Arlington Imaging Artificial Intelligence Workshop

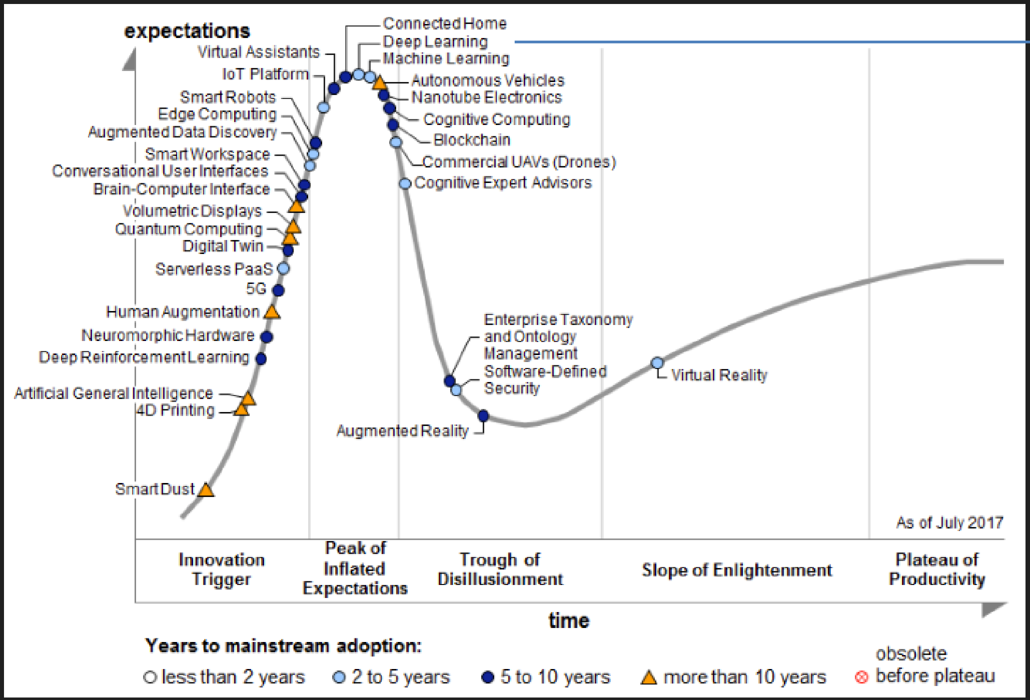
Making Clinical AI Relevant
5/09/2019

Riverain Technologies

Clinical AI in Action™

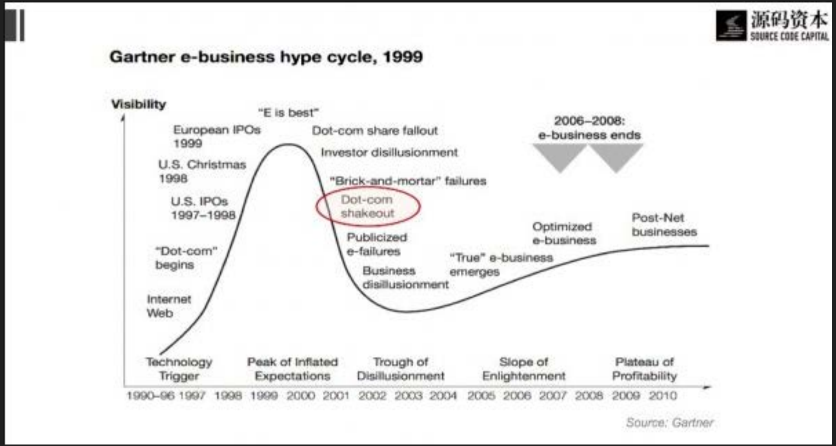
AI for Medical Applications

- Hype and disillusionment risk



Deep Learning is TOP of Hype Cycle

Internet, 2000



AI, Is it or isn’t it real

“AI is going to replace radiologists”

“AI is going to help us cure cancer”

One year later …

“AI can’t move across clinics”

“AI is not ready for routine adoption”

Is there a fundamental issue?

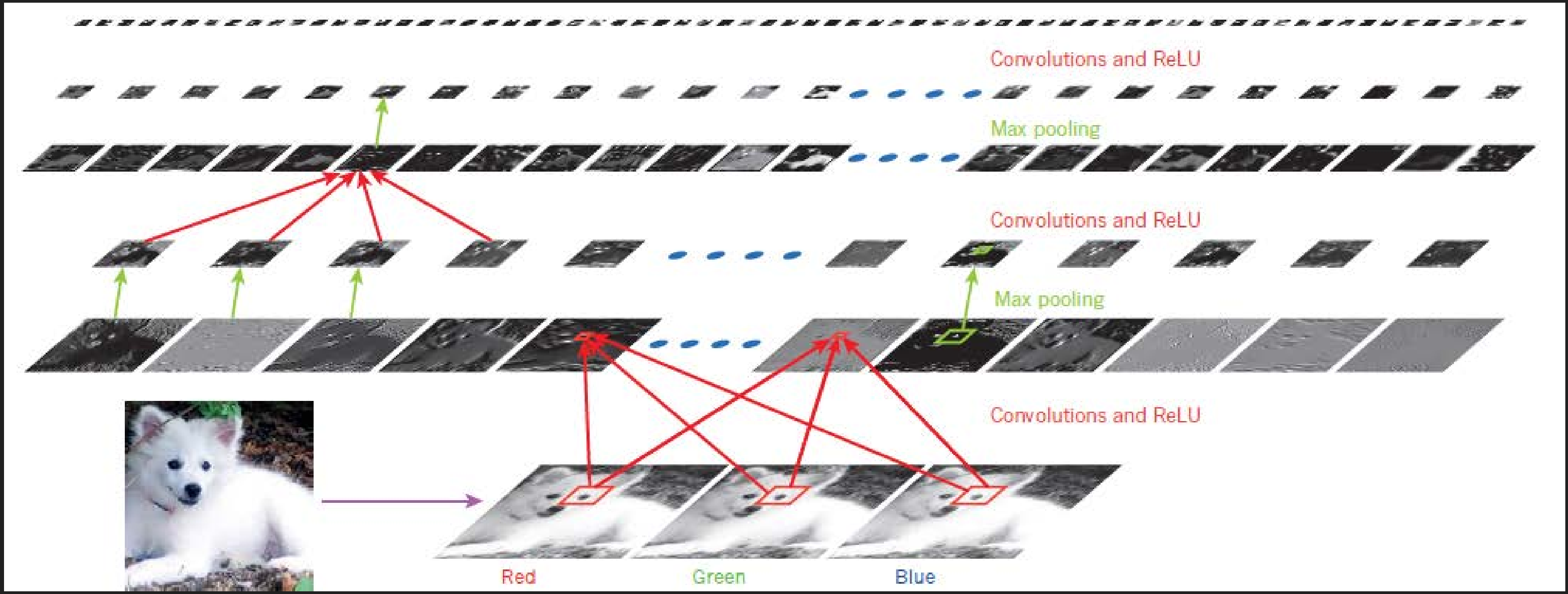
Bad designs lead to bad outcomes?

- Medical imaging devices have their own distinct properties
- Reconstruction and image formation software
- Drift and the need for calibration

More data isn't the answer

Designing in robustness is

Why AI is Sensitive to Acquisition



LeCun, Bengio, Hinton 436 | NATURE | VOL 531 | 28 May 2015

- Low-level features are lines, edges, blobs
- Variation in devices distort the low-level features
- This propagates through the network and distorts the output predictions leading to brittleness

Building Trust in AI

Normalization – Dealing with sources of Variance

Sampling and Contrast/Latitude Normalization

Original

↓

Normalize

Original

↓

Normalize

Same patient captured with different devices

Acquisition Variability

- Noise, contrast, appearance vary with device and institution preferences

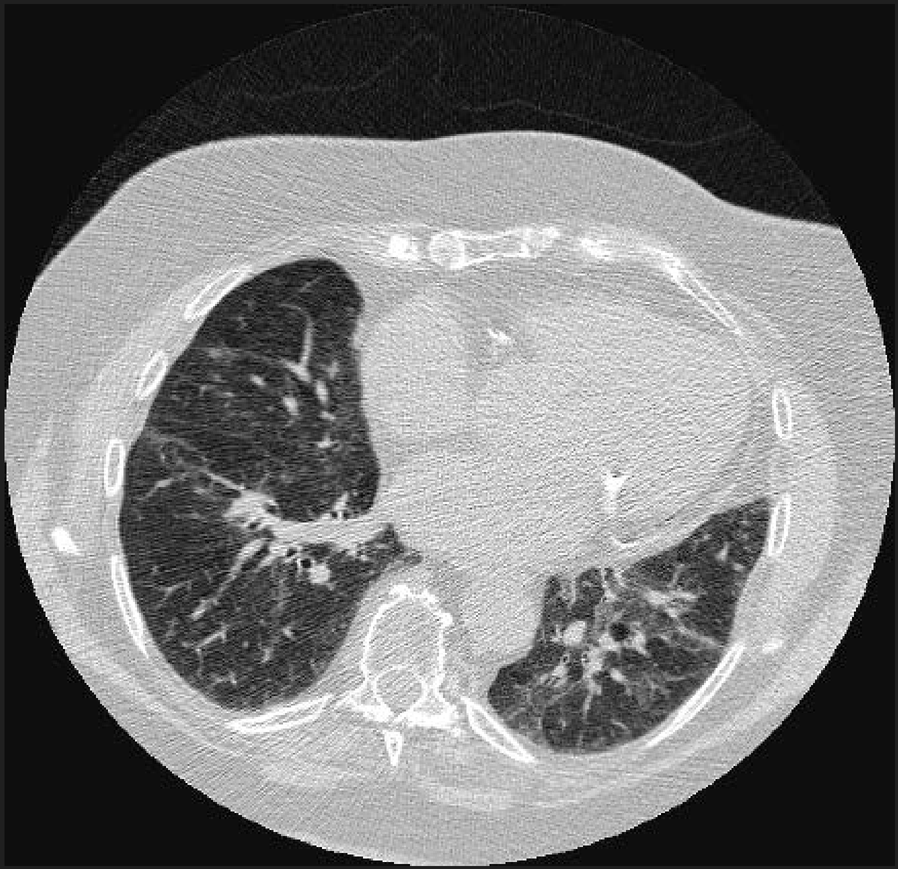
Acquisition variability easily handled by humans, challenging for machines

Noise and kernel normalization

Same for CT

Acquisition Variability

- Noise, contrast, calibration vary with device and institution preferences
- Challenging for machines



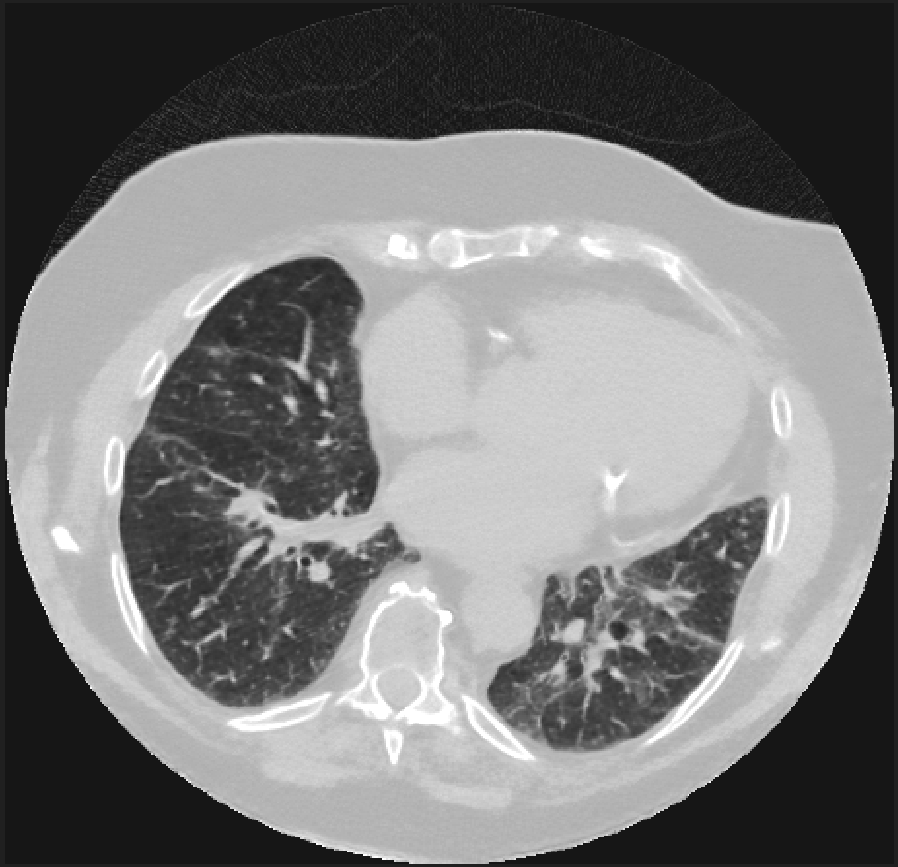
Low Dose CT Slice

Noise and kernel normalization

ClearRead CT

- Adaptive analysis of each scan
- Suppresses noise, adjust contrast and attenuation calibration
- Robust results, massive development time savings
- Future proof

Same for CT



Noise and contrast normalization

Slice thickness normalization

Conventional Interpolation

Slice thickness normalization

Model Based

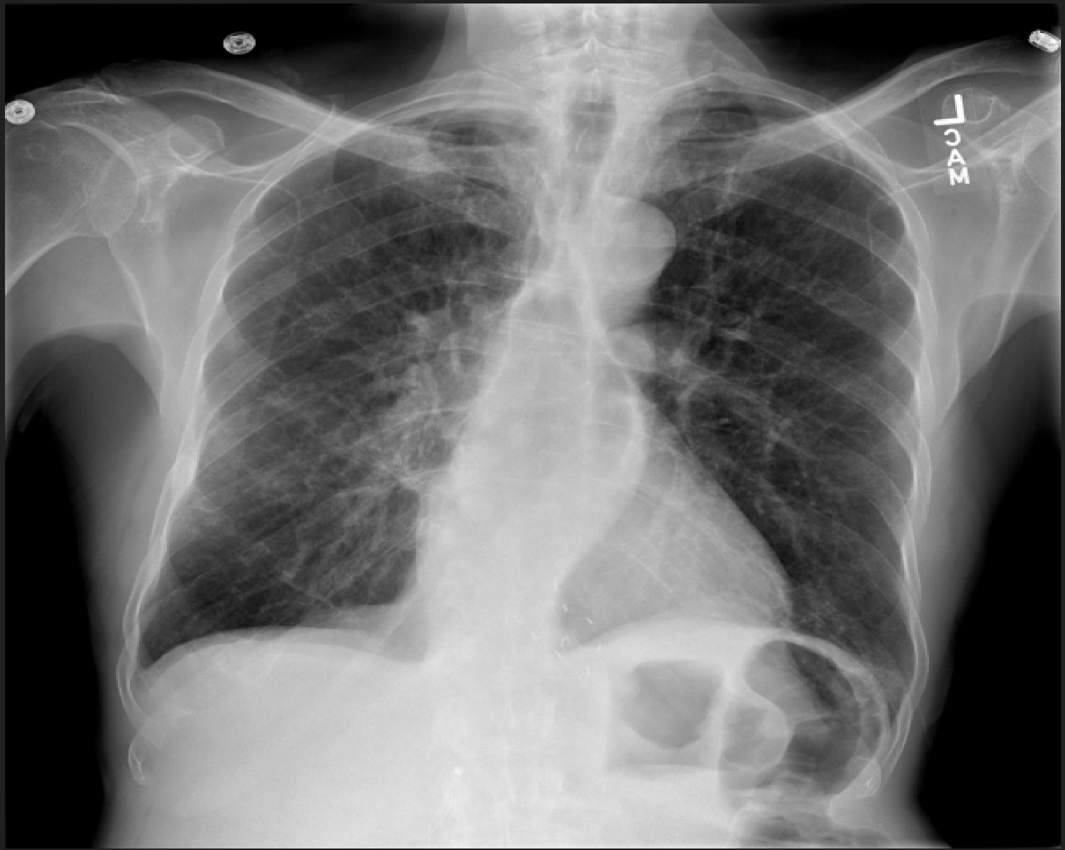
Building Trust in AI

Transparency and Predictability

Regression Applications are more Demanding

Consistency

- Preserved detail and tone
- Ability to toggle



Original

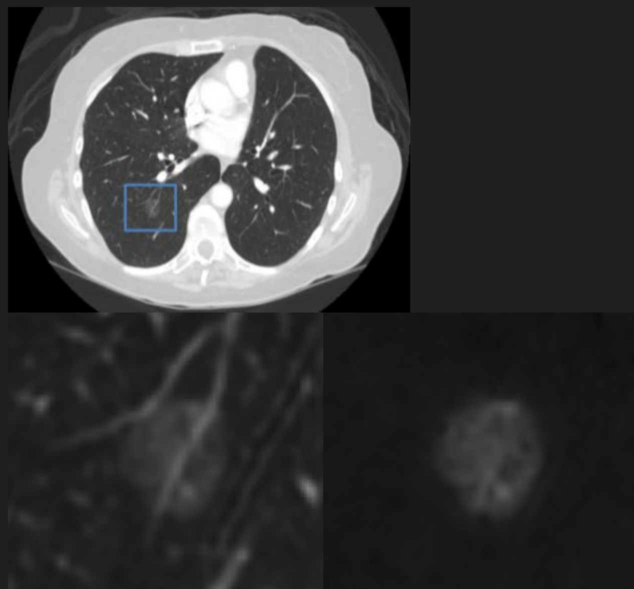
Regression Applications are more Demanding

Consistency

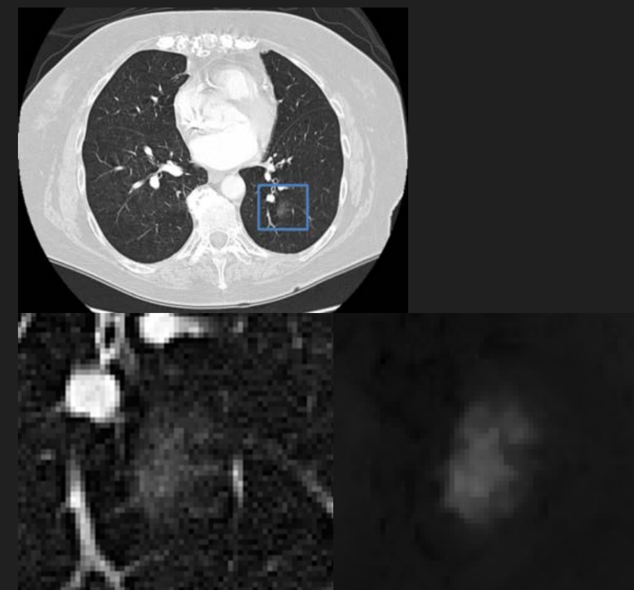
- Preserved detail and tone
- Ability to toggle

ClearRead Bone Suppression

Regression Applications are more Demanding



Ground Glass



Part-solid

- The question of “why” is difficult.
- By precisely controlling the input, we can get at the relevant factors and increase transparency of decisions and measurements.

Building Trust in AI

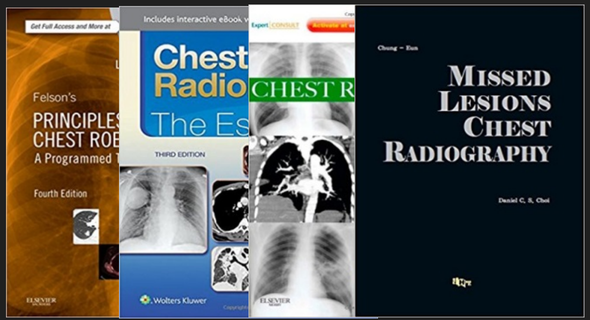
Use of Simulation

"What I cannot create, I do not understand."

Feynman

Why Simulation?

Medical Knowledge

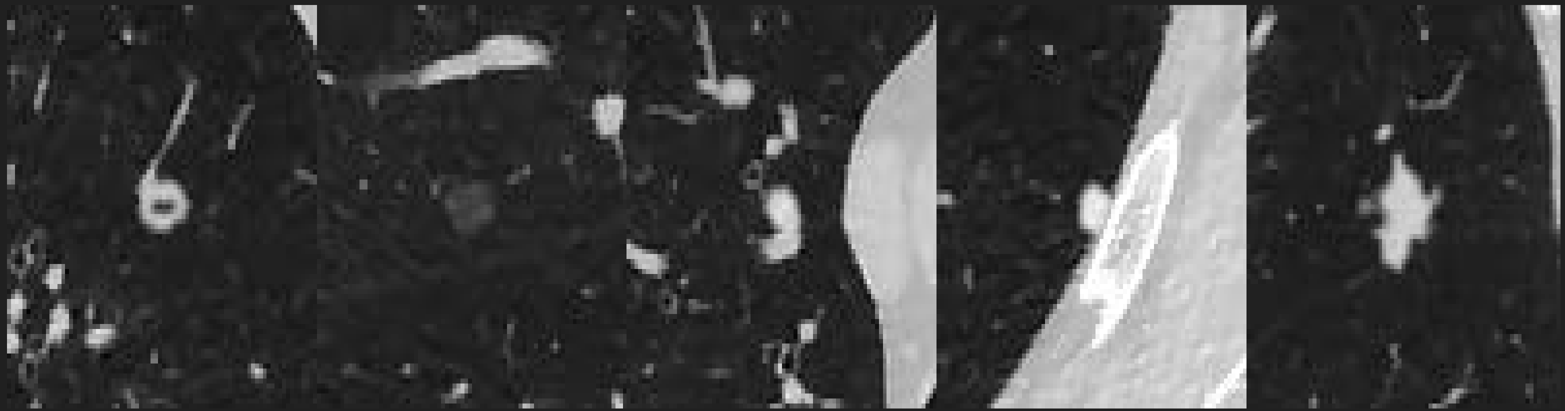


→ Programmed Simulators → AI Development

Database of Examples ↑ AI Development

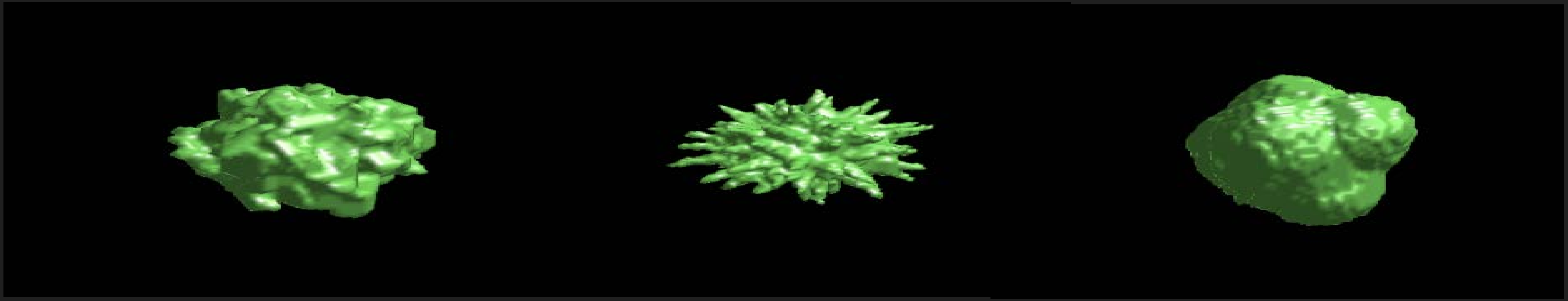
- Rarity, large variations, complex patterns
- Difficult problems require large models – large models need a lot of data with associated ground truth
- Potential for significant gaps, even with large collections

Variation in Disease and the Validation Process



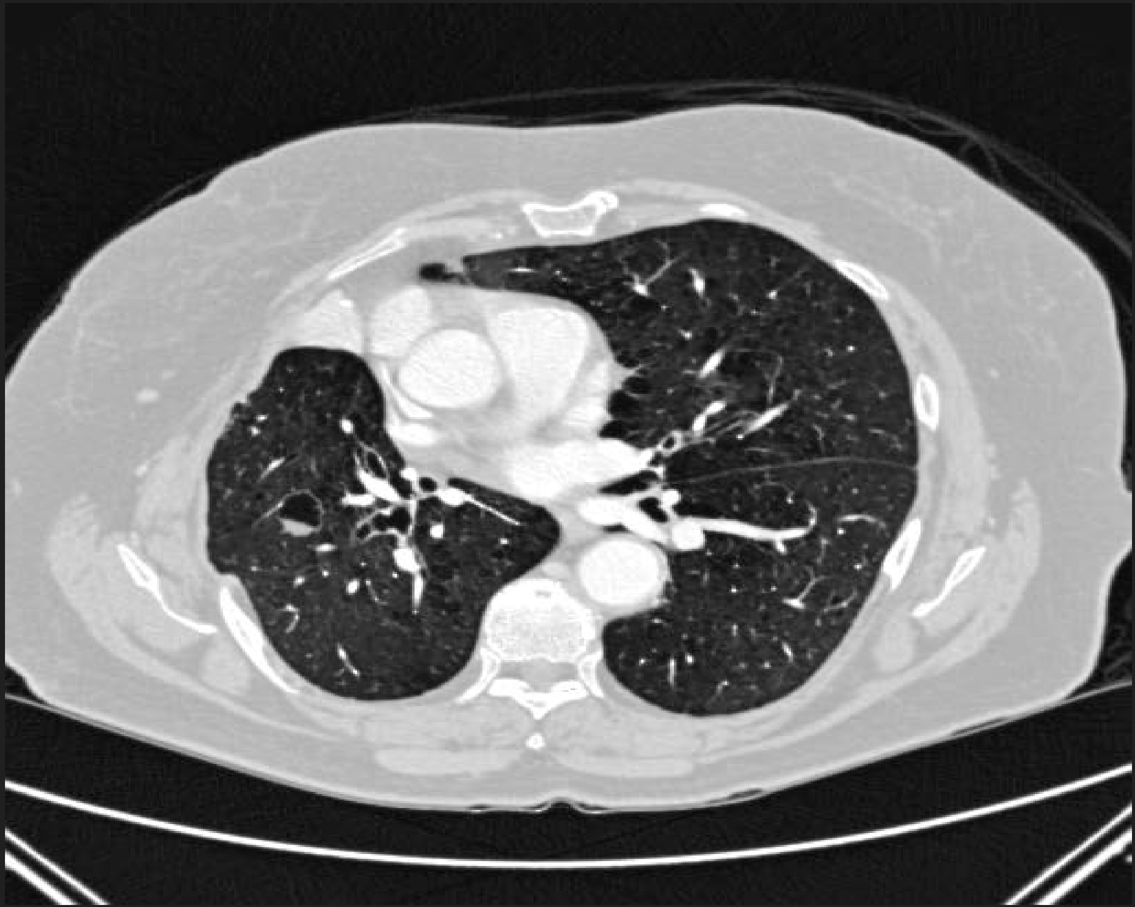
- What really matters is statistical size
- A lot of samples doesn’t necessarily imply sufficient samples in tails of distribution

Simulation: Product Development



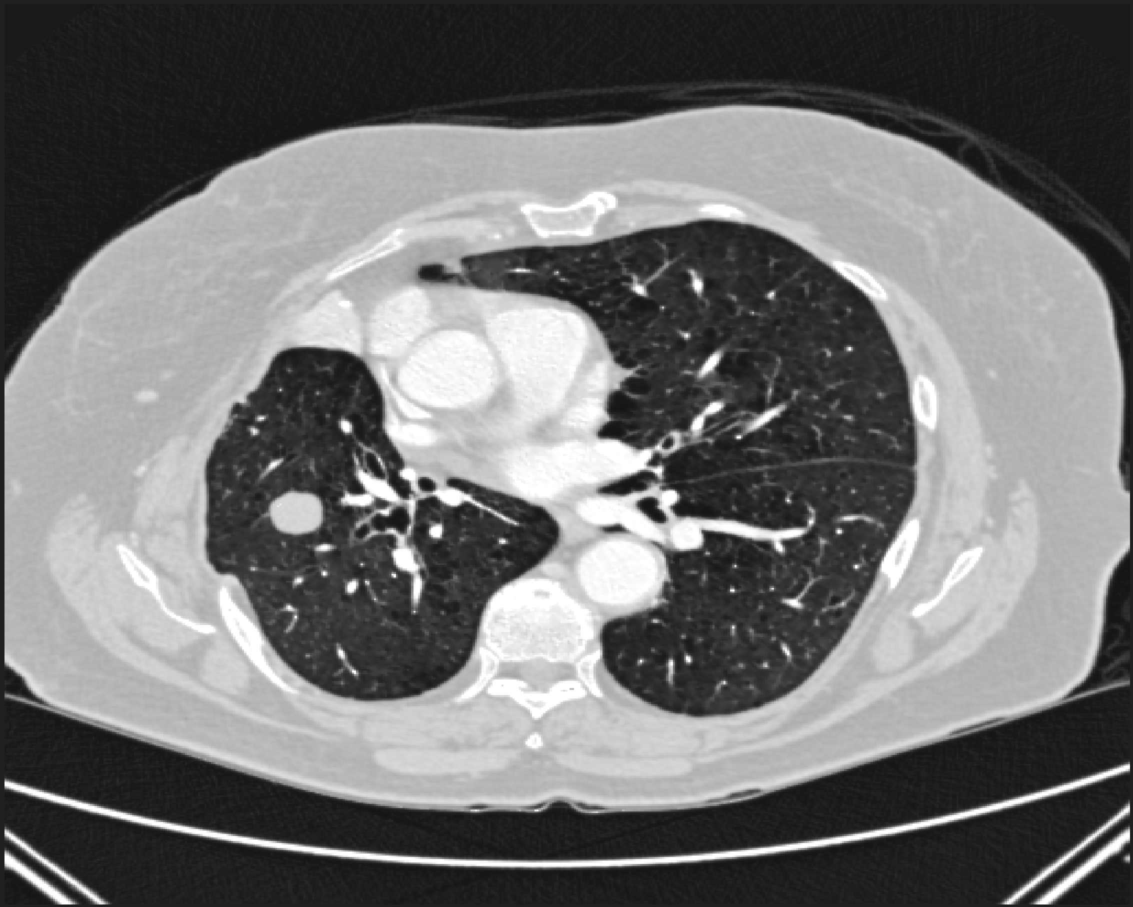
- Allows arbitrary amounts of data to be created cost effectively – critical for machine learning solutions
- Allows infrequent samples to be created
- Observed, prospective weaknesses (a particular class of FN) can be decomposed and then modeled to create adequate training samples
  - Not feasible using just measured data
- Provides precision ground truth, critical to achieving optimal performance

Leveraging Simulation



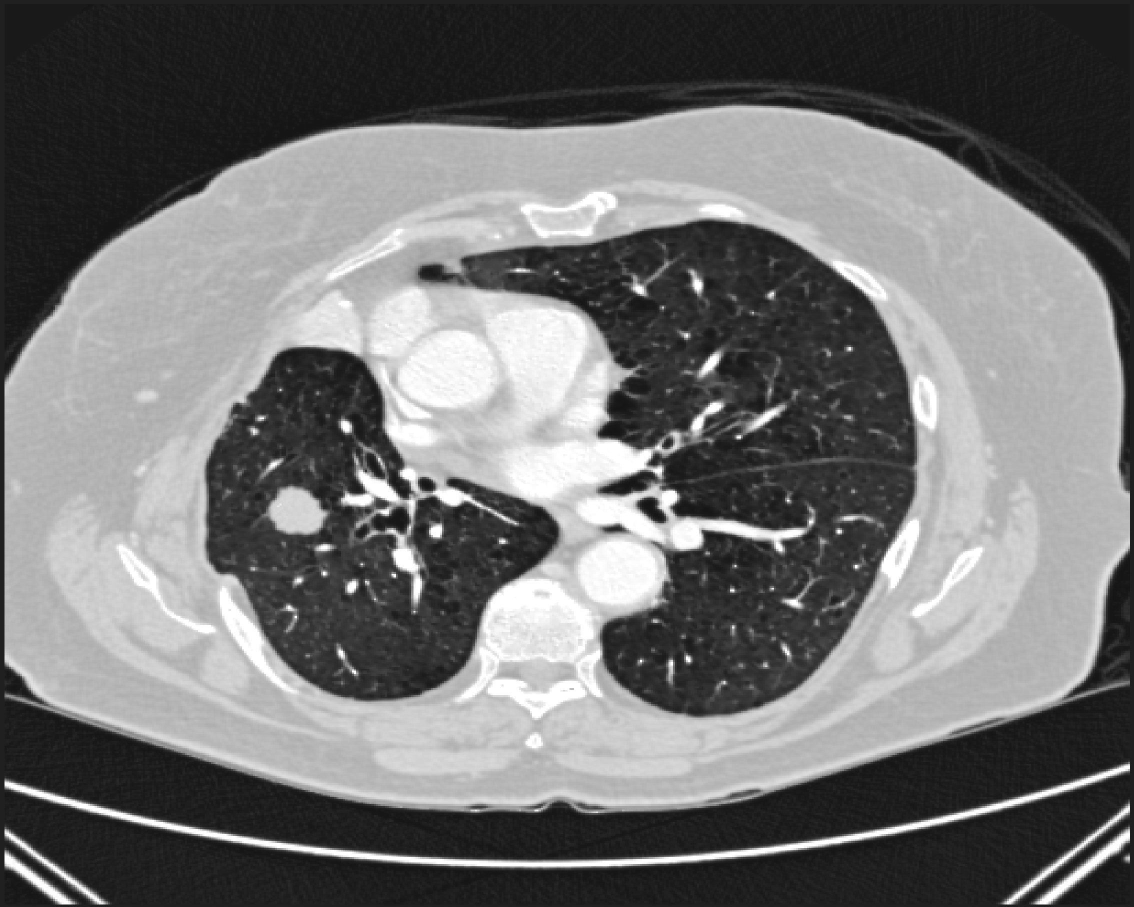
Cavitated

Leveraging Simulation



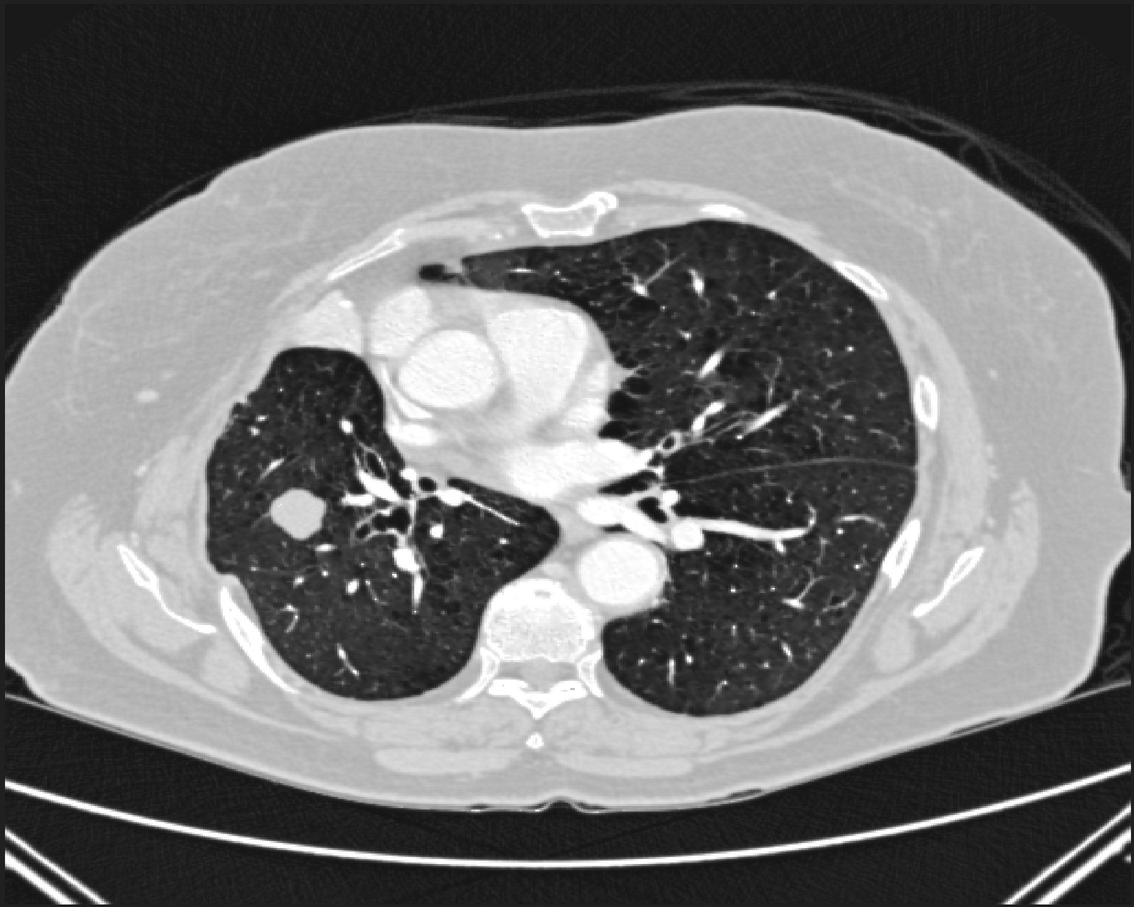
Smooth

Leveraging Simulation



Rough

Leveraging Simulation



Lobulated

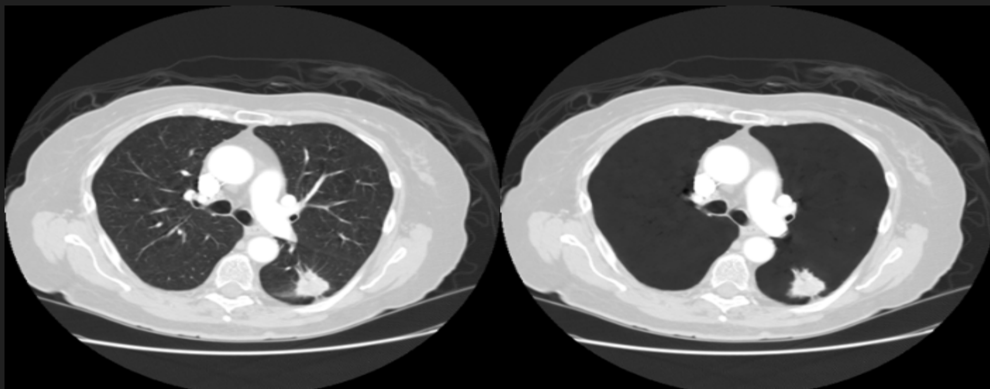
Leveraging Simulation

Spiculation

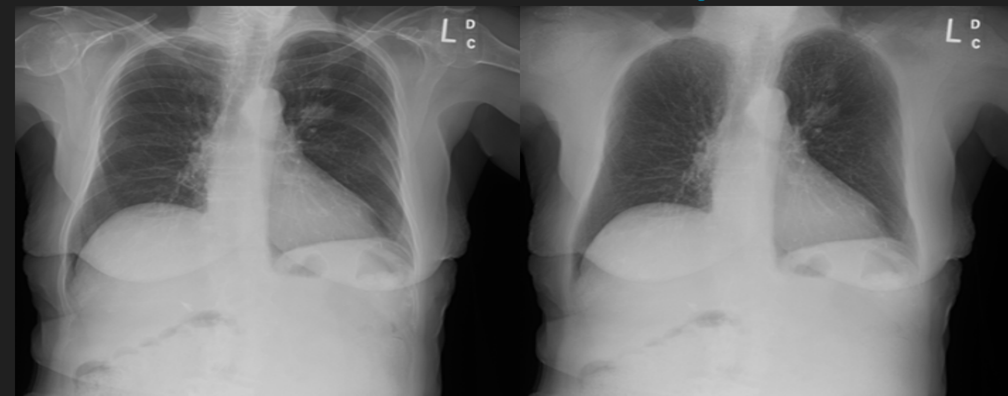
Bringing it all Together

Riverain Technologies – ClearRead Applications

ClearRead CT

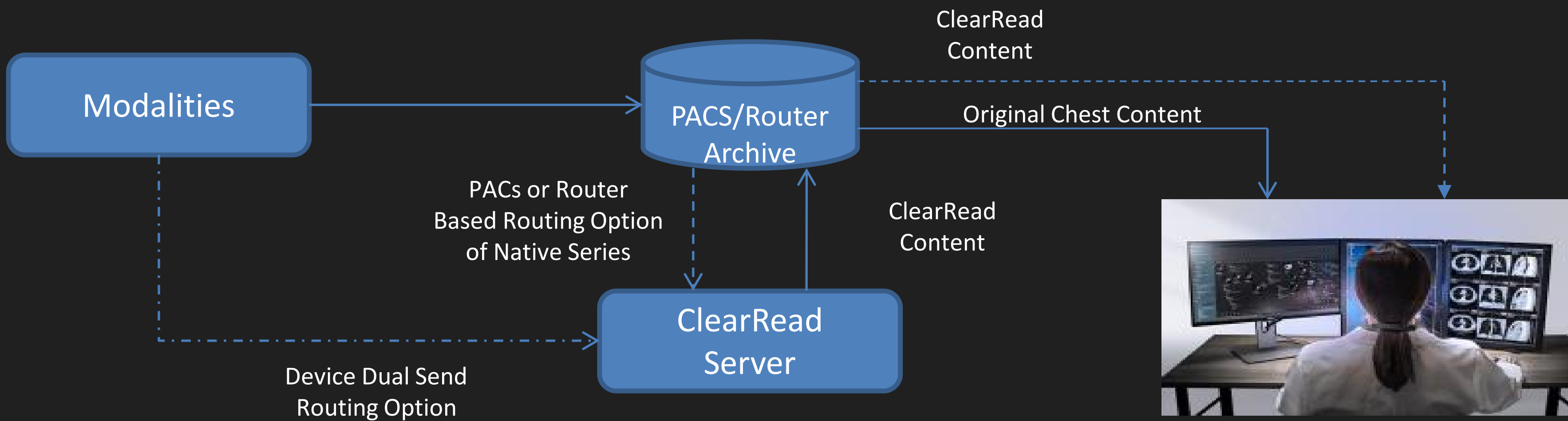


ClearRead Xray



- Five FDA approved products
- Focus is on thoracic imaging
- Clinical AI software at scale

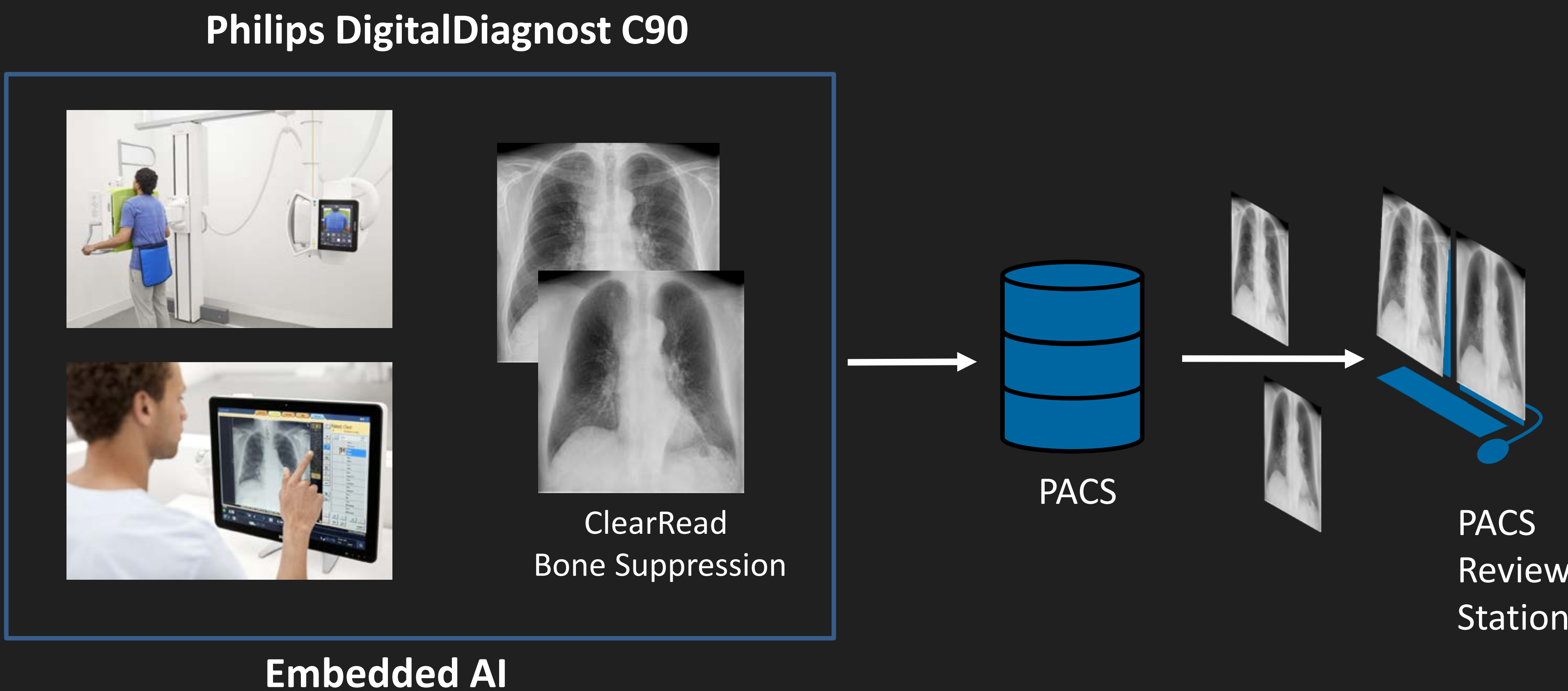
ClearRead Data Workflow



Data Flow:

- Processing occurs on local ClearRead server (physical or virtual machine)
- ClearRead content pushed to PACS archive or read directly from ClearRead server
- ClearRead content read on existing radiologist review station
- ClearRead content available in ‘Real Time’ at Point of Read based on automated routing and processing – No perceived delay by reader critical

ClearRead Modality Embedded Workflow



ClearRead Xray

ClearRead Xray | Bone Suppress

Original

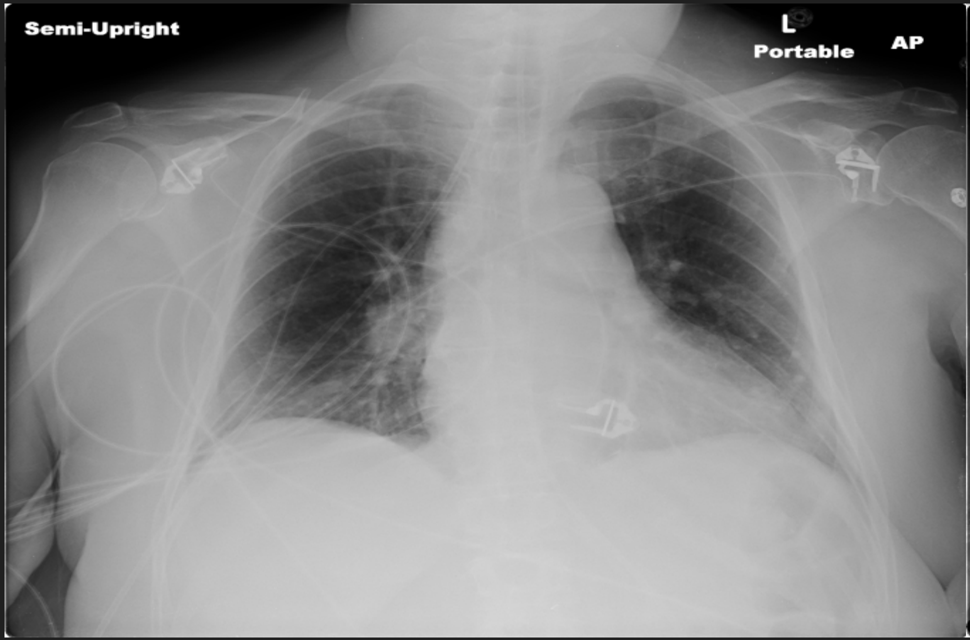
Bone Suppress

Key Features

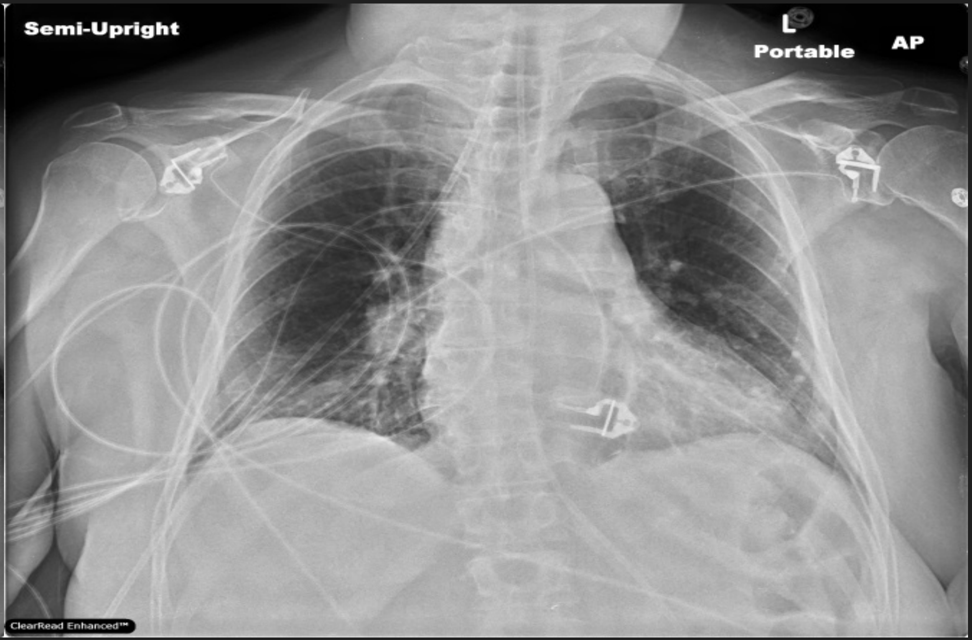
- First FDA approved software for bone suppression, proven to improve reader detection accuracy
- Robust, vendor neutral processing, for your site or entire enterprise
- Stacked review model allows for quick and easy comparison

ClearRead Xray | Enhance

Original



Enhance



Highlights

- Visualizing lines and tubes without distraction
- Vendor neutral image enhancement for consistent presentation

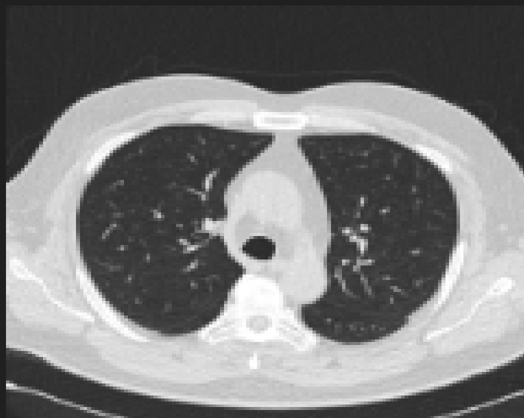
Evidence


Cardiopulmonary Imaging • Original Research
Improved Detection of Subtle Lung Nodules by Use of Chest Radiographs With Bone Suppression Imaging: Receiver Operating Characteristic Analysis With and Without Localization
Comparison of Dual-Energy Subtraction and Electronic Bone Suppression Combined With Computer-Aided Detection on Chest Radiographs: Effect on Human Observers' Performance in Nodule Detection
European Journal of Radiology
Bone suppressed images improve radiologists' detection performance for pulmonary nodules in chest radiographs
Small Lung Cancers: Improved Detection by Use of Bone Suppression Imaging—Comparison with Dual-Energy Subtraction Chest Radiography
Impact of Bone Suppression Imaging on the Detection of Lung Nodules in Chest Radiographs: Analysis of Multiple Reading Sessions
Lung Nodules: Improved Detection with Software That Suppresses the Rib and Clavicle on Chest Radiographs
Radiology

ClearRead CT

ClearRead CT Overview

CT Slice



Vessel Suppress

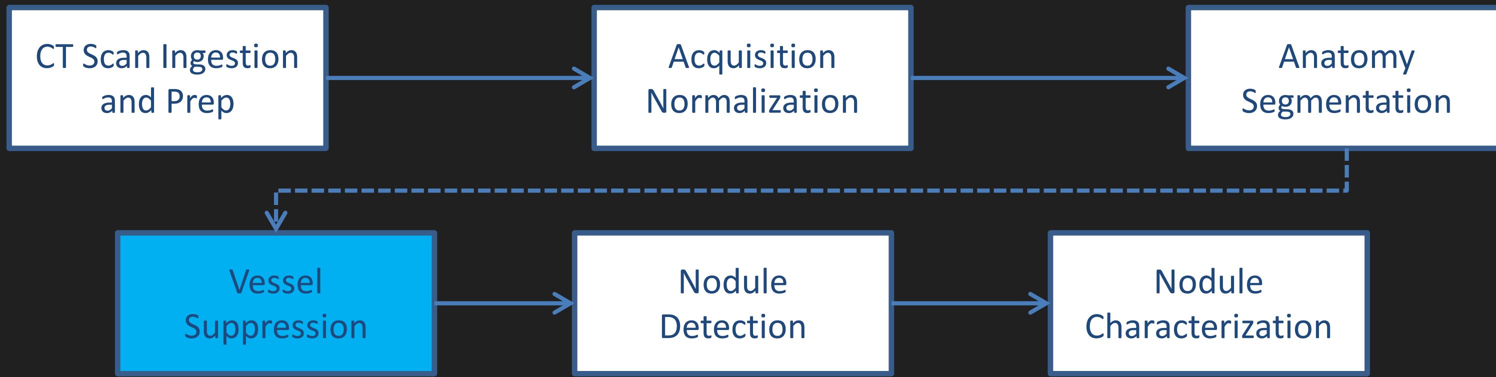
Detect

Highlights

- First FDA cleared system for concurrent reading
- First FDA cleared system to demonstrate improved reader accuracy and reading time
  - 26% reduction in reading time (nodule search)
  - 29% reduction in missed nodules
- First FDA cleared system for non-solid nodules
- Supports non-contrast and contrast chest CT

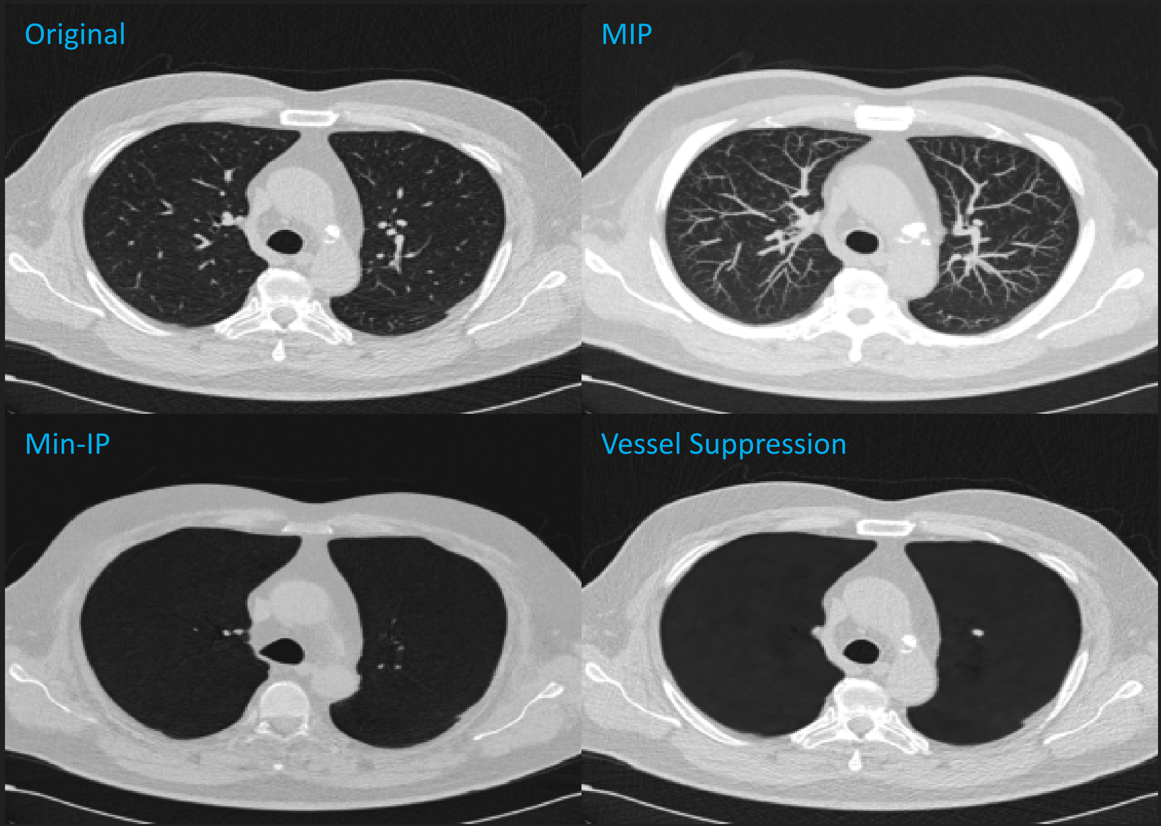
ClearRead CT

Algorithmic Overview



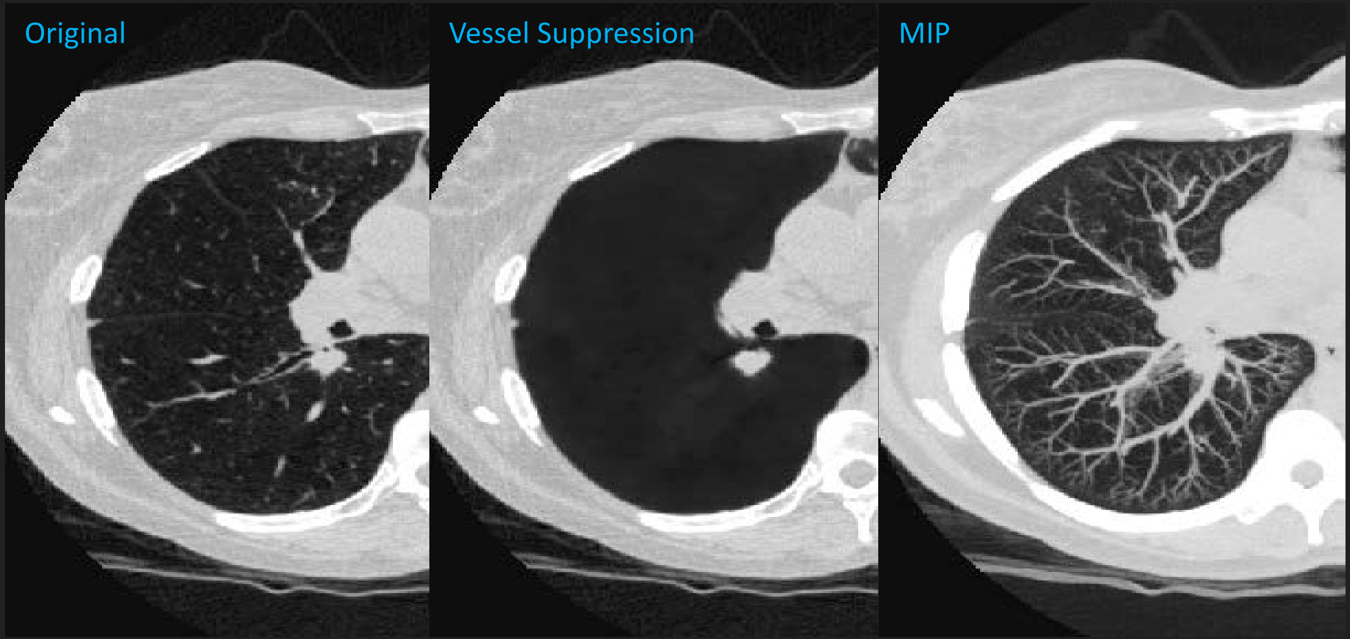
Data Ingestion & Prep:	Ingest CT Data and perform volume preparation
Volume Normalization:	Noise, contrast and sampling matched to target
Anatomy Segmentation:	Segment patient body and lungs
Vessel Suppression:	Suppress vessels based on voxel estimates
Nodule Detection:	Detect, Segment and Classify Nodules
Nodule Characterization:	Volumetrics, morphology and densitometry

Vessel Suppression Compared to MIPs



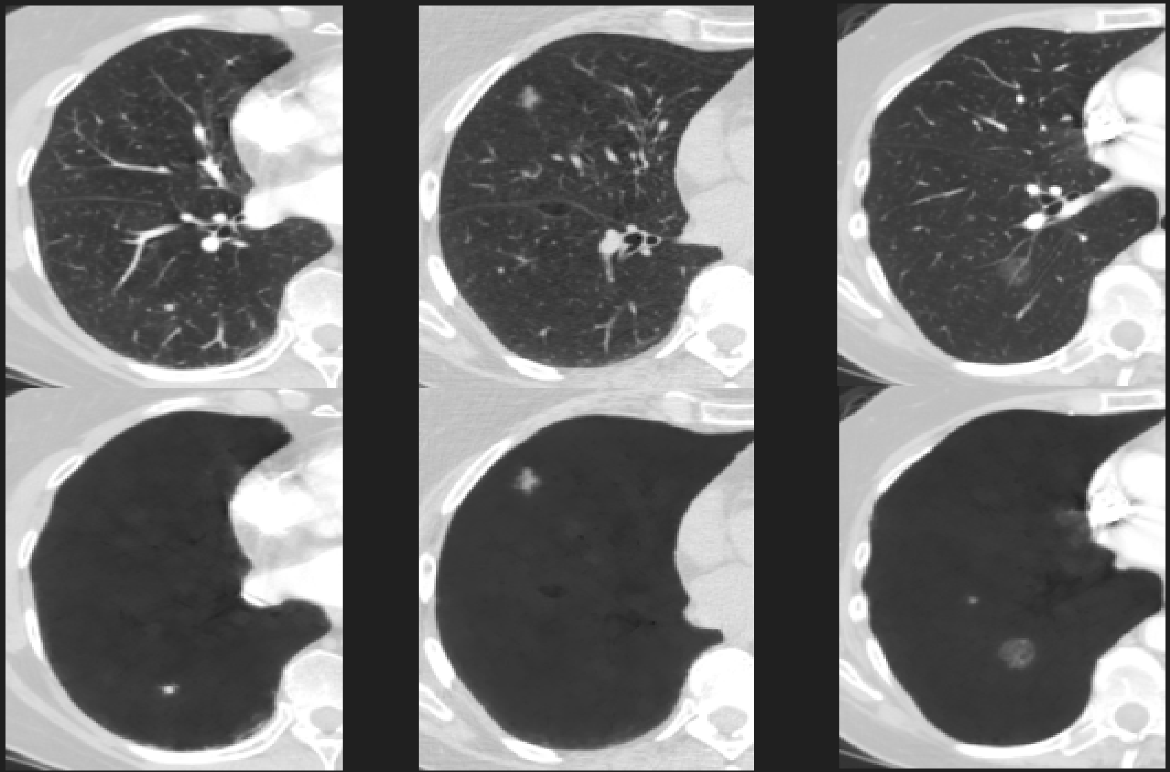
- MIPs are useful for small solid nodules, but problem of clutter and masking remains
- Minimum intensity projections (Min-IPs) are not a viable solution for general nodule enhancement
- Example above is a challenging nodule that was missed by 4/4 readers

Masking Effect of Maximum Intensity Projections



- FN case that is retrospectively very visible
- MIPs can “fuse” nodules with background structures, thus masking their appearance
- With Vessel Suppression, there is no ambiguity, no scrolling back-and-forth for confirmation

ClearRead CT | Vessel Suppress



Native CT Slice

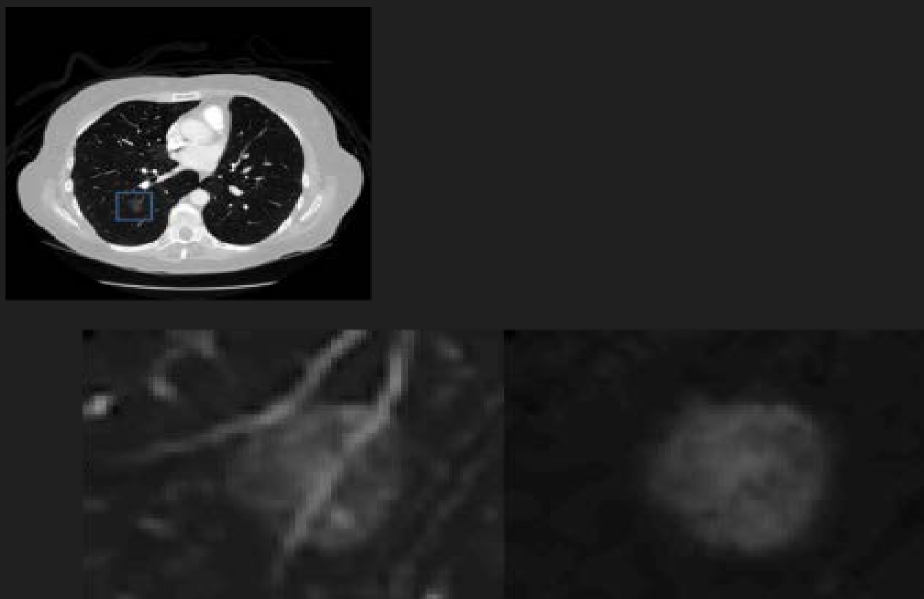
ClearRead CT | Vessel Suppress

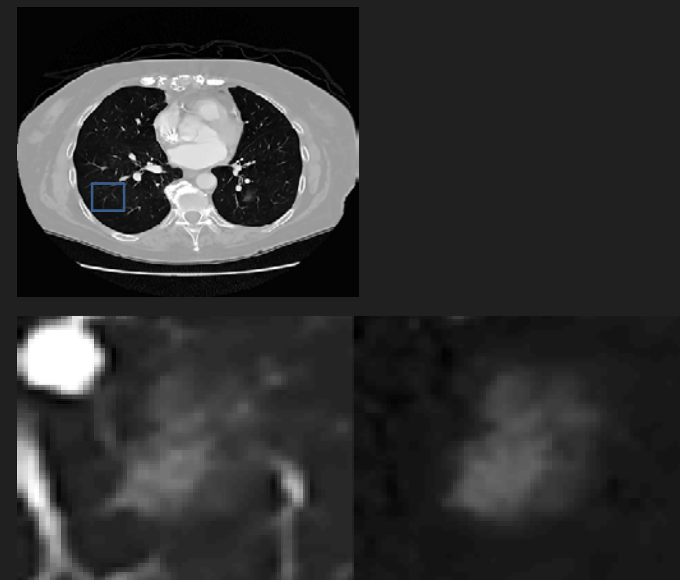
Aids the radiologist in seeing and characterizing solid, part-solid, and ground glass by removing distracting structured noise

ClearRead CT

Beyond Detection

Drilling down past detection, to the underlying structures, where MIPs cannot go



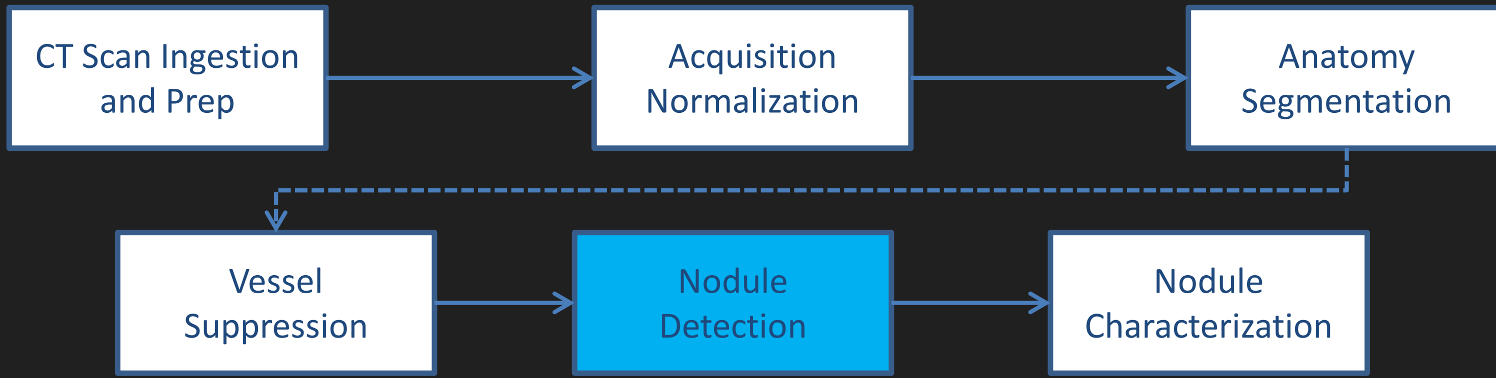


Radiologists have high disagreement (kappa < 0.4) when typing part-solid nodules

✓ Believe this can be significantly improved based on Vessel Suppression

ClearRead CT

Algorithmic Overview



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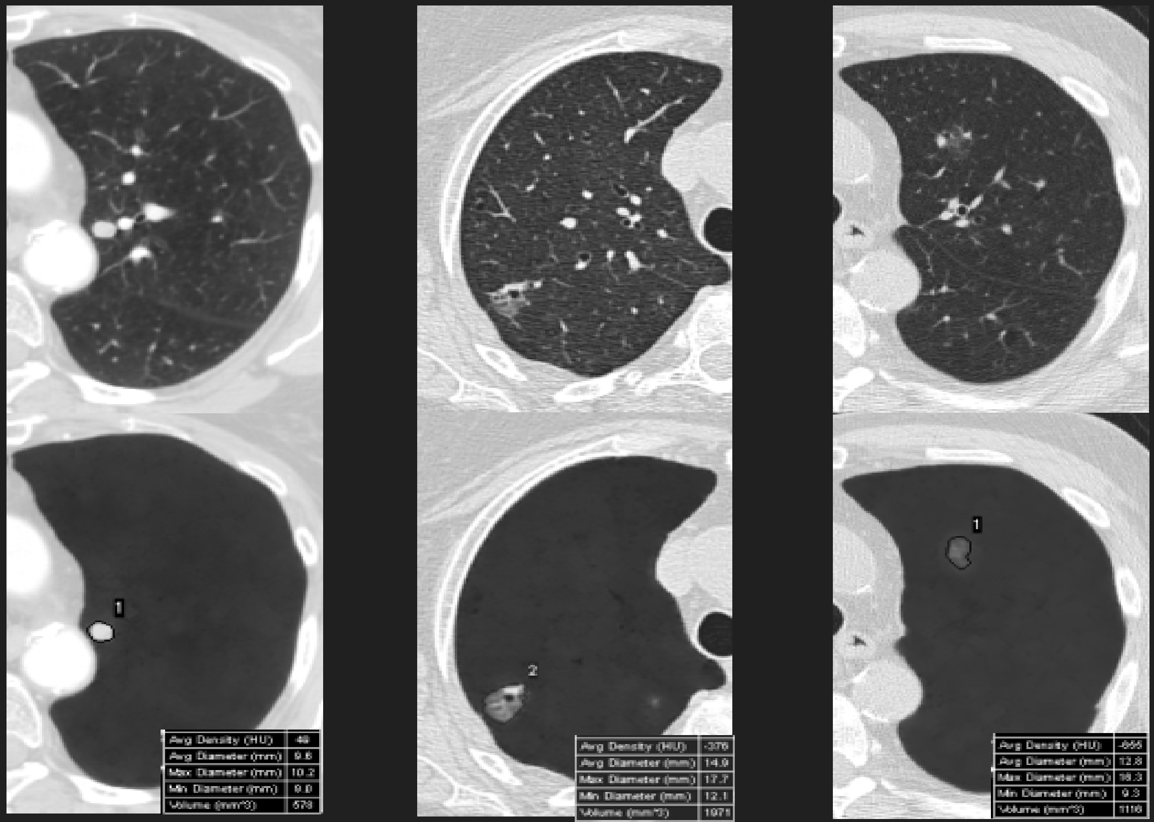
ClearRead CT | Detect

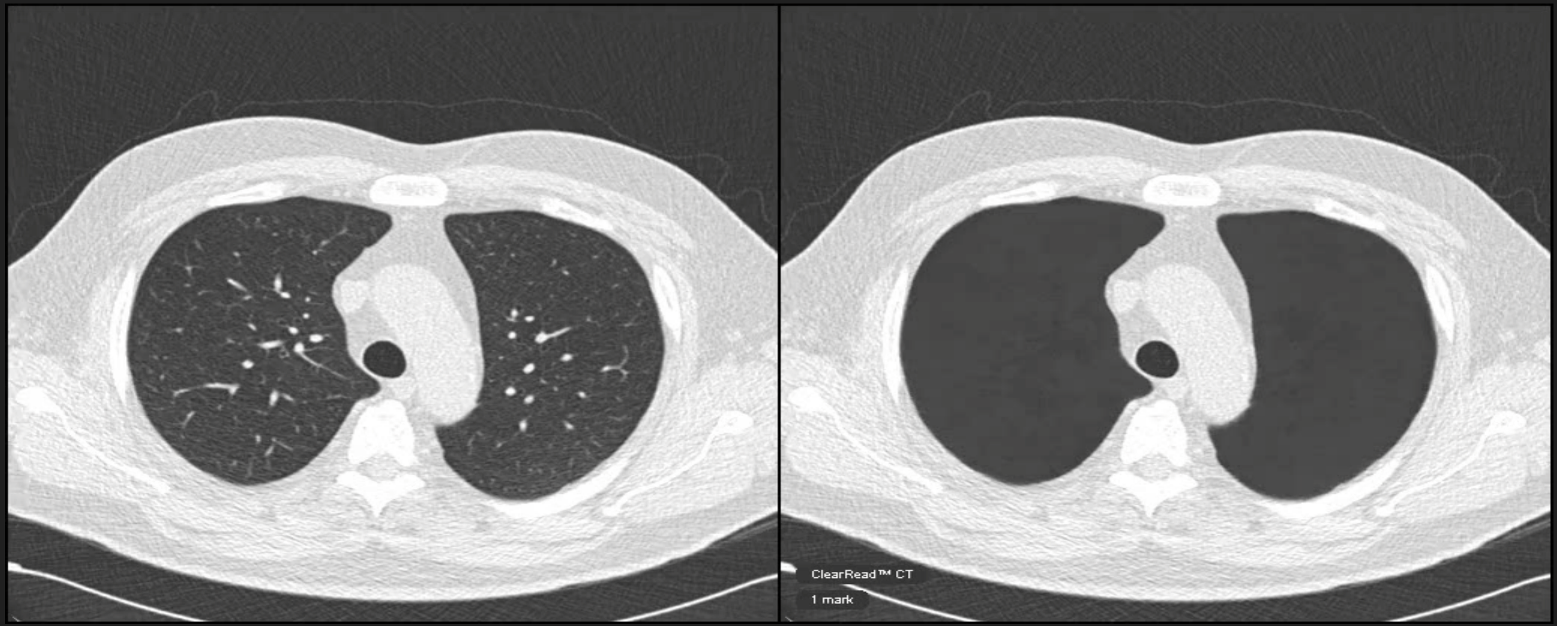


Native CT Slice

ClearRead CT | Detect

- Precisely detects and characterizes regions of interest (solid, part-solid and ground glass) that may be lung cancer

ClearRead CT | Detect



Fly Through

Evidence

Evidence: ClearRead CT Pivotal Study

Machine Test Results

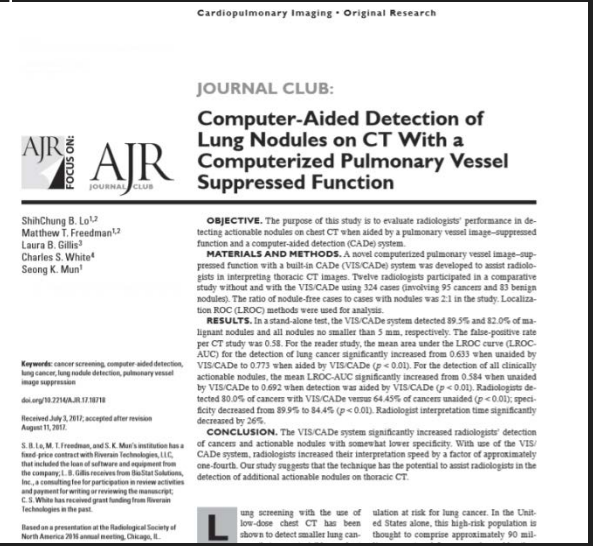
- Detection Results:
  - On a blind dataset comprised of solid, mixed, and ground glass actionable nodules, ClearRead CT detected 82.5% of the actionable nodules (89% of cancers) with an average false positive rate of 0.75 per patient .

Reader Study Results

- Detection Results:
  - In a MRMC reader study, ClearRead CT led to statistically significant improved area under t
    receiver operating curve for aided readers.
  - 2 Arm, blinded study
  - 12 readers, 324 cases with 2:1 normal to cancer cases

- Reading Efficiency
  - Radiologists reading with ClearRead CT read 26% faster than when unaided

- Reading Accuracy
  - Radiologists detected 29% of previously missed nodules


Cardiopulmonary Imaging • Original Research

JOURNAL CLUB:

Computer-Aided Detection of Lung Nodules on CT With a Computerized Pulmonary Vessel Suppressed Function

ShihChung B. Lo[1,2]
Matthew T. Freedman[1,2]
Laura B. Gillis[3]
Charles S. White[4]
Seong K. Mun[1]

OBJECTIVE. The purpose of this study is to evaluate radiologists' performance in detecting actionable nodules on chest CT when aided by a pulmonary vessel image–suppressed function and a computer-aided detection (CADe) system.

MATERIALS AND METHODS. A novel computerized pulmonary vessel image–suppressed function with a built-in CADe (VIS/CADe) system was developed to assist radiologists in interpreting thoracic CT images. Twelve radiologists participated in a comparative study without and with the VIS/CADe using 324 cases (involving 95 cancers and 83 benign nodules). The ratio of nodule-free cases to cases with nodules was 2:1 in the study. Localization ROC (LROC) methods were used for analysis.

RESULTS. In a stand-alone test, the VIS/CADe system detected 89.5% and 82.0% of malignant nodules and all nodules no smaller than 5 mm, respectively. The false-positive rate per CT study was 0.58. For the reader study, the mean area under the LROC curve (LROC-AUC) for the detection of lung cancer significantly increased from 0.633 when unaided by VIS/CADe to 0.773 when aided by VIS/CADe ($p < 0.01$). For the detection of all clinically actionable nodules, the mean LROC-AUC significantly increased from 0.584 when unaided by VIS/CADe to 0.692 when detection was aided by VIS/CADe ($p < 0.01$). Radiologists detected 80.0% of cancers with VIS/CADe versus 64.45% of cancers unaided ($p < 0.01$); specificity decreased from 89.9% to 84.4% ($p < 0.01$). Radiologist interpretation time significantly decreased by 26%.

CONCLUSION. The VIS/CADe system significantly increased radiologists' detection of cancers and actionable nodules with somewhat lower specificity. With use of the VIS/CADe system, radiologists increased their interpretation speed by a factor of approximately one-fourth. Our study suggests that the technique has the potential to assist radiologists in the detection of additional actionable nodules on thoracic CT.

Keywords: cancer screening, computer-aided detection, lung cancer, lung nodule detection, pulmonary vessel image suppression

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Received July 3, 2017; accepted after revision August 11, 2017.

S. B. Lo, M. T. Freedman, and S. K. Mun's institution has a fixed-price contract with Riverain Technologies, LLC, that included the loan of software and equipment from the company; L. B. Gillis receives from BioStat Solutions, Inc., a consulting fee for participation in review activities and payment for writing or reviewing the manuscript; C. S. White has received grant funding from Riverain Technologies in the past.

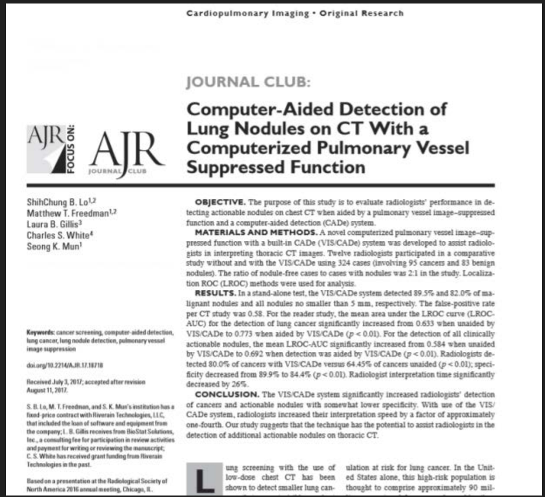
Based on a presentation at the Radiological Society of North America 2016 annual meeting, Chicago, IL.

Lung screening with the use of low-dose chest CT has been shown to detect smaller lung can- ulation at risk for lung cancer. In the United States alone, this high-risk population is thought to comprise approximately 90 mil-

Evidence: ClearRead CT

Objective: To evaluate whether vessel-suppressed computed tomography (VSCT) can be reliably used for semi-automated volumetric measurements of solid pulmonary nodules, as compared to standard CT (SCT)

Results: Semi-automated volumetric measurements on VSCT showed substantial agreement with the standard of reference (Lin's CCC=0.990 for Reader 1; 0.985 for Reader 2).


Cardiopulmonary Imaging • Original Research

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Lung screening with the use of low-dose chest CT has been shown to detect smaller lung can- ulation at risk for lung cancer. In the United States alone, this high-risk population is thought to comprise approximately 90 mil-

Conclusions: VSCT datasets are feasible for the measurements of solid nodules, showing an almost perfect concordance between readers and with measurements on SCT.

Evidence: ClearRead CT

Effect of Artificial Intelligence Based Vessel Suppression and Automatic Detection of Part-Solid and Ground-Glass Nodules on Low-Dose Chest CT RSNA 2018, Ramandeep Sign, et.al. Mass General Hospital

RESULTS

With addition of AI-VS images, R1 and R2 detected 290 nodules (126 PSN, 164 SSN) and 293 (132 PSN, 161 GGN), respectively, which were significantly greater than those detected without the AI-VS (p= 0.004). AI-VS aided in detection of solid component in 22 PSN which were deemed SSN by both readers.

CONCLUSION

AI-VS improves detection and characterization of GGN and PSN on LDCT of the chest. Specifically, improved and easier detection of the solid component in non-solid nodules with AIVScan avoid false down-grading of Lung-RADS category, and thus help in appropriate patient management.

Evidence: ClearRead CT

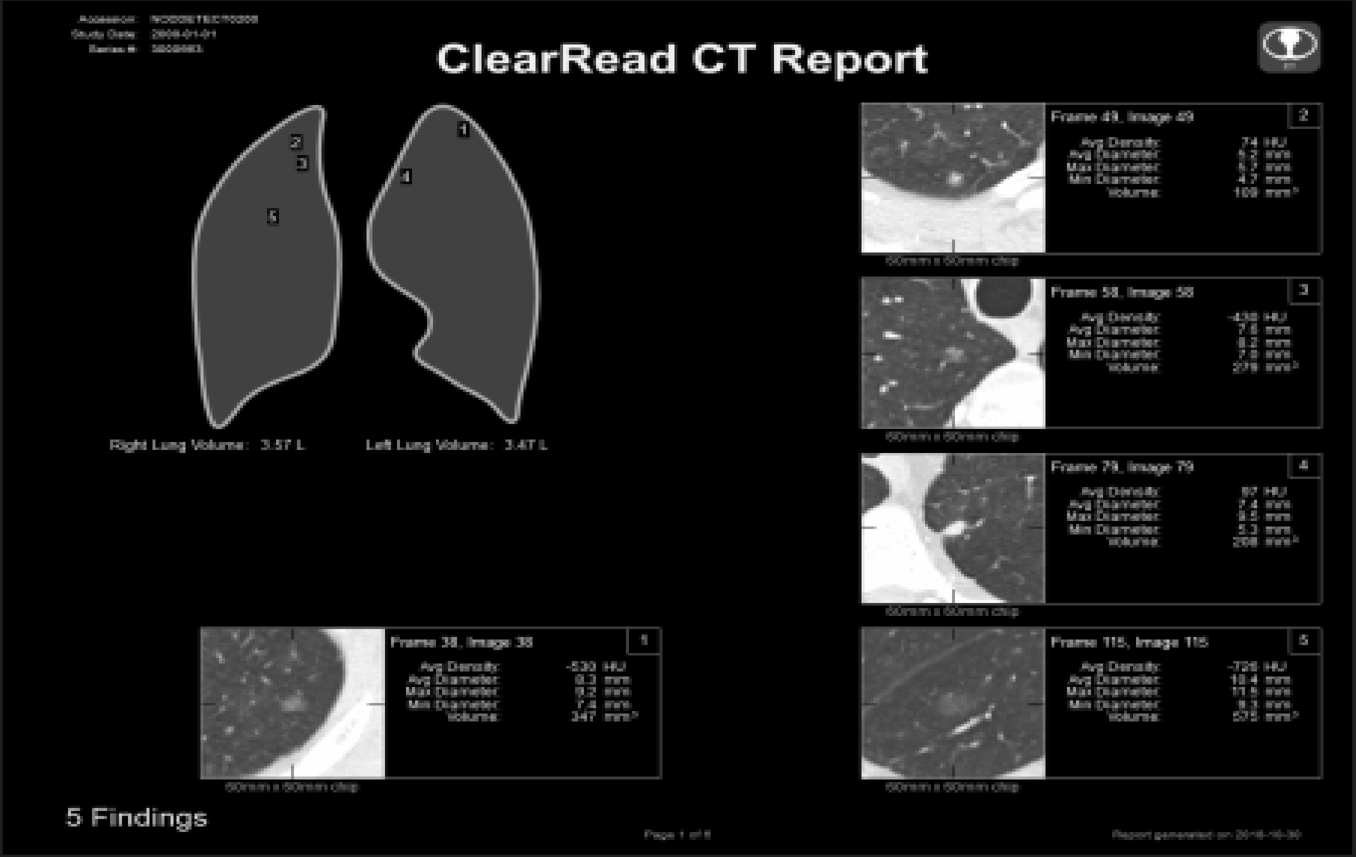
- Prospectively processing 100,000s Chest CTs Annually
- 20+ sites across AMCs, Rad Groups and VAs
- Select Sites
  - Duke Health
  - Michigan Medicine
  - Einstein Medical Center
  - University of Chicago Medicine
  - University of Maryland Medical System
  - University of Wisconsin Health

Multiple VA Centers

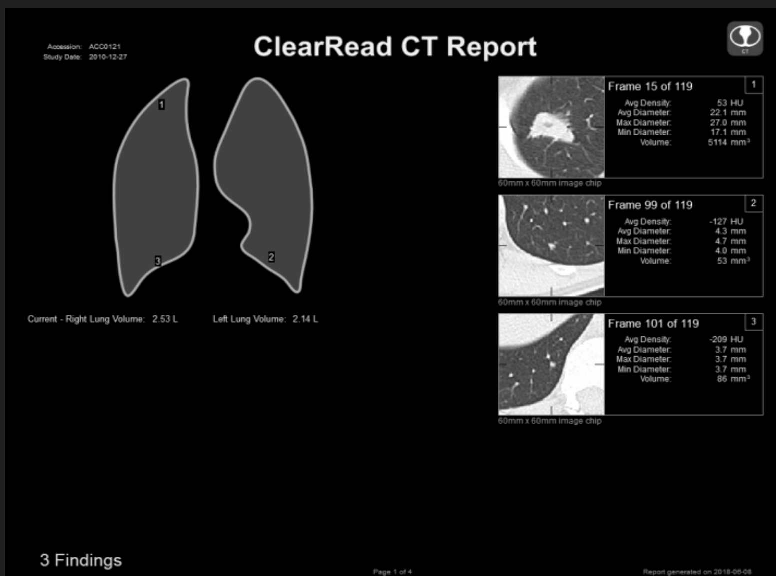
ClearRead CT Workflow

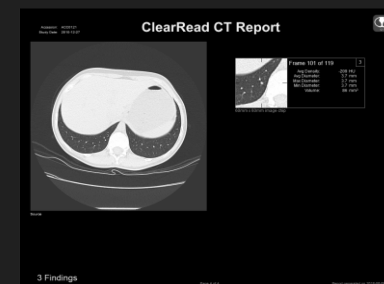
ClearRead CT Summary Report

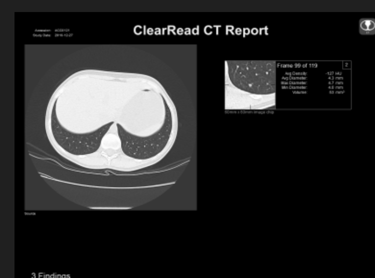
Secondary Capture Option



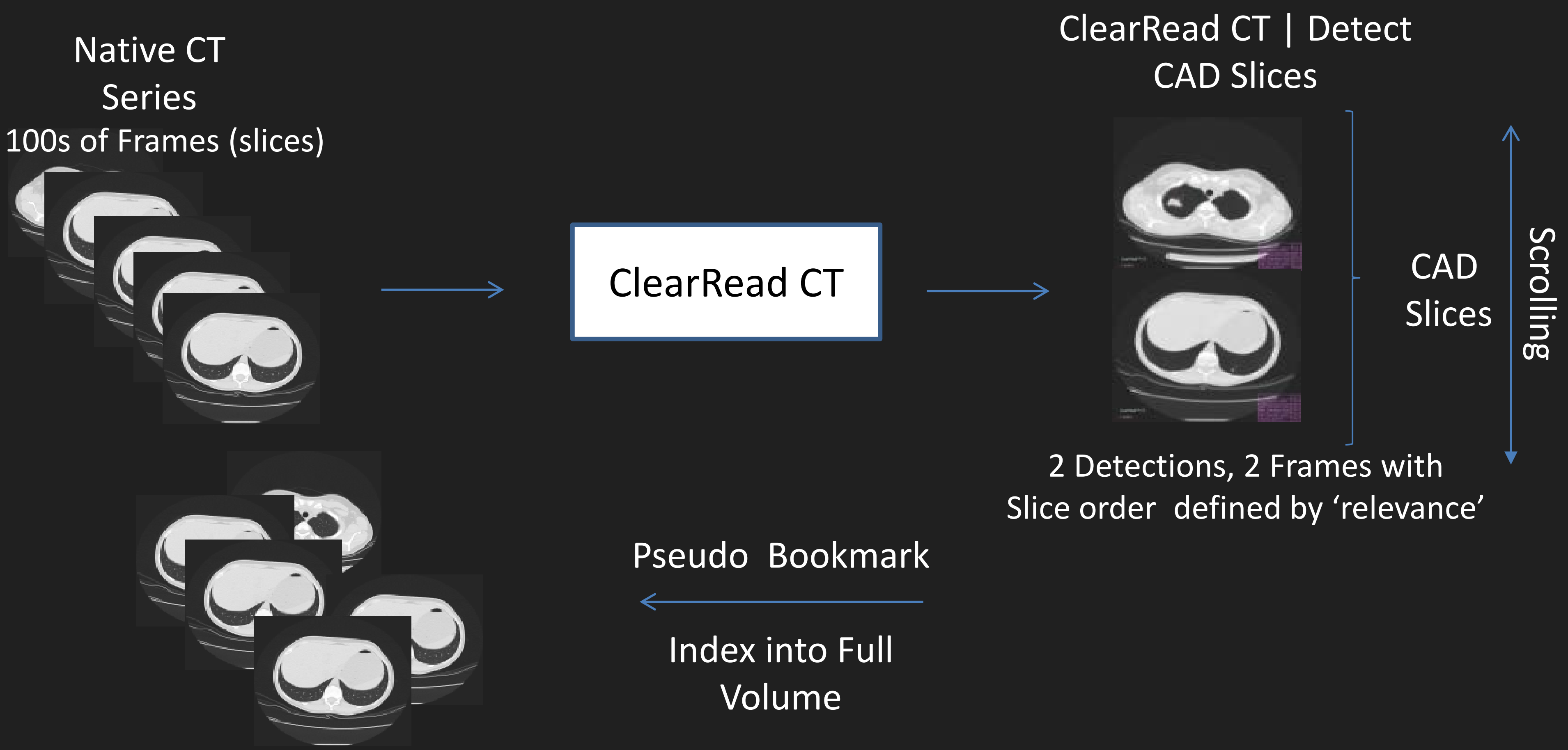
ClearRead CT Report with Findings Frames



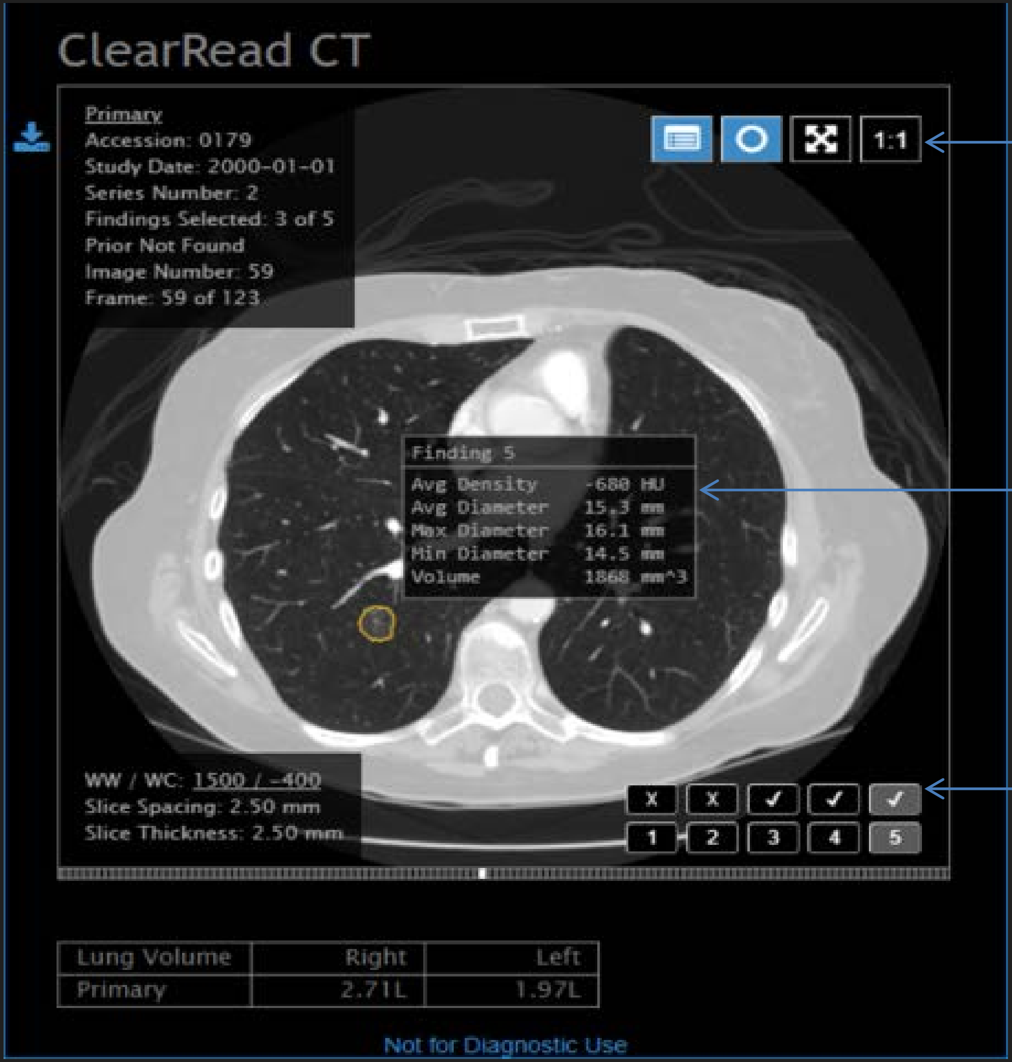




Bookmarking with CAD Slices



ClearRead Viewer



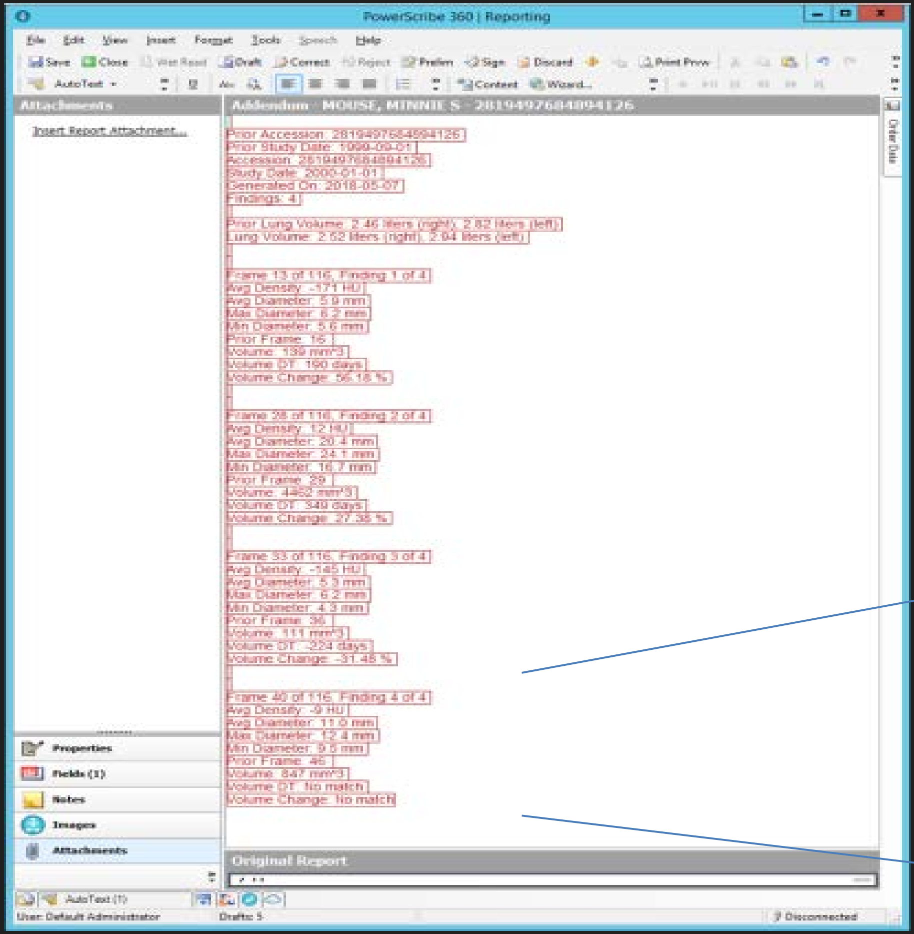
Standard Workstation Tools

Measurement Pane

Bookmark Navigation
Accept/Reject Marks for Reporting

Nuance PowerScribe 360

Integration/Reporting



The integration of ClearRead CT and Nuance PowerScribe 360 enables optimal clinical workflow by automatically updating the report with the ClearRead CT findings.

Frame 40 of 116. Finding 4 or 4	
Average Density	-9 HU
Average Diameter	11.0 mm
Max Diameter	12.4 mm
Min Diameter	9.5 mm
Prior Frame	46
Volume	847 mm^3
Volume DT	No Match
Volume Change	No Match

Critical Clinical Considerations

- Efficient, seamless workflow on existing workstations
- Improved reading and reporting efficiency
- Improved accuracy (High sensitivity and specificity)
- Predictability
  - Never underestimate the Importance of an anecdote - Users loose confidence quickly
  - A ‘small’ change in input cannot lead to a ‘large’ perceived change in output
    - A common issue with binary decision making
- Automatic reporting
- Robust handling of sources of variance
- Minimization of ‘black box’ effect

Conclusion

- Building systems that will work in a clinical environment requires more than just a lot of data and deep neural networks
  - Understand and account for sources of variance and neutralize by design
- Domain knowledge has to be utilized in order to design, build and deploy reliable systems
  - USE Cases
  - Workflow integration

Thank You