

## Research Article

# Feasibility of telecytology for rapid preliminary diagnosis of ultrasound-guided fine needle aspiration of axillary lymph nodes in a remote breast care center

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## Abstract

**Background:** In the recent years, the advances in digital methods in pathology have resulted in the use of telecytology in the immediate assessment of fine needle aspiration (FNA) specimens. However, there is a need for organ-based and body site-specific studies on the use of telecytology for the immediate assessment of FNA to evaluate its pitfalls and limitations. We present our experience with the use of telecytology for on-site evaluation of ultrasound-guided FNA (USG-FNA) of axillary lymph nodes in a remote breast care center. **Materials and Methods:** Real-time images of Diff-Quik-stained cytology smears were obtained with an Olympus digital camera attached to an Olympus CX41 microscope and transmitted via ethernet by a cytotechnologist to a pathologist who rendered preliminary diagnosis while communicating with the on-site cytotechnologist over the Vocera system. The accuracy of the preliminary diagnosis was compared with the final diagnosis, retrospectively. **Results:** A total of 39 female patients (mean age: 50.5 years) seen at the breast care center underwent USG-FNA of 44 axillary nodes. Preliminary diagnoses of benign, suspicious/malignant, and unsatisfactory were 41, 52, and 7%, respectively. Only one of the 23 cases that were initially interpreted as benign was reclassified as suspicious on final cytologic diagnosis. Seventeen of 18 suspicious/malignant cases on initial cytology corresponded with a malignant diagnosis on final cytology. One suspicious case was reclassified as benign on final cytologic diagnosis. All unsatisfactory cases remained inadequate for final cytologic interpretation. The presence of additional material in the cell block and interpretative error were the main reasons for discrepancy, accounting for the two discrepant cases. **Conclusions:** This retrospective study demonstrates that the on-site telecytology evaluation of USG-FNA of axillary lymph nodes in patients at a remote breast care center was highly accurate compared with the final cytologic evaluation. It allows pathologists to use their time more efficiently and makes on-site evaluation at a remote site possible.

**Key words:** Axillary lymph nodes, FNA, telecytology, ultrasound-guided FNA

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## INTRODUCTION

Locoregional axillary lymph node status has long been the gold standard in determining the management and prognosis of breast carcinoma patients. Chang *et al.* recently showed that ultrasound-guided fine needle aspiration (USG-FNA) of lymph nodes is highly sensitive and specific for the involvement of axillary lymph nodes in breast carcinoma and plays a role both in sparing sentinel lymph node biopsy and in triaging cases for systemic chemotherapy.<sup>[1]</sup> USG-FNA is a simple, inexpensive, and minimally invasive procedure that can detect the presence of metastatic carcinoma preoperatively in axillary lymph nodes, thereby helping in the selection of patients who should directly undergo axillary lymph node dissection or neoadjuvant treatment instead of sentinel lymph node biopsy.

Pathologists at several institutions perform on-site preliminary evaluation of material obtained from axillary lymph nodes by rapidly staining cytologic smears. Preliminary on-site evaluation provided to clinicians or radiologists facilitates triage of patients and immediate referral to other specialties in multispecialty breast care centers. However, distance of the radiology suites and physician-based FNA clinics from the office and laboratory of the pathologist and multiple locations for aspiration procedures are an impediment for a timely immediate on-site assessment by pathologists. In addition, these procedures can be time consuming.

Dynamic telepathology systems focus on the transmission of live 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 to distant observers.<sup>[2]</sup> Advancement in telepathology technology has made it feasible to use dynamic telepathology for cytologic specimens.<sup>[3]</sup> However, most of the studies using dynamic telecytopathology have been retrospective.<sup>[4,5]</sup> Only a few studies have focused on the application of dynamic telecytopathology for initial real-time on-site diagnosis in aspiration cytology and have been restricted mainly to the pancreas, thyroid, and mediastinum.<sup>[6-10]</sup> There is a further need for other organ-based and body site-specific studies on the use of telecytology 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 of USG-FNA of axillary lymph nodes in a breast care center.

## MATERIALS AND METHODS

The study involved USG-FNA biopsies of axillary lymph nodes performed by radiologists at a remote breast care center located a block away from the university hospital.

An on-site cytotechnologist prepared cytology smears that included Diff-Quik-stained slides and alcohol-fixed smears that were later stained with the Papanicolaou method in the laboratory. The total number of Diff-Quik-stained slides prepared on-site ranged from two to five slides per pass. Additional material was collected for the cell block as needed. A maximum of four passes were performed per axillary lymph node. Initially, two passes were performed and evaluated with the telecytopathology system. Additional passes were performed only if the initial two passes did not yield adequate material for preliminary diagnosis.

Telecytopathology was introduced at the breast care center in November 2010. A telepathology system consisting of an Olympus CX41 microscope and a digital camera with NetCam software was used to transmit the images [Figure 1]. A 2.11 megapixel cooled digital color camera (Olympus DP20, Olympus America, Center Valley, PA) was used for acquisition of the image along with the microscope and a Dell desktop computer with a direct ethernet connection. NetCam software (Olympus) used transmission control protocol/internet protocol (TCP/IP) to transmit live images over the Internet via an assigned static IP address [Figure 2]. The computer and the image server required logging 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.

Different cytotechnologists with 12 to 20 years of experience and conversant with the telecytopathology system operated the microscope at the remote site. The faculty cytopathologist could not control the microscope or camera and interacted with the cytotechnologist via speaker telephone. The preliminary diagnosis was communicated to the radiologist. The images were transmitted continuously as the cytotechnologist moved the slide on the stage and the pathologist could view on the screen what the cytotechnologist was seeing through the microscope. The Olympus microscope had objectives from ×4 to ×40. Low-power objectives ×10 and ×4 were used to assess overall cellularity of the smears and identify areas that may have required review under higher-power ×40 for better cytologic details.

Diagnostic categories that were used for preliminary on-site evaluation and final cytologic diagnosis included unsatisfactory, benign, and suspicious/malignant smears. Benign smears were defined as containing polymorphous lymphocytes representing reactive lymph nodes. Suspicious and malignant categories were combined into one group for assessing the rate of accuracy. Suspicious category included all cases that were considered suspicious for metastatic breast carcinoma or cases with atypical features that were suggestive but nondiagnostic for malignancy. Smears were considered unsatisfactory if they contained only adipose tissue or blood. The initial and final cytologic interpretations for the majority of

the telecytopathology cases were performed by the cytopathologist. The final cytologic diagnosis was made without using any ancillary techniques.

Accuracy was defined by agreement between the preliminary and final interpretations of the two groups. Cases were considered discrepant if the preliminary diagnostic category did not correspond to the final diagnostic category. All slides of discrepant cases were reviewed to assess the cause of discrepancy. The impact of telecytopathology evaluation on the number of passes performed was also assessed. Histology slides from surgical follow-up, when available, were also reviewed.

## RESULTS

There were 44 consecutive cases of axillary lymph nodes (20 right sided and 24 left sided) in 39 female patients (aged 28–67 years, mean: 50.5 years) that were evaluated by telecytopathology from November 2010 to April 2012.

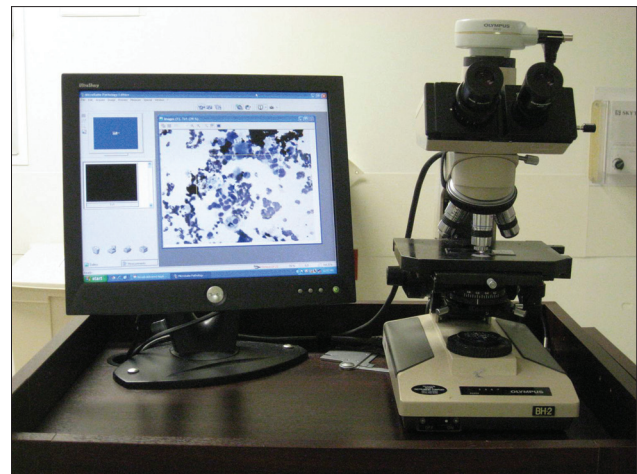
Table 1 shows the final cytologic diagnosis on all axillary lymph nodes and nodules along with preliminary diagnosis rendered via telecytopathology. Of the 23 cases with initial telecytopathology diagnosis as benign, 22 were benign on the final cytology and one was reclassified as suspicious. Of the 18 axillary lymph nodes with a preliminary telecytopathology diagnosis as suspicious/malignant, 17 were malignant on final cytologic assessment and one was reclassified as benign.

Three axillary lymph nodes with a preliminary telecytopathology evaluation of 'unsatisfactory' remained unsatisfactory on final cytologic assessment. The accuracy rate of preliminary telecytopathology diagnosis was 95.5% (42/44).

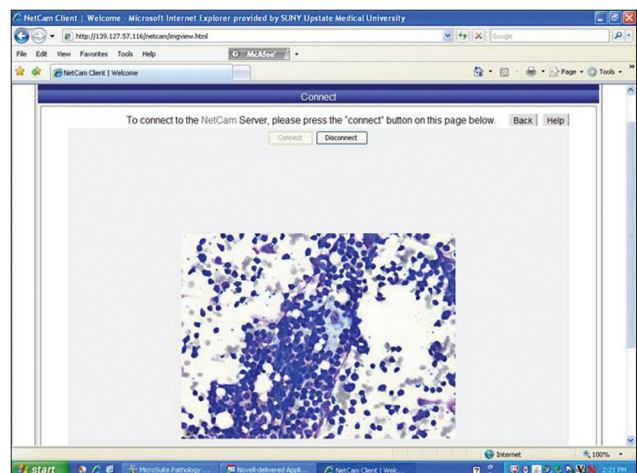
Telecytopathology cases with discordant preliminary and final diagnosis are shown in Table 2. One of the discrepant cases involved the axillary tail of a left breast that was interpreted as a lymph node on ultrasound examination. Telecytopathology evaluation of smears revealed a cluster of atypical epithelial cells with slight overlapping and increased nuclear cytoplasmic ratio. [Figure 3]. Benign

**Table 1: Preliminary onsite telecytopathology and final cytologic diagnosis**

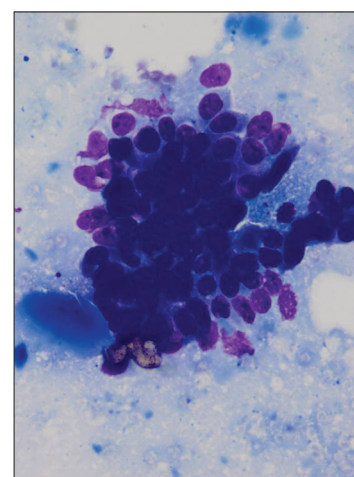
Preliminary telecytopathology cytologic diagnosis	Number of cases	Final cytologic diagnosis	Number of cases
Benign	23	Benign	22
		Suspicious	1
		Malignant	17
Suspicious/malignant	18	Benign	1
		Unsatisfactory	3
Unsatisfactory	3	Unsatisfactory	3
<b>Total</b>	<b>44</b>		<b>44</b>



**Figure 1: The telecytopathology digital system comprises an Olympus camera and a monitor with a microscope**



**Figure 2: Reactive lymph node in ultrasound-guided fine needle aspiration (USG-FNA) of axillary lymph node specimen viewed remotely on a computer screen using telecytopathology digital system (Diff-Quik)**

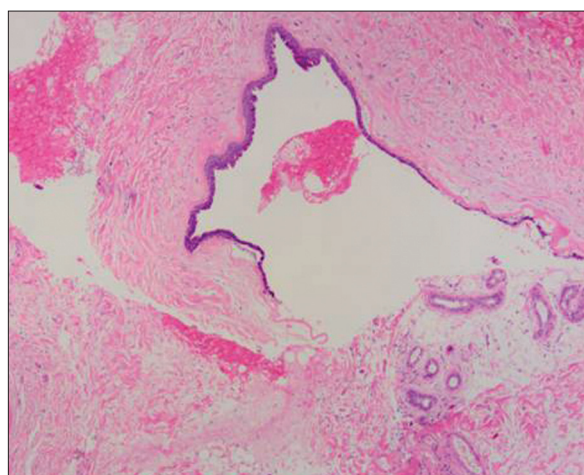


**Figure 3: Telecytopathology evaluation of smears revealed a cluster of atypical epithelial cells with slight overlapping and increased nuclear cytoplasmic ratio (Diff Quik stain)**

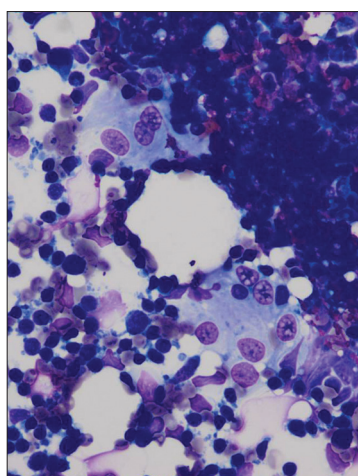
breast parenchyma with ductal ectasia was identified in the cell block [Figure 4] and the atypical epithelial cells identified on the smears correlated with those lining the ectatic duct in the cell block material.

The other case was given the preliminary diagnosis of reactive lymph node. However, one isolated cluster of large atypical cells was identified upon further review that were presumed to be histiocytes on telecytopathology review [Figure 5]. The final cytology on this case was rendered as suspicious. In our follow-up of this patient for eight months, no biopsy was performed on axillary lymph node at our institution.

Surgical follow-up was available in 15 of the 17 cases with final cytology diagnosis of malignancy. All of these 15 cases underwent axillary lymph node dissection and showed metastatic carcinoma involving the axillary lymph nodes. Of the 23 cases with final cytology diagnosis as benign, surgical follow-up was available in only eight cases. All of these eight cases underwent sentinel lymph node biopsy



**Figure 4: Benign breast parenchyma with ductal ectasia (cell block section H and E)**



**Figure 5: Isolated cluster of large atypical cells that were presumed to be histiocytes on telecytopathology review**

that revealed metastatic carcinoma in six cases and no evidence of tumor in two cases. All cases with metastatic carcinoma involving sentinel lymph nodes underwent axillary lymph node dissection. In the unsatisfactory category, surgical follow-up was available in only one case and included sentinel lymph node biopsy and axillary lymph node dissection showing metastatic carcinoma.

Table 3 shows the number of axillary lymph nodes in each of the diagnostic categories that underwent two or more passes. Of 23 benign axillary lymph nodes, eight

**Table 2: Discrepancies between preliminary telecytopathology and final cytologic diagnosis**

Case	Location	Preliminary diagnosis	Final diagnosis	Review
1	Left axillary lymph node	Suspicious: Atypical epithelial cells, cannot exclude malignancy	Benign breast parenchyma with areas of fibrosis and ductal ectasia	Cell Block: Benign breast parenchyma with ductal ectasia was identified in the cell block. Ductal epithelial cells in smears represented the ductal cells of the breast parenchyma and not metastatic tumor
2	Left axillary lymph node	Benign: Probable reactive lymph node	Suspicious cytology	One isolated cluster of large atypical cells was identified upon further review that was thought to be histiocytes on telecytopathology review.

**Table 3: Number of passes performed in the axillary node in each of the diagnostic categories**

Preliminary diagnostic category	Number of cases	Number of cases with 2 or less passes	Number of cases with 3 or more passes
Benign	23	15	8
Suspicious/malignant	18	6	12
Unsatisfactory	3	1	2
Total	44	22	22

(35%) required more than two passes to obtain adequate material for cytologic diagnosis. In the unsatisfactory category, two cases (67%) underwent more than two passes. Twelve of the 18 cases (67%) in the suspicious/malignant category required more than two passes to render a cytologic diagnosis.

## DISCUSSION

Innovations in telepathology have made it feasible to procure pathology consultation remotely.<sup>[11]</sup> Although increasing number of studies in the recent cytology literature have demonstrated the usefulness of dynamic and static telepathology systems to review cytology smears remotely over an internet connection, dynamic systems appear to be more accurate when compared with static systems.<sup>[4-10,12-17]</sup>

In the current study, we performed the initial on-site evaluation of USG-FNA biopsies of axillary lymph nodes in a remote breast care center via a dynamic live and remotely operated telecytopathology system. To the best of our knowledge, this is the first case series assessing the role of dynamic telecytopathology for rapid preliminary diagnosis of USG-FNA of axillary lymph nodes. We demonstrated a high concordance between preliminary telecytopathology cytologic diagnosis and final cytologic diagnosis.

Discrepancies in telecytopathology between on-site preliminary diagnosis and final diagnosis were mostly minor and could be attributed to the availability of additional material and interpretative difficulty at the time of preliminary telecytopathology interpretation. Unsatisfactory rate at the time of preliminary telecytopathology was 7% and did not alter at the time of final cytologic diagnosis.

We encountered one false-positive case that was initially considered to be suspicious for malignant neoplasm and received final interpretation of ductal ectasia. Retrospective review of the slides in this case showed that the atypical epithelial cells that were initially suspected to represent tumor cells at the time of initial telecytopathology evaluation actually represented ductal epithelium of the ectatic duct in breast parenchyma (of the axillary tail) captured in cell block material. Interpretative difficulty in the other case was related to distinguishing large atypical cells noted on further review from histiocyte aggregates, a dilemma that has been previously described.<sup>[18]</sup>

Our study has limitations. It is a pilot, observational study that involved a relatively small sample. The data was gathered retrospectively. The cytopathologist who gave the preliminary evaluation also rendered the final diagnosis and was not blinded. This may introduce bias. However, this is in accordance with the practice at our institution,

where the cytopathologist who gives a preliminary reading also gives the final diagnosis. Future larger prospective studies addressing these issues would be useful.

On-site telecytopathology evaluation accurately classified 50% of the axillary nodes as benign and communication of these results to the patients immediately after the procedure alleviated the anxiety of patients. Seventeen patients with suspicious or malignant diagnosis were appropriately triaged and referred to proper specialties without further delay.

In our study, preliminary telecytopathology on-site evaluation limited the number of passes to two per lymph node in 50% of the cases, and in 50% of the cases, more than two passes were performed. Adequate material for cytologic diagnosis was obtained in 93% (41 of 44 cases) of the axillary lymph nodes that underwent additional aspirations. To the best of our knowledge, none of the prior studies other than the ones related to thyroid have focussed on the optimal number of passes that may be needed to maximize diagnostic certainty, in the absence of immediate assessment of specimens by a cytopathologist.<sup>[19-21]</sup> If we apply recommendations of thyroid FNA studies to axillary lymph nodes, then at least four passes per axillary lymph nodes may be required to assure a good diagnostic yield, in the absence of immediate assessment of specimens by a cytopathologist. Based on our study, preliminary telecytopathology on-site evaluation minimized the number of passes required to procure adequate material for cytologic diagnosis to two passes in 50% percent of the axillary lymph nodes. Therefore, patient discomfort associated with each additional pass was reduced.

The success of telecytopathology depends on the experience of the on-site operator, for example, an experienced cytotechnologist or senior resident with interest in cytopathology or a cytopathology fellow who can operate the slides on the on-site microscope effectively, transmit real-time images, and project significant findings while being in audio contact with the attending cytopathologist.<sup>[3]</sup> Also, the pathologist must be familiarized with the use of telecytopathology for the interpretation of real-time images. In our study, both the pathologist and on-site operator were familiar 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. Whole-slide image scanning systems (virtual microscopy) have the potential to circumvent the need for on-site personnel for operating slides and transmitting real-time images. Presently, the long scanning time and large size of files make whole-slide imaging system very restrictive for use in cytopathology.<sup>[3]</sup>

Under the current practice, staff cytopathologists alone are able to bill (Current Procedural Terminology code 88172, 88177) for passes performed during telecytopathology

services as long as they participate in the preliminary evaluation of these passes and assess the need for additional passes to obtain material for cytologic diagnosis and ancillary studies.<sup>[22]</sup> The results of these preliminary evaluations have to be communicated to the physicians performing the procedure. Staff cytopathologists are legally responsible for all cases in which they provide diagnostic services, including telecytopathology. However, the importance of the experienced cytotechnologist and cytopathologist working as a team for the effectiveness of telecytopathology services cannot be overemphasized.

Telecytopathology allows for on-site evaluation at multiple sites by different cytopathologists and also facilitates consultation with a colleague in difficult cases. In this retrospective study, we did not focus on the time spent by the pathologist on each individual pass. However, based on experience, the estimated time that the cytopathologist spent evaluating each pass was two to four minutes.

In summary, we demonstrate that on-site preliminary telecytopathology evaluation for axillary lymph nodes USG-FNA is highly accurate when compared with the final cytologic evaluation. It assures adequacy of sampling and decreases the number of passes that are needed to procure the adequate material. The low cost of the telecytopathology equipment (approximately \$ 6,000 excluding the microscope) makes it a cost-effective alternative in situations where constraints of distance and time may preclude cytopathologists from rendering preliminary on-site evaluations at distant and multiple locations.

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