OBJECTIVES

• To introduce LDCT lung screening and guidelines.
• Discuss rationale for present recommendations.
• Discuss advantages and risks
• Take home points
A 64 year old male presents to your office for yearly wellness check-up. He is in general good health with a history of hypertension well controlled with medication. There is no history of previous cancer. The patient however has a history of smoking cigarettes 1 pack/day for 33 years however quit 5 years ago. Do you recommend chest screening?

- Lung cancer screening is controversial.
- Risks remain a concern.
- Can results of large studies be duplicated in clinical setting?
Lung cancer needs to be fought on two fronts.

1) Cigarette smoking cessation.
2) Early detection

LUNG CANCER

- 13% of all new cancers
- 27% of all cancer deaths

- 2015: 221,200 new cases
  115,610 – MEN
  105,590 – WOMEN

- Estimated deaths – 158,040

http://www.cancer.org/
Last Revised: 03/04/2015
LUNG CANCER

• INVOLVES MOSTLY AN OLDER POPULATION.
• 2/3 - 65 YEARS OR OLDER
• < 2 % UNDER AGE OF 45
• AVERAGE AGE AT DIAGNOSIS 70 YEARS.

http://www.cancer.org/
Last Revised: 03/04/2015

LUNG CANCER

• WHEN FOUND MAJORITy NOT LOCALIZED.
• OVERALL SURVIVAL RATE IS < 16%

EARLIER STAGE DIAGNOSIS FAVORS A BETTER PROGNOSIS

<table>
<thead>
<tr>
<th>Percent of cases by stage</th>
<th>5 Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOCALIZED</td>
<td>16 %</td>
</tr>
<tr>
<td>REGIONAL</td>
<td>22 %</td>
</tr>
<tr>
<td>DISTANT</td>
<td>57 %</td>
</tr>
<tr>
<td>UNKNOWN (unstaged)</td>
<td>5 %</td>
</tr>
</tbody>
</table>

• THAT’S WHY WE NEED TO DEVELOP A SCREENING TOOL FOR EARLY DIAGNOSIS.

LUNG CANCER

WORLD WIDE PROBLEM

Need an effective screening test to find lung cancer at early stage.

EFFECTIVE OR GOOD SCREENING EXAM

DISEASE
- Disease constitutes significant health problem with significant morbidity and mortality.
- Available treatment which improves prognosis with early detection.

EXAM
- Need to find disease in pre clinical state.
- Be safe and of reasonable cost.
- Improved outcomes and be widely available.
BACKGROUND

• 1970’s RCT - to evaluate screening utilizing chest x-ray and/or sputum cytology.
• No decrease in mortality demonstrated.
• At that time ACS and USPTF did not recommend screening.

BACKGROUND

• Investigators turned to CT for lung cancer screening.
• Conventional CT was not used for screening due to concerns of radiation dose.
• Advances in both hardware and software made low dose CT a viable modality for lung screening.
BACKGROUND

• Uncontrolled studies were performed in Europe, Japan and the United States.

• **Results:** 1) Low Dose CT was feasible
  2) Harms of screening were minimized when protocols for surveillance imaging were followed.

BACKGROUND

• Early uncontrolled studies showed increase in **survival rates**.
• Vulnerable to Lead Time bias.
• Randomized control trials needed.
• Need to show decrease in mortality.
National Lung Screening Trial (NLST)

- Sponsored by the National Cancer Institute.
- Investigated 2 methods of detecting lung cancer.
- Evaluated chest x-ray and Low Dose CT.
- Objective: To evaluate whether lung cancer mortality reduced with LDCT or Chest x-ray.

National Lung Screening Trial (NLST)

- Ran from 2002 to 2007.
- 53,457 volunteers.
- Participants randomly placed in LDCT or Chest x-ray protocol.
- Age ranged from 55 to 74 years old.
- Each had smoking history.
- Each agreed to baseline exam followed by 2 annual follow-up studies.
National Lung Screening Trial (NLST)

• In 2010 National Cancer Institute reported to the medical community that NLST trial was terminated.
• Study terminated because end point was reached – LDCT reduced death.
• Results - 20% reduction in lung cancer mortality with LDCT vs chest x-ray.

COMPARATIVE MORTALITY REDUCTION

<table>
<thead>
<tr>
<th>Modality</th>
<th>Number needed to be screened (NNS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Dose Chest CT</td>
<td>320</td>
</tr>
<tr>
<td>Mammogram (50 – 59)</td>
<td>351</td>
</tr>
<tr>
<td></td>
<td>(50 – 70)</td>
</tr>
<tr>
<td></td>
<td>400</td>
</tr>
<tr>
<td>Sigmoidoscopy</td>
<td>817</td>
</tr>
</tbody>
</table>
PATIENT PROTECTION AND AFFORDABLE CARE ACT

USPTF – July 2013 posted revised draft recommendations.

• Draft recommendation: to give lung cancer screening with LDCT a grade B recommendation for high risk individuals with appropriate smoking history.

SIGNIFICANCE:

• Grade B – High certainty that the net benefit is moderate.
• PPACA mandates a recommendation of B or above from USPTF requires private insurers must cover the procedure.

Centers for Medicare & Medicaid Services (CMS)

• 02 – 05 – 2015 issued an announcement.

• Medicare will cover lung cancer screening with LDCT once per year for Medicare recipients who meet the following criteria:

  • Age 55 – 77.
  • Either current smokers or have quit smoking within last 15 years.
  • Tobacco smoking history of at least 30 pack years.
  • Must receive a written order from a physician or qualified non-physician practioner.

• Coverage includes a visit “for counseling and shared decision-making on the benefits and risks of lung cancer screening”.

CMS.gov
Since NLCT report of mortality reduction with LDCT multiple organizations have issued guidelines.

- Majority follow eligibility requirements for high risk patients defined by the NLST.
- Majority recommend screening be performed by high quality, high volume, multidisciplinary lung screening programs.

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**Table 3. Guidelines for Lung-Cancer Screening with Low-Dose CT.**

<table>
<thead>
<tr>
<th>Organization</th>
<th>Year</th>
<th>Target Population**</th>
<th>Recommendation</th>
<th>Enforcement of Shared Decision Making</th>
<th>Additional Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Academy of Family Physicians</td>
<td>2013</td>
<td>Persons with a high-risk of lung cancer on the basis of age and smoking history</td>
<td>Insufficient evidence to recommend screening</td>
<td>No</td>
<td>Screening cannot be recommended on the basis of a single study conducted in major medical centers.</td>
</tr>
<tr>
<td>American Association for Thoracic Surgery</td>
<td>2012</td>
<td></td>
<td></td>
<td></td>
<td>Not specified</td>
</tr>
<tr>
<td>Tier 1</td>
<td>Persons 55-79 yr of age with a history of smoking 20 or more pack yr or current smoking</td>
<td>Recommendation on the basis of data from the NLST trial</td>
<td></td>
<td></td>
<td>Screening should be conducted at facilities that are capable of managing indeterminate and positive screens and that are able to efficiently transition patients to appropriate follow-up.</td>
</tr>
<tr>
<td>Tier 2</td>
<td>Persons 50-79 yr of age with a history of smoking 20 or more pack yr or current smoking</td>
<td>Recommendation on the basis of data from randomized trials</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tier 3</td>
<td>Persons who meet the NLST criteria</td>
<td>Consensus opinion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>American College of Chest Physicians, American Lung Association, American Thoracic Society</td>
<td>2012</td>
<td>Persons meeting the NLST eligibility criteria</td>
<td>Grad A recommendation (a conditional recommendation for moderate-strength evidence that the screening should be offered)</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>American College of Radiology</td>
<td>2012</td>
<td>Persons meeting the NLST eligibility criteria</td>
<td>Grad B recommendation (moderate certainty of moderate net benefit)</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>American Cancer Society**</td>
<td>2013</td>
<td>Persons meeting the NLST criteria</td>
<td>Consensus opinion</td>
<td>Yes</td>
<td>Screening should be performed only if there is access to a high-quality multidisciplinary lung screening program.</td>
</tr>
<tr>
<td>National Comprehensive Cancer Network**</td>
<td>2012</td>
<td>Persons meeting the NLST eligibility criteria</td>
<td>Patients should have a full understanding of risks and benefits.</td>
<td>No</td>
<td>Multiple-slice screening programs will be helpful to ensure that patients will have access to CT scanning.</td>
</tr>
<tr>
<td>Category 1</td>
<td>Persons meeting the NLST eligibility criteria</td>
<td>High-level evidence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 2B</td>
<td>Persons aged 65 to 79 yr with a history of smoking ≥20 pack yr (current or 20 yrs of smoking)</td>
<td>Lower-level evidence and consensus opinion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>U.S. Preventive Services Task Force**</td>
<td>2013</td>
<td>Persons meeting the NLST eligibility criteria, with upper limit for age extended to 80 yr</td>
<td>Grad B recommendation (moderate certainty of moderate net benefit)</td>
<td>Yes</td>
<td>Moderate net benefit depends on accuracy of imaging interpretation.</td>
</tr>
</tbody>
</table>

*Eligibility criteria for the National Lung Screening Trial (NLST) were an age of 55 to 74 years, at least a 30-pack-year smoking history for current and former smokers, and cessation of smoking within the previous 15 years. The American College of Chest Physicians (ACCP) guidelines were based on the NLST data supplemented with evidence from the literature. The American College of Radiology (ACR) guidelines were based on the NLST data and additional evidence from the literature. The American Cancer Society (ACS) guidelines were based on the NLST data and additional evidence from the literature. The National Comprehensive Cancer Network (NCCN) guidelines were based on the NLST data and additional evidence from the literature. The U.S. Preventive Services Task Force (USPSTF) guidelines were based on the NLST data and additional evidence from the literature.**
Benefits and harms of LDCT

USPTF felt that the benefits of lung cancer screening with LDCT outweighed the harms.

Benefits

- Early detection of lung cancer.
- Decrease in deaths when compared to chest x-ray.
- Reduced morbidity from lung cancer treatment

Harms

- INCIDENTALOMAS
- FALSE POSITIVES
- OVERDIAGNOSIS
- RADIATION EXPOSURE
- CHANGE IN SMOKING BEHAVIOIR.
INCIDENTALOMAS

Numerous lesions can be seen within thyroid, breasts, mediastinum (i.e., coronary arteries), liver, kidneys, and adrenal gland.

• Follow up of these lesions if indicated is warranted.
• NLST noted other causes for mortality in their study.
• Cardiovascular and pulmonary diseases as well as other cancers were the largest group.

INCIDENTAL FINDINGS

COPD

CORONARY ARTERY CALCIFICATION
FALSE POSITIVES

• Approximately 1 in 4 LDCT will be positive.
• Of these 96% were found to be false positives.
• Majority resolved with one follow up CT.
• Previous films reduce false positives.
• Significant decrease in false positives after 2 screening rounds.

OVERDIAGNOSIS

• Identification of a disease that would not have become clinically evident or cause death in a patient’s lifetime.
  
  • May contribute to increase cost, anxiety and morbidity.
  • Difficult to measure.
  • Inherent in all screening programs.
  • Recent JAMA article suggests 18% overdiagnosis.
  • Need new imaging modalities or tumor markers to differentiate non aggressive vs aggressive tumors.

RADIATION RISK

- Estimate of Radiation harms comes from radiation exposure from atomic bombs.
- Data is extrapolated to low dose radiation common in medical procedures.

RADIATION RISK

- Scientific unit of measurement is millisievert (mSv).
- Average adult in US receives about 3 mSv per year from background radiation sources.
- Largest source is from Radon in homes (approximately 2 mSv).
## Radiation Risk

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Approx. Radiation Dose</th>
<th>Comparable to Background</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest x-ray</td>
<td>0.1 mSv</td>
<td>10 days</td>
</tr>
<tr>
<td>Chest CT</td>
<td>7 mSv</td>
<td>2 years</td>
</tr>
<tr>
<td>Low Dose Chest CT</td>
<td>1.5 mSv</td>
<td>6 months</td>
</tr>
<tr>
<td>Mammogram</td>
<td>0.4 mSv</td>
<td>7 weeks</td>
</tr>
</tbody>
</table>


- NLST Estimates suggest 1 cancer death per 2,500 screenings.
- NLST - benefit in preventing lung cancer outweighs radiation risk.

- 1 Death per 2,500 screenings vs 320 screenings to save 1 life.
SMOKING HABITS

WHAT ARE CONCERNS?

• If in screening program – can continue to smoke.
• Negative study - Motivation to quit reduced – Health Certificate Effect.
• Abnormal results or cancer diagnosis – might discourage quitting.
• Limited studies however suggests screening itself does not influence smoking patterns.
• Continued studies are needed to assess patient management
• ACR – accreditation requires counseling or available smoking cessation materials.

Benefit of chest CT over Chest X-ray
PULMONARY NODULE

- .1 TO 3 CM IN SIZE
- >3 CM IS CONSIDERED A MASS

- CHEST X-RAYS DEMONSTRATING NODULE = 0.2%
- CHEST CT DEMONSTRATING A NODULE = 8 – 51%

- MINIMUM AVERAGE SIZE WHICH CAN BE SEEN
- CHEST X-RAY = 8 – 10 MM
- CHEST CT = 3 – 4 MM

MINIMUM AVERAGE SIZE

8 – 10 mm 3 – 4 mm

http://radiopaedia.org/images/2364718
What if a nodule is found?

- Challenge for Radiologist is when to act on a finding.
- Effort is made to decrease number of false positives.
- Some lesions are readily identifiable as benign appearing.
- Difficulty are lesions that are not clearly benign.

*The most confident sign of a nodule being benign is lack of growth over 2 years.*

CALCIFIED PULMONARY NODULE

HAMARTOMA

Perifissural nodule

http://radiopaedia.org/articles/solitary-pulmonary-nodules

Not typical for benign nodule

Different criteria have been utilized in lesions which do not fall into benign category.

- Nodule size
- Density/Attenuation
- Nodule margins

Nodule size

NLST protocol (non-calcified nodule)

- Nodule 4mm or larger – considered positive.
- Nodule < 4mm is considered negative.
- Nodule 10mm or > aggressive workup with PET/CT or biopsy.

*There are modifications for management using margin or density of a nodule.*
Density/Attenuation

Nodule density/attenuation can also modify how a nodule is managed.

3 types:
- Solid
- Partly solid
- Ground glass

Semi solid nodules which persist on follow up imaging have been shown to be malignant more often when compared to solid or partly solid nodules.

SOLID NODULE

Malignancy rate 7%

PARTLY SOLID NODULE

Malignancy rate 63%

http://www.radiologyassistant.nl/en/p460f9fcd50637/solitary-pulmonary-nodule-benign-versus-malignant.html#i4610035e5dd5a

SOLID OR PART-SOLID NODULE

| Size       | Action                          | PET/CT            | Low suspicion | Suspicious
|------------|---------------------------------|-------------------|---------------|-------------
| < 6 mm     | Annual LDCT for 2 years / consider annual LDCT * |                  |               | Biopsy/resection |
| 6 – 8 mm   | LDCT in 3 months                | Low suspicion - LDCT in 3 months. If increases-surgical resection |               |             |
| > 8 mm     | PET/CT                          | Suspicious        |               | Biopsy/resection |

*until patient no longer eligible for definitive treatment
GROUND GLASS NODULE

Malignancy rate 18%


GROUND GLASS

< 5mm

LDCT in 12 months

Change in size or character

Resect

>5 - 10mm

LDCT in 6 months

Change in size or character

Stable

Resect

>10mm

LDCT in 3-6 months

Change in size or character

Stable

Resect

LDCT Quarterly for 6-12 months or biopsy or resect

www.cancernetwork.com/screening/low-dose-spiral-ct-screening-and-evaluation-solitary-pulmonary-nodule/page/0/2
MARGINS

- Nodules have been assessed on whether they are smooth, lobulated or spiculated.
- Smooth nodules generally benign.
- Spiculated nodule has a higher likelihood of being malignant vs solid nodule.
- Unfortunately there is overlap.
- Management may be modified on the basis of margin characteristics.

MALIGNANT NODULES

**Fleischner Society 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 ≥55 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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**CONCERNS/CRITICISMS**

- Complications from biopsies and pulmonary resection. Complications increase with age.

- Older adults were poorly represented.

- Interpretation of LDCT and management of abnormal findings can vary wildly. Can NLST study results be reproduced in the community setting?
Can results of NLST study be reproduced?

- ACR has developed guidelines for performance of CT as well as interpretation.
- LUNG-Rads reporting system developed to characterize findings and to standardize management strategies.
- ACR has developed facility accreditation process.
- In order to be given a certificate of accreditation a screening center must have mechanism in place for counseling or smoking cessation materials.

### LUNG - RADS

Lung CT screening Reporting And Data Systems

<table>
<thead>
<tr>
<th>CLASSIFICATION</th>
<th>FOLLOW - UP</th>
<th>CHANCE OF MALIGNANCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAT 0 INCOMPLETE</td>
<td>Need additional imaging Check for old films</td>
<td></td>
</tr>
<tr>
<td>CAT 1 NEGATIVE</td>
<td>Annual screening</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>CAT 2 BENIGN</td>
<td>Annual screening</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>CAT 3 PROBABLY BENIGN</td>
<td>6 month follow up</td>
<td>1 - 2 %</td>
</tr>
<tr>
<td>CAT 4 SUSPICIOUS</td>
<td>3 month follow up or PET/CT</td>
<td>Ranging from 4 - 15 %</td>
</tr>
</tbody>
</table>

CAT 4 has sub categories (4a, 4b, 4x)
How is LDCT performed

• Must be able to identify pulmonary nodules using lowest dose possible. ALARA
• NLST decreased tube current resulting in approximate dose of 1.4 msv
• There are continued attempts at decreasing the dose with new technology

How is LDCT performed

• The patient is placed in multi-detector helical CT scanner in the supine position.
• NO contrast is used
• NO special preparation
• Scanning time approx. 10 –20 seconds
Does LDCT Fill requirements of a good screening exam?

YES IT DOES

• Lung cancer is a significant health problem and we do have effective treatments if caught early enough.
• Has potential for detecting disease before it becomes clinically apparent.
• Relatively safe and of reasonable cost.
• Improved health outcomes.
• Widely available.

A 64 year old male presents to your office for yearly wellness check-up. He is in general good health with a history of hypertension well controlled with medication. There is no history of previous cancer. The patient however has a history of smoking cigarettes 1 pack/day for 33 years however quit 5 years ago. Do you recommend chest screening?

64 years old - (*55 – 74 years old)
No previous history of cancer
33 pack year
Quit smoking 5 years ago - (*smoked within 15 years)

• Meets NLST and USPTF criteria for screening
• Can be offered screening and harms and benefits discussed with the patient.
• Should be advised that screening is not an excuse to keep smoking.

*Screening criteria
TAKE HOME POINTS

• Lung cancer is the leading cause of cancer death in US.
• When found the majority of lung cancers are not localized.
• Overall 5 year survival rate is <16%.
• NLST compared screening with LDCT vs Chest x-ray.
• NLST results: There was a 20% reduction in lung cancer mortality with LDCT vs chest x-ray.

TAKE HOME POINTS

• USPTF Gave LDCT a Grade B rating.
• PPACA mandates that a Grade B or above rating requires private insurers must cover procedure.
• 2015 – Medicare will cover lung cancer screening if patient meets criteria:

CRITERIA
• Age 55 – 77
• Current smoker or has quit smoking within last 15 years
• At least a 30 pack year history
**TAKE HOME POINTS**

- Lung cancer screening is the only screening test shown to lower chance of dying from lung cancer.

- The benefit of screening is increased if you are in a higher risk category.

**THE END**