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The diagnostic yield of CT-guided percutaneous lung biopsy in solid organ transplant recipients

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Abstract

Background—Despite the widespread use of computed tomography (CT)-guided percutaneous lung biopsy (PLB) in immunocompetent patients, the diagnostic yield and safety in solid organ transplant (SOT) recipients is unknown. The purpose of this investigation was to determine the test performance of CT-PLB in SOT recipients.

Methods—We performed a 10-year single-center, retrospective analysis among heart, lung, kidney and liver transplant recipients. We included all adult patients who underwent a PLB of a parenchymal lung nodule following their transplantation.

Results—Within the study period, 1754 solid organ transplants were performed of which 45 biopsies met study criteria. Overall the incidence of PLB in SOT was 3%. PLB established a diagnosis in 24 out of 45 cases. The yield of PLB was better for combined biopsy technique (fine needle aspiration biopsy (FNAB) and core biopsy (CB)) than for FNAB alone (odds ratio (OR): 4.2, 95% confidence interval (CI): 1.2, 15.6), and for lesions that were malignant (OR: 10.0, 95%

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CI: 1.8, 75.4) or caused by an invasive fungal infection (OR: 5.0, 95% CI: 1.1, 27.9). Complications occurred in 13% (6/45) of patients.

Conclusion—CT-guided PLB is a safe modality that provides a moderate yield for diagnosing pulmonary nodules of malignant or fungal etiology in SOT recipients.

Keywords

Percutaneous lung biopsy; invasive fungal disease; solid organ transplantation; malignancy; lung nodule

Introduction

Computed tomography-guided percutaneous lung biopsy (PLB) is widely used to diagnose pulmonary nodules and masses. Among immunocompetent patients, the sensitivity of the procedure exceeds 90% for malignant lesions and is 50%-80% for benign lesions (1, 2). The test performance characteristics of PLB among immunosuppressed solid organ transplant (SOT) recipients have not been established.

Lifelong immunosuppressive therapy renders SOT recipients susceptible to a wide range of pulmonary diseases. Among SOT recipients, pulmonary nodules may represent a spectrum of infectious, inflammatory, and malignant diseases (3-5). The development of a pulmonary nodule in an SOT recipient predicts a poor outcome with mortality rates of 70% in lung transplant patients (5). Establishing the etiology of a pulmonary nodule in an SOT recipient is critical in order to initiate effective treatment. Treatment may require modifying the intensity of immunosuppression, initiating anti-infective therapy, or surgical resection.

Despite its widespread use for the diagnosis of pulmonary lesions, little is known of PLB's test performance among SOT recipients. To address this knowledge gap, we performed a 10-year, retrospective analysis to determine the diagnostic yield of PLB for the evaluation of pulmonary nodules and masses among heart, lung, kidney and liver transplant patients.

Patients and Methods

Study Patients

We reviewed the medical records of all patients who were recipients of a heart, lung, liver, or kidney transplant and who had undergone one or more PLB of a pulmonary nodule or mass between January 1, 2000, and April 1, 2010. Study subjects were identified by a computer algorithm that cross-referenced the International Classification of Disease 9th revision procedural code for any solid organ transplant (v42) with the electronic medical record history of PLB. To validate this analysis, a chart review was also conducted for all patients who received a heart, lung, heart/lung, liver and kidney transplant during the 10-year study period. We included all patients who underwent a biopsy of a parenchymal lung nodule or mass following their transplantation date. Patients were excluded if they underwent a biopsy of pleural thickening or a mediastinal mass, or were less than 18 years of age at the time of biopsy. In one patient, the right lung was biopsied 2 months after the biopsy of the contralateral lung. For this individual, the first biopsy was used for evaluation for the purpose of model simplicity and to maintain the assumption of independence in the analysis. An institutional review board exemption (IRB number 4947) was obtained and data were collected and analyzed in compliance with the Health Insurance Portability and Accountability Act.

Protocol Imaging

Protocol—All biopsies were performed using a commercially available helical multi-detector row CT machine with CT-fluoroscopic capability. Unenhanced CT images were obtained through the region of interest with a section thickness of 2.5-5 mm. The maximal width and the length of the targeted nodule were measured in the axial plane using an electronic caliper and the median of these two dimensions was reported.

Biopsy Protocol—Board certified radiologists performed all biopsies determining patient positioning, skin entry site and trajectory. An on-site cytotechnologist was present for all procedures. Biopsies were performed using a coaxial technique with a 19-gauge thin wall coaxial introducer needle, 10 or 15 cm long, determined by the length of the trajectory. Fine needle aspiration biopsy (FNAB) was performed on all patients using a 21-gauge aspiration needle or a modified 21-gauge Menghini aspiration needle. Additional core biopsies (CB) were performed with a 20-gauge automated cutting needle biopsy gun in 21 (47%) patients. The decision to obtain additional core biopsies was based on physician preference and location of the target nodule. For example, if the nodule was adjacent to a pulmonary vessel, only FNAB was obtained. In 2006 there was a change in practice, where combined FNAB and CB were performed in a majority of patients (68% compared to 30% in years prior to 2006). A limited post-biopsy CT was obtained following the biopsy to evaluate for immediate complications such as a pneumothorax or pulmonary hemorrhage.

Samples of specimens obtained for cytology were placed on a glass slide and immediately smeared and stained using the Romanowski group of stains (proprietary name Diff-Quik, Richard-Allen Scientific, Kalamazoo, MI) followed by Papanicolau stain. Additional specimens for cell block and detailed cytological analysis were placed in saline. Microbiology specimens were sent for bacterial (anaerobic/aerobic), fungal, and mycobacterial cultures. The number of samples obtained was based on the cytopathologist's preliminary evaluation and/or the presence of acute complication that necessitated termination of the procedure.

Post-procedure Monitoring/Adverse Events

All patients were monitored for 4 hours after the biopsy. All patients received an upright postero-anterior chest radiograph, prior to hospital discharge, to evaluate for a delayed pneumothorax. Small (<20%), asymptomatic pneumothoraces were not treated. Symptomatic or expanding pneumothoraces were treated with nasal oxygen and thoracostomy tube insertion. Complications were classified as major (death, major permanent adverse sequelae, additional therapy, or unplanned increase in level of care) and minor (no therapy or consequence including overnight stay for observation only) based on Society of Interventional Radiology standards (6).

Clinical Follow-up

Patient characteristics including demographics, clinical course and radiographic characteristics were obtained from the medical record. Final cytology and microbiology results were reviewed in the medical record to evaluate the success of PLB. A finding of "atypical cells" was not considered to be a definitive diagnosis. Among patients in whom PLB failed to establish the diagnosis, an attempt to establish the etiology was made either by bronchoscopic biopsy, surgical biopsy, including video-assisted thoracoscopic surgery, mediastinoscopy, or thoracotomy. Empiric medical management with 3 months or longer clinical and radiographic follow-up was used to monitor response. Invasive fungal disease (IFD) was defined as "possible, probable or proven" based on European Organization for Research and Treatment of Cancer/Mycoses Study Group (EORTC/MSG) definitions (7).

Statistics

Adequacy of PLB was calculated for the entire cohort and statistical differences between the subgroups were calculated using Fisher's test or a chi-square test as appropriate. Logistic regression models were used to investigate the effect of lesion characteristics and biopsy type on the diagnostic yield of PLB. To assess the effect of lesion etiology on diagnostic yield, the logistic regression model included a categorical variable for etiology (non-fungal benign, IFD, and malignant). All tests were two-sided and were conducted at the 0.05 level of significance. All statistical analysis was performed using R Software (GNU General Public License).

Results

From January 1, 2000 to April 1, 2010 a total of 1754 patients received heart, liver, lung, kidney and heart/lung transplants. Based on our eligibility criteria, 45 patients underwent 46 PLB. Two patients underwent biopsies but were lost to follow-up, precluding the establishment of a definitive diagnosis. These individuals were included in the analysis. Patient characteristics are summarized in Table 1. The median age was 56 years (ranging from 18 to 69 years). Overall the incidence of PLB in SOT patients was 3% (46/1754). PLB was most frequently obtained among heart/lung (8%, 4/50), followed by heart (6%, 25/424), lung (3%, 8/237), liver (2%, 7/474), and renal transplant recipients (0.3%, 2/569). The study population had a median time from transplant to biopsy of 12.7 months. For recipients of heart transplants, the median time to biopsy was 4.3 months, whereas the median time until transplant among recipients of lung, liver, kidney, heart/lung and kidney transplants was 50.1 months. The time from transplant to biopsy was significantly different for those who underwent heart transplants versus those who underwent any other type of transplant ($p=0.02$).

Imaging Characteristics

Nodule and mass characteristics including size, location and appearance are reported in Table 1. Among SOT recipients, 50% had a single dominant nodule or a mass. The median length of the biopsied lesion was 2.3 cm, with a range 0.9-7.3 cm. The majority of biopsied lesions, 24 out of 45 (53%) were >2cm in size. Cavitary nodules were uniformly infectious in etiology (3 fungal, 1 atypical mycobacterial). Biopsied lesions were predominately located in the left and right lower lobes and left upper lobe. There were no significant differences in distribution of nodules by lung zone (central, middle and peripheral).

Procedures and complications

Of the 45 procedures, FNAB alone was performed in 24 (53%) cases. In the remaining 21 procedures, both FNAB and CBs were obtained. The overall complication rate was 13% (6/45). Five procedures resulted in an asymptomatic pneumothorax and an additional procedure required tube thoracostomy. Among the patients who sustained a post-biopsy pneumothorax, a combination technique of FNAB and CB was more common (67%; 4/6).

Diagnostic Yield

Characteristics associated with diagnostic yield are summarized in Table 2. Overall, PLB established a diagnosis in 24 of the 45 cases (53%). Among lesions diagnosed by PLB, 15 (63%) were non-malignant and 9 lesions were malignant. For patients who did not have a definitive diagnosis by PLB, 10 underwent a second diagnostic technique including surgical lung biopsy (7), or bronchoscopy (3). The remaining patients were diagnosed by clinical follow up (6), positive microbiologic blood culture (2), and pleural fluid cytology (1). A definitive diagnosis was not established for two patients due to a loss of follow-up and these

were considered “failed diagnoses” in our analysis. Malignant lesions, which accounted for 12 cases, included non-small cell lung cancer, metastatic disease, post-transplant lymphoproliferative disease (PTLD) and lymphoma. Among patients with malignant lesions, heart transplant recipients were the most common (4/12, 33%) followed by patients with liver (3/12, 25%) and lung transplants (3/12, 25%). Overall the sensitivity of PLB for diagnosing a malignant lesion was higher than for a non-malignant lesion, 75% and 48%, respectively, although this difference failed to reach statistical significance (p=0.09). Individuals with malignant lesions were 10 times more likely to have a definitive diagnosis established by PLB (9/12) than individuals who had other non-malignant, non-fungal etiologies (3/11) (adjusted odds ratio (OR)=10.0, 95% confidence interval (CI): (1.8, 75.4) p=0.01).

Among benign lesions, the most common diagnosis was fungal infection, accounting for 65% (20/31), of which 13 were due to *Aspergillus* species. The sensitivity of PLB for EORTC/MSG “proven” fungal infections was 75% (12/16). The sensitivity of PLB for all IFD (60%) was higher than the sensitivity for other benign, non-fungal lesions (20%). Lesions of IFDs were 5 times more likely to receive a diagnosis (12/20) than were lesions of other benign, non-fungal etiologies (3/11) (OR=5.0, 95% CI: (1.1, 27.9), p=0.05). Table 3 details the characteristics of the diagnosed fungal infections. For patients with fungal infections heart transplant recipients were the most common (16/20, 80%) followed by liver (2/20, 10%) and heart/lung (2/20, 10%) transplant recipients. 30% (6/20) were receiving empiric antifungal therapy at the time of diagnosis (Table 3).

FNAB alone had a significantly lower yield than the combination of FNAB and CB. A combination of FNAB and CB was 4.2 times more likely to yield a diagnosis than FNAB biopsy alone (OR=4.2, 95% CI: (1.2, 15.6) p=0.03). For benign lesions (22), FNAB biopsy was diagnostic in 9 cases (38%) and the combination of FNAB and CB was diagnostic in 15 cases (71%). For malignant lesions, CB and FNAB yielded a higher proportion of diagnoses than did FNAB alone, but this difference was not significant. No significant differences were found for the overall diagnostic yield by size (≤ 2cm: 47% vs. >2cm: 61%), nor did the diagnostic yield differ by size when modified by the status of malignancy.

Discussion

SOT recipients with pulmonary nodules or masses constitute a common clinical challenge. To our knowledge, this study represents the largest series that addresses the utility of PLB in SOT recipients. The differential diagnosis for lung nodules in SOT is broad and includes malignant (primary, metastatic, PTLD), infectious (fungal, nocardia, mycobacteria) and benign etiologies. The clinical picture is often unclear given immunosuppression and imaging studies have poor specificity. For example, although the “halo sign” in a patient after HSCT often represents an *Aspergillus* infection, it also may be observed in a variety of infectious (e.g., candidiasis, mucormycosis, atypical mycobacteria or cytomegalovirus), inflammatory (e.g., Wegener’s granulomatosis) and malignant conditions (8). Thus, possible treatment options could be a reduction in immunosuppression for PTLD, an increase in immunosuppression for Wegener’s granulomatosis, the administration of antimicrobials for a bacterial, fungal or viral infection or surgical resection for a malignancy. Because the potential treatment options for these pulmonary lesions are disparate a nodule’s clinical equipoise justifies the need for an aggressive diagnostic approach. Overall, the diagnostic yield of PLB among heart, lung, kidney and liver transplant recipients was 53%. The yield of the procedure varied for malignant and non-malignant etiologies, 75% and 48%, respectively. In a case series of immunocompetent patients, the overall diagnostic yield for PLB was 83% (sensitivity for malignant lesions 92%, and for benign lesions 67%) (2). Similarly, the overall sensitivity of PLB is in the range of 80% to 90%, in previous studies

from our institution (1). Differences in the diagnostic yields in these studies and in our analysis are likely attributable to the higher proportion of immunosuppressed patients in our cohort and, in turn, the unsurprising finding that more nodules were attributable to non-malignant diseases, including infections.

Three factors associated with a higher diagnostic yield were the biopsy type (use of FNAB and CB vs. FNAB, alone) and whether the lesions were of malignant or fungal etiology compared with a benign, non-fungal etiology. These findings are consistent with results from studies conducted in other patient populations. For malignant lesions in immunocompetent individuals, the biopsies combining FNAB and CBs (95%) have higher sensitivity than FNAB alone (85.1% to 89.7%) (9, 10). For benign lesions, Gong et al. demonstrated an increased yield of FNAB and CB (96%) compared with FNAB (40%) or CB (92%) alone (10). In our analysis, FNAB and CB appear to be superior to FNAB alone for both benign and malignant nodules, although differences did not achieve statistical significance.

Nearly half of the biopsied lung nodules were due to IFD and invasive pulmonary aspergillosis was especially common. Diagnostic yield was more likely for IFD than for other benign non-fungal etiologies. In analyses of hematopoietic stem cell transplant (HSCT) recipients and patients with other hematologic diseases PLB had sensitivities ranging from 62% to 80% (11-15). This modest efficacy is potentially related to the small volume of tissue available for microbiologic evaluation. One strategy to improve this limitation is to use non-culture based techniques, increasing the yield of biopsied samples. In a study of 61 immunosuppressed patients, Lass-Flörl et al. reported Calcofluor White staining combined with PCR and/or the tissue-based *Aspergillus* galactomannan (GM) assay was 100% sensitive and 100% specific for fungal detection (16). This is in marked contrast with the poor sensitivity (<30%), in SOT patients, of traditional culture and non-culture based techniques (serum *Aspergillus* GM) (17, 18). To date, a similar study has not been conducted solely in SOT recipients. A diagnostic strategy that combines PLB and non-culture based detection among SOT patients may be promising.

Of the 45 patients involved in our study, only 6 individuals experienced complications that were primarily asymptomatic pneumothoraces (13%), of which only 1 required tube thoracostomy. For HSCT and hematologic malignancy patients, a similar complication rate has been observed (12%, 15/127) (11-15). Overall, the complication rate for PLB is higher at 20-25% (19).

There are several limitations to our analysis. Because of the retrospective study design, we necessarily analyzed only those SOT recipients with pulmonary lesions who underwent PLB at the recommendation of treating physicians. We did not assign all SOT recipients with pulmonary nodules or masses to receive this diagnostic procedure. Accordingly, our findings may not be generalizable to other SOT recipients who may have had pulmonary lesions, but who were deemed inappropriate candidates for PLB during the 10-year period of analysis. Moreover, indications for performing a biopsy of a pulmonary nodule are not definitively established. Some providers may pursue a management strategy of watchful waiting or empiric therapy while others may have a lower threshold for pursuing early definitive diagnosis. This clinician “practice bias” is reflected in the current analysis, as heart transplant patients accounted for 80% of IFDs diagnosed by PLB, whereas the prevalence of pulmonary IFDs is highest among lung transplant recipients (6-16%) (20, 21). This discrepancy likely reflects a tendency for pulmonary nodules in lung transplant patients to be first evaluated by bronchoscopy rather than a higher incidence of IFD in heart transplant recipients. Thus, the performance of PLB in the evaluation of pulmonary nodules identified in all SOT recipients may be affected by factors we were not able to measure. Additionally,

we did not assess the concordance of the cytopathologist's preliminary assessment and final diagnosis. For example, a preliminary determination of a positive diagnostic finding that ultimately proved to be non-diagnostic would have likely terminated a procedure prematurely and reduced the diagnostic yield of the procedure. This "false positive" rate may have varied by cytopathologist.

In conclusion, PLB represents a rarely used, moderately efficacious, and safe modality for the diagnosis of pulmonary nodules in SOT patients. Although the overall diagnostic yield for PLB was only 53%, for "proven" IFD and malignancy, the two most common causes of pulmonary nodules in this case series, the sensitivity was 75%. Effective management of the SOT recipient with a pulmonary nodule or mass requires timely and accurate diagnosis. When non-invasive techniques fail, a biopsy may yield the diagnosis, dictating both a more narrow treatment choice and duration. For instance, a trial of empiric therapy with close follow-up may be reasonable if a malignancy is safely excluded. Future studies should focus on the use of PLB in conjunction with other non-culture based techniques, offering the promise of further improving diagnostic yield for IFD and possibly improved outcomes from these serious and difficult to diagnose infections.

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References

1. Geraghty PR, Kee ST, McFarlane G, Razavi MK, Sze DY, Dake MD. CT-guided transthoracic needle aspiration biopsy of pulmonary nodules: needle size and pneumothorax rate. Radiology. 2003; 229:475. [PubMed: 14595149]
2. Priola AM, Priola SM, Cataldi A, Errico L, Di Franco M, Campisi P, et al. Accuracy of CT-guided transthoracic needle biopsy of lung lesions: factors affecting diagnostic yield. Radiol Med. 2007; 112:1142. [PubMed: 18074198]
3. Haramati LB, Schulman LL, Austin JH. Lung nodules and masses after cardiac transplantation. Radiology. 1993; 188:491. [PubMed: 8327703]
4. Knollmann FD, Maurer J, Bechstein WO, Vogl TJ, Neuhaus P, Felix R. Pulmonary disease in liver transplant recipients. Spectrum of CT features. Acta Radiol. 2000; 41:230. [PubMed: 10866077]
5. Lee P, Minai OA, Mehta AC, DeCamp MM, Murthy S. Pulmonary nodules in lung transplant recipients: etiology and outcome. Chest. 2004; 125:165. [PubMed: 14718437]
6. Sacks D, McClenny TE, Cardella JF, Lewis CA. Society of Interventional Radiology clinical practice guidelines. J Vasc Interv Radiol. 2003; 14:S199. [PubMed: 14514818]
7. De Pauw B, Walsh TJ, Donnelly JP, Stevens DA, Edwards JE, Calandra T, et al. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/ Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Clin Infect Dis. 2008; 46:1813. [PubMed: 18462102]
8. Lee YR, Choi YW, Lee KJ, Jeon SC, Park CK, Heo JN. CT halo sign: the spectrum of pulmonary diseases. Br J Radiol. 2005; 78:862. [PubMed: 16110114]
9. Aviram G, Greif J, Man A, Schwarz Y, Marmor S, Graif M, et al. Diagnosis of intrathoracic lesions: are sequential fine-needle aspiration (FNA) and core needle biopsy (CNB) combined better than either investigation alone? Clin Radiol. 2007; 62:221. [PubMed: 17293214]
10. Gong Y, Sneige N, Guo M, Hicks ME, Moran CA. Transthoracic fine-needle aspiration vs. concurrent core needle biopsy in diagnosis of intrathoracic lesions: a retrospective comparison of diagnostic accuracy. Am J Clin Pathol. 2006; 125:438. [PubMed: 16613349]
11. Carrafiello G, Lagana D, Nosari AM, Guffanti C, Morra E, Recaldini C, et al. Utility of computed tomography (CT) and of fine needle aspiration biopsy (FNAB) in early diagnosis of fungal

pulmonary infections. Study of infections from filamentous fungi in haematologically immunodeficient patients. Radiol Med. 2006; 111:33. [PubMed: 16623303]

12. Crawford SW, Hackman RC, Clark JG. Biopsy diagnosis and clinical outcome of persistent focal pulmonary lesions after marrow transplantation. Transplantation. 1989; 48:266. [PubMed: 2667210]
13. Kallenberg MH, Gill RR, Factor RE, Bryar JM, Rubin RH, Jacobson FL, et al. Diagnostic efficacy and safety of computed tomography-guided transthoracic needle biopsy in patients with hematologic malignancies. Acad Radiol. 2009; 16:1408. [PubMed: 19683945]
14. Nosari A, Anghilieri M, Carrafiello G, Guffanti C, Marbello L, Montillo M, et al. Utility of percutaneous lung biopsy for diagnosing filamentous fungal infections in hematologic malignancies. Haematologica. 2003; 88:1405. [PubMed: 14687995]
15. Shi JM, Cai Z, Huang H, Ye XJ, He JS, Xie WZ, et al. Role of CT-guided percutaneous lung biopsy in diagnosis of pulmonary fungal infection in patients with hematologic diseases. Int J Hematol. 2009; 89:624. [PubMed: 19468797]
16. Lass-Flörl C, Resch G, Nachbaur D, Mayr A, Gastl G, Auberger J, et al. The value of computed tomography-guided percutaneous lung biopsy for diagnosis of invasive fungal infection in immunocompromised patients. Clin Infect Dis. 2007; 45:e101. [PubMed: 17806041]
17. Pfeiffer CD, Fine JP, Safdar N. Diagnosis of invasive aspergillosis using a galactomannan assay: a meta-analysis. Clin Infect Dis. 2006; 42:1417. [PubMed: 16619154]
18. Reichenberger F, Habicht J, Matt P, Frei R, Soler M, Bolliger CT, et al. Diagnostic yield of bronchoscopy in histologically proven invasive pulmonary aspergillosis. Bone Marrow Transplant. 1999; 24:1195. [PubMed: 10642808]
19. Covey AM, Gandhi R, Brody LA, Getrajdman G, Thaler HT, Brown KT. Factors associated with pneumothorax and pneumothorax requiring treatment after percutaneous lung biopsy in 443 consecutive patients. J Vasc Interv Radiol. 2004; 15:479. [PubMed: 15126658]
20. Pappas PG, Alexander BD, Andes DR, Hadley S, Kauffman CA, Freifeld A, et al. Invasive fungal infections among organ transplant recipients: results of the Transplant-Associated Infection Surveillance Network (TRANSNET). Clin Infect Dis. 2010; 50:1101. [PubMed: 20218876]
21. Silveira FP, Husain S. Fungal infections in solid organ transplantation. Med Mycol. 2007; 45:305. [PubMed: 17510855]

Table 1

Patient and Nodule Characteristics

Variable	Total (%)
Patient Demographics	
Median Age, y (Range)	56 (18, 69)
Male gender	26 (57.8)
Female gender	19 (42.2)
Transplant Type	
Heart	25 (55.6)
Lung	8 (17.7)
Liver	6 (13.3)
Heart/lung	4 (8.9)
Kidney	2 (4.4)
Nodule Characteristics	45
Lobar location	
Right upper lobe	8 (18)
Right middle lobe	1 (2)
Right lower lobe	15 (33)
Left upper lobe	10 (23)
Left lower lobe	11 (23)
Lung zone location *	
Peripheral only	29 (64.4)
Middle only	7 (15.6)
Central only	1 (2.2)
Peripheral/middle	4 (9.0)
Middle/central	2 (4.4)
All lung zones	2 (4.4)
Nodule size	
Median width (Range)	2.0 (0.7, 6.0)
Median length (Range)	2.3 (0.9, 7.3)
> 2cm	24 (53.3)
≤ 2cm	21 (46.7)

* Lung zones: represent cross sectional divisions by thirds (peripheral, middle, central)

Table 2

Diagnostic Yield Characteristics

	Total (%)
Overall	**45**
Diagnosis by PLB	24 (53)
Diagnosis by secondary method	19 (42)
Lost to follow-up	2 (4)
Diagnosed by Percutaneous Lung Biopsy	**24**
Benign etiology	
"Proven" fungal disease *	12 (26)
Bacterial infection	1 (2)
Atypical mycobacterial infection	1 (2)
Other benign #	1 (2)
Malignant etiology	
Primary lung cancer	4 (9)
Metastatic disease	3 (7)
Post-transplant lymphoproliferative disease	1 (2)
Unknown primary	1 (2)
PLB Diagnosis by Type of Biopsy ‡	
FNAB	9 (38) **
FNAB + CB	15 (71) **
Diagnosed by Secondary Method	**19**
Benign etiology	
All invasive fungal disease *	8 (18)
"Proven" fungal disease	4 (9)
"Probable" fungal disease	1 (2)
"Possible" fungal disease	3 (7)
Bacterial infection	4 (9)
Atypical mycobacterial infection	1 (2)
Other benign #	3 (7)
Malignant etiology	
Primary lung cancer	2 (4)
Lymphoma	1 (2)
Secondary Diagnostic Method	19
Surgical lung biopsy	7 (16)
Bronchoscopy	3 (7)
Clinical follow-up	6 (13)
Microbiologic culture (blood)	2 (4)
Fluid cytology (pleural)	1 (2)

*: Based on EORTC/MSG criteria for diagnosis of fungal infections

‡: FNAB: Fine Needle Aspiration biopsy, CB: Core biopsy

**: Denominator based on biopsy type: FNAB, n=24; FNAB + CB, n=21

#: Other benign etiology includes: fibrous tissue, old granulomatous disease

Table 3

Characteristics of Invasive Fungal Infections

***EORTC/MSG* Classification**	**Total (%)**
"Proven" fungal disease	**16**
Method of Diagnosis	
Culture only	3 (19)
Histology only	4 (25)
Histology and culture	9 (50)
Antifungal Therapy at Diagnosis	4 (25)
Fungal Species (n)	*Aspergillus* species (12) *
	Cryptococcus neoformans (2)
	Coccidioides immitis (1)
"Probable" fungal disease	**1**
Method of Diagnosis	
Culture only (nonsterile site)	1 (100)
Antifungal Therapy at Diagnosis	0
Fungal Species (n)	*Aspergillus fumigatus* (1)
"Possible" fungal disease	**3**
Method of Diagnosis	
Clinical manifestation	3 (100)
Antifungal Therapy at Diagnosis	2 (67)

* Includes (n): *A. fumigatus* (10), *A. nidulans* (1), *A. terreus* (1)