Solitary Pulmonary Nodule
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Introduction:

A solitary pulmonary nodule (SPN) is also called a coin lesion. A SPN is a lesion that is less than 3 centimeter in diameter and is surrounded by lung parenchyma without other abnormalities. Lesions that are larger than 3 cm are called masses. Up to 0.09 to 0.20% of all chest radiographs have a solitary pulmonary nodule, which means approximately 150,000 nodules are identified each year.[1]

In general, solitary pulmonary nodules can be categorized as either benign or malignant. There is a broad differential of solitary pulmonary nodules.

Table 1. DIFFERENTIAL DIAGNOSIS OF A SOLITARY PULMONARY NODULE

Neoplasm	Benign	Hamartoma
		Inflammatory pseudotumor
	Malignant	Bronchogenic carcinoma
		Carcinoid tumor
		Lymphoma (Non-Hodgkin's)
		Metastasis
Infection	Granuloma	Mycobacteria
		Fungi
	Septic embolus	
	Abscess	Bacteria (anaerobes, Staphylococcus, gram-negative)
		Nocardia
	Round pneumonia	Pneumococcus
	Parasitic	Echinococcus
		Dirofilaria (dog heartworm)
Inflammatory	Connective tissue	Wegener's granulomatosis
		Rheumatoid (necrobiotic) nodule
	Sarcoidosis (rare)	
Vascular	Arteriovenous malformation	
	Hematoma	
	Pulmonary infarct	
	Pulmonary artery aneurysm	
	Pulmonary venous varix	
Airway	Congenital lesion	Bronchogenic cyst
		Bronchial atresia
	Mucocele	
	Infected bulla	

Leef JL, and Klein JS. The solitary pulmonary nodule. Radiologic Clinics of North America 2002; 40:123-143

In the United States, lung cancer is the leading cause of cancer death although it may not be the most common type of cancer.[1] The cure rate can be up to 70% if lung cancer is detected in Stage 1. Survival rates may be as high as 80% at 5 years in those patients with resected malignant nodules. Survival drops down to less than 5% at 5 years after diagnosis in advance lung malignancies.[1]

In the retrospective study at the Mayo clinic[4], 629 patients (320 men, 309 women) were evaluated for solitary pulmonary nodules. The findings include that most lesions of solitary pulmonary nodules are benign(65% of total lesions). Of these benign lesions, 79% were

granulomas (granuloma can be from past infection with *Mycobacterium tuberculosis* or regional fungal disease such as histioplasmosis or coccidiomycosis), 7% are hamartomas, and the rest are organizing pneumonia, fibrosis, sclerosing hemangioma or infarctions. Of the malignant lesions, 49% were adenocarcinomas, 29% squamous cell carcinoma, 8% large cell cancer, 4% small cell cancer, and 2% carcinoid tumor of bronchus. Bronchogenic carcinoma is increasing especially amongst the elderly.

Demographic risk factors of malignant nodules:

There are some characteristics that may suggest malignancy in a SPN. Demographic factors such as age, smoking history, history of prior malignancies, and environmental exposures can help determine if the SPN is more likely to be malignant. Studies indicate that there are less lung malignancies in people less than 40 years of age, but increasing malignancies in people between 40 to 80 years old. [2,3] Tobacco smoke is also a risk factor for malignancy. [3] Environmental exposures such as Asbestos after a latency period of 20 to 40 years, especially when combined with tobacco exposure, predisposes to lung cancer. Other environmental exposures including uranium and heavy metals such as cadmium and nickel cause increase susceptibility to lung malignancies.

Radiological features of benign and malignant nodules:

Imaging may shed insight in the determination of a nodule is benign versus malignant and assist in guiding the direction of diagnostic procedures.

Nodular size can be used to distinguish malignant or benign lesions. 80% of benign nodules are less than 2 cm in diameter while only 15% of malignant lesions are less than 1cm in diameter.[3] A lesion's growth rate can denote malignancy. If the doubling time of a nodule is between 30-360 days, then the lesion should be sampled for biopsy or resected.[4] Malignant bronchogenic tumors' doubling time is often greater than 1 month or less than a year.[1] In a lesion that is spherical, a 30% increase in diameter is twice the volume. This growth pattern can signify that a nodule that was not present 2 months ago is most likely benign.

Malignant nodules have several morphologic characteristics including spiculation or scalloped borders. An indication of malignancy is the corona radiata sign, which involves fine lines extending 4-5 mm away from a nodule in a Computed Tomography (CT) scan. This sign gives the appearance of spiculation on plain radiological film.[1] Another signal of cancer are scalloped borders but this sign is more intermediate in interpretation for malignancy. Malignant lesions can have more vascularity because of expansion in angiogenic factors like vascular endothelial growth factor.[5] These angiogenic factors lead to magnifying microvessel density causing increase capillary perfusion and permeability, which can enhance the tumor if contrast dye is used with the CT scan. Tumors with lymph node metastasis or vessel invasion can have coarse spiculations and thickening of the bronchovascular bundles around the tumor.[5]

Other radiological features of SPN can guide the clinician toward a benign explanation. Fat deposits within a nodule with smooth margins can signify a benign lesion. Up to 50% of harmatomas have fat deposits. Calcification within a lesion can be seen in benign nodules. Compared to CT scan as a gold standard, a plain radiograph has a sensitivity of 50%, specificity of 87% and a positive predictive value of 93%.[1] Laminated or central pattern of calcification is often observed in benign lesions such as granuloma. [3]

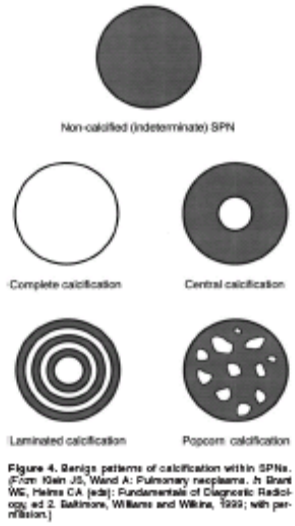


Figure 4. Benign patterns of calcification within SPNs. (From Klein JS, Weed A: Pulmonary neoplasms. In Grant WE, Helms CA [eds]: Fundamentals of Diagnostic Radiology, ed 2. Baltimore, Williams and Wilkins, 1999; with permission.)

Leef JL, and Klein JS. The solitary pulmonary nodule. Radiologic Clinics of North America 2002; 40:123-143

However, absence of calcium cannot distinguish between benign or malignant nodules because 67% of carcinoid tumors and almost 94% of all lung cancer do not contain appreciable calcium.[3]

Cavitation can be seen in both benign and malignant lesions such as squamous cell carcinoma, inflammatory nodules (abscesses), infectious granulomatous lesions, Wegener's granulomatosis and pulmonary infarcts. Wall thickness of cavitary lung nodules can assist in characterizing a benign versus malignant nodule. Cavitary SPN with the greatest wall thickness that is less than 5mm often are benign, while malignant lesions often have a wall thickness greater than 15mm.[3]

The bronchus sign on CT occurs when one or more bronchus leads directly to a peripheral pulmonary nodule. Air bronchograms (bronchus sign), or cystic appearance in a nodule can suggest adenocarcinoma, especially the localized form of bronchoalveolar cell carcinoma, or lymphoma . However, the appearance of the radiographic sign can be observed in benign lesions including organizing pneumonia, pulmonary infarct, tuberculosis, harmatoma or sarcoidosis.[3,4]

The bronchus sign can be utilized as guidance to aid in the selection of a diagnostic procedure to further evaluate a SPN. A nodule with a bronchus sign can be appropriately investigated with bronchoscopy because the yield is greater since the bronchoscope has easier access to the nodule. The bronchoscopic yield can increase dramatically from 44% to 82%.[5]

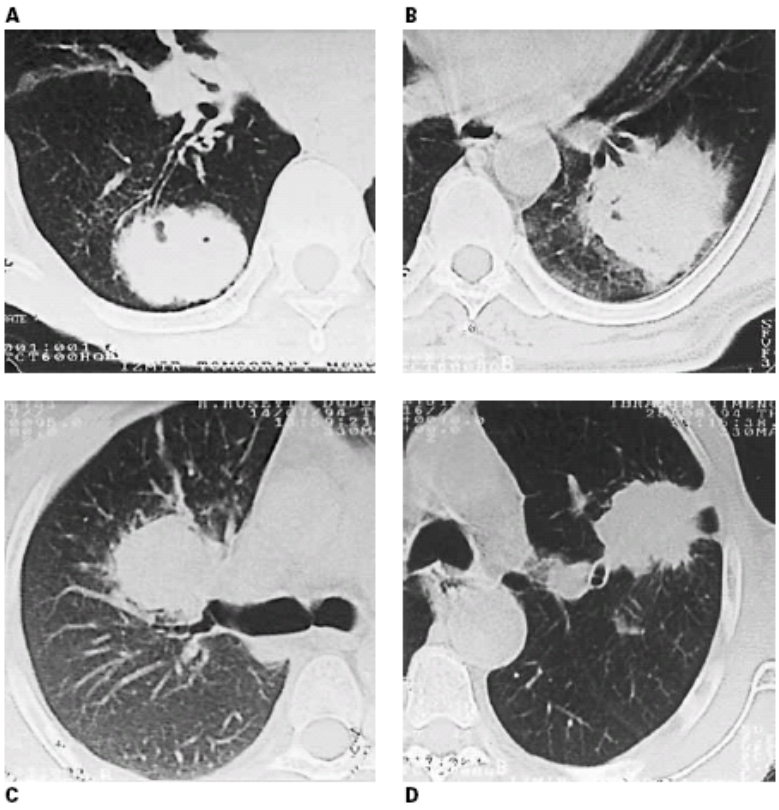


Fig. 1. The types of bronchus sign depicted by 2-mm thick CT sections in 4 patients whose resected specimens were examined and proven for mass-bronchus relationship. **A** A fifth-order bronchus cut-off by a 5-cm Tsuboi type 1 mass in the right lower lobe superior segment. **B** Three segmental bronchi contained within a 5-cm Tsuboi type 2 mass in the posterior basal segment of the left lower lobe. **C** A 4.5-cm mass compressing the posterior segmental bronchus (Tsuboi type 3) and also narrowing and thickening the anterior segmental bronchus of the right upper lobe (Tsuboi type 4). **D** A 5-cm mass thickening and slightly narrowing two fourth-order bronchi in the posterior segment of the left upper lobe (early-stage Tsuboi type 4).

Bilaceroglu S, Kumcuoglu Z, Alper H, Osma E, Cagirici U, Gunel O, Bayol U, Celikten E, Perim K, Kose T. CT bronchus sign-guided bronchoscopic multiple diagnostic procedures in carcinomatous solitary pulmonary nodules and masses. Respiration 1998; 65:49-55

Diagnostic evaluation of Solitary Pulmonary Nodules:
Noninvasive methods

Morphologic radiographic features can assist to distinguish between malignant and benign nodules. Physicians utilize noninvasive methods to investigate a solitary pulmonary nodule noticed in a plain radiograph. A spiral CT with contrast enhancement can improve visualization of a solitary pulmonary nodule. Despite various features on radiographs to help a clinician interpret a SPN, clinicians must be wary of analyzing plain film of small nodules especially those with indistinct border or obscured by ribs because they are difficult to assess. Also the limit of detectable change in a plain film is only 3-5 mm.[1] On chest CT scan the limit of detectable change is 0.3mm.[1]

Another investigational tool involves the Positron Emission Tomography (PET) scan. PET scan includes the uptake of 18-fluorodeoxyglucose to measure glucose metabolism. The theory is that most lung tumor will have enhanced uptake of 18-fluorodeoxyglucose than normal tissue because of increased metabolic activity.

In a metanalysis of PET scans, Gould et al, analyzed 727 studies from 1966-2000 in Medline and Cancerlit database and concluded that the mean sensitivity is 93.6% and mean specificity is 85.8% for detecting malignancy in pulmonary nodules and masses.[6]

The downside of PET scans encompass false negative that can occur especially with bronchioloalveolar carcinoma, carcinoids, 5% of all stage 1 lung cancer and tumors less than one centimeter in diameter.[7] False positives is associated with infectious or inflammatory processes.

Integrated PET/CT magnifies the sensitivity to 96% and specificity 88%.[7] However, both PET and PET/CT is not an appropriate imaging modality to investigate nodules that are less than one centimeter because the spatial resolution of current PET scans is 7-8mm, which is not enough to detect these subcentimeter malignancies.[6]

Sputum cytology is another noninvasive method that was used in the past to investigate pulmonary nodules. Based on the Early Lung Cancer detection program at Hopkins, there is evidence that sputum cytology does not help with distinguishing benign versus malignant lesions.[8] There may be the occasional situation involving squamous cell carcinoma that may be seen in sputum cytology because the malignant cells are shed intrabronchially.[8]

Invasive methods:

Bronchoscopy

Bronchoscopy is a popular method to diagnose a solitary pulmonary nodule. Bronchoscopy, in general, has a sensitivity for detecting malignancy in a pulmonary nodule that ranges from 20-80%.[1] The sensitivity is affected by nodular size, proximity to the bronchial tree and prevalence of carcinoma in a study population. Bronchoscopic technique involving nodules less than 1.5 centimeter in diameter has a sensitivity of 10% but this increases to 40-60% when nodules are 2-3 centimeter in diameter.[1] The yield of bronchoscopy in malignant lesions is much greater than in benign lesions. The lower yield in benign lesions may be influenced by the tendency of most benign lesion being less than 2 centimeter in size.[9]

In a retrospective analysis of 177 men (active or ex smokers) with pulmonary nodule evaluated by bronchoscopies over a 4 year period in the Houston Veteran affairs medical center, found that the diagnostic yield of malignancy is 64%, and of benign lesions is 35%. Also the investigators noticed that the more central to the bronchial tree the lesion is, the greater the yield with bronchoscopy. In addition, the right middle lobe or lingular segment had the highest yield in bronchoscopy. The right upper lobe had the most incidence of lung cancer in the study.

Table 3—*Bronchoscopy Yield by Distance From the Hilum

Location	Malignant	Benign	Total
Central	18/22 (82)	0/0	18/22 (82)
Intermediate	40/64 (62)	6/12 (50)	46/76 (61)
Peripheral	39/65 (60)†	3/14 (21)	42/79 (53)‡

*Data are presented as No. of lesions/total lesions (%).
†p = 0.2, χ^2 analysis across diagnostic yields of malignant lesions in three elliptical locations around the hilum.
‡p = 0.05, χ^2 analysis across diagnostic yields of all lesions in three elliptical locations around the hilum.

Table 5—*Bronchoscopy Yield by Bronchopulmonary Segment

Segments	Total	Malignant	Benign
RUL	46/78 (59)	42/70 (60)	4/8 (50)
RML	10/12 (83)	9/11 (82)	1/1
RLL	18/28 (64)	16/20 (80)	2/8
LUL	20/37 (54)	19/33 (58)	1/4
Lingula	4/6 (67)	4/5 (80)	0/1
LLL	8/16 (50)	7/12 (58)	1/4

*Data are presented as No. of lesions/total lesions (%); RLL = right lower lobe; LUL = left upper lobe; LLL = left lower lobe.

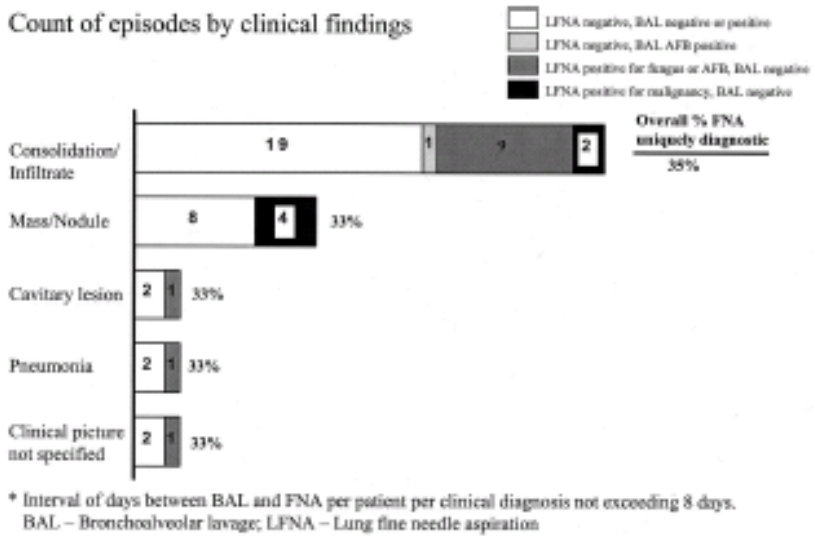
Baaklini WA, Reinoso MA, Gorin AB, Sharafkaneh A, Manian P. Diagnostic yield of fiberoptic bronchoscopy in evaluating solitary pulmonary nodules. Chest 2000;117:1049-1054

Complication rate of bronchoscopy is approximately 2%. Most common complications include hemorrhage (1.1%) and pneumothorax (0.2%).[10]

Bronchoscopy incorporates multiple techniques: bronchial washing, endobronchial biopsy, bronchial brushing, bronchoalveolar lavage, and transbronchial needle aspiration to

obtain specimens for analysis.[11] Bronchoscopy often involves a combination of techniques depending on the physician who performs the procedure.

Bronchoalveolar lavage (BAL) is the procedure that occur when a fiberoptic bronchoscope is directed distally into a subsegment bronchus, saline flush is introduced and then there is suctioning of the saline and cellular material out of the lung. There are few complications from a BAL including benign post bronchoscopy fever, short spans of decrease in alveolar oxygen concentration, laryngospasm, and rarely pneumothorax, hemothorax, or exacerbations of respiratory failure. Clark et al, in a retrospective study[10] involving 45 patients pulmonary disease evaluated by both BAL and fine needle aspiration at NIH Clinical center, resulted in 12 events of pulmonary mass and nodules, in which 35% of the time fine needle aspiration was positive while the BAL was negative. The authors of the study conjectured that the BAL did poorly compared to fine needle aspiration because the BAL technique and amount of saline used was varied. The optimal volume of BAL fluid should be 200-300ml but in the study the volume ranged from 3 to 50ml perhaps because the patients were too sick to tolerate larger amounts of fluid.[10]



Clark BD, Vezza PR, Copeland C, Wilder AM, Abati A. Diagnostic sensitivity of bronchoalveolar lavage versus lung fine needle aspirate. Mod Pathol 2002;15:1259-1265

In a study from a university hospital based in Switzerland[12], 172 patients underwent diagnostic bronchoscopy for a peripheral pulmonary lesion, The bronchoscopist determines which patients have bronchial washings, bronchial brushing,or transbronchial biopsy. Patients whose nodule was accessible through bronchoscopy had transbronchial needle aspiration, which is a retractable 22 gauge needle with a length of 13mm within a flexible catheter under fluoroscopy. After the needle enters the tissue, suction is applied with a 20 ml syringe at the side port of the proximal end of the catheter. The transbronchial needle aspiration was considered a

success if diagnosis can be made with either a positive tuberculosis culture or diagnosis of malignancy. Results indicated that 50% of 172 patients had diagnosis by bronchoscopy, 22% had diagnostic thoractomy, 9% had CT guided needle biopsy and 12% had follow up with history, plain film and clinical follow up. [12] Transbronchial needle biopsy was not attempted in certain patients because of lack of access to the lesion under fluoroscopy.

Diagnostic Procedures in the Workup of Peripheral Pulmonary lesions

Procedures	No. of Lesions	Malignant	Benign
Bronchoscopy	87	81	6
Sputum after bronchoscopy	2	1	1
CT-guided TNB	16	13	3
Thoracotomy	39	24	15
FNA of extrathoracic lesions	3	3	—
Autopsy	2	2	—
TB clinically	1	—	1
History, CXR, and follow-up	22	2	20
Total	172	126	46

*FNA = fine needle aspiration; CXR = chest radiograph.

Reichenberger F, Weber J, Tamm M, Bolliger CT, Dalquen P, Perruchoud AP, Soler M. The value of transbronchial needle aspiration in the diagnosis of peripheral pulmonary lesions. Chest 1999;116:704-708

Of the 50% of patients successfully evaluated by bronchoscopy, 22% had diagnosis by bronchial washing, 30% through bronchial brushing, and 17% by transbronchial biopsy. Bronchial washing, brushing and transbronchial biopsy together has a sensitivity of 33%. Additional use of transbronchial needle aspiration (TBNA) increased the overall diagnostic yield of bronchoscopy to approximately 50%. Also the success rate for TBNA was significantly greater in lesions with greater than 3 cm in diameter. [11,12]

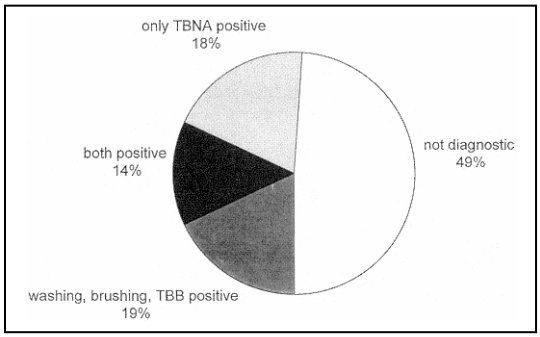


Figure1. Bronchoscopic workup of 172 pulm nodules In regard to the impact on the diagnositic yield of Different bronchoscopic methods

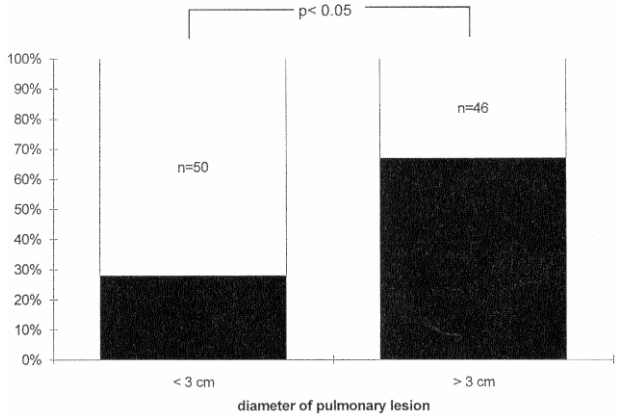


Figure2. Percentage of positive TBNA results by pulm. lesion size in a subgroup of 96 malignant lesions

Reichenberger F, Weber J, Tamm M, Bolliger CT, Dalquen P, Perruchoud AP, Soler M. The value of transbronchial needle aspiration in the diagnosis of peripheral pulmonary lesions. Chest 1999;116:704-708

Diagnostic Yield of Different Bronchoscopic Sampling Techniques

Techniques	Applications, % (No.)	Diagnostic Result, % (No.)	Only Technique With a Diagnostic Result, % (No.)
Bronchial washing	100 (172)	22 (37)	6 (10)
TBNA	89 (152)	35 (54)	20 (30)
Bronchial brushing	45 (77)	30 (23)	10 (8)
TBB	27 (47)	17 (8)	—
Total	172	51%	28%

Reichenberger F, Weber J, Tamm M, Bolliger CT, Dalquen P, Perruchoud AP, Soler M. The value of transbronchial needle aspiration in the diagnosis of peripheral pulmonary lesions. Chest 1999;116:704-708

Complications of TBNA, include pneumothorax 6-57%, hemoptysis or hemorrhagic complications 3-10%, rarely air embolism or hemothorax. [13]

Transthoracic Needle Aspiration

The transthoracic needle aspiration is another method for evaluation of SPN. It involves the guidance of a needle through the side of the patient by CT guidance to access tissue. One of the most common reasons for transthoracic needle biopsy or aspiration is an indeterminate nodule that needs further workup to guide medical treatment and the patient is not a surgical candidate. Levine et al.[14] conducted a study that retrospectively examined 262 patients at the University of California/San Diego School of Medicine, 58 patients of whom had a nondiagnostic fiberoptic bronchoscopy followed by transthoracic needle aspirate biopsy. The results indicated that the sensitivity for identification of malignant lesion is 80-95%, with specificity 50-88%. Their data also showed that 2 negative procedures of diagnostic bronchoscopy followed by transthoracic needle aspiration do not mean a benign lesion. They found that the procedure is best for the most peripheral of lesions but not optimal for lesions located in high apical location or near the hemidiaphragm.[15] Ultrasound guidance is another expansion on the same principle technique but it is still very new. Ultrasound guidance provide real time image guidance, and has other benefit of no radiation, and low cost. The difficulty with ultrasound guidance is that the nodules have to be close to the visceral pleura to make them detectable.[16]

Thoracotomy versus Video Assisted Thoracic Surgery (VATS)

Video Assisted Thoracic surgery is a procedure in which a patient is placed under anesthesia, then a double lumen endobronchial tube is placed to allow ventilation of the contralateral lung, while collapsing the ipsilateral lung. Approximately 3 incision made to allow the surgeon access to place a telescope camera and 2 biopsy forceps. Thoractomy is similar except a rib retractor is utilized. In the Annals of Thoracic Surgery[17], there was a randomized prospective trial of video assisted thoracic surgery versus muscle sparing lateral thoracotomy. 44 patients with solitary pulmonary nodules were randomized into 22 patients undergoing VATS and 22 patients with lateral thoracotomy. Main inclusion criteria involved maximum nodule size 2.5cm, located in peripheral third of the lung and the nodule is classified as indeterminate after diagnostic procedures.[17]

Table 3. Postoperative Patient Characteristics

Characteristic	VATS	LT	*p* Value
Operating room time (min)	97.2 ± 32.9	130.5 ± 14.0	>0.05
Transfusion	0	0	...
Air leak > 7 days	0	0	...
Postoperative stay (days)	4.6 ± 1.08	7.8 ± 0.89	<0.01
Pain[a]	26.5 ± 11.6	48.3 ± 12.8	<0.05
Ketorolac (mg)	106.6 ± 15.7	143.3 ± 26.1	<0.05
Anxiety[a]	25.5 ± 7.44	31.7 ± 17.0	NS

[a] Visual analogue scale, 0 to 100.

LT = lateral thoracotomy; VATS = video-assisted thoracic surgery.

Santambrogio L, Nosotti M, Bellaviti N, Mezzetti M. Videothoracoscopy versus thoracotomy for the diagnosis of the indeterminate solitary pulmonary nodule. Ann Thorac Surg 1995;59:868-71

In the VATS procedure, there was significantly less pain and hospital stay. The sensitivity and specificity of both is 100%.

Algorithms for Benign versus Malignant nodules

There is not a single technique that is best at analyzing the solitary pulmonary nodule. There are always new procedures and different guidelines for evaluation of the SPN. Some authors attempt to quantify the characteristics of a SPN to help guide the clinician towards a diagnostic procedure. Swenson et al.[18] created a complex clinical model to predict the probability of malignancy in a SPN using within their analysis age, sex, cigarette smoking status, history of asbestos exposure, extrathoracic malignant neoplasm, diagnosis of Chronic obstructive pulmonary disease (COPD), and plain radiographic data including diameter, location, margin and cavitation.

(1) Probability of Malignancy= $e^x/(1+e^x)$

(2) x = -6.8272 + (0.0391 * Age) + (0.7917 * cigarettes) + (1.3388 * Cancer) + (0.1274 * diameter) + (1.0407 * speculation) + (0.7838 * Upper)

Gurney used the Bayesian univariate analysis of SPN by estimating ratios for demographic and radiological features from previous literature to combine each probability into an estimation of the odds of having a malignancy in a pulmonary nodule.[15] The traditional Bayesian analysis does not take into account new imaging like PET/CT.

In the New England Journal of Medicine[1], there is a recommendation to use a pretest probability of cancer based on various demographic and clinical characteristics to steer the clinician to the most appropriate initial diagnostic test.

Table 1. Assessment of the Risk of Cancer in Patients with Solitary Pulmonary Nodules.

Variable	Risk of Cancer		
	Low	Intermediate	High
Diameter of nodule (cm)	<1.5	1.5–2.2	≥2.3
Age (yr)	<45	45–60	>60
Smoking status	Never smoked	Current smoker (≤20 cigarettes/day)	Current smoker (>20 cigarettes/day)
Smoking-cessation status	Quit ≥7 yr ago or never smoked	Quit <7 yr ago	Never quit
Characteristics of nodule margins	Smooth	Scalloped	Corona radiata or spiculated

Ost D, Fein AM, Feinsilver SH. The solitary pulmonary nodule. N Engl J Med 2003;348:2535-2542

Figure 2. Approach to the Management of Solitary Pulmonary Nodules.

Ost D, Fein AM, Feinsilver SH. The solitary pulmonary nodule. N Engl J Med 2003;348:2535-2542

Management approaches vary according to several factors, including the degree of surgical risk, the presence or absence of coexisting conditions, the patient's preferences, and local radiologic and surgical expertise. The probabilities of cancer shown are approximations. CT denotes

computed tomography, FEV_1 forced expiratory volume in one second, VO_2 max maximal oxygen consumption, and PET positron-emission tomography.

American college of radiology[1] also has its own recommendation for the testing of solitary pulmonary nodule.

Table 2. American College of Radiology Recommendations for the Testing of Solitary Pulmonary Nodules.*

Level of Clinical Suspicion	Size of Nodule on Plain-Film Radiography	
	<1 cm	≥1 cm
Low		
Initial evaluation	High-resolution CT	High-resolution CT or transthoracic fine-needle aspiration biopsy
Follow-up	Follow-up CT	Follow-up CT
Moderate to high	Transthoracic fine-needle aspiration biopsy	Contrast-enhanced high-resolution CT

* The information is based on data from Henschke et al.[31] CT denotes computed tomography.

Ost D, Fein AM, Feinsilver SH. The solitary pulmonary nodule. N Engl J Med 2003;348:2535-2542

Conclusion:

In conclusion, the investigation of the solitary pulmonary nodule remains an inexact science. There are multiple imaging modalities and diagnostic techniques to choose from. It is important for the clinician to understand each modality and diagnostic technique to best serve the patient. Each patient is different and most studies recommended taking into account a patient's history and clinical picture to help guide the best technique to use. It is interesting to note that there is a varied professional opinion in different fields, thoracic surgeons would be more aggressive and promote removal of the lesions, radiologist would more often recommend short term follow up and pulmonologist would advise less invasive procedures such as bronchoscopy.[19] It is important to take cost into consideration, since Medicare reimbursement for PET imaging is $1912, noncontrast CT of the thorax $276 and a CT guided needle biopsy is $560. [6]

References:

1. Ost D, Fein AM, Feinsilver SH. The solitary pulmonary nodule. N Engl J Med 2003;348:2535-2542
2. Jeong YJ, Yi CA, Lee KS. Solitary pulmonary nodules: detection, characterization, and guidance for further diagnostic workup and treatment. AJR 2007;188:57-68
3. Leef JL, and Klein JS. The solitary pulmonary nodule. Radiologic Clinics of North America 2002; 40:123-143
4. Libby DM, Smith JP, Altorki NK, Pasmantier MW, Yankelevitz D, Henschke CI. Managing the solitary pulmonary nodule discovered by CT. Chest 2004;125:1522-1529
5. Bilaceroglu S, Kumcuoglu Z, Alper H, Osma E, Cagirici U, Gunel O, Bayol U, Celikten E, Perim K, Kose T. CT bronchus sign-guided bronchoscopic multiple diagnostic procedures in carcinomatous solitary pulmonary nodules and masses. Respiration 1998; 65:49-55
6. Gould MK, Maclean CC, Kuschner WG, Rydzak CE, Owens DK. Accuracy of positron emission tomography for diagnosis of pulmonary nodules and mass lesions: a metanalysis. JAMA 2001;285:914-924
7. Rezaei MK, Schwartz AM, Orenstein JM. Solitary pulmonary nodule: the benign variety. Pathology Case Reviews;12:89-92
8. Khouri NF, Meziane MA, Zerhouni EA, Fishman EK, Siegelman SS. The solitary pulmonary nodule: assessment, diagnosis, and management. Chest 1987;91:128-133
9. Baaklini WA, Reinoso MA, Gorin AB, Sharafkaneh A, Manian P. Diagnostic yield of fiberoptic bronchoscopy in evaluating solitary pulmonary nodules. Chest 2000;117:1049-1054
10. Clark BD, Vezza PR, Copeland C, Wilder AM, Abati A. Diagnostic sensitivity of bronchoalveolar lavage versus lung fine needle aspirate. Mod Pathol 2002;15:1259-1265
11. Liam CK, Pang YK, Poosparajah S. Diagnostic yield of flexible bronchoscopic procedures in lung cancer patients according to tumour location. Singapore Med J 2007;48:625-631
12. Reichenberger F, Weber J, Tamm M, Bolliger CT, Dalquen P, Perruchoud AP, Soler M. The value of transbronchial needle aspiration in the diagnosis of peripheral pulmonary lesions. Chest 1999;116:704-708
13. Sawabata N, Yokota S, Maeda H, Nakagawa M, Yamaguchi T, Okada T, Itho M. Diagnosis of solitary pulmonary nodule: optimal strategy based on nodal size. Interactive cardiovascular and thoracic surgery 2006;5:105-108
14. Levine MS, Weiss JM, Harrell JH, Cameron TJ, Moser KM. Transthoracic needle aspiration biopsy following negative fiberoptic bronchoscopy in solitary pulmonary nodules. Chest 1988;93:1152-1155
15. Katis K, Inglesos E, Zachariadis E, Palamidas P, Paraskevopoulos I, Sideris G, Tamvakopoulou E, Apostolopoulou F, Rasidakis A. The role of transbronchial needle aspiration in the diagosis of periphera lung masses or nodules. Eur Respir J 1995;8:963
16. Yuan A, Yang PC, Chang DB, Yu CJ, Lee YC, Kuo SH, Luh KT. Ultrasound-guided aspiration biopsy of small peripheral pulmonary nodules. Chest 1992;101:926-930
17. Santambrogio L, Nosotti M, Bellaviti N, Mezzetti M. Videothoracoscopy versus thoracotomy for the diagnosis of the indeterminate solitary pulmonary nodule. Ann Thorac Surg 1995;59:868-71

18. Swenson SJ, Silverstein MD, Ilstrup DM, Schleck CD, Edell ES. The probability of malignancy in solitary pulmonary nodules. Arch Intern Med 1997;157:849-855
19. Prosch H, Strasser G, Oschatz E, Schober E, Schneider B, Mostbeck GH. Management of patients with solitary pulmonary nodules: a survey of radiologists, pulmonologists and thoracic surgeons. AJR 2006;187:143-148
20. Mohammed TL, White CS, Yankelevitz DF. Percutaneous needle biopsy in single lung patients. J Comput Assis Tomogr 2006;30:267-269
21. Tan BB, Flaherty KR, Kazerooni EA, Iannettoni MD. The solitary pulmonary nodule. Chest 2003;123:89S-96S