Developing a New Low-Dose CT Image Library to Facilitate Artificial Intelligence (AI) Development for Lung Cancer Screening

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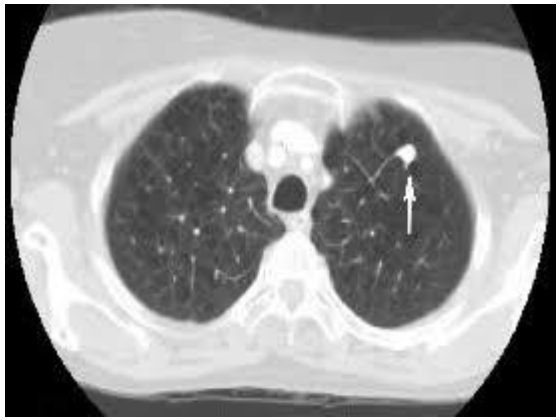
Problem

Low-dose CT (LDCT) screening for lung cancer has been shown to reduce lung cancer mortality, BUT with a high false-positive rate (FPR)

- National Lung Screening Trial (NLST)
  ~ 25% rounds 1-2; 16% round 3
- Current clinical practice: 17% (baseline), 11% (post-baseline) using Lung-RADS
  - Use of Lung-RADS may also lower sensitivity from that seen in the NLST

Positive LDCT Screens



- Usually a lung nodule
- Positivity – based on nodule size & attenuation
- Usually benign (> 90%)

Diagnostic follow-up:

- 3 or 6 month LDCT
- Less commonly: PET/CT, Chest CT
- Biopsy if high probability of malignancy

Burden of False Positives & Diagnostic Uncertainty

The high false-positive rate:

- Constitutes significant patient harm - short-term anxiety, radiation from f/u CTs, complications from diagnostic procedures
- Contributes to increased healthcare costs and utilization of healthcare resources, and serves to lower uptake of screening due to perceived burden (uptake currently < 10% of eligibles)

Impact of Reducing FPR by 50%

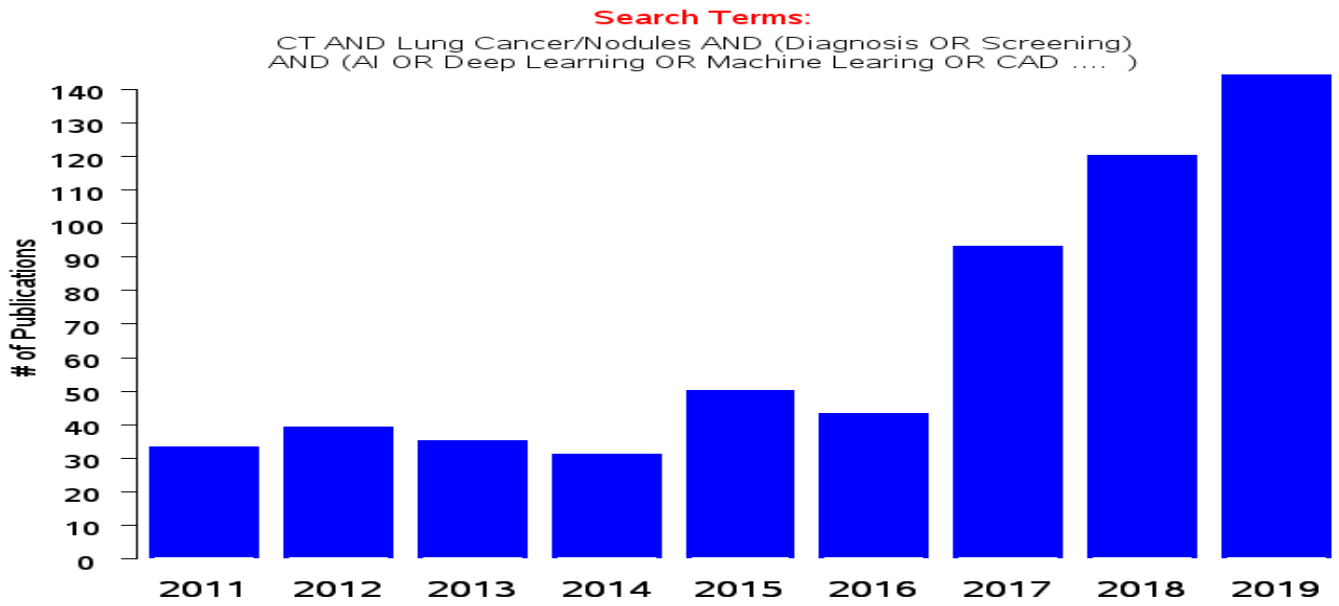
- 40,000 fewer false positives per year (current screening rate)
- 250,000 fewer false positives per year (50% adherence)
- **Diagnostic Uncertainty**:
- ~ 50% of biopsies following positive screens negative
- Diagnostic delay: ~20% had >18 month “delay”

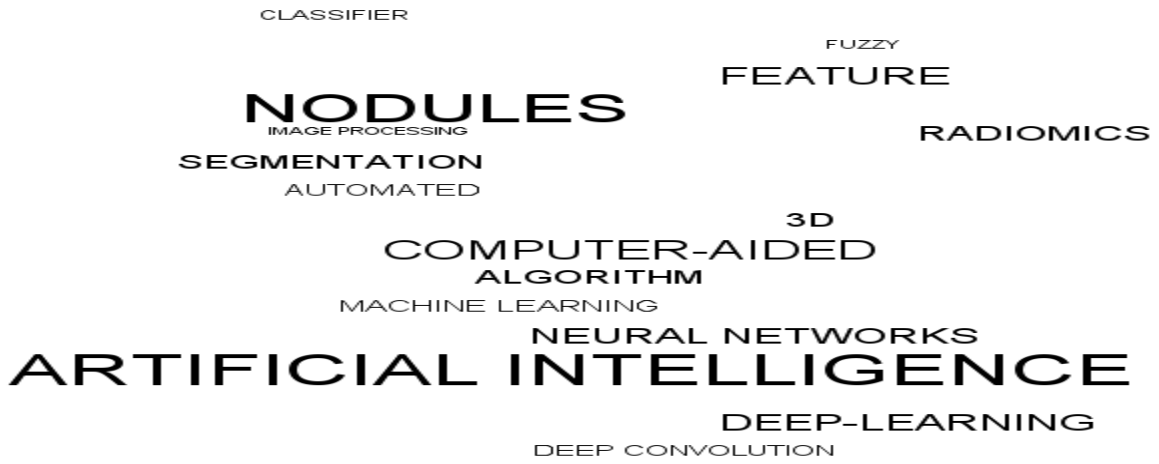
Resolving the Problem Through AI

- To make screening more efficient and reduce screening-related harms, the false-positive rate must be substantially reduced, while leaving test sensitivity essentially unchanged

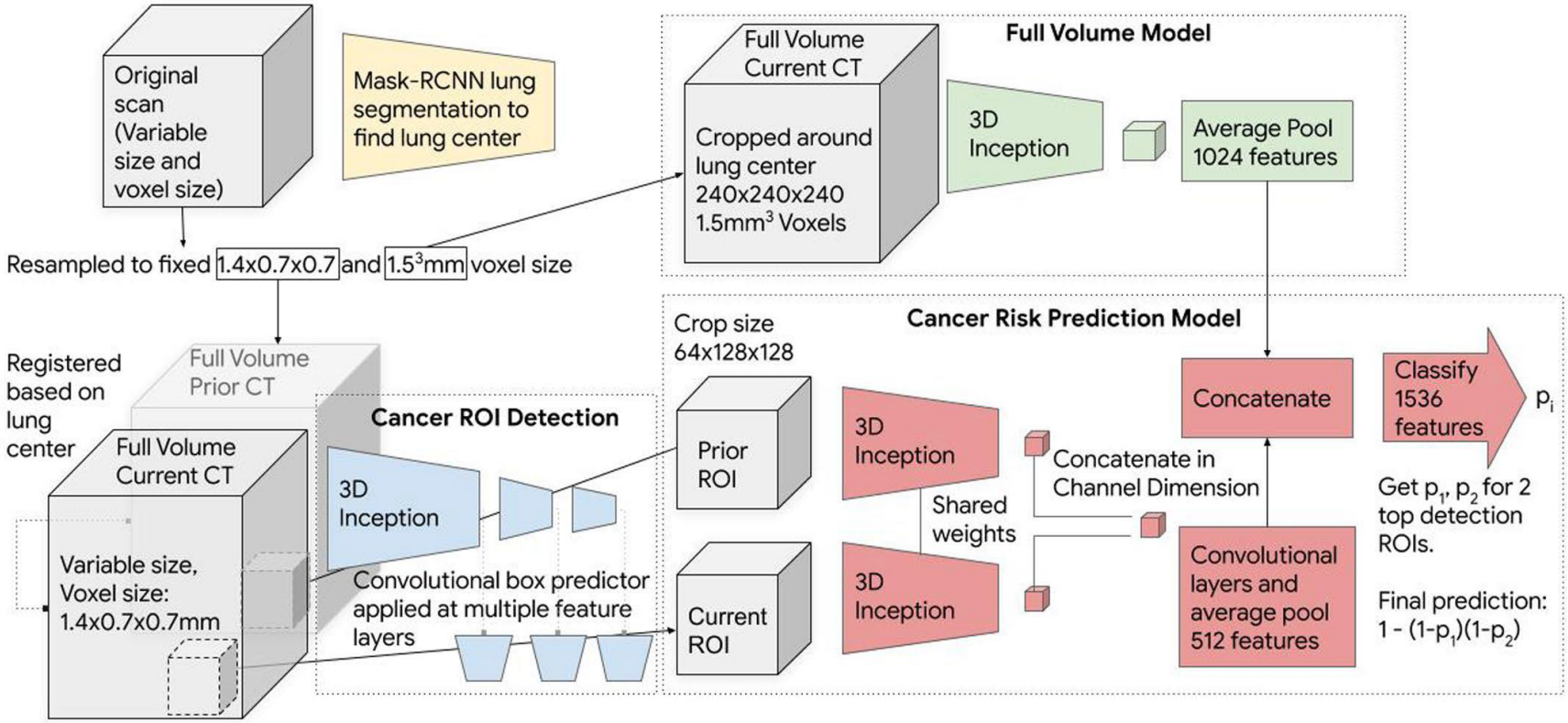
- One approach to reduce the false-positive rate is through development of artificial intelligence (AI) and machine learning tools to assist radiologists in interpreting LDCT screening and diagnostic images

AI Research for Detection of Lung Nodules/Cancer





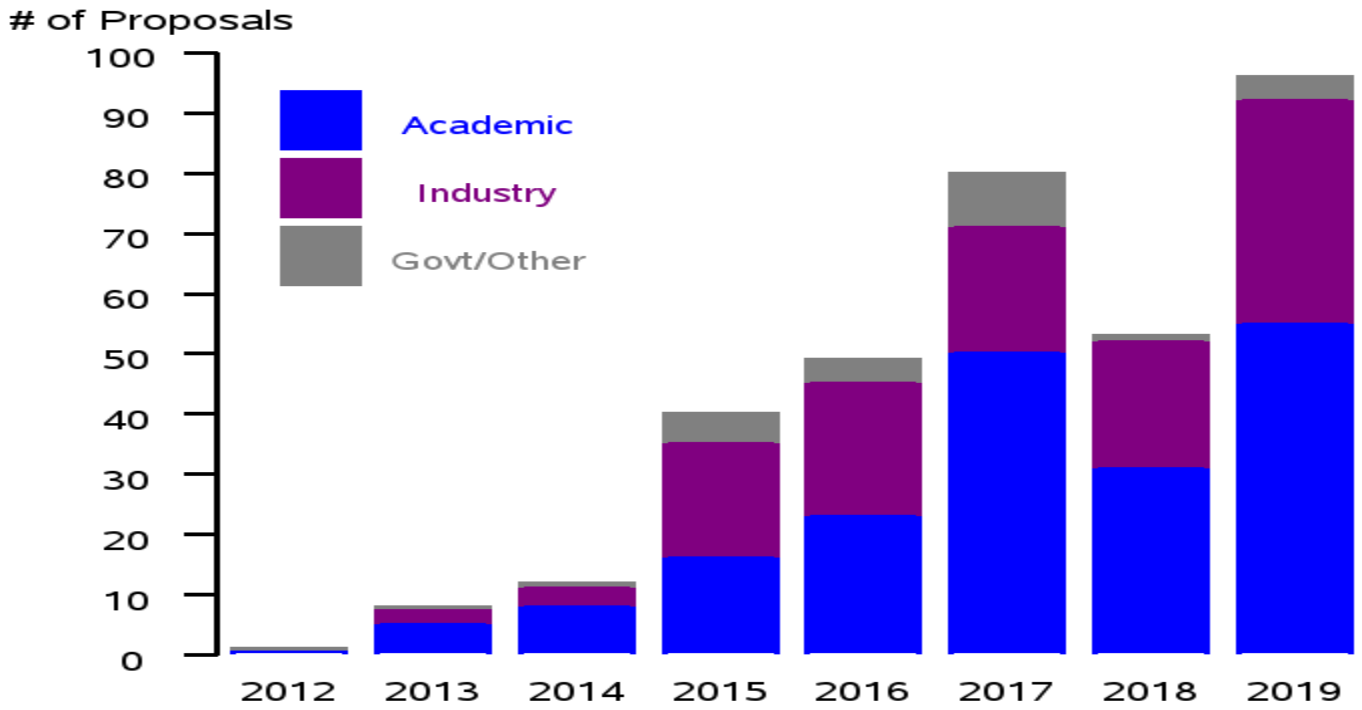
“End-to-End Cancer Risk Prediction” – Google AI
Ardila, et al., Nature Medicine, 2019



Used NLST CT Images for Training

NLST CT Image Library

- The NLST CT image library is the main resource for the development of AI tools to predict lung cancer in LDCT screens
- Images available to the general research community
- 339 proposals for CT images (through 2019)



Shortcomings of NLST Image Library

- CT images in the library are from 2002-2006 and CT technology has changed appreciably from 2006 to present
- The NLST images have been widely disseminated, making true validation of AI algorithms problematic
- The NLST was a volunteer population and not representative of LDCT screening in current clinical practice
- The NLST image library has only screening LDCT exams, not diagnostic f/u CT exams

Demographics of LDCT Screened Subjects NLST vs. Current Clinical Practice

	NLST	Current Clinical Practice
Age 70+	11%	24%
Women	41%	48%
Black	4.5%	7.1% *
Current Smoker	48%	58%
COPD	17%	32% *

* - Of non-missing responses

Request for Proposal (RFP)

- Create a new LDCT lung cancer screening image library
- Obtained with current LDCT technology and in standard clinical (non-research) settings
- Also includes diagnostic f/u CT images
- Includes demographic, screening outcome & clinical outcome (lung cancer incidence) data
- No enrolling/consenting of patients: only retrospective collection of de-identified images & data
- Make available to the research community through a controlled process
- Hold back a subset of images for algorithm validation

Scale of Project

	Proposed #
Unique Subjects *	15,000
Screening LDCT Images	22,500
Diagnostic CT Images	6,000-8000
Subjects with lung cancer-associated image (diagnosed within 18 months of a screen)	1500
Subjects with Lung-RADS positive screen (no cancer)	9000
Subjects with (only) Lung-RADS negative screens (no cancer)	4500

* Enrich for Racial/Ethnic Minorities, Other Special Populations

Using the LDCT Image Library for Algorithm Validation

- Subset of collected images held back as a validation set

- MDDT (Medical Device Development Tool)
- New FDA (CDRH) program to qualify tools that sponsors can use in the development and evaluation of medical devices
- Once qualified, an MDDT can be utilized by multiple sponsors
- Contractor will submit the validation set to FDA as a potential MDDT
- AI developers can utilize this MDDT when submitting algorithms for FDA approval

- Currently, 5 approved MDDTs (2 in imaging space)

Timeline and Budget (Total Costs)

- Five-year contract
- Collection of data and images, set-up for image storage - up to 3 years [$ 4.5 million]
- Image storage and dissemination – up to 3 years [$ 500 K per year]
- Image validation set activities, including qualification as MDDT – 2 years [~ $0.5-1 million]

- **Post-contract** – Plan to continue with image storage/dissemination in some manner

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Extra Slides

Feasibility of New LDCT Image Collection

Jan 2017 - June 2019: ~ 1.2 million LDCT exams performed at 3,300 facilities in standard clinical practice

Estimated # of associated lung cancers – 10,000

Top 100 facilities: ~ 500,000 LDCT exams, 4200 cancers

Top 250 facilities: ~ 650,000 LDCT exams, 5500 cancers

# of lung cancers required for resource ~ 1500 (NLST had 700)

Example: Contacting top 100 facilities, would need about 35 to participate. Include some smaller facilities for diversity.

Note: Consider exams through June 2019 in order to have 18 months follow-up for cancer incidence at time of collection.

FDA Approved/Cleared Algorithms for Lung CT

Device Name	Company	Year Approved/Cleared
Syngo CT Lung CAD	Siemens, AG	2020
ClearRead CT	Riverain Technologies	2016
ImageChecker CT CAD	Hologic	2007
Advanced Lung Analysis	GE Medical	2004
Lung CAR 1.1	MEDICSIGHT	2004
MEDICLUNG	MEDICSIGHT	2003
LungCare CT	Siemens AG	2003

All approved/cleared for lung nodule detection, not lung cancer