Outcomes in the NLST

Health system infrastructure needs to implement screening

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Disclosures

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  U01 CA196408  Integrated Molecular, Cellular and Imaging Characterization of Screen-detected Lung Cancer

  PCORI  Lung Nodule Surveillance Trial

  U01 CA037403  ECOG-ACRIN Early Detection and Diagnosis

  R01 LM011333  RUMI: A Patient Portal for Retrieving Understandable Medical Information

  T32 EB016640  Medical and Imaging Informatics Training Program
What have we learned & how do we translate this to practice?

- Eligibility
- Diffusion of screening across at-risk populations
- Standardized image acquisition & interpretation
- Data collection & longitudinal FU
- Smoking cessation
• 24% CT screens positive (nodule ≥ 4 mm) | PPV ~4%
• Few complications, especially in those with false [+] screens: < 0.1%
• 20% relative decrease in lung cancer-specific mortality
• 6.7% relative decrease in all-cause mortality
• NNS to prevent 1 death: 320
• Overdiagnosis estimated at 10-20%

Eligibility criteria: Age 55-74 | ≥ 30 pack yrs | Current or former smoker
For former smokers: YSQ ≤ 15 years

Ineligibility was infrequent in NLST

Referrals for ineligible patients is a current concern.

Risk to benefit ratio is unknown

Their screens are not a covered benefit
Goal: Enroll cohort representative of the eligible general population
Based on US Census Department’s Tobacco Use Supplement 2002-2004

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NLST</th>
<th>Tobacco Use Supplement</th>
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<tbody>
<tr>
<td>Male %</td>
<td>59.0%</td>
<td>58.5%</td>
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<td>Age group</td>
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<td>55-59 yr.</td>
<td>42.8%</td>
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<td>60-64 yr.</td>
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<td>Hispanic</td>
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<td>Current smoker</td>
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<td>Median pack years</td>
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Targeted enrollment efforts

- NLST initiated target enrollment plan after trial launch

  - 7 ACRIN sites based on accrual performance | regional demographics | resources
  - Worked with ACS, NCI Office of Communications, NMA
  - Costs of individual strategies varied from $146-749/enrollee
  - Target sites: 9.3% to 15.2% (p < 0.0001) vs. Non-target sites: 3.5% to 3.8% (p = 0.46)
  - Across ACRIN: 8.4% minority participants | 7 Sites accounted for 77.6% of minorities

- Start early
- Sustainable plan
**Standardized image acquisition**

- Detection task: Detect & follow *changes* in nodules of ≥ 4 mm diameter
- “Low dose” | Balance spatial resolution & noise
- Radiologist panel reviewed various images from various acquisitions
- CT physicist team individually calibrated each of 16 scanner platforms

![Thick section | smooth kernel](image1) ![Thin section | sharp kernel](image2)

Nodule characterization

- Image acquisition & reconstruction are critical to characterization
- Two methods of nodule characterization
  - Semantic (visual): Agnostic to technique | low reader agreement
  - Quantitative features: Reproducible | sensitive to acquisition
- Nodule classification: Size, location, consistency, margins, evolution
- To calibrate readers: Training module (image quality & nodule types)
- In retrospective analyses reader agreement was moderate (N = 9)
  - Nodule growth: $K$ coefficient = 0.55 (0.52 - 0.58)
  - Change in attenuation: $K$ coefficient = 0.31 (0.27 - 0.52)
  - High level FU (Actionable change): $K$ coefficient = 0.66 (0.63 – 0.69)

Quantitative analysis

- Volumetry & mass (segmentation & feature extraction)
- NELSON used VDT to determine screen result in solid nodules
  - Feature analysis by nodule consistency
    - Solid: Volumetry (~ 90%) | Reproducible & accurate | VDT ≤ 400 days ➔ suspicious
    - Subsolid: SW only recently been developed for nodule segmentation
    - Subsolid: Volume & VDT | mass & MDT [where MDT = Δt x (In (2))/ln (M2/M1)]
    - Pairwise comparisons of CAD vs. Expert: K coefficient 0.54-0.72

Gietema HA. Radiology 2006; 24:251-257.
Take home for nodule characterization

- Nodule features are important in classifying benign vs. malignant
  - Semantic | Computational | Some combination

- Semantic features are relatively insensitive to technique but have only moderate inter-reader agreement
  - Illustrated lexicons will be critical to “calibrating” across centers

- Computer vision features are sensitive to acquisition & reconstruction
  - Reduce variance
  - Measure reproducibility & accuracy across heterogeneous datasets
Data element collection

- Baseline risk of lung cancer: Eligibility, smoking, health status
- Screen results: [-] | [+] short term FU | [+] definitive FU
- Follow-up tests & results
  - Types of diagnostic testing performed: Histology | stage
  - Treatment approaches & complications
  - Outcomes: Lung cancer and all-cause mortality
  - Deaths: Lung cancer | management-related | other
- Other:
  - Medical resource utilization and costs
  - Tissue acquisition: Tumor | ACRIN (blood, sputum, urine)
Challenges to data collection

- **NLST experience**
  - Vital status known for 97% of CT arm | 96% of CXR arm
  - Diagnosis | Treatment completed at *non-NLST* sites
  - LTF: Relocation | Lack of contact information

- **Alternatives to direct participant contact**
  - Google searches
  - Other personal contacts
  - National Death Index

Must have reliable staff to maintain contact & track patients

- Variable evidence on screening as motivational tension
- Smoking cessation is significantly associated with positive screen

<table>
<thead>
<tr>
<th>Screening Result</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Referent group</td>
<td></td>
</tr>
<tr>
<td>Positive screen</td>
<td>Stable from previous</td>
<td>0.785 (0.706 to 0.872)</td>
</tr>
<tr>
<td>Positive screen</td>
<td>New or changed</td>
<td>0.663 (0.607 to 0.724)</td>
</tr>
</tbody>
</table>

- 5As: Ask, Advise, Assess, Assist and Arrange (FU]
- Examined PCP 5As practices and smoking cessation rates post-screen
- Frequency of PCP interventions:
  - 77.2% ask | 75.6% advise | 63.4% assess | 56.4% assist | 10.4% arrange
- Less intensive interventions were not associated with increased quit rates
- OR for assist = 1.40 (1.21-1.63) | for arrange = 1.46 (1.19 – 1.79)

Implications for national implementation

- Ensure screen eligibility
- Adequate representation of at-risk minorities
  - Plan early for targeting special populations
  - Establish more robust mechanisms within communities of interest
- Standardized acquisition: low dose & enable computer vision
- Interpretation: Standardize terminologies using illustrated lexicons
- Longitudinal follow-up: Dedicated program staff & tracking SW
- Incorporate smoking cessation into screening program
Thanks!
Challenges to data collection

- **Screening and treatment locations**
  - NLST sites performed screening
  - *Other* facilities completed diagnosis and/or treatment

- **Lost to FU**
  - Vital status known for 97% of CT arm | 96% of CXR arm
  - Relocation | Lack of reliable contact information

- **Alternatives to direct participant contact**
  - Other personal contacts
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These challenges hamper documentation of screening benefit
<table>
<thead>
<tr>
<th>NLST CT Technique Chart</th>
<th>Siemens 64 Sensation</th>
<th>GE – VCT (64)</th>
<th>Toshiba Aquilion</th>
<th>Philips MX8000 16 slice</th>
</tr>
</thead>
<tbody>
<tr>
<td>kV</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>Gantry rotation time</td>
<td>0.50 sec</td>
<td>0.50 sec</td>
<td>0.50 sec</td>
<td>0.5 sec</td>
</tr>
<tr>
<td>mA (Regular – Large patient values)</td>
<td>50-100</td>
<td>50-100</td>
<td>80-160</td>
<td>75-150</td>
</tr>
<tr>
<td>mAs (Reg – Lg)</td>
<td>25-50</td>
<td>25-50</td>
<td>40-80</td>
<td>37.5-75</td>
</tr>
<tr>
<td>Scanner effective mAs (Reg – Lg)</td>
<td>25-50</td>
<td>27-53</td>
<td>26.7-53.3</td>
<td>25-50</td>
</tr>
<tr>
<td>Detector collimation (mm) - T</td>
<td>0.6 mm</td>
<td>0.625</td>
<td>2 mm</td>
<td>.75 mm</td>
</tr>
<tr>
<td>Number of active channels - N</td>
<td>32</td>
<td>64</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Detector configuration – N · T</td>
<td>32 x 0.6 mm</td>
<td>64 x 0.625</td>
<td>16 x 2 mm</td>
<td>16 x .75 mm</td>
</tr>
<tr>
<td>Collimation (operator console)</td>
<td>64 x 0.6 mm</td>
<td>.625/.984/39.37</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Table incrementation (mm/rotation) - I</td>
<td>19.2 mm</td>
<td>39.37 mm</td>
<td>48 mm</td>
<td>18 mm</td>
</tr>
<tr>
<td>Pitch ([mm/rotation]/ beam collimation – I/NT</td>
<td>1.0</td>
<td>0.984</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Table speed (mm/second)</td>
<td>38.4 mm/sec</td>
<td>78.74 mm/sec</td>
<td>96 mm/sec</td>
<td>36 mm/sec</td>
</tr>
<tr>
<td>Scan time (40 mm thorax)</td>
<td>11 sec</td>
<td>5.1 sec</td>
<td>4.2 sec</td>
<td>11 sec</td>
</tr>
<tr>
<td>Nominal reconstructed slice width</td>
<td>2 mm</td>
<td>2.5 mm</td>
<td>2 mm</td>
<td>2 mm</td>
</tr>
<tr>
<td>Reconstruction interval</td>
<td>1.8 mm</td>
<td>2.0 mm</td>
<td>1.8 mm</td>
<td>1.8 mm</td>
</tr>
<tr>
<td>Reconstruction algorithm</td>
<td>B30</td>
<td>STD</td>
<td>FC 10</td>
<td>B or C</td>
</tr>
<tr>
<td># Images/data set (40 cm thorax)</td>
<td>223</td>
<td>200</td>
<td>223</td>
<td>223</td>
</tr>
<tr>
<td>CTDI vol (Dose in mGy)</td>
<td>1.9 – 3.8 mGy</td>
<td>2.2 – 4.4 mGy</td>
<td>2.7 – 5.4 mGy</td>
<td>1.9 – 3.8 mGy</td>
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= Modifiable parameters on technologist console
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