Lung Cancer Screening: Radiologic and Clinical Implications

Katherine R. Birchard, M.D.
University of North Carolina at Chapel Hill
“I need someone well versed in the art of torture—do you know PowerPoint?”
Nothing to disclose...
Objectives

• In context of NLST:
  • Review Imaging Techniques
  • Review Current Data on Radiation Doses from medical imaging
  • Review Appearances of False Positives
  • Review Pathology that may cause “Overdiagnosis”
A Brief History...

- Many Randomized and non-randomized controlled trials over the years:
  - 1970’s: Trials with Sputum Culture and Chest xray
  - Mayo CT Screening Study-1999-2008 No control arm (model as control arm)
  - ELCAP Study 1999- Large! 65,000 pts; No control arm
  - DANTE Trial- Small nos., LDCT and control = same
A Brief History...

- In many studies, groups that were “intervened upon” had/were found to have:
  - More lung cancers
  - More early stage lung cancers
  - More resectable lung cancers
  - But! No significant reduction in lung cancer mortality, especially compared to overall mortality (Mayo)

- Enter the NLST...
The National Lung Screening Trial

- 53,454 patients, 55-74, 30 pack-years, quit ≤ 15 years ago
- 26,722 LDCT; 26,732 Chest X-ray
- Three annual exams, median follow-up time = 6.4 years
The National Lung Screening Trial

- Chest X-Ray Technique:
  - Single PA Film

The National Lung Screening Trial

• Chest X-Ray Technique:
  • Single PA Film
    • Median effective dose = 0.0344 mSv; (95th percentile = 0.1150 mSv; 5th percentile = 0.0104 mSv)

• Context:
  • US citizen average effective dose = 3mSv/year
  • 1/100 of the dose

The National Lung Screening Trial

- CT Technique:
  - Non-contrast, helical

The National Lung Screening Trial

- CT Technique:
  - Non-contrast, helical
  - Standardization across sites quite complicated

Section 1: Radiation Dose from a Single Geometric Phantom

**Low dose helical CT technique**
- Primary Reviewer: [Name]
- Reviewer ID: [ID]
- Action(s) Required or Notes: [Notes]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measured</th>
<th>Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTDI Body Phantom</td>
<td>5.0 (mGy)</td>
<td>5.0 (mGy)</td>
</tr>
<tr>
<td>Active Chamber length</td>
<td>3.75 mm</td>
<td>3.75 mm</td>
</tr>
<tr>
<td>Chamber correction factor</td>
<td>7.0</td>
<td>7.0</td>
</tr>
<tr>
<td>Isocenter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measured 1 (mGy)</td>
<td></td>
<td></td>
</tr>
</tbody>
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**CTDI at Isocenter in position 12 o'clock**
- Primary Reviewer: [Name]
- Reviewer ID: [ID]
- Action(s) Required or Notes: [Notes]

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<tbody>
<tr>
<td>CTDI Normal 12 o'clock position in phantom (mGy)</td>
<td>DLP(mGy)</td>
<td>DLP(mGy)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.17</td>
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</table>

**CTDI at 12 o'clock position in phantom**
- Primary Reviewer: [Name]
- Reviewer ID: [ID]
- Action(s) Required or Notes: [Notes]

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The National Lung Screening Trial

- CT Technique:
  - Non-contrast, helical
  - Standardization quite complicated
  - Average effective dose of NLST CT scan = 1.4 mSv

- Context:
  - US citizen average effective dose = 3mSv/year
  - 1/2 of the dose

The National Lung Screening Trial: Early Results

- LDCT group had more detected cancers and more early stage cancers than X-ray group
- We are not so surprised...
The National Lung Screening Trial: Early Results

- LDCT group had more detected cancers and more early stage cancers than X-ray group
- We are not so surprised...
- “Significant reduction in lung cancer mortality” announced in November 2010 by NCI
National Lung Screening Trial: Abstract Data

LDCT

• 247 lung cancer deaths per 100,000 person-yrs

-20% relative reduction in mortality from lung cancer in LDCT group compared to Chest X-ray group (95CI, p=0.004)

-6.7% fewer deaths from any cause in LDCT group compared to Chest X-ray group (95CI, p=0.02)

Chest X-Ray

• 309 lung cancer deaths per 100,000 person-yrs

NLST, NEJM Aug 2011. 365;5:395-409
# National Lung Screening Trial: The Numbers

<table>
<thead>
<tr>
<th></th>
<th>LDCT Deaths</th>
<th>X-Ray Deaths</th>
<th>Difference of 121 = 6.1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Cancer:</td>
<td>427*</td>
<td>503*</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular:</td>
<td>486</td>
<td>470</td>
<td></td>
</tr>
<tr>
<td>Respiratory Illness:</td>
<td>175</td>
<td>226</td>
<td></td>
</tr>
<tr>
<td>Complic. Med/Surg:</td>
<td>12†</td>
<td>7†</td>
<td></td>
</tr>
<tr>
<td>Other:</td>
<td>349</td>
<td>343</td>
<td></td>
</tr>
<tr>
<td>Unknown:</td>
<td>12‡</td>
<td>7‡</td>
<td></td>
</tr>
<tr>
<td><strong>Total Deaths:</strong></td>
<td><strong>1865</strong></td>
<td><strong>1998</strong></td>
<td></td>
</tr>
</tbody>
</table>

National Lung Screening Trial: False Positives

**LDCT**
- False Positives: 96.4%

**Chest X-Ray**
- False Positives: 94.5%

(NLST, NEJM Aug 2011. 365;5:39)
National Lung Screening Trial: “Overdiagnosis”

<table>
<thead>
<tr>
<th>LDCT</th>
<th>Chest X-Ray</th>
</tr>
</thead>
<tbody>
<tr>
<td>• BAC Stage 1A = 83</td>
<td>• BAC Stage 1A = 17</td>
</tr>
</tbody>
</table>
National Lung Screening Trial

- Lung cancer screening: not ready for primetime

- Why?
  - False Positives - risks outweigh benefits?
  - Overall mortality needs to be further investigated
  - Must assess impact/meaning of overdiagnosis further
  - Must assess morbidity associated with screening, as well as emotional burden on patients
  - Determine Cost and who will pay
  - Probably “okay” on radiation front
Effective Doses of Common Exams:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Effective dose (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA chest radiograph</td>
<td>0.01-0.02</td>
</tr>
<tr>
<td>CT Head</td>
<td>2.0</td>
</tr>
<tr>
<td>Lumbar Spine radiograph</td>
<td>1.5</td>
</tr>
<tr>
<td>Bone Scan (Nuclear)</td>
<td>6.3</td>
</tr>
<tr>
<td>Chest CT</td>
<td>5-7</td>
</tr>
<tr>
<td>Abdomen CT</td>
<td>6-8</td>
</tr>
<tr>
<td>Chest CTA</td>
<td>8-15</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
<td>8-17</td>
</tr>
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</table>
Lung Cancer Screening

- Where do we go from here?
- Use current guidelines for abnormalities detected on CT
# Current Guidelines

**Recommendations for Follow-up and Management of Nodules Smaller than 8 mm Detected Incidentally at Nonscreening CT**

<table>
<thead>
<tr>
<th>Nodule Size (mm)*</th>
<th>Low-Risk Patient†</th>
<th>High-Risk Patient‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4</td>
<td>No follow-up needed§</td>
<td>Follow-up CT at 12 mo; if unchanged, no further follow-up‖</td>
</tr>
<tr>
<td>&gt;4–6</td>
<td>Follow-up CT at 12 mo; if unchanged, no further follow-up‖</td>
<td>Initial follow-up CT at 6–12 mo then at 18–24 mo if no change‖</td>
</tr>
<tr>
<td>&gt;6–8</td>
<td>Initial follow-up CT at 6–12 mo then at 18–24 mo if no change</td>
<td>Initial follow-up CT at 3–6 mo then at 9–12 and 24 mo if no change</td>
</tr>
<tr>
<td>&gt;8</td>
<td>Follow-up CT at around 3, 9, and 24 mo, dynamic contrast-enhanced CT, PET, and/or biopsy</td>
<td>Same as for low-risk patient</td>
</tr>
</tbody>
</table>

Note.—Newly detected indeterminate nodule in persons 35 years of age or older.

* Average of length and width.

† Minimal or absent history of smoking and of other known risk factors.

‡ History of smoking or of other known risk factors.

§ The risk of malignancy in this category (<1%) is substantially less than that in a baseline CT scan of an asymptomatic smoker.

‖ Nonsolid (ground-glass) or partly solid nodules may require longer follow-up to exclude indolent adenocarcinoma.

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MacMahon H et al. Guidelines for Management of Small Pulmonary Nodules Detected on CT Scans: A Statement from the Fleischner Society Radiol 2005
Lung Cancer Screening

• Where do we go from here?

• Use current guidelines for abnormalities detected on CT

• Await NELSON Trial results, ItalaLUNG Trial
Conclusions:

- In context of NLST:
  - Reviewed Imaging Techniques
  - Reviewed Current Data on Radiation Doses from medical imaging
  - Reviewed Appearances of False Positives
  - Reviewed Pathology that may be cause “Overdiagnosis”
Thank you for your attention!