

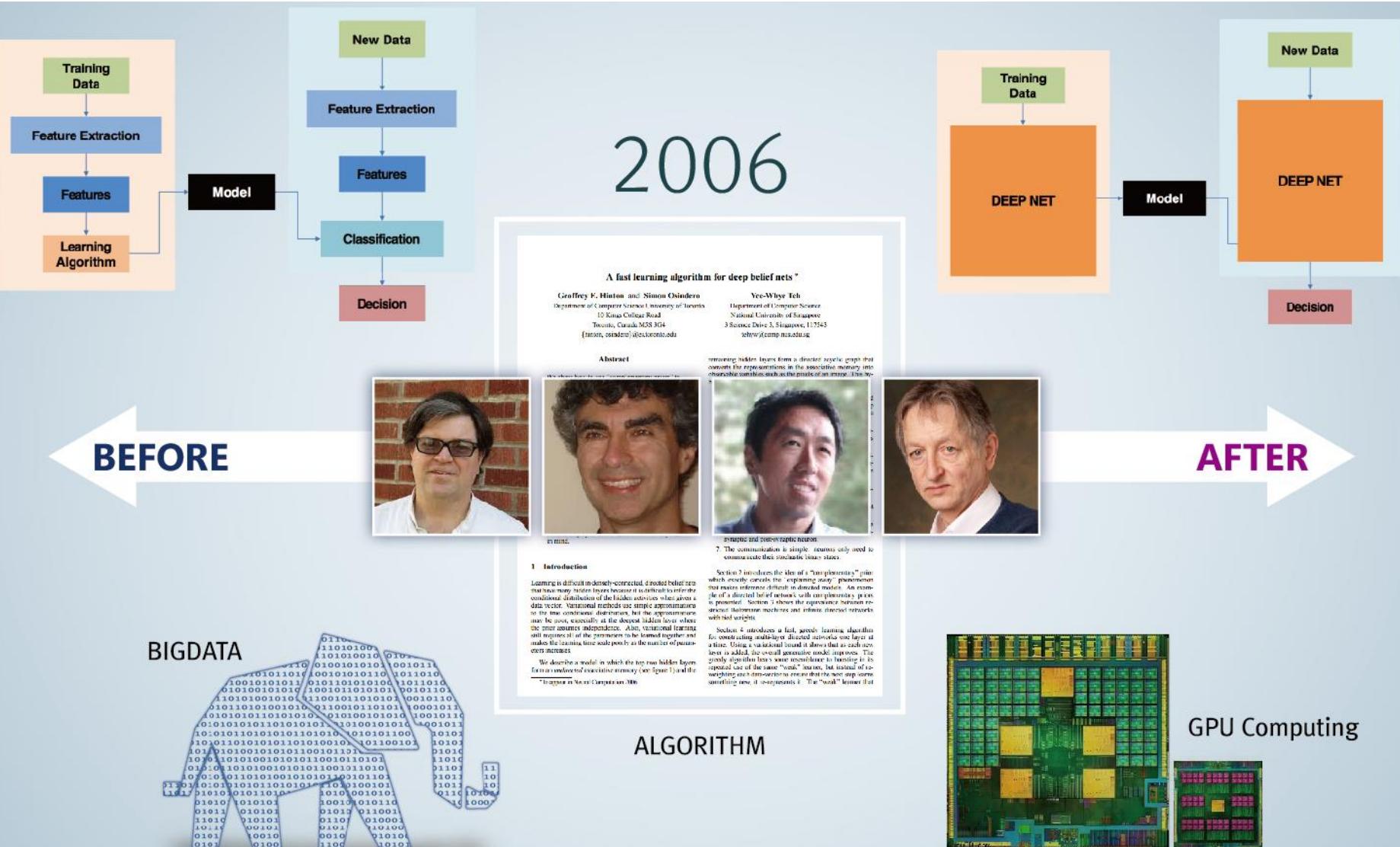
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# Medical Imaging with AI

Hyunna Lee

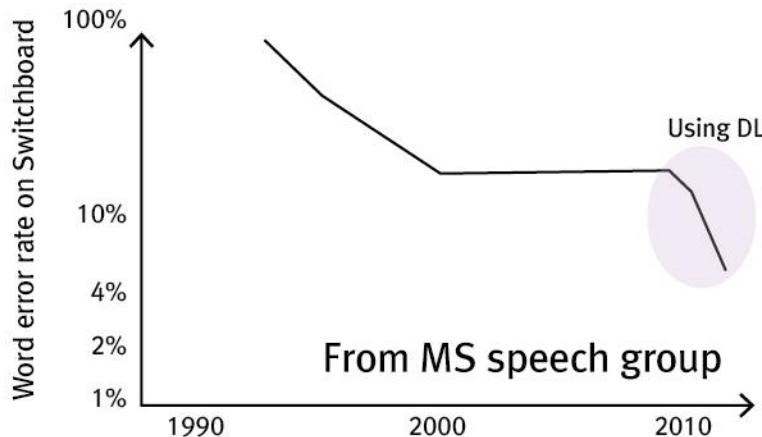
Medical Imaging & Intelligent Reality Lab ( MIR<sup>2</sup>L )  
Health Innovation Big Data Center, Asan Medical Center  
South Korea

# 인공지능 기술의 혁신: 딥러닝

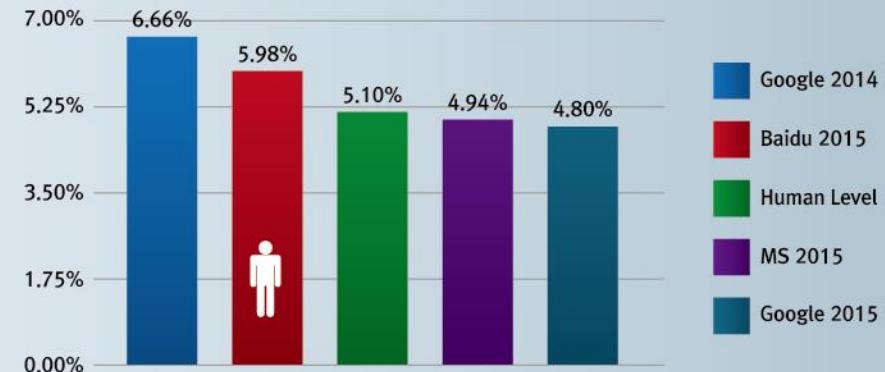


# 인공지능 기술의 혁신: 딥러닝

## Speech Recognition

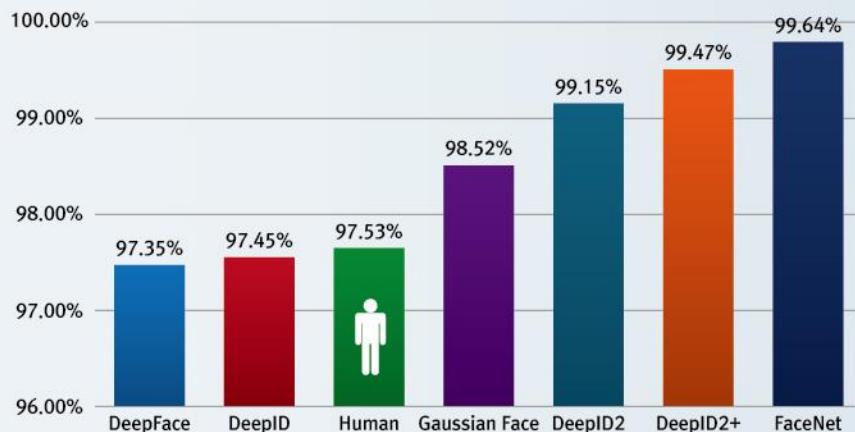


## Object (Image) Recognition (ImageNet)



Research

## Face Verification



JAMA | Original Investigation | INNOVATIONS IN HEALTH CARE DELIVERY

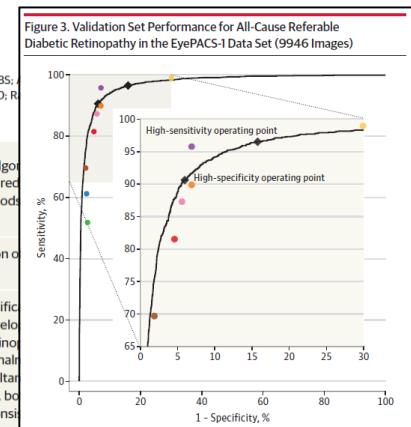
## Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs

Varun Gulshan, PhD; Lily Peng, MD, PhD; Marc Coram, PhD; Martin C. Stumpe, PhD; Derek Wu, BS; Subhashini Venugopalan, MS; Kasumi Widner, MS; Tom Madams, MEng; Jorge Cuadros, OD, PhD; Rajiv Raman, MS, DNB; Philip C. Nelson, BS; Jessica L. Mega, MD, MPH; Dale R. Webster, PhD

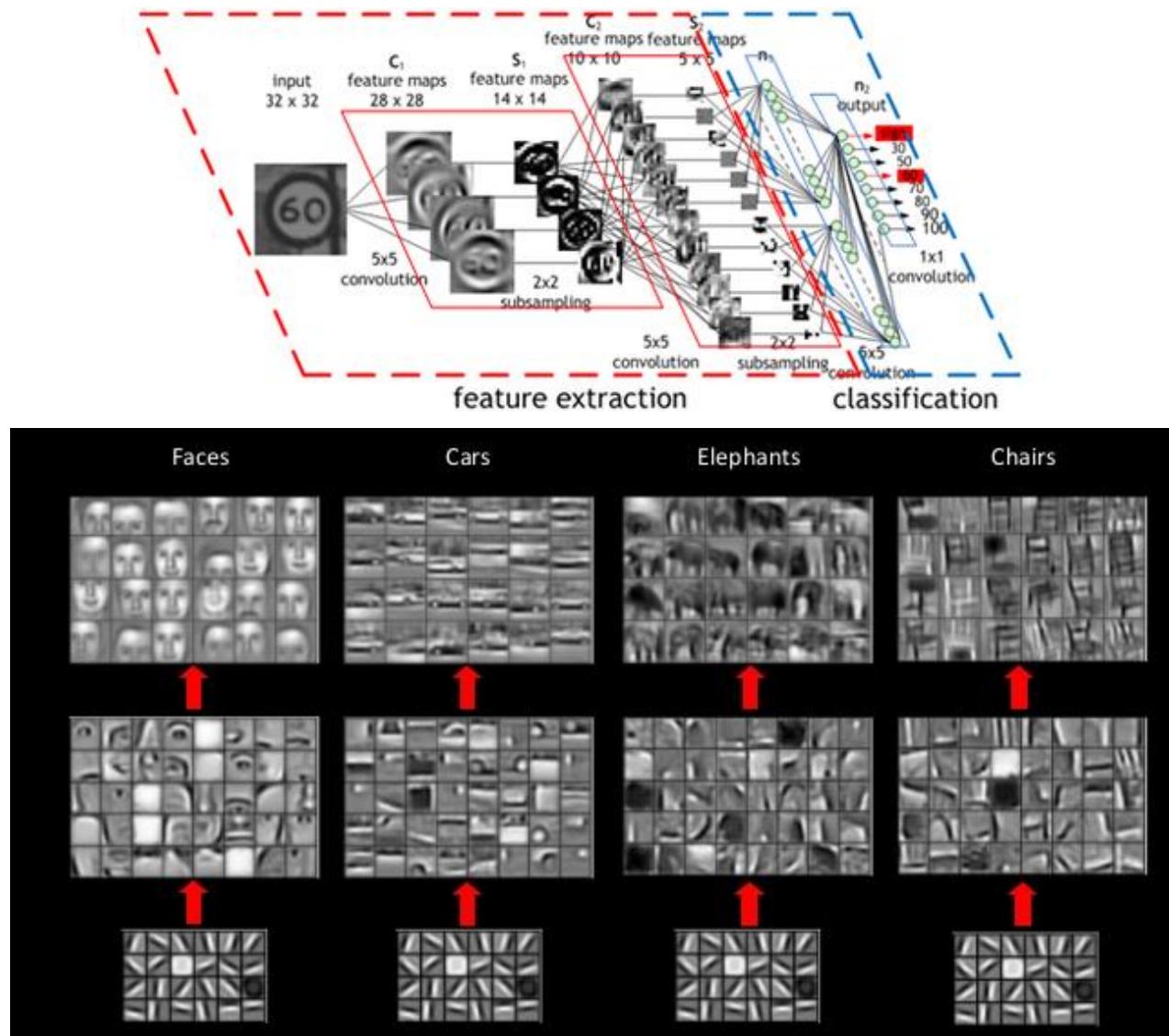
**IMPORTANCE** Deep learning is a family of computational methods that allow an algorithm to program itself by learning from a large set of examples that demonstrate the desired behavior, removing the need to specify rules explicitly. Application of these methods to medical imaging requires further assessment and validation.

**OBJECTIVE** To apply deep learning to create an algorithm for automated detection of diabetic retinopathy and diabetic macular edema in retinal fundus photographs.

**DESIGN AND SETTING** A specific type of neural network optimized for image classification called a deep convolutional neural network was trained using a retrospective development data set of 128 175 retinal images, which were graded 3 to 7 times for diabetic retinopathy, diabetic macular edema, and image gradability by a panel of 54 US licensed ophthalmologists and ophthalmology senior residents between May and December 2015. The resultant algorithm was validated in January and February 2016 using 2 separate data sets, both graded by at least 7 US board-certified ophthalmologists with high intragrader consistency.



# Convolutional Neural Net



# Convolutional Neural Net

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[www.cybercontrols.org](http://www.cybercontrols.org)



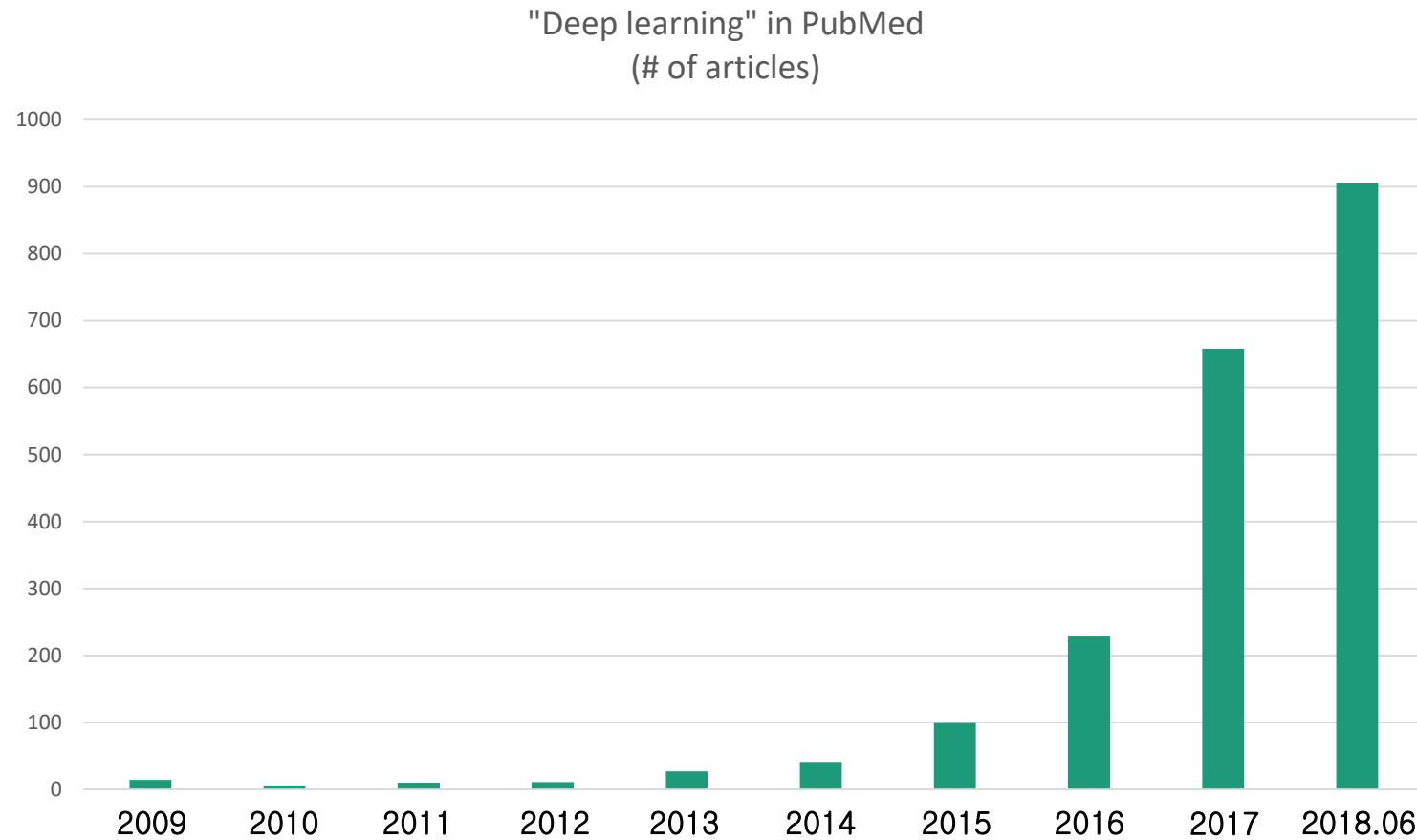
UNIVERSITY OF ULSAN  
COLLEGE MEDICINE



ASAN  
Medical Center

# 인공지능 기술의 혁신: 의료영상

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# 인공지능 기술의 혁신: 의료영상

Research

JAMA | Original Investigation | INNOVATIONS IN HEALTH CARE DELIVERY

## Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs

Varun Gulshan, PhD; Lily Peng, MD, PhD; Marc Coram, PhD; Martin C. Stumpe, PhD; Derek Wu, BS; Arunachalam Narayanaswamy, PhD; Subhashini Venugopalan, MS; Kasumi Widner, MS; Tom Madams, MEng; Jorge Cuadros, OD, PhD; Ramasamy Kim, OD, DNB; Rajiv Raman, MS, DNB; Philip C. Nelson, BS; Jessica L. Mega, MD, MPH; Dale R. Webster, PhD

**IMPORTANCE**  
program itself  
behavior, rem  
medical imagi

**OBJECTIVE** To  
retinopathy ai

**DESIGN AND S**  
called a deep  
data set of 128  
diabetic macu  
and ophthalm  
algorithm was  
graded by at li

**EXPOSURE** De

**MAIN OUTCOM**  
referable diab  
referable diab

## LETTER

doi:10.1038/nature21056

## Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva<sup>1\*</sup>, Brett Kuprel<sup>1\*</sup>, Roberto A. Novoa<sup>2,3</sup>, Justin Ko<sup>2</sup>, Susan M. Swetter<sup>2,4</sup>, Helen M. Blau<sup>5</sup> & Sebastian Thrun<sup>6</sup>

Skin cancer, the most common human malignancy<sup>1–3</sup>, is primarily diagnosed visually, beginning with an initial clinical screening and followed potentially by dermoscopic analysis, a biopsy and histopathological examination. Automated classification of skin

images (for example, smartphone images) exhibit variability in factors such as zoom, angle and lighting, making classification substantially more challenging<sup>23,24</sup>. We overcome this challenge by using a data-driven approach—1.41 million pre-training and training images

Research

JAMA | Original Investigation

## Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer

Babak Ehteshami Bejnordi, MS; Mitko Veta, PhD; Paul Johannes van Diest, MD, PhD; Bram van Ginneken, PhD; Nico Karssemeijer, PhD; Geert Litjens, PhD; Jeroen A. W. M. van der Laak, PhD; and the CAMELYON16 Consortium

ChosunBiz  
2018. 6. 23 (토)

뉴스

증권

부동산

정책·금융

기업

오피니언

기업 -

바이오·제약

인공지능(AI)으로 빼 나이 판독...식약처, 뷰노 개발 의료기기 첫 판매 허가

리자운 기자 ▾

기사

100자 평(0)

입력 : 2018.05.16 11:11

의료현장에서 인공지능 기술을 활용해 뼈(骨)나이를 판독할 수 있게 됐다. 규제당국이 국내에서 개발한 인공지능(AI) 기반 의료기기 판매를 처음으로 허가했다.

시품의약품안전처는 국내 의료기기업체 '뷰노'가 개발한 인공지능(AI) 기술이 적용된 의료영상분석장치 소프트웨어 '뷰노메드 본에이지(VUNomed-BoneAge)'를 16일 허가했다고 밝혔다.



▲ 뷰노의 시기반 의료영상분석장치 소프트웨어 '뷰노메드 본에이지(VUNomed-BoneAge)'./식약처 제공

# Beyond computer vision

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Computer Vision  
To Discern  
Clinician Behaviors

**“Bedside Computer Vision”**

Yeung S, Fei-Fei Li et al. NEJM 2018 April

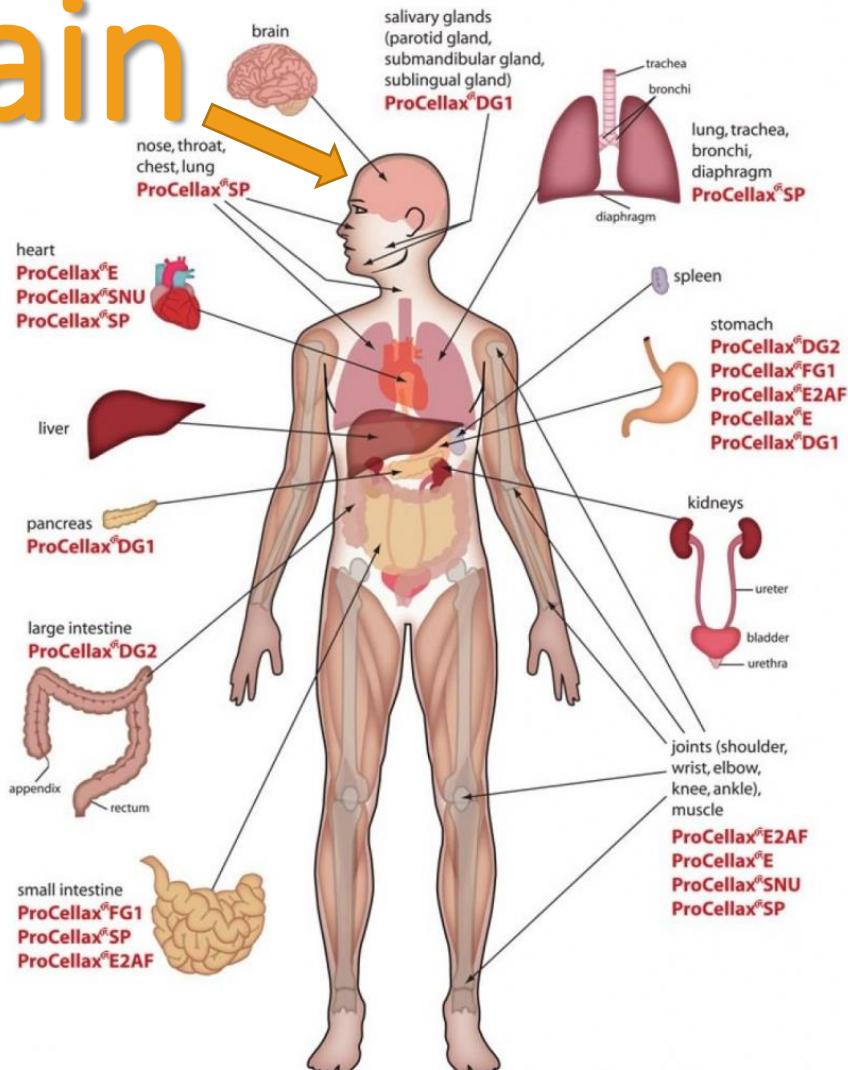


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# Brain

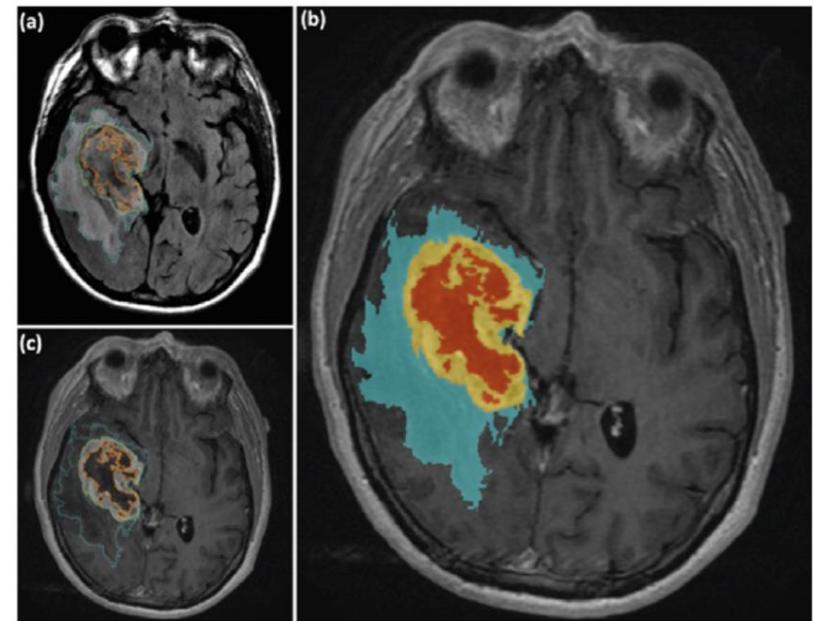


## ■ Segmentation of Glioblastoma Malformation (GBM)

- Multi-class segmentation

- ✓ Necrosis
- ✓ Enhancing tumor
- ✓ Edema

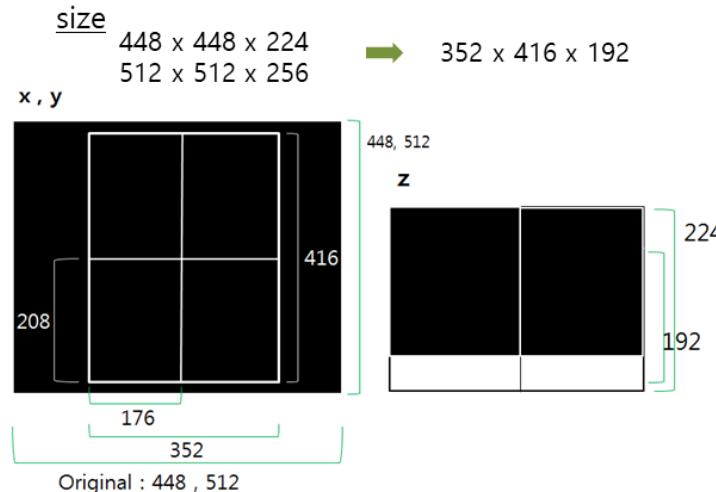
- AMC dataset
  - ✓ 103 patients
  - ✓ 3D enhanced-T1w



- Segmentation of Glioblastoma Malformation (GBM)
  - Phase 1: localization (coarse segmentation)

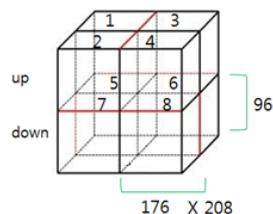
### Data dividing to 8 cube

#### 1. Image & Mask cropping

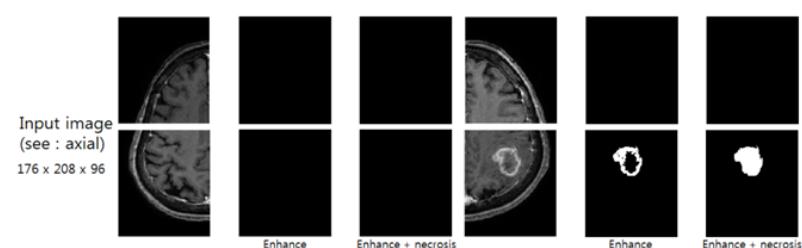


#### 2. Divided to 8 cube

size  
352 x 416 x 192       $\rightarrow$  176 x 208 x 96

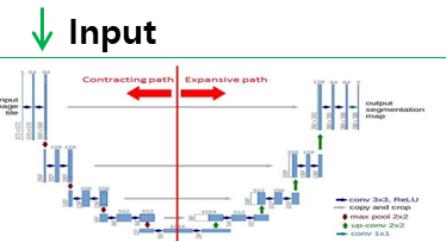


	Label	Set
T1ce	Enhanced	Train 600 Valid 112 Test 112
	Enhanced + Necrosis	Train 600 Valid 112 Test 112

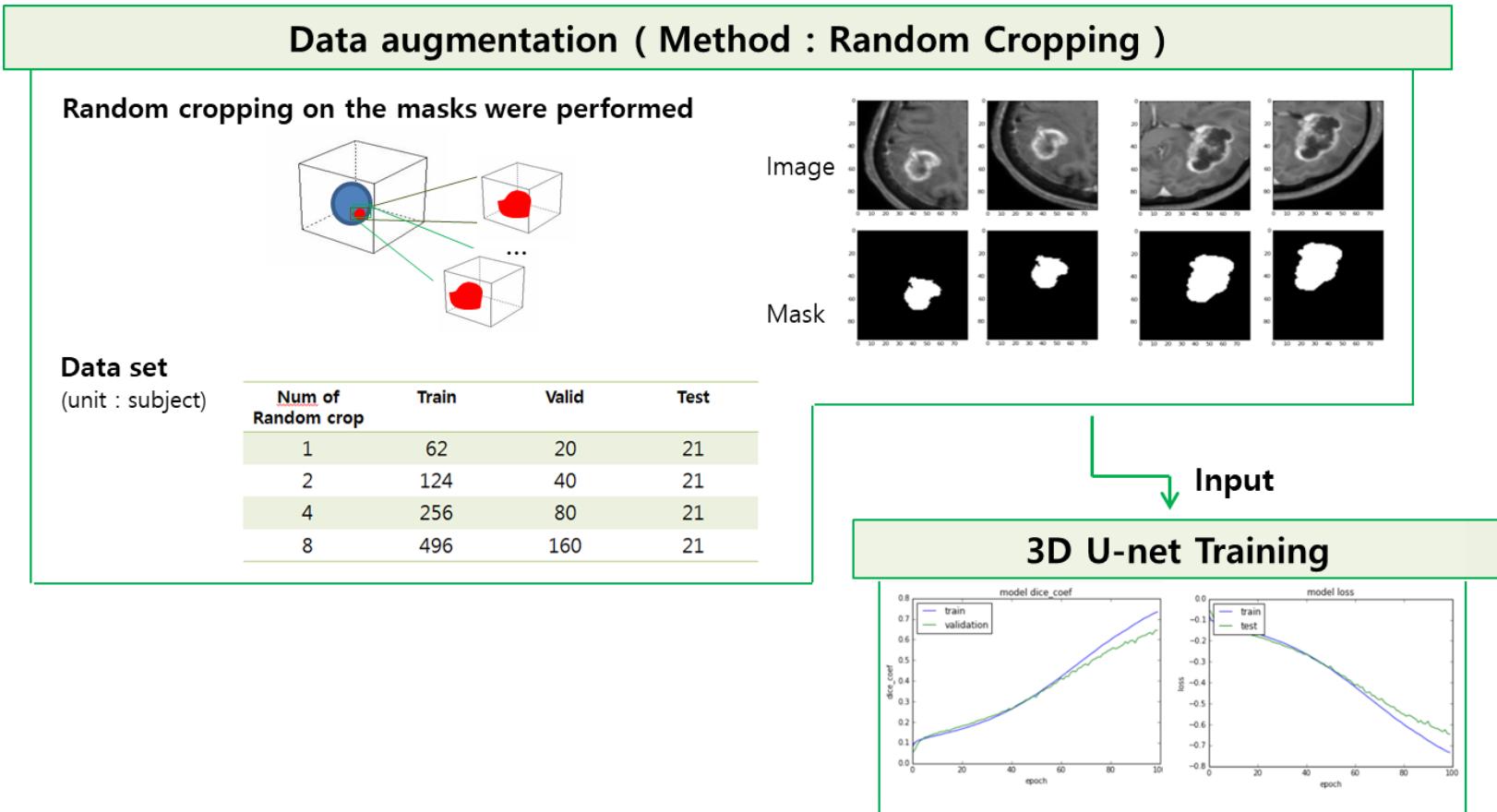


### 3D U-net Training

one of the most widely used CNN architectures for image segmentation



- Segmentation of Glioblastoma Malformation (GBM)
  - Phase 2: fine segmentation



# Tumor

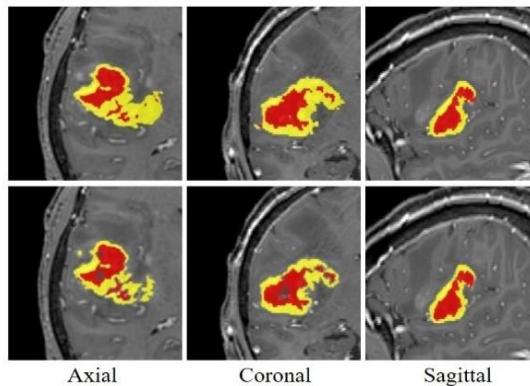
## ■ Segmentation of Glioblastoma Malformation (GBM)

- Results

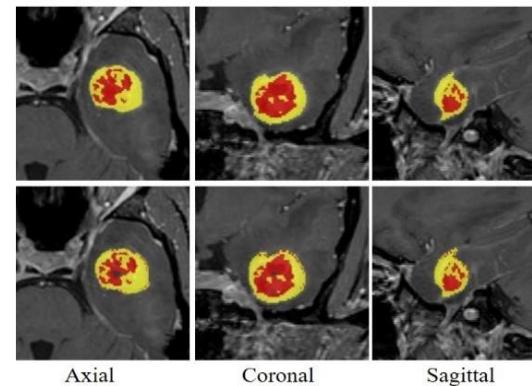
Enhancing	Dice	Jaccard
coarse	0.819	0.701
x1	0.648	0.511
x2	0.707	0.567
x4	0.771	0.642
x8	0.823	0.711
x16	0.834	0.725

Necrosis	Dice	Jaccard
coarse	0.788	0.684
x1	0.445	0.324
x2	0.641	0.517
x4	0.717	0.594
x8	0.778	0.658
x16	0.848	0.759

Gold standard



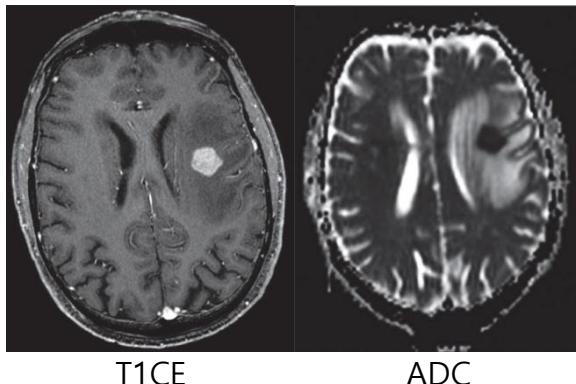
Test



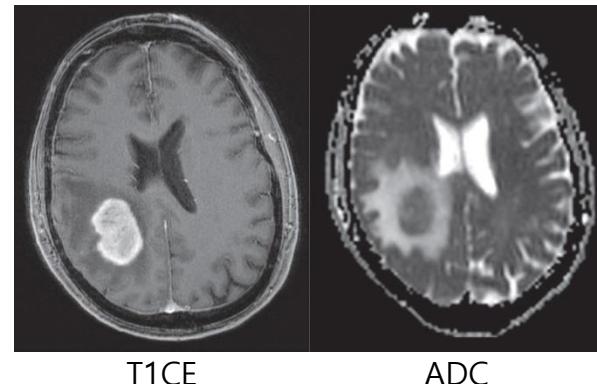
## ■ Classification

- Binary classification: PCNSL vs. GBM

**PCNSL (primary CNS lymphoma)**



**GBM(glioblastoma)**



VS.

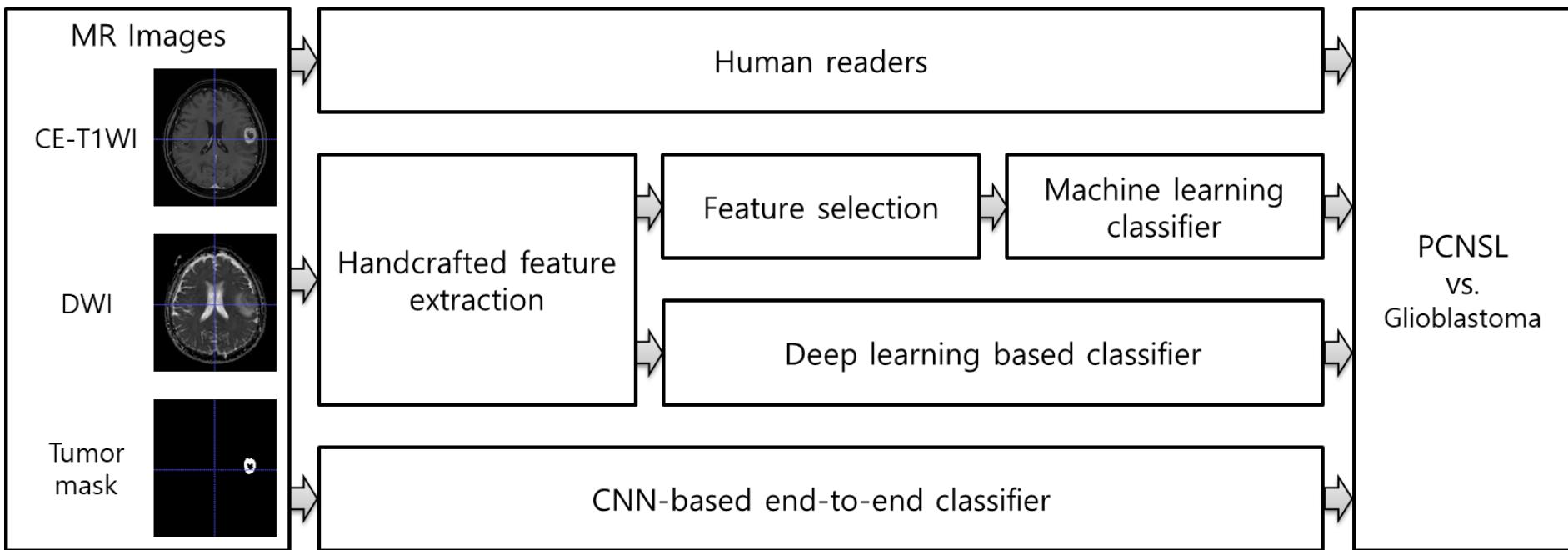
- Multi-center: AMC and Samsung Medical Center

	ASAN Medical Center		Samsung Medical Center	
Pathology	PCNSL	GBM	PCNSL	GBM
Patients (N)	62	91	14	28

	Training		Internal validation	
Pathology	PCNSL	GBM	PCNSL	GBM
Patients (N)	50	73	12	18

## ■ Classification

- Binary classification: PCNSL vs. GBM



## ■ Classification

- Pre-processing

- ✓ Bias correction

- ✓ Intensity normalization

- Handcrafted features

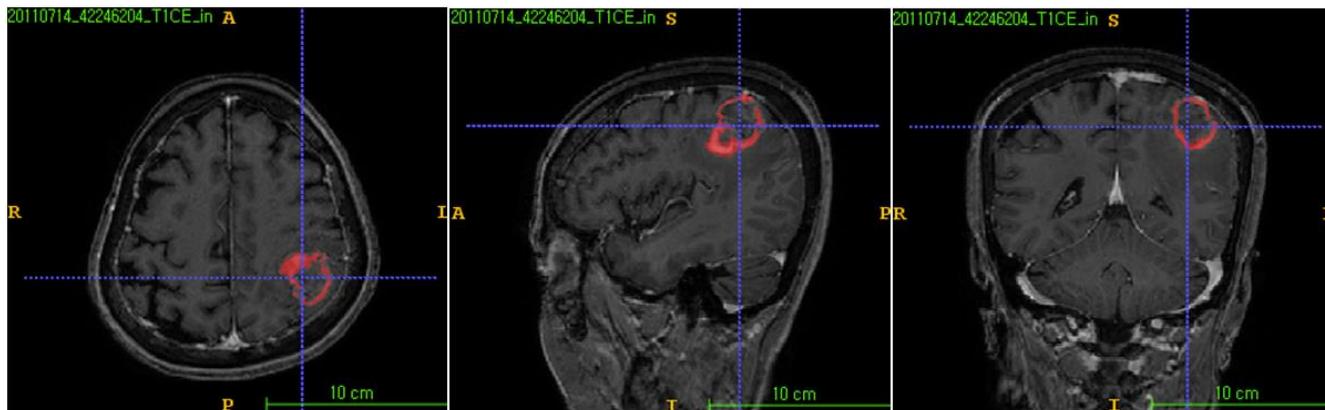
- ✓ First order: 17

- ✓ GLCM (dist=1,2,3):  $25 \times 3 = 75$

- ✓ GLRLM: 12

104 features

- $\times 9$  wavelets (original + 8 wavelets) = 936 features



## ■ Classification

- Results: Handcrafted features + NN

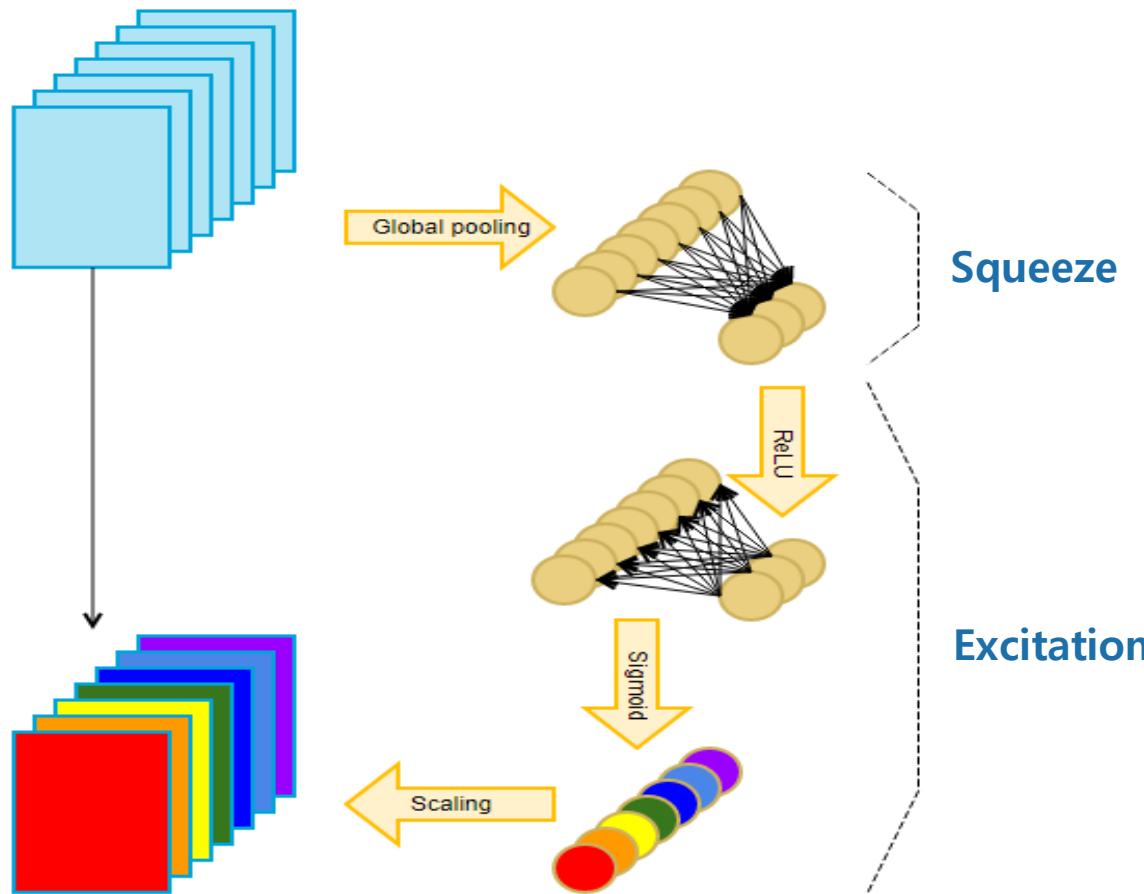
Network	Data	Internal validation				External validation (z-scoring with training dataset)				External validation (z-scoring with test dataset)			
		AUC (95% CI)	Acc. (%)	Sen. (%)	Spec. (%)	AUC (95% CI)	Acc. (%)	Sen. (%)	Spec. (%)	AUC (95% CI)	Acc. (%)	Sen. (%)	Spec. (%)
100-10	T1	0.9652 (0.9589, 0.9715)	93.33	91.67	94.44	0.9179 (0.9137, 0.9221)	83.33	78.57	85.71	0.9107 (0.9067, 0.9147)	85.71	85.71	85.71
	ADC	0.9692 (0.9603, 0.9781)	93.33	91.67	94.44	0.8598 (0.8351, 0.8845)	80.95	92.86	75.00	0.8426 (0.8254, 0.8598)	78.57	64.29	85.71
	T1 +ADC	0.9907 (0.9869, 0.9945)	100	100	100	0.9466 (0.9372, 0.9560)	85.71	92.86	82.14	0.9503 (0.9448, 0.9558)	85.71	92.86	82.14
500-100-10	T1	0.9655 (0.9602, 0.9708)	86.67	91.67	83.33	0.9152 (0.9081, 0.9223)	83.33	78.57	85.71	0.9100 (0.9042, 0.9158)	83.33	78.57	85.71
	ADC	0.9680 (0.9566, 0.9794)	93.33	91.67	94.44	0.8366 (0.8109, 0.8623)	73.81	100	60.71	0.8428 (0.8278, 0.8578)	76.19	64.29	82.14
	T1 +ADC	0.9903 (0.9873, 0.9933)	100	100	100	0.9345 (0.9245, 0.9445)	85.71	92.86	82.14	0.9480 (0.9412, 0.9548)	83.33	85.71	82.14
500-100-50-10	T1	0.9556 (0.9493, 0.9619)	86.67	91.67	83.33	0.9101 (0.9022, 0.9180)	83.33	78.57	85.71	0.9103 (0.9048, 0.9158)	83.33	78.57	85.71
	ADC	0.9638 (0.9526, 0.9750)	93.33	91.67	94.44	0.8342 (0.8084, 0.8600)	80.95	92.86	75.00	0.8359 (0.8194, 0.8524)	76.19	64.29	82.14
	T1 +ADC	0.9893 (0.9853, 0.9933)	100	100	100	0.9245 (0.9163, 0.9327)	85.71	92.86	82.14	0.9418 (0.9328, 0.9508)	85.71	92.86	82.14

## ■ Classification

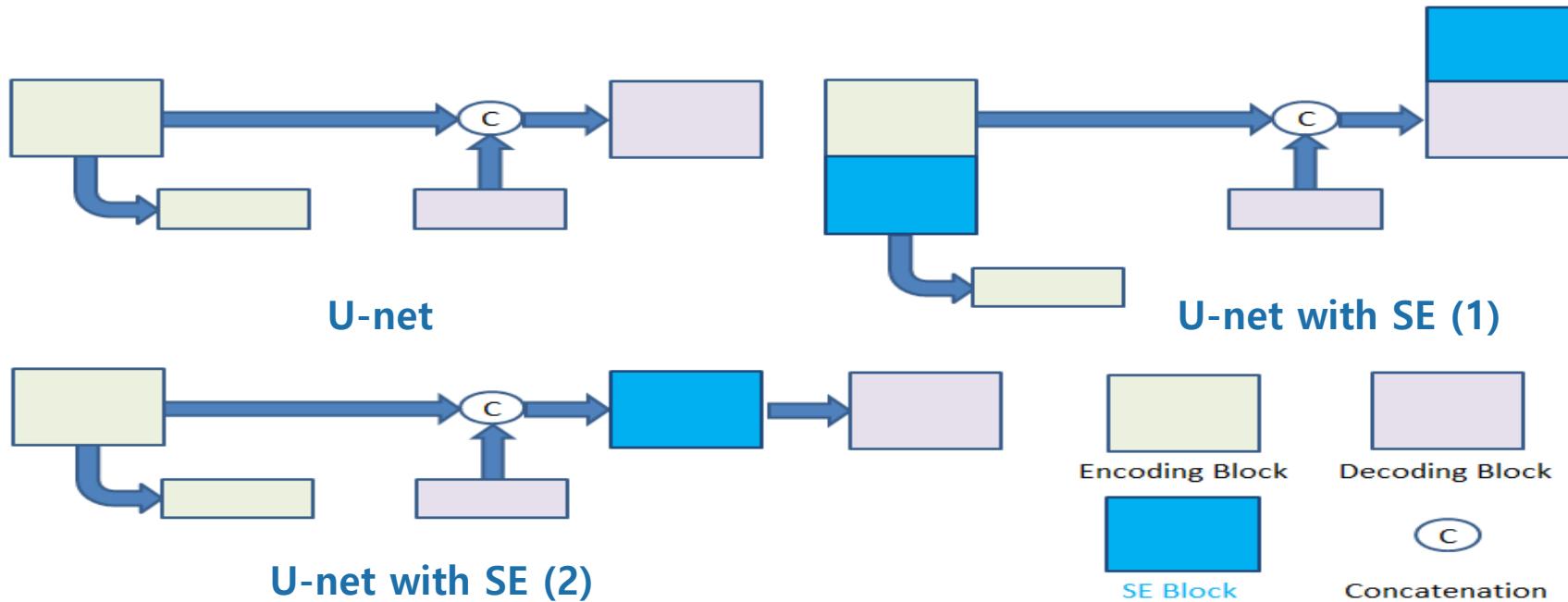
- Results: CNN-based end-to-end

	Data	Internal validation				External validation			
		AUC (95% CI)	Acc. (%)	Sen. (%)	Spec. (%)	AUC (95% CI)	Acc. (%)	Sen. (%)	Spec. (%)
Inception v3 (without data augmentation)	T1CE	0.8197 (0.7881, 0.8513)	73.33	41.67	94.44	0.5091 (0.4945, 0.5237)	42.86	57.14	35.71
	ADC	0.8794 (0.8568, 0.9020)	83.33	83.33	83.33	0.4857 (0.4687, 0.5027)	35.71	100	3.57
	T1CE+ADC	0.7945 (0.7719, 0.8171)	76.67	41.67	100	0.6019 (0.5845, 0.6193)	40.48	50.00	35.71

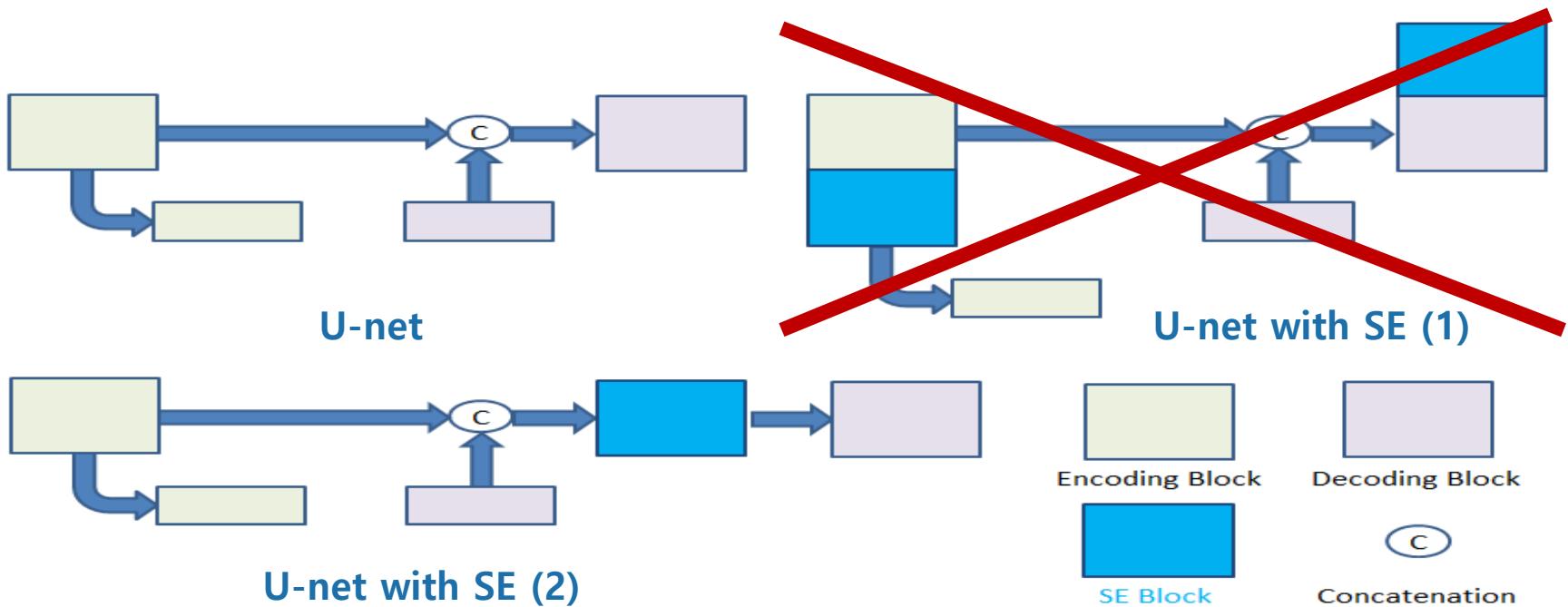
- Infarct segmentation with SE block
  - Squeeze-and-Excitation Block



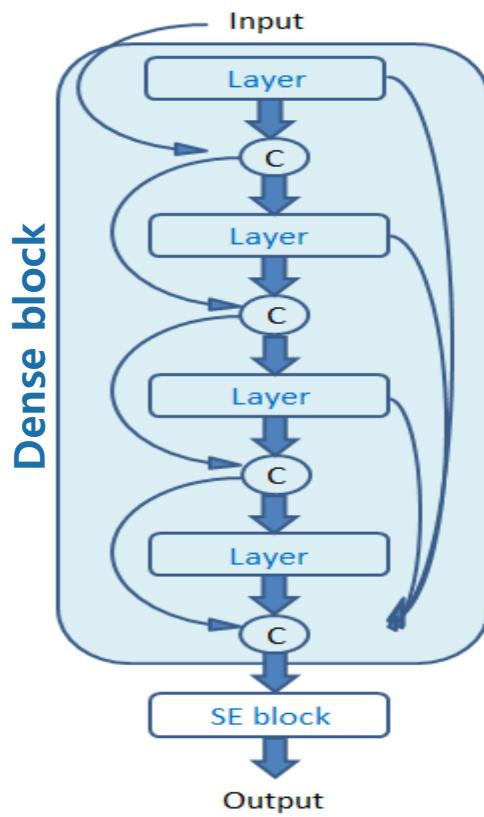
- Infarct segmentation with SE block
  - Networks: U-net and Dense-net



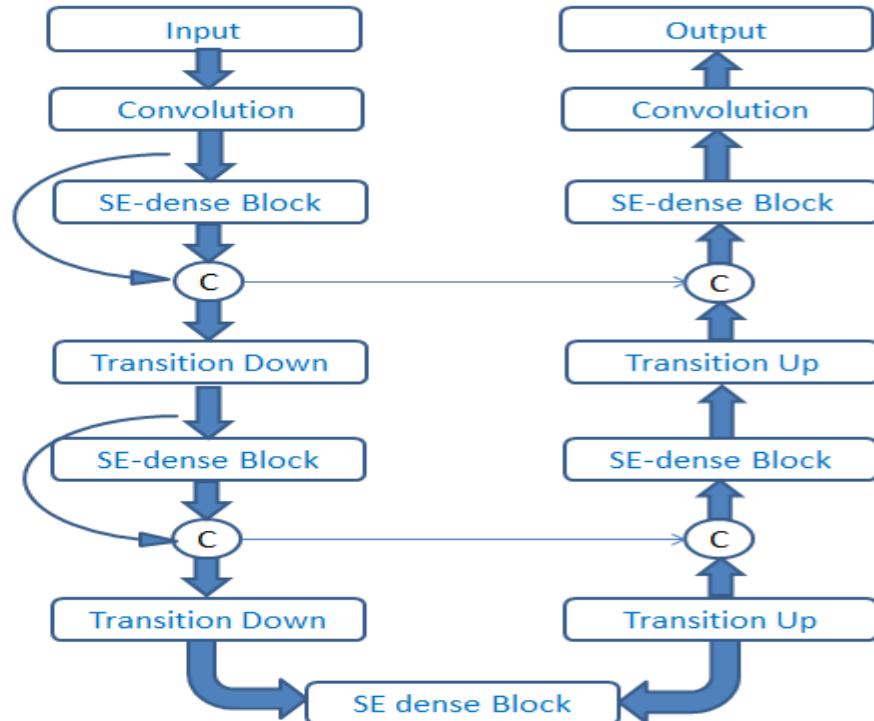
- Infarct segmentation with SE block
  - Networks: U-net and Dense-net



- Infarct segmentation with SE block
  - Networks: U-net and Dense-net



**SE-dense block**



**Dense-net with SE**

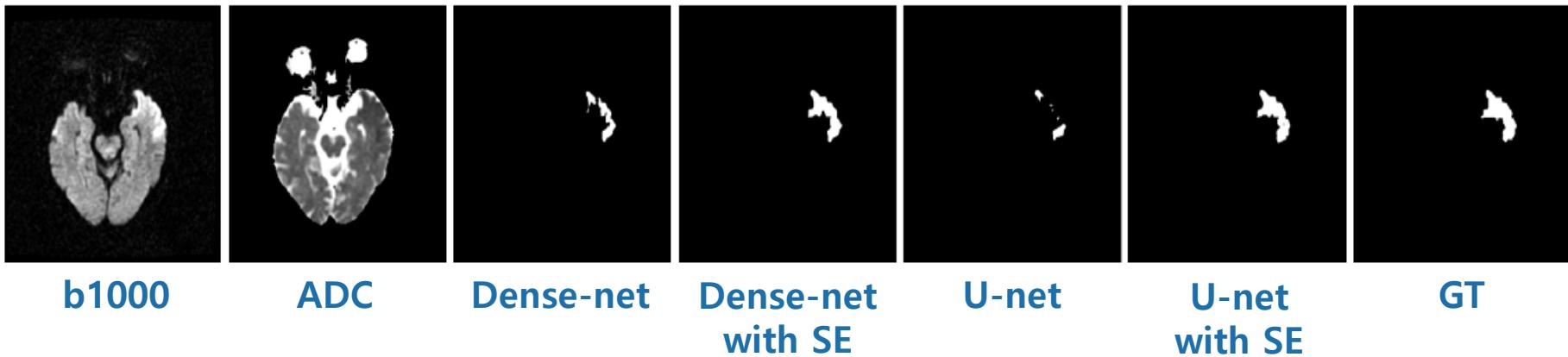
## ■ Infarct segmentation with SE block

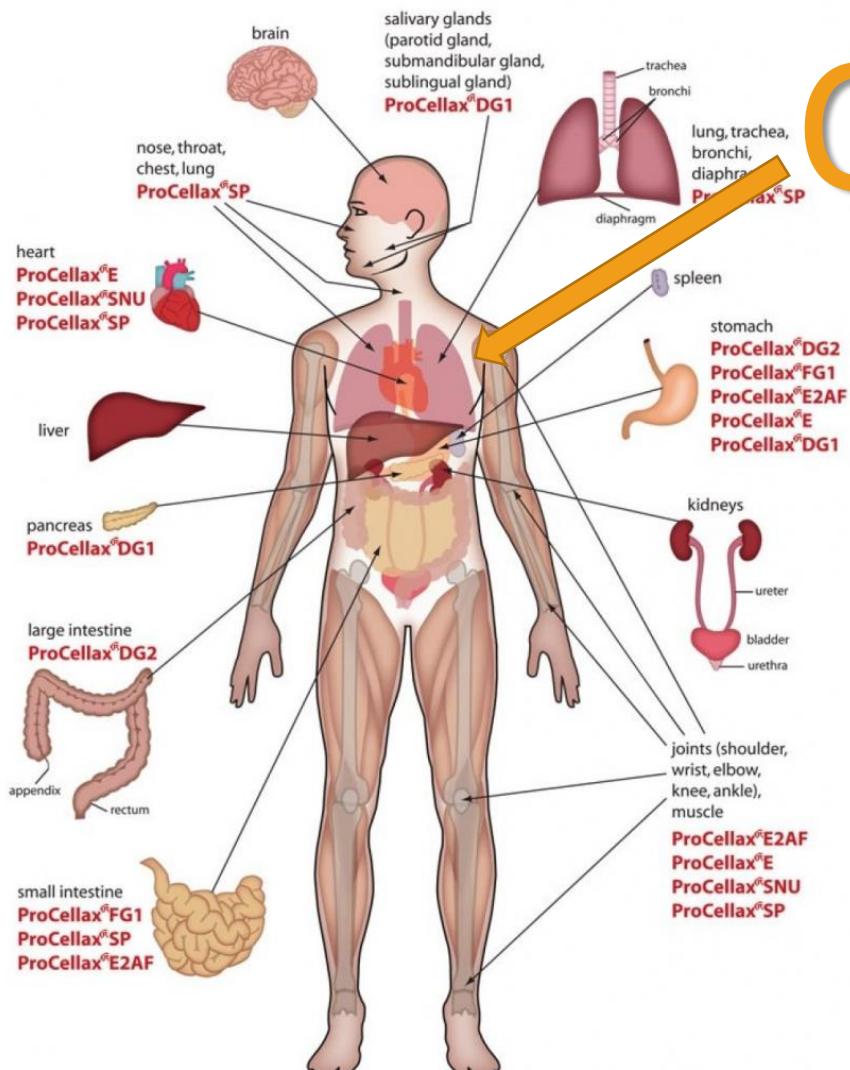
- AMC dataset
  - ✓ 436 acute stroke patients
  - ✓ DWI scans: b1000 and ADC
- Pre-processing
  - ✓ Resized volume size: 384 x 384 x 20
  - ✓ Fixed pixel spacing: 0.6510 mm x 0.6510 mm x 6.9 mm
  - ✓ Intensity normalization

## ■ Infarct segmentation with SE block

- Results

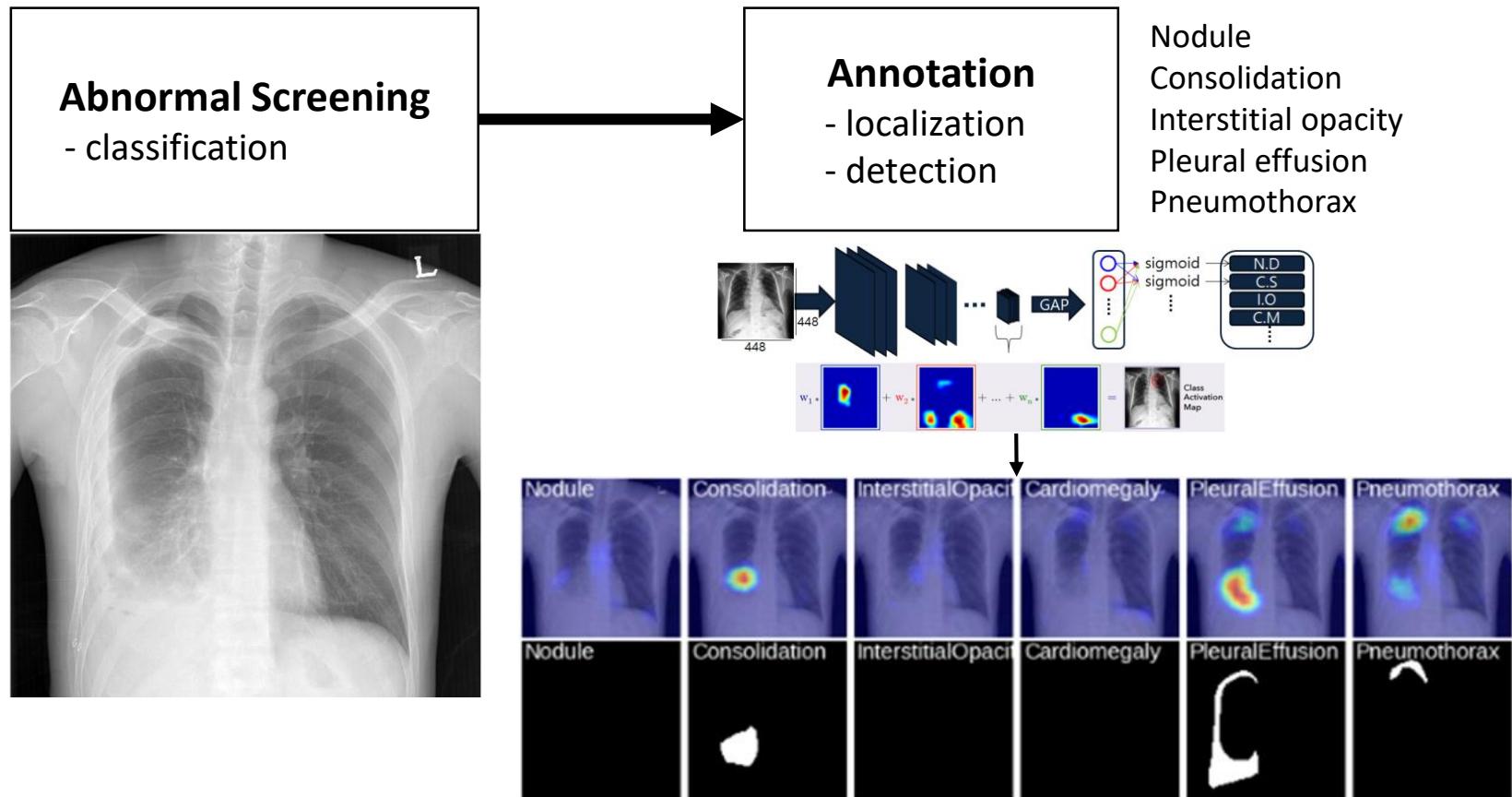
Original	Dice	Jaccard	With SE	Dice	Jaccard
2D En-/De-coder	0.749	0.617	2D En-/De-coder	0.768	0.640
2D U-net	0.823	0.713	2D U-net	0.832	0.723
2D Dense-net	0.809	0.694	2D Dense-net	0.820	0.711
3D FCN	0.632	0.494	3D FCN	0.612	0.477
3D U-net	0.764	0.639	3D U-net	0.743	0.615





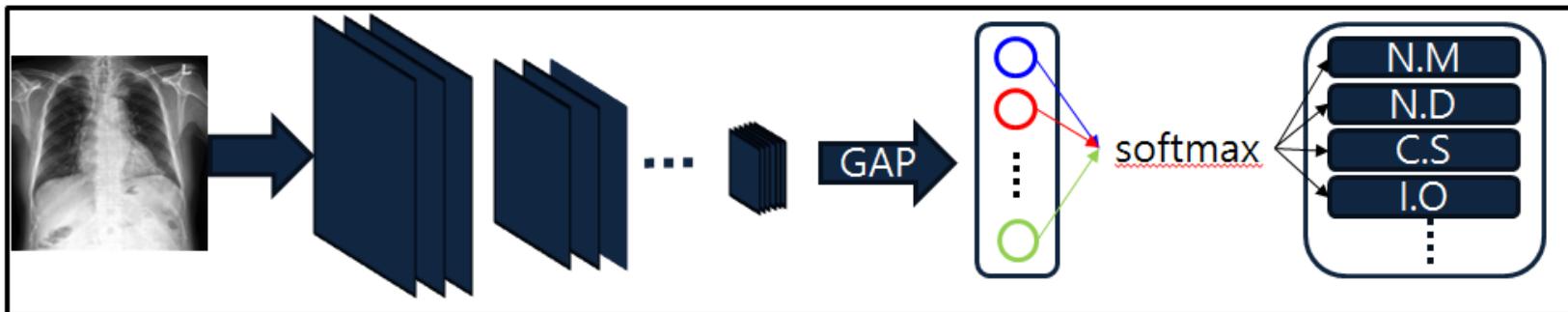
# Chest PA: Curriculum learning

- Curriculum learning for multi-label classification
  - 5-label classification



# Chest PA: Curriculum learning

- Curriculum learning for multi-label classification
  - Multi-class classification
    - ✓ Each instance **exclusively** belong to **single class**

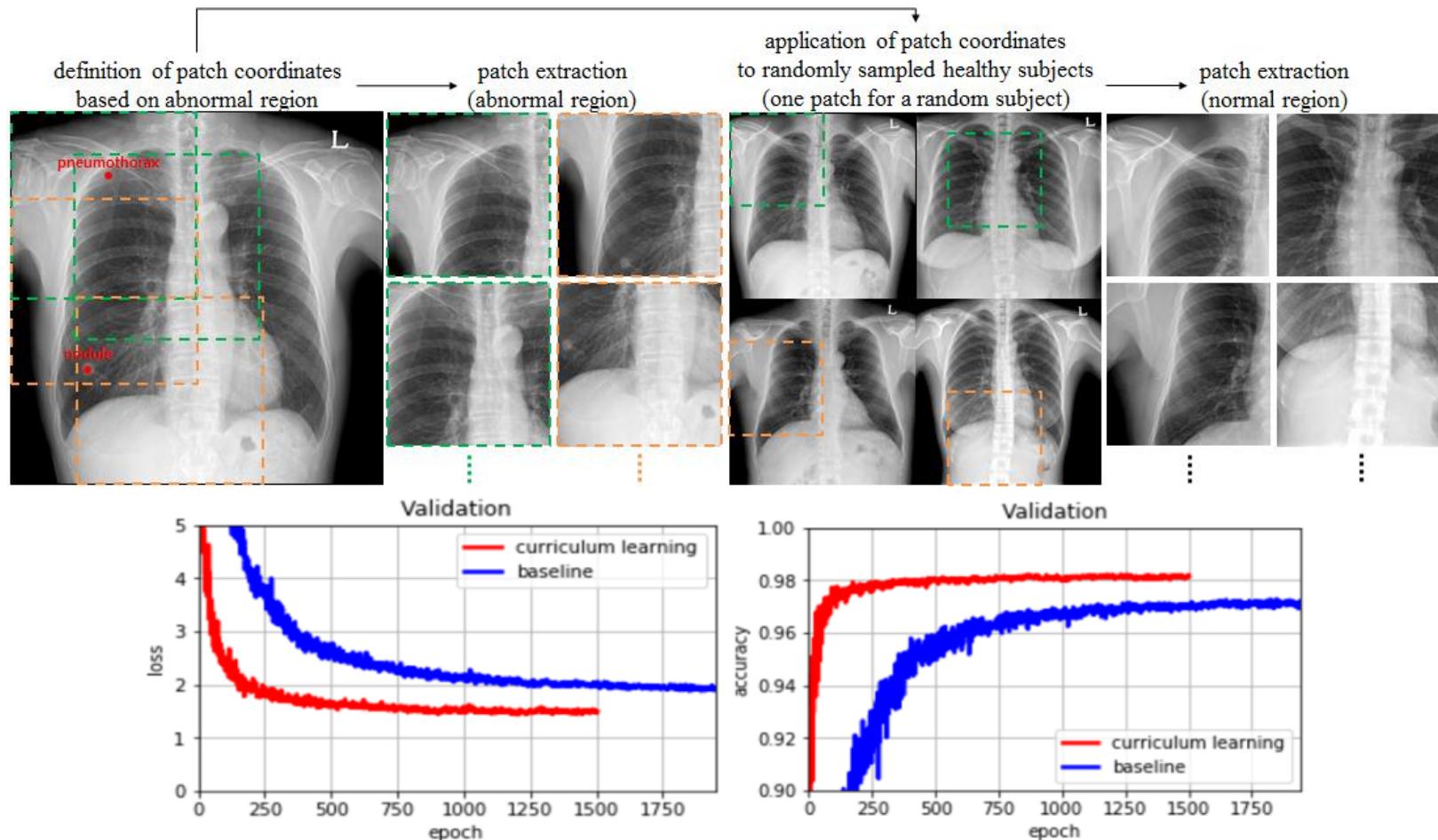


- Multi-label classification
  - ✓ Each instance can belong to **multiple classes**



# Chest PA: Curriculum learning

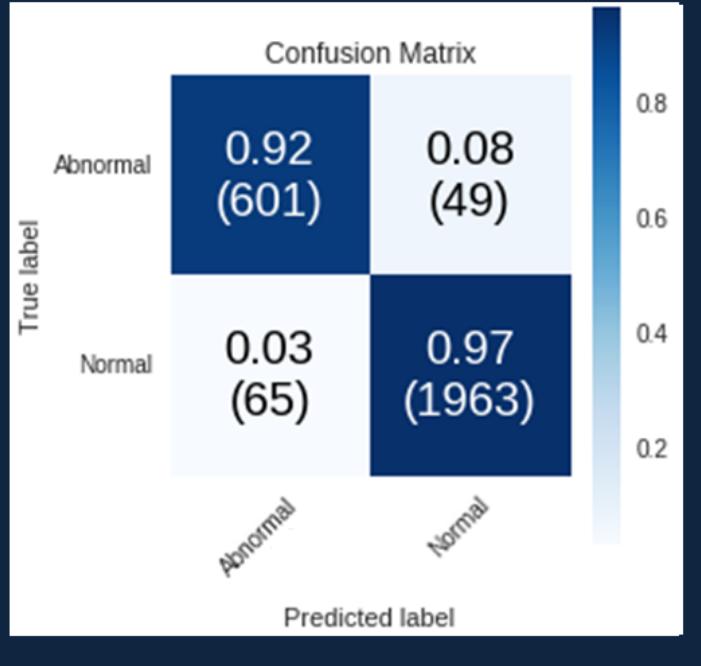
- Curriculum learning for multi-label classification
  - Curriculum learning: from patch to entire image



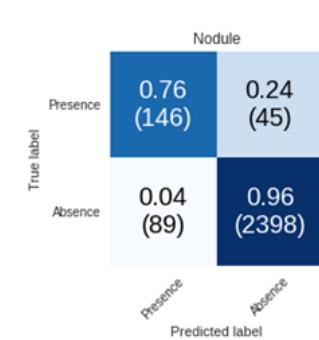
# Chest PA: Curriculum learning

- Curriculum learning for multi-label classification
  - Results

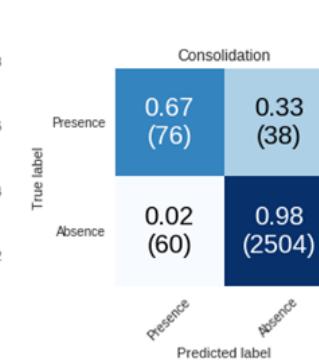
## Normal vs Abnormal



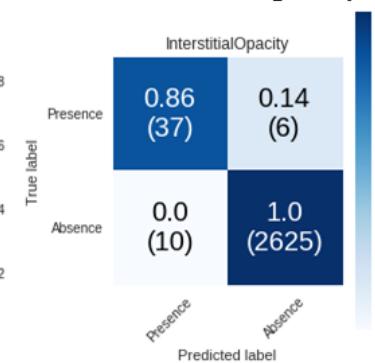
## Nodule



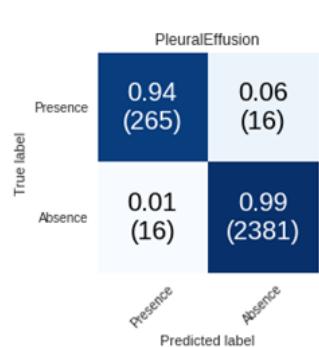
## Consolidation



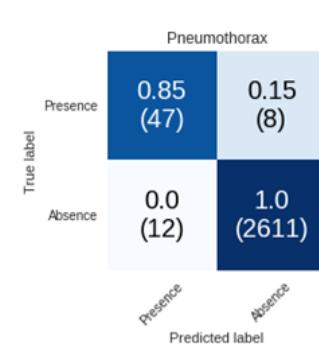
## Interstitial Opacity



## Pleural Effusion



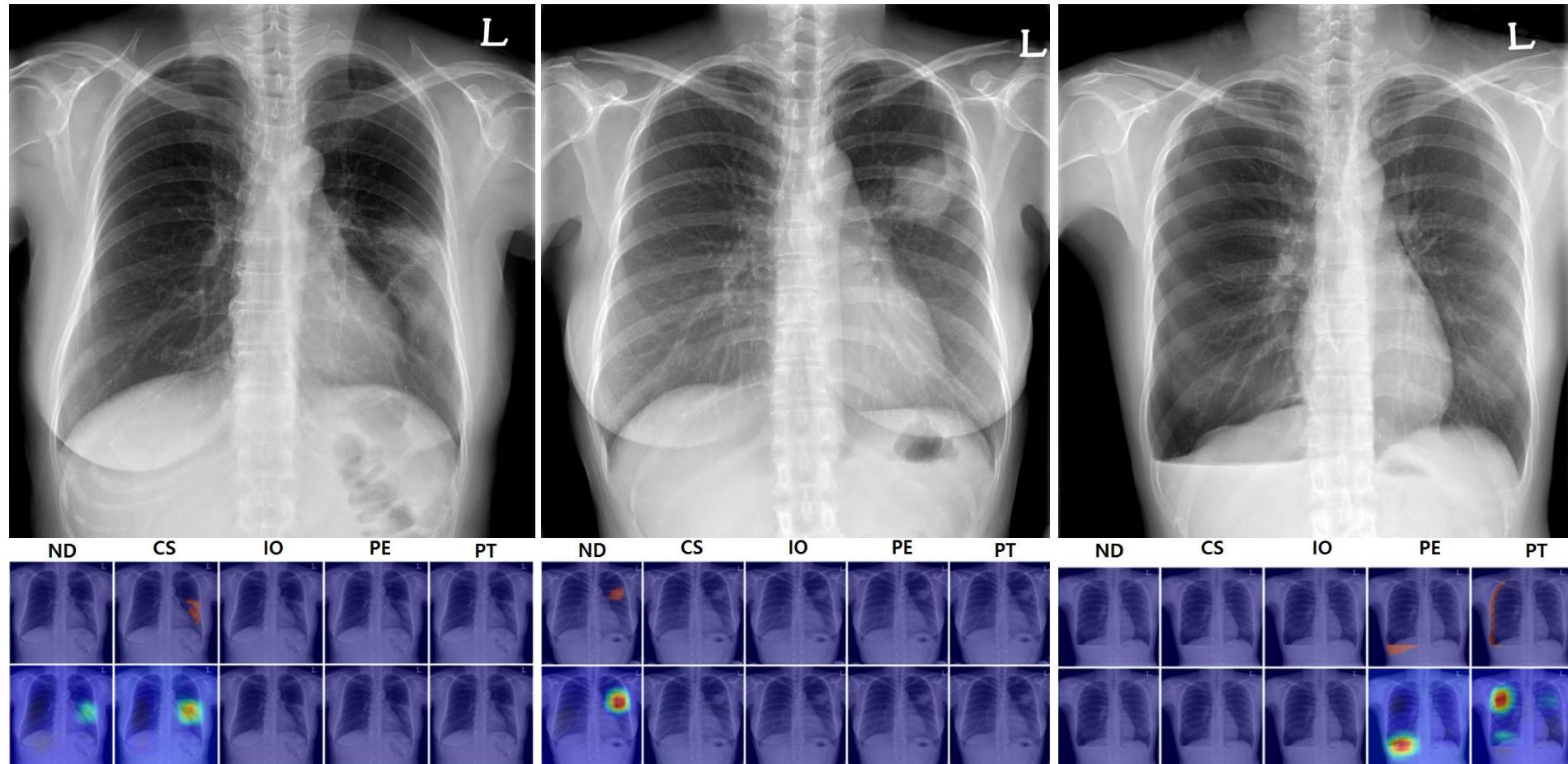
## Pneumothorax



# Chest PA: Curriculum learning

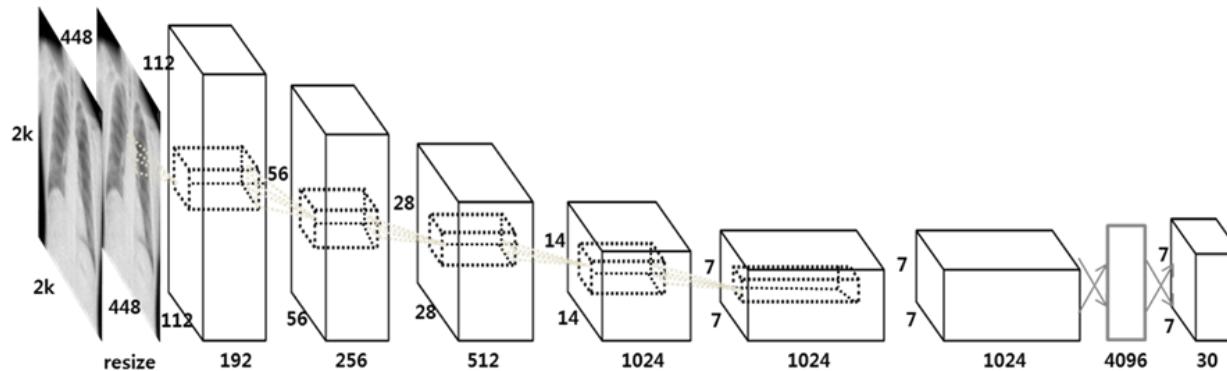
M<sup>2</sup>L

- Curriculum learning for multi-label classification
  - Results



# Chest PA: Reproducibility

- Reproducibility analysis on CNN-based detection
  - Using image pairs within short-term period (7 days)
  - 5-class detection
    - ✓ Nodule
    - ✓ Consolidation
    - ✓ Interstitial Opacity
    - ✓ Pleural Effusion
    - ✓ Pneumothorax
  - Network: YOLO v2



# Chest PA: Reproducibility

- Reproducibility analysis on CNN-based detection
  - Results

Nodule (N = 121)		1st	
2nd	P	P	N
	N	90	3
2nd	P	19	1
	N	4	4

Consol. (N = 27)		1st	
2nd	P	P	N
	N	19	1
2nd	P	4	4
	N	4	4

I. O. (N = 12)		1st	
2nd	P	P	N
	N	12	0
2nd	P	0	0
	N	0	0

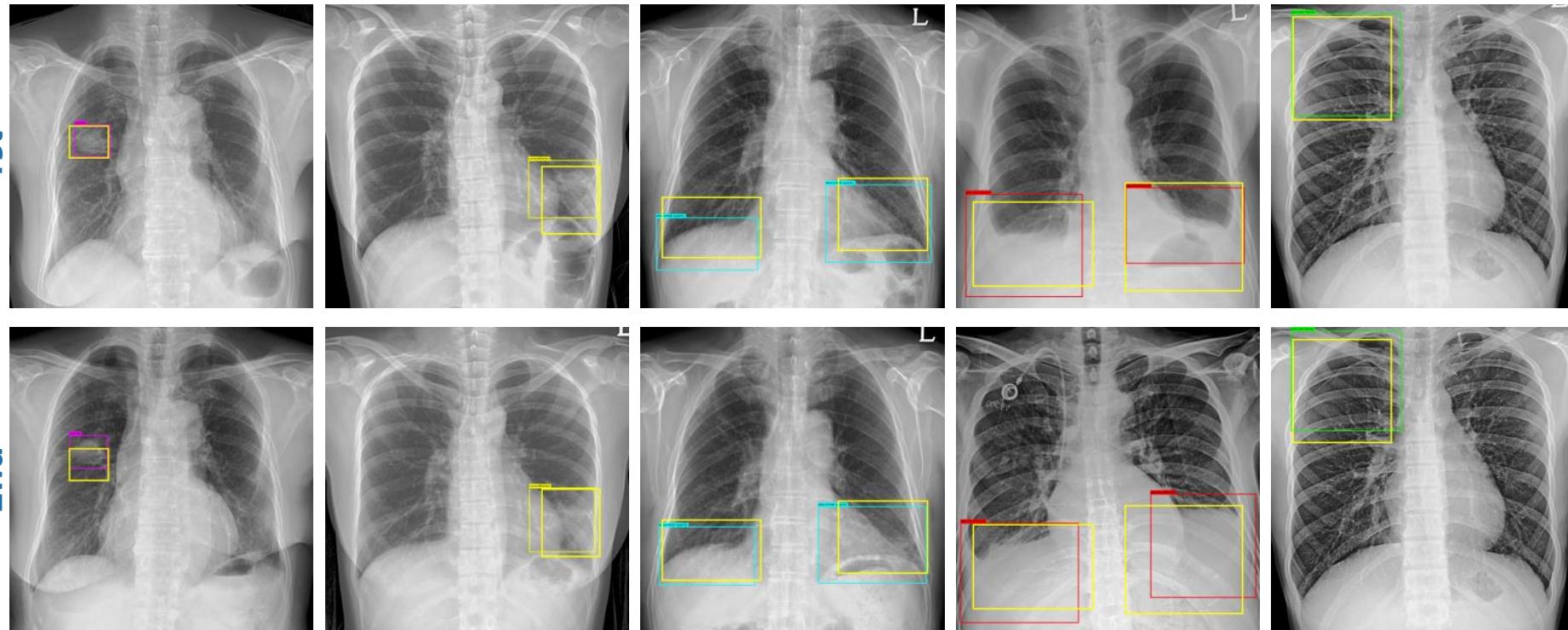
P. E. (N = 67)		1st	
2nd	P	P	N
	N	61	0
2nd	P	2	4
	N	4	2

Pneumotho. (N = 21)		1st	
2nd	P	P	N
	N	13	1
2nd	P	2	4
	N	4	2

# Chest PA: Reproducibility

M<sup>2</sup>L

- Reproducibility analysis on CNN-based detection
  - Results



# Chest PA: Reproducibility

- Reproducibility analysis on CNN-based detection
  - Comparison of various networks

✓ YOLO v2

Nodule (N = 121)		1st	
2nd	P	P	N
	N	94	3
		15	9

✓ Faster RCNN

Nodule (N = 121)		1st	
2nd	P	P	N
	N	11	12
		90	8

✓ VUNO-net

Nodule (N = 121)		1st	
2nd	P	P	N
	N	14	6
		97	4

✓ Mask RCNN

Nodule (N = 121)		1st	
2nd	P	P	N
	N	13	15
		90	3

# Chest PA: Reproducibility

- Reproducibility analysis on CNN-based detection
  - Comparison with human readers

✓ Reader 1

Nodule (N = 121)		1st	
2nd	P	P	N
	N	116	1
		2	2

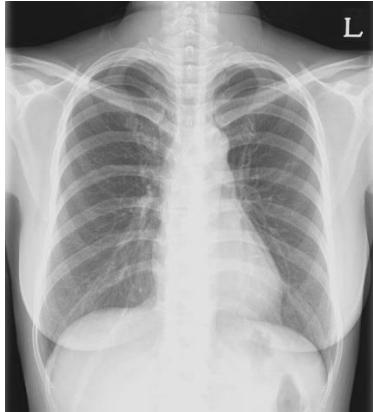
✓ Reader 2

Nodule (N = 121)		1st	
2nd	P	P	N
	N	111	3
		4	3

# Chest PA: Automatic delineation

M<sup>2</sup>L

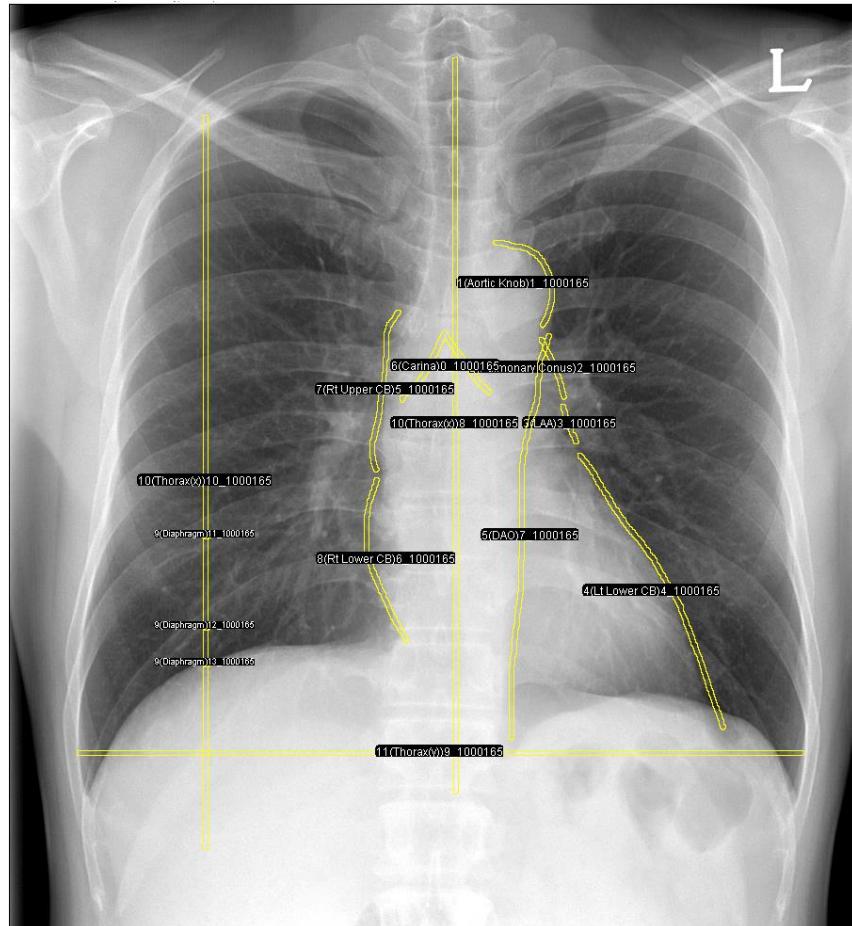
- Curved line detection for cardiomegaly patients



Normal



Cardiomegaly

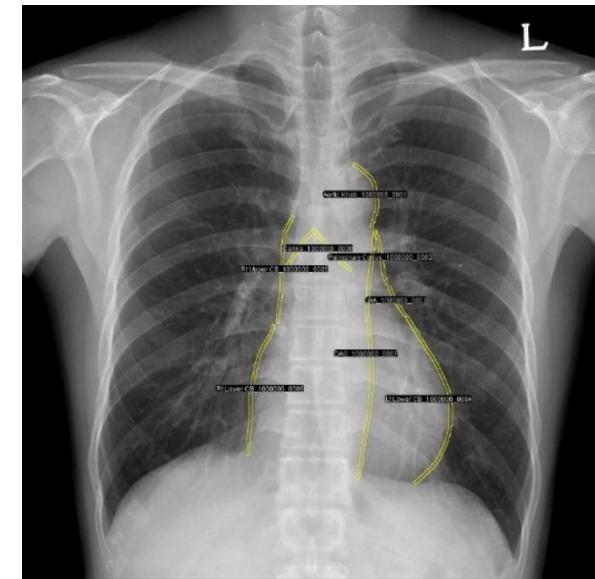


# Chest PA: Automatic delineation

M<sup>2</sup>L

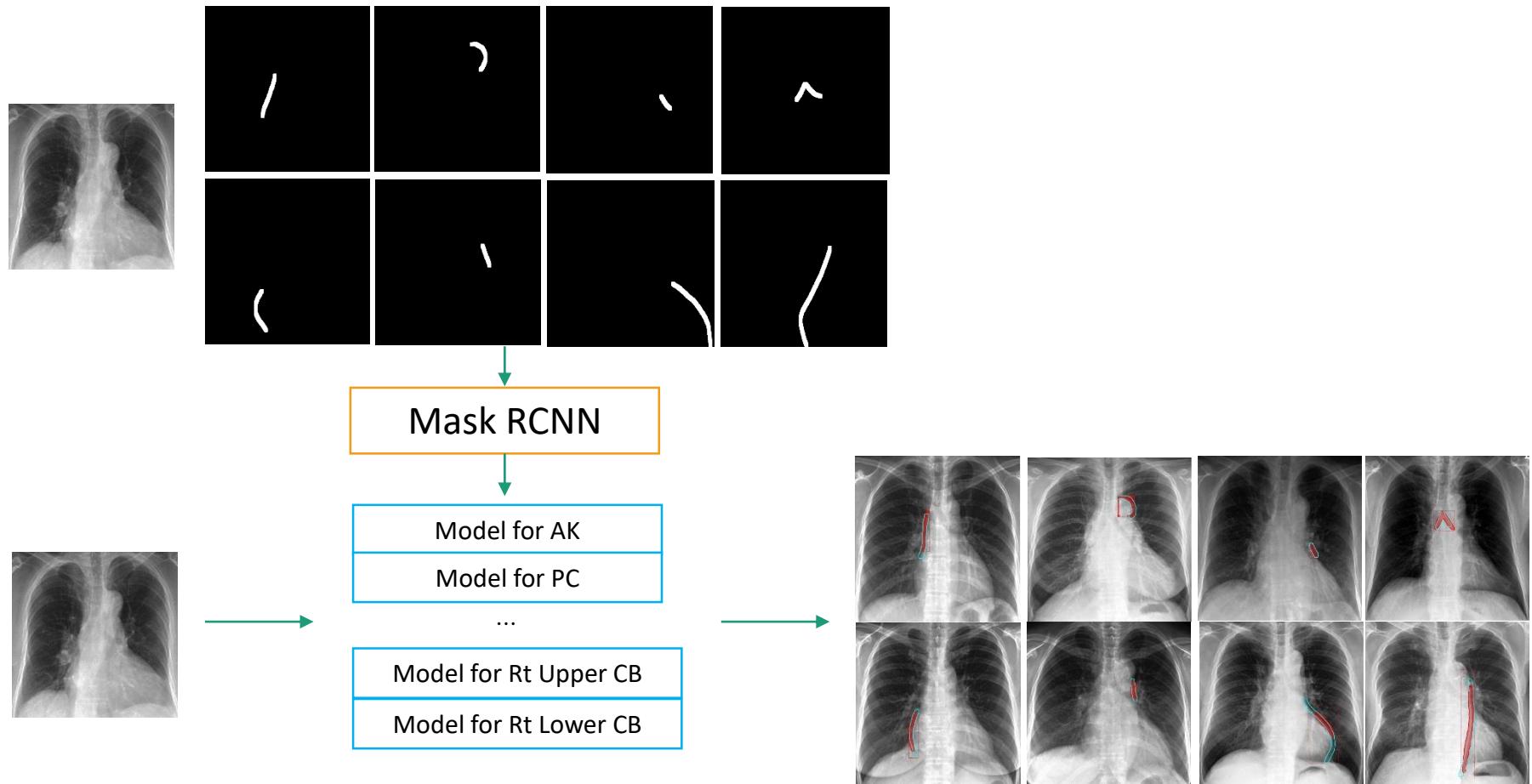
- Curved line detection for cardiomegaly patients

- AMC dataset
  - ✓ Normal 1020 cases
  - ✓ cardiomegaly 1000 cases
- 8-class curved lines
  - ✓ Aortic knob (AK)
  - ✓ Pulmonary conus (PC)
  - ✓ Left atrial appendage (LAA)
  - ✓ Descending aorta (DAO)
  - ✓ Carina (C)
  - ✓ Boundaries of left ventricle (Lt lower CB)
  - ✓ Boundaries of right atrium (Rt upper CB)
  - ✓ Boundaries of right ventricle (Rt lower CB)
  - ✓ Each line was drawn as a mask, **with 10 pixel width**



# Chest PA: Automatic delineation M<sup>2</sup>L

- Curved line detection for cardiomegaly patients
  - Network: Mask RCNN



# Chest PA: Automatic delineation

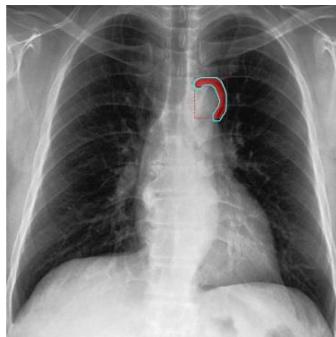
M<sup>2</sup>L

- Curved line detection for cardiomegaly patients
  - Results

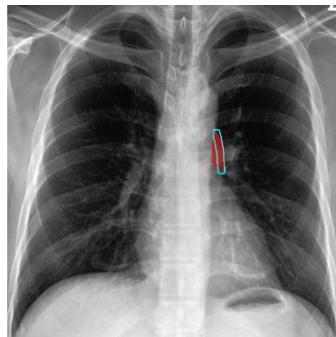
	IOU	Detection ratio
AK	0.8029	0.9975
PC	0.5658	0.8222
LAA	0.3990	0.7171
DAO	0.6925	0.8949
Carina	0.7034	1.0000
Lt lower CB	0.7831	1.0000
Rt upper CB	0.6427	0.9927
Rt lower CB	0.6888	0.9829

# Chest PA: Automatic delineation M<sup>2</sup>L

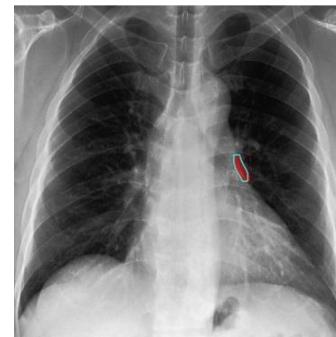
- Curved line detection for cardiomegaly patients
  - Results



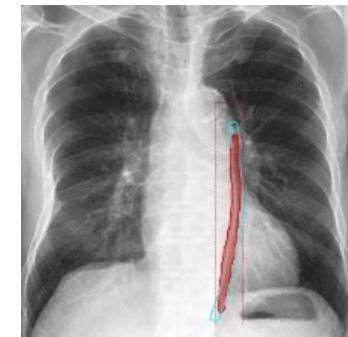
**AK**  
 $0.79 \pm 0.08$



**PC**  
 $0.50 \pm 0.20$



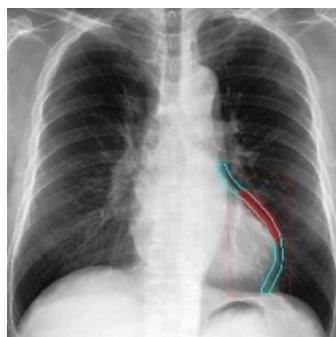
**LAA**  
 $0.40 \pm 0.24$



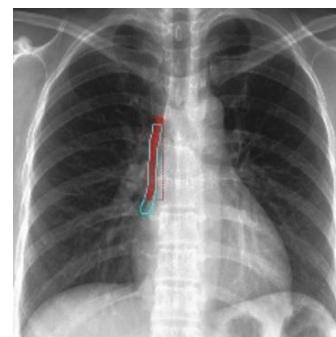
**DAO**  
 $0.60 \pm 0.26$



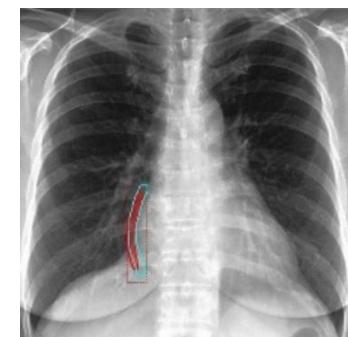
**Carina**  
 $0.70 \pm 0.13$



**Lt lower CB**  
 $0.72 \pm 0.13$

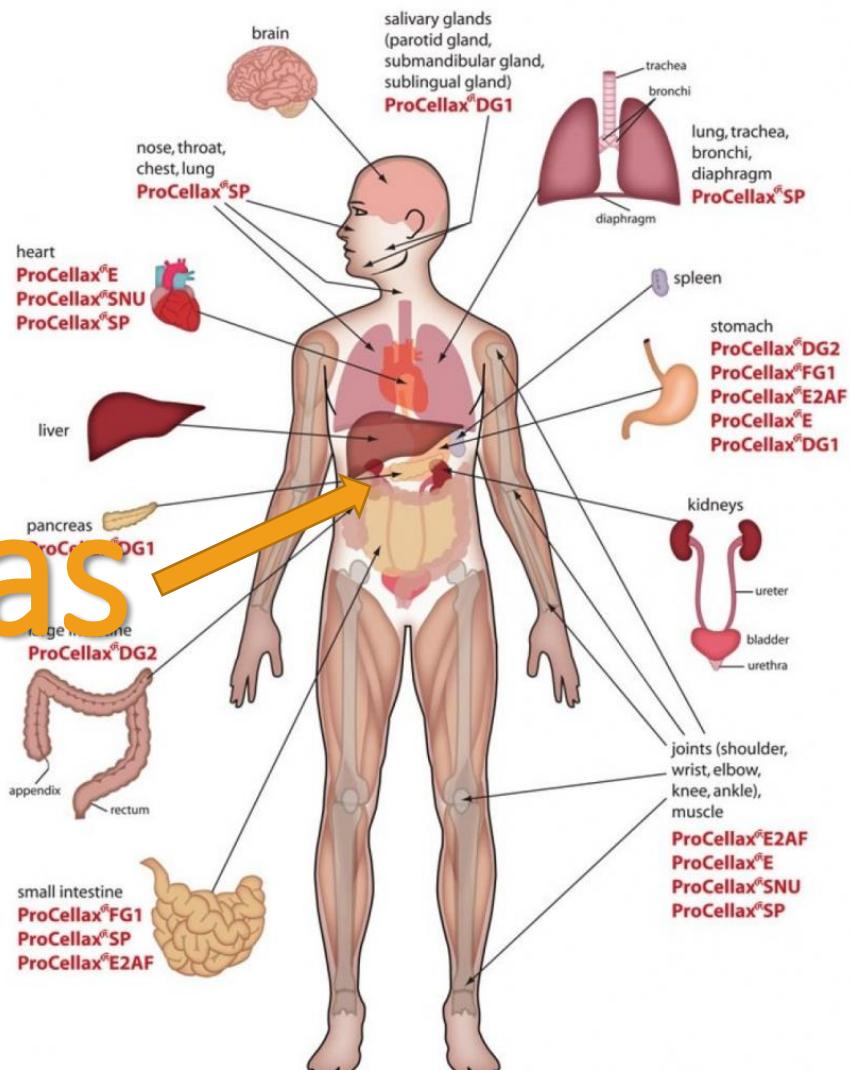


**Rt upper CB**  
 $0.63 \pm 0.16$



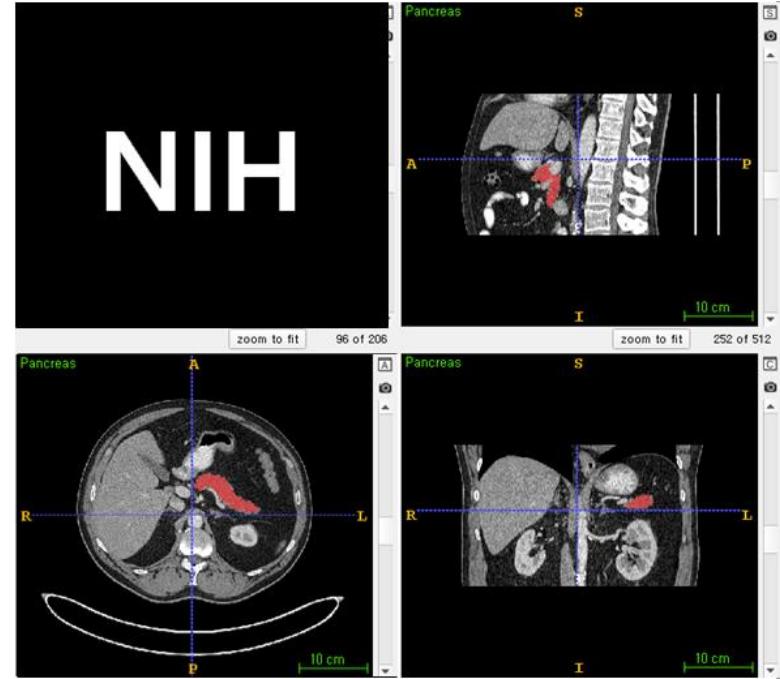
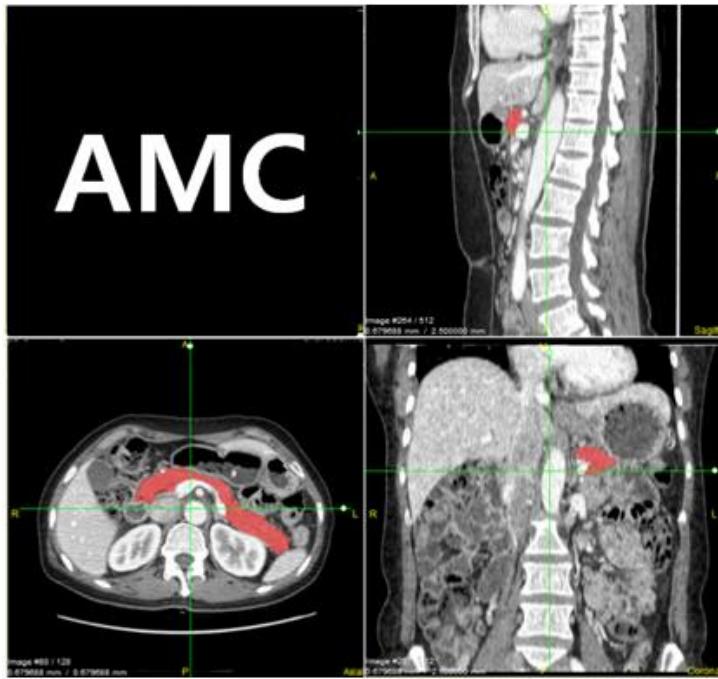
**Rt lower CB**  
 $0.63 \pm 0.14$

# Pancreas



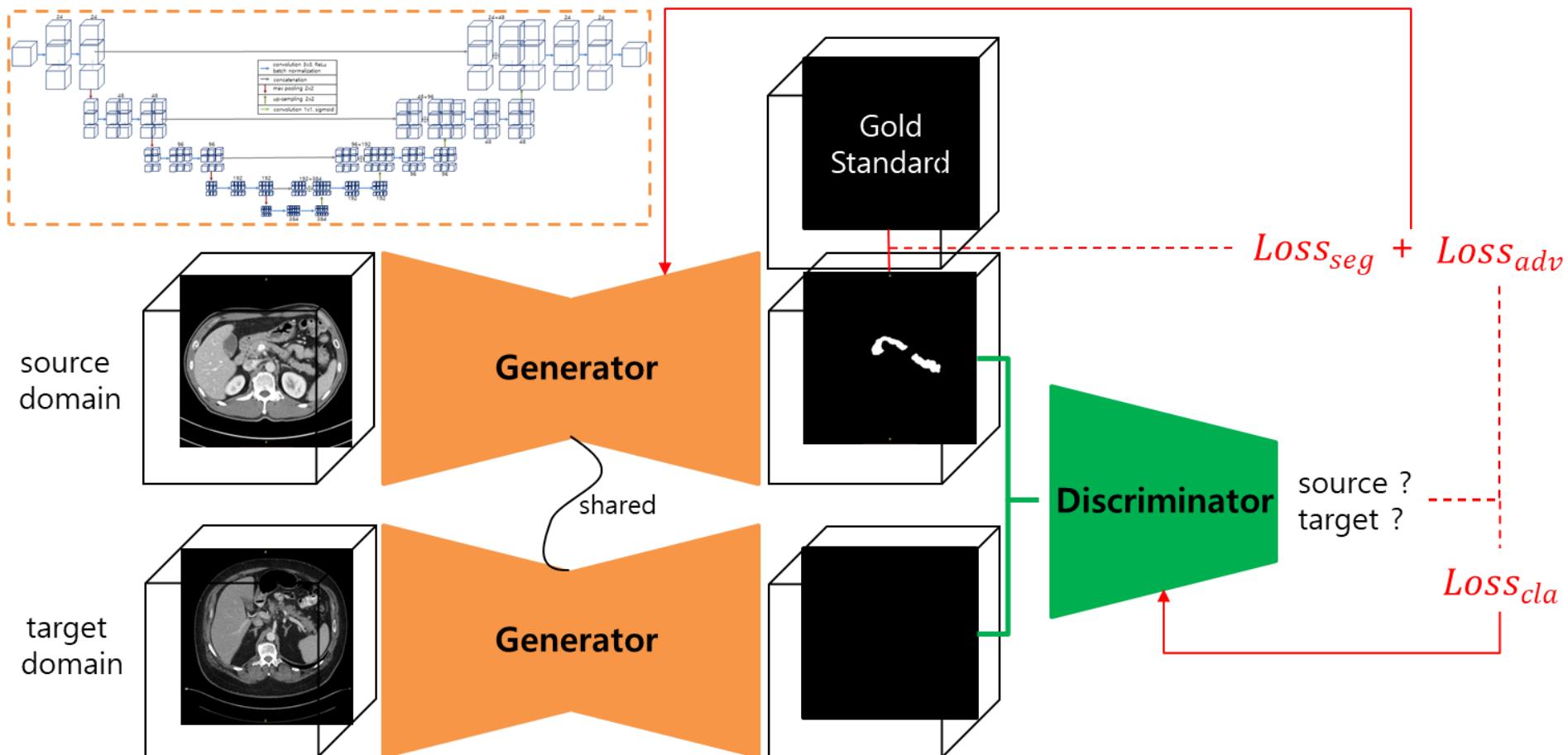
# Pancreatic Cancer

- Pancreas segmentation using domain adaptation
  - Multi-center datasets: AMC and NIH
    - ✓ AMC: 220 patients
    - ✓ NIH: 82 patients



# Pancreatic Cancer

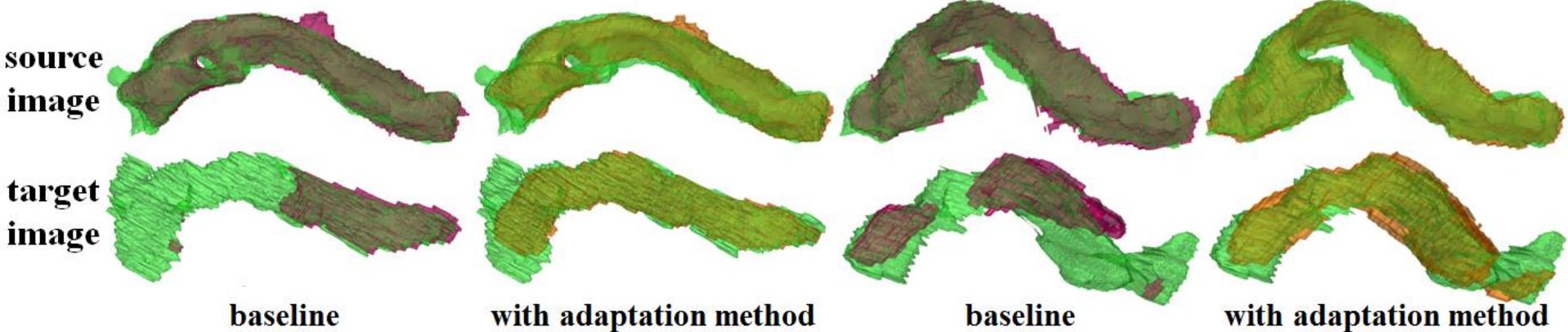
- Pancreas segmentation using domain adaptation
  - Domain adaptation



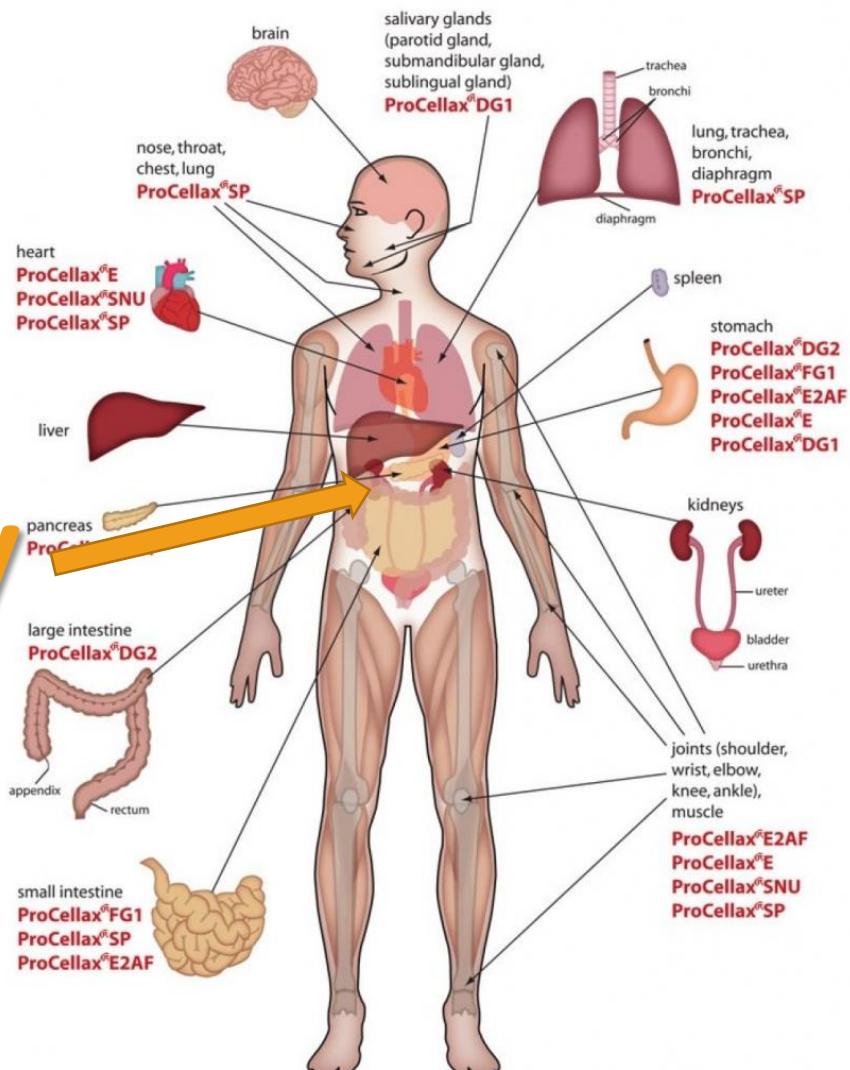
# Pancreatic Cancer

- Pancreas segmentation using domain adaptation
  - Domain adaptation

Source	Target	Dice
NIH	NIH	0.7601
	AMC	0.5833
AMC (baseline)	AMC	0.8466
	NIH	0.4649
AMC (with DA)	AMC	0.8284
	NIH	0.6770

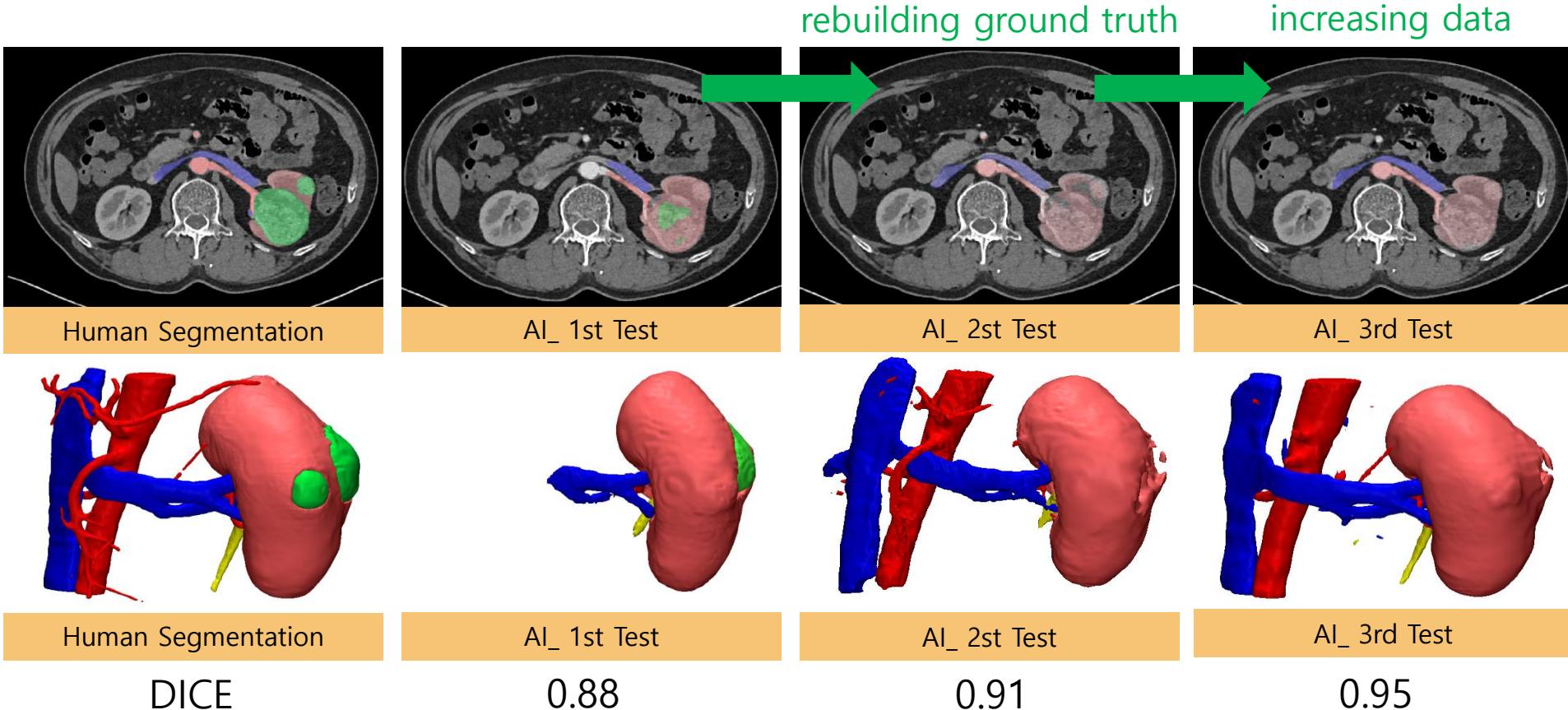


# Kidney



# Kidney segmentation

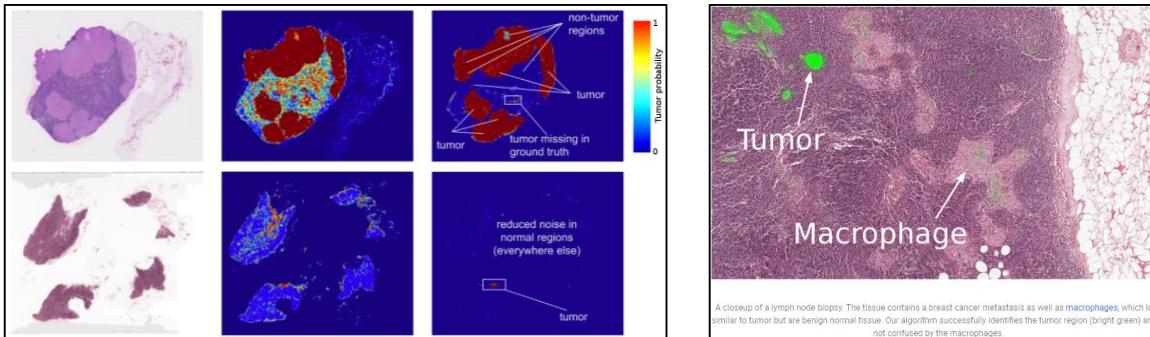
- Kidney segmentation
  - Results



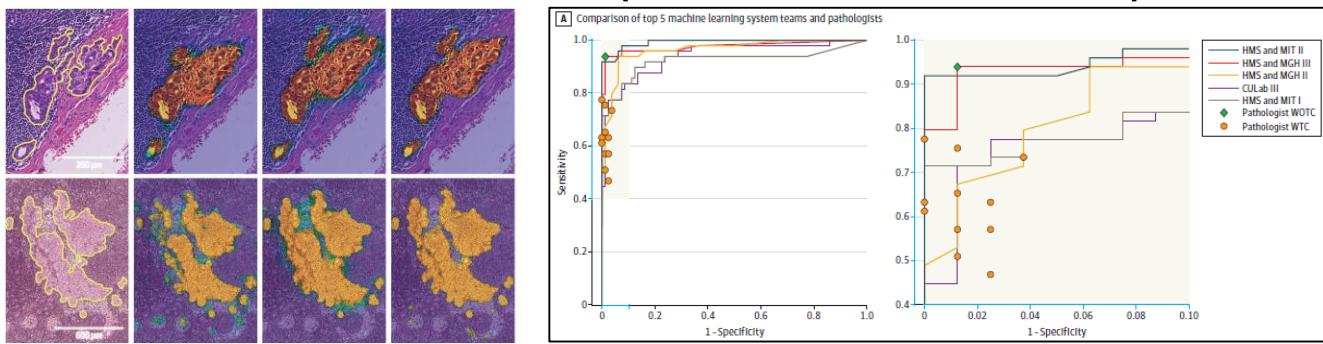
# Pathology

## ■ Survey

- Assisting Pathologists in Detecting Cancer with Deep Learning,  
*Google Research Blog*, Mar. 2017

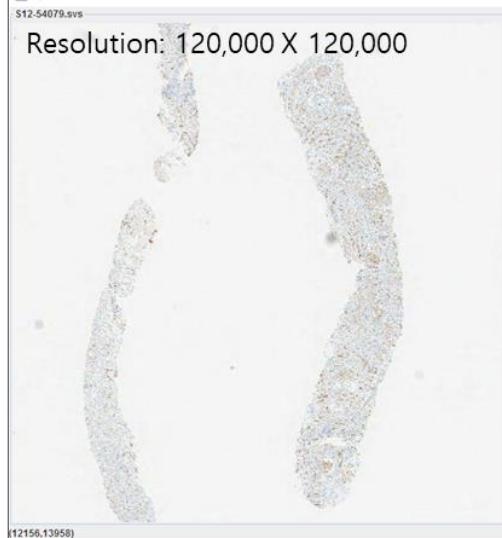


- Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer, *JAMA*, Dec. 2017 (from CAMELYON16)

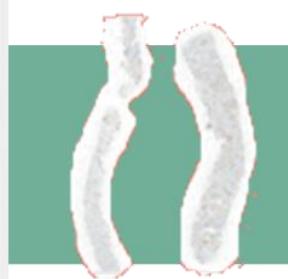


# Pathology

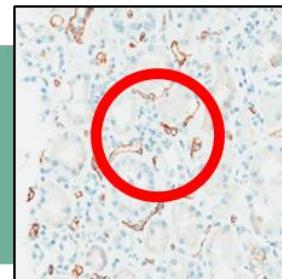
## ■ Peri-tubular capillary (PTC) counting



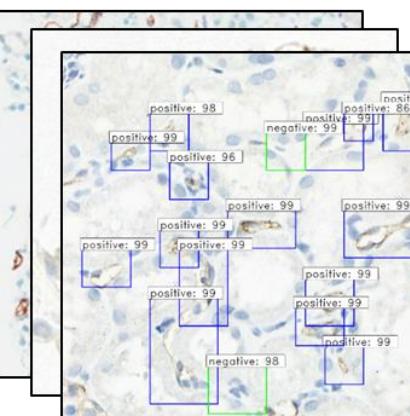
1. Input digital pathology image



2. Image processing  
for extracting only cells



3. Classification of  
feasible ROI  
(Deep learning task 1)



4. Detection of \*PTC for  
all feasible ROIs  
(Deep learning task 2)

### 5. Scoring by Banff criteria (Grade 0~4)

	Detected Area	C4d+ PTC	C4d- PTC
	1	35	8
	...	...	...
	13	22	20
	sum	523	325
Feature	B	3	
Interstitial inflammation (% of nonfibrotic cortex) <sup>a</sup>	i	>50%	
Total inflammation (% all cortex)	ti	>50%	
Tubulitis (maximum mononuclear cells/tubule) <sup>b</sup>	t	>10	
Arterial inflammation (% lumen endarteritis) <sup>c</sup>	V	Transmural or necrosis	
Glomerulitis (% glomeruli involved) <sup>d</sup>	g		
Capillaritis (cells per cortical PTC*, requires >10% of PTC to be affected for scoring)	ptc	None (<10%)	<25% <5/PTC
C4d deposition in PTC (% positive) <sup>e</sup>	C4d	0%	1%-9% 10%-50% >50%

TABLE 29.3 Banff scores of individual features

# Pathology

## ■ Peri-tubular capillary (PTC) counting

- AMC dataset

✓ Phase 1: ROI classification

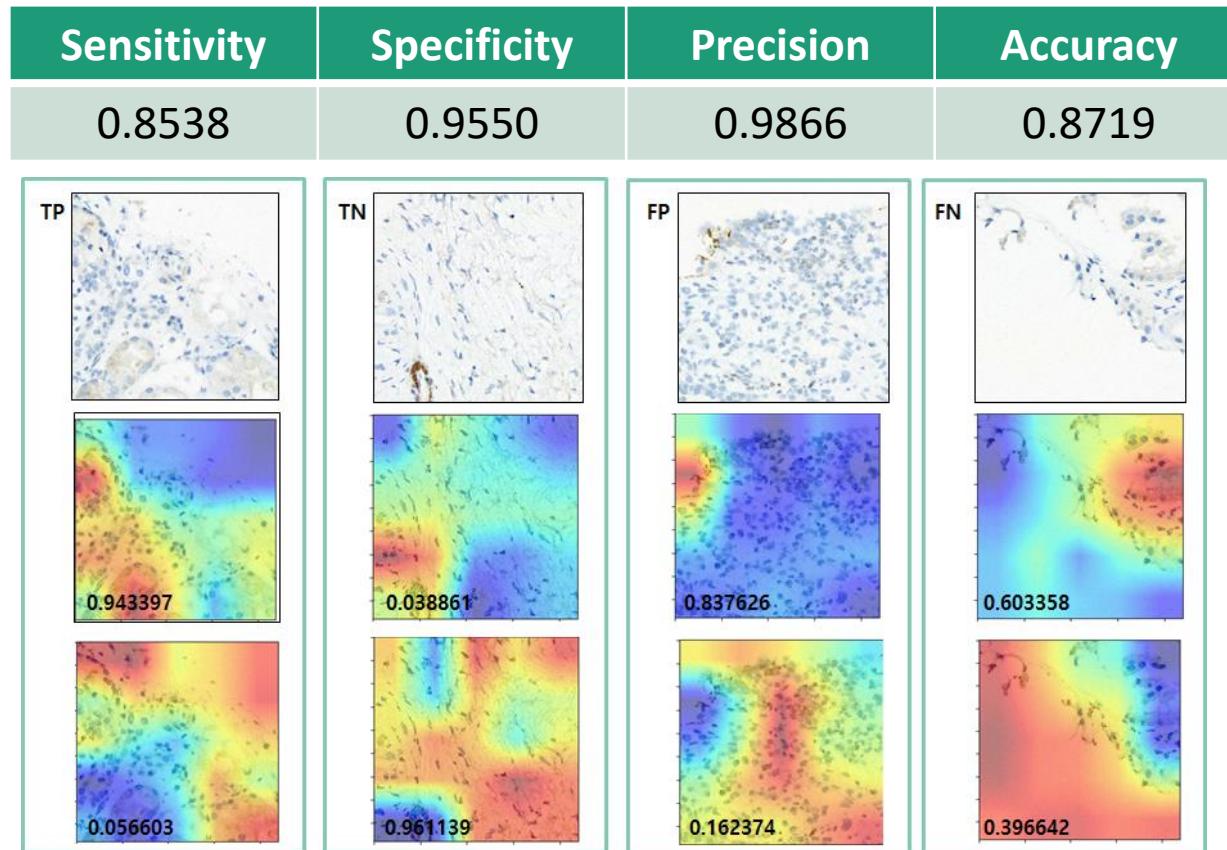
Class	Training		Validation	Test
	Subset 1 (Slide 1~200)			Dataset 2 (Slide 381~480)
Feasible	1108		431	431
Non-feasible	222		100	100

✓ Phase 2: PTC detection

Class	Hard labeled dataset			AI-assisted dataset		
	Training	Validation	Test	Training	Validation	Test
	Subset 1 (Slide 1~200)				Subset 2 (Slide 201~380)	
positive	423	277	202	1,503	486	496
negative	1,200	800	422	2,025	674	651

# Pathology

- Peri-tubular capillary (PTC) counting
  - Phase 1: ROI classification
    - ✓ Network: Inception V3



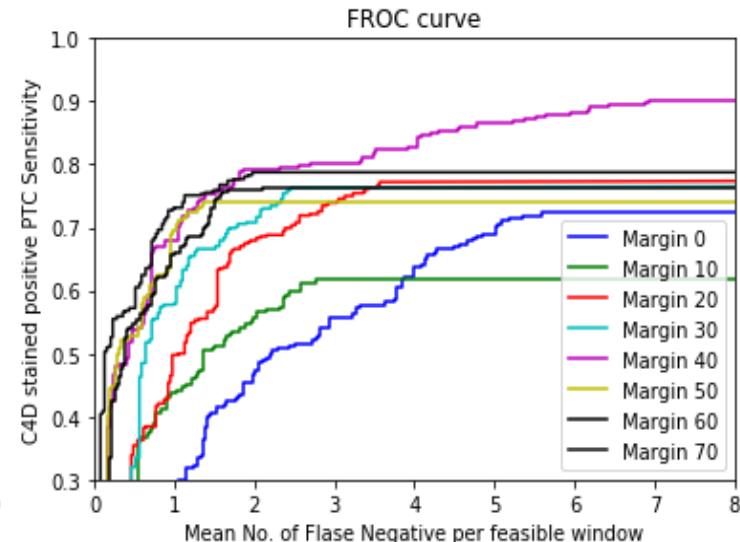
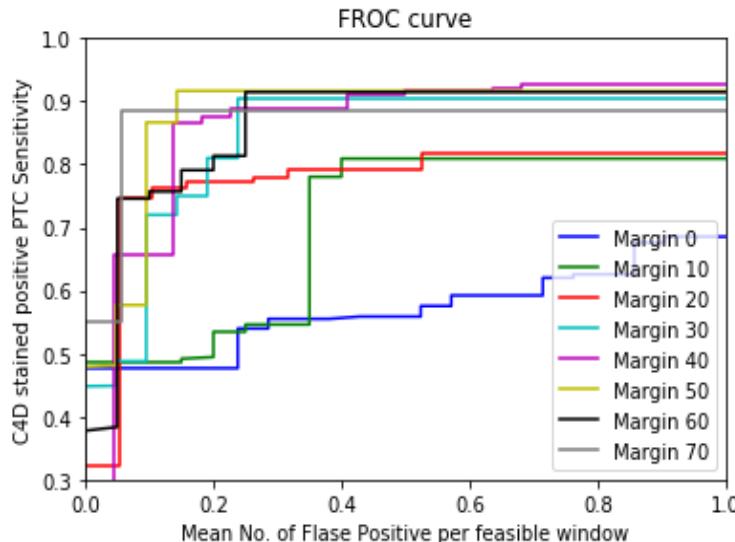
# Pathology

## ■ Peri-tubular capillary (PTC) counting

- Phase 2: PTC detection

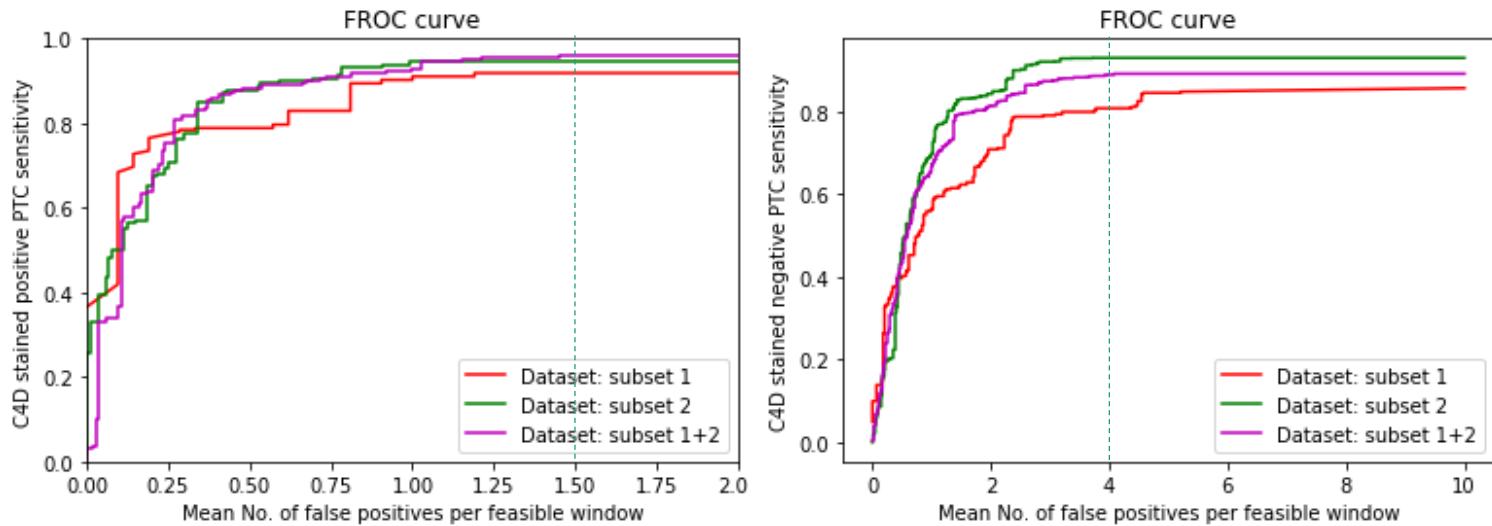
- ✓ Network: Faster RCNN

- ✓ Margin including various size to **include neighborhood region**



# Pathology

- Peri-tubular capillary (PTC) counting
  - Feasibility of AI-assisted labeled data



Data labeling	C4d positive	C4d negative
Hand-labeled	0.9273	0.8193
AI-assisted	0.9413	0.8864
Fusion	0.9522	0.8523

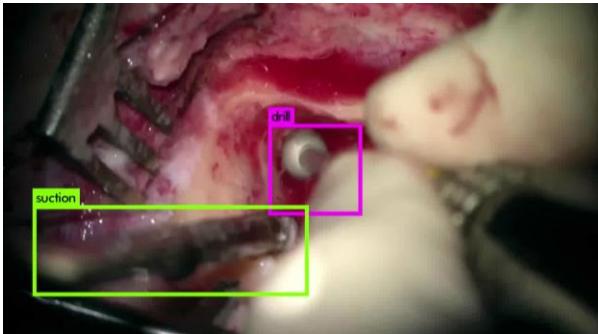
# Surgical video

M<sup>2</sup>L

- Mastoidectomy
  - Scene understanding



- Tool/structure detection



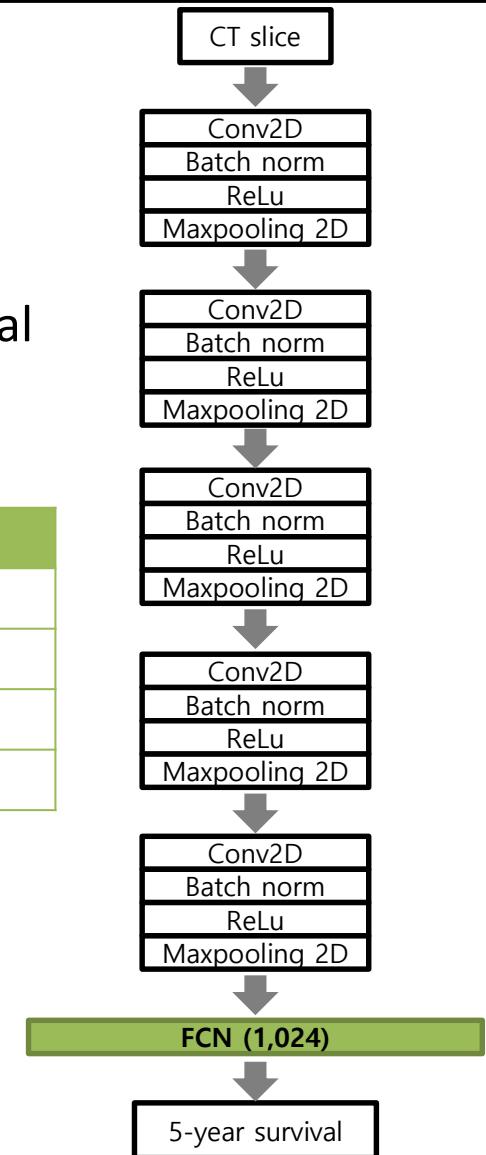
# COPD deep radiomics



## ■ Survival analysis

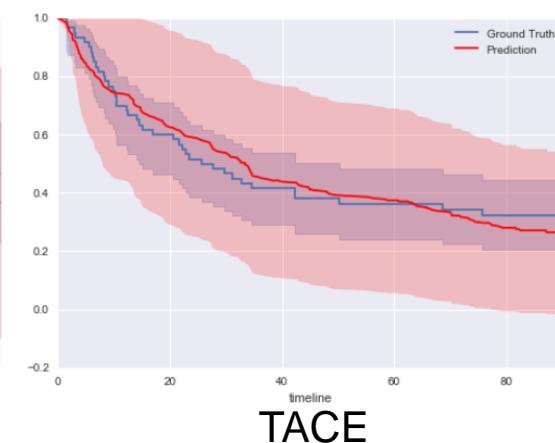
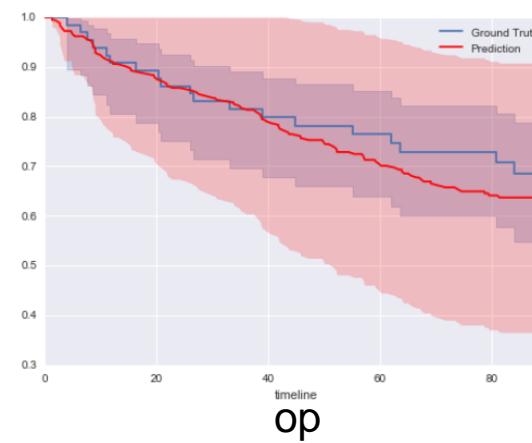
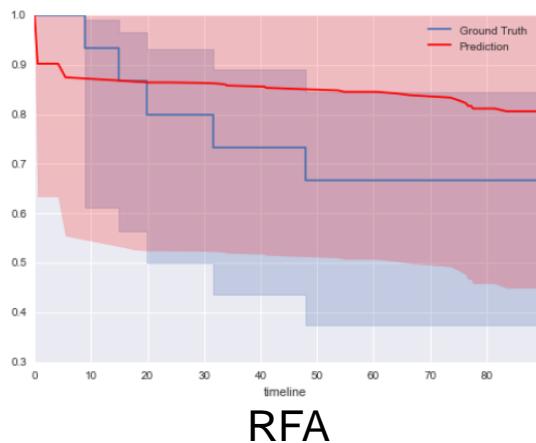
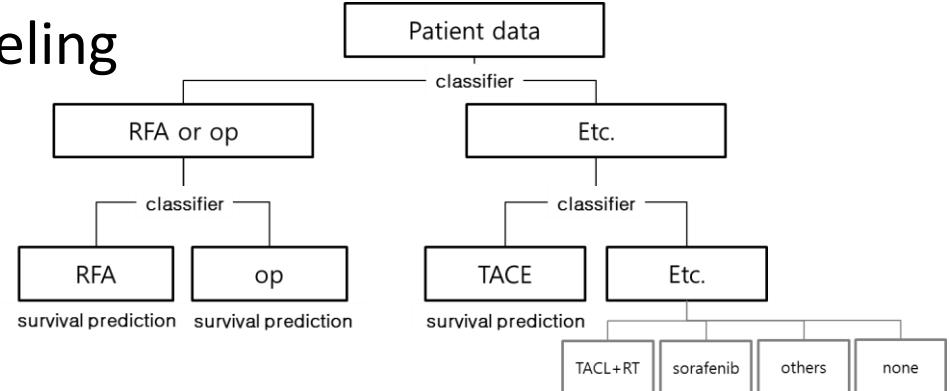
- Random survival forest
- Extraction of deep features
  - Design a CNN model for classifying 5-year survival

Data	C-index
Deep radiomics features (A1+A2+A3+A4+A5+A6)	<b>0.8412</b>
Demographic information	0.7688
PFT	0.7498
Handcrafted features	0.5994



# CDSS on Liver Cancer

- Treatment recommender system for liver cancer
  - Patient's baseline data: 39 variables
  - 1,000 patients
  - Hierarchical decision modeling





Medical  
Imaging  
Intelligent  
Reality  
Lab

## Clinical Collaborators@Asan Medical Center

Radiology: Joon Beom Seo, SangMin Lee<sup>A,B</sup>, Dong Hyun Yang, Hyung Jin Won, Ho Sung Kim, Seung Chai Jung

Neurology: Dong-Wha Kang, Chongsik Lee, Jaehong Lee, Sangbeom Jun, Misun Kwon, Beomjun Kim

Cardiology: Jaekwan Song, Jongmin Song, Younghak Kim

Internal Medicine: Jeongsik Byeon

Pathology: Hyunjeong Go

Surgery: Bumsuk Go, JongHun Jeong, Songchuk Kim

