Improving the Quality of Cytology Diagnosis

Root Cause Analysis for Errors in Bronchial Washing and Brushing Specimens

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Abstract

Detailed root cause analysis to determine causes of pulmonary cytology errors has not been used to design specific practice changes. We performed root cause analysis of all false-negative bronchial brushing and washing specimen errors (n = 32) detected by the cytologic-histologic correlation process in 2002. Medical records and all slides were reviewed. Based on the correlation process, 10 errors were interpretive, 16 sampling, and 6 combined interpretive/sampling. Root cause analysis showed that the lesion was not accessible in 8 cases and tumor was readily identified on the slides in only 1 case. In 11 cases, the malignant cells were few and not recognized, and in 13 cases, obscuring artifacts (eg, cellular crushing and air drying) limited interpretation. Sampling issues had a major role in the misdiagnosis in 31 cases (97%), and recommendations for error reduction include immediate interpretation and the use of transmucosal fine-needle aspiration.

Anatomic pathology errors are estimated to occur in approximately 1% to 5% of all specimens, and the majority of these errors do not lead to patient harm.[1-12] Error frequencies depend on the method of detection, and commonly used methods are secondary review for cytologic-histologic (CH) correlation, hospital or departmental conferences, clinician-directed concerns, extradepartmental consultation, and other quality assurance practices.[1-12] Although error frequencies, based on these detection methods, have been published in the medical literature, little study on how to reduce these errors has occurred.[1]

Six institutions are participating in an Agency for Healthcare Research and Quality (AHRQ; Rockville, MD) project focused on developing quality improvement programs to reduce pathology-detected errors that occur more frequently and/or are associated with greater clinical severity.[1] Based on the CH correlation error-detection process, Clary et al[8] reported that errors related to pulmonary specimens were the most frequent organ-specific errors, partly because lung specimens are of high volume. In pulmonary specimens, Clary et al[8] reported that 90.9% of errors were false-negative diagnoses and 9.1% of errors were false-positive diagnoses.

In the pathology literature, informal root cause analysis has focused on determining diagnostic pitfalls or on documenting the findings in unusual cases that led to misdiagnosis.[1] This approach implies that errors are related to failures in diagnostic ability rather than to system flaws that might lead to individuals performing poorly. Formal root cause analysis has not been performed and is a method that systematically examines for all sources of error and provides information that may be used to target errors at their source.[13-16]

This study represents a second step in our project that uses pathology-detected errors to redesign systems to improve

patient safety. In the first step, we established baseline error frequencies based on errors detected at multiple institutions using a number of pathology-driven methods.[1] In this study, we performed root cause analysis of 1 year of pulmonary false-negative errors from one institution. Our method of root cause analysis classified errors into specific system-focused causes rather than into specific failures of diagnosis.[1] These findings have led to the third step of devising and implementing error-reduction plans to target and reduce these causes of error.

Materials and Methods

Background and Design

In September 2002, the AHRQ funded 4 institutions to share deidentified anatomic pathology diagnostic error data using a Web-based database, determine baseline error frequencies detected by different methods, collect patient outcome information to determine the clinical impact of diagnostic errors, perform root cause analysis to derive error-reduction strategies, and assess the success of these error-reduction strategies using quantitative and qualitative measures.[1] Additional institutions have joined this project during the past several years.

In this study, we performed root cause analysis of specific 2002 error data obtained at the University of Pittsburgh Medical Center (UPMC; Pittsburgh, PA). We chose to report data from a single institution because errors are correlated with specific system processes that differ widely by institution.[1] We wanted to determine how the clinical and laboratory processes resulted in error. For this study, we selected errors related to bronchial brushing and washing specimens detected through the CH correlation process. Bronchoscopy with bronchial brushing and/or washing is a commonly performed procedure, and previous data have shown that errors occur relatively frequently with this specimen type. We obtained institutional review board approval for performance of this project.

The CH Correlation Review Process

Because the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88)[17] did not mandate how the CH correlation process is to be performed, laboratories perform CH correlation quite differently, which leads to bias in error reporting.[18] In the beginning of the project, we first standardized the CH correlation process in the participating institutions. On a monthly basis, a cytotechnologist used an existing laboratory information system program to identify all patients who had both cytology and surgical specimens from the same anatomic site that had been obtained within 6 months of each other before the date of review. A designated "review" pathologist selected cases in which the cytologic and surgical specimens were discrepant. The cytotechnologist then retrieved the patient slides and reports and generated a hard-copy review sheet. The review pathologist examined the material and determined the cause of error.

The patients included in this study underwent procedures at 1 of 2 UPMC hospitals, and, despite our efforts at standardization, the CH correlation process was performed slightly differently at each hospital. At one hospital, a designated pathologist performed CH correlation, and this pathologist was blinded to the original pathologist of record. At the other hospital, 1 of 5 pathologists performed CH correlation, and these pathologists were not blinded.

Definition of CH Error and Cause

We defined a *discrepancy* as a difference between the cytologic and histologic diagnoses. Because cytology and surgical diagnostic schema are somewhat different, we considered the diagnoses in a scaled categorical context to determine whether a discrepancy occurred. To determine step differences, we classified all cytologic and histologic diagnoses into the categories of unsatisfactory, benign, atypical, "suspicious," and malignant. We defined a *CH correlation error* as at least a 2-step discrepancy.[1] We evaluated only 2-step or greater CH correlation discrepancies because of the lack of reproducibility and clinical import of 1-step discrepancies. For example, a diagnostic error occurred if a patient's bronchial brush specimen was diagnosed as benign and the patient's lung biopsy specimen was diagnosed as non–small cell carcinoma. This example falls within the scope of the Institute of Medicine's definition of error because in at least 1 specimen, the definitive pathologic diagnosis was not reached. A cytologic diagnosis of suspicious and a histologic diagnosis of non–small cell carcinoma would not be considered a 2-step discrepancy for this study.

The review pathologist microscopically examined all slides and determined whether the cytology, surgical, both, or neither diagnosis was in error.[8] The pathologist then assigned a "cause" of the error, using the categories of interpretation, sampling, or both. An *interpretation error* was an error in disease categorization, and this error was further classified as an overcall (if the review diagnosis was categorically lower than the original diagnosis) or an undercall (if the review diagnosis was higher than the original diagnosis). A *sampling error* was an error in which the diagnostic material was not present on the slide, even on review. In the aforementioned example, if the review pathologist concurred with the original lung biopsy and brushing diagnoses, a sampling error occurred in the brushing specimen, because material diagnostic of cancer was not present on the cytology slides.

CH Correlation Data Collection

We developed a 2-part CH correlation data collection instrument. The first part contained pathology items, including

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date of cytology and surgical specimen collection, specimen type, original and review diagnoses, original and review pathologist and cytotechnologist, limitations in specimen quality, and causes of error. The second part contained patient management and outcomes items, including additional tests ordered, unnecessary or additional treatment protocols initiated, morbidity or mortality related to additional tests or treatments, and delays in diagnosis.

A data collector reviewed the pathology CH correlation logs and pathology reports to complete the first part of the instrument. An honest broker reviewed the hospital electronic and paper medical records to complete the second part of the instrument. An honest broker was a clinical outcomes data collector who was the only person exposed to clinical data linked to individual patient identifiers. Use of the honest broker satisfied the Health Insurance Portability and Accountability Act requirements regarding use of medical record data for research purposes.

UPMC Data

A total of 119 bronchial brushing specimens and 446 bronchial washing specimens were obtained during 2002. The discrepancy frequency (total number of discrepant bronchial brushing or washing specimens divided by the total number of paired cytology and surgical pathology specimens) was 9.43%. We chose to examine the cases in which the cytology specimen was diagnosed as benign and the surgical specimen as malignant (n = 32); a false-negative error was detected in 7 bronchial brushing specimens and 25 bronchial washing specimens. These errors were seen in 28 patients (4 patients had an error in both a brushing specimen and a washing specimen). In 12 (38%) of 32 cases, the cytology and surgical specimens were not obtained at the same time. For a third of these cases, the cytology had been obtained with a surgical specimen that also was negative, and in two thirds of the cases, a surgical specimen had not been obtained at the time of the first bronchoscopy.

Second Pathologist CH Correlation Review

A second pathologist reperformed the CH correlation to establish the diagnostic variability with the original CH correlation process. The second pathologist was a cytology fellow (L.N.). Our purpose in reperforming the CH correlation was to confirm the findings of Clary et al,[8] who showed only moderate pairwise κ values between pathologists performing CH correlation. We determined a pairwise κ statistic for the original and CH correlations between the review and second pathologists. To perform this analysis, we collapsed the cytologic diagnoses into the categories of malignant and not malignant; we could not perform the analysis using all categories (including atypical and suspicious), because the second pathologist did not use all these categories. For the root cause analysis, we used the original error assessment.

Root Cause Analysis

We used Toyota Production System methods to perform root cause analysis.[13-16,19-21] We assumed that errors resulted from system flaws that had an active and a latent component.[22,23] An error could occur anywhere along the process of procuring, transporting, processing, signing out, and reporting the findings of a specimen. For each case, we attempted to determine the reasons for the discrepant cytologic and histologic diagnoses by examining all possible causes of error. Broadly speaking, we classified error according to the traditional taxonomy of sampling and interpretation. **Table 1** shows examples of interpretive errors, and **Table 2** shows examples of sampling errors; these examples are not exhaustive. In our root cause analysis, we determined how system flaws in the different steps

Table 1
Sources of Interpretive Error

Sampling contributions
Sample contains few malignant cells
Sample contains large amount of obscuring material
Sample is poorly preserved (eg, crushing)
Preparation contributions
Preparation contains a large amount of obscuring material
Preparation contains few malignant cells
Preparation is poorly preserved
Preparation is poorly stained
Screening contributions
Malignant cells not dotted (or few malignant cells dotted)
Cytotechnologist classified as benign (type of bias)
Diagnostic contributions
Few malignant cells (single cells or fragments)
Malignant cells not recognized because of obscuring factors
Malignant cells not recognized because of poor preservation
Unexpected malignancy in clinical context
Well-differentiated malignancy
Unclear
Correlative surgical biopsy tissue diagnosed as benign
Pathologist factors (eg, experience, time of day)

Table 2
Preanalytic and Analytic Factors That Are Sources of Sampling Error

Lesion factors
Lesion located peripherally
Lesion located subbronchially
Lesion located only in lymphovascular spaces
Specimen procurement factors
Specimen poorly prepared (eg, excessively thick or bloody; air dried; inflamed; necrotic; degenerated; lysed; crushed; obscured by foreign material, mucus, or other artifacts; or poorly smeared or stained)
Slides or material lost
Specimen preparation factors
Specimen poorly prepared (eg, excessively thick or bloody; air dried; inflamed; necrotic; degenerated; lysed; crushed; obscured by foreign material, mucus, or other artifacts; or poorly smeared or stained)
Slides or material lost
Screening factors
Cytotechnologist failed to dot or classify significant cells
Patient or physician factor
Procedure discontinued before diagnostic material obtained

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between procurement and reporting could lead to a sampling error, an interpretive error, or both.

We performed slide and medical record review. For slide review, 2 reviewers (L.N. and S.S.R.) independently reevaluated the cytology and histology slides. The reviewers were provided the original diagnoses and were instructed that an error had been detected through the CH correlation process. Each cytology case was graded subjectively on overall cellularity (and the number of neoplastic cells, bronchial cells, macrophages, and inflammatory cells) on a 4-part Likert scale. Cellular preservation was classified as excellent, good, or poor. The reviewers also graded each case for the amount of obscuring factors (blood, inflammation, and upper airway contaminant). Other artifacts (eg, cellular crushing) also were graded on a 4-part Likert scale. If the 2 reviewers disagreed regarding the assessment on an individual case, the case was examined jointly to reach consensus. For purposes of analysis, subgrading using the Likert scale was not useful for the analysis, and we collapsed all categories into present or absent.

In the medical record review, we obtained data from the electronic pathology report and from the hospital information system. From the cytology report, we obtained information on the type of specimen (brushing or washing), gross appearance of the specimen, number of smears and/or cytocentrifuged preparations, type of stains used (Papanicolaou or rapid Romanowsky), clinical history (if provided), original diagnosis by cytotechnologist, original diagnosis by pathologist, adequacy statement by cytotechnologist, and adequacy statement by pathologist. From the surgical pathology report, we obtained information on the type of specimen, number of tissue fragments (if biopsy), clinical history (if provided), specimen limitations, original diagnosis, and review diagnosis. From the hospital records, we reported the bronchoscopic and computed tomography (CT) findings. We could not obtain bronchoscopic findings in all cases because the electronic medical record did not include the bronchoscopic report for all clinicians or because the bronchoscopic report contained no significant case description. For the bronchoscopic findings, we classified the cases as showing normal findings, extrinsic compression with normal mucosa, and mucosa abnormalities. For the CT findings, we determined whether a mass was present, the size of the lesion, and the radiologic impression of malignancy.

Based on the slide and medical record review, we assigned at least 1 specific error cause to each case. We then redetermined whether sampling and/or interpretation components had a role in the false-negative diagnosis. For root cause analysis, we classified the error as secondary to interpretation if malignant cells had been seen on review, sampling if no malignant cells were seen on review, and interpretation and sampling if malignant cells were seen on review and sampling factors had a role in the false-negative diagnosis. For example, if the original CH error assessment was secondary to interpretation and on root cause analysis we determined that rare malignant cells were obscured by excess blood, we concluded that the false-negative diagnosis was secondary to interpretation and sampling. We then determined the number of cases in which an error was caused by interpretation alone, sampling alone, and interpretation and sampling.

We tallied the number of sampling and interpretive errors with specific error causes. We did not have a sufficient number of cases to perform statistical significance testing to determine whether some error types occurred at a statistically higher or lower frequency than other error types.

We derived error-reduction initiatives that could target specific error types. For example, if tumor was present submucosally and was not sampled cytologically, transbronchial fine-needle aspiration would be a method that could reduce the frequency of this error type. We calculated the total number of errors that could be reduced using each error-reduction initiative.

Results

Table 3 shows the gross appearance and type of preparation for the cytologic specimens and type of surgical specimens. Of all cytology specimens, 13 (41%) were reported as bloody. The mean number of tissue pieces reported on surgical biopsy specimens was 5.1.

Table 4 shows the original cytologic, original surgical, CH correlation cytologic review, and second pathologist CH correlation cytologic review diagnoses. Based on the surgical tissue diagnoses, 26 (81%) of cases were non–small cell carcinoma, 3 (9%) were small cell carcinoma, and 3 (9%) were sarcoma. In 1 case, the diagnosis was granular cell tumor. The original CH correlation review cytologic diagnosis was malignant in 10 (31%) of cases, suspicious in 1 (3%), atypical in 5 (16%), benign in 15 (47%), and unsatisfactory in 1 (3%); based on these data, a pure sampling error was seen in 50.0%, a combined sampling and interpretive error was seen in 18.7%, and a pure interpretive error was seen in 31.3%. The pairwise κ value between the original CH correlation and the second pathologist review diagnoses was 0.178.

Table 5 shows the bronchoscopic and CT scan findings. In 27 (84%) of the cases, a mass lesion was present; the range in mass size was 1.0 × 1.0 cm to 8.0 × 5.0 cm. In the radiologic reports, 12 lesions (38%) were described as malignant or suspicious for malignancy. In 11 cases (34%), bronchoscopic findings were not available; in 15 cases (47%), a mucosal lesion was identified; in 2 cases (6%), compression only was observed; and in 4 cases (13%), the bronchoscopic findings were normal.

Table 6 shows causes of sampling and interpretation error. In 8 cases (25%), the tumor was submucosal and was not accessible by brushing or washing. There was no correlation

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Table 3
Information on Cytology and Surgical Pathology Specimens*

Case No.	Cytology					Surgical Pathology		
	Type	Gross Appearance	Prep	Stains	History	Type	No. of Blocks	No of Pieces
1	Brush	Brush in saline	7 DSM	7 P	Yes	Excision	7	—
2	Wash	Bloody	4 DSM	4 P	Yes	Excision	7	—
3	Wash	Bloody	4 DSM	4 P	Yes	TB	1	7
4	Brush	Brush	4 CC	4 P	Yes	EB	1	5
5	Wash	Mucoid	4 DSM	1 RR, 3 P	No	TB	1	5
6	Wash	Mucoid	4 DSM	1 RR, 3 P	No	Excision	7	—
7	Wash	Cloudy, blood-tinged	4 DSM	1 RR, 3 P	Yes	TB	1	5
8	Brush	Brush, bloody fluid	2 DSM, 2 CC	1 RR, 3 P	Yes	TB	1	6
9	Wash	Bloody	4 DSM	1 RR, 3 P	No	TB	1	4
10	Wash	Bloody	4 DSM	1 RR, 3 P	No	TB	1	7
11	Wash	Bloody and cloudy	1 DSM, 2CC	1 RR, 3 P	Yes	TB	1	4
12	Wash	Bloody	4 DSM	1 RR, 3 P	No	TB	1	3
13	Wash	Blood-tinged	4 DSM	1 RR, 3 P	No	TB	1	5
14	Wash	Blood-tinged	2 DSM, 2 CC	1 RR, 3 P	No	TB	1	3
15	Wash	Mucoid	2 DSM, 2 CC	1 RR, 3 P	Yes	TB	1	4
16	Wash	Bloody	2 DSM, 2 CC	1 RR, 3 P	No	TB	1	5
17	Wash	Blood-tinged	4 DSM	1 RR, 3 P	No	TB	1	9
18	Wash	Bloody	2 DSM, 2 CC	1 RR, 3 P	No	TB	1	3
19	Wash	Bloody	2 DSM, 2 CC	1 RR, 3 P	Yes	Excision	5	—
20	Wash	Blood-tinged	2 DSM, 2 CC	1 RR, 3 P	Yes	TB	1	5
21	Wash	Bloody	4 DSM	1 RR, 3 P	No	Core	1	3
22	Brush	Brush in saline	2 DSM, 2 CC	4 P	Yes	TB	1	3
23	Wash	Cloudy	2 DSM, 2 CC	1 RR, 3 P	Yes	Excision	7	—
24	Brush	Brush in bloody fluid	2 DSM, 2 CC	1 RR, 3 P	No	Excision	7	—
25	Wash	Blood-tinged	2 DSM, 2 CC	1 RR, 3 P	Yes	EB	1	7
26	Brush	Brush in fluid	2 DSM, 2 CC	4 P	Yes	EB	1	7
27	Wash	Blood-tinged	2 DSM, 2 CC	1 RR, 3 P	Yes	TB	1	7
28	Brush	Brush in saline	2 DSM, 2 CC	4 P	Yes	TB	1	7
29	Wash	Bloody	4 DSM	1 RR, 3 P	Yes	TB	1	5
30	Wash	Cloudy	4 DSM	4 P	Yes	TB	2	3
31	Wash	Bloody	2 DSM, 2 CC	1 RR, 3 P	No	TB	1	6
32	Wash	Blood-tinged	2 DSM, 2 CC	1 RR, 3 P	No	Excision	8	—

CC, cytocentrifuged; DSM, direct smear; EB, endometrial biopsy; P, Papanicolaou stain; RR, rapid Romanowsky stain; TB, transbronchial biopsy.
* History indicates that clinical history data were provided on the cytology requisition form. For excision specimens, the number of blocks is number of blocks of tumor processed; for biopsy specimens, the number of pieces is the number of pieces obtained on biopsy material.

between the presence of a mass lesion and the original CH correlation frequency of interpretation or sampling error. In 11 cases (34%), the tumor broached the mucosal surface on the surgical biopsy tissue, although tumor was not present on the cytologic specimen (even after review). The original CH correlation process showed that in 13 cases (41%), tumor was present on the cytologic specimen. In 1 case (3%), the malignancy was poorly differentiated and readily identified on review; in the other 12 cases (38%), sampling issues had a role in misdiagnosis and the malignant cells were partially obscured, crushed, air dried, or few. In 3 cases, malignancy was diagnosed on the cytology specimen even though a lesion was not seen on bronchoscopy. In 4 cases, a lesion was identified bronchoscopically, although malignant cells were not seen on the cytologic specimen. In 4 cases (13%), the malignancy was well differentiated and mimicked reactive conditions, and in 3 cases (9%), the malignancy represented an unusual tumor for this location. In 8 cases (25%), the tumor had not been identified by the cytotechnologist but was seen on review. Sampling issues had a major role in underdiagnosis of 31 (97%) of the cases.

Table 7 shows recommendations to reduce error and the number of cases in which this error type might have been prevented if these recommendations had been implemented. We believe that immediate interpretation at the time of the procedure would have been the most effective method to reduce error because the pathologist would have asked for additional specimen samples.

Discussion

Our findings showed that in pulmonary brushing and washing specimens, interpretive error was linked closely to sampling error and that separation of these 2 error causes in individual cases was not always possible. Most errors, even those that originally were classified by CH correlation as interpretive, had a component that was secondary to poor sampling.[8]

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Table 4
Original and Review Diagnoses

Case No.	Original		Second Cytologic-Histologic Correlation Review	Original Cytologic-Histologic Correlation Review
	Cytology	Surgical		
1	Negative	Squamous cell carcinoma	Negative	Negative
2	Negative	Squamous cell carcinoma	Negative	Negative
3	Negative	NSCC	Negative	Negative
4	Negative	Granular cell tumor	Negative	Negative
5	Negative	Rhabdomyosarcoma	Negative	Malignancy
6	Negative	Rhabdomyosarcoma	Negative	Malignancy
7	Negative	NSCC	NSCC	Atypical
8	Negative	NSCC	Negative	Negative
9	Negative	Adenocarcinoma	Negative	Adenocarcinoma
10	Negative	NSCC	Negative	NSCC
11	Negative	Small cell carcinoma	Negative	Small cell carcinoma
12	Negative	NSCC	Negative	Negative
13	Negative	Small cell carcinoma	Small cell carcinoma	Negative
14	Negative	Squamous cell carcinoma	Negative	Atypical
15	Negative	NSCC	Negative	Negative
16	Negative	Adenocarcinoma	Negative	NSCC
17	Negative	Leiomyosarcoma	Negative	"Suspicious"
18	Negative	Adenocarcinoma	NSCC	Adenocarcinoma
19	Negative	NSCC	NSCC	Atypical
20	Negative	NSCC	NSCC	Negative
21	Negative	Small cell carcinoma	Malignant	Carcinoma
22	Negative	Adenocarcinoma	Negative	Atypical
23	Negative	Adenocarcinoma	Negative	Negative
24	Negative	Adenocarcinoma	Negative	Atypical
25	Negative	Adenocarcinoma	Negative	Negative
26	Negative	Adenocarcinoma	Negative	Negative
27	Negative	NSCC	NSCC	Negative
28	Negative	NSCC	Suspicious	Negative
29	Negative	Squamous cell carcinoma	NSCC	Squamous cell carcinoma
30	Negative	NSCC	Negative	Negative
31	Negative	NSCC	Unsatisfactory	Unsatisfactory
32	Negative	Adenocarcinoma	NSCC	NSCC

NSCC, non–small cell carcinoma.

These data indicated that errors mainly were a result of system problems[22] and were caused by poor quality specimens that did not contain diagnostic material or were misinterpreted partly owing to their less-than-optimal nature. An obvious misinterpretation occurred in only 1 case.

Devising effective error-reduction strategies to reduce specific error types necessitates changes in the laboratory and the clinical services involved in specimen procurement.[1] Targeting clinical sampling would seem to offer the greatest opportunity for reducing errors for 2 reasons.[24] First, improved sampling might help obtain diagnostic material that otherwise would not be obtained, and, second, improved samples might lead to improved interpretations. An error-reduction strategy that involves immediate cytologic interpretation would provide benefit in allowing clinicians to obtain additional material or change techniques if the samples did not contain diagnostic material. We have shown that increasing clinician focus on specimen procurement leads to higher quality specimens, and we currently are testing this hypothesis in pulmonary cytology specimens.[24] Such extensions of cytologic services increase costs and require developing a different type of expertise but lead to lower health care costs because of less invasive testing and the performance of fewer tests. We are examining the costs of false-negative cytologic diagnoses, and the results are forthcoming.[1]

Both cytology and surgical tissues may be obtained during bronchoscopy, and one could argue that a clinically significant error has not occurred as long as the appropriate diagnosis is made on one component. In this series, 12 (38%) of 32 specimens were not obtained at the same time (eg, a biopsy specimen was not obtained), indicating that, for at least these errors, additional procedures were needed to establish a diagnosis. Although service changes (such as immediate interpretation services) add expense, they also might lead to fewer additional procedures with associated morbidities. A cost-effectiveness analysis was beyond the scope of this study but could add insight into the tradeoffs of additional vs immediate interpretation testing. In addition, for patients who have conflicting cytology or surgical pathology diagnoses, clinicians must act on a discrepancy pair; although clinicians usually act on a malignant diagnosis (on the cytology or surgical specimen),

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Table 5
Computed Tomography Scan and Bronchoscopic Findings

	Scan Findings				Bronchoscopic Findings
Case No.	Mass Lesion	Size (cm)	Location	Impression	Impression
1 and 2	Yes	6.4 × 4.7	Right hilar region, narrowing bronchus intermedius and right middle lobe bronchus, postobstructive pneumonia; small subpleural nodules	Likely bronchogenic carcinoma	Submucosal and infiltrative mucosal lesion in bronchus intermedius; occlusion of right middle and lower lobes
3	Yes	3.1 × 2.8	Lateral segment right lower lobe, noncalcified with irregular margins	Likely bronchogenic carcinoma with lymphangitic spread	Normal
4	Yes	1.0 × 1.0	Right tracheal bronchial angle	1.0-cm mass lesion that looks like a lymph node	Plaque-like lesion (2-3 mm) with a granular surface
5 and 6	Yes	4.0 × 5.0	Left lower lobe, located paraspinally with possible invasion into pulmonary artery	"Suspicious" for malignancy	Endobronchial tumor emanating into proximal airways
7	Yes	3.0 × 3.5	Left perihilar region with abnormal lymph nodes	Perihilar mass	Not available
8 and 31	Yes	3.1 × 3.2	Proximal anterior segment confluent with left hilar region	Mass lesion	Not available
9	Yes	5.0 × 4.4	Right upper lobe with confluent right hilar adenopathy	Mass lesion may represent primary malignancy	Not available
10	No	—	Consolidation and infiltrative change in the right upper and middle lobes; right-sided paratracheal adenopathy	Consolidation	Extrinsic compression of wall; orifice occluded by soft tissue
11	Yes	Unknown	Left upper lobe, apical subsegmental spiculated lesion	Spiculated lesion	Endobronchial lesions identified
12	Yes	6.0 × 5.0	Right upper lobe and mediastinal mass with encasement of right upper lobe bronchus	Very suspicious for malignancy	Fleshy lesion emanating from upper lobe bronchus; procedure aborted because of bleeding
13	Yes	2.0 × 3.0	Right lower lobe with extension into right hilum; mediastinal mass present	Most likely malignant	Extrabronchial compression
14	No	—	Interstitial infiltrates with hilar and mediastinal lymphadenopathy	Interstitial infiltrates	Not available
15	Yes	4.2 × 3.0	Left lower lobe superior segment with satellite nodules	Left lower lobe mass	Not available
16	Yes	4.0 × 4.5	Anterior middle of right side of chest with enlarged retrocaval lymph node	Large lobular mass	Normal
17	Yes	Not measured	Large perihilar mass	Mass lesion	Left lower lobe, medial segment mass; no lesion seen
18	No	—	Right lower lobe, infiltrative process	Infiltrates	No endobronchial lesions seen
19	Yes	4.0 × 4.0	Right upper lobe, mass with irregular margins	Mass lesion	Not available
20	Yes	8.0 × 5.0	Subcarinal mass extending into the right inferior hilum	Mass lesion	Tumor originating from lower lobe; appears to infiltrate the main-stem bronchus
21	Yes	3.0 × 3.0	Left upper lobe and hilar mass that narrows lingular segment bronchus	Consistent with bronchogenic carcinoma	Heaped-up bronchial mucosa; friable tumor that bled easily in medial aspect of minor carina
22	Yes	4.0 × 4.0	Right-sided pleural based mass	Mass lesion	Right upper lobe bronchus with erythema and edema
23	Yes	Not stated	Right lower lobe peripheral mass	Mass lesion	No communication of tumor to mucosa; compression present
24	Yes	4.0 × 5.0	Right upper lobe mass with spiculated margins	Highly suspicious for malignancy	Not available
25 and 26	Yes	4.5 × 4.7	Soft tissue mass in the posterior mediastinum extending into the right subcarina; no masses in lung parenchyma	Suspicious for lung malignancy	Extrinsic compression of major carina with submucosal disease extending down left and right main-stem bronchi; mucosa not broken
27 and 28	Yes	4.7 × 4.4	Right middle lobe, soft tissue mass and right-sided hilar lymphadenopathy	Mass lesion	Not available
29	No	—	Infiltrate in left upper lobe; consolidated region in suprahilar and perihilar areas	Infiltrate	Submucosal studding, thought to be recurrence
30	No	—	Massive adenopathy; no lung mass present	Adenopathy	Apical segment of left upper lobe occluded; mucosa friable
32	Yes	13.2	Left upper lobe collapse with extensive mass	Lung mass	Not available

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Table 6
Root Cause Analysis of Sampling and Interpretation Contributions to Error

Case No.	Error Assessment	Root Cause Analytic Factors
1	Sampling	Malignant cells not interpretable because of air-drying artifact and excessive thickness
2	Sampling	Malignant cells not interpretable because of air-drying artifact and excessive thickness
3	Sampling	Malignant cells located in submucosal lymphangitic spaces and not accessible by brushing or washing
4	Sampling	Malignant cells located in submucosa and not accessible by brushing or washing
5	Interpretation	Only rare malignant cells seen admixed in larger tissue fragments; malignant cells partially obscured with blood; malignant cells not dotted by cytotechnologist; abundant squamous contaminant present; surgical biopsy specimen showed only a small focus of tumor extending through mucosa
6	Interpretation	Only rare malignant cells seen admixed in larger tissue fragments; malignant cells partially obscured with blood; cytotechnologist did not dot malignant cells; abundant squamous contaminant present; surgical biopsy specimen showed only a small focus of tumor extending through mucosa
7	Sampling and interpretation	Rare, single atypical cells admixed with abundant acute inflammation; <10 malignant cells present; well-differentiated tumor; cytotechnologist did not dot malignant cells
8	Sampling	Scantily cellular specimen that contained only a few benign bronchial cells; tumor did not penetrate the mucosa and observed only in the submucosa
9	Interpretation	Only 2 malignant cell groups admixed with a large amount of blood and acute and chronic inflammation; malignant cell groups present in very thick areas of debris and blood; malignant cells somewhat overstained and showed dark nuclei; cytotechnologist did not dot groups of malignant cells
10	Interpretation	Only 4 small malignant cells groups and few single malignant cells present; cytotechnologist did not dot malignant cells; large amount of obscuring mucus and acute and chronic inflammation present; crushing of the tumor cells observed
11	Interpretation	Rare malignant cells seen on smears, which were crushed and showed air-drying artifact; rare malignant cells seen in cytocentrifuged preparations and were obscured with acute inflammation and mucus; cytotechnologist did not dot malignant cells; acellular cytocentrifuged preparation
12	Sampling	Preparations showed excessive blood and acute inflammation and were extremely thick; scant normal pulmonary cellularity indicating poorly sampled lesion; surgical pathology specimen showed malignant cells and an ulcer
13	Sampling	Malignant cells located in submucosa and were not accessible by brushing or washing; cytology preparations showed benign bronchial cells and a large amount of blood
14	Sampling and interpretation	A single cell showed an enlarged nucleus and high N/C ratio; cytology specimens predominantly showed blood, benign bronchial cells, and macrophages; surgical pathology specimen showed malignant cells within lymphatics and no ulcer
15	Sampling	Cytocentrifuged and smear preparations showed abundant blood and acute inflammation; rare metaplastic cells and bronchial cells observed; sections of the biopsy tissue showed malignant cells appearing to breach the mucosa
16	Interpretation	Cytocentrifuged preparations showed abundant blood and necrotic debris that partially obscured the slides; air-drying artifact limited interpretation; scattered malignant cells seen on smears and cytocentrifuged preparations; cytotechnologist did not dot malignant cells; sections of biopsy specimen showed necrosis and clusters of malignant cells
17	Sampling and interpretation	One smear showed a fragment of spindle cells "suspicious" for metastatic leiomyosarcoma; other smear and cytocentrifuged preparations showed blood, acute inflammation, reactive bronchial cells, and macrophages
18	Interpretation	Numerous malignant cells seen on cytocentrifuged and smear preparations; very well-differentiated malignancy, although occasional cells showed features diagnostic of malignancy; an absence of background acute inflammation
19	Sampling and interpretation	Sections of surgical specimen showed well-differentiated adenocarcinoma adjacent to reactive epithelial cells; smears and cytocentrifuged preparations showed numerous atypical epithelial cells with slightly hyperchromatic nuclei and slightly increased N/C ratios; differential diagnosis included reactive change and malignancy
20	Sampling	Cytocentrifuged and smear preparations showed acute and chronic inflammation and blood; only rare bronchial cells observed; sections of biopsy tissue showed an ulcer with tumor admixed with acute and chronic inflammation
21	Interpretation	Single malignant cells admixed with abundant acute inflammation and necrotic debris; malignant cells were few and showed considerable nuclear crushing artifact; cytotechnologist did not dot malignant cells
22	Sampling and interpretation	Cytocentrifuged and smear preparations predominantly showed benign bronchial cells and macrophages; single group of atypical cells observed; sections of the biopsy specimen showed an intact mucosa without an ulcer
23	Sampling	Cytocentrifuged and smear preparations showed necrotic debris and acute inflammation; tumor insufficiently sampled; sections of biopsy tissue showed necrosis with tumor fragments
24	Sampling and interpretation	Cytocentrifuged and smear preparations showed benign bronchial cells, macrophages, and blood; a single group of cells showed slight atypia; tumor insufficiently sampled; sections of biopsy tissue showed an adenocarcinoma that was underneath an intact mucosa
25	Sampling	Cytocentrifuged and smear preparations sparsely cellular and predominantly showed blood and mucus; only rare bronchial cells observed; tumor not sampled; sections of biopsy tissue showed tumor extending through mucosa
26	Sampling	Cytocentrifuged and smear preparations sparsely cellular and predominantly showed blood and mucus; only rare bronchial cells observed; tumor not sampled; sections of biopsy tissue showed tumor extending through mucosa
27	Sampling	Cytocentrifuged and smear preparations cellular and showed numerous bronchial epithelial cells, chronic inflammation, and mucus; slight crushing observed on the smears; tumor not sampled; sections of biopsy tissue showed tumor extending through mucosa
28	Sampling	Cytocentrifuged and smear preparations cellular and showed numerous bronchial epithelial cells, chronic inflammation, and mucus; slight crushing seen on smears; tumor not sampled; sections of biopsy tissue showed tumor extending through mucosa
29	Interpretation	Smear preparations showed abundant blood and acute inflammation; numerous squamous cells seen; majority of squamous cells appeared mature, although single malignant cells were seen; sections of biopsy tissue showed well-differentiated squamous cell carcinoma; blood and inflammation compromised the specimen, and original pathologist may have thought that all squamous cells were contaminant or metaplastic
30	Sampling	Cytocentrifuged and smear preparations showed necrosis and acute inflammation; tumor not sampled; sections of biopsy tissue showed an ulcer with rare single malignant cells in a densely fibrotic stroma
31	Sampling	Scantily cellular specimen with no bronchial cells; cytology specimen unsatisfactory for diagnosis; tumor did not penetrate the mucosa and was seen only in the submucosa
32	Interpretation	Rare malignant cells admixed with abundant acute inflammation; sections of the biopsy tissue showed tumor extending through the mucosa

N/C, nuclear/cytoplasmic.

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Table 7
Recommendations to Reduce Errors Based on 32 Cases

Error Source/Recommendation	No. (%) of Cases Possibly Affected
Sampling	
Perform immediate interpretation during procedure.	23 (72)
Initiate the use of transbronchial fine-needle aspiration.	10 (31)
Prepare cell block in all cases in which material is available.	22 (69)
Use procedures to remove excess blood or inflammation.	9 (28)
Use technology that removes blood or inflammation and creates more uniform preparation.	9 (28)
Interpretation	
Perform blinded double viewing of a portion of all cases before sign-out.	13 (41)
Limit sign-out to subspecialized individuals.	7 (22)
Have more than 1 cytotechnologist screen the case.	8 (25)
Create a teaching file of difficult cases.	4 (13)
Contact clinician before sign-out.	Unknown
Address interpretive biases (ie, biases discussed by Reason[22,23]).	Unknown
Sampling and interpretation	
Prepare additional material in cases in which the clinician visualized a lesion during bronchoscopy and material is not seen on initial preparation (ie, obtain bronchoscopic findings before final sign-out).	9 (28)
Prepare additional material when slides are bloody or thick or show abundant inflammation.	9 (28)
Perform real-time correlation on same-procedure surgical and cytology specimens.	Unknown

false-positive diagnoses (even on surgical tissue samples) lead to major clinical consequences. This study was designed to look at discrepant diagnoses based on the CH correlation process and was not intended to determine overall error pulmonary frequencies (based on the failure of both cytology and surgical tissue samples to obtain a malignant diagnosis) or to specifically target surgical pathology errors. In fact, one of the reasons so many surgical biopsies had been obtained on bronchoscopy cases was in an attempt to reduce error.

Our data imply that cytology laboratory processes did not change when specimens were prepared poorly. Probable reasons for the failure to reprepare specimens included cost and time factors and the lack of connection that links poor specimen quality with errors. Change is difficult because it requires cytotechnologists and cytologists to request additional preparations knowing that case sign-out will be delayed and that the additional preparations might not alter the diagnosis in any specific case.

Manufacturers have shown that some technologies decrease sampling errors by decreasing the amount of blood, inflammation, and debris in specimen preparations. We infer from our data that although technologies have a role in the improvement of specimen quality, improvement also highly depends on human factors. For example, trusting that a monolayer preparation automatically improves Papanicolaou test sensitivity falsely assumes that the sample was obtained adequately and that poorly processed specimens are sufficient for diagnosis. The interplay between sensitivity and specificity depends highly on clinical skill and judgment.

The pairwise κ statistic showed poor agreement between the original and review CH correlation assessments of sampling and interpretive errors. These data confirm the results of Clary et al,[8] who reported interobserver κ values ranging from 0.02 to 0.45. Some laboratories use cytology fellows to perform CH correlation,[18] and our data and the data presented by Clary et al[8] indicate that fellows and cytologists have similar pairwise κ statistics when performing correlations. The CH correlation process typically involves the reexamination of challenging cases in which few malignant cells may be present. CLIA '88 does not mandate a method for performing CH correlation, and assessing for the presence or absence of malignancy on review is left to reviewer discretion. In our study, the original CH correlation reported malignant cells in 10 cases, and root cause analysis showed that sampling error strongly contributed to the original failure to recognize these cells. Thus, depending on reviewer characteristics, the original diagnosis in these 10 cases could be classified simply as a misinterpretation or a misinterpretation strongly biased by poor specimen quality. The difference between these assessments has medical-legal consequences. Low interobserver agreement is why we chose to investigate error from the viewpoint of the original CH correlating pathologists, assuming that their expertise would result in the more correct assessments.

The low interobserver agreement also raises the validity of performing double pathologist case viewing before sign-out as a means of error reduction. Double viewing has been shown to detect errors when performed after sign-out and to decrease errors when performed before sign-out.[3-5] Novis[25] showed that double viewing of all cases before sign-out reduced subsequent amended report frequency. In our study, double viewing potentially could reduce interpretive errors because malignant cells were detected by CH correlation review in 10 (31%) of all cases. A difficulty in the effective use of pre–sign-out double viewing is the resistance of pathologists to spend additional time.[26] The lack of cytotechnology dotting and the obscuring artifacts could have hampered detection of the malignant cells even on secondary review.

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Errors may be assessed using other reporting schemes. For example, Reason[22,23] reported that errors have an active and a latent component, and we focused on examining the latent factors. Reason[22,23] reported that active errors are subclassified as slips or mistakes. An example of a slip is the failure of a pathologist to concentrate on the dotted areas because that pathologist is too busy or tired; an example of a mistake is the failure to make a malignant diagnosis because of a low pretest probability of cancer. Targeting these error types would entail implementing a different set of error-reduction plans (eg, limiting the number of slides viewed per day and attempting to reduce particular biases). Further study is necessary to characterize these error types in this context.

The clinical workup of patients with lung lesions is highly variable, and the tests that are ordered strongly influence the probability of producing adequate samples. Grzybicki et al[27] reported that clinicians show poor agreement on the proper ordering of tests in patients with lung masses. Pulmonologists often perform bronchoscopy as the first-line test, whereas in the same scenario, surgeons are more apt to perform definitive surgery.[27] The biases inherent in ordering practices affected the cases that were encountered at UPMC and, consequently, affected the error frequencies and causes. Recommendations for error reduction could differ at other institutions because of the inherently different nature of patients who undergo bronchoscopy.

These data show that the CH correlation process may be used to design error-reduction initiatives. We are testing some of these initiatives in real-time practice.

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