

Imaging–Histologic Discordance at Percutaneous Biopsy of the Lung

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Rationale and Objectives: The purpose of this study was to quantify the degree of imaging–histologic discordance in a cohort of patients undergoing computed tomography (CT)–guided lung biopsy for focal lung disease.

Materials and Methods: A retrospective review was performed of 186 patients who underwent percutaneous lung biopsy of a parenchymal lesion at our institution between January and December 2009. Diagnostic radiology reports of CT or positron emission tomography–CTs performed before biopsy were used to classify the lesion as malignant or benign by five readers. Pathology reports of the biopsied lesions were classified by three readers. Inter-reader agreement and imaging–histologic concordance were quantified using kappa statistics. Discordant benign cases were then revisited to determine downstream effects.

Results: Inter-reader agreement on report content was substantial or almost perfect with kappas >0.783 . Kappas for concordance were as follows: malignant (0.448), primary lung cancer (0.517), metastatic disease to lung (0.449), benign (0.510), and overall agreement (0.381). Of the twelve discordant benign cases that were revisited, four were found to be false negatives, resulting in a delay in diagnosis.

Conclusions: Our study of imaging–histologic discordance in percutaneous biopsy of lung lesions supports the need for imaging report standardization and improved integration and communication between the fields of radiology and pathology.

Key Words: Radiologic–pathologic correlation; standardized reporting; imaging–histologic discordance.

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Radiology and pathology play central roles in cancer diagnosis but typically report findings independently of one another. Independent reporting can increase radiologic–pathologic discordance, defined as a discrepancy between imaging interpretation and histologic findings (1). Radiologic–pathologic correlation has been studied in various imaging specialties to gauge interpretive performance and accuracy, and to identify radiographic features corresponding to histologic findings (2–7). However, few studies have attempted to assess the utility of integrated radiologic–pathologic correlation for establishing imaging–histologic concordance or discordance as a method to prospectively identify missed carcinomas due to biopsy sampling error (8).

Radiologic–pathologic discordance may be categorized as either discordant malignant or discordant benign. The former refers to a lesion that appears radiologically benign, but is malignant on histology; the latter refers to a lesion suspicious

for malignancy on imaging but benign histologically (9). In mammography, with the adoption of the Breast Imaging–Reporting and Data System (BI-RADS), this notion of discordance fits naturally due to strict, unambiguous radiologic guidelines governing diagnostic conclusions. BI-RADS provides a framework that allows instances of discordance to receive special consideration such that ostensibly negative pathology in cases of high radiographic suspicion warrant prompt repeat biopsy (10–14).

In contrast to breast imaging, there exists no standardized set of reporting guidelines for thoracic imaging (15). This fact makes the study of discordance challenging as radiology reports can contain more than one diagnosis for a lung lesion (eg, organizing pneumonia vs primary neoplasm) or no diagnoses at all. Discordance resulting from such ambiguity can be confusing to the referring physician because it may obscure the likelihood of malignancy (16). Furthermore, in instances of high suspicion of carcinoma by imaging, a nonspecific benign histologic diagnosis resulting from inadequate tissue sampling could lead to delayed diagnosis of a missed cancer by the referring clinician (17).

By nature, lung cancer imaging is relatively more complex than breast cancer imaging, with greater anatomic and pathologic diversity. It is therefore understandable that lung cancer imaging reports reflect this complexity through differential diagnoses, which may naturally conflict. However, it is nonetheless important to correlate radiology and pathology diagnoses to appraise accuracy in imaging interpretation,

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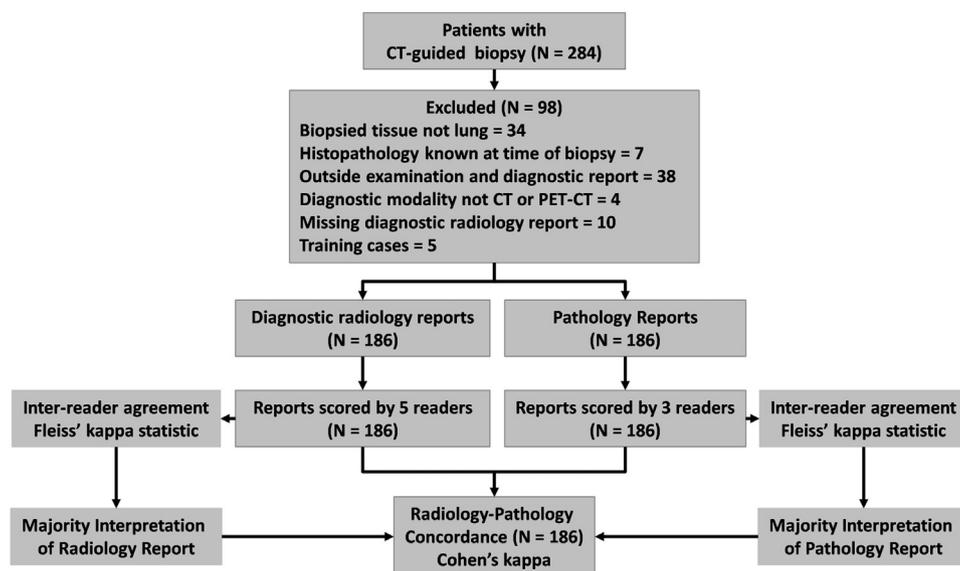


Figure 1. Experimental design. CT, computed tomography; PET, positron emission tomography.

identify potential causes of discordance, and make efforts to resolve these disparities.

To the best of our knowledge, there have been no previous studies to measure discordance in thoracic oncology. In this article, we sought to develop and apply a reliable scale for categorizing radiologic and pathologic findings to quantify the degree of imaging–histologic discordance in a cohort of patients undergoing computed tomography (CT)–guided lung biopsy for focal lung disease.

MATERIALS AND METHODS

With institutional review board approval, 186 patients undergoing image-guided core needle biopsy of the lung were studied retrospectively. Informed consent was waived because of the retrospective nature of the study. The cohort included all individuals in whom a diagnostic CT or positron emission tomography (PET)–CT was acquired and interpreted at our institution within 1 month of percutaneous lung biopsy. We limited the analysis to parenchymal lung lesions to constrain the diversity of thoracic pathology to lesions potentially related to lung carcinoma. The study cohort was established by querying our institutional radiology information system for procedures coded as CT-guided lung biopsy during the calendar year 2009 (Fig 1). In 2010, the thoracic radiology section at our institution began experimenting with various standardized templates for radiology reporting. However, as the need for, and composition of, such templates is debated, they are used by only a subset of radiologists who complete them to varying degrees. Therefore, to establish the degree of discordance during the most recent time period in which all radiologists were reporting in their most “natural” state, our study was limited to the year 2009. The query returned 299 lesions in 284 patients. Of these, 93 patients were excluded for the following reasons: the biopsy was of the

tissue other than the lung ($n = 34$), such as the pleural or chest wall lesions ($n = 34$); histopathology was known at the time of diagnostic interpretation ($n = 7$); diagnostic radiology reports were not generated from our institution ($n = 38$); a diagnostic radiology report was not obtained before biopsy or did not reference the lesion of interest ($n = 10$); or the diagnostic imaging modality was neither CT nor PET-CT ($n = 4$). Five randomly selected cases were used to train readers in the classification procedure and were not included in the results. All statistical analyses were performed using R, version 3.0.1 (18).

Inter-reader Agreement on Interpretation Content

Text reports of diagnostic CT or PET-CT examinations rendered by institutional radiologists before biopsy were retrieved and deidentified. Radiologic diagnoses were independently classified as benign or malignant by five readers representing different levels of medical experience to measure the degree of agreement between readers on report content. Given the straightforward nature of the task, nonradiologists were included as readers. The group was composed of a biomedical informatician, a general internist, a pathologist, a radiologist, and a medical student, none of whom had previously reviewed the radiology reports. All readers were blinded to the corresponding pathology results and received standardized instructions on how to classify reports (Supplementary Appendix 1); five training cases were used to ensure an understanding of the classification task. Table 1 lists sample reader scoring. Responses were dichotomous (1 = yes or 0 = no) for each of the four independent determinations: malignant (not otherwise specified), primary lung cancer, metastatic disease, and benign disease. Interobserver agreement on the information content of the report among the five readers was determined using Fleiss kappa statistic, which adjusts the percent agreement for the level of agreement that would be expected entirely due to chance

TABLE 1. Sample Reader Scoring of Radiology and Pathology Diagnostic Interpretations

Original Semantic Reports	Reader Interpretation of Report			
	Malignant	Primary Lung Cancer	Metastatic Disease	Benign Disease
Radiology impression: focal nodule in the right lower lobe with central necrosis. Primary consideration is malignant disease, in particular primary lung cancer or metastatic disease.	1	1	1	0
Pathology final diagnosis: lung, left lower lobe (biopsy): <ul style="list-style-type: none"> ■ Very scant fragments of necrotic tissue, suboptimal for evaluation ■ No evidence of necrotic neoplasm by immunohistochemistry ■ GMS, PAS, and AFB stains negative for organisms (see comment) Comment: although special stains are negative for organisms, an infectious etiology is favored.	0	0	0	1

“1” indicates that the diagnosis was included as a possible etiology of the lesion of interest; “0” indicates that the diagnosis was not included.

TABLE 2. Inter-reader Agreement on Information Content of Diagnostic Imaging and Pathology Reports

Radiology Classification Agreement between Readers	Fleiss Kappa*	Pathology Classification Agreement between Readers	Fleiss Kappa*
Radiology–malignant, not otherwise specified	0.783	Pathology–malignant, not otherwise specified	0.974
Radiology–primary lung cancer	0.904	Pathology–primary lung cancer	0.964
Radiology–metastatic disease to the lung	0.849	Pathology–metastatic disease to the lung	0.926
Radiology–benign	0.915	Pathology–benign disease	0.972
Radiology–combined	0.817	Pathology–combined	0.925

*Kappa values between 0.61 and 0.80 have “substantial” agreement. Kappa values >0.81 have an “almost perfect” agreement.

(Table 2). Following the literature (19), the strength of agreement for the kappa scores was interpreted as “poor” (kappa value 0); “small” (0.01–0.20); “fair” (0.21–0.40); “moderate” (0.41–0.60), “substantial” (0.61–0.80), and “almost perfect” (0.81–1.00).

The original pathology interpretations of biopsied lesions rendered by institutional lung pathologists were deidentified and then classified by three independent readers, which included a biomedical informatician and two radiologists, none of whom had previously reviewed the reports. Although the biomedical informatician served as one of the five radiology report readers mentioned earlier, a washout period of 6 weeks was allotted before classification of corresponding pathology reports. As mentioned previously, a numerical value (1 = yes or 0 = no) was assigned to classify the final description of histology as malignant, benign, primary lung cancer, or metastasis; interobserver agreement among the three readers was determined using the Fleiss kappa statistic (Table 2).

Radiologic–Pathologic Concordance

For purposes of determining concordance between imaging and histologic interpretations, the standard of reference was the majority (dominant) classification for both diagnostic imaging (five readers) and pathology (three readers) reports. Concordance was defined as agreement between radiology and pathology reports. Discordance was divided into the

TABLE 3. Cohen Kappa Scores Comparing the Majority of Radiology Diagnosis with Majority of Pathology Diagnosis

Disease Category	Cohen Kappa Coefficient between Radiology and Pathology Diagnoses
Malignant, not otherwise specified	0.448 (0.304–0.592)
Primary lung cancer	0.517 (0.396–0.638)
Metastatic disease to the lung	0.449 (0.315–0.583)
Benign process	0.510 (0.374–0.647)
Combined	0.381 (0.300–0.461)

following: 1) discordant benign—imaging interpretations indicated a malignant lesion, but the pathology was benign, and 2) discordant malignant—imaging interpretations indicated a benign etiology, but the pathology was malignant.

Concordance was quantified using the Cohen kappa. Five kappa scores were obtained (Table 3). Pairwise comparisons were made between each of the four individual (malignant, primary lung cancer, metastatic disease, and benign) imaging interpretations relative to the reference pathology report classifications. A fifth kappa score for a “combined” category was calculated by treating each unique combination of responses (four dichotomous variables resulting in 16 possible combinations) for a lesion to the four yes/no questions as a distinct answer and comparing to pathology. The “combined” category score was calculated to compare a comprehensive

TABLE 4. Frequencies and Percentages of Conclusions Observed on Radiology and Pathology Reports

Radiology or Pathology Report Description	Radiology		Pathology	
	n	%	n	%
Definitively malignant or benign				
Malignant, not otherwise specified	15	8.1	0	0.0
Primary lung cancer	55	29.6	81	43.5
Metastatic disease to the lung	45	24.2	38	20.4
Benign process	25	13.4	48	25.8
Primary lung cancer or metastatic disease ¹	8	4.3	13	7.0
Ambiguous (malignant or benign)				
Primary lung cancer or metastatic disease or benign process	5	2.7	0	0.0
Primary lung cancer or benign process	8	4.3	0	0.0
Metastatic disease or benign process	12	6.5	0	0.0
Malignant, not otherwise specified or benign process	6	3.2	0	0.0
Nondiagnostic				
Indeterminate	7	3.8	6	3.2
Total	186	100.0	186	100.0

Data are based on the majority interpretation by readers for the imaging and pathology reports.

¹Cases in which neither benign nor malignant disease were included in the imaging diagnosis.

representation of radiology and pathology reports, rather than treating the diagnostic categories independently.

RESULTS

Inter-reader Agreement on Report Content

An almost-perfect agreement was observed between readers of radiology reports for all categories of diagnosis except “malignant, not otherwise specified” ($\kappa = 0.783$). Concordance was highest in reports indicating “primary lung cancer” or “benign disease” as diagnostic considerations. Overall, 148 (80%) of 186 radiology reports decisively categorized lesions as only malignant (including “malignant, not otherwise specified,” “primary lung cancer,” or “metastatic disease”) or benign disease (Table 4). Small percentages (16%) were ambiguous or noncommittal, prescribing combinations of malignant and benign disease with no indication of certainty, or did not mention a diagnosis (3.8%).

As expected, pathology reporting was consistently more definitive and there was an almost-perfect agreement between readers ($\kappa > 0.81$). In all, 167 (90%) of 186 pathology reports definitively characterized the biopsied lesion as “primary lung cancer,” “metastasis,” or “benign disease.” Thirteen of 186 cases were classified as either primary lung cancer or metastasis due to nonspecific immunohistochemical staining; six cases were indeterminate owing to insufficient sampling.

For purposes of this analysis, pathology was considered the gold standard; these six cases were not included in the determination of imaging–histologic concordance.

Concordance between Radiology and Pathology Reports

Cohen kappa (Table 3) to compare the concordance of diagnoses between imaging and pathology reports for each of the four diagnostic imaging categories were as follows: malignant, 0.448; primary lung cancer, 0.517; metastatic disease of the lung, 0.449; and benign process, 0.510. A combined score that factored all diagnostic categories was 0.381.

To further illustrate concordance, Table 5 shows the percent agreement between pathologic diagnosis and the radiologic report at the individual case level. We simplified pathology into malignant versus benign and compared to radiologic interpretations grouped into four categories: malignant disease, benign disease, combined malignant or benign disease, and indeterminate.

Outcomes in Discordant Benign Cases

Twelve cases in our cohort had a definitive radiologic diagnosis of malignancy but were discordant benign, meaning that the histologic interpretation was benign (Table 6). Four cases were histologic false negatives with benign histologic diagnoses secondary to improper tissue sampling. The final diagnoses of metastatic disease in these four cases occurred 2–12 months after the initial biopsy and were ultimately diagnosed either on imaging findings (continued growth of the index lesion or development of new lesions) or rebiopsy of the lesion. Six cases had initial radiologic diagnoses of malignancy, but had specific benign histologic diagnoses (granulomatous infection, hamartoma, and amyloidoma) sufficient to confirm a false-positive radiologic diagnosis of malignancy, and no further diagnostic testing was pursued. In the remaining two cases, discordance was never reconciled because the patients were lost to follow-up at our institution.

DISCUSSION

We conducted a retrospective study to quantify discordance within standard of practice radiology and pathology reporting in patients undergoing percutaneous lung biopsy. The analysis of concordance was not straightforward. We initially sought to investigate imaging–histologic correlation in lung biopsy cases with the intent of emphasizing discordance as a method to prospectively identify missed carcinomas, as is done in breast imaging (8,10–13). However, we found that radiology reports varied significantly in diagnostic coverage and clarity depending on a radiologist’s personal style, an observation also reported in the literature (20,21). Therefore, it is difficult to determine diagnostic accuracy (and thus radiology–pathology concordance) when a radiology report includes multiple differential diagnoses. In contrast to lung

TABLE 5. Relationships between Benign and Malignant Pathologic Diagnosis and Radiologic Report

Pathologic Truth (<i>n</i> = 180)	Categories of Radiology Interpretation, <i>n</i> (%)				
	Pathologic Diagnosis, <i>n</i> (%)	Malignant Only	Benign Only	Malignant or Benign	Neither*
Malignant = 132 (71)		108 (82)	4 (3)	17 (13)	3 (2)
Benign = 48 (26)		12 (24)	20 (42)	14 (30)	2 (4)

In six cases (3%), there was insufficient tissue for pathologic diagnosis; these cases are not included.

*Cases in which neither benign nor malignant disease were included in the imaging diagnosis.

TABLE 6. Features of Cases with Benign Discordance (Radiographic Malignant Diagnosis with Benign Histology)

<i>n</i>	Age (years)	Sex	Radiologic Diagnosis	Pathologic Diagnosis	Final Diagnosis and Mode of Diagnosis
1	74	M	Metastatic colon cancer	Hepatic parenchymal sampling	Metastatic colon carcinoma, repeat biopsy 3 months later
2	70	M	Metastatic thyroid cancer	Alveolar tissue with nonspecific fibrosis and chronic inflammation with focus of granulomatous inflammation	Metastatic thyroid carcinoma, repeat imaging 2 months later
3	81	M	Metastatic sarcoma	Lymphoplasmacytic infiltrate	Metastatic sarcoma, repeat imaging 5 months later, repeat biopsy 12 months later
4	65	M	Metastatic adenoid cystic carcinoma	Benign alveolar tissue with focal fibrosis	Metastatic adenoid cystic carcinoma, repeat imaging 3.5 months later
5	73	M	Metastatic squamous cell carcinoma	Amyloidoma	Amyloidosis
6	58	F	Primary lung cancer	Necrotizing granulomatous inflammation, coccidioidomycosis	Disseminated coccidioidomycosis
7	48	M	Primary lung cancer	Pulmonary hamartoma	Hamartoma
8	75	F	Primary lung neoplasm	Necrotizing granuloma, coccidioidomycosis	Granuloma
9	51	M	Primary lung neoplasm	Necrotizing granuloma, likely coccidioidomycosis	Granulomatous disease, clinical diagnosis
10	55	F	Metastatic breast cancer	Fragments of bronchioalveolar tissue and mucin with eosinophils	Inflammatory, surgical biopsy 1 month later
11	46	M	Primary lung neoplasm	Lung with hemosiderin-laden macrophages, mild chronic inflammation	Indeterminate, lost to follow-up
12	51	F	Malignant, not otherwise specified	Benign tissue with focal fibroelastosis, old hemorrhage, rare refractile, nonpolarizable foreign material	Lost to follow-up

F, female; M, male.

imaging, the success of percutaneous breast biopsy programs and their strength in detecting malignancies through discordance is predicated on precise, unambiguous delivery of imaging findings in addition to clear communication between the radiologist and pathologist (22). Historically, no such standardized reporting system has existed in thoracic imaging, where imaging interpretations use natural language, address a larger range of pathologic conditions, and do not require reference to a level of suspicion, all of which factors into making direct comparisons to pathology challenging.

The simplified scale we developed to characterize the diagnoses from radiology and pathology reports (ie, “malignant,” “benign,” “primary lung cancer,” and “metastatic disease”) enabled us to quantify imaging–histologic concordance. Although more granular levels of suspicion for a lesion

were considered (eg, 0%–25%, 26%–50%, 51%–75%, and 76%–100%), the unstructured narrative text of radiology reports inhibit such an evaluation. Specifically, the assignment of quantitative levels of suspicion to semantic descriptions is difficult to generalize (eg, two radiologists may have different opinions on the quantitative suspicion of “possibly malignant”).

We found moderate concordance between radiology and pathology for the four individual diagnostic categories we defined. However, when all categories were viewed collectively under the “combined” category, agreement was only fair. These findings were not unexpected: when individual differential diagnoses in a single report are considered independently, there will naturally be increased concordance as the pathology diagnosis needs to only match one of the radiology differentials. In contrast, when all differential diagnoses

are considered together, any radiologic differential that is not also a diagnosis in the pathology report results in discordance. This is a common scenario as pathology reports typically contain a single diagnosis, and radiology reports often contain multiple diagnoses. It is possible that a more contextual view of concordance, accounting for each patient's history and individual findings, could lead to different observations of concordance. However, such an analysis would be more time intensive and possibly less reliable as it would require increased clinical interpretation among readers.

Although the sheer diversity of pathology in thoracic radiology makes it less amenable to decisive radiologic reporting relative to mammography, a more systematic appraisal of the certainty conveyed in the radiology report akin to BI-RADS would not only help encode ambiguity, but also allow for efficient detection of discordance and improve clinical decision making (23). Efforts are underway to develop such standards. For example, the first version of a standardized reporting system for lung cancer screening, Lung-RADS, has been released by the American College of Radiology (22) and is designed to serve as a standard for screening interpretation, reporting, and quality assurance.

We looked specifically at discordant benign cases, which in breast imaging are considered the most deleterious as they may prove to be pathologic false negative. In breast disease, it is understood that these cases warrant repeat biopsy or surgical excision (10). Among our 12 discordant benign cases, there were four instances of metastatic disease in which diagnosis was delayed until either repeat biopsy or subsequent disease progression on imaging confirmed the initial radiographic suspicion of malignancy. Unlike discordant benign cases, in which pathologic false-negative findings can delay diagnosis, discordant malignant cases infrequently increase harms to the patient because management is comparable to situations of radiology–pathology concordance for malignancy. However, discordant malignant cases afford opportunities for critical feedback; the radiologist can review the features that influenced judgment in underestimating the severity of the lesion and use these cases as teaching tools to audit false negatives and measure quality assurance (9).

Our study had several limitations. First, our methodology for weighting report content excluded potential diagnoses, if the reporting radiologist favored one diagnosis over another, which contributed to lower multireader concordance on imaging reports and to lower radiologic–pathologic concordance. Second, our cases were drawn from a cohort of patients undergoing percutaneous biopsy. This introduced a selection bias as patients may also receive pathologic diagnoses through other sampling techniques (eg, surgical excision), and we did not correlate with radiology in these cases. Third, our findings apply to our tertiary-care center, which serves a population of patients who have a larger variety of pathologies relative to other hospitals and clinics. Finally, our results are influenced by our institution's reporting practices among radiologists and pathologists.

CONCLUSIONS

We observed only moderate concordance between independently rendered radiology and pathology reports on patients undergoing percutaneous lung biopsy. The reasons for this are several and are as follows: 1) the pathology encountered in focal lung disease is diverse, 2) similar imaging features may have very different histologies, which limits the degree of specificity in reporting, 3) radiology reports use free text without a controlled vocabulary or standardized approach to description or degree of suspicion for a particular pathology, and 4) interpreting radiologists have varying degrees of confidence in stipulating a primary diagnosis. These factors conspire to create ambiguity when there is discordance between diagnostic imaging and histologic interpretation. Our experience underscores opportunities to improve communication in diagnostic imaging through more standardized reporting that conveys levels of suspicion for different pathologies. Moreover, the coupling of radiology and pathology into an integrated report developed by closer communication between disciplines may better serve the needs of referring clinicians by identifying potential causes of discordance and providing recommendations for management in the setting of disagreement.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.acra.2014.11.009>.

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