

Telecytologic Diagnosis of Breast Fine Needle Aspiration Biopsies

Intraobserver Concordance

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OBJECTIVE: To determine the intraobserver concordance between telecytologic and glass slide diagnosis of breast fine needle aspirates.

STUDY DESIGN: Twenty-five cases, originally received in consultation, were each examined by three cytopathologists. An average of seven compressed digital images per case were presented, together with a brief clinical history, using the http protocol and an internet browser.

RESULTS: Agreement between the telecytologic and glass slide diagnosis ranged from 80% to 96%. Nevertheless, two cases that had been unequivocally diagnosed as malignant based upon video images were considered to be benign by the same pathologist when reviewing the glass slides. Both diagnostic confidence and self-concordance were higher for one pathologist having significant previous video microscopy experience.

A high degree of concordance between glass slide diagnosis and telecytologic diagnosis may be achieved for breast FNAs.

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CONCLUSION: *Although intraobserver concordance between telecytologic and glass slide diagnoses of breast fine needle aspirates is high, refinement of existing criteria for diagnosis of malignancy, taking account of the particular limitations associated with telecytologic diagnosis, may be prudent prior to widespread use of telecytology for fine needle aspiration evaluation.* (Acta Cytol 2000;44:175-180)

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The use of automated devices relying on the capture and analysis of video images for screening or rescreening of Pap smears is now routine. Given the

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major roles played by both fine needle aspiration (FNA) and exfoliative cytology in anatomic diagnosis, it is surprising that the investigation of telepathology as a tool for cytopathology diagnosis has been far exceeded by the vigorous investigation of this approach for surgical pathology diagnosis and consultation.¹⁻¹⁶ Although there are apparently a number of laboratories employing telecytology as a diagnostic modality and remote cytodiagnosis has been discussed by an expert panel,¹⁷ only a very few studies of factors influencing the accuracy and reliability of remote cytopathologic diagnosis (telecytology) have been published.¹⁸⁻²² Some authors have considered the results obtained in these investigations encouraging²¹; others have suggested that telecytology is a "dead end," at least when the diagnosis depends upon the interpretation of preselected fields of view.^{22,23}

Given the small number of studies and the heterogeneity of their interpretation, there is a need to identify factors influencing the accuracy and reproducibility of telecytopathologic diagnosis. We carried out a small study in which we identified factors that may influence the ability of a cytopathologist to reproduce his or her slide-based diagnosis when presented only with representative fields selected by a referring pathologist distant from the consultant.

Materials and Methods

Twenty-five FNAs of the breast, initially submitted for a second opinion, were selected randomly from the Registry of Cytopathology, Armed Forces Institute of Pathology. The patients ranged in age from 19 to 82 years (mean, 43; median, 40). Seven cases had been signed out as malignant and 16 as benign (cyst, fibroadenoma, ductal hyperplasia); 2 cases carried a descriptive diagnosis incorporating the designation *atypical*. Because these cases were received in consultation and were in many cases interpreted as benign, tissue diagnoses were not available. The slides had been previously stained with Papanicolaou stain, hematoxylin and eosin, and/or Diff-Quik and representative fields dotted by a cytotechnologist (S-BB) for teaching purposes. These fields had been selected to provide information routinely used in cytologic diagnosis, such as cellularity and background; reference cells, such as normal epithelium, neutrophils and red cells; and representative fields showing abnormal features. Between five and eight dotted fields were photographed at 100× and/or 400× using Kodak Ectachrome 64 daylight film (Rochester, New York), digitized and stored as 4-5-Mb images on CD-ROM disc (Kodak) in PCD format; this resulted in essentially no loss of resolution.

Images were subsequently rendered as 50-150-Mb JPEG files, transferred to an internet site and presented to the participating observers via the http protocol on a Silicon Graphics Indigo II computer (Mountain View, California) equipped with a 1,280×1,024 pixel display (Figure 1). In addition, small, "thumbnail" representations of each image, together with a brief clinical history, including patient age and signs/symptoms, were presented (Figure 1).

Three pathologists (C.F.A., L.D.T., M.V.T.), all of whom hold certificates of added qualification in cytopathology from the American Board of Pathology and all of whom have had at least some prior experience with telepathology consultation, reviewed each of the 25 cases and recorded their findings on a template (Figure 2). Several weeks later, each of these pathologists was asked to evaluate the glass slides from these cases, in random order. There was no identifying information on the glass slides or video images that would allow the examining pathologist to relate any group of images to the corresponding glass slide nor did any pathologist believe that he/she could definitely identify any of the cases previously viewed on the computer screen.

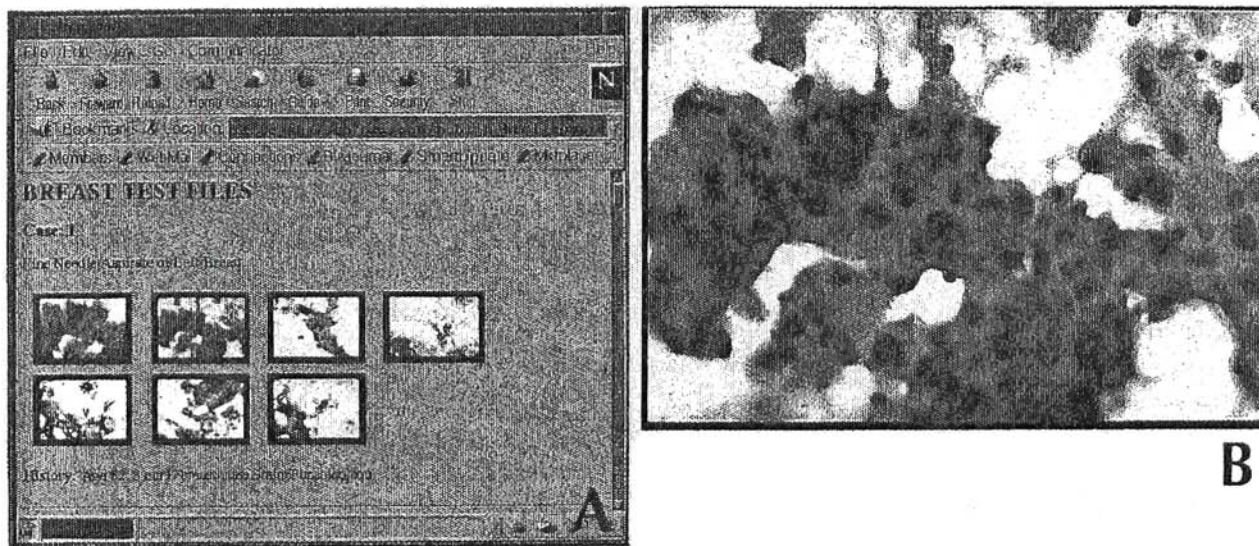


Figure 1 (A) Thumbnail images and clinical history provided to examining pathologists. (B) Enlarged image provided to examining pathologist when he/she "clicked" on the second thumbnail image shown in Figure 1A.

Each of the pathologists was permitted to use his or her customary criteria both for specimen adequacy and for arriving at a diagnosis.

To evaluate the intraobserver concordance between the telecytologic diagnosis and the glass slide diagnosis, we divided diagnoses into two groups— atypical/malignant and benign.

Intraobserver variability for each of the three pathologists was assessed using Cohen's Kappa.²⁴ Significance of $2 \times n$ contingency table results was assessed using Yates-corrected χ^2 ; significance of 2×2 contingency table results was assessed using Fisher's Exact Test.

Results and Discussion

Each of the three observers thought that either 20 or 21 of the cases presented enough information to permit remote diagnosis (Table I). No observer identified more than two cases as less than adequate on both telecytologic and glass slide examination, and the three observers did not all agree on any single case as "insufficient" on either glass slide or telecytologic examination.

Observers were clearly more confident of their glass slide diagnoses than of their telecytologic diagnoses. Given the difficulty, each observer expressed at least some reservations regarding approximately 40% of their telecytologic diagnoses (Table II). Two of the three observers expressed reservations about their glass slide diagnoses in a

similar percentage of cases. This is not surprising since these were difficult cases originally sent for a second opinion.

It is not surprising, therefore, that all three observers "hedged" a significant number of both glass slide and telecytologic diagnoses with terms such as "atypical, favor malignant" (Table III). Each observer hedged more cases using telecytology than they did on glass slide. Although this did not achieve statistical significance for any individual pathologist, the total number of hedged telecytologic diagnoses (33) was significantly greater than the total number of hedged glass slide diagnoses (19, $P = .016$). Interobserver differences in the number of hedged diagnoses were not statistically significant for either the telecytologic or glass slide diagnosis.

Intraobserver concordance for each of the three pathologists is summarized in Table IV. Typically, intraobserver reproducibility, evidenced by values of $\kappa > .6$, are considered "substantial," though there is no universally accepted interpretation.²⁴ By this criterion, all three observers performed adequately, though one clearly outperformed the others. This particular pathologist, who had significantly more experience than the others using video microscopy, considered the fewest cases to be "inadequate," expressed the greatest confidence in his/her diagnoses and hedged the fewest diagnoses—utilizing either the glass slides or telecytology.

Only two benign telecytologic diagnoses were

<p>CASE INFORMATION</p> <p>Number:</p> <p>Adequacy</p> <p>Material Sufficient: Y N</p> <p>Image Quality: Y N</p> <p>Cellular Detail: Y N</p>	<p>DIAGNOSTIC PARAMETERS USED</p> <p>Cellularity</p> <p>Background</p> <p>Fragment characteristics</p> <p>Individual cytologic features</p> <p>Entity specific patterns</p> <p>Other</p>
<p>CLASSIFY/RECOMMEND</p> <p>Benign/Follow</p> <p>Atypia/favor benign; correlate clinically</p> <p>Atypia/cannot r/o malignancy/excise</p> <p>Malignant/excise</p> <p>Cannot evaluate/defer</p>	<p>COMMENTS</p>
<p>DIAGNOSIS</p>	
<p>CONFIDENCE</p> <p>Very confident</p> <p>Pretty confident</p> <p>Not confident</p>	

Figure 2 Template used for recording telecytologic findings.

Table I Perception of Adequacy

Medium	Adequate	Less than adequate
Telectyology		
Observer 1	20	5
Observer 2	21	4
Observer 3	21	4
Glass slide		
Observer 1	21	4
Observer 2	19	6
Observer 3	22	3

thought to be malignant by the same pathologist upon reviewing the glass slides; in both cases, the initial diagnosis had been hedged. In contrast, a total of seven atypical or malignant telectyologic diagnoses were thought to represent benign processes when the same pathologist reviewed the glass slides. In three of these seven cases, the telectyologic diagnosis had been unqualified, the pathologist was very confident of the diagnosis, and the specimen was believed to be adequate on telectyologic examination. No specimen characteristic, such as staining or cellularity, was found useful in predicting which telectyology diagnoses were likely to be refuted when the same pathologist examined glass slides.

Although all three observers were cytopathologists who had examined specimens previously using video microscopy, observer 3 had previously examined significantly more cytopathologic specimens using video microscopy than had either observer 1 or observer 2. This fact, rather than any particular characteristic of the cases themselves, seems to explain the high concordance between his/her telectyologic and glass slide diagnoses.

These results, which are similar to those previously reported for Pap smears diagnosed by video microscopy¹⁹ for breast fine needle aspirates^{21,22}

Table II Observer Confidence

Medium	Confident	Telectyologic diagnosis	
		Atypical/malignant	Benign
Telectyology			
Observer 1	15	5	5
Observer 2	13	8	4
Observer 3	15	9	1
Glass Slide			
Observer 1	15	8	2
Observer 2	18	5	2
Observer 3	24	1	0

Table III Hedged Diagnoses

Medium	Diagnosis	
	Hedged	Not hedged
Telectyology		
Observer 1	7	18
Observer 2	15	10
Observer 3	11	14
Glass slide		
Observer 1	4	21
Observer 2	8	17
Observer 3	6	19

and for remote diagnosis of surgical pathology specimens,¹⁻¹⁶ allow us to conclude that a high degree of concordance between glass slide diagnosis and telectyologic diagnosis may be achieved for breast FNAs. Although our criteria for "agreement" differ somewhat from those used previously, our concordance rates between the telectyologic diagnosis and glass slide diagnosis, 80% for two of the pathologists and 96% for the third, are similar to the 84% concordance reported by Della Mea et al²¹ and the 67–91% concordance reported by Galvez et al.²² This level of concordance between telectyologic and glass slide diagnoses is encouraging; it seems highly unlikely that the intraobserver reproducibility of glass slide diagnoses will be perfect, particularly when the interpretation of difficult consultation cases is considered. The fact that a photographic step preceded the acquisition of digital images is not expected to affect our results; the practical limits on system performance resulted from subsequent digitization and compression, together with selection of a limited number of fields for diagnostic evaluation.

Both the confidence in the telectyologic diagnosis

Table IV Concordance Between Glass Slide Diagnoses and Telectyologic Diagnoses

Glass slide diagnosis	Telectyologic diagnosis	
	Atypical/malignant	Benign
Observer 1 ($\kappa = .63$)		
Atypical/malignant	6	0
Benign	4	15
Observer 2 ($\kappa = .63$)		
Atypical/malignant	6	2
Benign	2	15
Observer 3 ($\kappa = .92$)		
Atypical/malignant	9	0
Benign	1	15

and the concordance with the glass slide diagnosis appear to be greater for pathologists who have had more experience with the technique. Nevertheless, particular caution, even for experienced observers, would appear to be prudent when considering a malignant diagnosis. Although it is possible that use of the "triple test" (agreement between mammographic, physical examination and FNA findings) would prevent inappropriate therapy in patients for whom a misdiagnosis of malignancy was made by telecytology, we do not have adequate information on physical examination or mammographic findings to draw this conclusion. Refinement of existing criteria for diagnosis of malignancy, taking account of the particular limitations associated with telecytologic diagnosis, may be prudent prior to widespread use of telecytology for FNA evaluation.

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