RADLogics™

YOUR OWN VIRTUAL-RESIDENT™

Virtual Resident ™: Deep Learning Image Analysis for Efficient and Enhanced-Value Radiology Reporting

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AuntMinnie.com
BEST NEW RADIOLOGY VENDOR
2015

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Talk Outline

- Identifying the Need
- The Virtual Resident solution
- Developing an App
- Deep Learning image analysis example Apps:
  - Chest CT
  - Chest X-ray
  - MR lesions
- Developing a Platform for Apps & A complete Ecosystem
- Final thoughts

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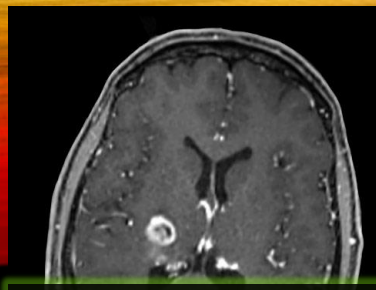
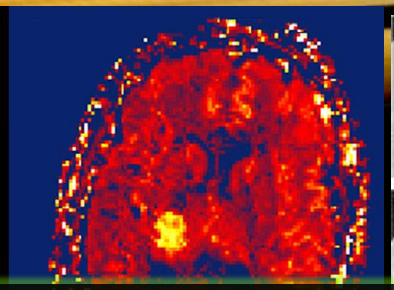
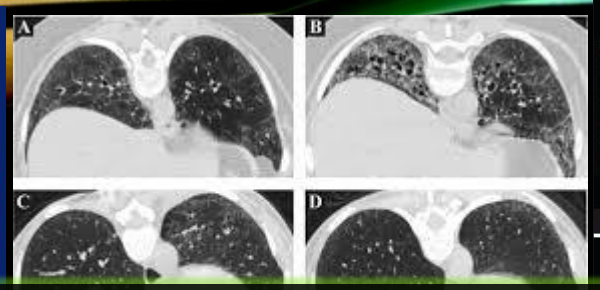

IMAGING

25 second CT scans produce up to 2000 images

PET/CT requires review of up to 6000 images

Breast US can create 5000 images

5 Billion studies per year worldwide, and growing

Pain Point

Limited Time to Review Ever increasing Number of Images

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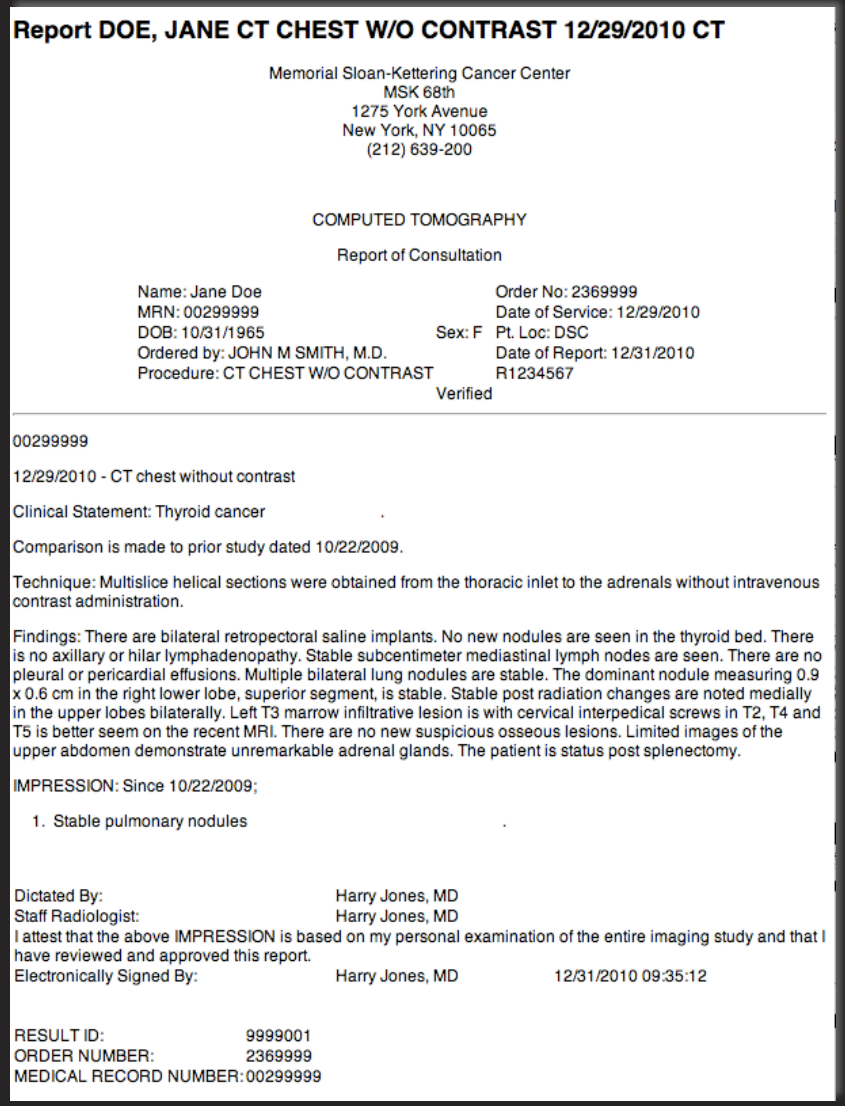
Radiologist Report Example

Textual Report of Findings and Diagnosis



Report DOE, JANE CT CHEST W/O CONTRAST 12/29/2010 CT

Memorial Sloan-Kettering Cancer Center
MSK 68th
1275 York Avenue
New York, NY 10065
(212) 639-200

COMPUTED TOMOGRAPHY

Report of Consultation

Name: Jane Doe		Order No: 2369999
MRN: 00299999		Date of Service: 12/29/2010
DOB: 10/31/1965	Sex: F	Pt. Loc: DSC
Ordered by: JOHN M SMITH, M.D.		Date of Report: 12/31/2010
Procedure: CT CHEST W/O CONTRAST		R1234567

Verified

00299999

12/29/2010 - CT chest without contrast

Clinical Statement: Thyroid cancer .

Comparison is made to prior study dated 10/22/2009.

Technique: Multislice helical sections were obtained from the thoracic inlet to the adrenals without intravenous contrast administration.

Findings: There are bilateral retropectoral saline implants. No new nodules are seen in the thyroid bed. There is no axillary or hilar lymphadenopathy. Stable subcentimeter mediastinal lymph nodes are seen. There are no pleural or pericardial effusions. Multiple bilateral lung nodules are stable. The dominant nodule measuring 0.9 x 0.6 cm in the right lower lobe, superior segment, is stable. Stable post radiation changes are noted medially in the upper lobes bilaterally. Left T3 marrow infiltrative lesion is with cervical interpedical screws in T2, T4 and T5 is better seem on the recent MRI. There are no new suspicious osseous lesions. Limited images of the upper abdomen demonstrate unremarkable adrenal glands. The patient is status post splenectomy.

IMPRESSION: Since 10/22/2009;

1. Stable pulmonary nodules .

Dictated By:	Harry Jones, MD	
Staff Radiologist:	Harry Jones, MD	

I attest that the above IMPRESSION is based on my personal examination of the entire imaging study and that I have reviewed and approved this report.

Electronically Signed By:	Harry Jones, MD	12/31/2010 09:35:12

RESULT ID:	9999001
ORDER NUMBER:	2369999
MEDICAL RECORD NUMBER:	00299999

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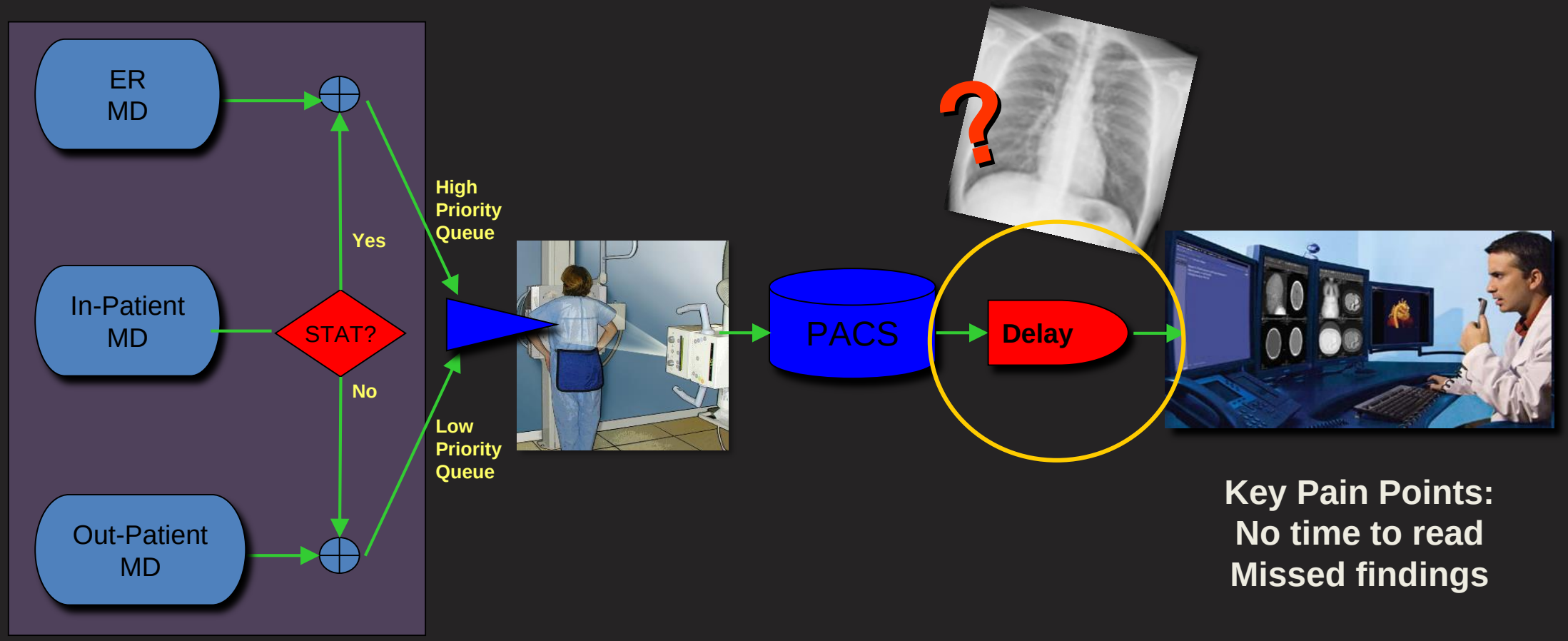
The Problem:
Current Radiologist's Workflow



Key Pain Points:
No time to read
Missed findings

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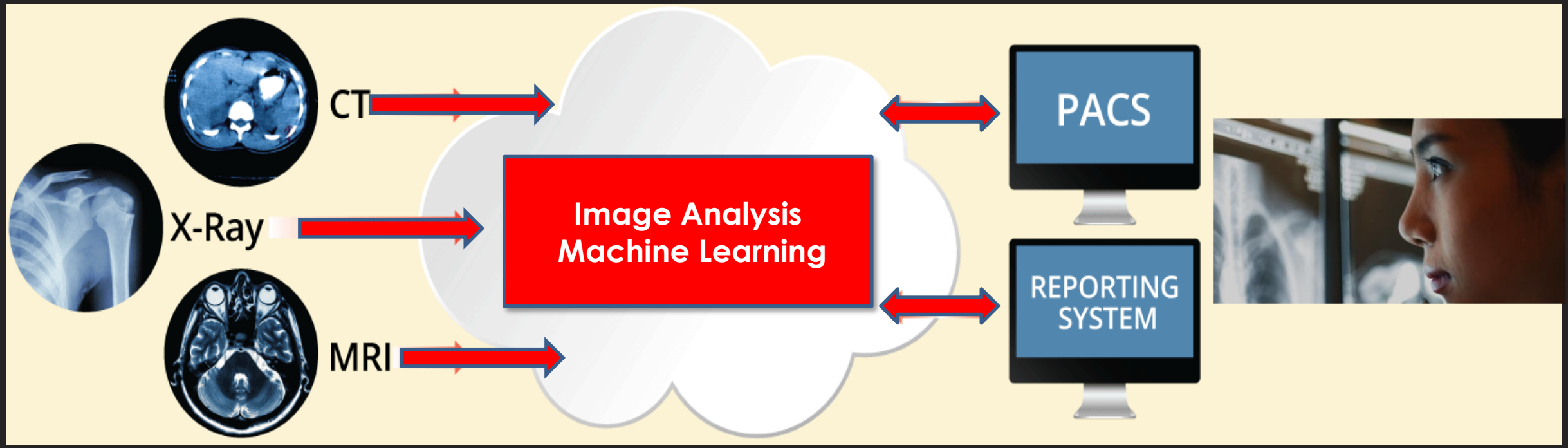
The Solution: Bridging the Gap between Technology and Radiology



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Radiologist Workflow Analysis

Hospitals
Private clinics
HMOs
University Hospitals

Spent months in Reading Rooms
& interviewed in medical conferences
→ Understanding how Radiologists work
→ Generating an App Portfolio

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Radiologist Tasks

- Search
- Measure
- Diagnose
- Report

- **Take 80% of Radiologist Reading Time**
- **30% Error Rate in Reports***

* Accuracy of Radiology Procedures, L Berlin, American Journal of Roentgenology, May 2007

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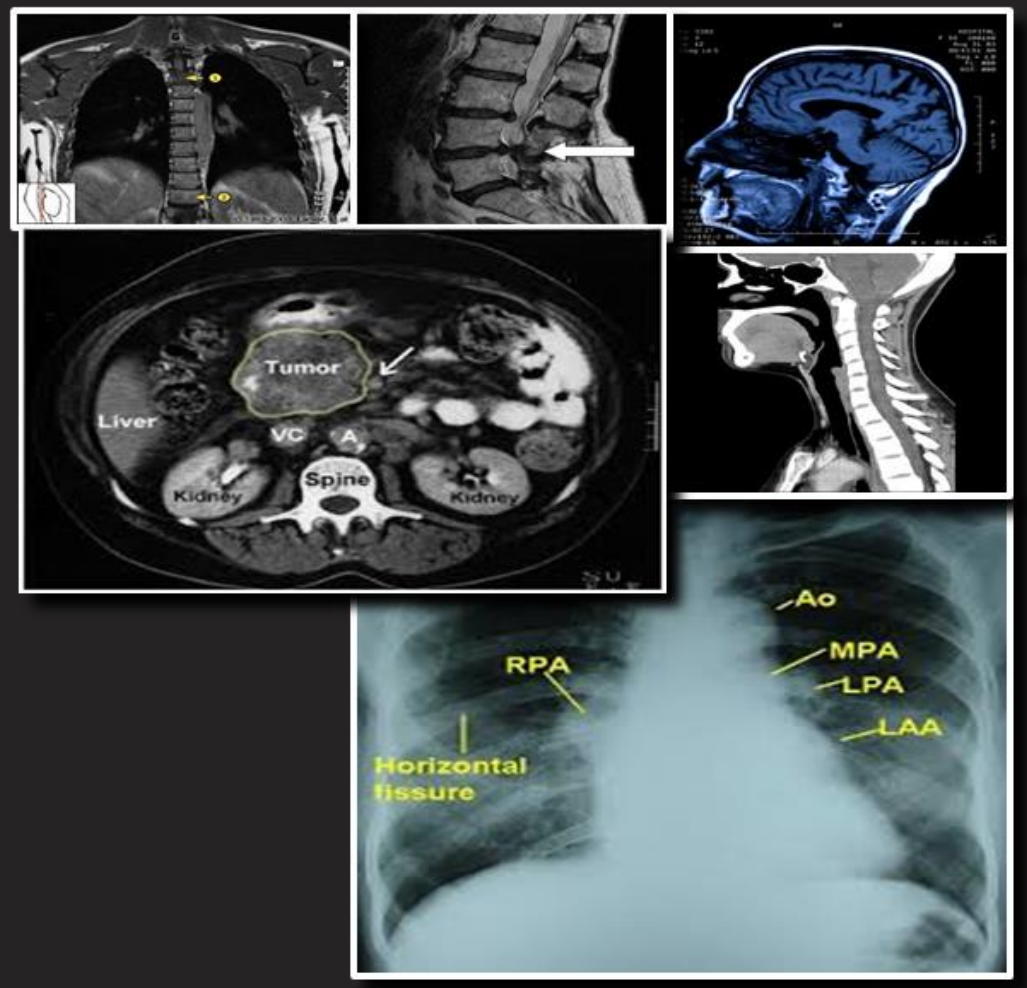
Clinical Use Cases

- Oncology
  - Lung Cancer (Avail. Now)
  - Liver Cancer
  - Stomach Cancer
- Emergency Care
  - Chest CT (Avail. Now)
  - XRAY
  - Neuro MRI
  - Neuro CT
  - Abdomen CT
- Chronic Disease & Elderly Population
  - Neuro CT (musculoskeletal)
  - Neuro MRI (neurodegenerative)



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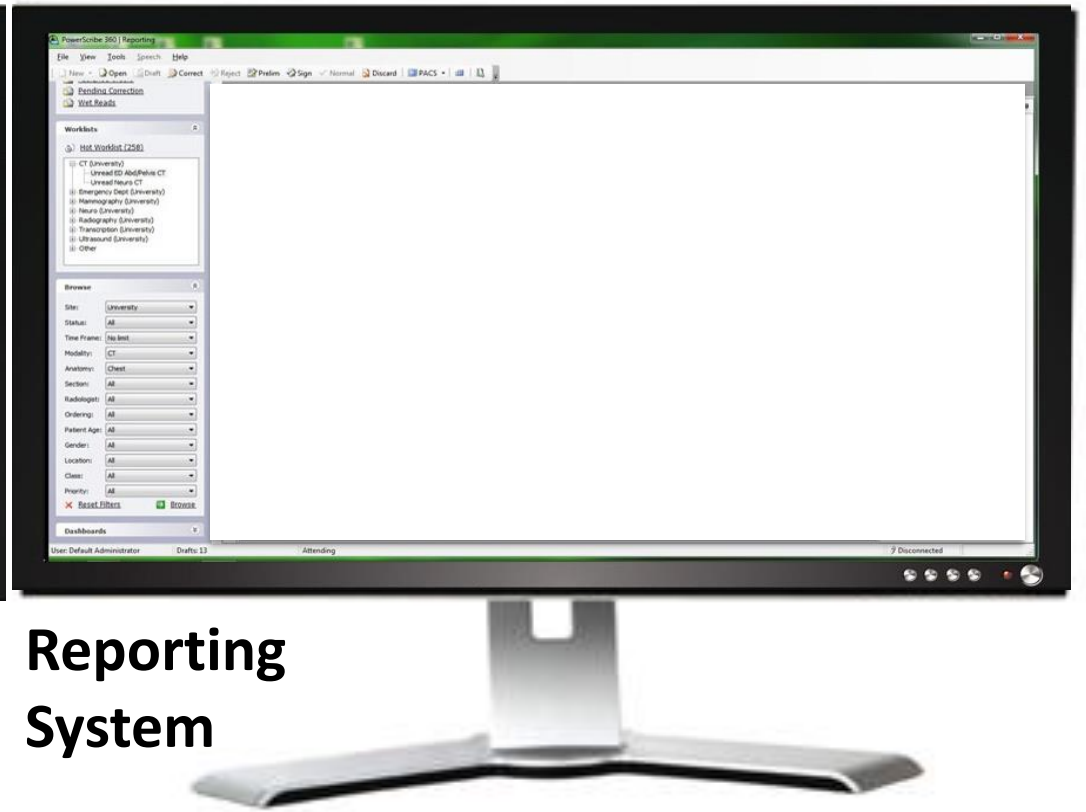
Radiologist Workflow:

Seamless integration into their familiar reading environment

PACS



Reporting System

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II. The Virtual Resident Solution

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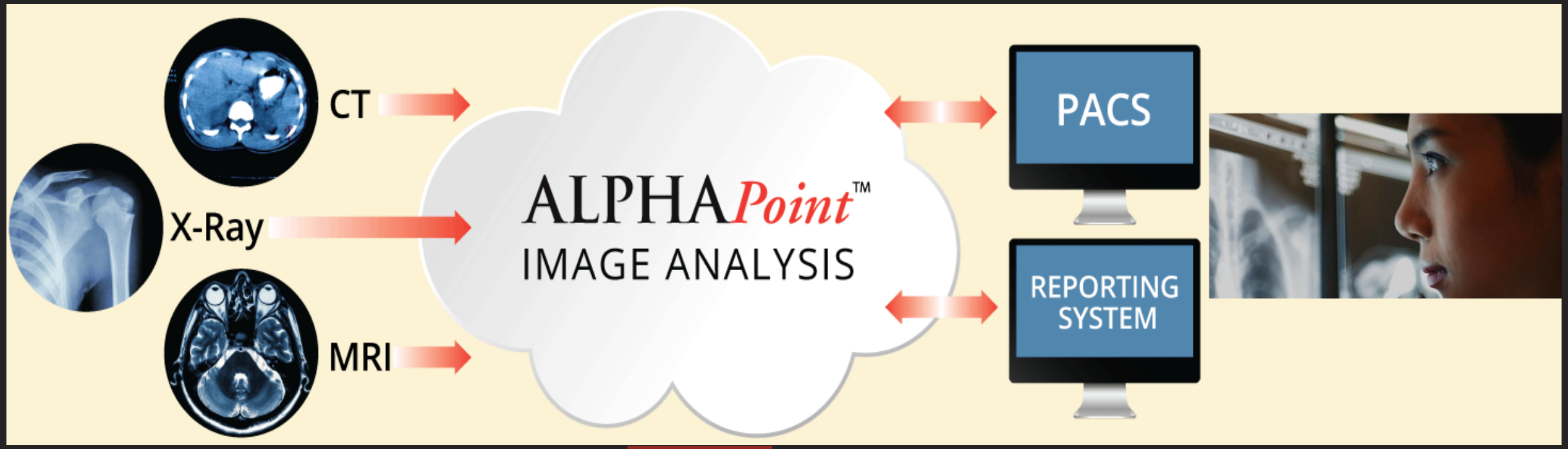
Solution = ALPHAPoint Virtual Resident™



Clinical Data Archive

US Patents 8953858, 9418420, 9582880;
other patents pending

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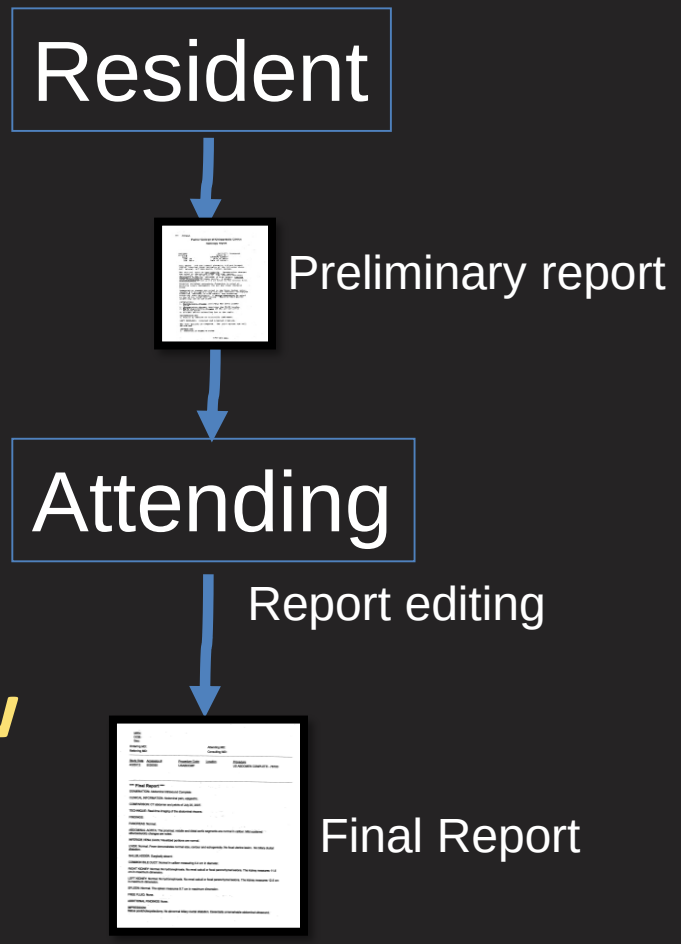
Human vs. Virtual Resident-enabled Workflow

- The radiology report is the primary communication "product" of a working radiologist
- In teaching institutions, radiology trainees ("residents") review imaging scans and dictate Preliminary Reports
- Attending radiologists later edit and finalize the Resident's preliminary reports into Final Reports



AlphaPoint-enabled Workflow

=

Resident-enabled Workflow

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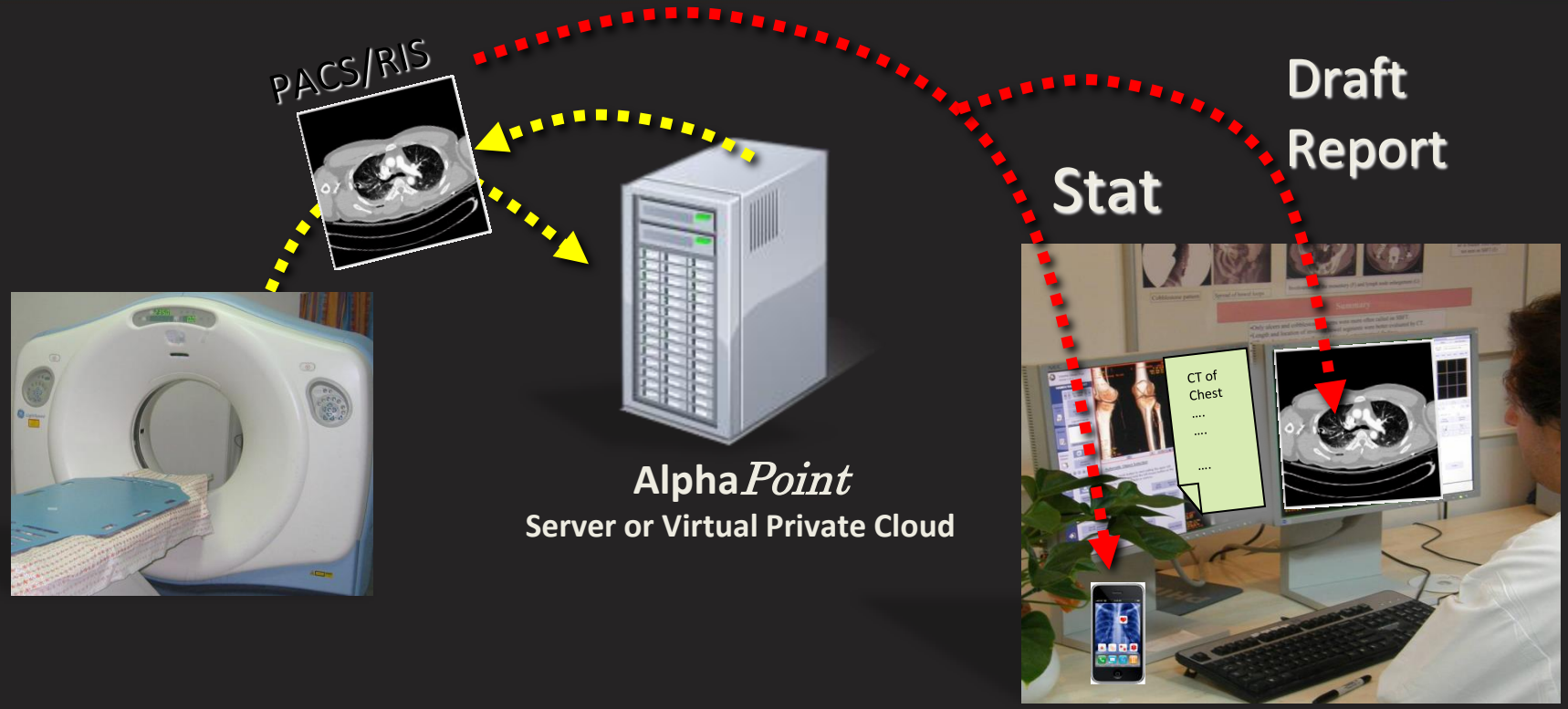
Solution



AlphaPoint ™ automatically generates prior to radiologist review:

- Key findings
- Key images
- Quantified measurements
- Automatic draft report
- Stat alerts for critical findings

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Machine Learning for Image Analysis

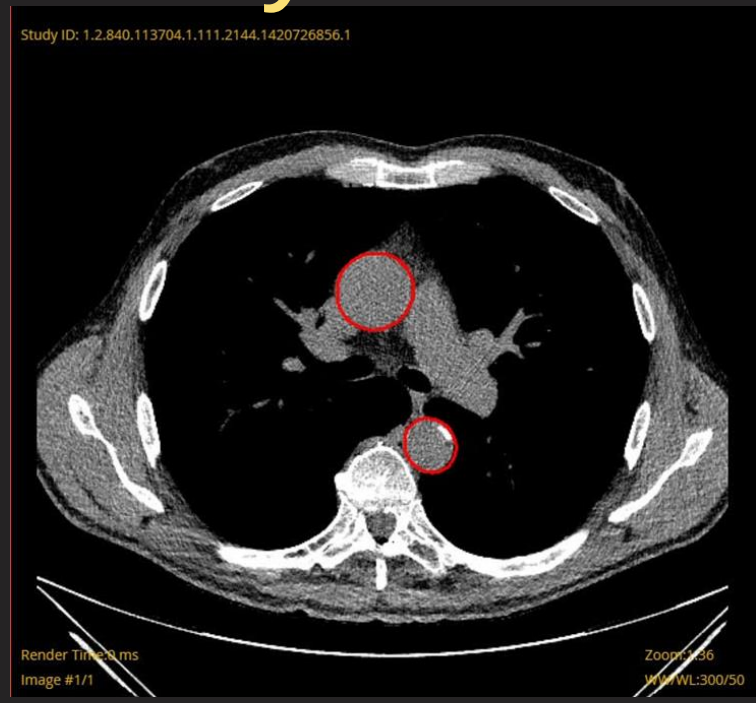
ALPHAPoint "Virtual-Resident"

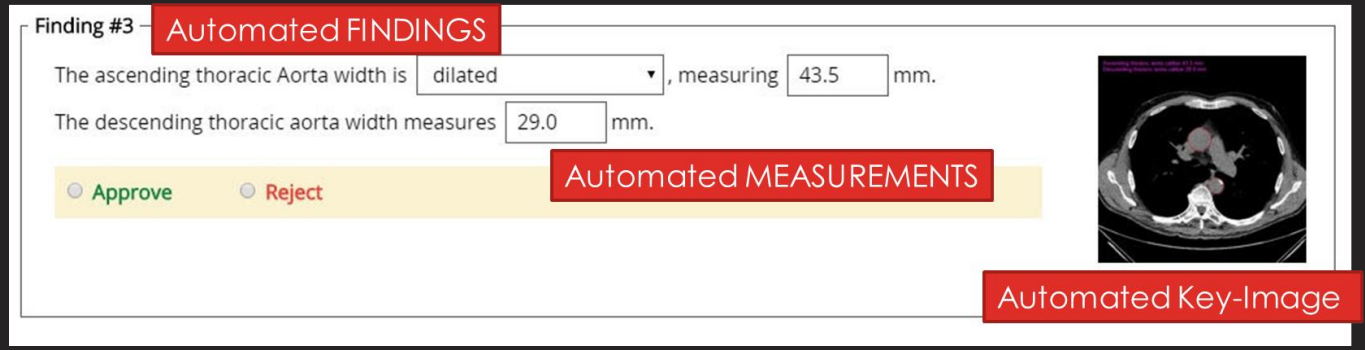
prior to radiologist review,

prepares a detailed list of:

- Findings
- Characterization
- Measurements
- Visualization

Report Finding = "App"





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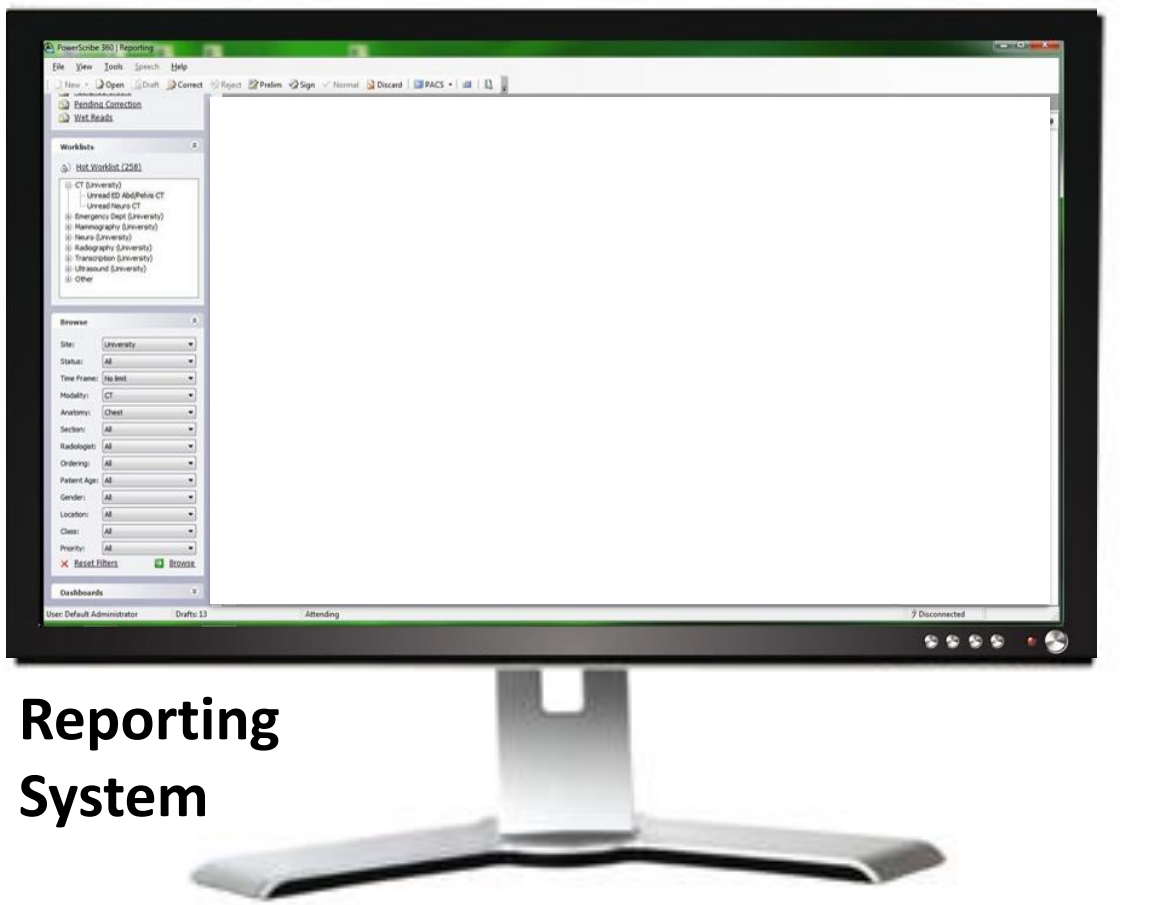
Radiologist Experience

PACS



Reporting System

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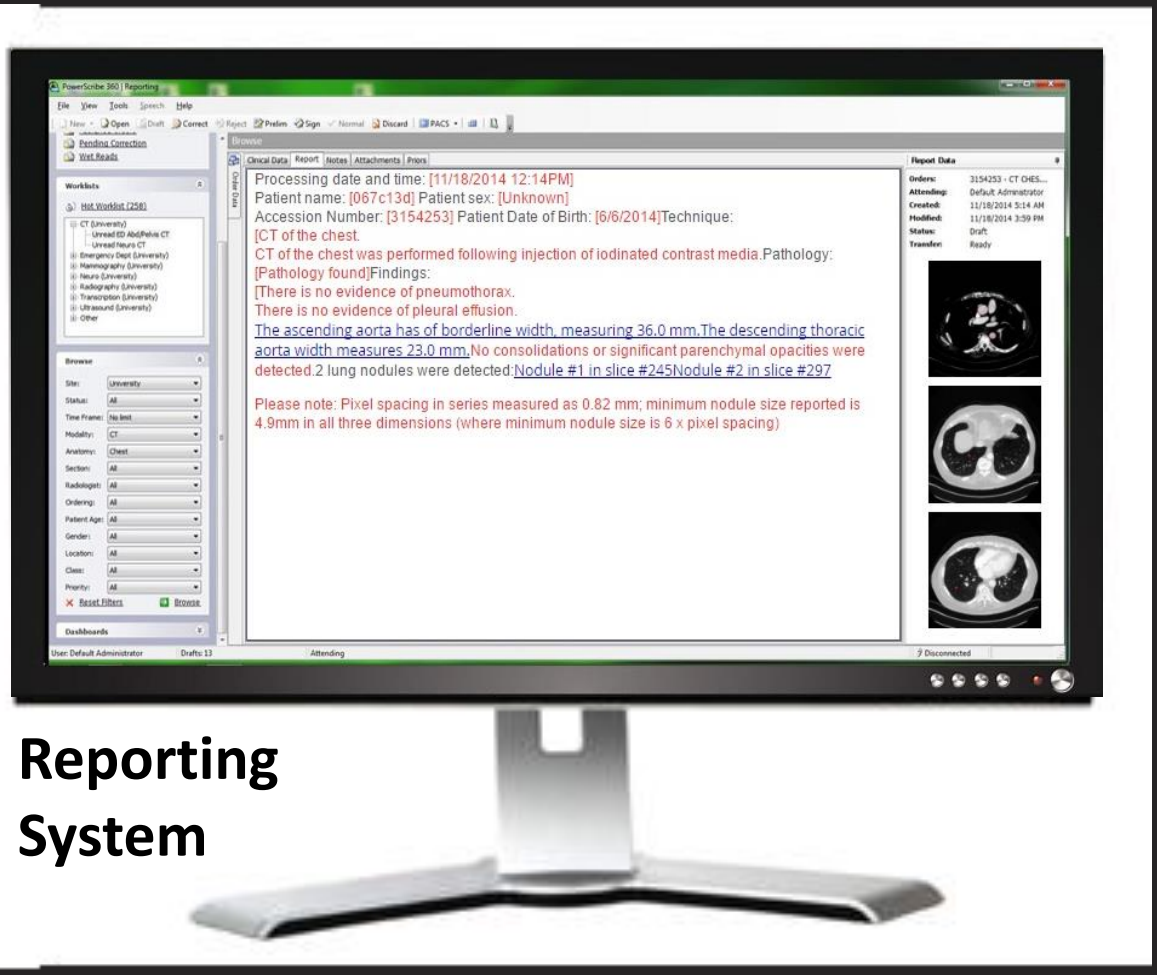
Radiologist Experience

PACS



Reporting System

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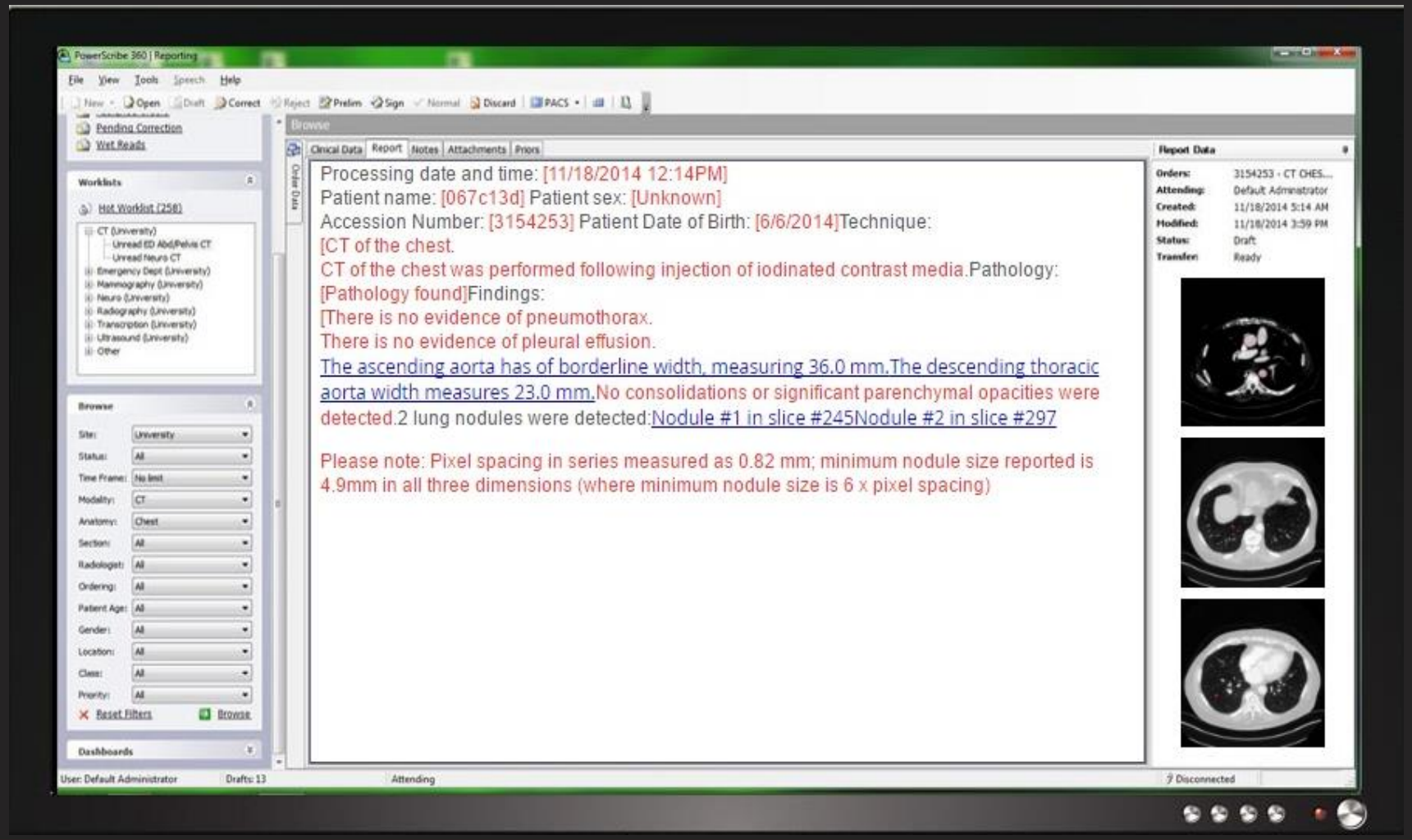
Prepopulated Preliminary Report – example 1

Radiologist Review Starting Point



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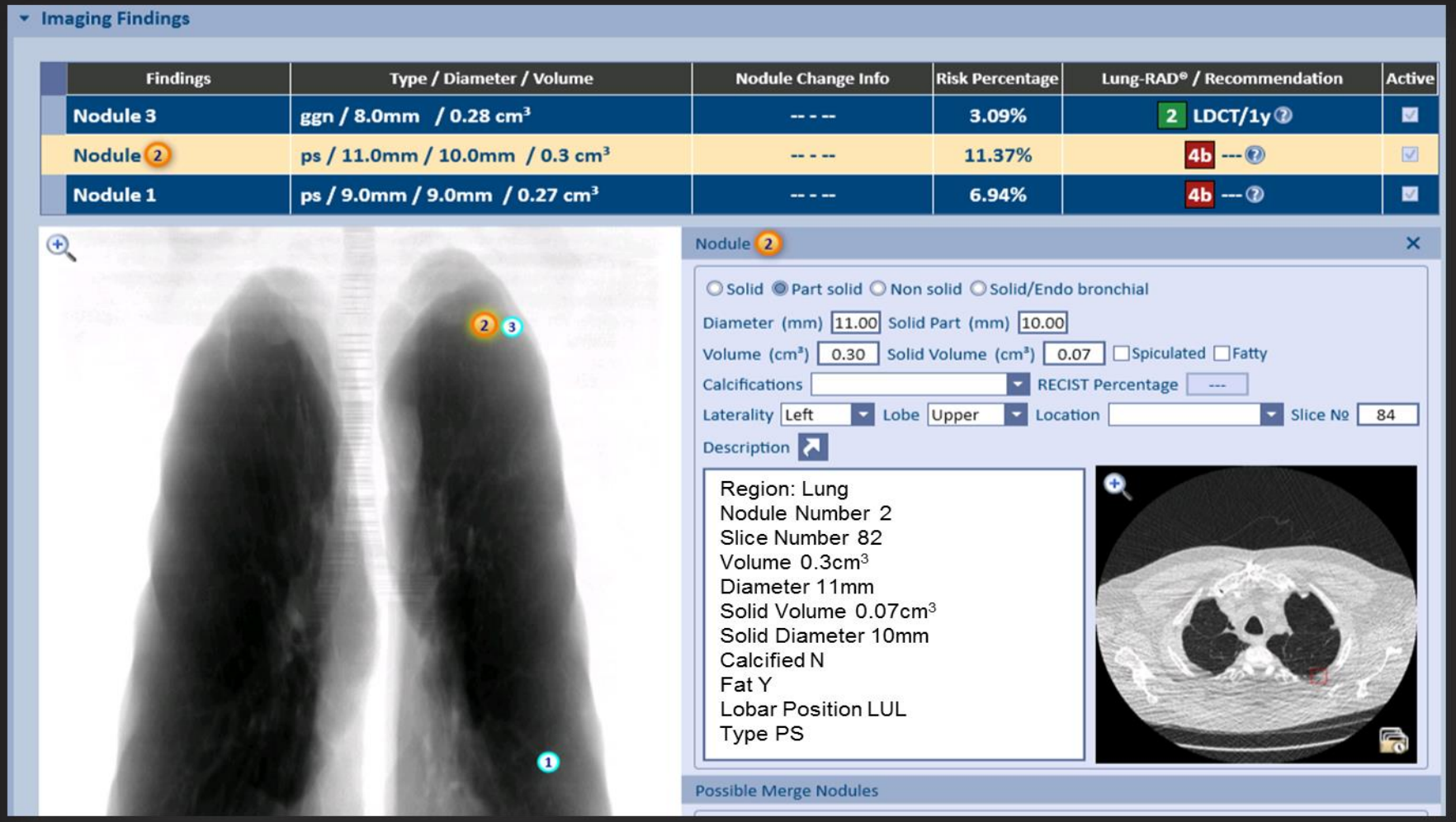
Prepopulated Preliminary Report – example 2



MRS Medical Reporting Software

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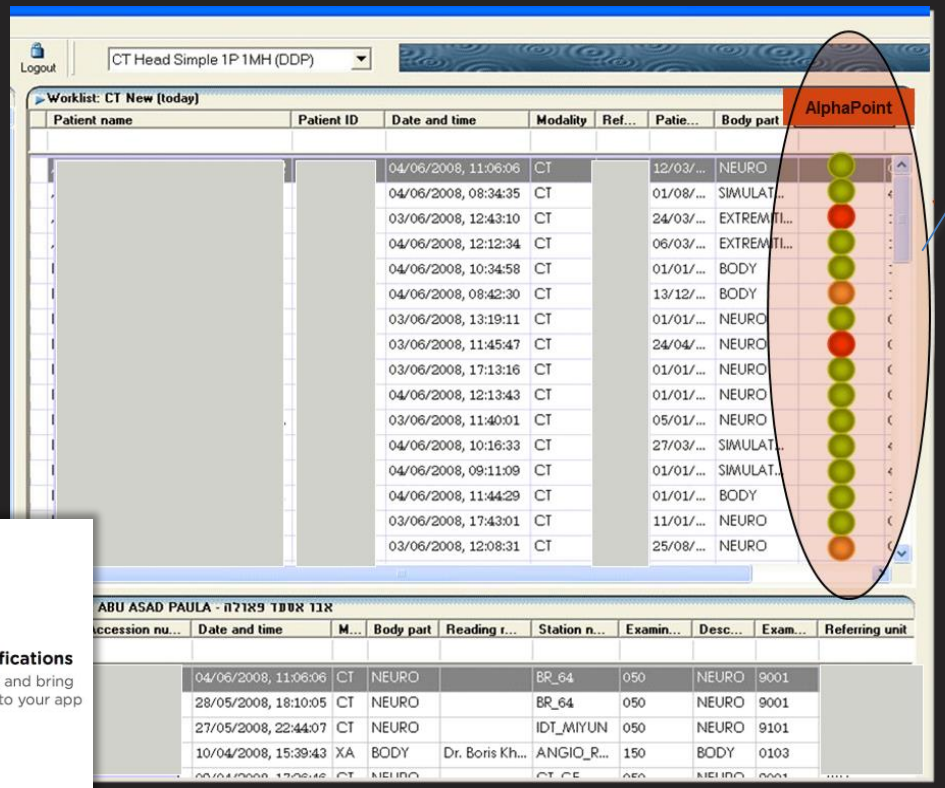
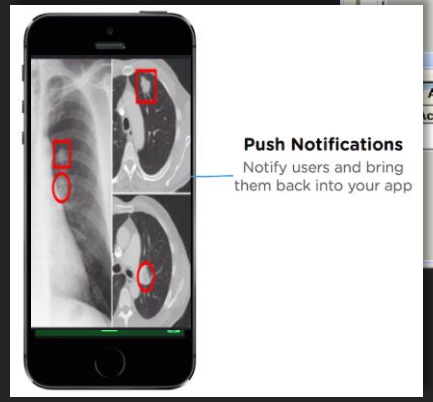
Enhanced Worklist & Alerts

- Augmented Worklist



- Critical Push Notifications



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Key Benefits

- Improve patient outcomes with case prioritization and consistent quantitative measurements
- Increase radiologist productivity
- …all this while maintaining existing radiological workflow protocols

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III. Developing an App

There's an App for That

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Deep Learning within the Apps

- Tasks
  - Detection, Segmentation, Categorization
  - Organ level, Pathology level
  - Reducing false-positives while maintaining high sensitivity
- Data Representations
  - Input to network: Pixels, Patches, ROIs, Full image labeling
- Methodologies
  - Combine classical with deep vs All deep
  - Transfer Learning methods & Fine Tuning
  - Supervised Learning: new networks, fully trained

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The Data Challenge

Difficult to find & extract from archives

Pathologies even more difficult

Need expert labeling

Long tedious process

Noisy labels

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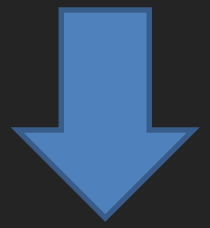
Solving the Data Challenge



Data Representation

Data Augmentation

Transfer Learning

Know your Context

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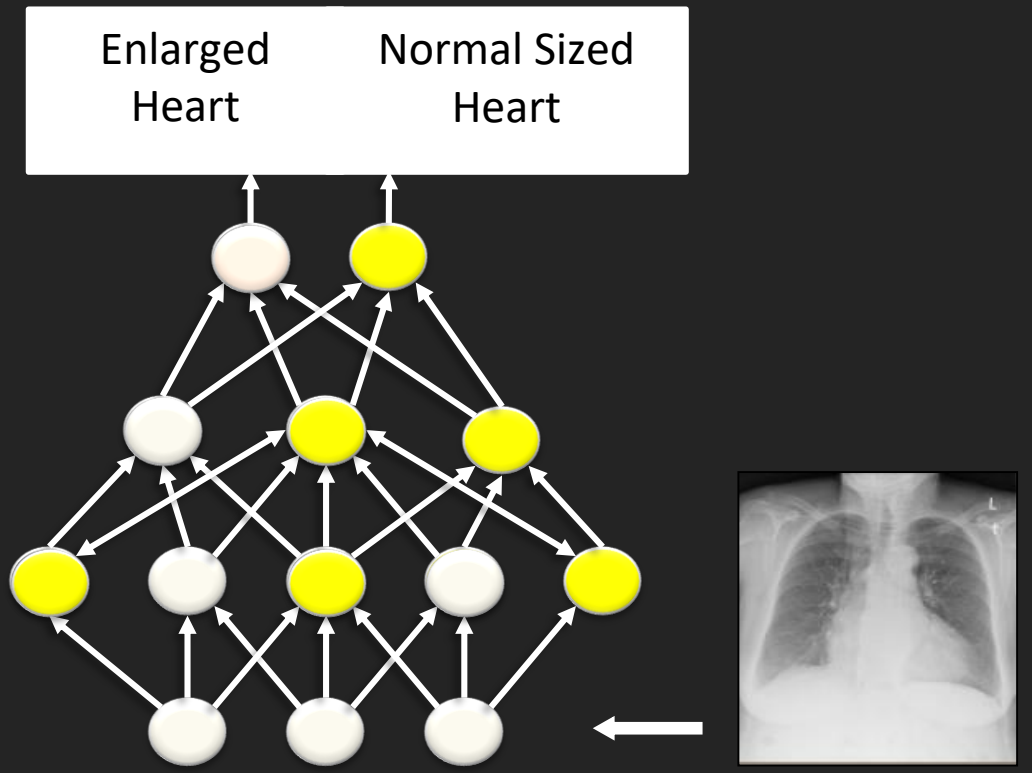
Deep Learning within the Apps

- Chest CT Applications
  - Free Pleural Air
  - Lung Opacities
  - Lung nodules
- Chest X-ray Applications
  - Lung Segmentation
  - Free Pleural Air
  - Free Pleural Fluid
  - Enlarged Heart
  - Enlarged Mediastinum



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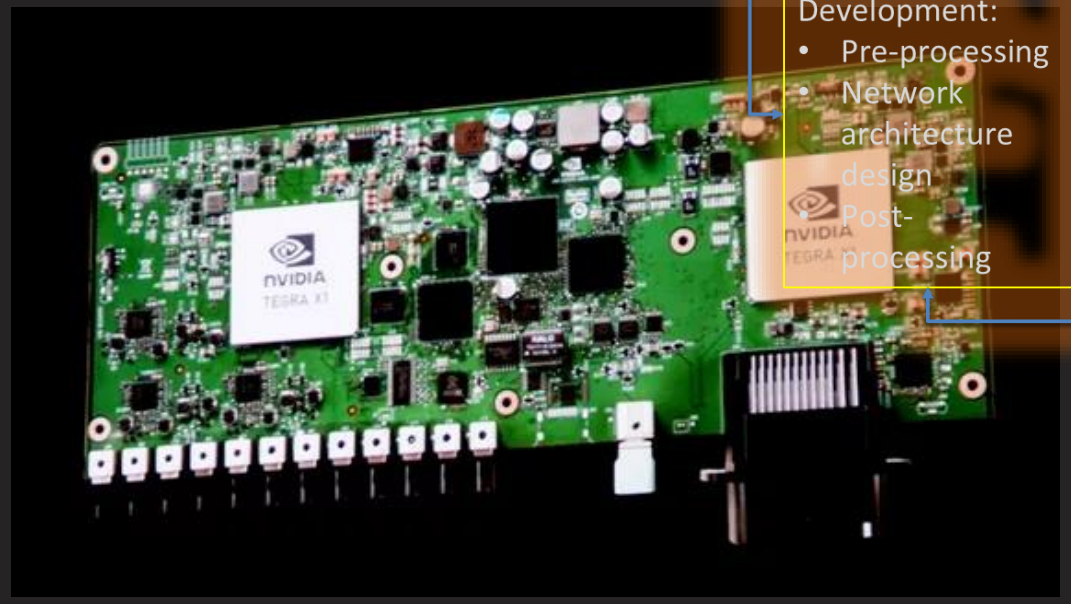
App Development Platform



Define Requirements

Solution Design:
- Computer Vision
- Image Processing
- Deep Learning

Data Collection

Labeling:
- Develop Labeling tool
- Run Labeling by expert

Application Development:
- Pre-processing
- Network architecture design
- Post-processing

Validation & hyper-parameters optimization

Testing on test-set

Release Alpha version

Alpha-Site Validation

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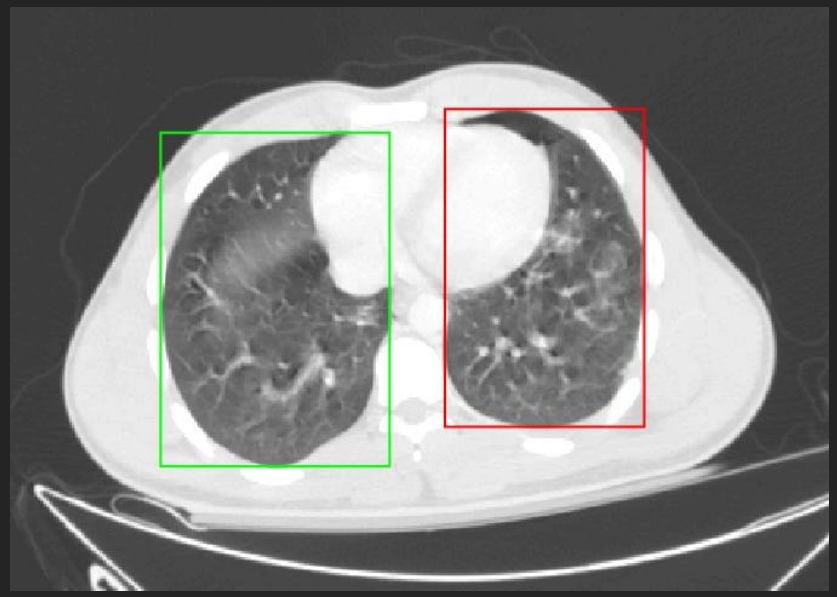
1. Chest CT Global & Distributed Findings:
Free Pleural Air, Opacities & Pleural Fluid Applications

- Classification is done per side for each slice, on an ROI around the lung.
- Each ROI is classified to:
  - "Contains"/"doesn't contain" free pleural air
  - "Contains"/"doesn't contain" opacities
  - "Contains"/"doesn't contain" pleural fluid
- A "global" (per side) classification is done according to these slice-based results.



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Opacities Detection

Detection of consolidations and parenchymal opacities in the lungs

Example sentences in Report:

"There is evidence of consolidations or parenchymal opacities in the left lung"

Clinical validation results (n=442):

- Sensitivity: 96 %
- Specificity: 99 %

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Pleural Fluid Detection

Clinical validation results (n=321):

- Sensitivity:
  - Mild: 76 %
  - Moderate or Severe: 97 %
- Specificity: 91 %

Pleural Air Detection

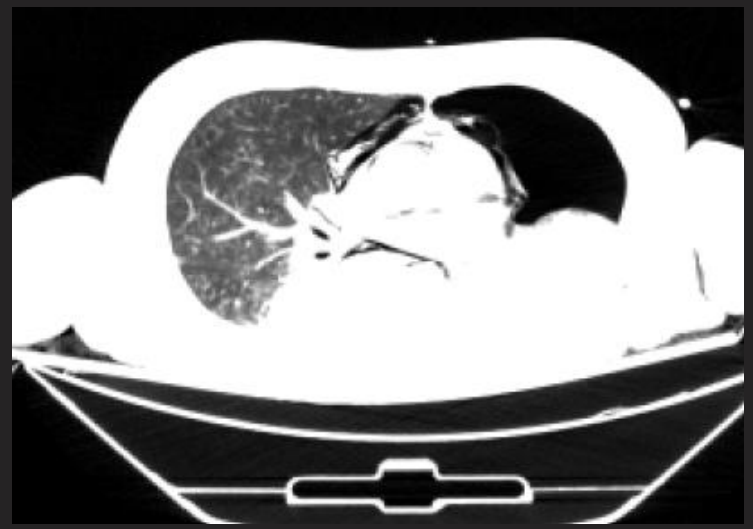
Clinical validation results (n=494):

Sensitivity:

Mild: 72 %

Moderate or Severe: 95 %

Specificity: 97 %



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2. Chest CT Local findings: Nodule App

- 2 Main Stages:
  - Candidate Generation – Classical methods
  - False Positive reduction – Using a CNN
- The false positive reduction stage is done by creating 2.5D representations of the candidates, and via massive data augmentation, a CNN was trained for the classification

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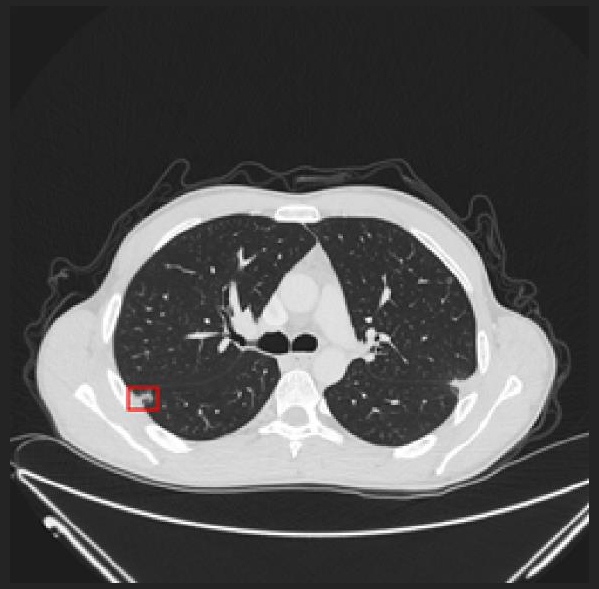
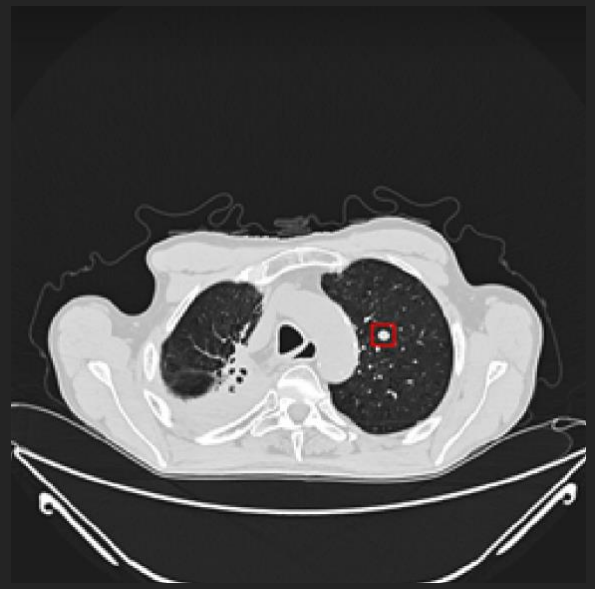
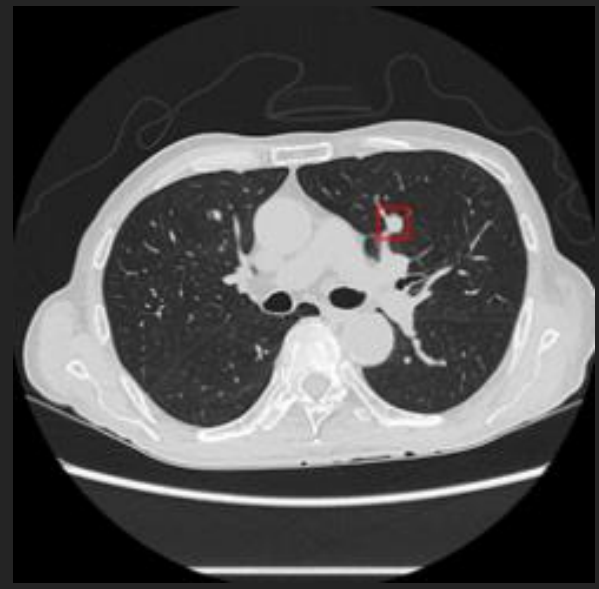
Examples From Clinical Sites



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3. Chest X-ray Apps

X-ray: The most common exam in radiology with 2B procedures/year (CT: 500M)

No. of Examinations (2012)	Modality
28,689	MR
66,968	CT
50,207	US
162,492	CR
115,653	**CR CHEST**

Courtesy: Sheba

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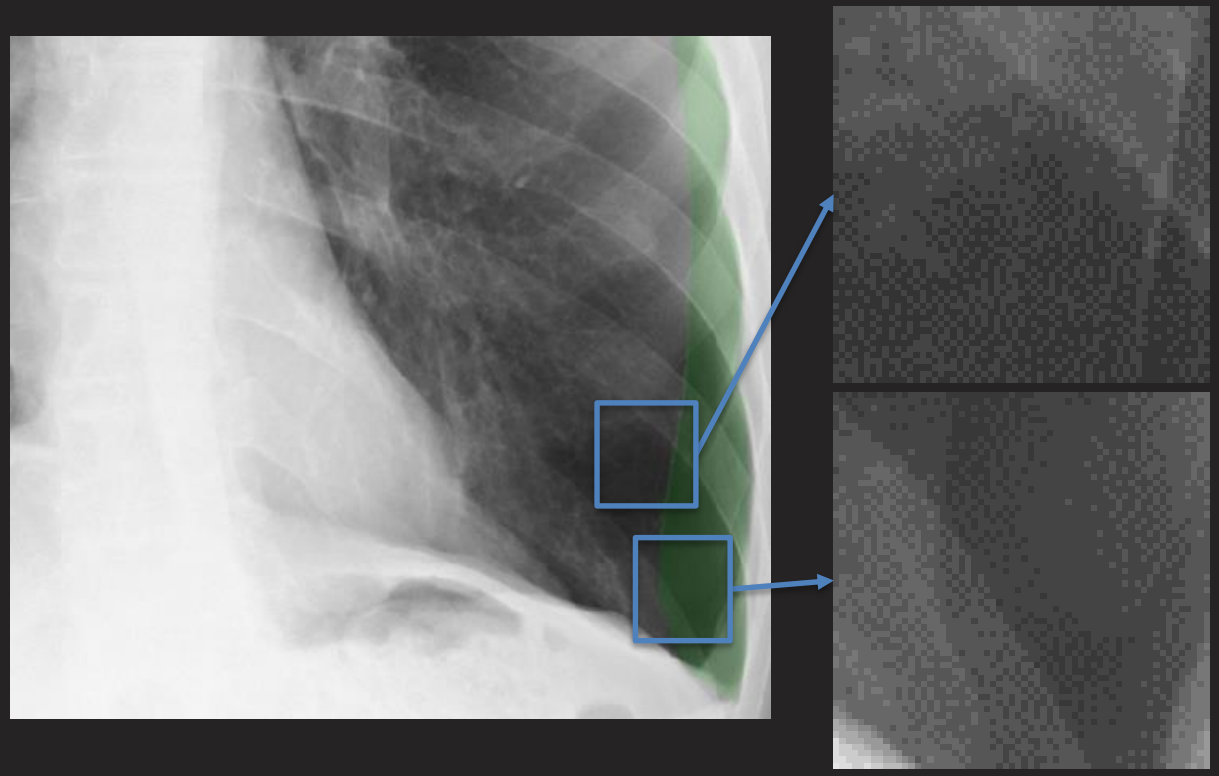
Free Pleural Air Application

- Pixelwise classification: free air vs. lung tissue
- CNN is capable of learning typical textures for lungs/ free air
- Transferring from hundreds of training samples to ~5M training patches



Clinical validation results (n=86):
AUC: 0.950

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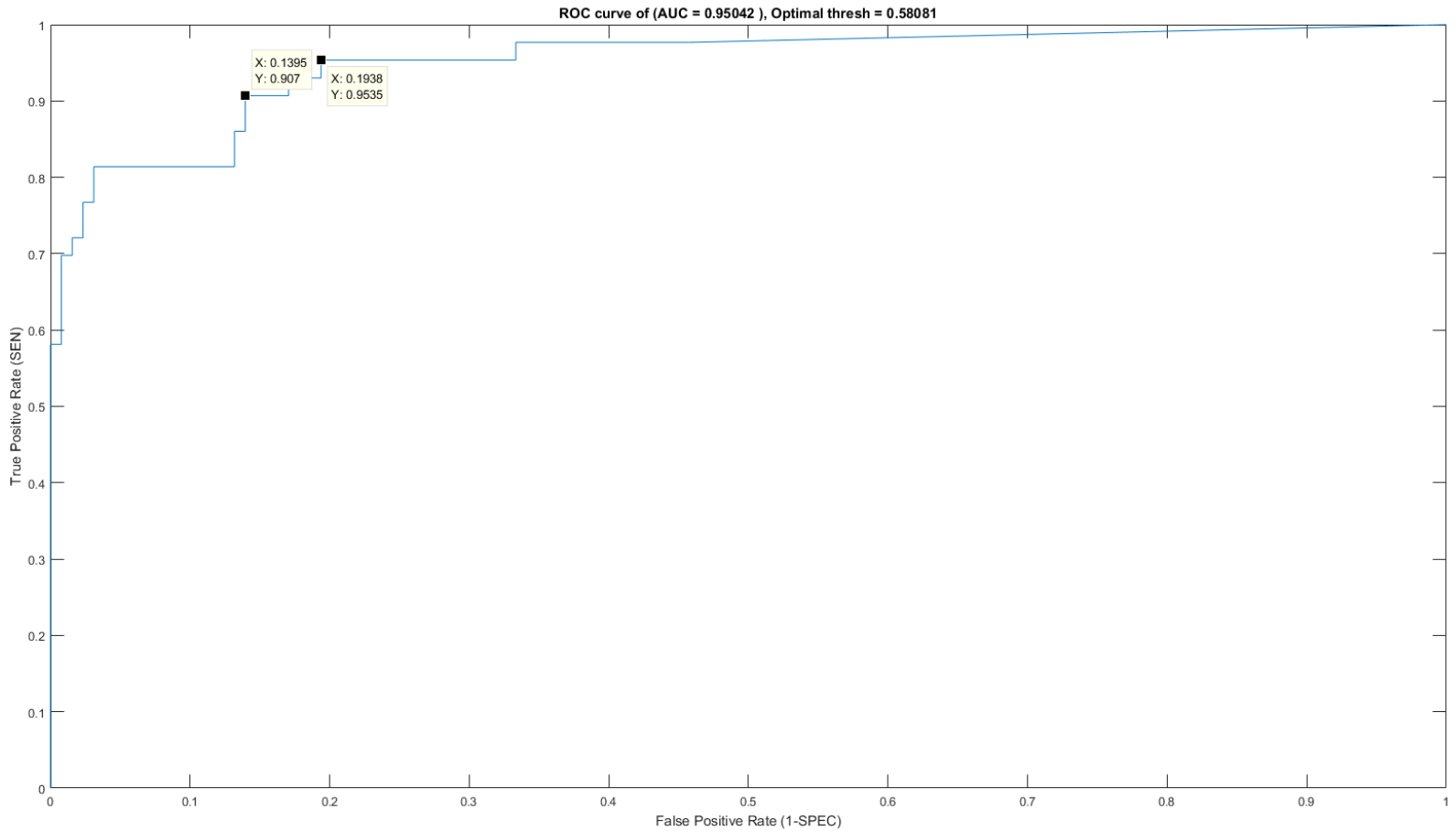
Pleural Air Detection: ROC curve



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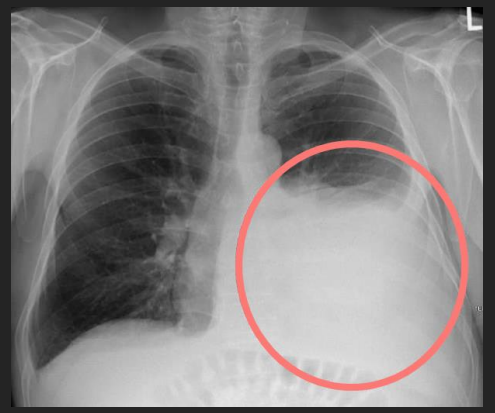
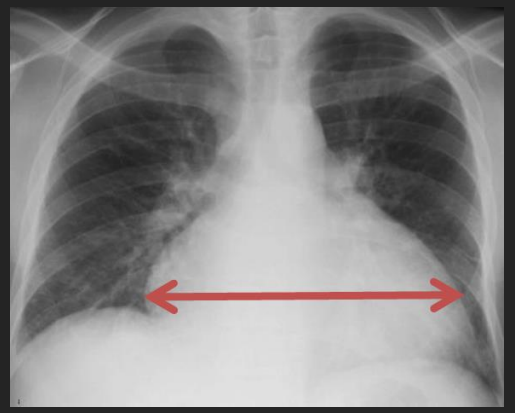
4. Chest X-ray Global Findings

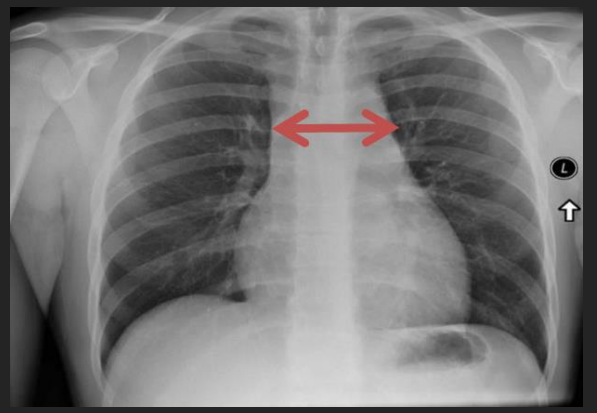
- Global appearance and hard to segment in single image.
- Data challenge very significant!
- Solution: use *Transfer Learning*



Pleural Fluid



Enlarged Heart



Enlarged Mediastinum

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Image-level Labeling Using Transfer Learning

Pre-trained network for ImageNet: VGG-S

Features aggregation from layers:
FC5
FC6
FC7

Optimized SVM per each pathology

- Right pleural fluid Y/N
- Left pleural fluid Y/N
- Enlarged heart Y/N
- Enlarged mediastinum Y/N

Return of the Devil in the Details: Delving Deep into Convolutional Networks', *Ken Chatfield, Karen Simonyan, Andrea Vedaldi, and Andrew Zisserman,* BMVC 2014

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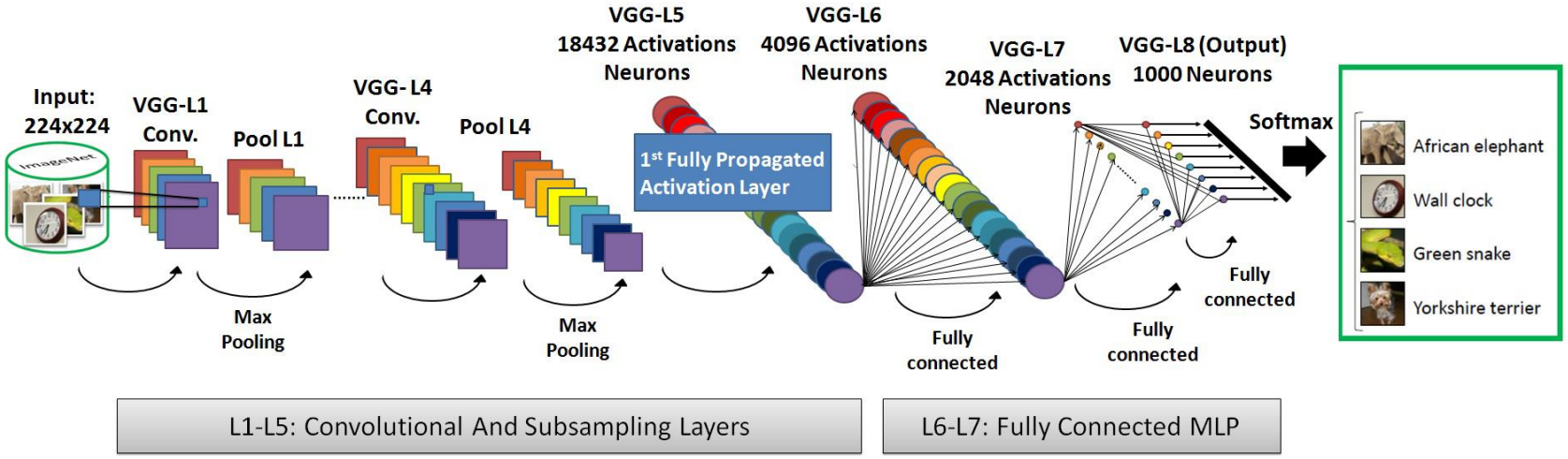
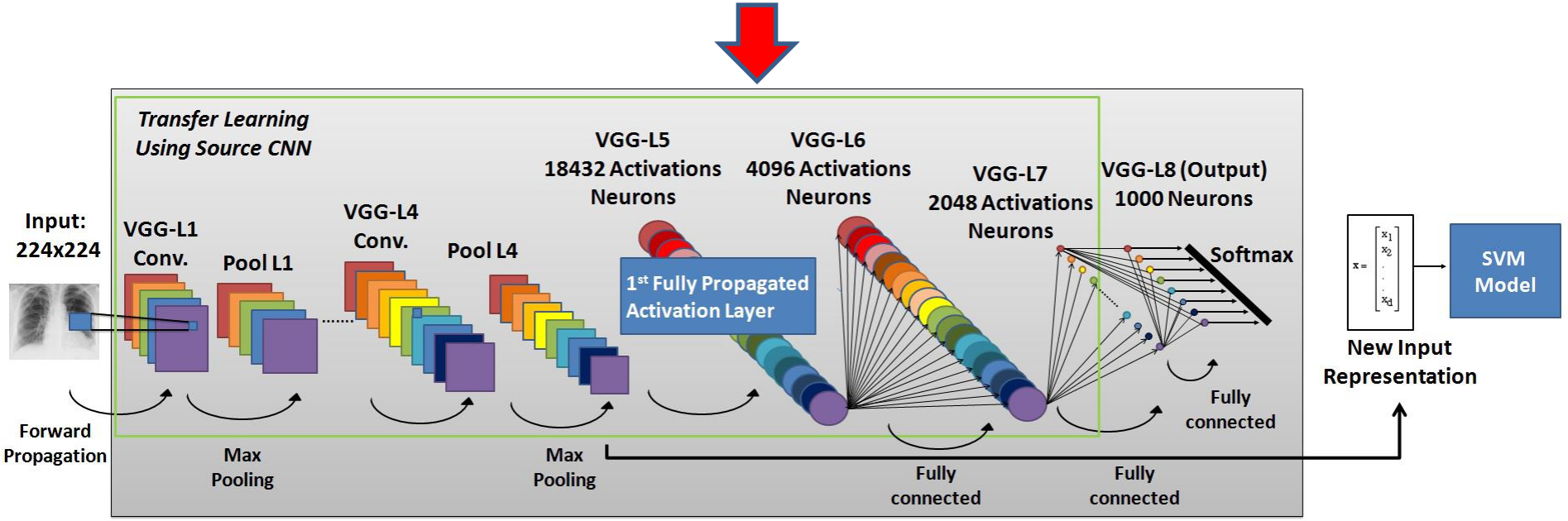
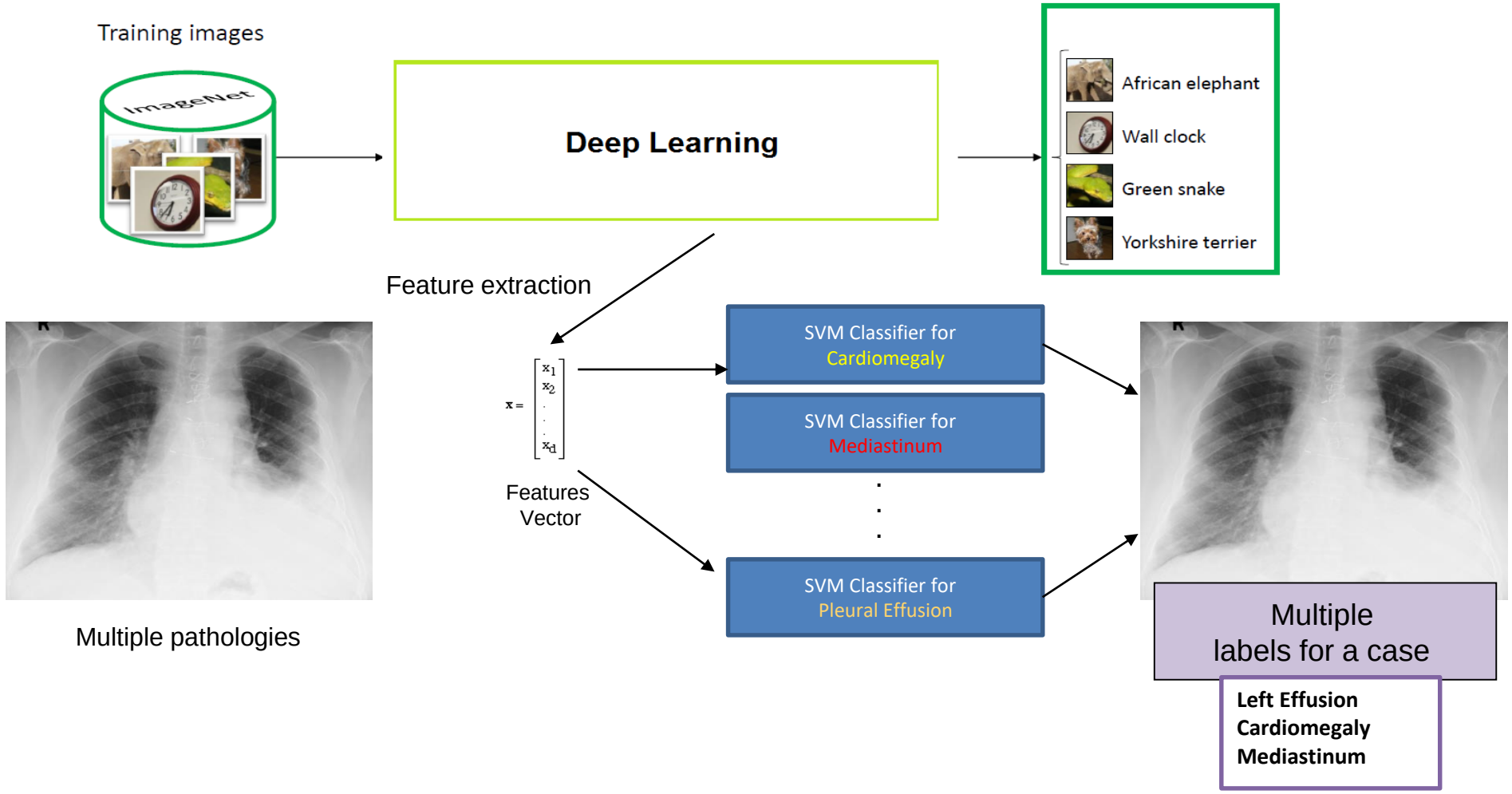
Transfer Learning





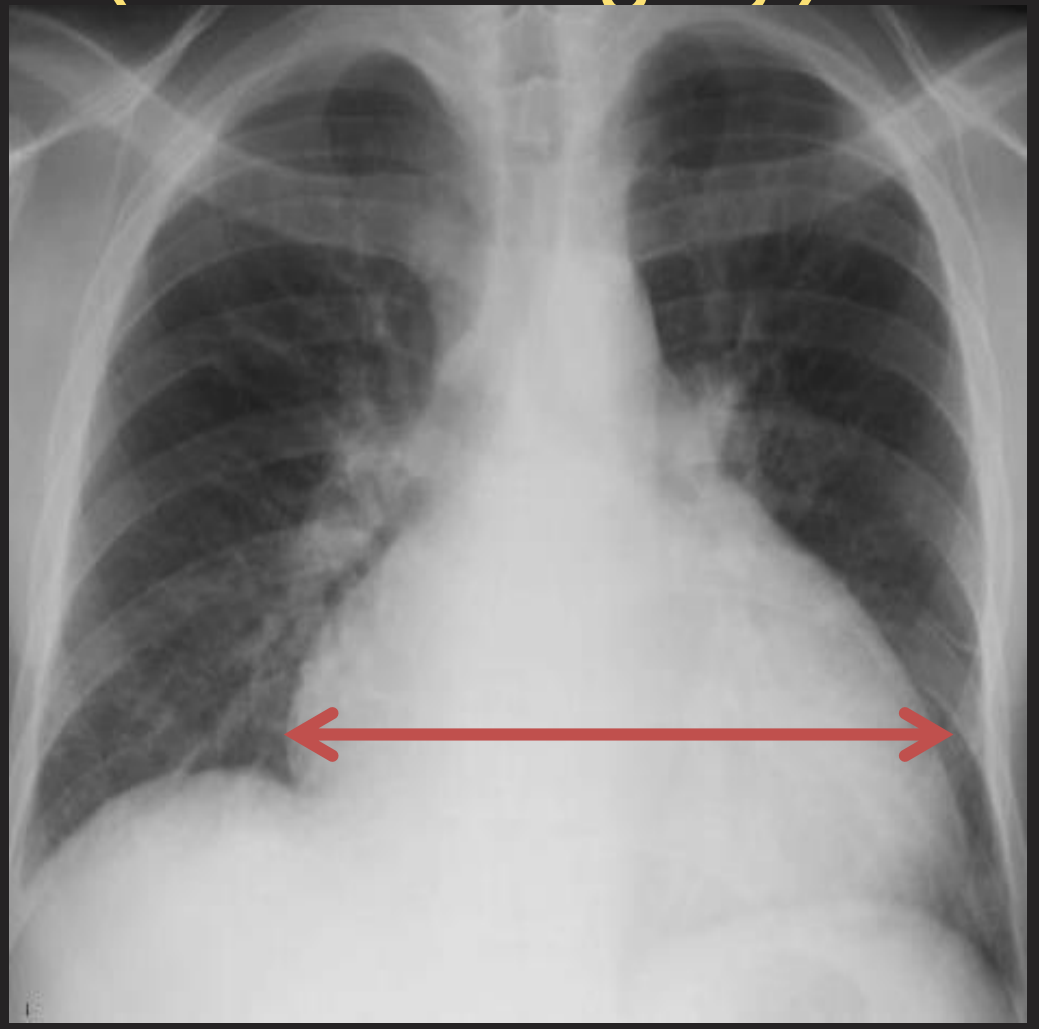
System Overview



Enlarged Heart Detection (Cardiomegaly)

- Detection of abnormal enlargement of the cardiac silhouette
- Includes: Automated detection of an abnormal state
- Outputs finding (yes/no enlarged heart) to report

- <u>Clinical validation results (n=404):</u>
  - AUC: 0.947



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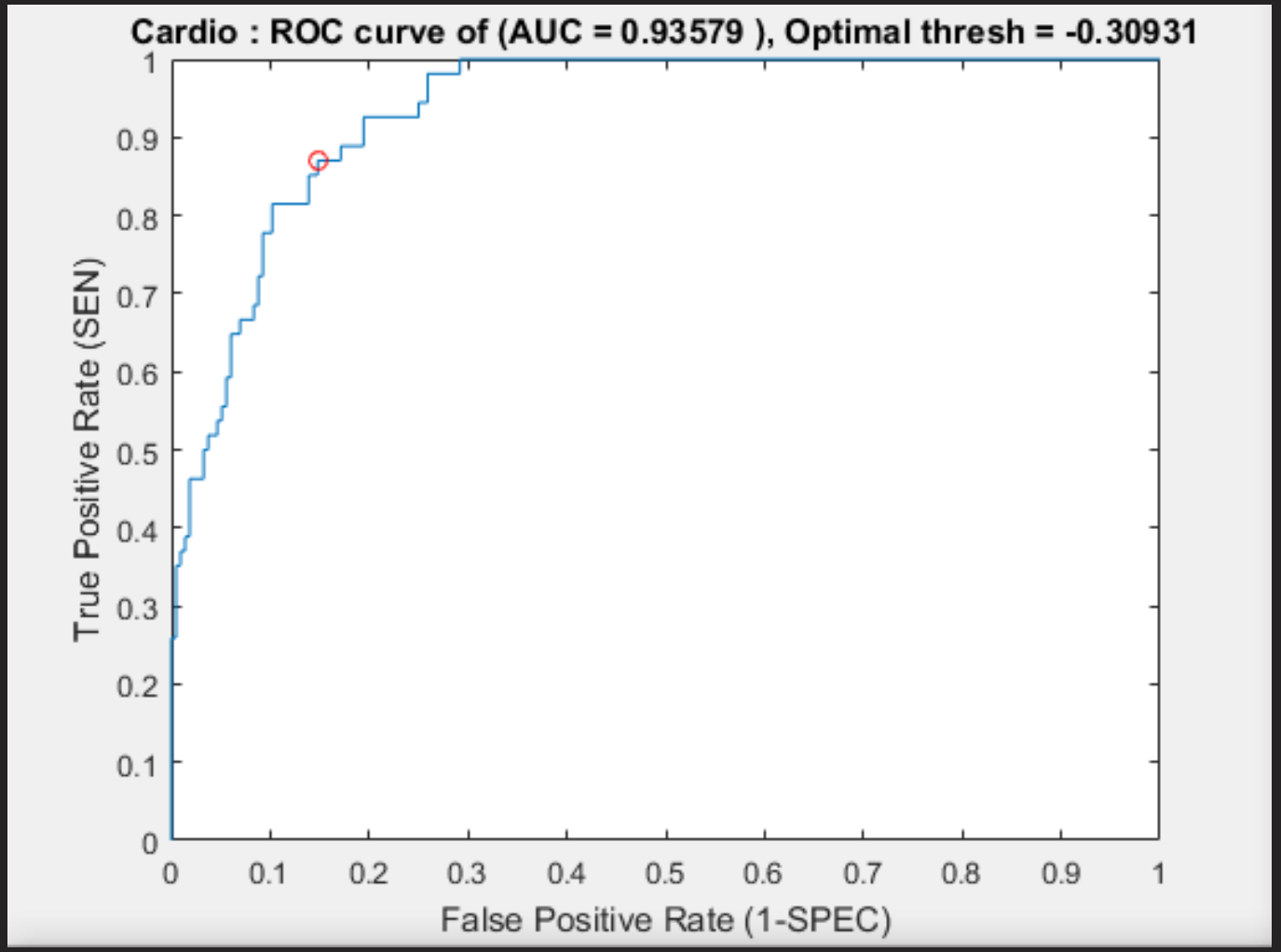
Enlarged Heart Detection (Cardiomegaly)



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Results (1000+)

	Enlarged Heart Cardiomegaly	Enlarged Mediastinum	Right Pleural Fluid	Left Pleural Fluid
AUC	0.9475	0.9216	0.9303	0.9128
Spec. at ~95% Sens.	0.7799	0.6752	0.7348	0.7956
Spec. at ~90% Sens.	0.8511	0.8121	0.8702	0.8066
Sens. at ~90% Spec.	0.7973	0.7536	0.7143	0.6667

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5. Work in Progress

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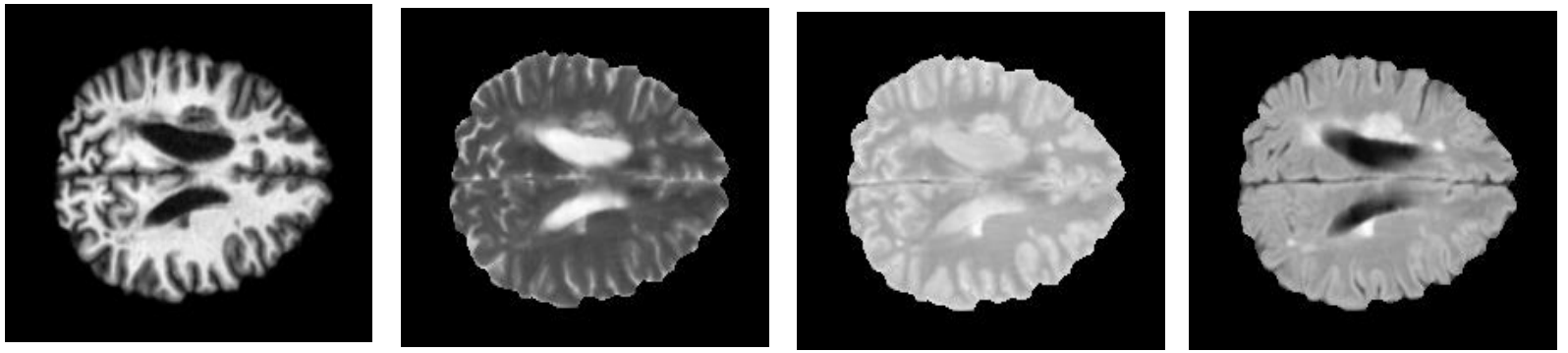
LONGITUDINAL MULTIPLE SCLEROSIS LESION SEGMENTATION

MRI data

Multi-View Convolutional Neural Networks

Multiple Sclerosis Lesion Segmentation

- MS is one of the most common neurological diseases in young adults. It affects approximately 2.5 million people worldwide
- The immune system attacks the central nervous system and damages the myelin, a fatty tissue which protects the nerve fibers - This leads to deficiency in sensation, movement and cognition
- MS lesions (scars) are formed in damaged regions, mostly in the WM

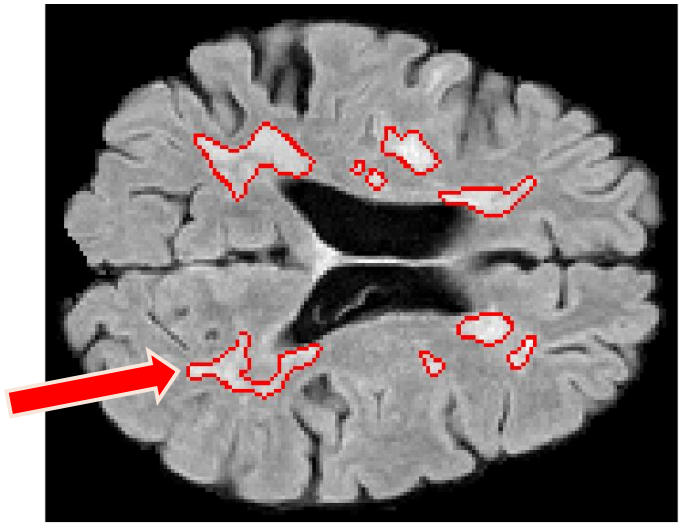


T_1-w T_2-w PD-w FLAIR

Multiple Sclerosis Lesion Segmentation

- Efficient MS treatment: reduces lesion volume
- Manual segmentation: time consuming and subjective
- Automatic segmentation algorithms are needed!

- Very challenging: MS lesions vary in size, location, texture and shape

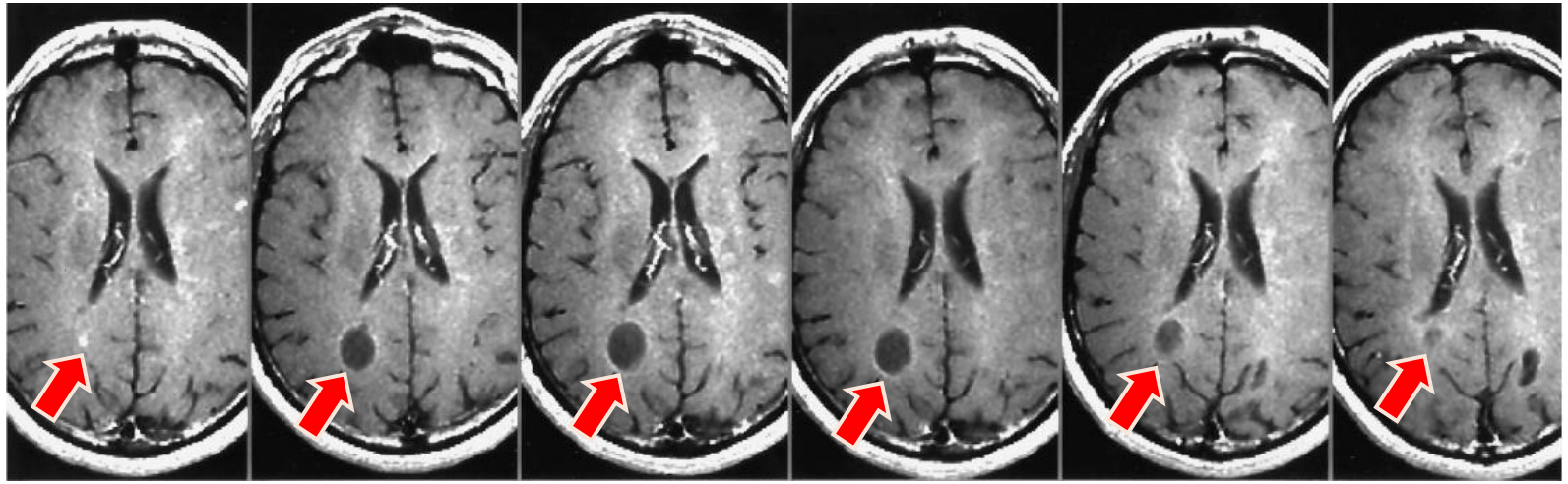


Lesions in Time

- Studies have shown: MS lesions change significantly over time
- ISBI2015: Longitudinal MS lesion segmentation challenge

- Current state-of-the-art methods:
  - Many algorithms: Random Forests (Geremia et al. 2013), Sparse Dictionary Learning (Weiss et al. 2013) , Deep Learning (Brosch et al. 2016)
  - But… No use of temporal data!

T_1-w



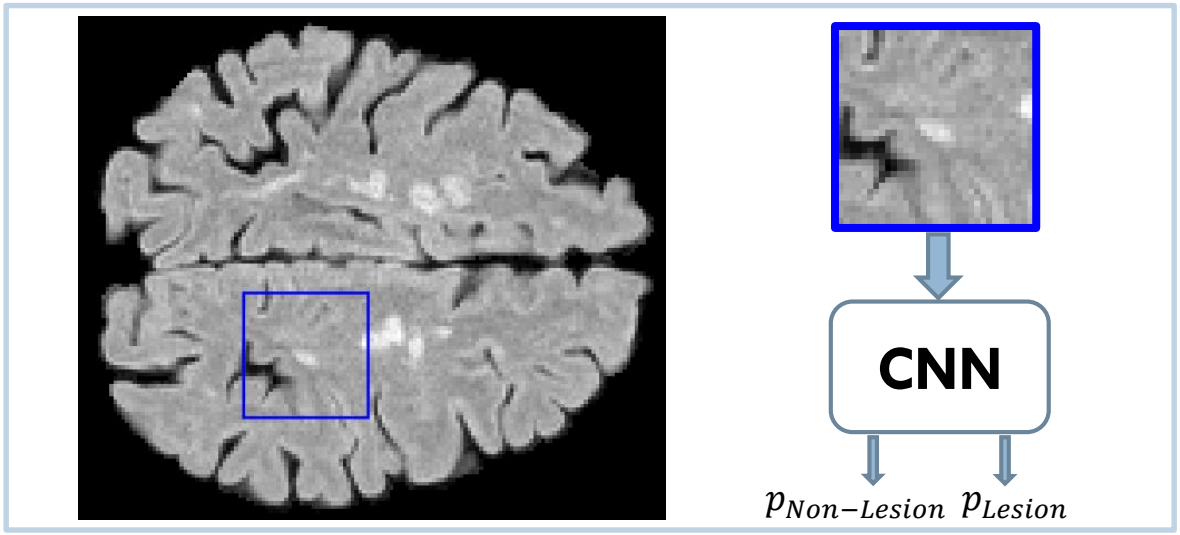
Guttmann et al. 1995

ISBI 2015: Data Set Description

- Training Set:
  - 5 Patients, 4-5 time points per patient (Total scans: 21)
  - Manually segmented by 2 expert raters
- Test Set:
  - 14 Patients, 4-6 time points per patient (Total scans: 61)
  - No publicly available manual segmentations
  - Evaluated online
- 3T MR scanner
- 4 Contrast images:
  - T_1-w: voxel dimensions = $0.82\text{x}0.82\text{x}1.17$ mm
  - FLAIR, T_2-w, PD-w: voxel dimensions = $0.82\text{x}0.82\text{x}2.2$ mm
- Follow-up time: 1 year

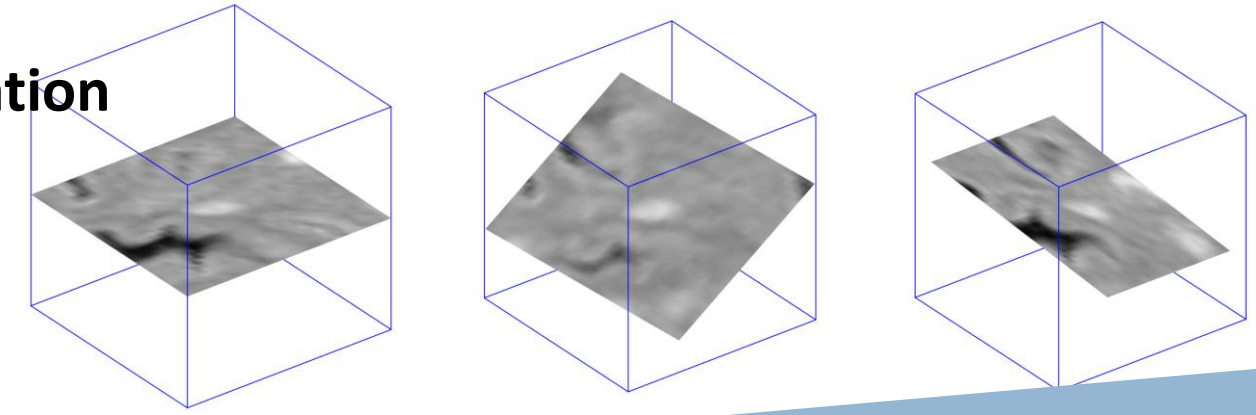
Solution: Segmentation as a voxel classification task

- Total segmented lesion voxels: ~250K



Solution #1:
Patch based training (and classification) for segmentation

Solution #2:
3D **Data Augmentation**

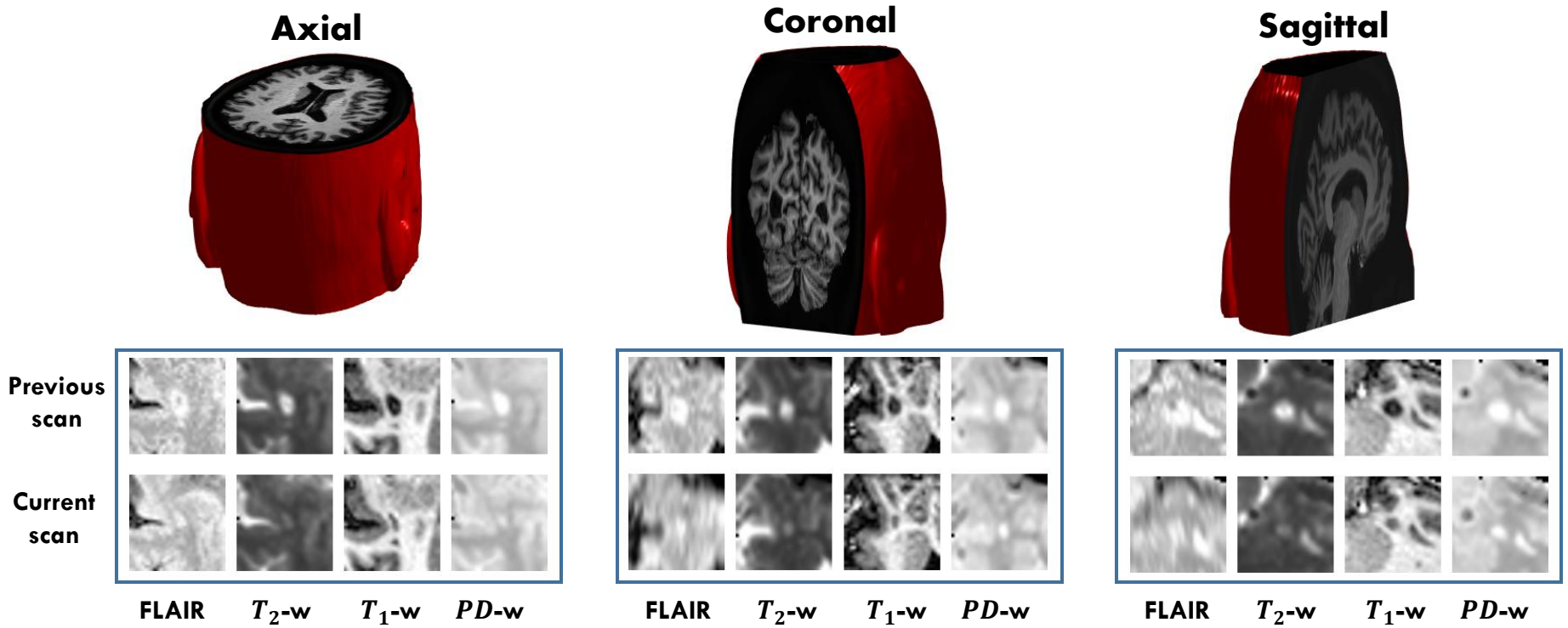


Patch Extraction

Extract 24 32x32 patches around each candidate lesion voxel:

3 views (Axial, Coronal, Sagittal); 4 images (FLAIR, T1, T2, PD);

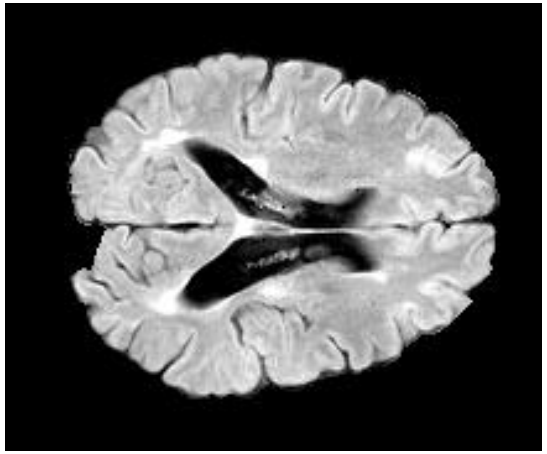
2 time points for each view



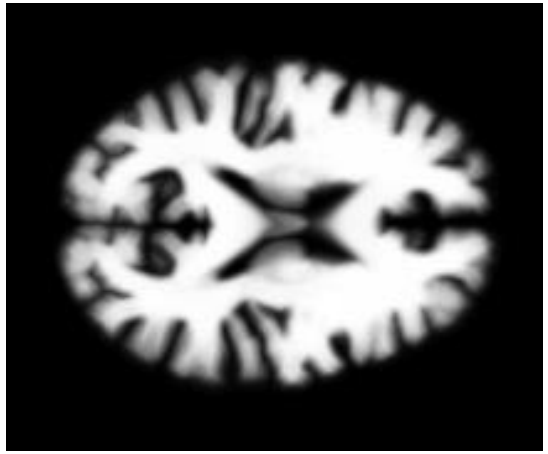
Solution: Candidate Extraction

- Based on two observations:
  - Lesions are hyper intense in FLAIR
  - Lesions are located in WM or on the border between WM and GM
- Candidate mask:

$$M(p) = \begin{cases} 1, I_{FLAIR}(p) > \theta_{FLAIR} \cap Dilate_R\big(WM(p)\big) > \theta_{WM} \\ 0, otherwise \end{cases}$$



I_{FLAIR}

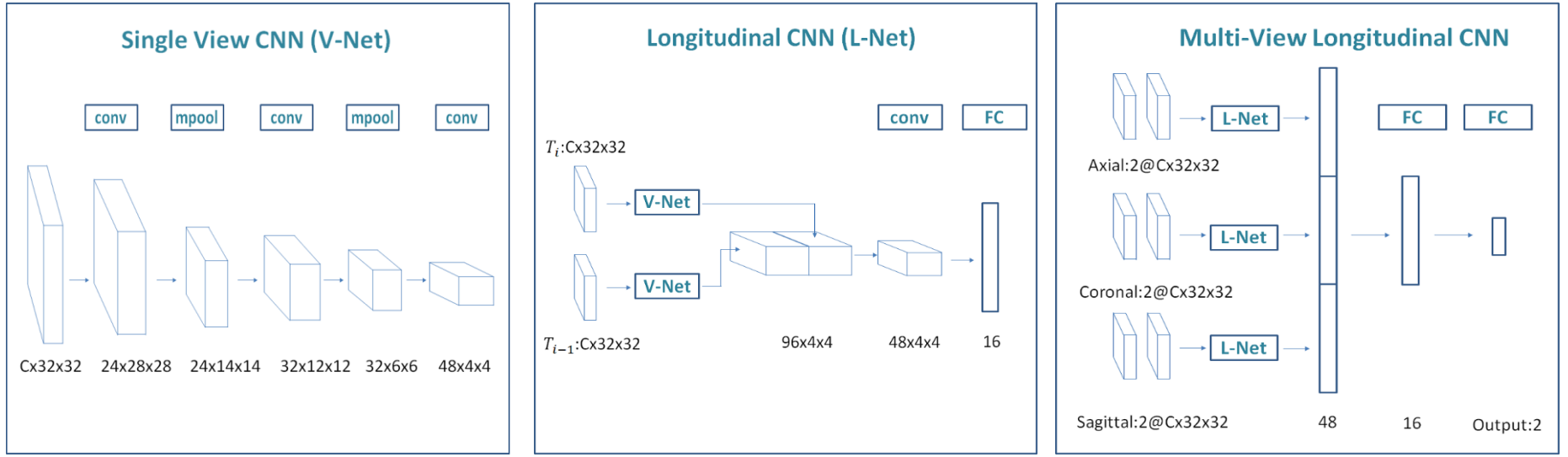


$Dilate_R(WM)$

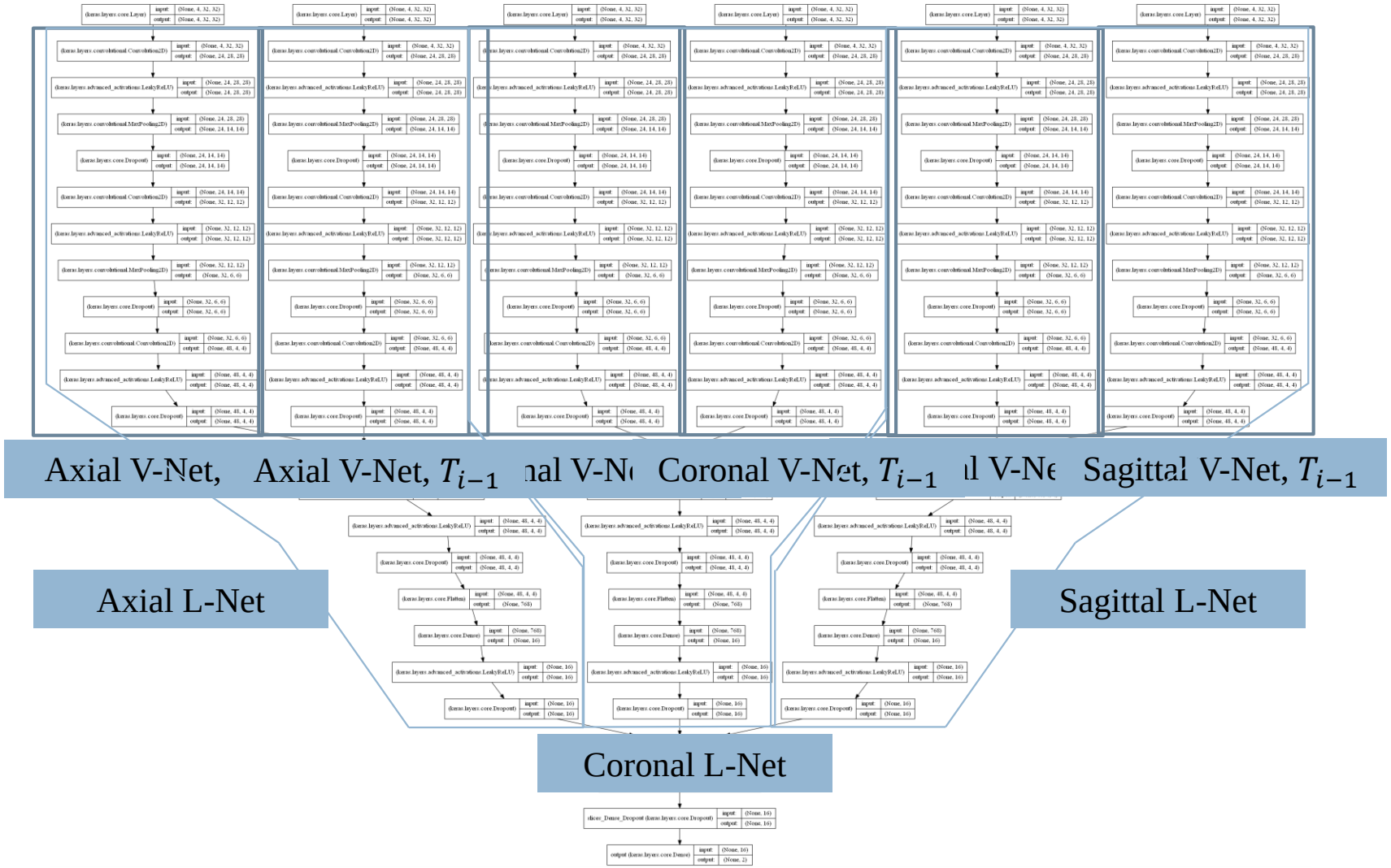
M

Network Architecture (I)

- All 24 extracted patches are fed into a convolutional neural network, which outputs a lesion probability for each voxel
- CNN data fusion:
  - Modalities – Fused at first layer. Utilizes fine-level voxel intensity correlations
  - Time Points – Fused at intermediate layer. Able to detect larger scale features such as change in lesion size
  - Views – Fused by fully connected layers, rather than convolutions (since they are not connected spatially). Utilizes high level features.



Network Architecture (II)

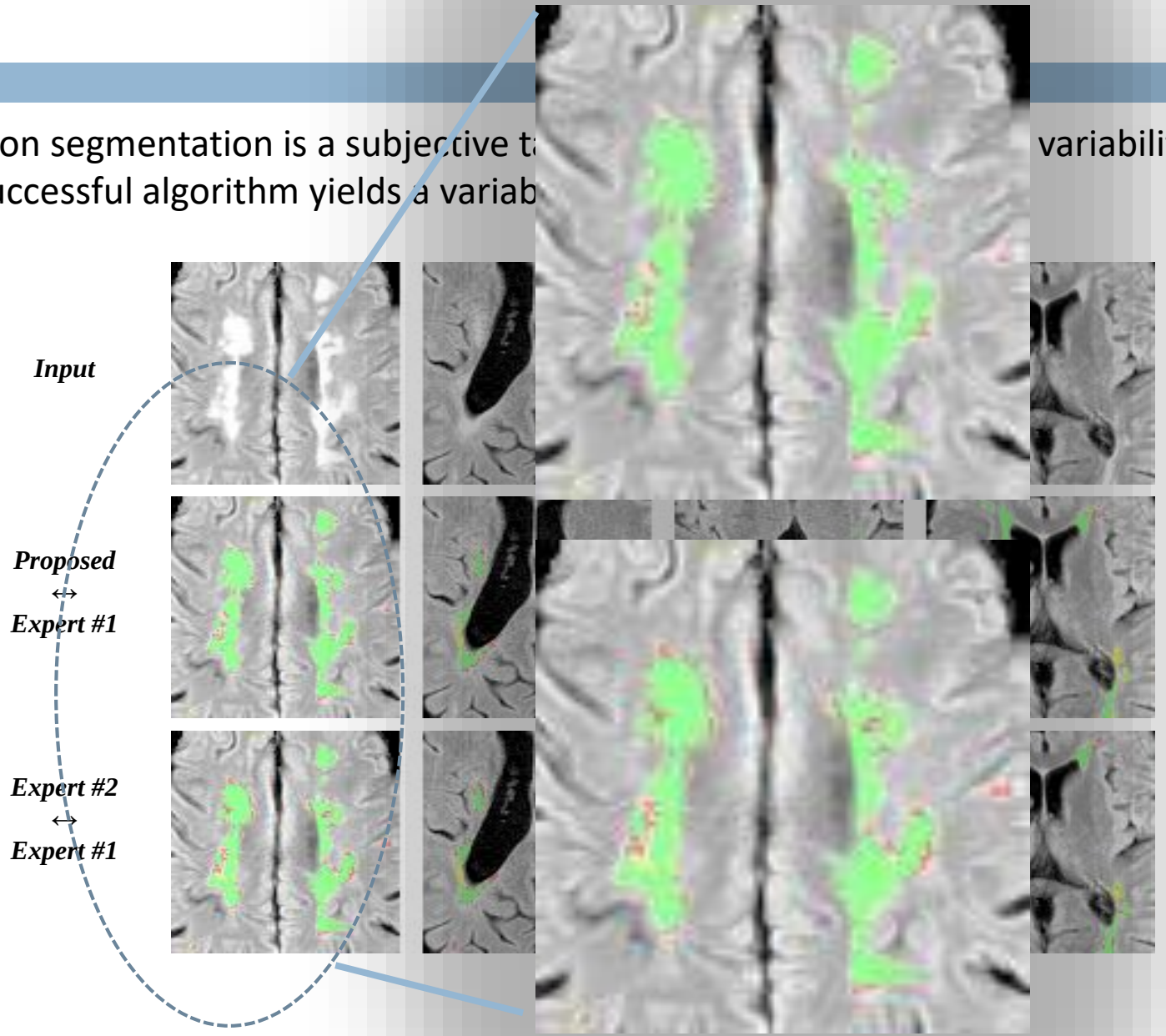


Technical Details

- Training infrastructure: Keras (Theano wrapper)
- Nonlinearity: Leaky ReLU ($\alpha = 0.3$)
- Leave-Patient-out cross validation (4 training / 1 validation)
- Avoiding overfitting:
  - Dropout ($p = 0.25$) after every convolutional and fully connected layer
  - Weight Sharing: Shared weights for T_i and T_{i-1} V-Nets
  - Data Augmentation: Rotations in 3D drawn from Gaussian distribution ($\mu = 0°, \sigma = 5°$)
- Class Balancing: Equal number of positive and negative samples in each batch (size = 128)
- Training objective: Categorical Cross-Entropy (voxel-wise lesion/non-lesion)
  Solver: AdaDelta
- 500 training epochs
- Running Times:
  - Training: 4 Hours
  - Classification: 27 seconds

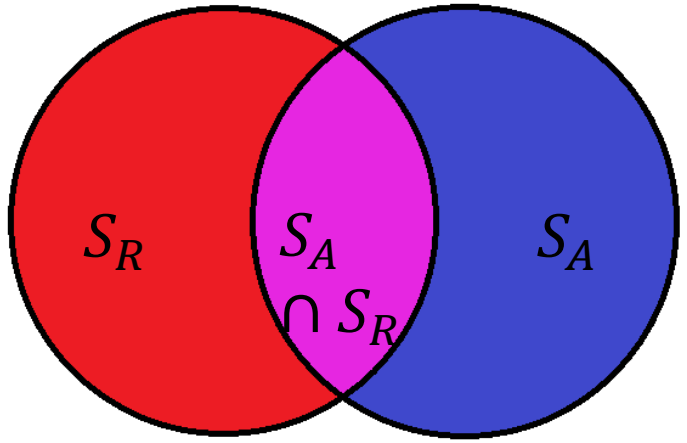
Qualitative Example

- Lesion segmentation is a subjective t variability (IRV)
- A successful algorithm yields a variab



Quantitative Analysis

- Comparing automatic and manual rater segmentation:
  - S_A, S_R - Automatic and Rater segmentation volumes
  - Λ_A, Λ_R- Automatic and Rater lesion lists
- Cross validation metrics:
  - Volume correlation: $VC(S_A, S_R) = \rho(S_A, S_R) \in [-1,1]$
  - $Dice(S_A, S_R) = 2\frac{|S_A \cap S_R|}{|S_A|+|S_R|} \in [0,1]$
  - $PPV(S_A, S_R) = \frac{|S_A \cap S_R|}{|S_A \cap S_R|+|S_A \cap S_R^C|} \in [0,1]$
  - $LTPR(S_A, S_R) = \frac{|\Lambda_A \cap \Lambda_R|}{|\Lambda_A \cap \Lambda_R|+|\Lambda_A^C \cap \Lambda_R|} \in [0,1]$
  - $LFPR(S_A, S_R) = \frac{|\Lambda_A \cap \Lambda_R^C|}{|\Lambda_A \cap \Lambda_R^C|+|\Lambda_A^C \cap \Lambda_R^C|} \in [0,1]$



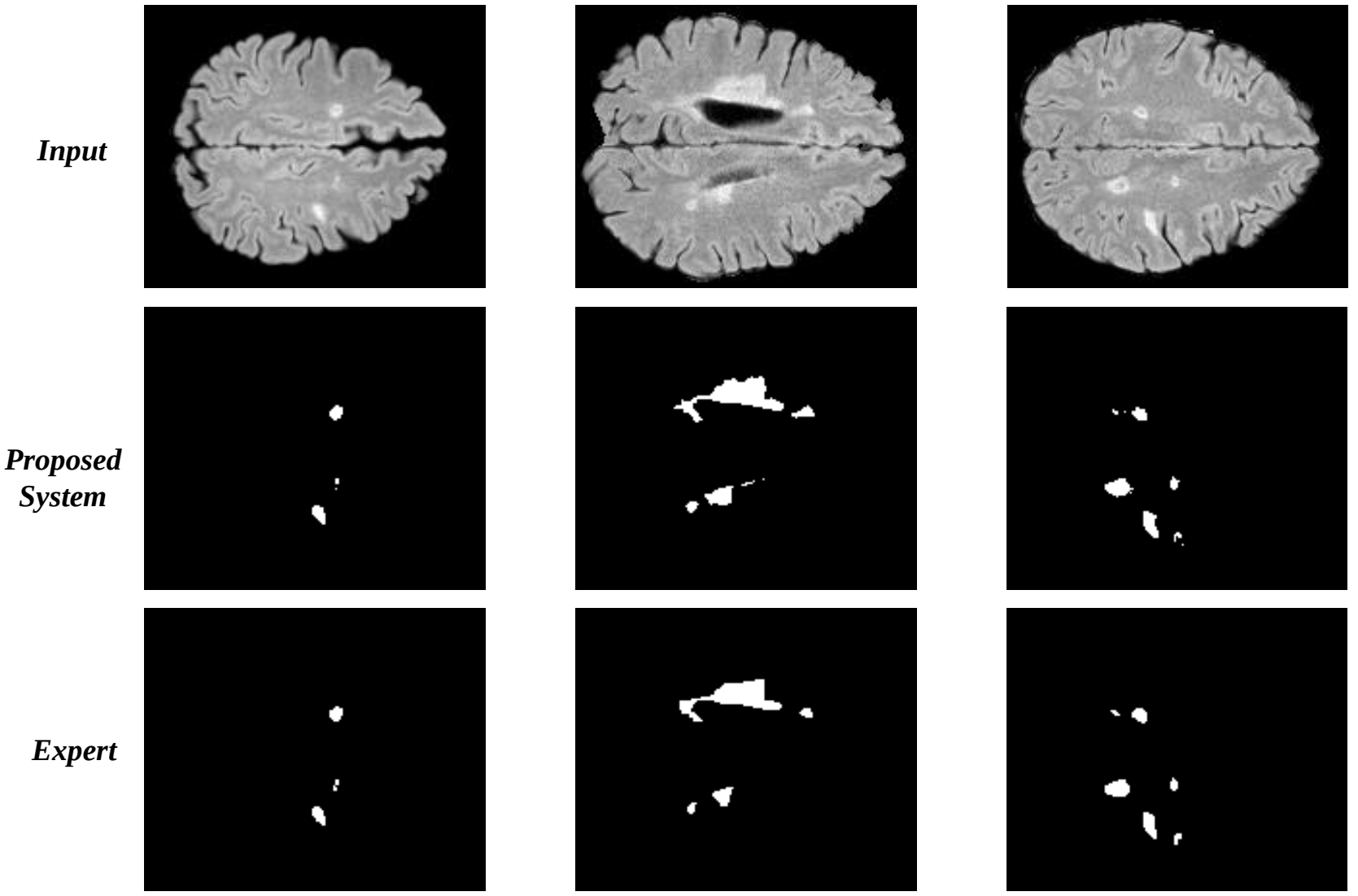
- Test Evaluation metric:
  - $Sc(S_A, S_R) = \frac{1}{8}Dice(S_A, S_R) + \frac{1}{8}PPV(S_A, S_R) + \frac{1}{4}LFPR(S_A, S_R) + \frac{1}{4}LTPR(S_A, S_R) + \frac{1}{4}VC(S_A, S_R)$
  - Averaged across all cases and all raters
  - Normalized such that the lower inter-rater score is equal to 90

Quantitative Analysis

Time Points	Images	Dice (R1)	Dice (R2)	p-value
1	***FLAIR***	0.669	0.649	< 0.001
1	T_1,T_2, ***PD, FLAIR***	0.702	0.672	0.006
2	***FLAIR***	0.714	0.692	0.02
2	T_1, T_2, ***PD, FLAIR***	**0.727**	**0.707**	-
Rater #1		-	0.744	-

- Multiple images improve accuracy
- Multiple time points enhance segmentation even further
- Best model nearly reaches human level accuracy

Examples



Test Set Results

Test Set Results: Top 5 groups out of 18 groups

Rank	Method	ISBI score	Dice
1	**Proposed System**	**91.267**	**0.627**
2	PVG1	90.137	0.579
3	Proposed System, no post-processing	90.070	**0.627**
4	IMI	89.673	0.573
5	VISAGES2	89.265	0.560

- State-of-the art in challenge score and Dice
- Post processing improves overall score, as predicted in cross validation
- Challenge score higher than 90, comparable to performance of an expert

IV. Developing a Platform for 3rd Party Apps & Complete Ecosystem

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It's all about the TEAM

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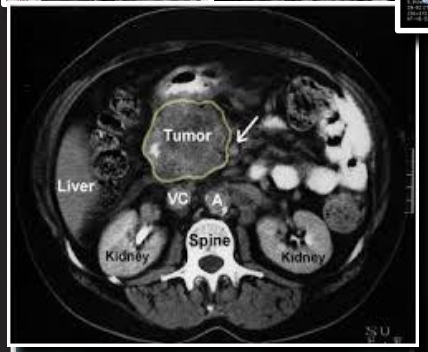
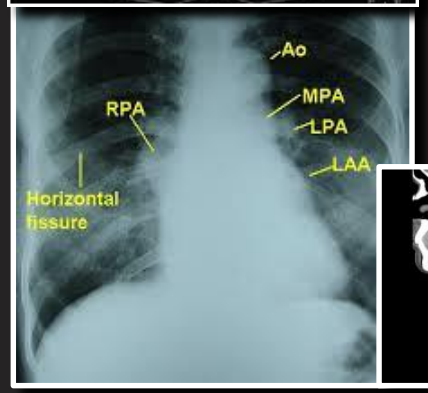
Ecosystem

App Developers





Apps →

← **Access to Market**
Revenue Share $$$
Clinical Data
Regulatory Coverage
Publications

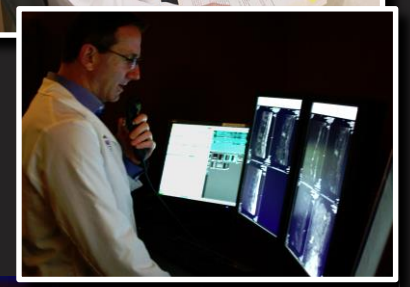
ALPHA*Point* Platform

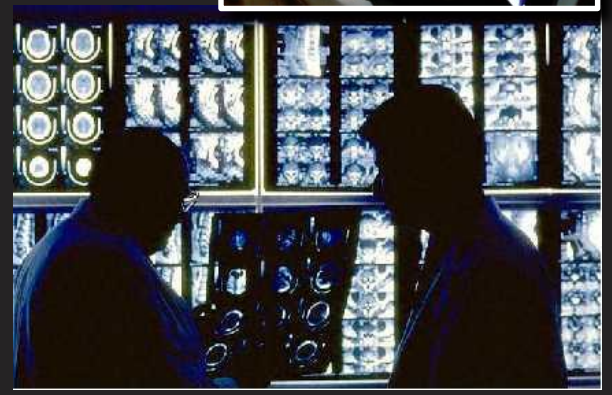
Clinical Data Archive

Premium Workflow Experience →

← **Premium $$$**

Customers





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V. Final Thoughts: Implications of a "Machine Learning" Virtual Resident

Adaptation

Continuous improvement

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Thank You

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