PCF Quantitative Imaging Workshop XVI:
Lung Cancer, COPD and Cardiovascular Disease –
On the Cusp of Transformation

• Welcome!
  • Why are we here?
    • What is needed?
    • What is possible?
  • What will we decide to do?
NELSON - 10-year Mortality Reduction

- The Dutch-Belgian NELSON Trial evaluated LDCT screening compared to usual care in a population-based trial of high-risk current and formers smokers.
- Randomized-15,792, 50-74 years of age, greater than 10 cigarettes/day for >30 years or >15 cigarettes/day for >25 years, smoking cessation <= 10 years.
- LDCT performed at baseline 1, 3, 5.5 years later.
- LDCT can significantly reduce deaths from lung cancer by at least 26% in men and up to from 39-61% in women.
- Harms reported in screening arm as modest.

De Koning HJ et al. Effects of Volume CT Lung Cancer Screening: Mortality Results of the NELSON Randomised-Controlled Population Based Trial. IASLC WCLC 2018. PL02.05
Frequency of a positive result and cases of lung cancer diagnosed within 12 mo of baseline enrollment

**I-ELCAP: 73 Institutions; 60,869 Participants & 131,942 CT scans**

Curative Screening Requires Precise Imaging

<table>
<thead>
<tr>
<th>Max Nodule Diameter</th>
<th>+1mm Volume Change %</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.00</td>
<td>59%</td>
</tr>
<tr>
<td>7.00</td>
<td>49%</td>
</tr>
<tr>
<td>8.00</td>
<td>42%</td>
</tr>
<tr>
<td>9.00</td>
<td>37%</td>
</tr>
<tr>
<td>10.00</td>
<td>33%</td>
</tr>
</tbody>
</table>
QIBA LDCT Conformance Phantom

• Total Cost- $250 shipped
• Integrated with automated software for rapid data acquisition (<5 min)
• Output is a structured report that evaluates fundamental imaging properties using machine vision via web (< 30 min)
QIBA had proposed standardized process for accurate screening nodule measurement.

Quality process touches the entire imaging chain: acquisition devices, technologists, radiologists, reconstruction software, and image analysis tools involved in screening.

RSNA has launched a cloud-based quality service to measure conformance for optimal image acquisition.

PCF has funded performance analysis with RSNA across global locations.

IASLC may partner to scale this quality process globally.
Slow US Screening Implementation

- CMS reimbursement reduced, raising concerns with access and disparities
- Concerns with medical radiation harms receding
- Concerns with “false-positivity” but volumetric approaches lower false positivity rates from 28%-3%
- Concerns with over-diagnosis but at 10 yrs. follow-up of NLST demonstrate rate is <3%
- LDCT image quality inadequate in 40% of VA screening pilot cases
- Slow uptake allowing quality measures to emerge
Thought Experiment  Lung Cancer Deaths

2019-24 Global LDCT Impact

Global Lung Cancer Deaths – 1.76 Million in 2018
(https://www.who.int/news-room/fact-sheets/detail/cancer)
Without screening about 10% Stage I rate -of them 50-75% are cured then from 88K-132K/yr. cured
With screening, perhaps 50-75% Stage I rate- of them 50-75% are cured the from 432K-990K/yr. cured
Theoretical 5-year screening impact could be to save an additional 1.76-4.29 million lives across the world
US Healthcare Costs, 2017

The United States spends more on health care than any other country in the world, and a large share of that spending comes from the federal government. In 2017, the United States spent about $3.5 trillion, or 18 percent of GDP, on health expenditures – more than twice the average among developed countries.
UN Health Ministers Declaration, 2011:

“Within the next two decades, 50% of the world’s economic productivity will be required to support the healthcare costs of people with chronic diseases derived from life style choices. The impact of obesity, tobacco, diet and related personal habits will disrupt the social order as we know it.”

<table>
<thead>
<tr>
<th>Disease</th>
<th>Rank 1990</th>
<th>Rank 2016</th>
<th>% Change</th>
<th>Deaths 2016*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Heart Disease</td>
<td>1</td>
<td>1</td>
<td>-19.5</td>
<td>544.8</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>2</td>
<td>2</td>
<td>13.6</td>
<td>191.5</td>
</tr>
<tr>
<td>COPD</td>
<td>4</td>
<td>3</td>
<td>69.8</td>
<td>163.8</td>
</tr>
<tr>
<td>Alzheimer</td>
<td>7</td>
<td>4</td>
<td>78.7</td>
<td>105.3</td>
</tr>
<tr>
<td>Colon Cancer</td>
<td>6</td>
<td>5</td>
<td>15.7</td>
<td>79.3</td>
</tr>
</tbody>
</table>

State of US Health, 1990-2016, JAMA 319:1444, 2018 (* #s in 1000s)
Differences: Smokers & Nonsmokers

Cause Specific Mortality Rates

Why isn’t the disease, Tobacco syndrome?

*CPS II Data Thun et al 1997*
• Identify bottlenecks with innovative solutions to safely implement effective CT based management with self evolving continuous process improvement

• Included integration of optimal quantitative imaging methodology within an efficient clinical workflows

• Leverage the full extent of tobacco injury evident on thoracic CT field-of-view (COPD, CAD)

• Reframe screening as for tobacco-injury assessment encounter to ensure optimal preventive management with smoking cessation approaches & for other lifestyle changes to reduce risk of premature tobacco-related mortality

*Supported over many years by IASLC
Molecular Effect of Tobacco on Lung Tissue

Contribution of the Inflammatory Response in Chronic Injury to Lung CA

Carcinogenic Exposure

- Normal Epithelium
- Cell Injury
- Initiated Cell
- Clonal Expansion
- Invasion Competence

Inflammation

- 5-LO
- COX-2
- Cytokines

IL1B Effect on CVD and Lung Cancer

• Phase III randomized Cantos trial of antibody to IL-1B to treat people with prior MI and elevated risk of CVD
• Active arm had objective reduction in CVD occurrence and reduced mortality with lung cancer
• Article suggests that inflammasome contributed to CVD and lung cancer pathogenesis

Ridker PM et al NEJM 377: 1119-1131, 2017
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• Progress Snap-shop - Long-term results reported this year: NELSON, MILD, Hitachi City, NLST—all showing durable, objective, significant mortality reduction benefit.

• Results of PCF supported studies to be reported by QIBA-Accumetra

• Components of Screening Improving: diagnostic work-ups more efficient; surgical results improving, frequency of detecting COPD/CAD

• Screening software tools VA and Siemens emerging

• Higher resolution commercial CTs as well as prototype now available; also new software tools including AI emerging

• Progress with IASLC LDCT image archive
Impact of 3 Leading Causes of Death

- Coronary Artery Disease, Lung Cancer, COPD account for 44% of the mortality related to the top 25 causes of premature death
- These three are the leading causes of premature death across the world
- Lung cancer accounts for only 26% of this mortality burden
- To address NCD Crisis we need integrated care of all thoracic tobacco-induced diseases

Mulshine JL Am J Publ Health, Oct, 2018
Promoting Trust Between Patients and Physicians in the Era of Artificial Intelligence

• Trust
  • Competency
  • Motive
  • Transparency

“By affirming the foundational importance of trust to health outcomes and engaging in deliberate systems transformation, the benefit of AI could be realized while strengthening patient-physician (subject-clinician) relationships.”

Nundy S, Montgomery T, Wachter RM. JAMA 322:497, 2019
Impact of Patient-donated Specimens

Cell Lines

33,207 Publications

4,700 Citing Patents

1,232,329 Citations

422 Linked Clinical Trials

1,019 Supporting Funders

Cell Line Supplement Revisited, 2019
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• What will we decide to do?
Karma in Crystal City