Incidental Lung Nodules - Initial evaluation
Key Studies and guidelines

General Information

Lung nodules:

- A lung nodule is defined as ≤ 3cm
- A lung mass is defined as > 3 cm
- Majority of incidental nodules are benign
- Nodules can be described as: solid, sub-solid, ground-glass
- Incidental lung nodules found on a CT chest (Not a lung cancer screening CT): Use Fleischner Society 2017 management guidelines.

Lung Cancer and Lung Cancer Screening (LCS):

- Currently, overall 5-years survival for ALL patients with lung cancer is 18%.
- Early diagnosis of lung cancer at stage I disease has a 5-year survival of 73-90%
- Lung Cancer Screening: Use Lung-RADS for management guidelines.
- Lung-RADS is to minimize variation in the management of LCS CT–detected lung nodules and is an important component of LCS CT quality assurance and registry reporting.

Incidental Nodule Management

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017

- Fleischner Society, founded in 1969, is an international, multidisciplinary medical society for thoracic radiology, who are dedicated to the diagnosis and treatment of diseases of the chest.
- These guidelines apply to patients > 35 years old, with incidental nodules found on a CT chest.
- Nodules are divided by their characteristics: Solid nodules versus Sub-solid/ground glass nodules

Guideline Summary:

Single solid nodules:

	<6mm	6-8mm	>8mm	Follow-up considerations
Low risk	No follow-up	CT 6-12 mo, then consider CT at 18-24 mo	CT 3 mo, PET/CT or Bx	
High risk	Optional CT 12 mo	CT 3-6mo, then CT 18-24 mo	CT 3 mo, PET/CT or Bx	Suspicious nodules and/or upper lobe location warrant a 12 mo CT follow-up

Multiple solid nodules:

	<6mm	6-8mm	>8mm
Low risk	No follow-up	CT 3-6 mo, then consider CT at 18-24 mo	CT 3-6mo, then consider CT at 18-24 mo
High risk	Optional CT 12 mo	CT 3-6mo, then CT 18-24 mo	CT 3-6mo, then at 18-24 mo

Single sub-solid nodules:

	<6mm	≥ 6mm
Ground glass opacity	No follow-up	CT at 6-12 mo, then every 2 yrs x 5 yrs
Part solid	No follow-up	CT at 3-6 mo, if unchanged and solid component is <6mm, annual CT x 5 years

Multiple sub-solid nodules:

<6mm	≥ 6mm
CT at 3-6mo, if stable consider CT at 2 & 4 yrs	CT at 3-6 mo, subsequent imaging based on nodule suspicion

RISK CALCULATIONS

Models to estimate the probability of Malignancy in patients with pulmonary nodules

- Estimate the chances that a pulmonary nodule is malignant by combining clinical and imaging features that are known to be independent predictors of lung cancer.
- There are 8 probability models to date that have been externally validated and cover both incidental nodules and lung cancer screening (See table 4).
- Some models rely on clinical and CT features: Gurney (1993), Mayo (1997), Department of Veterans Affairs (VA 2007), Peking University People's Hospital (PKUPH 2012) and Brock (2013)
- Other models incorporate PET scan results in addition to clinical and CT features: Herder (2005) , Thoracic Research Evaluation and Treatment (TREAT 2014) and Bayesian Inference Malignancy Calculator (BIMC 2015)
- Study results indicate that risk calculators, along with patient risk factors, nodule features and multidisciplinary expert evaluation can help to discriminate benign versus malignant nodules,

and drive diagnostic decision-making. Advances in molecular biomarkers and Genomic testing are likely to improve malignancy probability.

- Each calculator has a specific use. Depending on your specific population would determine which calculator you would use.
- It is important to choose a single calculator to be used consistently at your institution for continuity of practice between providers (see table 5) that is reflective of your population.

Table 4.

Table 4. List of websites where probability calculators can be found for clinical use

Model	Website
Gurney	http://www.chestx-ray.com/index.php/calculators/spn-calculator
	https://www.merckmanuals.com/medical-calculators/SolitaryPulmNod_Cummings.htm
Mayo Clinic	https://reference.medscape.com/calculator/solitary-pulmonary-nodule-risk
	http://www.chestx-ray.com/index.php/calculators/spn-calculator
Herder	http://www.nucmed.com/nucmed/spn_risk_calculator.aspx
	http://spn.azurewebsites.net/Herder
VA	http://ebmcalc.com/SolitaryPulmNod_VA.htm
Brock	https://brocku.ca/lung-cancer-risk-calculator
	http://spn.azurewebsites.net/Brock
TREAT	https://treat.mc.vanderbilt.edu/calculator
BIMC	http://www.simoneperandini.com/bimc/

Table 5.

Table 3. Suggested populations for clinical application of pulmonary nodule malignancy probability models

Model	Population to Consider Clinical Application	Comments
Gurney	High risk of lung cancer May consider in cavitary nodules	Presence of cavitation and growth is considered in this model.
		Its accuracy was lower in direct comparisons with the PKUPH and BIMC models (12, 14, 21).
Mayo	Low to moderate risk of lung cancer	This is the most externally validated model.
		It does not include growth rate, FDG-PET results, or history of any cancer within 5 yr.
		Accuracy was lower in comparison studies in populations with high lung cancer prevalence that were sent for surgical evaluation (13, 14).
Herder	FDG-PET result available	Accuracy was higher than the Mayo Clinic, VA, and BIMC models in comparison studies (20, 24).
VA	Males with history of smoking	Accuracy has been overall lower in comparison studies with the other models (14, 18–20, 23).
PKUPH	High risk of lung cancer	It was developed from a Chinese population with high lung cancer prevalence.
		External validation in different geographic and ethnic populations is necessary.
Brock	Lung cancer screening	It was developed in a lung cancer screening population, but it has demonstrated high accuracy even in populations with high lung cancer prevalence (20, 23, 26).
	General lung nodule population	The model includes PN multiplicity and attenuation on CT scans.
TREAT	High risk of lung cancer	This model was designed for use during preoperative evaluation of high-risk PNs.
	PET and serial imaging available	It is one of the newer models and one of the least externally validated.
BIMC	Moderate to high risk of lung cancer	FDG-PET results and PN growth are considered in this model.
	PET and serial imaging available	Its accuracy was lower when compared with the Herder model (24).
		It is one of the least externally validated models.

Radiologic Findings that determine suspicion for Lung Cancer

INTERMEDIATE (5-65%) AND HIGH RISK (>65%)

High risk nodule characteristics:

- Spiculated or irregular nodule margins
- Upper Lobe location
- Larger nodules (>6mm)
- Singular or Multiple nodules up to 4
- Solid nodule with volume doubling w/in 100-400 days
- Sub-solid nodule with volume doubling time w/in 3-5 years

Risk factors associated with lung cancer:

- Chronic Obstructive Pulmonary Disease
- Idiopathic Pulmonary Fibrosis
- Female with sub-solid nodules
- Family Hx of lung cancer – whether the patient is a smoker or non-smoker
- Smoker: 20 pack-years or more and quit smoking w/in the past 15 years
- Second hand smoke exposure or other inhaled carcinogens
- African Americans and native Hawaiian

LOW RISK (< 5% risk of cancer)

Lower risk nodule characteristics:

- Multiple nodules > 5 w/less risk
- Small nodule size (<6mm)
- Regular nodule margins
- Non-upper lobe nodules

Low risk factors for lung cancer:

- Under age 40
- Non-smoker

In Summary:

Incidental lung nodule management and lung cancer screening has been well studied for more than 20 years. Guidelines for management of an incidental nodule, lung cancer risk stratification, and staging for lung cancer are ever evolving in the era of new technology. Patient-specific factors and nodule characteristics on imaging are important when calculating the probability risk of malignancy in incidental nodules. The goals of these guidelines and risk calculators are to reduce lung cancer mortality through early identification, diagnosis and oncologic management.

Although this module focuses on incidental nodules, the information below is comprehensive to also include: radiology reading, biomarkers, modes of biopsies, lung cancer screening and its guidelines.

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Pre-Biopsy Testing:

"Liquid biopsy" (like *Biodesix CDT*):

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