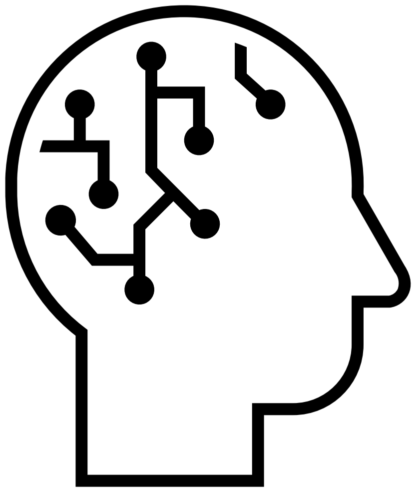
Lung Cancer Screening:
is there a role for Artificial Intelligence?



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Wellstar Health System

Disclosures

- Consultant, Philips
- Consultant, Medtronic

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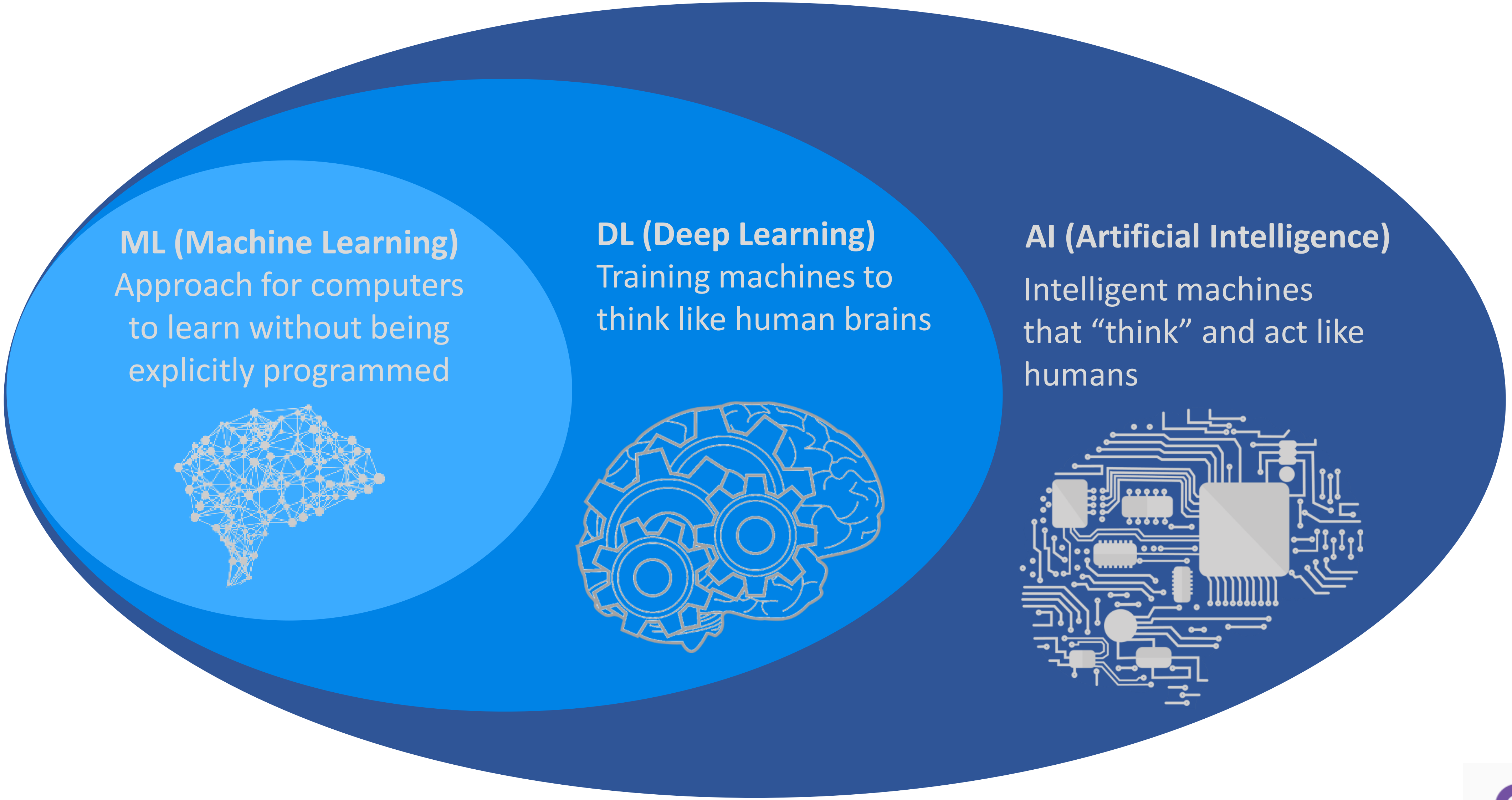
Overview

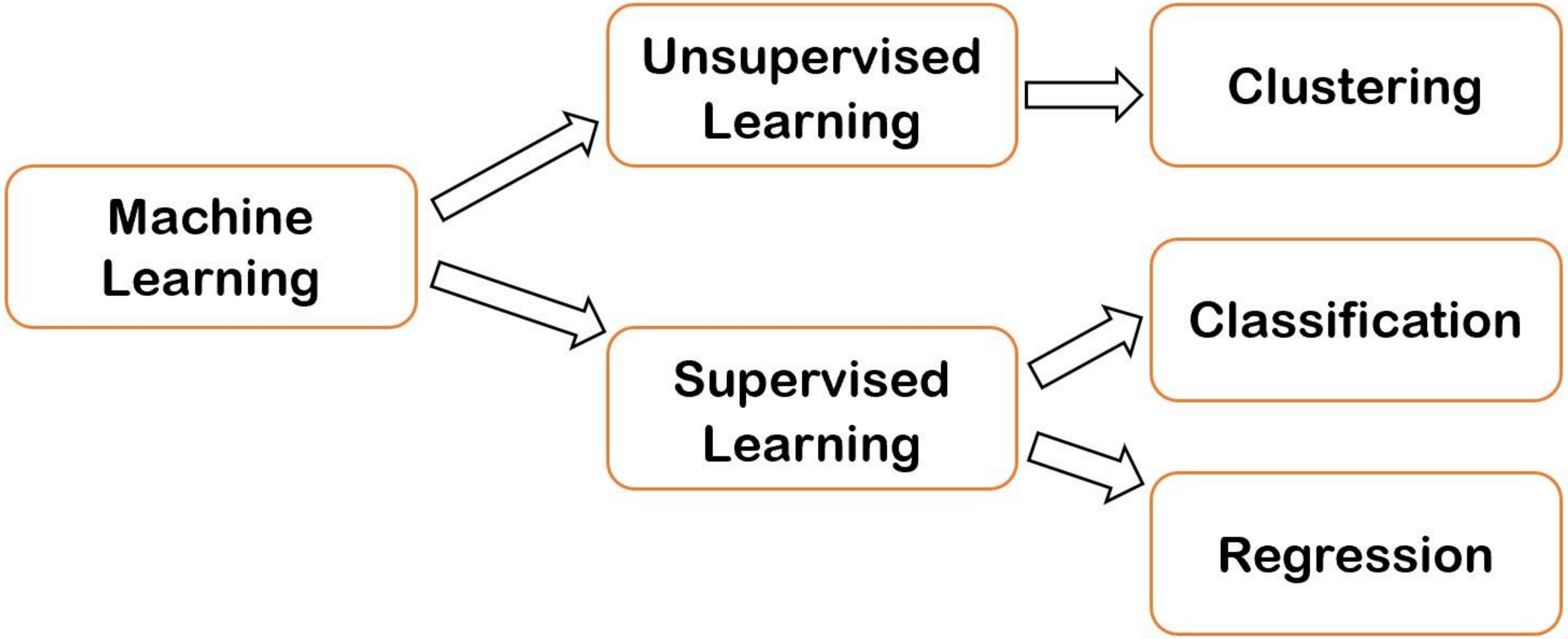
- What is Artificial Intelligence?
- Applications of AI in Imaging
- Applications of AI in Lung Cancer
- Future opportunities for AI in Early Detection of Lung Cancer

Artificial intelligence definitions



Sources: Deep Learning in Medical Imaging: General Overview - Korean J Radiol. 2017 Jul-Aug;18(4):570-584
and Machine Learning for Medical Imaging - RadioGraphics (2017) VOL. 37, NO. 2

Machine Learning

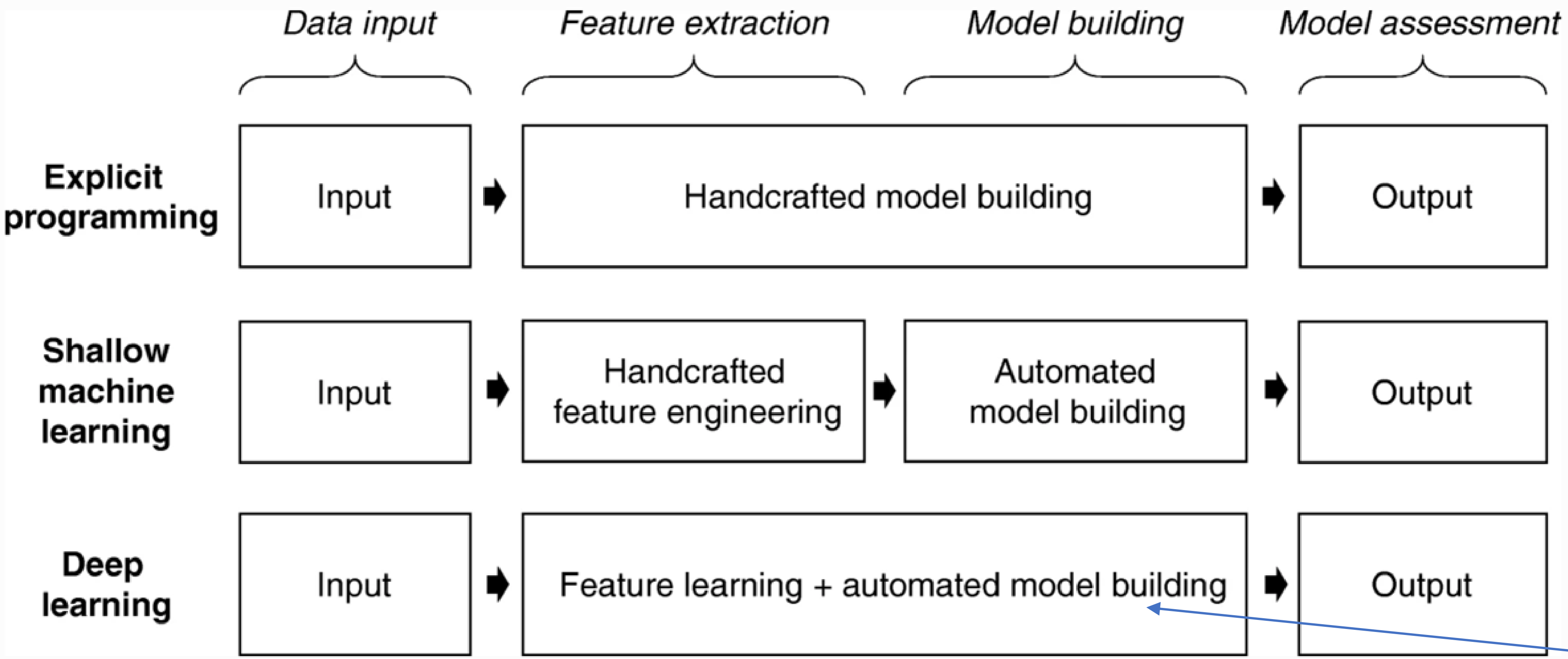


Infer patterns without known outcomes

Data management by written algorithms, known labeled outcomes

Deep Learning

From: Machine learning and deep learning



Process of analytical model building (inspired by Goodfellow et al. 2016, p. 10)

Learns from problem-specific training data to *automate* the process of analytical model building and solve associated tasks.
The machine improves its own performance with time.

Janiesch C, Zschech P, Heinrich K, "Machine Learning and Deep Learning" in Electronic Markets Vol 31, pp685-695, April 8, 2021

Radiology Images are huge amounts of pure digital data

ORIGINAL RESEARCH ■ SPECIAL REPORT

Radiomics: Images Are More than Pictures, They Are Data[1]

In the past decade, the field of medical image analysis has grown exponentially, with an increased number of pattern recognition tools and an increase in data set sizes. These advances have facilitated the development of processes for high-throughput extraction of quantitative features that

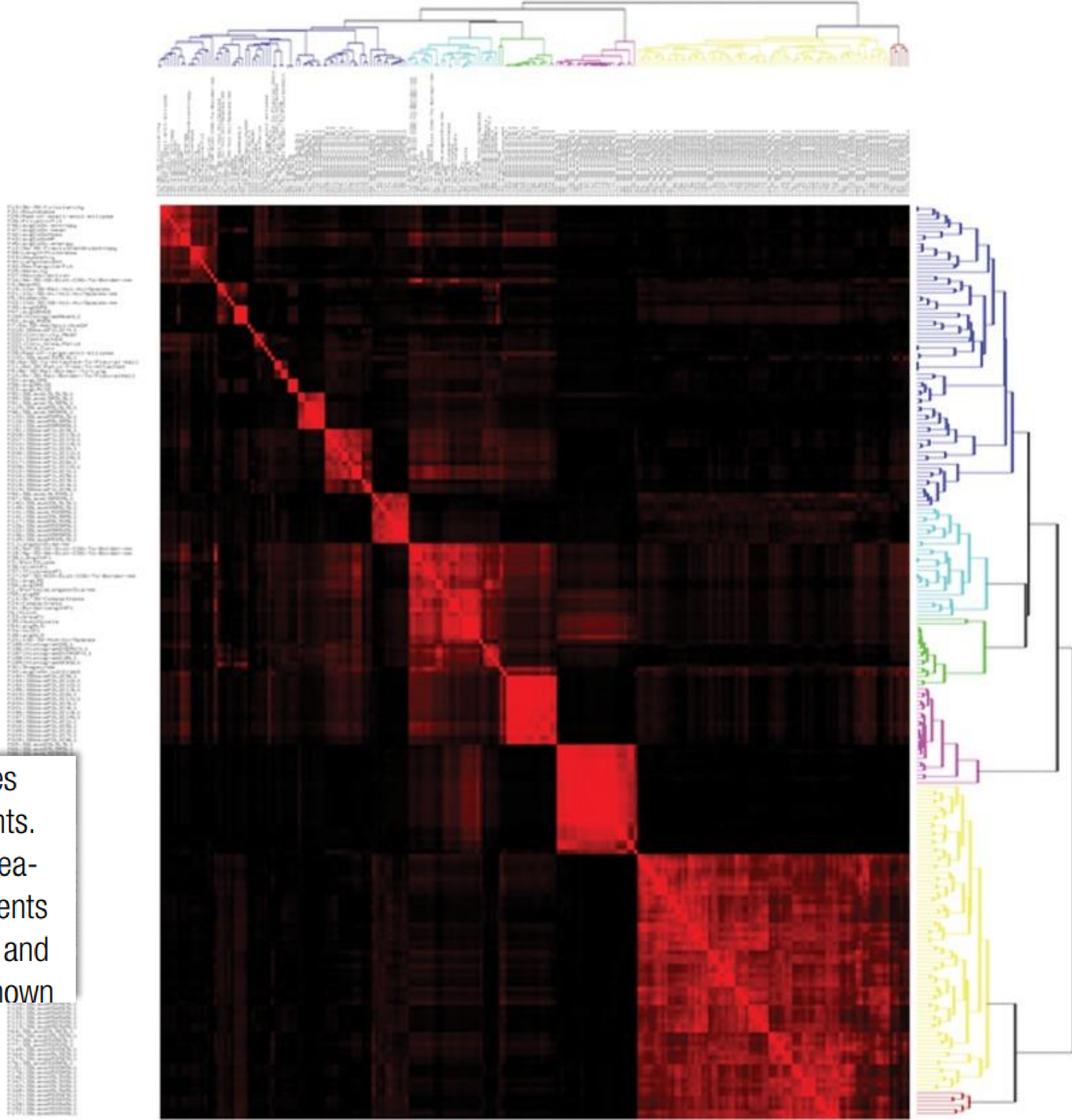


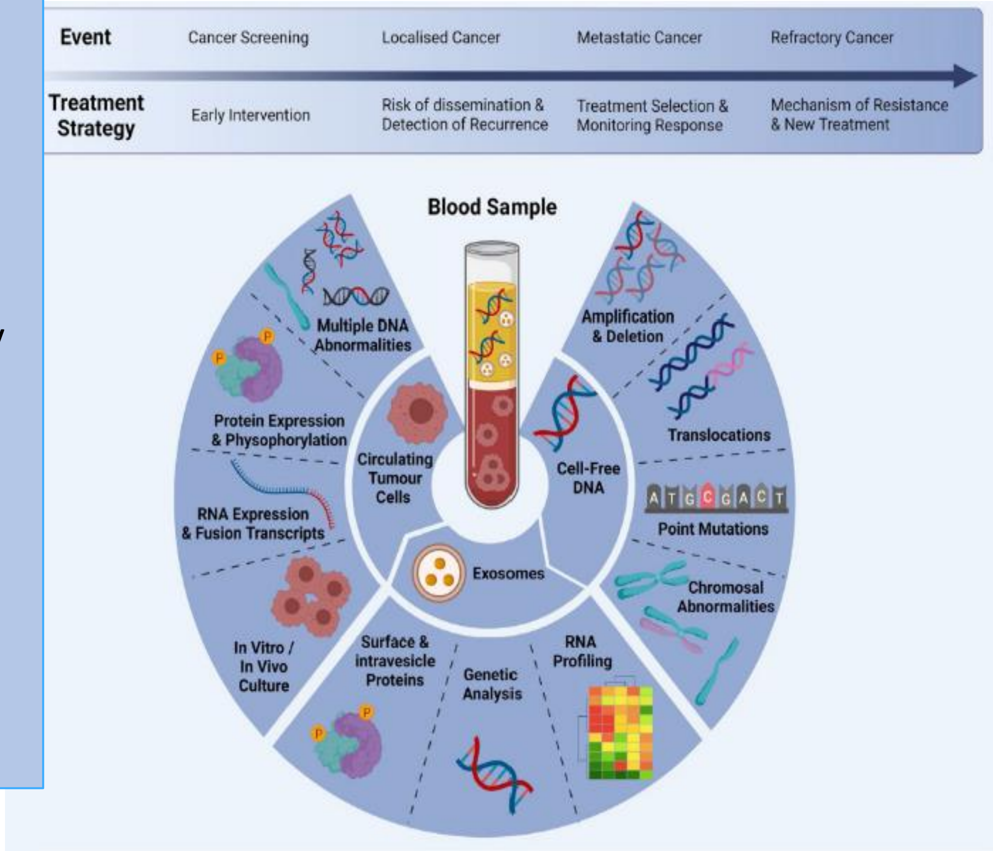
Figure 3: Covariance matrix of radiomic features. A total of 219 features were extracted from each non–small cell lung cancer tumor in 235 patients. Across all tumors, each feature was individually compared with all other features by using regression analysis, thereby generating correlation coefficients (R^2). Individual features were then clustered and plotted along both axes, and R^2 is shown as a heat map, with areas of high correlation ($R^2 > 0.95$) shown

Source: Radiology: Volume 278: Number 2—February 2016

Lung Cancer Care requires huge amounts of data: **largely unstructured**

Demographics
Risk factors
Health Factors
Imaging
Serology tests
Lung function
Cardiac Function
Histology
Immunohistochemisty
Biomarkers
- Immune
- Mutations

Radiation
Chemotherapies
Immune Therapies
Outcomes data
Follow up data



Can we gain insights by allowing AI to trend and sort metadata across large populations?

type	Strength	Weakness	Clinical application in oncology
effusion	• Reflective of tumor molecular alterations/mutations • Stable up to 2 days in blood samples • Reflective of tumor heterogeneity • Highly sensitive assays (NGS, PCR)	• Contamination of germinal cfDNA • Cannot reflect every gene mutation • Low amount in plasma • Undetectable in many patients with early-stage cancer • Less stable than non-tumor DNA	• Elevated in cancer patients compared to healthy individuals • Increases with tumor size and stage
all body	• Stable source of tumor genetic material (DNA, RNA, protein, miRNA) • Commercial kits available	• required standardization for extraction and detection • Unreliable isolation procedures	• Elevated in cancer patients compared to healthy individuals • Exosome size positively correlates with unfavorable outcomes
ral	• Assessment of tumor markers (PD-L1) during treatment • Demonstration of signal co-localization • Cell morphology and functional studies	• Not predictive of therapeutic benefit in metastatic setting • Undetectable in most patients with early-stage cancer • Rare to capture in the bloodstream	• Predictive of early relapse after primary treatment • CTC number correlates with progression-free survival and overall survival
	• Different profile among early-stage cancer patients • Distinguishable between cancer patients and healthy individuals	• Loss of epithelial specific markers during epithelial mesenchymal transition (EMT) • High variability • Lack of standardization • Unspecific for a cancer type	• cmi-RNA expression correlates with tumor development, progression and metastasis
ral blood	• TEP-RNA is reflective of tumor transcriptome • Abundant • Dynamic mRNA repertoire because of short life-span	• Reproducibility • Lack of validated assay	• Distinguishable between healthy individuals •

The sample type, strength, weakness and clinical applications of each marker is discussed.

Source: The Role of Circulating Biomarkers in Lung Cancer - Front. Oncol., 21 January 2022 Sec. Thoracic Oncology

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Artificial intelligence that may simulate “intelligent behavior” (perform critical thinking comparable to a human being) **can be used to analyze and interpret complex medical data.**

Can it help produce meaningful insights on lung cancer Early Detection, making it easier, faster and more efficient?

Image from Engineering Application of Artificial Intelligence & Machine Learning by Shahab D. Mohaghegh

First AI applications

WIRED STAFF SCIENCE JUN 26, 2012 11:15 AM

Google's Artificial Brain Learns to Find Cat Vi

When computer scienti network of 16,000 com and let it browse YouTube, it did what many web users might do -- it began to look for cats.

Picking up on the most commonly occurring images featured on YouTube, the system achieved 81.7 percent accuracy in detecting human faces, 76.7 percent accuracy when identifying human body parts and 74.8 percent accuracy when identifying cats.

"The network is sensitive to high-level concepts such as cat faces and human bodies. Starting with these learned features, we trained it to obtain 15.8 percent accuracy in recognizing 20,000 object categories, a leap of 70 percent relative improvement over the previous state-of-the-art [networks]."

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Computer-aided lung nodule detection – as a starting point

Radiology

Kyongtae T. Bae, MD, PhD
Jin-Sung Kim, MS[2]
Yong-Hum Na, MS
Kwang Gi Kim, PhD
Jin-Hwan Kim, MD[3]

Published online before print
10.1148/radiol.2361041286
Radiology 2005; 236:286–294

Abbreviations:

Pulmonary Nodules: Automated Detection on CT Images with Morphologic Matching Algorithm—Preliminary Results[1]

With early CADe tools, Bae et al. in **2005** reported a **sensitivity of 95.6%** for the detection of pulmonary nodules nonetheless **with a number of false positives per examination of 6.9 and 4.0** for detection sensitivity thresholds of 3 and 5 mm, respectively

Source: Radiology 2005; 236:286–294

Eur Radiol (2012) 22:2076–2084
DOI 10.1007/s00330-012-2437-y

CHEST

Performance of computer-aided detection of pulmonary nodules in low-dose CT: comparison with double reading by nodule volume

"*Commercially available CADe tool has **sensitivity of 96.7%**, whereas **double reading has only 78.1% sensitivity**. Nonetheless, these CADe tools are known to encounter a **high number of false positives** and insufficient performances for the detection of subsolid nodules*"

Source: Eur Radiol (**2012**) 22:2076–2084

ELSEVIER

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Computer-aided diagnosis (CAD) of subsolid nodules: Evaluation of a commercial CAD system

Joseph Benzakoun (MD)[a,b,*], Sébastien Bommart (MD PhD)[c,d], Joël Coste (MD PhD)[a,b], Guillaume Chassagnon (MD PhD)[b,e], Mathieu Lederlin (MD PhD)[f,g], Samia Boussouar (MD)[b,h], Marie-Pierre Revel (MD PhD)[b,e]

"*With sensitivity adjusted for 3-mm nodule detection, **50%** of subsolid nodules were detected, **26%** at the 5-mm setting. And at the highest sensitivity setting (2-mm nodule detection), the nodule detection rate only increased to **54%***"

Source: European Journal of Radiology 85 (**2016**) 1728–1734

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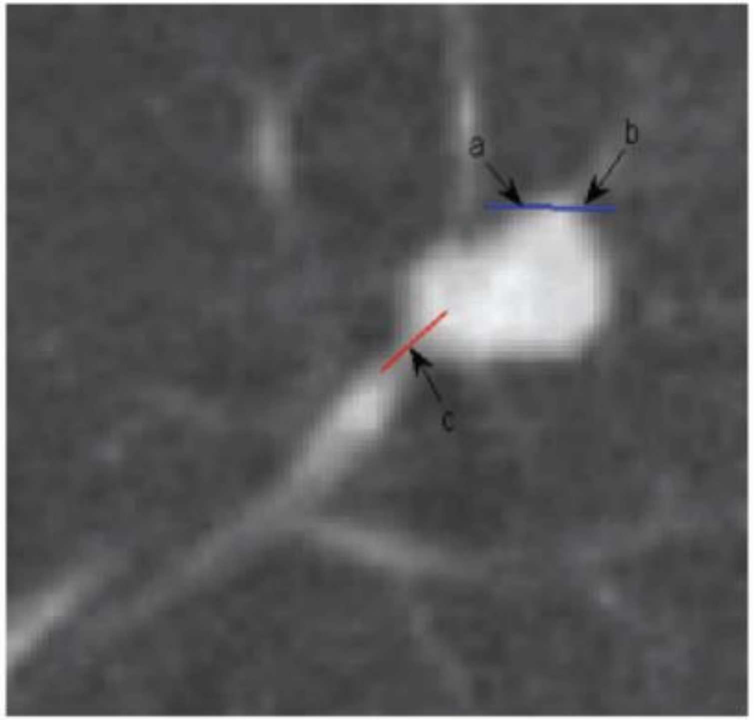
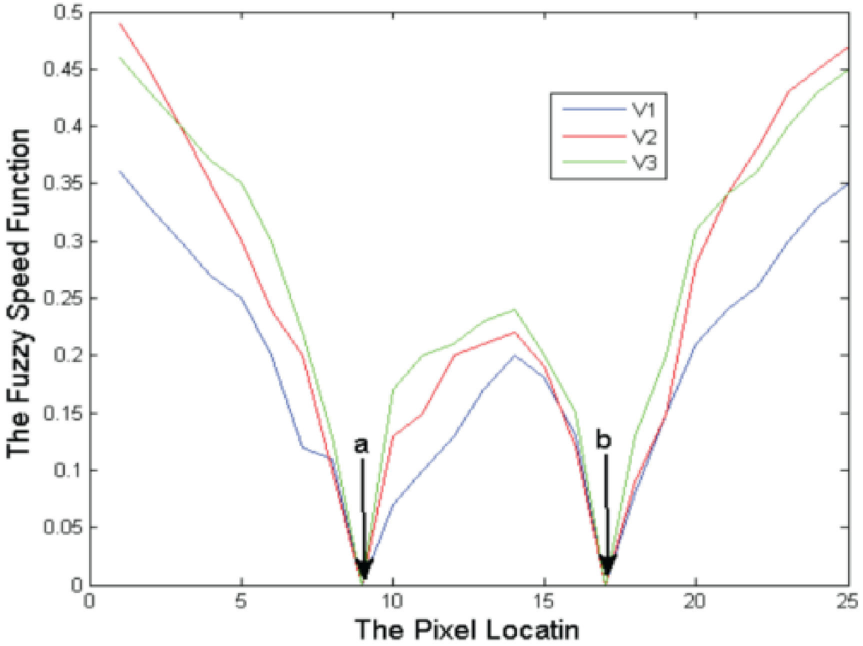
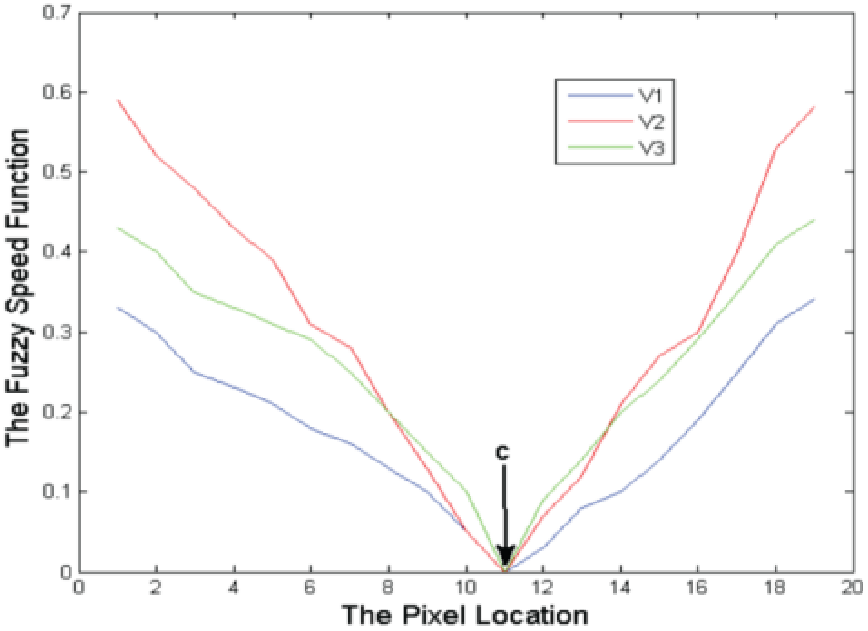
Fuzzy Speed Function Based Active Contour Model for Segmentation of Pulmonary Nodules

Kan Chen, Bin Li[*] , Lian-fang Tian, Wen-bo Zhu and Ying-han Bao
School of Automation Science and Engineering, South China University of Technology, Guangzhou, Guangdong, China







Source: Fuzzy Speed Function Based Active Contour Model for Segmentation of Pulmonary Nodules - Bio-Medical Materials and Engineering 24 (**2014**) 539–547

Featured Prediction Competition

Data Science Bowl 2017

Can you improve lung cancer detection?

$1,000,000
Prize Money

Booz Allen Hamilton · 1,972 teams · 6 years ago

A total of US$1 million in prize money for the ten best algorithms that could predict lung cancer from a single screening CT scan. The task was to predict whether an individual patient would be diagnosed with lung cancer within 1 year of the scan

2017 Data Science Bowl winners include:

- First Place: Liao Fangzhou and Zhe Li, two researchers from China's Tsinghua University who have no formal medical background but were able to apply their analytics skills to an unfamiliar but challenging area of research.
- Second Place: Julian de Wit and Daniel Hammack, both software and machine learning engineers based in the Netherlands. Julian came in third in the Data Science Bowl 2016.
- Third Place: Team Aidence, members of which work for a Netherlands-based company that applies deep learning to medical image interpretation.

Source: Data Science Bowl 2017 | Kaggle

Source: Nearly 10,000 Compete in 3rd Data Science Bowl to Improve Lung Cancer Detection (boozallen.com)

Google AI project 2019

analysis, into a product currently remains to be seen. All of the solutions developed by Google AI so far are proprietary. In the *Nature Medicine* letter, the authors state that their code has "dependencies on internal tooling, infrastructure and hardware, and its release is therefore not feasible. However, all experiments and implementation details are

LUNG CANCER

…gle's lung cancer AI: …mising tool that needs …er validation

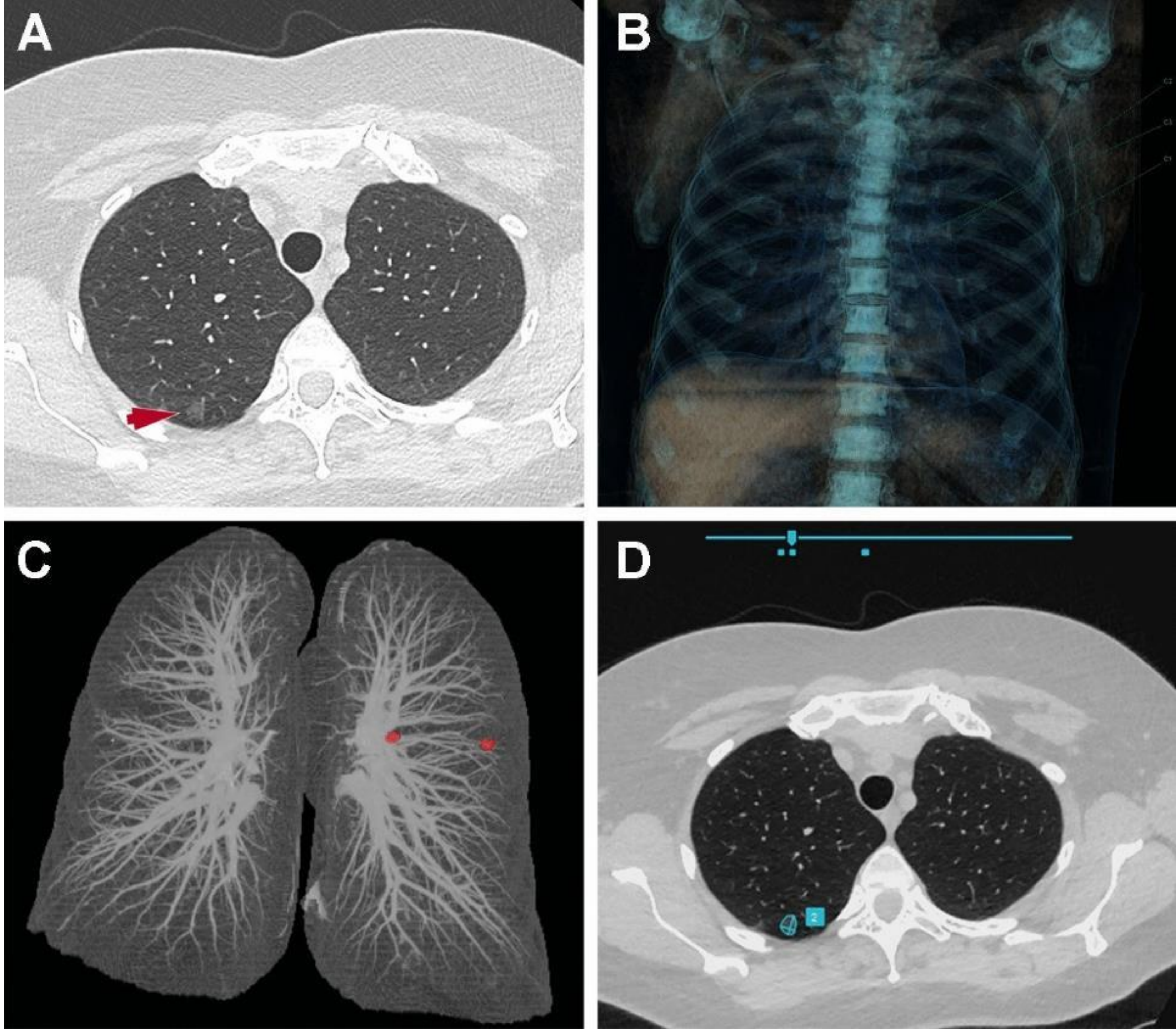
…s and Bram van Ginneken

…from Google AI have presented results obtained using a deep learning model for the detection of lung cancer in screening CT images. The authors report a level of performance similar to, or better than, that of radiologists. However, these claims are currently too strong. The model is promising but needs further validation and could only be implemented if screening guidelines were adjusted to accept recommendations from black-box proprietary AI systems.

Refers to Ardila, D. et al. End-to-end lung cancer screening with three-dimensional deep learning on low-dose chest computed tomography. *Nat. Med.* **25**, 954–961 (2019).

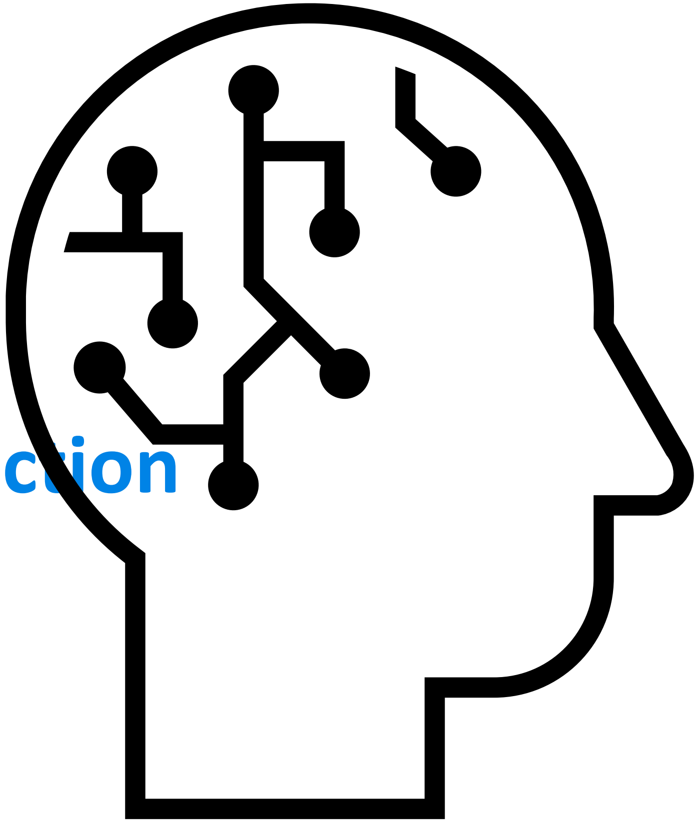
Deep Learning vs. Machine Learning 2022

Detection of a pulmonary ground-glass nodule. **A** Axial chest CT image shows a 10 × 8 mm ground-glass nodule (arrow) in the right upper lobe. **The ground-glass nodule is not detected by two different computer-aided detection tools based on classical machine learning methods** (**B** and **C**) but is **correctly detected by the one based on deep learning** (**D**)



Source: Artfcial intelligence in lung cancer: current applications and perspectives - Japanese Journal of Radiology (November 9, 2022)

Current applications of AI in Early Detection



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2015 COMPUTER-AIDED NODULE DETECTION

DynaCAD Lung

Advanced visualization for CT chest exams

DynaCAD Lung is a vendor neutral Computer-Aided Detection (CAD) system that provides a robust set of automated tools for radiologists to analyze multi-slice CT exams of the chest.

- Standard CT scans
- Comparison to prior exams
- Standardized nodule table (structured data)

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NATURAL LANGUAGE PROCESSING TO DETECT INCIDENTAL FINDINGS

NUANCE

Wellstar Incidental Nodule
2019-2022 (800 days)

92,000 **Chest Imaging Reports referred by NLP to reviewers**

Released By: KEVIN S EARLY, MD 9/17/2020 12:50 AM The Results Reporting Office (F1) will complete appropriate follow-up actions based on defined processes. F1 EXAM: KH CT ABDOMEN/PELVIS W/O IV CONTRAST TECHNIQUE: CT scan of the abdomen and pelvis with multiplanar reformatted images generated from the data set without IV contrast. Dose reduction techniques were utilized. CLINICAL INDICATION: urinary frequency, incontinence and hematuria. Pain FINDINGS: COMPARISON: No comparison studies are available at this time. Liver: Hepatic steatosis. Lower chest: 5 mm pleural-based noncalcified pulmonary nodule left lower lobe image 15. Additional smaller pulmonary nodules are seen in the left lower lobe. Pancreas: Normal. Gallbladder: Normal. Adrenals: Normal. Spleen: Normal. Gastrointestinal: The stomach, small bowel, and colon appear normal. The appendix is not identified, but there is no evidence of inflammation. Kidneys: 3 mm calculus in the right kidney, nonobstructing.. No evidence of hydronephrosis. Left kidney normal. Vasculature: Abdominal and pelvic vasculature appears normal on unenhanced images. Pelvis: Prostate and seminal vesicles are normal. Bones: No destructive osseous lesion. Lymph nodes: No enlarged lymph nodes. Nonobstructing right renal calculus IMPRESSION: . . of the chest at 12 months could be performed. There are noncalcified solid and/or part solid nodules as above. Per 2017 Fleischner Society guidelines, the recommendation for a patient with multiple < 6 mm noncalcified nodules is usually no followup scan. In a high risk patient, optional (

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2021 AI assisted DIAGNOSIS

Optellum

ABOUT US PRODUCTS & SOLUTIONS RESOURCES

NEWS & EVENTS

US PRESS RELEASE: Optellum Receives FDA Clearance for the World's First AI-Powered Clinical Decision Support Software for Early Lung Cancer Diagnosis

Rhiannon Lassiter - March 23, 2021 - Clinical / News and PR

- AI-powered Radiomics-based *digital biomarker* for lung cancer
- Features a clinically-validated Lung Cancer Prediction (LCP) score
- The score is computed from full patterns of 3D pixels in standard CT images
- Deployed inside "Lung Cancer Orchestrator" Nodule Clinic App

Optellum.com

Future for Screening: Machine Learning of VOCs

sensors

MDPI

Article

A Study of Diagnostic Accuracy Using a Chemical Sensor Array and a Machine Learning Technique to Detect Lung Cancer

Chi-Hsiang Huang [1,2], Chian Zeng [3], Yi-Chia Wang [1,2], Hsin-Yi Peng [3], Chia-Sheng Li
Che-Jui Chang [3,5] and Hsiao-Yu Yang [3,6,*]

Characteristics	Lung Cancer Cases (n = 56)	Non-Tumour Controls (n = 188)
Age (year), mean (SD)	65.3 (8.8)	53.5 (16.1)
Male, no. (%)	12 (21.4)	106 (56.4)
Cigarette smoking		
Pack-years, mean (SD)	21.0 (10.7)	20.6(18.3)
Smoking status		
Current smokers, no. (%)	2 (3.6)	25 (13.3)
Former smokers, no. (%)	8 (14.3)	11 (5.9)
Never smoked, no. (%) [a]	44 (78.6)	150 (79.8)
Second-hand smokers (%)	2 (3.6)	2 (1.1)
Tumour histological type		
Squamous cell carcinoma, no. (%)	1 (1.8%)	
Adenocarcinoma, no. (%)	52 (92.9%)	
Small cell lung cancer, no. (%)	1 (1.8%)	
Other carcinomas, no. (%)	2 (3.6%)	
Clinical stage		
I	37 (66.1%)	
II	7 (12.5	
III	11 (19.6	
IV	1 (1.8	

Source: Sensors 2018, 18(9), 2845

Opportunities for AI in Lung Cancer

Data management

- Convert unstructured data to Structured
- Collate relevant data for work-up and treatment

Population Health

- Refine Population Risk assessment
- Refine Lung Screening criteria
- Address Social Determinants of Health

Risk stratification

- Refine Lung Screening criteria
- Refine NLP referral for review
- Address Social Determinants of Health

Nodule Management

- Improved specificity in nodule detection
- Improved sensitivity for GGOs

Treatment and Outcomes

- Determine best treatment based on all factors known
- Predict outcomes based on all factors known

For example

Volumes of Patient Data are very high to detect 1 lung cancer

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Lung Screening

33,645 scans

11,866 unique patients

406 Lung Cancers

55 non-lung cancers

Incidental Nodule

2019-2022 (800 days)

92,000 Imaging Reports referred by NLP to reviewers

35,000 Imaging Reports referred to NP and RN for review

1014 cases reviewed by Physicians

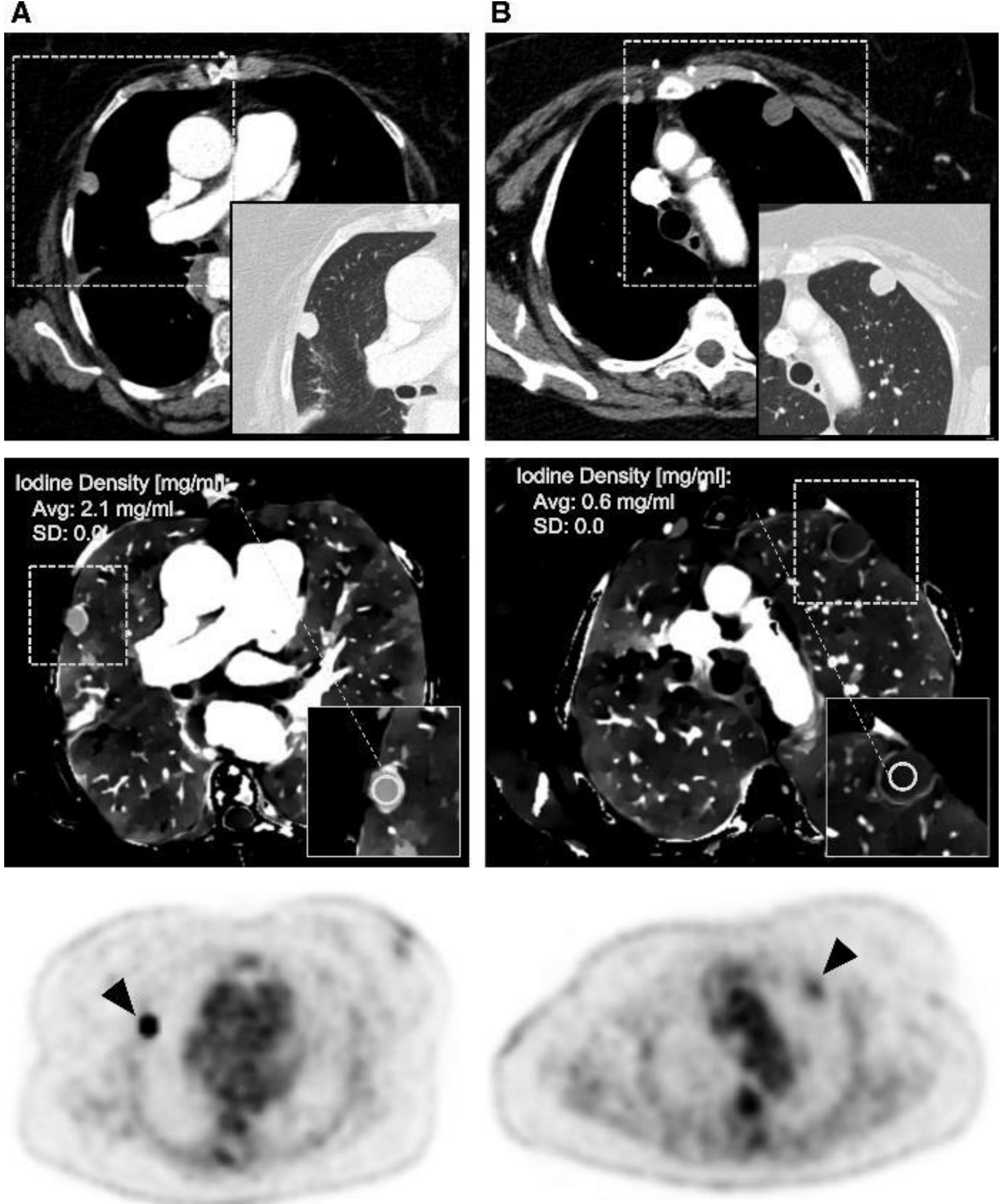
76 Lung Cancers detected and treated

14 non-lung cancers

New tool: Spectral CT

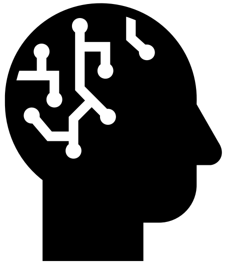
Conventional CT images (upper row) show two pulmonary nodules in the right (A) and left (B) upper lobe, both of which are considered **suspicious for malignancy based on their size and appearance**.
Iodine maps available from **dual-layer, dual-energy CT** (center row) clearly indicate significant **uptake of the iodinated contrast media** by the right pulmonary nodule (**A, 2.1 mg/ml**), whereas the left pulmonary nodule did not take up iodine (**B, 0.6 mg/ml**).

Concordant findings were obtained on FDG18 – PET (lower row), with low hypermetabolic activity associated with the left pulmonary nodule (maximum standardized uptake value = 1.7, arrowhead in B), and the right nodule demonstrating significant fludeoxyglucose avidity (maximum standardized uptake value = 7.1, arrowhead in A).



Source: Stratification of Pulmonary Nodules Using Quantitative Iodine Maps from Dual-Energy Computed Tomography - Am J Respir Crit Care Med Vol 199, Iss 2, pp e3–e4, Jan 15, 2019

Summary

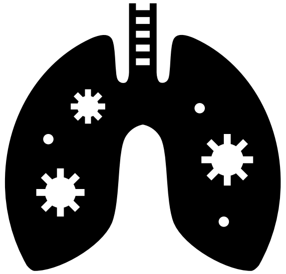


Artificial Intelligence has several forms:

Machine Learning

Deep Learning

Artificial Intelligence



There are several applications already in clinical practice

NLP
Computer-aided Detection
Radiomics Digital biomarker

Unsolved problems remain

Unstructured data
Population Health
Risk assessment improvement

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