Radiographically Detected Solitary Pulmonary Nodule
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Muller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. *Radiology* 2008; 246(3):697-722.	Review/Other -Dx	N/A	Glossary of terms for thoracic imaging.	N/A	4
2. Lillington GA. Disease-a-Month. 37th ed. St Louis, Mo: Mosby-Year Book; 1991:271-318.	Review/Other -Dx	N/A	Textbook; review of SPN diagnosis and management.	Conventional tomographies, CT, transthoracic needle aspiration biopsy are useful in SPN evaluation. Decision analysis computer techniques should be employed in management decision making.	4
3. Godoy MC, Naidich DP. Subsolid pulmonary nodules and the spectrum of peripheral adenocarcinomas of the lung: recommended interim guidelines for assessment and management. *Radiology* 2009; 253(3):606-622.	Review/Other -Dx	N/A	Review on subsolid pulmonary nodules and the spectrum of peripheral adenocarcinomas of the lung.	New appreciation of the importance of subsolid nodules has led to the need for a reappraisal of the natural history of such lesions. While numerous controversial aspects remain, the main purpose of this report has been to set out interim guidelines based on best-guess estimates, the authors' extensive albeit anecdotal experience, and especially currently available published data. It cannot be overemphasized that the guidelines proposed in this review pertain to subsolid nodules only and are not intended to supplant guidelines regarding the management of solid nodules that have already been published both as a consensus statement of the Fleischner Society and more recently by the American College of Chest Physicians. It is anticipated that future developments based on multidisciplinary efforts will result in greater consensus regarding optimal CT classification of subsolid lesions and ultimately more definitive, evidence-based guidelines leading to more rigorous standardization and ultimately improved clinical treatment of patients with subsolid lung nodules.	4
4. Brandman S, Ko JP. Pulmonary nodule detection, characterization, and management with multidetector computed tomography. *J Thorac Imaging* 2011; 26(2):90-105.	Review/Other -Dx	N/A	To review evidence-based guidelines to help guide the appropriate management of pulmonary nodules.	Pulmonary nodule detection and characterization continue to improve with technological advancements. The noninvasive methods available for assisting in nodule detection and for characterizing nodules as benign, malignant, or indeterminate will be discussed.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
5. Gurney JW. Determining the likelihood of malignancy in solitary pulmonary nodules with Bayesian analysis. Part I. Theory. *Radiology* 1993; 186(2):405-413.	Review/Other -Dx	N/A	To determine the likelihood of malignancy in SPNs through the application of the Bayes Theorem.	Explains how Bayes Theorem can be used to evaluate various clinical and radiologic findings to determine the probability of malignancy in SPNs. The most important features were radiographic and include thickness of cavity wall, spicular edge and diameter >3 cm.	4
6. Henschke CI, Yankelevitz DF, Mateescu I, Brettle DW, Rainey TG, Weingard FS. Neural networks for the analysis of small pulmonary nodules. *Clin Imaging* 1997; 21(6):390-399.	Review/Other -Dx	28 nodules; 14 benign; 14 malignant	To evaluate neural networks in differentiating benign from malignant SPNs on CT images.	S-MODALS were able to correctly identify all but 3 benign nodules. S-MODALS classified a nodule as malignant because it looked similar to other malignant nodules. It identified the most similar nodules to display them to the radiologist. The specific features of the nodule that determined its classification were also shown, so that S-MODALS is not simply a "black box" technique but gives insight into the neural networks diagnostics. This initial evaluation of S-MODALS neural networks using pulmonary nodules whose CT features were very suspicious for lung cancer demonstrated the potential to reduce the number of biopsies without missing malignant nodules. S-MODALS performed well, but additional optimization of the techniques specifically for CT images would further enhance its performance.	4
7. Nakamura K, Yoshida H, Engelmann R, et al. Computerized analysis of the likelihood of malignancy in solitary pulmonary nodules with use of artificial neural networks. *Radiology* 2000; 214(3):823-830.	Observational -Dx	56 chest radiographs; 34 primary lung cancers, 22 benign nodules	To develop a computer-aided diagnostic scheme by using an ANN to assist radiologists in the distinction of benign and malignant pulmonary nodules.	Performance of the ANN was considerably greater with objective features (area under the ROC curve, Az = 0.854) than with subjective features (Az = 0.761). Performance of the ANN was also greater than that of the radiologists (Az = 0.752). The computerized scheme has the potential to improve the diagnostic accuracy of radiologists in the distinction of benign and malignant SPNs.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
8. Swensen SJ, Silverstein MD, Ilstrup DM, Schleck CD, Edell ES. The probability of malignancy in solitary pulmonary nodules. Application to small radiologically indeterminate nodules. *Arch Intern Med* 1997; 157(8):849-855.	Observational -Dx	419 patients; 210 controls	To differentiate benign from malignant nodules using multivariate regression model.	65% of the nodules were benign, 23% were malignant, and 12% were indeterminate. Three clinical characteristics (age, cigarette-smoking status, and history of cancer [diagnosis, ≥5 years ago]) and 3 radiological characteristics (diameter, spiculation, and upper lobe location of the SPNs) were independent predictors of malignancy. The area (+/-SE) under the evaluated ROC was 0.8328 +/- 0.0226. Three clinical and 3 radiographic characteristics predicted the malignancy in radiologically indeterminate SPNs.	4
9. Truong MT, Sabloff BS, Ko JP. Multidetector CT of solitary pulmonary nodules. *Radiol Clin North Am* 2010; 48(1):141-155.	Review/Other -Dx	N/A	To review the role of imaging in the detection and characterization of SPNs. Strategies for evaluating and managing SPNs are also discussed.	With the increasing use of MDCT, small nodules are being detected more often. Although most incidentally discovered nodules are benign, usually the sequelae of pulmonary infection and malignancy, either primary or secondary, remains an important consideration in the differential diagnosis of SPNs.	4
10. Matsuki Y, Nakamura K, Watanabe H, et al. Usefulness of an artificial neural network for differentiating benign from malignant pulmonary nodules on high-resolution CT: evaluation with receiver operating characteristic analysis. *AJR* 2002; 178(3):657-663.	Review/Other -Dx	155 cases	To use an ANN to differentiate benign from malignant pulmonary nodules on HRCT findings and to evaluate the effect of ANN output on the performance of radiologists using ROC analysis.	The ANN showed a high performance in differentiating benign from malignant pulmonary nodules (A(z) = 0.951). The average A(z) value for all radiologists increased by a statistically significant level, from 0.831 to 0.959, with the use of the ANN output. Our computerized scheme using the ANN can improve the diagnostic accuracy of radiologists who are differentiating benign from malignant pulmonary nodules on HRCT.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
11. de Hoop B, Gietema H, van de Vorst S, Murphy K, van Klaveren RJ, Prokop M. Pulmonary ground-glass nodules: increase in mass as an early indicator of growth. *Radiology* 2010; 255(1):199-206.	Observational -Dx	52 ground-glass nodules	To compare manual measurements of diameter, volume, and mass of pulmonary ground-glass nodules to establish which method is best for identifying malignant ground-glass nodules by determining change across time.	The kappa values for intra- and interobserver agreement for identifying a solid component were 0.55 and 0.38, respectively. Intra- and interobserver coefficients of variation were smallest for ground-glass nodules mass (P<.001). 13 malignant ground-glass nodules were resected. Mean growth-to-variability ratios were 11, 28, and 35 for diameter, volume, and mass, respectively (P=.03); mean times required for growth to exceed the upper limit of agreement were 715, 673, and 425 days, respectively (P=.02). Mass measurements can enable detection of growth of ground-glass nodules earlier and are subject to less variability than are volume or diameter measurements.	4
12. Kostis WJ, Yankelevitz DF, Reeves AP, Fluture SC, Henschke CI. Small pulmonary nodules: reproducibility of three-dimensional volumetric measurement and estimation of time to follow-up CT. *Radiology* 2004; 231(2):446-452.	Observational -Dx	115 pulmonary nodules: 94 nodules (with no or minimal artifact); 105 nodules (including those with moderate artifacts)	To determine reproducibility of volume measurements of small pulmonary nodules on CT scans and to estimate critical time to follow-up CT.	The SD of percentage volume change decreased with increasing nodule size from 18.5% in 2-5 mm nodules to 10.6% in 5-8 mm nodules and to 7.47% in 8-10 mm nodules. Inclusion of cases with moderate motion artifacts increased the SD of percentage volume change to 27.4% in 2-5 mm nodules, to 17.1% in 5-8 mm nodules, and to 19.3% in 8-10 mm nodules. Critical time to follow-up CT for nodules detected at baseline screening was 12, 5, and 3 months and 1 month for those with initial sizes of 2, 5, 8, and 10 mm, respectively. For nodules detected at annual repeat screening, it was 4 and 3 months and 1 month for nodules that were 3, 4, and 5 mm or larger in size, respectively. Mean monthly volumetric growth index in 94 standard cases was 0.06%, and standard error was 0.21%. Factors that affect reproducibility of nodule volume measurements and critical time to follow-up CT include nodule size at detection, type of scan (baseline or annual repeat) on which the nodule is detected, and presence of patient-induced artifact.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
13. Brown MS, Goldin JG, Rogers S, et al. Computer-aided lung nodule detection in CT: results of large-scale observer test. *Acad Radiol* 2005; 12(6):681-686.	Observational -Dx	22 nodules in 8 patients	To study the incremental effects of using a CAD system on the performance of a large pool of observers.	In an analysis involving only the first randomly selected case read by all 202 participants, there were statistically significant increases in nodule detection rates and numbers of false-positive results for all types of observers. There was a significant difference in detection rates between radiologists and non-radiologists before CAD, but after CAD, there was no significant difference in detection rates between these observer types. In a second analysis involving 13 participants who read all 8 cases, mean detection rates were 64.0% before CAD and 81.9% after CAD. Mean numbers of false-positive results were 0.144 per case before CAD and 0.173 after CAD. In a large observer study, use of a CAD system for nodule detection resulted in an incremental increase in detection rate, but also led to an increase in number of false-positive results. Also, CAD appears to be an equalizer of detection rates between observers of different levels of experience.	3
14. Li F, Aoyama M, Shiraishi J, et al. Radiologists' performance for differentiating benign from malignant lung nodules on high-resolution CT using computer-estimated likelihood of malignancy. *AJR* 2004; 183(5):1209-1215.	Observational -Dx	56 total: 28 primary lung cancers (6-20 mm) 28 benign nodules	To evaluate whether a CAD scheme can assist radiologists in distinguishing small benign from malignant lung nodules on HRCT.	The area under the ROC curve (Az value) of the CAD scheme alone was 0.831 for distinguishing benign from malignant nodules. The average Az value for radiologists was improved with the aid of the CAD scheme from 0.785 to 0.853 by a statistically significant level (P=0.016). The radiologists' diagnostic performance with the CAD scheme was more accurate than that of the CAD scheme alone (P<0.05) and also that of radiologists alone. CAD has the potential to improve radiologists' diagnostic accuracy in distinguishing small benign nodules from malignant ones on HRCT.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
15. Nietert PJ, Ravenel JG, Taylor KK, Silvestri GA. Influence of nodule detection software on radiologists' confidence in identifying pulmonary nodules with computed tomography. *J Thorac Imaging* 2011; 26(1):48-53.	Observational -Dx	131 cases	To examine the extent to which CT nodule detection software influences the confidence of radiologists in identifying small pulmonary nodules.	Total of 327 unique nodules were identified. Declines in confidence were significantly ($P<0.05$) associated with the absence of an nodule detection software mark and smaller nodules (OR=71.0, 95% CI=14.8-339.7). Among nodules with prenodule detection software confidence less than 100%, increases in confidence were significantly ($P<0.05$) associated with the presence of a nodule detection software mark (OR=6.0, 95% CI=2.7-13.6) and larger nodules. Secondary findings showed that nodule detection software did not improve reader diagnostic accuracy. Although in this study nodule detection software does not seem to enhance reader accuracy, the confidence of the radiologists in identifying small pulmonary nodules with CT is greatly influenced by nodule detection software.	3
16. White CS, Pugatch R, Koonce T, Rust SW, Dharaiya E. Lung nodule CAD software as a second reader: a multicenter study. *Acad Radiol* 2008; 15(3):326-333.	Observational -Dx	109 patients from 4 sites	To evaluate the performance of CT lung nodule CAD software as a second reader.	The average increase in area under the curve for the 10 readers with CAD software was 1.9% for a 95% CI (0.8%-8.0%). The area under the curve without CAD software was 86.7% and with CAD software was 88.7%. A nonsignificant correlation was observed between the improvement in sensitivity and experience of the radiologists. The readers also showed a greater improvement in patients with cancer as compared to those without cancer. In this multicenter trial, CAD software was shown to be effective as a second reader by improving the sensitivity of the radiologists in detecting pulmonary nodules.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
17. Swensen SJ, Viggiano RW, Midthun DE, et al. Lung nodule enhancement at CT: multicenter study. *Radiology* 2000; 214(1):73-80.	Observational -Dx	356 patients	To test the hypothesis that absence of statistically significant lung nodule enhancement (≤15 HU) at CT is strongly predictive of benignity.	The prevalence of malignancy was 48%. Malignant neoplasms enhanced (median: 38.1 HU; range: 14.0 to 165.3 HU) significantly more than granulomas and benign neoplasms (median: 10.0 HU; range: -20.0 to 96.0 HU; P<0.001). With 15 HU as the threshold, the sensitivity was 98%, the specificity was 58%, and accuracy was 77%. The PPV was 68% and the NPV was 96%. If a threshold of 10 HU was selected, the sensitivity would be 100%, specificity 50.3%, accuracy 74.2%, PPV 65% and NPV 100%.	2
18. Jeong YJ, Lee KS, Jeong SY, et al. Solitary pulmonary nodule: characterization with combined wash-in and washout features at dynamic multi-detector row CT. *Radiology* 2005; 237(2):675-683.	Observational -Dx	107 patients	To prospectively assess the accuracy of combined wash-in and washout characteristics at dynamic contrast material-enhanced MDCT in distinguishing benign from malignant SPNs.	There were 49 malignant and 58 benign nodules. When diagnostic criteria for malignancy of both wash-in of 25 HU or greater and washout of 5-31 HU were applied, sensitivity, specificity, and accuracy for malignancy were 94% (46/49 nodules), 90% (52/58 nodules), and 92% (98/107 nodules), respectively. Of 58 benign nodules, 27 showed less than 25 HU wash-in, 14 showed persistent contrast enhancement without washout and with wash-in of 25 HU or greater and 11 showed washout greater than 31 HU and wash-in of 25 HU or greater. Evaluation of SPNs by analyzing combined wash-in and washout characteristics at dynamic contrast-enhanced MDCT showed 92% accuracy for distinguishing benign nodules from malignant nodules.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
19. Yi CA, Lee KS, Kim EA, et al. Solitary pulmonary nodules: dynamic enhanced multi-detector row CT study and comparison with vascular endothelial growth factor and microvessel density. *Radiology* 2004; 233(1):191-199.	Observational -Dx	131 patients	To evaluate enhancement dynamic of benign and malignant nodules at MDCT.	With 30 HU or more of net enhancement as a cutoff value in differentiation of malignant and benign nodules, sensitivity for malignant nodules was 99% (69/70 malignant nodules), specificity was 54% (33/61 benign nodules), PPV was 71% (69/97 malignant readings), NPV was 97% (33/34 benign readings), and accuracy was 78% (102/131 nodules). Peak attenuation was correlated positively with extent of microvessel density (r = 0.369, P=.006) and vascular endothelial growth factor staining (r = 0.277, P=.042). Malignant nodules showed significantly higher vascular endothelial growth factor expression (P=.009) than that of benign nodules. Dynamic enhancement with MDCT shows high sensitivity and NPVs for diagnosis of malignant nodules but low specificity because of highly enhancing benign nodules. Extent of enhancement reflects underlying nodule angiogenesis.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
20. Chae EJ, Song JW, Seo JB, Krauss B, Jang YM, Song KS. Clinical utility of dual-energy CT in the evaluation of solitary pulmonary nodules: initial experience. *Radiology* 2008; 249(2):671-681.	Observational -Dx	49 patients	To determine the clinical utility of dual-energy CT in evaluating SPNs.	CT numbers on virtual nonenhanced and nonenhanced weighted average images and CT numbers on the iodine-enhanced image and the degree of enhancement showed good agreements (intraclass correlation coefficients: 0.83 and 0.91, respectively). Diagnostic accuracy for malignancy by using CT numbers on iodine-enhanced image was comparable to that by using the degree of enhancement (sensitivity, 92% and 72%; specificity, 70% and 70%; accuracy, 82.2% and 71.1%, respectively). On virtual nonenhanced image, 85.0% (17/20) of calcifications in the SPN and 97.8% (44/45) of calcifications in the lymph nodes were detected, and the apparent sizes were smaller than those on the nonenhanced weighted average image. Radiation dose (average dose-length product, 240.77 mGy cm) was not significantly different from that of single-energy CT (P=.67). Dual-energy CT allows measurement of the degree of enhancement and detection of calcifications without additional radiation dose.	3
21. Kang MJ, Park CM, Lee CH, Goo JM, Lee HJ. Dual-energy CT: clinical applications in various pulmonary diseases. *Radiographics* 2010; 30(3):685-698.	Review/Other -Dx	N/A	To review the clinical applications of dual-energy CT in various pulmonary diseases.	By using dual-energy CT angiography for the evaluation of perfusion defects in cases of pulmonary embolism, and using xenon CT for the evaluation of ventilation defects, it may be possible to replace perfusion and ventilation scanning. An iodine map from dual-energy CT can demonstrate the distribution of pulmonary perfusion, whereas xenon ventilation CT can be used to generate a ventilation map. Furthermore, the virtual nonenhanced dual-energy CT technique can be used for the evaluation of pulmonary nodule characteristics without acquisition of true nonenhanced CT images. Knowledge of the applications of dual-energy CT and the typical images produced may lead to wider use of dual-energy CT for pulmonary applications and better interpretation of the results.	4

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22. Schroeder T, Ruehm SG, Debatin JF, Ladd ME, Barkhausen J, Goehde SC. Detection of pulmonary nodules using a 2D HASTE MR sequence: comparison with MDCT. *AJR* 2005; 185(4):979-984.	Observational -Dx	30 patients	To determine the diagnostic performance of MRI based on a HASTE sequence for the detection of pulmonary nodules in comparison with MDCT.	Compared with the sensitivity of CT, the sensitivity values for the HASTE MR sequence were as follows: 73% for lesions <3 mm, 86.3% for lesions between 3 and 5 mm, 95.7% for lesions between 6 and 10 mm, and 100% for lesions >10 mm. The overall sensitivity of the HASTE sequence for the detection of all pulmonary lesions was 85.4%. An MRI examination that consists of a HASTE sequence allows one to detect, exclude, or monitor pulmonary lesions that are ≥5 mm. Suspicious lesions <5 mm still need to be validated using CT.	2
23. Kim JH, Kim HJ, Lee KH, Kim KH, Lee HL. Solitary pulmonary nodules: a comparative study evaluated with contrast-enhanced dynamic MR imaging and CT. *J Comput Assist Tomogr* 2004; 28(6):766-775.	Observational -Dx	81 patients: 31 dynamic MRI; 27 dynamic CT; 23 both	To compare the diagnostic performance of dynamic MRI and CT for the differentiation of benign and malignant pulmonary nodules.	The malignant SPNs revealed significantly greater degrees of peak enhancement on dynamic MRI (mean +/- SD [p%SI] 131.2 +/- 46.1 vs 54.2 +/- 45.3; range [p%SI] 82.6-260.0 vs -0.7-171.7; P <0.0001) and CT (mean +/- SD [DMI] 37.8 +/- 15.1 vs 17.9 +/- 21.8; range [DMI] 14.1-68.2 vs -5.4-107.6; P=0.0004). Although dynamic MRI was somewhat superior to dynamic CT, the diagnostic performances of the 2 modalities based on ROC analysis were not statistically significant. Dynamic MRI and CT seem to be equally well suited for the differentiation between benign and malignant SPNs.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
24. Schaefer JF, Vollmar J, Schick F, et al. Solitary pulmonary nodules: dynamic contrast-enhanced MR imaging--perfusion differences in malignant and benign lesions. *Radiology* 2004; 232(2):544-553.	Observational -Dx	58 patients	To evaluate dynamic MRI in the evaluation of SPN's.	Frequency of malignancy was 53% (27/51 nodules). Malignant nodules showed stronger enhancement with a higher maximum peak and a faster slope (P<.001). Significant washout (>0.1% increase in signal intensity per second) was found only in malignant lesions (14/27 lesions). Sensitivity, specificity, and accuracy were 96%, 88%, and 92%, respectively, for maximum peak; 96%, 75%, and 86% for slope; and 52%, 100%, and 75% for washout. When curve profiles and morphologic enhancement patterns were combined, sensitivity increased to 100%. Dynamic MRI delineates significant kinetic and morphologic differences in vascularity and perfusion between malignant and benign SPNs. Washout seems to be highly specific for malignancy.	2
25. Kono R, Fujimoto K, Terasaki H, et al. Dynamic MRI of solitary pulmonary nodules: comparison of enhancement patterns of malignant and benign small peripheral lung lesions. *AJR* 2007; 188(1):26-36.	Observational -Dx	202 SPNs	To compare enhancement patterns of malignant and benign small peripheral lung lesions on dynamic contrast-enhanced MRI.	For 122 (85%) of 144 primary lung cancers, time at maximum enhancement ratio was 4 minutes or less. For all tuberculomas and hamartomas, time at maximum enhancement ratio was >4 minutes or gradual enhancement occurred without a peak time (P<0.0001). Lung cancers had different maximum enhancement ratios and slopes than benign lesions (all P<0.005). With 110% or lower maximum enhancement ratio as a cutoff value, the PPV for malignancy was 92%; sensitivity, 63%; and specificity, 74%. With 13.5%/min or greater slope as a cutoff value, sensitivity, specificity, PPV, and NPV for malignancy were 94%, 96%, 99%, and 74%, respectively. Dynamic contrast-enhanced MRI is helpful in differentiating benign from malignant SPNs. Absence of significant enhancement is a strong predictor that a lesion is benign.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
26. Mavi A, Lakhani P, Zhuang H, Gupta NC, Alavi A. Fluorodeoxyglucose-PET in characterizing solitary pulmonary nodules, assessing pleural diseases, and the initial staging, restaging, therapy planning, and monitoring response of lung cancer. *Radiol Clin North Am* 2005; 43(1):1-21, ix.	Review/Other -Dx	N/A	To assess pleural diseases and the initial staging, restaging, therapy planning and monitoring response of lung cancer by evaluating FDG-PET in characterizing SPNs.	The authors present a growing body of evidence that demonstrates and supports the utility of FDG-PET in the differentiation of benign and malignant pulmonary nodules, the assessment of lung cancer in various stages of disease, and the characterization of pleural diseases. In addition, new developments–such as prospects for potential utility of novel radiotracers and delayed imaging–that can further refine the role of FDG scans in the work-up of lung nodules and cancer and forecast the future place of PET in these common modalities are discussed.	4
27. Christensen JA, Nathan MA, Mullan BP, Hartman TE, Swensen SJ, Lowe VJ. Characterization of the solitary pulmonary nodule: 18F-FDG PET versus nodule-enhancement CT. *AJR* 2006; 187(5):1361-1367.	Observational -Dx	42 nodules	To compare nodule-enhancement CT and FDG-PET in the characterization of SPN.	Nodule-enhancement CT was positive in all 25 malignant nodules and in 12 benign nodules, with sensitivity and specificity of 100% and 29%, respectively, and with a PPV and NPV of 68% and 100%, respectively. Qualitative FDG-PET interpretations were positive in 24/25 malignant nodules and in 4 benign nodules. FDG-PET was considered negative in one malignant nodule and in 13/17 benign nodules. This correlates with a sensitivity and specificity of 96% and 76%, respectively, and with a PPV and NPV of 86% and 93%, respectively. Original prospective FDG-PET and semiquantitative SUV analysis showed sensitivity, specificity, PPV, and NPV of 88%, 76%, 85%, and 81% and 84%, 82%, 88%, and 78%, respectively. Due to its much higher specificity and only slightly reduced sensitivity, FDG-PET is preferable to nodule-enhancement CT in evaluating indeterminate pulmonary nodules. However, nodule-enhancement CT remains useful due to its high NPV, convenience, and lower cost. Qualitative FDG-PET interpretation provided the best balance of sensitivity and specificity when compared with original prospective interpretation or SUV analysis.	2

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28. 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(2):475-481.	Observational -Dx	846 consecutive patients	To retrospectively evaluate the effect of needle size of pneumothorax rate and the diagnostic accuracy of CT-guided needle aspiration biopsy.	Pneumothorax occurred in 226/846 patients. Coaxial needle size and patient age had a significant effect on pneumothorax rate. Pneumothorax occurred in 124 (38%) of 324 patients who underwent procedures with 18-gauge needles and in 121 (23%) of 522 patients who underwent procedures with 19-gauge needles (P<.001). The overall diagnostic accuracy was 96% for procedures performed with 18-gauge needles and 92% for procedures performed with 19-gauge needles, with a sensitivity of 95% and 89% and a specificity of 100% and 99%, respectively. Pneumothorax occurred in 153 patients older than 60 years, in 99 patients 60 years and younger (P<.02), in 90 patients older than 70 years, and in 162 patients younger than 70 years (P<.01). The relationship between pneumothorax rate and age as a continuous distribution was not significant (P<.07), nor were the 50- or 75-year age cutoffs (P<.06 and P<.9, respectively). Use of a smaller coaxial stabilizing needle produces a substantially decreased risk of pneumothorax with comparable diagnostic accuracy, sensitivity, and specificity for histopathologic diagnosis of pulmonary nodules.	3

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29. Wallace MJ, Krishnamurthy S, Broemeling LD, et al. CT-guided percutaneous fine-needle aspiration biopsy of small (< or =1-cm) pulmonary lesions. *Radiology* 2002; 225(3):823-828.	Observational -Dx	61 patients	To determine the accuracy of percutaneous CT-guided biopsy of small lung nodules.	Overall sensitivity was 82% (32/39); specificity, 100% (18/18); and diagnostic accuracy, 88% (50/57) on the basis of 57 patients being evaluable. Results for 47 0.8-1.0 cm lesions were considerably better (sensitivity, 88%; accuracy, 92%) than those for 10 0.5-0.7 cm lesions (sensitivity, 50%; accuracy, 70%). Sensitivity (75% vs 87%) and accuracy (87% vs 89%) also improved when comparing subpleural (≤1.0 cm from pleural surface, n=30) with deeper (>1 cm from pleural surface, n=27) pulmonary lesions, but the improvement did not indicate statistical significance. Core biopsy did not reveal malignancy in any of the nine patients in whom preliminary cytologic results were inconclusive and did not improve diagnostic yield. Thirty-eight (62%) patients had pneumothorax, with 19 (31%) requiring thoracostomy tube placement. CT-guided FNA biopsy of pulmonary lesions ≤1.0 cm can yield high diagnostic accuracy rates approaching those of larger lesions; FNA biopsy of 0.8-1.0 cm lesions that are not subpleural offers the best opportunity for success.	3
30. Westcott JL. Needle biopsy of the chest. In: Tavares J, Ferruci J, eds. *Imaging-Diagnosis- Intervention.* Philadelphia, Pa.: Lippincott; 1993:1-3.	Review/Other -Dx	N/A	Textbook to review aspects of FNA of SPN's.	FNA is highly useful to diagnose malignancy. Benign diagnoses are possible but are often nonspecific.	4
31. Yankelevitz DF, Wisnivesky JP, Henschke CI. Comparison of biopsy techniques in assessment of solitary pulmonary nodules. *Semin Ultrasound CT MR* 2000; 21(2):139-148.	Review/Other -Dx	N/A	To review the various techniques that provides specimens for pathology.	Workups will vary from institution to institution, based on availability of equipment and skill.	4

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32. Baaklini WA, Reinoso MA, Gorin AB, Sharafkaneh A, Manian P. Diagnostic yield of fiberoptic bronchoscopy in evaluating solitary pulmonary nodules. *Chest* 2000; 117(4):1049-1054.	Observational -Dx	177 patients	To evaluate factors affecting the diagnostic yield of fibroptic bronchoscopy in evaluating SPN's.	The diagnostic accuracy of bronchoscopy in malignant and benign lesions were 64% (97/151) and 35% (9/26), respectively. The yield of bronchoscopy was directly related to lesion size (P<0.001, chi(2)). When lesions were grouped according to distance from the hilum, yields of bronchoscopy in central, intermediate, and peripherally located lesions were 82%, 61%, and 53%, respectively (P=0.05, chi(2)). When we stratified distance from the hilum by lesion size, the difference in yield was not significant. However, lesions ≤2 cm had a diagnostic yield of 14% (2/14) when located in the peripheral third vs 31% (5/16) when located in the inner two thirds of the lung. There was a trend toward higher combined diagnostic yield in right middle and lingular lobes when compared to all other segments (P=0.09, chi(2)). Transbronchial biopsy, washing, and brushing were complementary in improving the yield of bronchoscopy. Size is the strongest determinant of diagnostic yield in bronchoscopy when evaluating SPNs. The yield of bronchoscopy is particularly low in lesions ≤2 cm that are located in the outer third of the lung. Thus, alternative diagnostic approaches may be preferable in this situation.	3

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Yamagami T, Iida S, Kato T, et al. Usefulness of new automated cutting needle for tissue-core biopsy of lung nodules under CT fluoroscopic guidance. *Chest* 2003; 124(1):147-154.	Observational -Dx	110 biopsies	To evaluate a new type of automated cutting needle for tissue-core biopsy using CT fluoroscopic guidance.	The rate of success for the diagnosis for specimens that were adequate for histopathologic analysis was 94.5% (104/110 specimens). The sensitivity, specificity, and accuracy in diagnosing malignancy were 95.1%, 100%, and 96.2%, respectively. A specific cell type could be characterized in 95.2% of those 104 lesions (99 lesions; malignant, 76 lesions; benign, 23 lesions). The specific cell type was precisely diagnosed, and was confirmed after surgery in 65 malignant lesions and 23 benign lesions. The biopsy-induced complications encountered were pneumothorax in 34.5% (38/110 patients) and hemoptysis in 6.4% (7/110 patients). No patient had a serious complication. CT fluoroscopy-guided lung biopsy using the Auto Surecut needle provides a high degree of diagnostic accuracy, allows for the specific characterization of lung nodules, and can be performed safely.	3

Radiographically Detected Solitary Pulmonary Nodule
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
34. Savage C, Walser EM, Schnadig V, Woodside KJ, Ustuner E, Zwischenberger JB. Transthoracic image-guided biopsy of lung nodules: when is benign really benign? *J Vasc Interv Radiol* 2004; 15(2 Pt 1):161-164.	Observational -Dx	836 cases	To evaluate transthoracic image-guided biopsy in the management of a non-malignant diagnosis at lung biopsy.	Non-malignant result at lung biopsy is classified as: 1. Benign specific, 2. Benign non-specific, or 3. Non-diagnostic; the last two diagnoses need further workup. 95/836 total cases with FNA +/- core biopsies over the 5-year period were identified as nonmalignant and had complete pathologic or radiologic follow-up. 21/95 had a benign specific diagnosis; all were true-negative for malignancy on radiologic (n=17) or surgical (n=4) follow-up. The remaining 74 had either benign nonspecific (n=53) or nondiagnostic (n=21) diagnoses. 7/53 benign nonspecific specimens (13%) and 6/21 nondiagnostic specimens (29%) were malignant at excisional biopsy or radiologic follow-up. 16/95 (17%) had a postprocedural pneumothorax requiring a chest tube. Transthoracic FNA +/- core biopsy may yield a nonmalignant diagnosis as (i) benign specific, (ii) benign nonspecific, or (iii) nondiagnostic. Diagnosis-directed medical management is recommended for a benign specific diagnosis. Additional diagnostic studies, repeat biopsy, or resection is necessary for benign nonspecific and nondiagnostic biopsy results as a result of an unacceptably high rate of malignancy.	3

Radiographically Detected Solitary Pulmonary Nodule
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Dendo S, Kanazawa S, Ando A, et al. Preoperative localization of small pulmonary lesions with a short hook wire and suture system: experience with 168 procedures. *Radiology* 2002; 225(2):511-518.	Observational -Dx	150 patients 168 lesions	To evaluate the use of a short hook wire and suture system for preoperative localization of SPN.	The hook wire was successfully placed without dislodgment in 146 patients, accounting for 164 (97.6%) of 168 lesions. Group A2 showed a success rate of 100%. There was no difference in patients among the 3 groups in regard to size of lesions or their distance from the pleural surface. In patients in groups A2 and B, the proportion of nodules with ground-glass opacity and primary lung carcinoma at CT was significantly greater than that in patients in group A1. In 168 placements, nonsymptomatic pneumothorax cases were observed in 54 (32.1%), hemorrhages into the lung were observed in 25 (14.9%), and hemorrhage into the pleural space was observed in one (0.6%). No patient complained of notable pain during or after the procedure, and no serious complication was experienced. Unsuccessful placement was caused by too shallow a puncture with the introducer needle. This system with a flexible suture for preoperative localization has a high success rate.	4
36. Hanninen EL, Langrehr J, Raakow R, et al. Computed tomography-guided pulmonary nodule localization before thoracoscopic resection. *Acta Radiol* 2004; 45(3):284-288.	Review/Other -Dx	24 patients 25 pulmonary nodules	To access the success rate and complications of a CT guided nodule marker system.	Mean lesion size was 7 mm (range 4-15 mm) and mean lesional distance to the pleura was 13 mm (range 2-31 mm). The pulmonary nodule-marker system was positioned successfully in all 25 pulmonary nodules within 5-11 min (mean 7.5 min). Minimal pneumothoraces were observed in 5 patients with no requirements of chest drains. In addition, no bleeding complications or hematothorax were observed. All 25 pulmonary nodules could be resected thoracoscopically. However, in one patient (4%), the guide-wire dislocated during thoracoscopy, but the lesion could be successfully resected during thoracoscopy. The CT-guided placement of the pulmonary nodule-marker system used here offers a safe and accurate guide for the localization of small pulmonary nodules during thoracoscopic resection.	4

Radiographically Detected Solitary Pulmonary Nodule
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Henschke CI, Yankelevitz DF, Naidich DP, et al. CT screening for lung cancer: suspiciousness of nodules according to size on baseline scans. *Radiology* 2004; 231(1):164-168.	Observational -Dx	2,897 patients	To retrospectively assess the frequency with which a particular, possibly optimal workup of noncalcified nodules <5.0 mm in diameter identified on initial CT images at baseline screening leads to a diagnosis of malignancy prior to first annual repeat screening, compared with a possibly optimal workup of larger nodules.	The frequency with which malignancy was or could have been diagnosed when the largest noncalcified nodule was <5.0 mm in diameter was 0/378, whereas when the largest noncalcified nodule was 5.0-9 mm in diameter, the frequency was 13 or 14 of 238. If persons with only nodules <5.0 mm had merely been referred for first annual repeat screening without immediate further workup, the referrals for such workup would have been reduced by 54% (from 817 [28%] to 385 [13%] of 2,897). In modern CT screening for lung cancer at baseline, detected noncalcified nodules <5.0 mm in diameter do not justify immediate workup but only annual repeat screening to determine whether interim growth has occurred.	3
38. MacMahon H, Austin JH, Gamsu G, et al. Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. *Radiology* 2005; 237(2):395-400.	Review/Other -Dx	N/A	To review guidelines for follow-up of small pulmonary nodules.	Nodules ≤4 mm should be followed in 1 year. The current practice in the United States of recommending follow-up studies for all indeterminate opacities is partly related to perceived liability if a cancer should develop. When the medical community has preached the importance of early detection of cancer for so long, it may prove difficult to convince physicians and the public that follow-up CT of every nodule in every patient is unnecessary.	4
39. Gould MK, Fletcher J, Iannettoni MD, et al. Evaluation of patients with pulmonary nodules: when is it lung cancer?: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 2007; 132(3 Suppl):108S-130S.	Review/Other -Dx	N/A	Evidence-based clinical practice guidelines based on a systematic literature review to develop for the evaluation of patients with pulmonary nodules.	Recommendations stress the value of risk factor assessment, the utility of imaging tests (especially old films), the need to weigh the risks and benefits of various management strategies (biopsy, surgery, and observation with serial imaging tests), and the importance of eliciting patient preferences. Patients with pulmonary nodules should be evaluated by estimation of the probability of malignancy, performance of imaging tests to characterize the lesion(s) better, evaluation of the risks associated with various management alternatives, and elicitation of patient preferences for treatment.	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

ANN = Artificial neural network

CAD = Computer-aided detection

CI = Confidence interval

CT = Computed tomography

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

FNA = Fine-needle aspiration

HASTE = Half-Fourier acquisition single-shot turbo spin-echo

HRCT = High-resolution computed tomography

MDCT = Multidetector computed tomography

MRI = Magnetic resonance imaging

NPV = Negative predictive value

OR = Odds ratio

PPV = Positive predictive value

ROC = Receiver-operator characteristic

SD = Standard deviation

SPN = Solitary pulmonary nodule

SUV = Standardized uptake value