Update on LUNG-RADS™

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Disclosures

- No financial disclosures
- Chair, American Cancer Society National Lung Cancer Roundtable
- Chair, American College of Radiology Lung Cancer Screening Committee
- Chair, ACR Lung Cancer Screening Registry
- Vice-Chair NCCN Lung Cancer Screening Panel
- Chair, ACR LungRADS committee
US: Lung Cancer Screening

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening
The National Lung Screening Trial Research Team*

Cost-Effectiveness of CT Screening in the National Lung Screening Trial

U.S. Preventive Services Task Force

Current Recommendation
Release Date: December 2013

- The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults ages 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.
Grade: B recommendation.
LungRADS Update - Outline

- v1.0 Released April 2014
- Use & Data from the AC Lung Cancer Screening Registry
- V1.1 coming in 2018
- Future updates
ACR LungRADS™ 1.0 - Released April 2014

- Modeled after 20+ year experience with BIRADS
- Now part of a suite of ACR Radiology Reporting & Data Systems
- Structured reporting and management tool for lung cancer screening CT interpretation
- Categories 0-4 with increasing risk of lung cancer
- Modifier S for other significant findings
- Variables to evaluate quality assurance & improvement

http://www.acr.org/Quality-Safety/Resources/LungRADS
ACR RADS newly formed RADS steering committee
ACR LungRADS™ - Why?

- To provide a common lexicon & definitions
- To standardize practice among radiologists for communicating with ordering providers
- To define a positive screen
- To address uncertainty in positive screen management
- To facilitate quality assurance & improvement
- To be updated as knowledge evolves
2180 consecutive high-risk patients undergoing clinical CT screening between 1/2012-05/2014 reclassified using LungRADS

Lung-RADS:
- Reduced positive screen rate from 27.6% to 10.6%
- No false negatives in the 152 patients with >12-month follow-up reclassified as benign
- Increased PPV for malignancy from 6.9% to 17.3%

http://www.jacr.org/article/S1546-1440(14)00473-6/abstract
Reclassified NLST CT screening exams using LungRADS
26,722 LDCT arm subjects (26,309 baseline; 48,671 post-baseline)

<table>
<thead>
<tr>
<th></th>
<th>BASELINE LungRADS</th>
<th>BASELINE NLST</th>
<th>POST BASELINE LungRADS</th>
<th>POST BASELINE NLST</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPR (1-Specificity)</td>
<td>12.9% (26.6%)</td>
<td>5.3% (27.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>86.1% (93.8%)</td>
<td>78.6% (94.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPV</td>
<td>6.9% (3.8%)</td>
<td>10.9% (2.4%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
False negative LungRADS screens were nodules with no growth and/or pure nonsolid nodules (5 year survival 64% TPs vs. 73% FNs)

Compared to the original NLST criteria
- FPRs with LungRADS were ½ at baseline and ¼ post-baseline
- Sensitivity was 8% and 15% lower at baseline and post-baseline
- PPV was 2-3 fold higher for LungRADS
ACR LungRADS™ 4X: Subsolid Nodules

<table>
<thead>
<tr>
<th>Category Descriptor</th>
<th>Category Descriptor</th>
<th>Primary Category</th>
<th>Expected Distribution</th>
<th>Probability of Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspicious</td>
<td>Radiologist discretion to upcode categories based on additional findings and nodule features</td>
<td>4X</td>
<td></td>
<td>?</td>
</tr>
<tr>
<td>Suspicious</td>
<td>Findings for which additional diagnostic testing and/or tissue sampling is recommended</td>
<td>4B</td>
<td>2%</td>
<td>&gt; 15%</td>
</tr>
</tbody>
</table>

Malignancy Rates for Lesions Upgraded to Category 4X

<table>
<thead>
<tr>
<th>Observer</th>
<th>Total Upgraded to Category 4X</th>
<th>Upgraded from Lung-RADS 3</th>
<th>Upgraded from Lung-RADS 4A</th>
<th>Upgraded from Lung-RADS 4B</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30/58 (52)</td>
<td>8/18 (44)</td>
<td>2/3 (67)</td>
<td>20/37 (54)</td>
</tr>
<tr>
<td>2</td>
<td>42/74 (57)</td>
<td>14/28 (50)</td>
<td>8/12 (67)</td>
<td>20/34 (59)</td>
</tr>
<tr>
<td>3</td>
<td>35/64 (55)</td>
<td>10/19 (53)</td>
<td>6/10 (60)</td>
<td>19/35 (54)</td>
</tr>
<tr>
<td>4</td>
<td>29/55 (53)</td>
<td>9/19 (47)</td>
<td>4/8 (50)</td>
<td>16/28 (57)</td>
</tr>
<tr>
<td>5</td>
<td>42/91 (46)</td>
<td>11/30 (37)</td>
<td>8/12 (67)</td>
<td>23/49 (47)</td>
</tr>
<tr>
<td>6</td>
<td>35/66 (53)</td>
<td>8/19 (42)</td>
<td>7/9 (78)</td>
<td>20/38 (53)</td>
</tr>
<tr>
<td>Average (%)*</td>
<td>53 (49, 56)</td>
<td>46 (40, 52)</td>
<td>65 (55, 74)</td>
<td>54 (50, 58)</td>
</tr>
</tbody>
</table>

4X malignancy rate was 46-57% per observer & substantially higher than malignancy rates of categories 3, 4A & 4B SSNs

Radiology 2016 Chung et al
ACR LungRADS™ - Update

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- To standardize practice among radiologists for communicating with ordering providers
- To define a positive screen
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- To facilitate quality assurance & improvement
- To be updated as knowledge evolves
## ACR Lung Cancer Screening Registry

<table>
<thead>
<tr>
<th></th>
<th>2015*</th>
<th>2016</th>
<th>2017~</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong># of facilities</strong></td>
<td>908</td>
<td>905</td>
<td>307</td>
<td>2120</td>
</tr>
<tr>
<td></td>
<td></td>
<td>new since 2015</td>
<td>new since 2016</td>
<td></td>
</tr>
<tr>
<td><strong># of screening exams</strong></td>
<td>42,126</td>
<td>167,663</td>
<td>171,075</td>
<td>380,864</td>
</tr>
</tbody>
</table>

* 2015 facility enrollment began in September 2015
~ 2017 data through 8/30/2017 (8 months)
## Positive Screen Rate (LungRADS 3, 4A/B/X)

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>baseline screens</td>
<td>21.2 %</td>
<td>19.6%</td>
<td>18.3%</td>
</tr>
<tr>
<td>subsequent screens</td>
<td>14.2%</td>
<td>12.7%</td>
<td>11.2%</td>
</tr>
<tr>
<td>overall</td>
<td>20.7%</td>
<td>18.6%</td>
<td>16.8%</td>
</tr>
<tr>
<td># of screens</td>
<td>41,407</td>
<td>166,158</td>
<td>167,228</td>
</tr>
</tbody>
</table>

* 2015 facility enrollment began in September 2015
  ~ 2017 data through 8/30/2017 (8 months)
<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV 2a for LR 3 with 6 month recommended CT</td>
<td>0.01</td>
<td>0.01</td>
<td>0.00</td>
</tr>
<tr>
<td>PPV 2b for LR 4A with 3 month recommended CT</td>
<td>0.14</td>
<td>0.12</td>
<td>0.08</td>
</tr>
<tr>
<td>PPV 3 all known biopsies with tissue diagnosis of cancer at 1 year</td>
<td>0.62</td>
<td>0.62</td>
<td>0.76</td>
</tr>
</tbody>
</table>

* 2015 facility enrollment began in September 2015
~ 2017 data through 8/30/2017 (8 months)
Lung-RADS: Pushing the Limits

In response to the recommendation of the U.S. Preventive Services Task Force and the coverage decision by the Centers for Medicare and Medicaid Services for lung cancer screening (LCS) computed tomography (CT), the American College of Radiology introduced the Lung CT Screening Reporting and Data System (Lung-RADS) in 2014 to standardize the reporting and management of screening-detected lung nodules. As with many first-edition guidelines, questions arise when such reporting systems are used in daily practice. In this article, a collection of 15 LCS-related scenarios are presented that address situations in which the Lung-RADS guidelines are unclear or situations that are not currently addressed in the Lung-RADS guidelines. For these 15 scenarios, the authors of this article provide the reader with recommendations that are based on their collective experiences, with the hope that future versions of Lung-RADS will provide additional guidance, particularly as more data from widespread LCS are collected and analyzed.
Scenario 1: New LungRADS category 3 solid lung nodule in a patient who is aging out of the screening program.
Scenario 2: Lung mass in a patient with vague symptoms.
Scenario 3: Solid suspicious (Lung-RADS category 4B) nodule with very slow growth rate.
Scenario 4: Ground-glass nodule that increases in density but remains stable in size.
Scenario 5: Ground-glass nodule with slow growth rate.
Scenario 6: How to measure and classify a part-solid nodule.
Scenario 7: Nodule that decreases in size but increases in attenuation.
Scenario 8: Nodule with characteristic features of an intrapulmonary lymph node.
Scenario 9: Airway (endotracheal or endobronchial) nodule.
Scenario 10: Incidental potentially important finding other than lung cancer detected at low-dose LCS CT.
Scenario 11: Reenrolling patients in the LCS CT program after a stable abnormality.
Scenario 12: Low-dose LCS CT of a patient with a recent respiratory infection.
Scenario 13: Categorization of a cavitary lung nodule or nodules.
Scenario 14: Low-dose LCS CT of a patient with a history of a treated lung malignancy.
Scenario 15: Low-dose LCS CT of a patient with a treated low-risk non lung malignancy.
Lung cancer screening using low-dose CT scanning reduces lung-cancer-specific and overall mortality in high-risk patients. A significant limitation of lung cancer screening is the false-positive rate. The American College of Radiology Lung Imaging Reporting and Data System (Lung-RADS) was designed to standardize reporting of low-dose lung cancer screening results and to decrease the false-positive rate without significantly compromising sensitivity. Implementing Lung-RADS can also improve cost-effectiveness. However, Lung-RADS has never been studied in a prospective fashion. It also does not have a specific reporting category for patients with isolated hilar and mediastinal adenopathy or pleural effusion in the absence of lung nodules. We report four such cases from our lung cancer screening program. We believe that this is a significant limitation of Lung-RADS and should be revised in its new version.

CHEST 2017; 151(3):539-543

does not have a specific reporting category for patients with isolated hilar and mediastinal adenopathy or pleural effusion in the absence of lung nodules
Define perifissural nodules

Current:
- Nodules with features of an intrapulmonary lymph node should be managed by mean diameter and the 0-4 numerical category classification

Future:
- Solid nodules with smooth margins, an oval, lentiform or triangular shape, and maximum diameter less than 10 mm (perifissural nodules) should be classified as category 2
A perifissural nodule is a fissure-attached, homogeneous, solid nodule that had smooth margins and an oval, lentiform, or triangular shape [1]. They represent about 20% of nodules detected in lung cancer screening, are invariably benign, and do not require follow-up [1,2,3].

More broadly, smooth or attached NCNs comprised 83% of all indeterminate solid pulmonary nodules detected in the NELSON trial [4]. At 1 year follow-up, no cancer was found in smooth (0/654) or attached (0/503) 5-10 mm nodules. Xu et al concluded that 1 year follow-up is sufficient.

PANCAN & BCCA pooled: probability of lung cancer in perifissural nodules was zero (0 of 571 nodules; one-sided 97.5% CI, 0 to 0.006) [5]

2. de Hoop B et al. Pulmonary perifissural nodules on CT scans: rapid growth is not a predictor of malignancy. Radiology. 2012;265(2):611-6
3. Fleischner revision
4. Xu DM et al. Smooth or attached solid indeterminate nodules detected at baseline CT screening in the NELSON study: cancer risk during 1 year of follow-up. Radiology. 2009;250(1):264-72
5. McWilliams A et al. Probability of Cancer in Pulmonary Nodules Detected on First Screening CT. NEJM2013;369;910-919
LungRADS Update #2 – ’18 – Non Solid Nodules

- Raise the size threshold for pure non solid nodules from 20 mm to 30 mm

- Current: Category 2
  - non solid nodule(s) (GGN):
    - < 20 mm OR
    - ≥ 20 mm and unchanged or slowly growing

- Future: Category 2
  - non solid nodule(s) (GGN):
    - < 30 mm OR
    - ≥ 30 mm and unchanged or slowly growing
LungRADS Update #2 – ’18 – Non Solid Nodules

- NSNs slow-growing & with longer volume doubling times than solid nodules

- Mean volume doubling time for growing NSNs

- No growth:
  - 90% did not grow on long-term follow-up (median 59 months) Chang et al. Chest 2013;143:172

- Indolent course:

- Management evolved to selective surgery & longer annual follow-up
  - 2017 Fleischner Guideline solitary GGO > 8 mm: CT in 6-12 months to confirm persistence, then every 2 yrs until 5 yrs; if grows or new solid component, consider resection
Address management for new large nodules

Current: Category 4B Management
- Chest CT with or without contrast, PET/CT and/or tissue sampling depending on the *probability of malignancy and comorbidities. PET/CT may be used when there is a $\geq 8$ mm solid component. For new large nodules that develop on an annual repeat screening CT

Future: Category 4B Management
- Chest CT with or without contrast, PET/CT and/or tissue sampling depending on the *probability of malignancy and comorbidities. PET/CT may be used when there is a $\geq 8$ mm solid component. For new large nodules that develop on an annual repeat screening CT, a 1 month LDCT may be considered
Change in how nodule diameter is measured & recorded

Current:
- Report average diameter (of long and short axis diameters) rounded to the nearest whole number

Future:
- To calculate nodule mean diameter, measure both the long and short axis to one decimal point, and report mean nodule diameter to one decimal point
Change in how diameter is measured & recorded

Change in nodule size represents a combination of true change plus measurement error.

Using average diameter measurements, in order to overcome measurement error and confirm true change, growth of at least 1.5 mm is required. If using volumetric techniques, true change can be determined using the QIBA Lung Nodule Profile Calculator (v0.1) [http://services.accumetra.com/NoduleCalculator.html](http://services.accumetra.com/NoduleCalculator.html)
LungRADS Update - Future

Size & growth defined in mm to volume

- Current: Mean diameter
- Future: Volumetric; new QIBA small nodule profile and growth profile to aid in measuring system performance and the variance around size measurements
- Obstacles:
  - Availability of accurate, robust software tools
  - Fully integrated into radiologist workflow
  - Reimbursement for lung nodule CAD/CAD-like tools which require facility investment & radiologist time to translate
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