Optimizing imaging-based lung cancer screening

Alex Bui, PhD
Professor, Departments of Radiological Sciences, Bioengineering & Bioinformatics
David Geffen School of Medicine at UCLA

Sunday, October 7, 2018
The impact of lung cancer

Lung cancer is the single largest cause of cancer-related mortality in the United States and worldwide

- In 2018, approximately 154,000 related deaths are estimated due to lung cancer (*more than colon, breast, and prostate cancer deaths, combined*)
- Earlier detection is key to survival, with significant improvement in 5-year survival and curative chances if detected during Stage I/II (most lung cancers are detected in Stage III/IV)
More comprehensive characterization of at-risk populations through electronic health records (EHRs) and omics

Machine learning/data science approaches for earlier detection of actionable lung cancer (vs. indolent disease)

Operationalizing precision medicine techniques in real-world populations to maximize individual health outcomes

Several opportunities exist to improve imaging-based lung cancer screening

1. High false positive rate for detection (NLST positive screen rate of 24%, but positive screen rate <4%)
2. Concerns regarding overdiagnosis
3. Current guidelines for screening only cover up to a third of individuals who will develop lung cancer

Launched in 2002, the National Lung Screening Trial (NLST) aimed to understand to what extent low-dose computed tomography (LDCT) could reduce lung-cancer specific mortality.

- 53,000 participants in a prospective randomized controlled trial receiving imaging annually
- Study revealed that individuals who received LDCT had a 15-20% lower mortality from lung cancer than those who received chest x-rays
- NLST findings resulted in a recommendation from the US Preventative Task Force that is the basis for today's Medicare coverage of LDCT lung cancer screening
Enabling precision medicine in LAC-DHS

Risk stratification is essential to implementing lung cancer screening and precision medicine in LAC-DHS

- Second largest public health system in the United States, with ~600,000 patients
- Many individuals are underrepresented and/or from lower socioeconomic groups, with less access to healthcare (i.e., underserved)
- No current lung cancer screening program
- Highly resource constrained environment
- Screening decisions must be targeted to those who will benefit most
- LDCT screening cannot be implemented for the entire LAC-DHS population
- Downstream consequences of lung cancer detection must consider the cost of treatment (immunotherapies and other lung cancer treatments are cost prohibitive)

Integration
Combining what we have and what we know

Navigation
Building a process for tailored care & resources

Engagement
Working with patients, community, and stakeholders
Interpretation is labor-intensive and challenging, even for experts

- Many indeterminate pulmonary nodules (IPNs) are found on LDCT
- Nodules vary in size, and it is difficult to know if a nodule is benign or malignant

Construct a CNN for nodule detection and diagnosis

- Nodule detection is straightforward, with >95% accuracy
- Classification is much more challenging, given limited real-world data and changing imaging (e.g., Kaggle competition)
- Still an active area of research with clinical translation of deep learning still challenging
New continuous time models to handle real-world data, integrating new observations for risk assessment

Exploring approaches to optimize sequential decision making processes based on stratified risk

Methods are needed to understand when risk models need to be retrained over time

Cancer is a complex, evolving entity, and phenotypes change over time and across subgroups

**Screening**
- infrequent data collection
- high-risk, increased monitoring

**Diagnosis/Treatment**
- measurable disease, more frequent monitoring
- intervention, high frequency monitoring to assess response

**Long-term Outcomes**
- resolution, less frequency
- return to minimal monitoring

1. Decreased false positive rate for LDCT
2. Performance equal to the experts, and in many cases recommending a diagnostic action before the expert
3. Recommendations were understandable to experts

---

no disease
pre-disease state, asymptomatic
indolent disease
disease, symptomatic
treatment
survival, sequelae
Open questions for lung cancer risk models

Determining appropriate strategies to mitigate overdiagnosis and optimize resource allocation

- Not all lung nodules will become malignant; as we begin to better understand characterization of these nodules, can we do a better job of risk stratification over time?
- What combination of screening methods (imaging, genetics, genomics) will likely be appropriate for risk assessment?
- Not all patients are compliant with longitudinal screening and treatment over time, can we do a better job of identifying individuals who will therefore likely benefit from resource utilization?