Prevent Cancer Foundation
"Quantitative Imaging Workshop XV: Lung Cancer, COPD and Cardiovascular Disease - Quality is a Gateway to Deep Learning"

James L. Mulshine, MD
Co-Chair, QIIBA Small Nodule Profile Committee
Assoc Director, Institute for Translational Research
Chair, IASLC Screening and Early Detection Committee
Vice Chair, Scientific Director, Prevent Cancer Foundation
AND A SPECIAL THANKS ALSO GOES TO THE

Carolyn R. “Bo” Aldigé
Prevent Cancer Foundation

STEERING COMMITTEE

Chair:

• James L Mulshine, *Rush University*

Members:

• Laurie Fenton Ambrose
  *Lung Cancer Alliance*
• Ricardo S. Avila
  *Accumetra, Inc*
• Daniel C. Sullivan
  *Duke University*
• Elisha Malanga
  *COPD Foundation*
• Raul San Jose Estepar
  *Brigham&Women’s*
• David F. Yankelevitz
  *Mount Sinai Med. Center*
10-year Mortality Reduction with NELSON

- 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
Comparison NLST and NELSON Cancer Detection and Stage I Rates T0, T1

NLST

• ROUND 1 NO. OF CA/TOTAL SCREENED 168/24,715 (0.67%)
• ROUND 2 NO. OF CA/TOTAL SCREENED 211/24,102 (0.87%)

• Stage 1/All Cases Total- 104/165 (63%)

NELSON

• ROUND 1 STAGE I/ALL DETECTED CA 40/7289 (0.5%)
• ROUND 2 STAGE I/ALL DETECTED CA 57/7289 (0.8%)

• Stage 1/ All CA Cases Total- 42/57 (73.7%)

Improved LCA & Mortality Prediction Accuracy: Survival Models of SA CT Image Measurements
A. Schreuder et al. WCLC, 2018

• Analysis on 17 features including CAD measures of atherosclerosis and COPD
• Analyzed large number of NLST cases with 7 yr f/u
• Conclusion: CAD measures of emphysema and atherosclerosis and CAD-supported pulmonary nodule annotations are of added value for predicting lung cancer and mortality. These new models may be used to further personalize lung cancer CT screening follow-up protocols
Societal Impact of Screening Implementation

• Our goal is for better, cheaper, faster implementation of cloud-enabled LDCT screening of the three leading causes of tobacco-related premature death

• How do we ensure that the populations that are at the highest risk have access to these services

• How do we make sure these services are supported so that continued rapid evolution and dissemination are ensured?
Progress Check From QIW XIV

Recommendation from Technical Breakout was to assemble preliminary data and submit a grant on a pivotal trial showing the benefits of applying advanced methods for lung nodule change measurements versus the current standard of care

• Align RSNA/QIBA and Workshop participants activities regarding CT image quality
Moving to the Cloud

• Economical, global, easily accessible, cloud-centered services
• QIBA Profile Conformance Testing to validate appropriate CT screening performance to reliably measure pulmonary nodule volume change
• Cloud can serve as a central (infinitely scalable), vendor-neutral resource to enable nodule measurement precision with hosted tools
• Data aggregated on the cloud services as a data quality resource to monitor delivered CT performance
• Vast compacity to monitor data security
QIBA Dedicated LDCT Conformance Phantom

• Lost 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)
Potential IASLC Partnership with QIBA to Enhance Accuracy of Screening

• 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
• Should IASLC to partner to accelerated and scale this quality process globally to reduce potential harms and cost of CT screening?
The IASLC Early Lung Image Confederation

1. Develop an IASLC hub and spoke system.
   - ELIC Software System
   - ELIC Governance

2. Provision of Global high-quality screening services.
   - CT Image Quality Pilot Project
   - Education & Training Pilot
   - Image Archive to support AI progress
ELIC: Enabling QI as an Tool for Clinical Decision Support for Screening & Therapeutic Management

• Precision & consistency required for QI integration either for routine care/or trials is vastly more demanding than for routine qualitative imaging
  • ELIC could be used to disseminated QI, workflow friendly profiles, economical QI tools (simple phantoms evaluated with integrated software analysis) are crucial to enable QI quality and can be delivered via cloud-based processes
  • ELIC archive could support software tool development for efficient lung nodule detection and characterization as well as screen for other tobacco-induced diseases of the thorax
  • ELIC could support accelerated tool development to monitor RX response through the collaborative development of an integrated research and care cloud environment
Uptake with Screening

• In 2015 of the 6.8 million U.S. smokers eligible for LDCT screening, only 262,700 received it.
• According to the study’s authors, their findings underscore the need to educate clinicians and smokers about the benefits and risks of LDCT to engage in informed decision-making conversations with clinicians.

*Jemal A, Fedewa SA. JAMA Oncol. 2/2/17*
CDC Fast Facts 2017

• Smoking is the leading cause of preventable death.
• Cigarette smoking is responsible for more than 480,000 deaths per year in the United States, including more than 41,000 deaths resulting from secondhand smoke exposure. This is about one in five deaths annually, or 1,300 deaths every day.
• On average, smokers die 10 years earlier than nonsmokers
• If smoking continues at the current rate among U.S. youth, 5.6 million of today’s Americans younger than 18 years of age are expected to die prematurely from a smoking-related illness. This represents about one in every 13 Americans aged 17 years or younger who are alive today.
Impact of Non-Communicable Disease

**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>Isch. Hrt. D is</td>
<td>1</td>
<td>1</td>
<td>-19.5</td>
<td>544.8</td>
</tr>
<tr>
<td>Lung CA</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 CA</td>
<td>6</td>
<td>5</td>
<td>15.7</td>
<td>79.3</td>
</tr>
</tbody>
</table>
CT Technological Opportunities for COPD

Nodularity
Airway / Vasculature Phenotypes
Pleural Thickening

Emphysema Phenotypes
Calcium Scoring

Effective Linear Attenuation Coefficient
Density

Morphology & Shape
Size

Edge detection

Dynamic (INSP EXP)
Registration

Deformation
Gas trapping
Parenchyma Inhomogeneities

R. Estepar, 2015
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
LDCT Screening As A Health Encounter

• Preventive care for major smoking-related diseases is a significant opportunity for lifestyle changes to reduce risk
• Annual CT-based tobacco health encounter could bundle coaching on smoking cessation along with other relevant wellness information into an efficient ambulatory prevention encounter addressing major modifiable risk
• LDCT can be developed as a quantitative health evaluation tool to guide management for asymptomatic, tobacco-exposed individuals assessing for CAD, lung CA and COPD
• For success, collaboration across leading professions—primary care, cancer, cardiology, pulmonary, nursing, behavioral scientists & others is essential to optimally integrate care and support healthy life styles
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
Impact of Tobacco Control Efforts on Lung Cancer Deaths Among U.S. Males, 1975-2000

S Moolgavar et al. JNCI, 2012
Conclusion

• Imaging technology is rapidly evolving.
• The process optimization routine clinical QCT is emerging rapidly to allow for more robust quantitative imaging to integrate into routine screening management processes
• A quality screening acquisition process can be disseminated rapidly via the cloud within workflows across the US and the world at modest expense
• International collaboration such as with ELIC can rapidly assemble outcomes from deployed QI processed images to improve the implementation of LDCT screening and enable multi-disciplinary care of early lung cancer and related tobacco-induced diseases