



This work was based on my Ph.D. dissertation at Arizona State University, supervised by Dr. Jianming Liang. I thank N. Tajbakhsh, J. Shin, V. Sodha, M. M. Rahman Siddiquee, J. Pang, R. Feng, L. Zhang, S. Bajpai, F. Haghghi, M. R. Hosseinzadeh Taher, Z. Guo, P. Zhang for their helps in paper writing and experiments.

Towards Annotation-Efficient Deep Learning for Computer-Aided Diagnosis

Zongwei Zhou, PhD

Postdoc, Department of Computer Science
Johns Hopkins University, Baltimore, MD
P: 1-(480)738-2575 | E: zzhou82@jh.edu



Imaging data account for about 90% of all healthcare data

Introduction

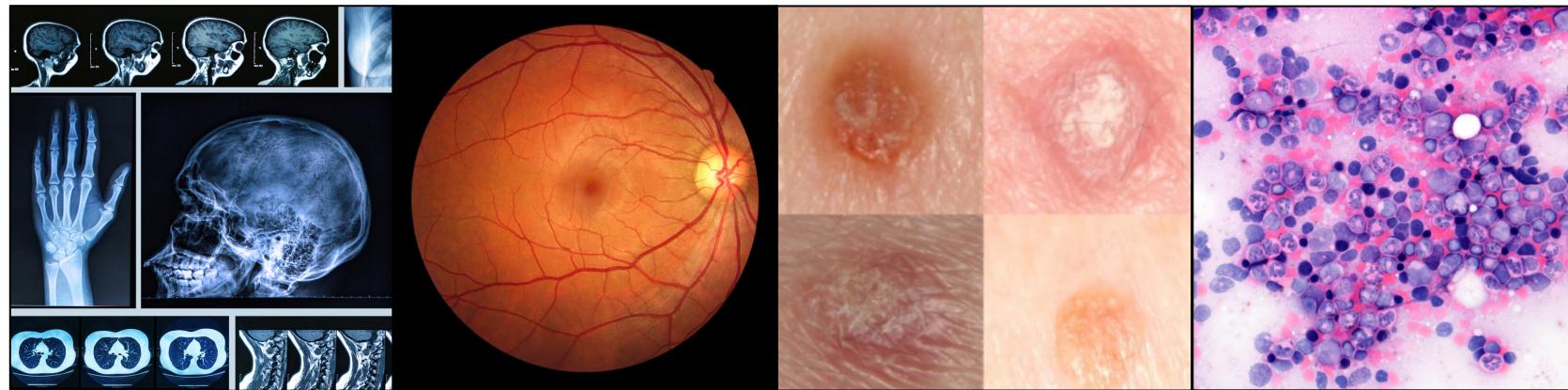
Objective

Aim 1

Aim 2

Aim 3

Summary



Radiology

Ophthalmology

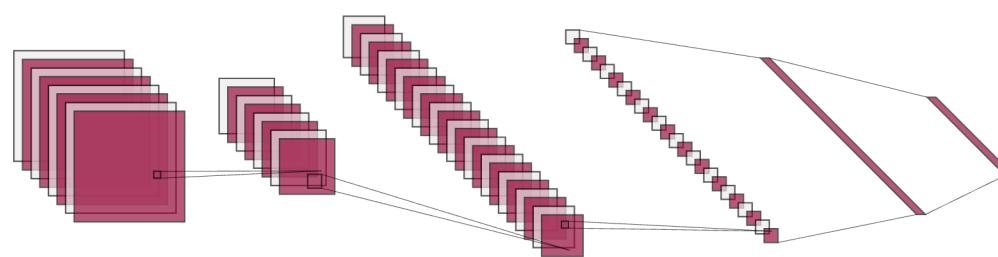
Dermatology

Pathology

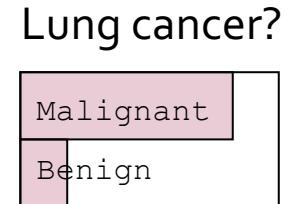
Deep Learning has ushered in a revolution in medical imaging



Input image



Hidden layers

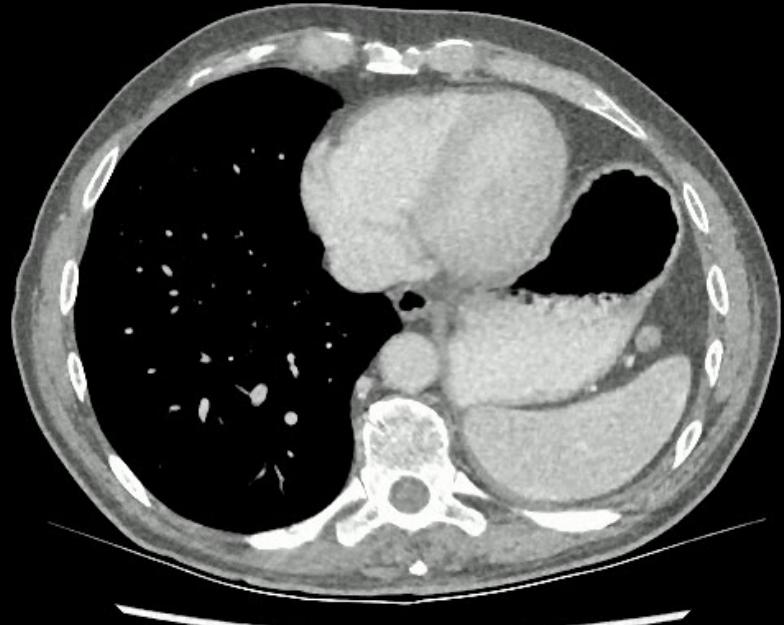


Output

1. "The Digital Universe Driving Data Growth in Healthcare." published by EMC with research and analysis from IDC (12/13)
2. LeCun, Yann, et al. "Deep learning." Nature, 2015.

Radiologists hate annotation, but computer scientists love annotation.

CT



Ground Truth
annotated by human experts

Deep Learning

- Liver
- Liver tumor

- I thank S. Bajpai for this experiment; the code can be found at <https://github.com/MrGiovanni/UNetPlusPlus/tree/master/pytorch>
- 1. Bajpai, Shivam. "Pre-Trained Models for nnUNet." Master diss., Arizona State University, 2021.
- 2. Zhou, Zongwei, et al. "Unet++: A nested u-net architecture for medical image segmentation." DLMIA, 2018.
- 3. Zhou, Zongwei, et al. "Unet++: Redesigning skip connections to exploit multiscale features in image segmentation." TMI, 2019.



To match human diagnostic precision, deep learning requires enormous annotation cost.

- **1,511,400** radiologist-annotated CT images for pancreatic cancer detection (*15 years to create*)
- **42,290** radiologist-annotated CT images for lung cancer diagnosis
- **129,450** dermatologist-annotated images for skin cancer classification

↑
The FELIX Project
at JHU

Introduction

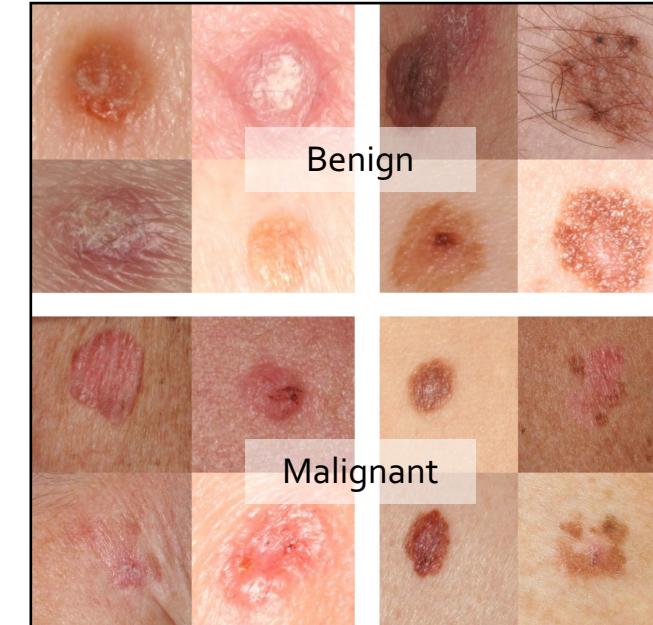
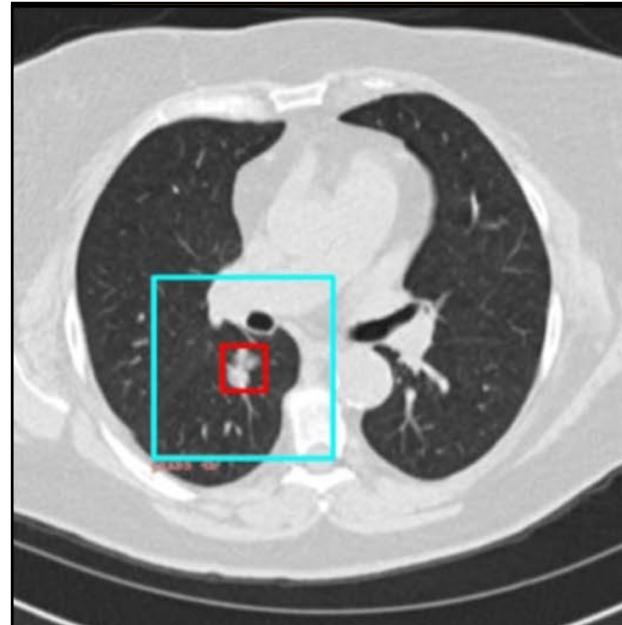
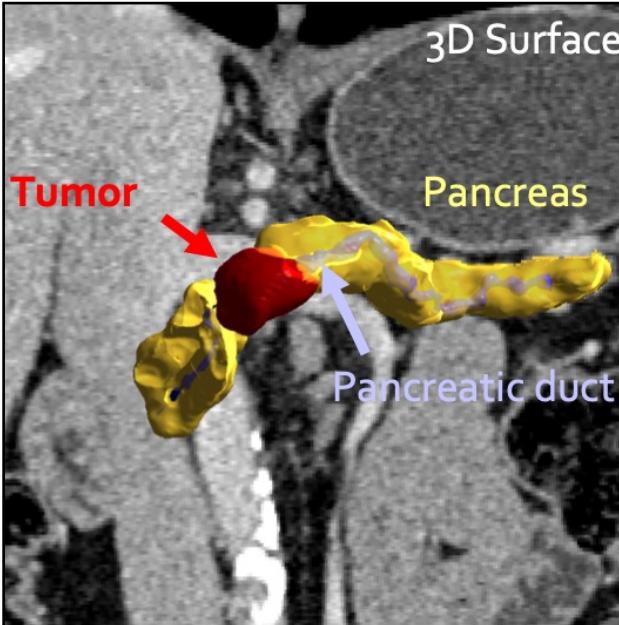
Objective

Aim 1

Aim 2

Aim 3

Summary



1. Xia, Yingda, et al. "The FELIX project: Deep networks to detect pancreatic neoplasms." medRxiv, 2022.
2. Ardila, Diego, et al. "End-to-end lung cancer screening with three-dimensional deep learning on low-dose chest computed tomography." Nature medicine 25.6 (2019): 954-961.
3. Esteva, Andre, et al. "Dermatologist-level classification of skin cancer with deep neural networks." Nature, 2017.



To match human diagnostic precision, deep learning requires enormous annotation cost.

- **1,511,400** radiologist-annotated CT images for pancreatic cancer detection (*15 years to create*)
- **42,290** radiologist-annotated CT images for lung cancer diagnosis
- **129,450** dermatologist-annotated images for skin cancer classification

Introduction

Objective

"How to develop annotation-efficient deep learning without such BIG annotated data?"

Aim 1

Significant, consider these scenarios:

- A flood of patients are waiting for imaging results during an outbreak
- Doctors do not have time to annotate every case for algorithm development
- Not many doctors have expertise for novel/rare diseases

Summary



Introduction

Computer-*Aided* Diagnosis

Assisting human experts to see more patients and
to deliver more accurate diagnosis (*beyond human eye*)

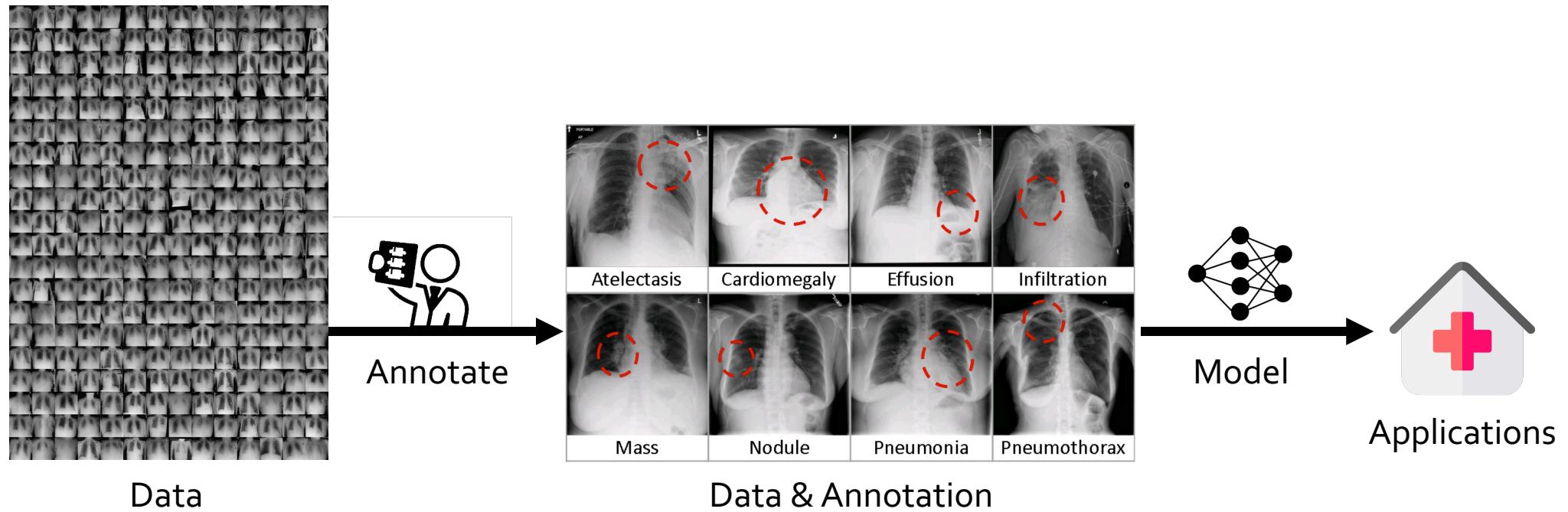
Objective

Aim 1

Aim 2

Aim 3

Summary





Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Introduction

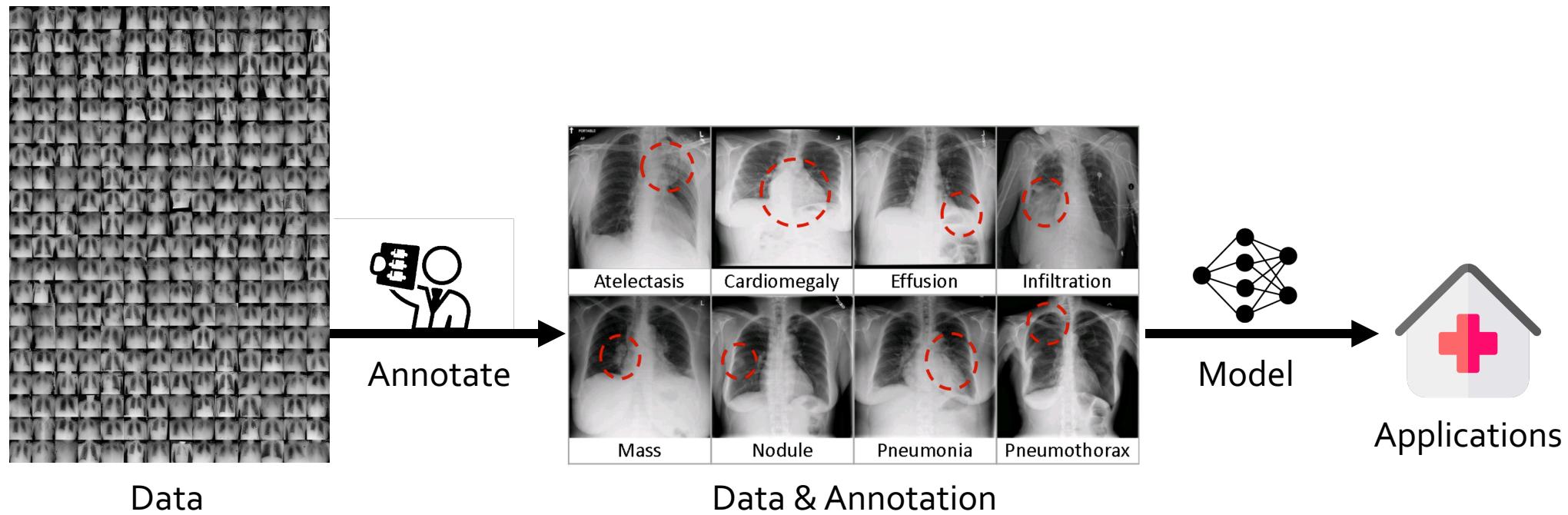
Objective

Aim 1

Aim 2

Aim 3

Summary





Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems
Aim 1: Acquiring necessary annotation efficiently from human experts

Introduction

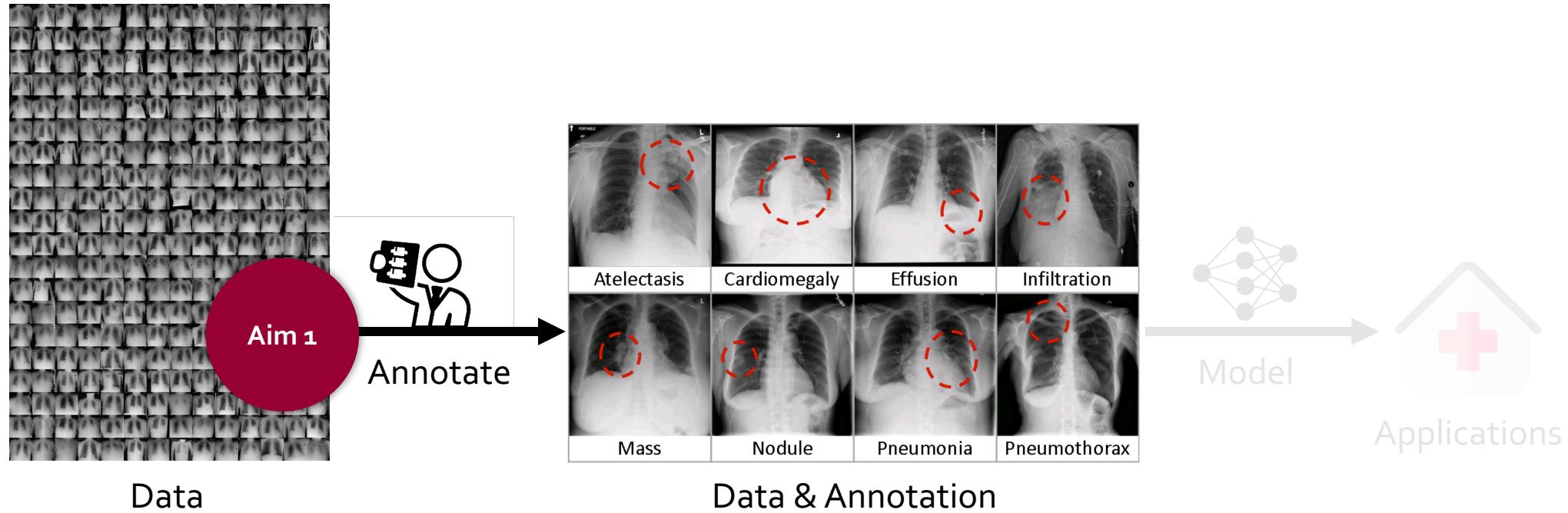
Objective

Aim 1

Aim 2

Aim 3

Summary





Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Introduction

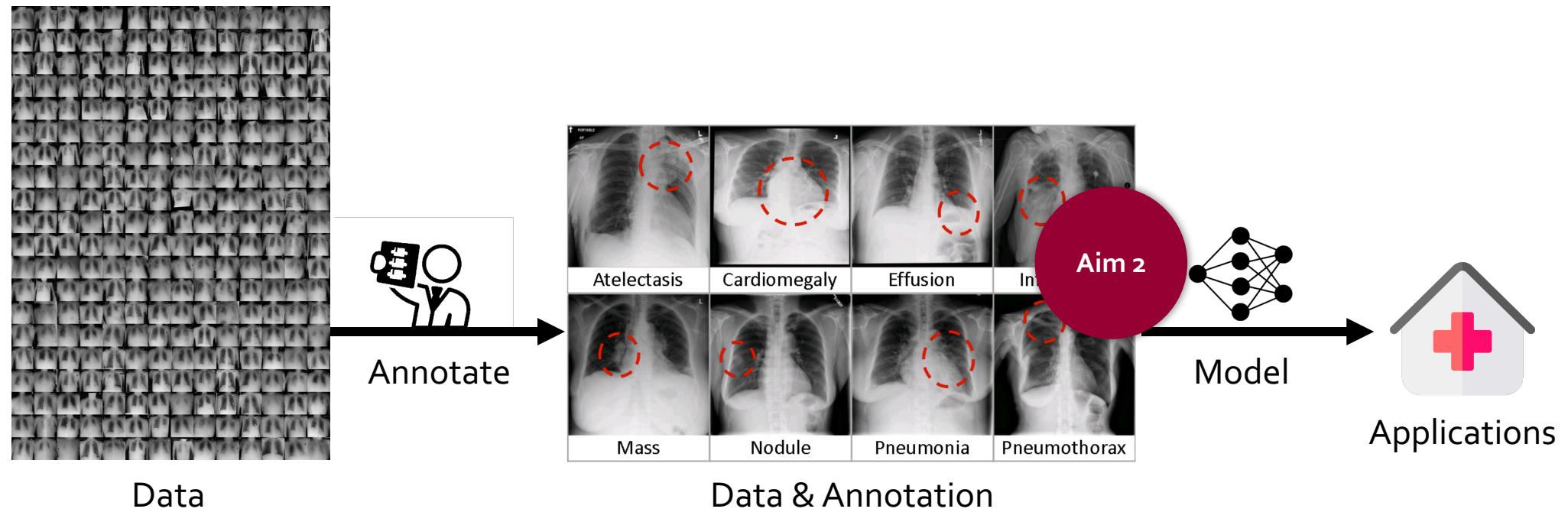
Objective

Aim 1

Aim 2

Aim 3

Summary





Introduction

Objective

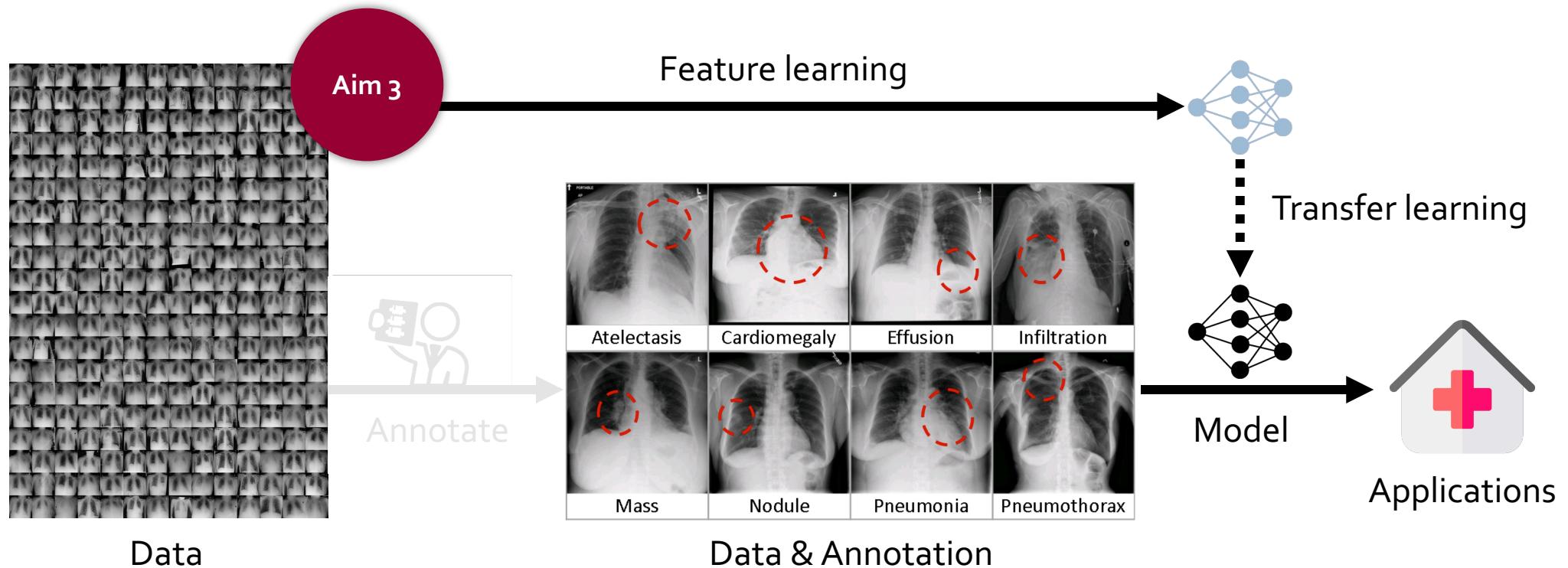
Aim 1

Aim 2

Aim 3

Summary

- Goal:** Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems
- Aim 1:** Acquiring necessary annotation efficiently from human experts
- Aim 2:** Utilizing existing annotation effectively from advanced architecture
- Aim 3:** Extracting generic knowledge directly from unannotated images



Introduction

Objective

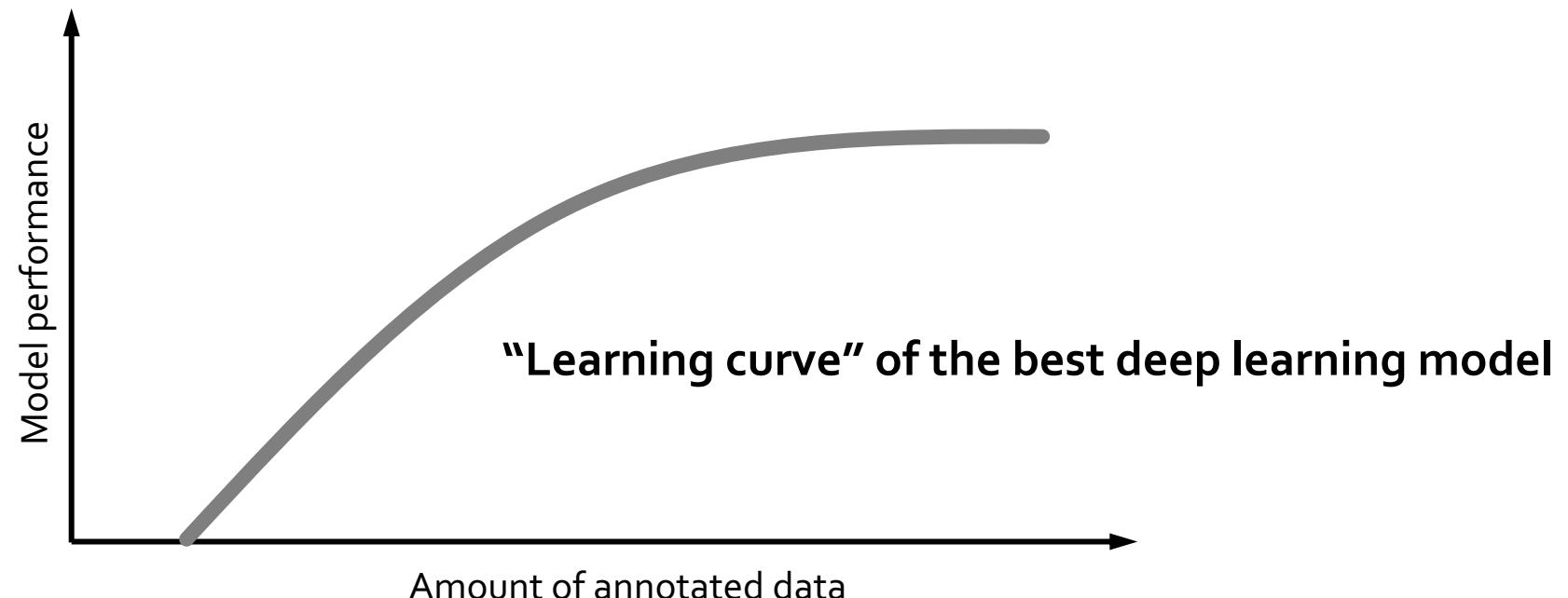
Aim 1

Aim 2

Aim 3

Summary

- Goal:** Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems
- Aim 1:** Acquiring necessary annotation efficiently from human experts
- Aim 2:** Utilizing existing annotation effectively from advanced architecture
- Aim 3:** Extracting generic knowledge directly from unannotated images



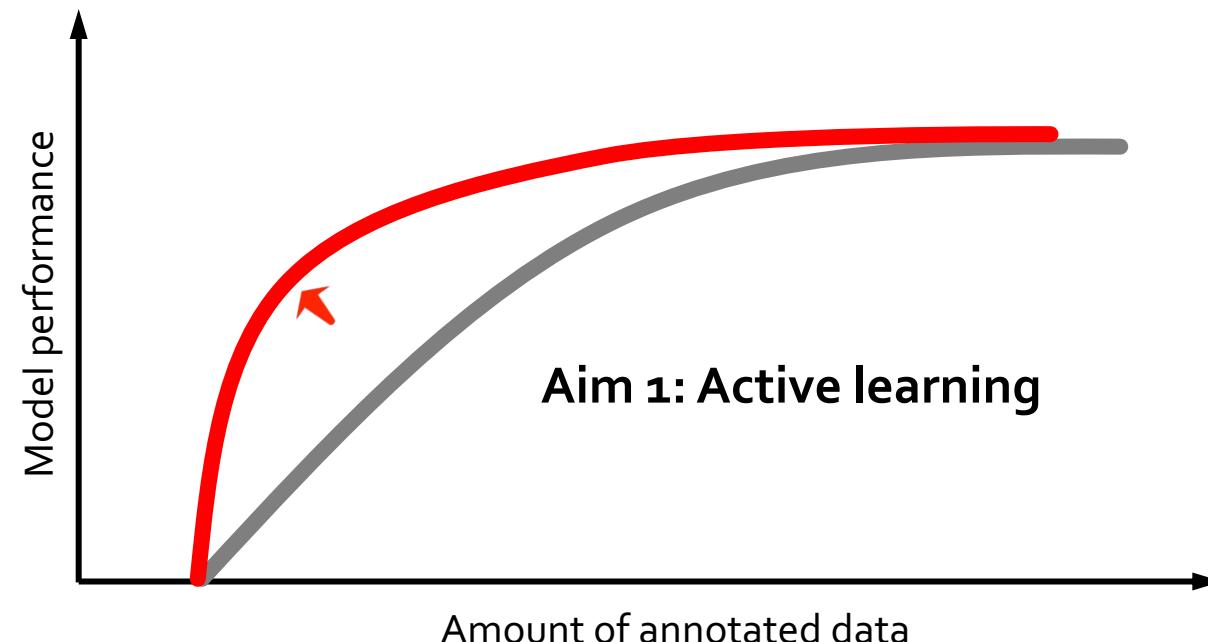
Aim 1

Aim 2

Aim 3

Summary

- Goal:** Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems
- Aim 1:** Acquiring necessary annotation efficiently from human experts
- Aim 2:** Utilizing existing annotation effectively from advanced architecture
- Aim 3:** Extracting generic knowledge directly from unannotated images



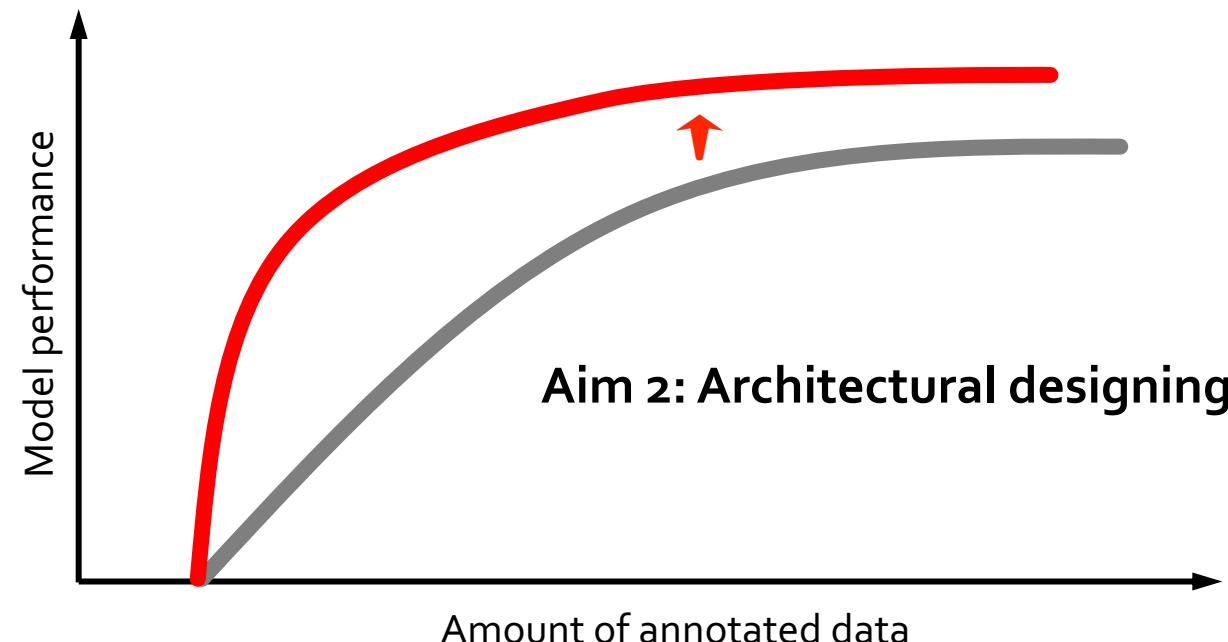
Aim 1

Aim 2

Aim 3

Summary

- Goal:** Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems
- Aim 1:** Acquiring necessary annotation efficiently from human experts
- Aim 2:** Utilizing existing annotation effectively from advanced architecture
- Aim 3:** Extracting generic knowledge directly from unannotated images



Introduction

Objective

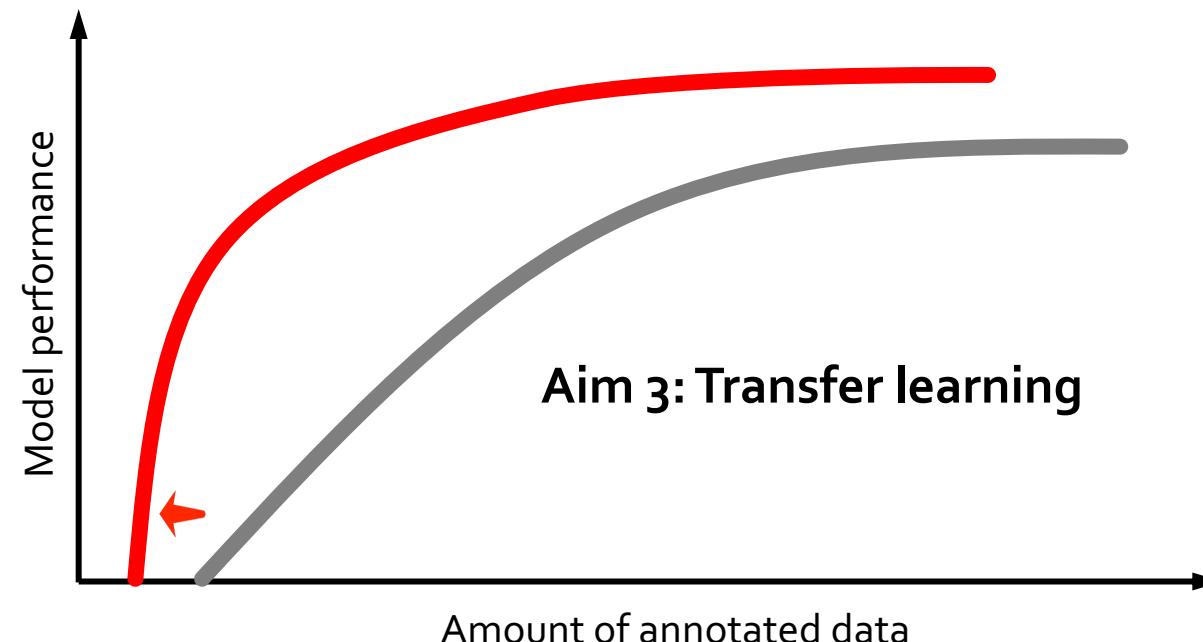
Aim 1

Aim 2

Aim 3

Summary

- Goal:** Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems
- Aim 1:** Acquiring necessary annotation efficiently from human experts
- Aim 2:** Utilizing existing annotation effectively from advanced architecture
- Aim 3:** Extracting generic knowledge directly from unannotated images



Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary

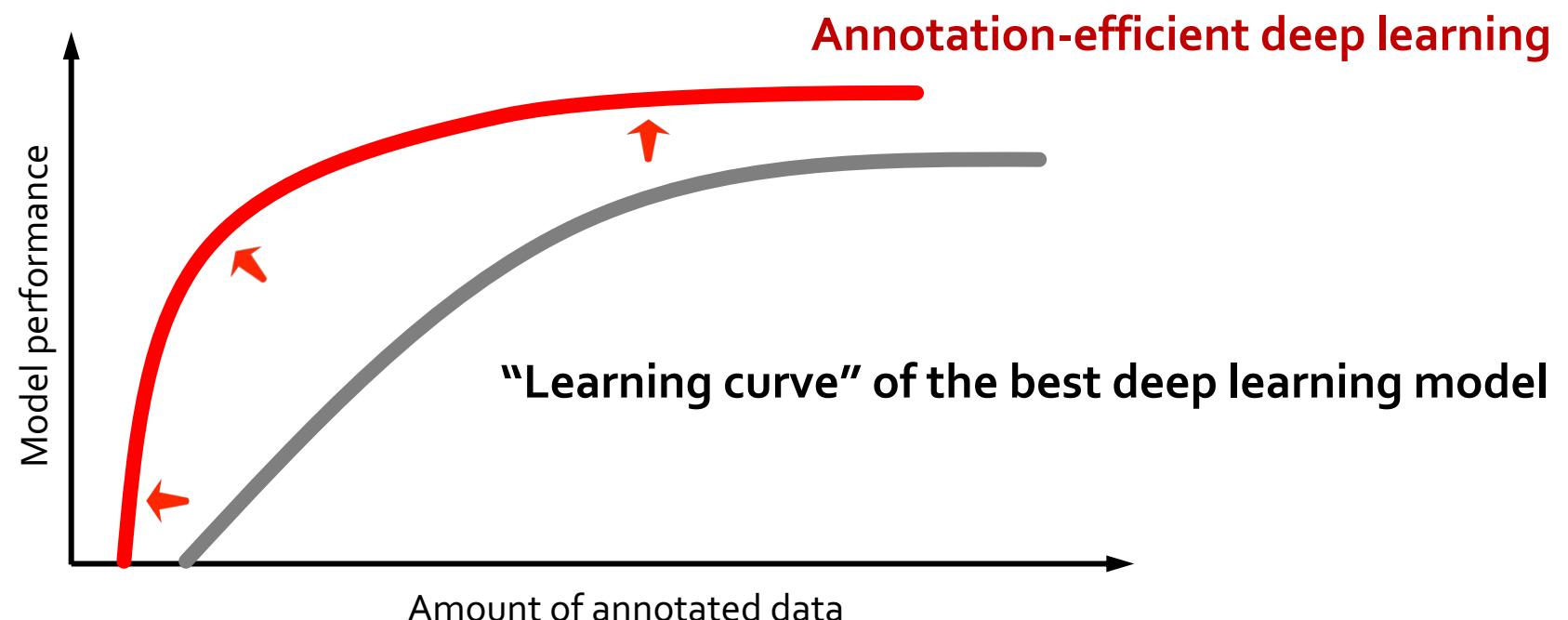
Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Aim 3: Extracting generic knowledge directly from unannotated images

Hypothesis: With a small part of the dataset annotated, we can deliver deep models that approximate or even outperform those that require annotating the entire dataset.





Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary

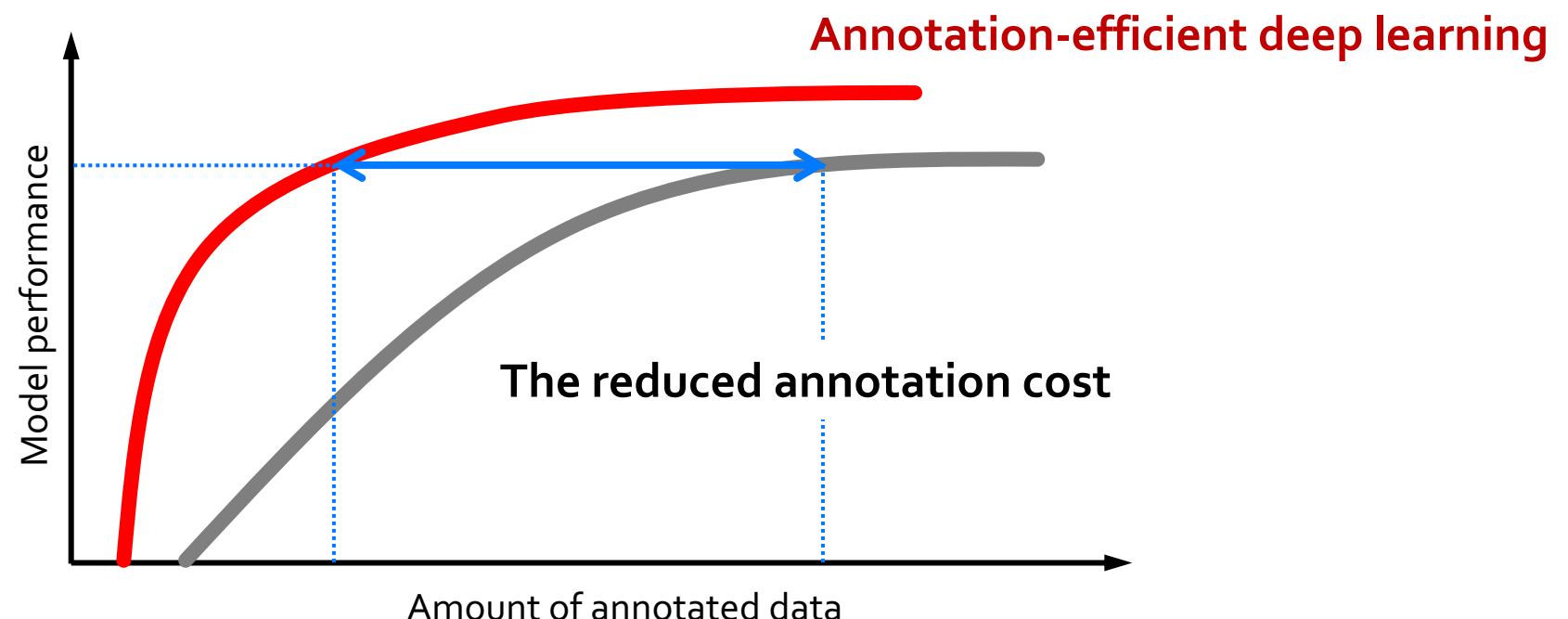
Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Aim 3: Extracting generic knowledge directly from unannotated images

Hypothesis: With a small part of the dataset annotated, we can deliver deep models that approximate or even outperform those that require annotating the entire dataset.



Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary

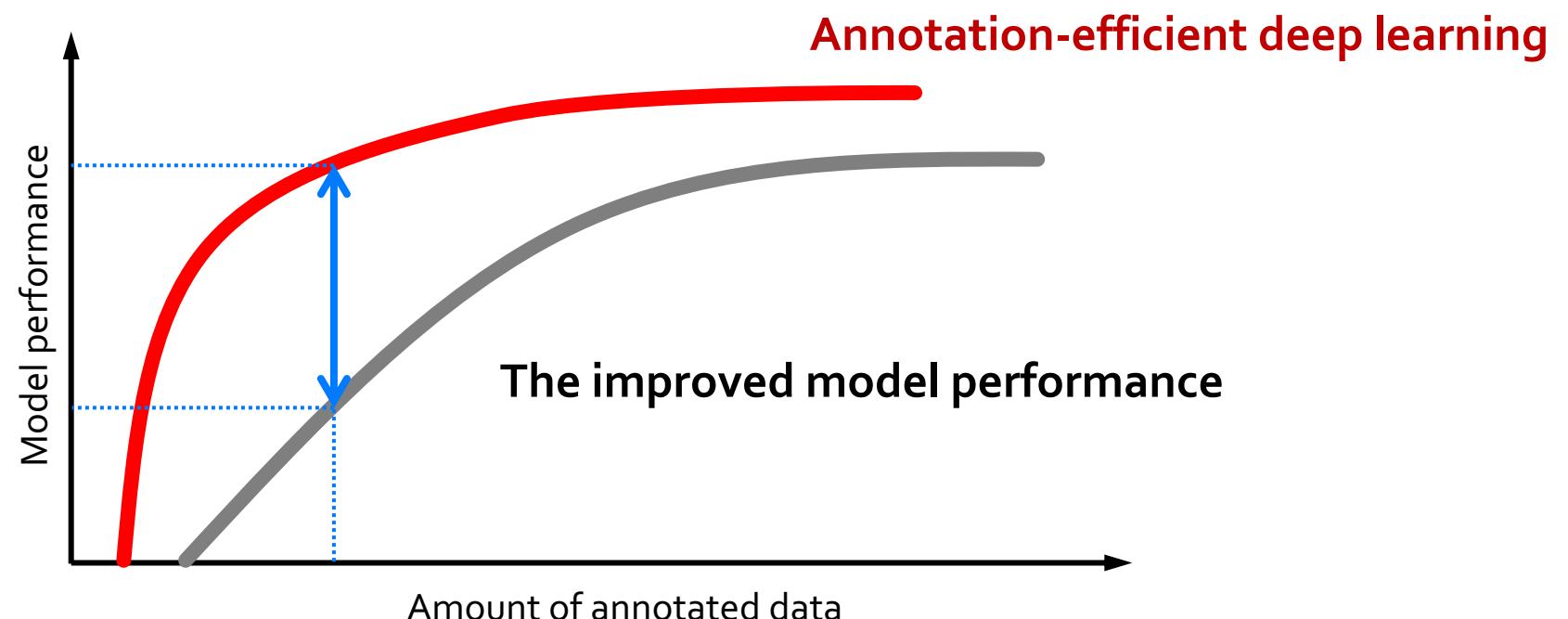
Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Aim 3: Extracting generic knowledge directly from unannotated images

Hypothesis: With a small part of the dataset annotated, we can deliver deep models that approximate or even outperform those that require annotating the entire dataset.

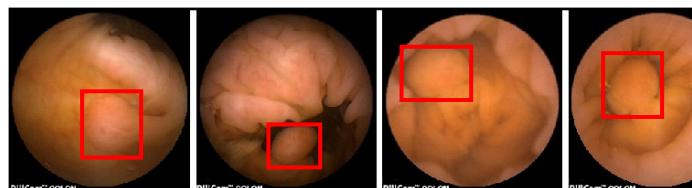




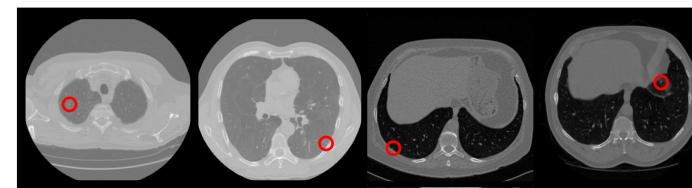
Introduction

Objective

Aim 1



Polyp detection

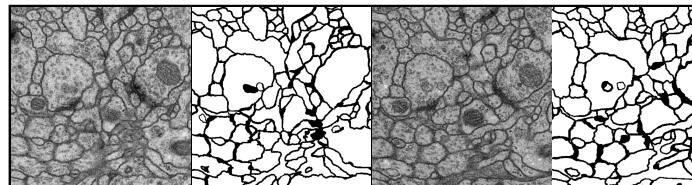


Lung nodule detection

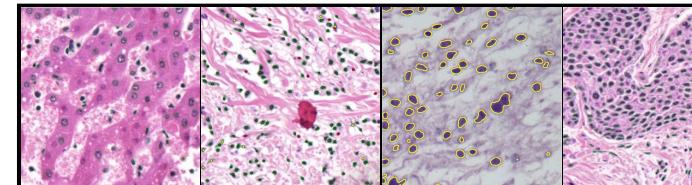


Pulmonary embolism detection

Aim 2



Neuronal structure segmentation

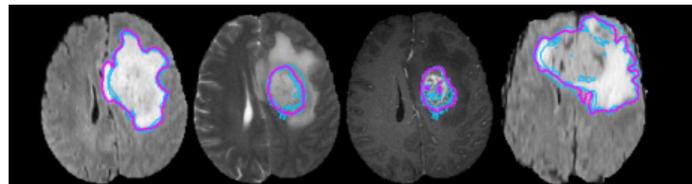


Cell/nuclei segmentation



Liver/lesion segmentation

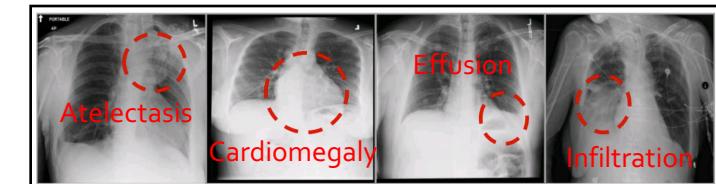
Summary



Brain/tumor segmentation



Kidney/lesion segmentation



Pulmonary diseases classification

Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Aim 3: Extracting generic knowledge directly from unannotated images



Aim 1: Acquiring necessary annotation efficiently from human experts

Task: Find the most important 1,000 images from 1,000,000 images

Introduction

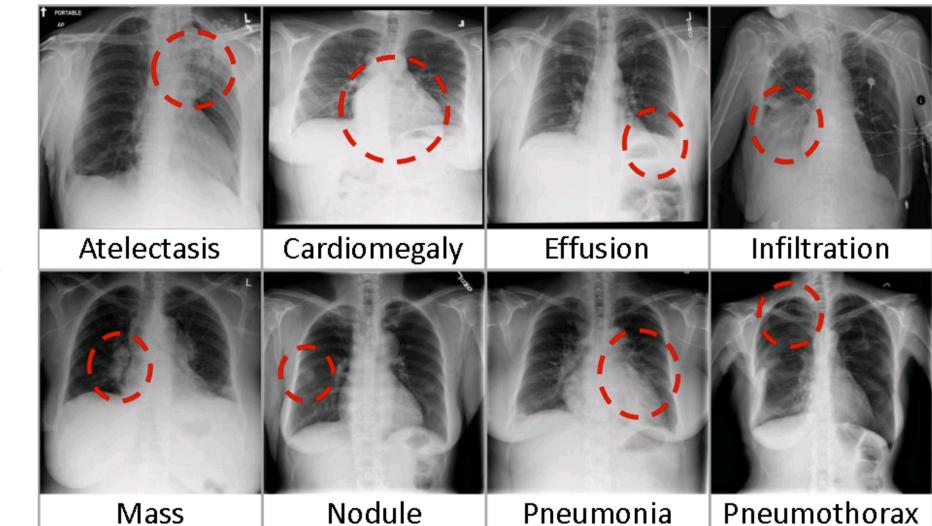
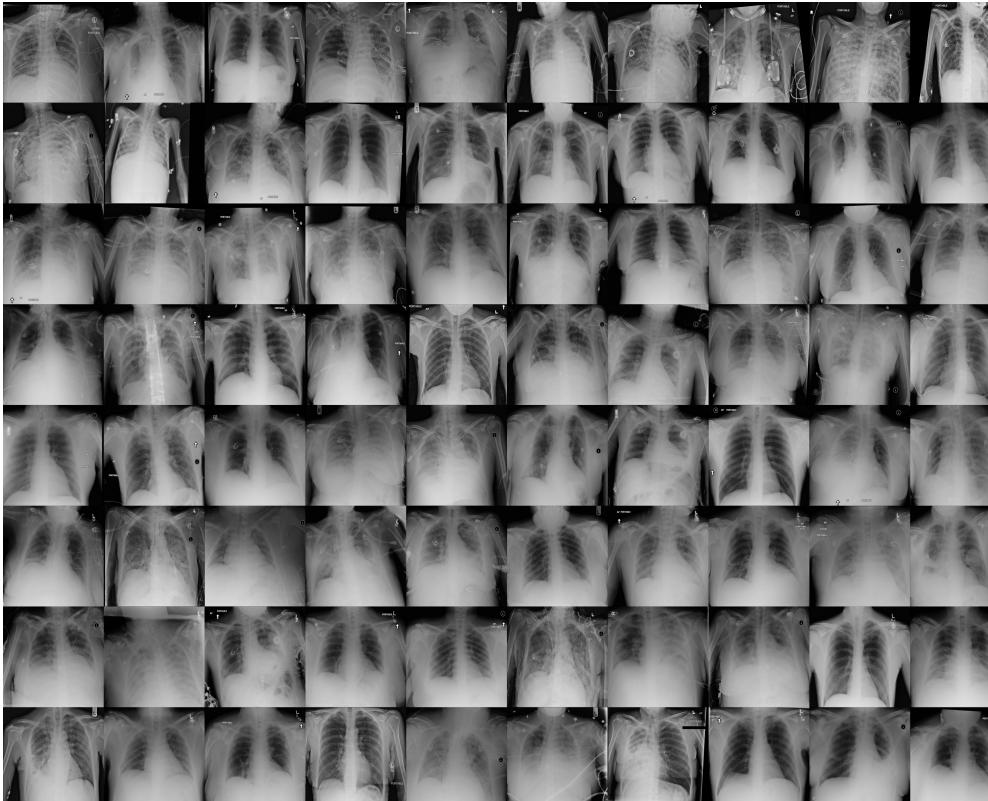
Objective

Aim 1

Aim 2

Aim 3

Summary





Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure

Introduction

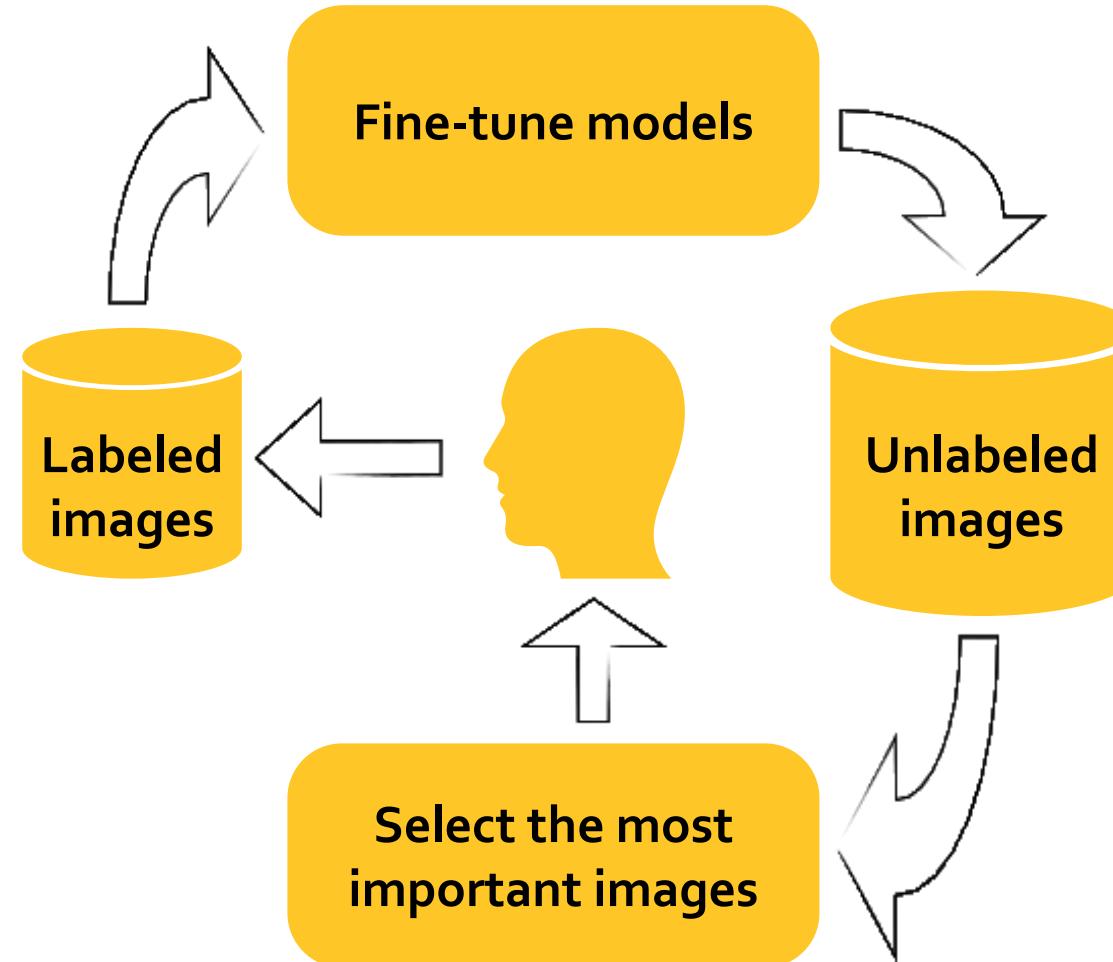
Objective

Aim 1

Aim 2

Aim 3

Summary





Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure

Introduction

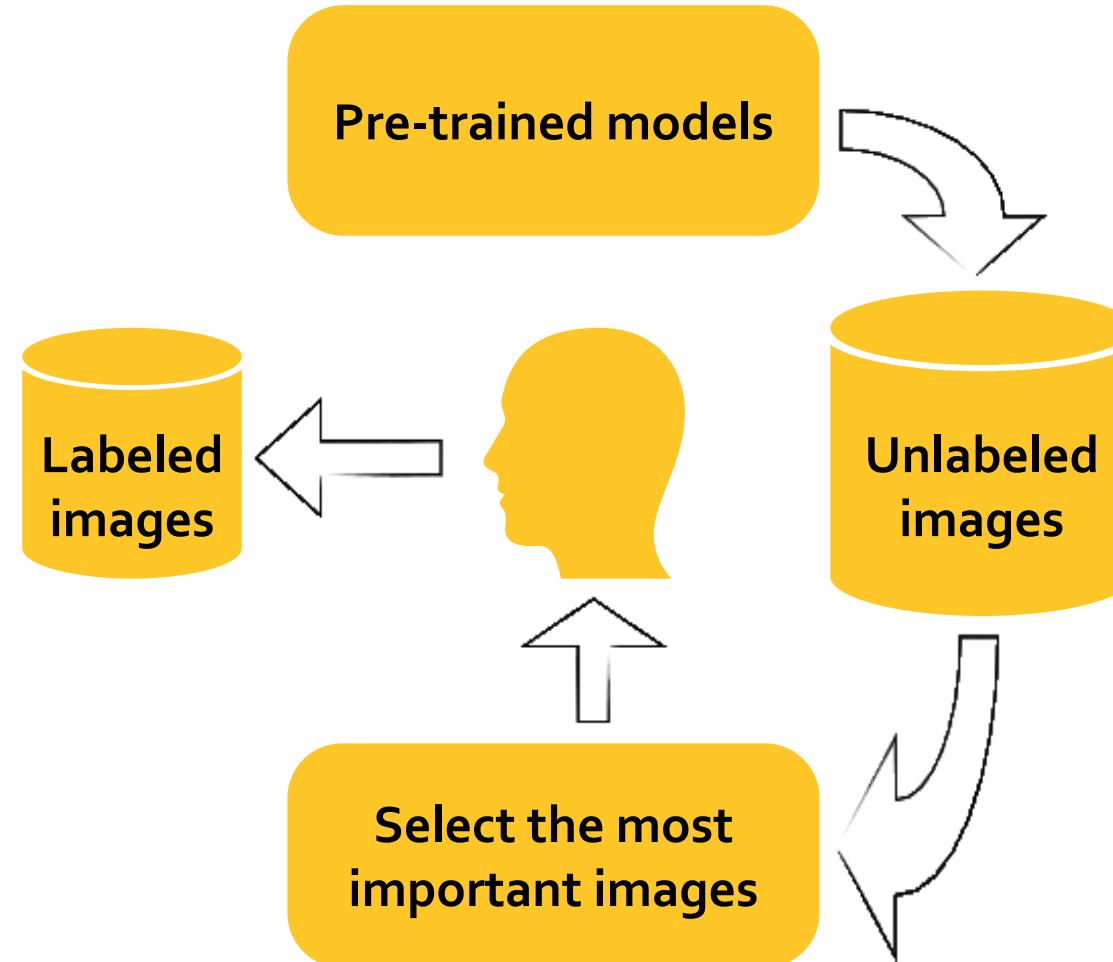
Objective

Aim 1

Aim 2

Aim 3

Summary





Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure

Introduction

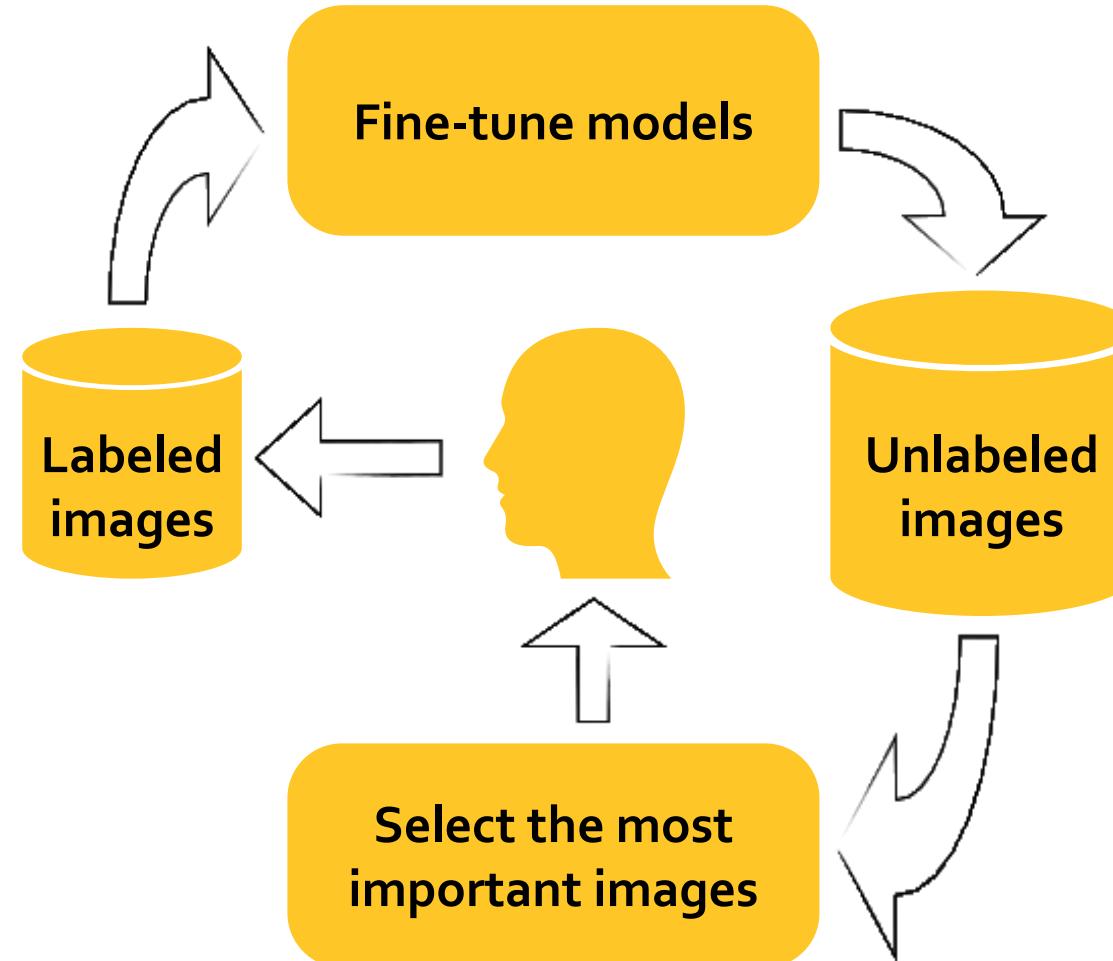
Objective

Aim 1

Aim 2

Aim 3

Summary





Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure

Introduction

Objective

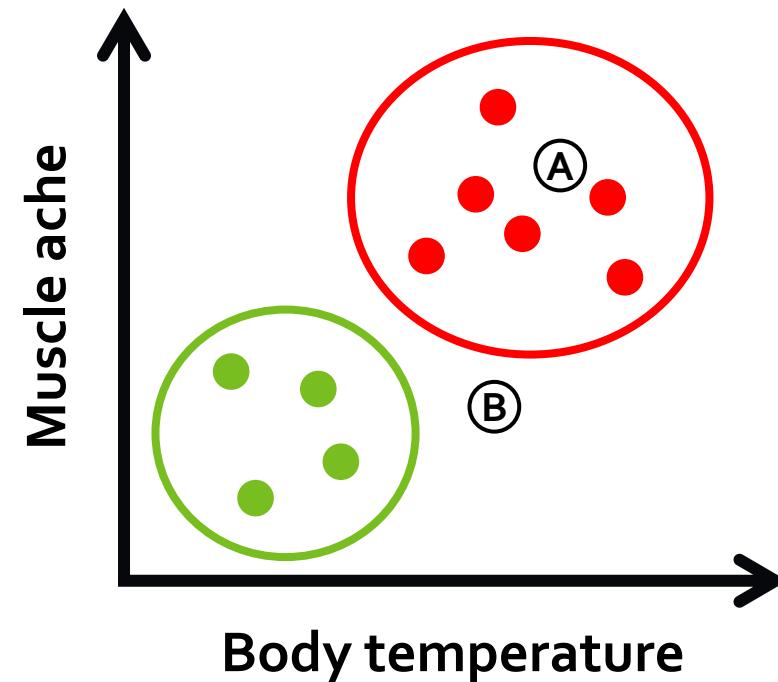
Aim 1

Aim 2

Aim 3

Summary

- Flu
- Healthy



Select the most
important images

Which sample would you
annotate first, A or B?



Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure

Introduction

Objective

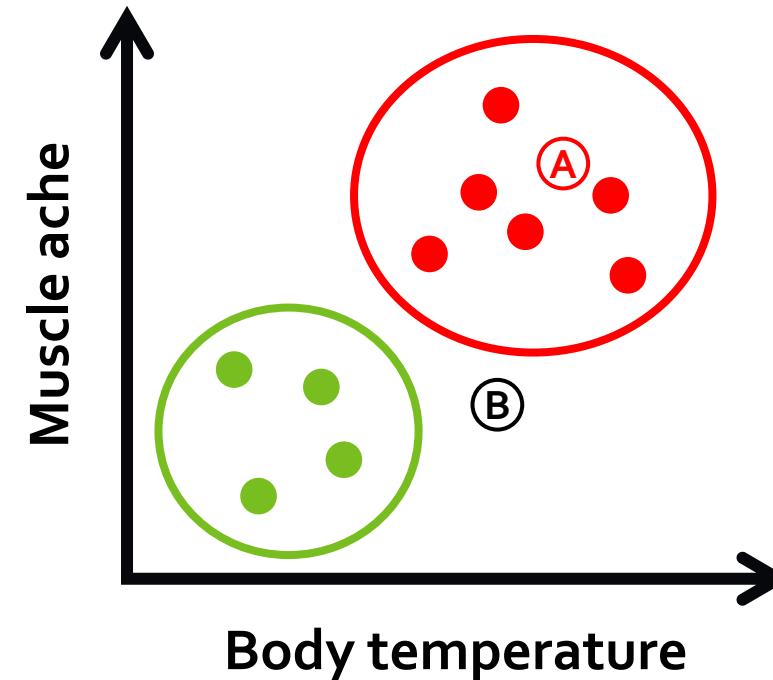
Aim 1

Aim 2

Aim 3

Summary

- Flu
- Healthy



Select the most
important images

Which sample would you
annotate first, A or B?



Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure

Introduction

Objective

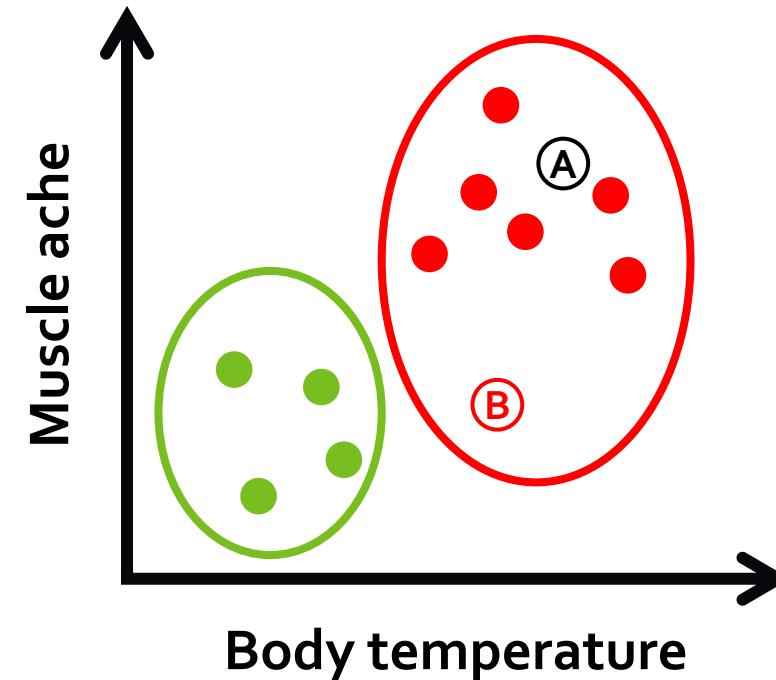
Aim 1

Aim 2

Aim 3

Summary

- Flu
- Healthy



Select the most
important images

Which sample would you
annotate first, A or B?



Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure

Introduction

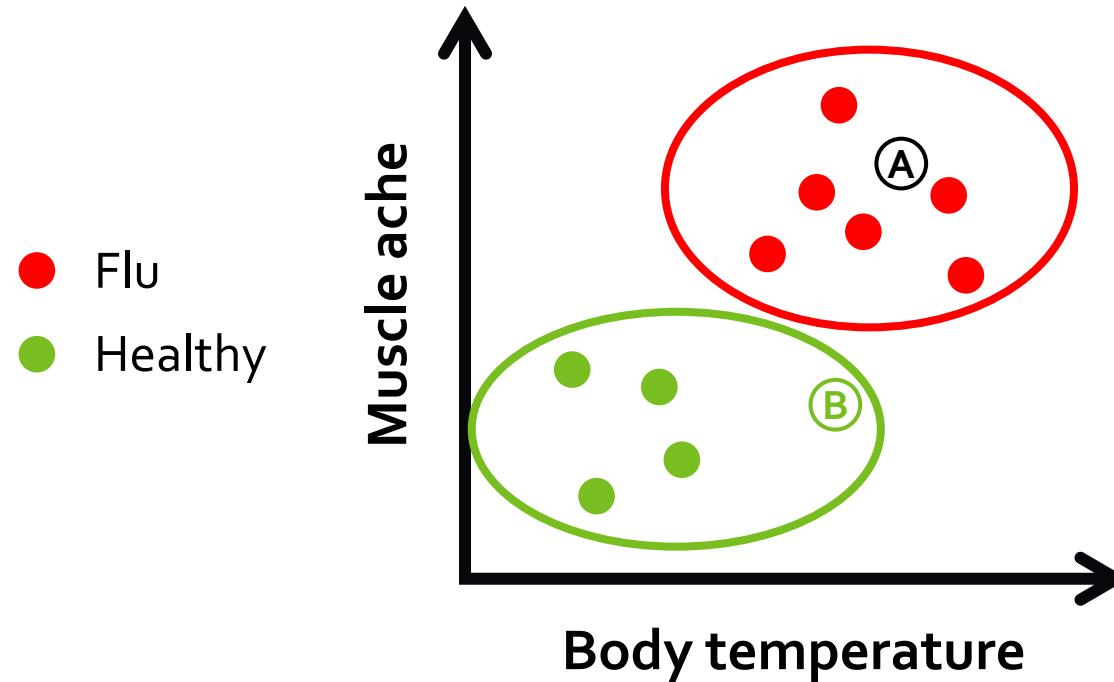
Objective

Aim 1

Aim 2

Aim 3

Summary



Select the most
important images

Which sample would you
annotate first, A or B?



Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure, *uncertainty-based*

Introduction

Objective

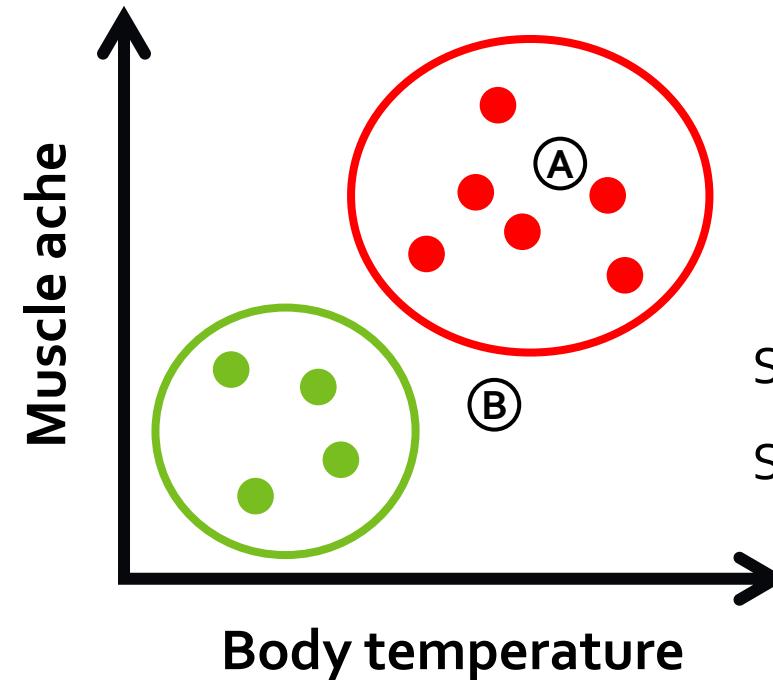
Aim 1

Aim 2

Aim 3

Summary

- Flu
- Healthy



Sample A: *low uncertainty*

Sample B: *high uncertainty*

Select the most
important images

Which sample would you
annotate first, A or B?



Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure, *diversity-based*

Introduction

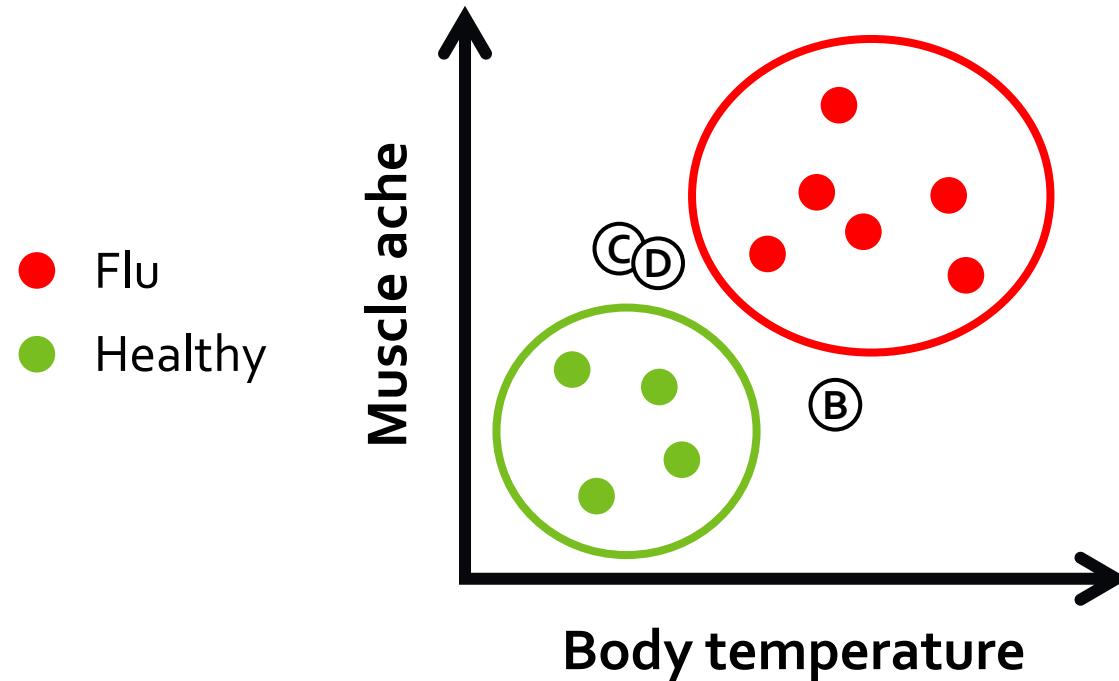
Objective

Aim 1

Aim 2

Aim 3

Summary



Select the most
important images

Which two samples would
you annotate first?



Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure, *diversity-based*

Introduction

Objective

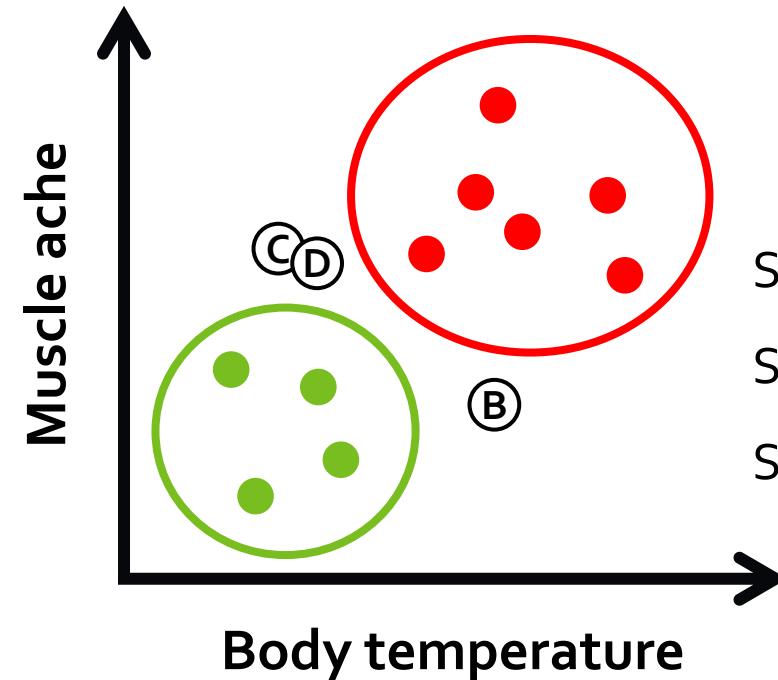
Aim 1

Aim 2

Aim 3

Summary

- Flu
- Healthy



Samples B, C: *highest* diversity

Samples B, D: *high* diversity

Samples C, D: *low* diversity

Select the most
important images

Which two samples would
you annotate first?



Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure, *diversity-based*

Introduction

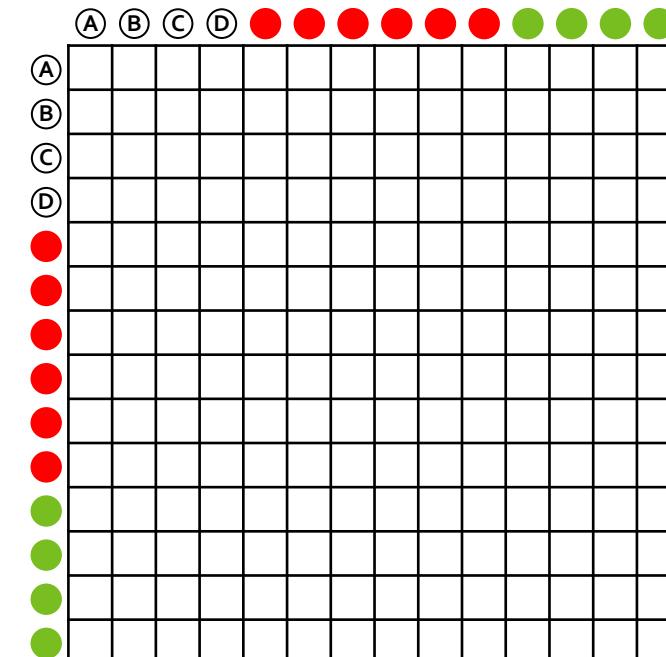
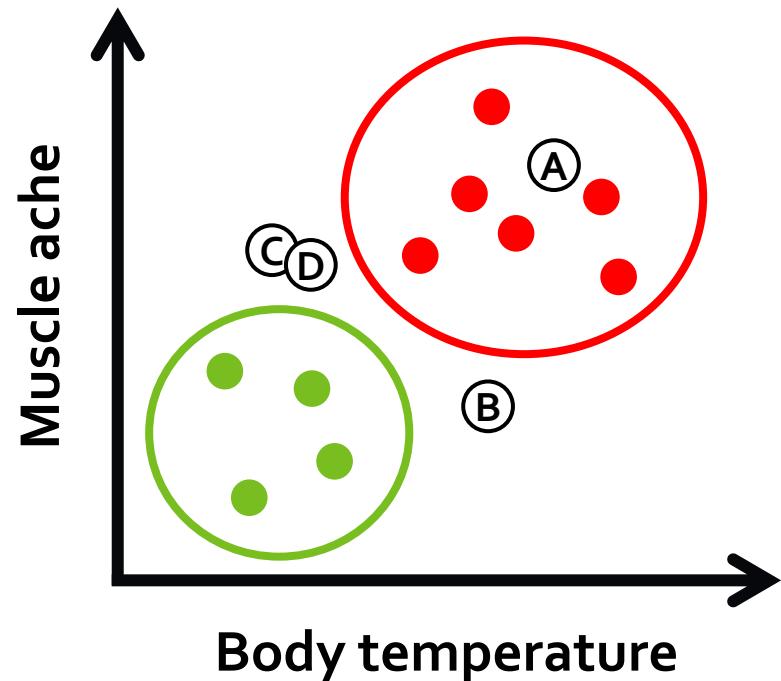
Objective

Aim 1

Aim 2

Aim 3

Summary





Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure, *diversity-based*

Introduction

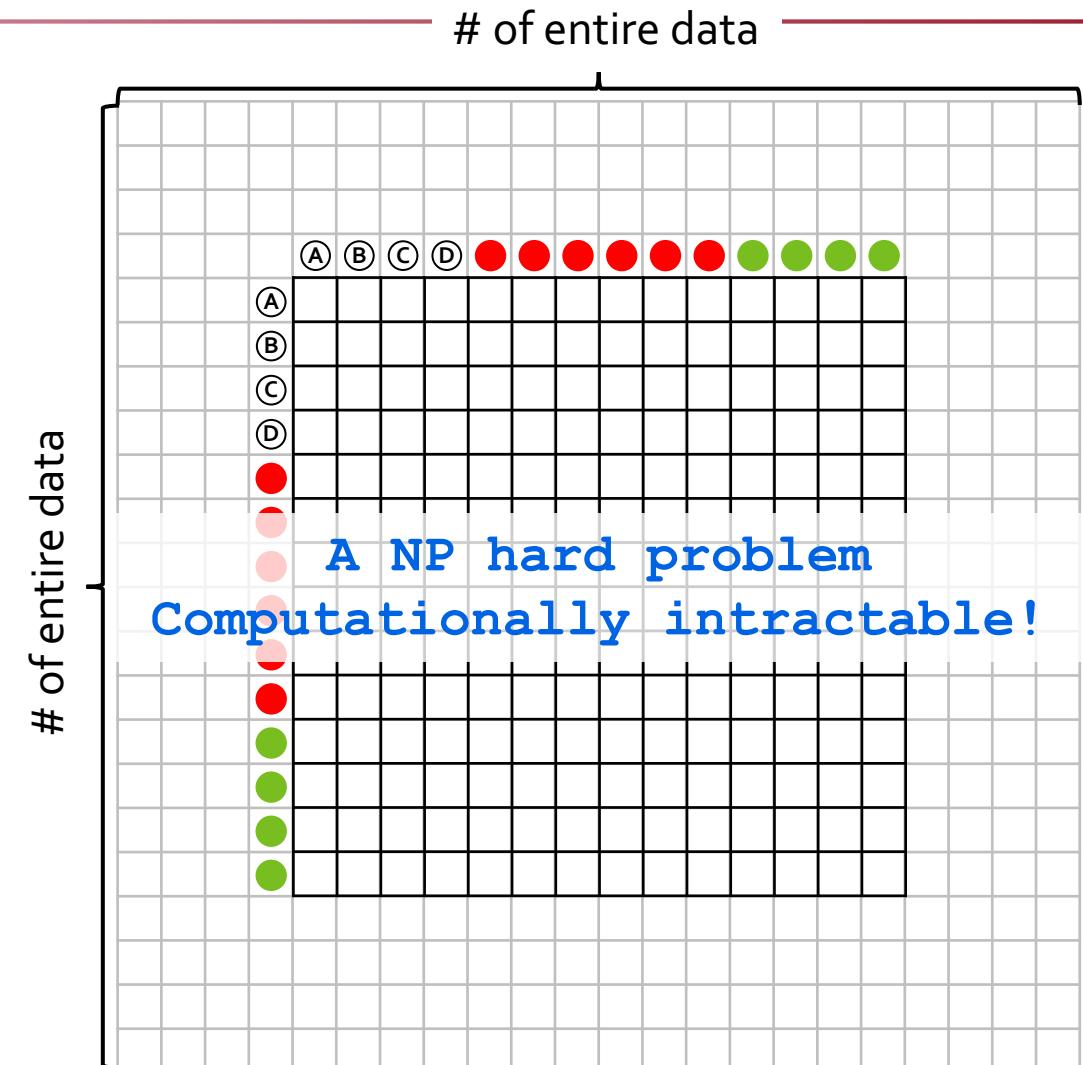
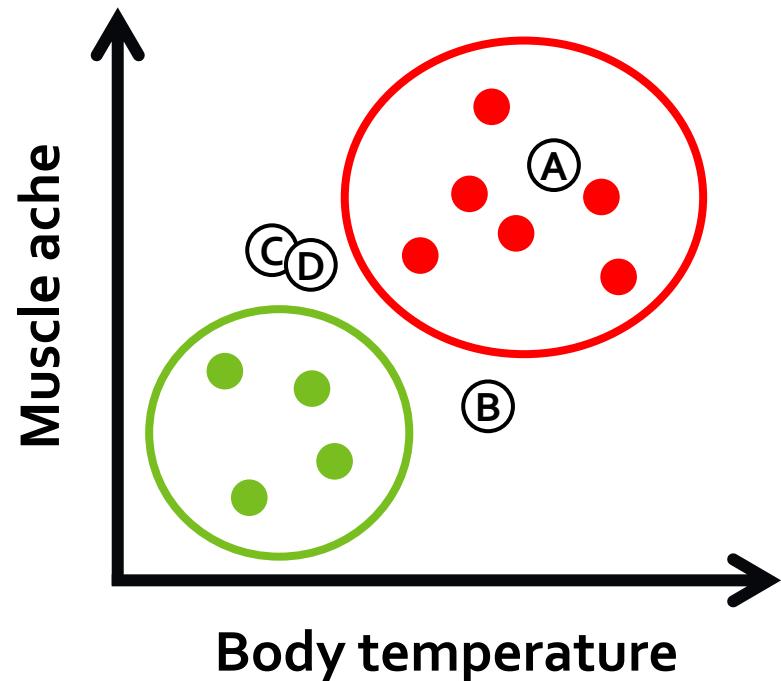
Objective

Aim 1

Aim 2

Aim 3

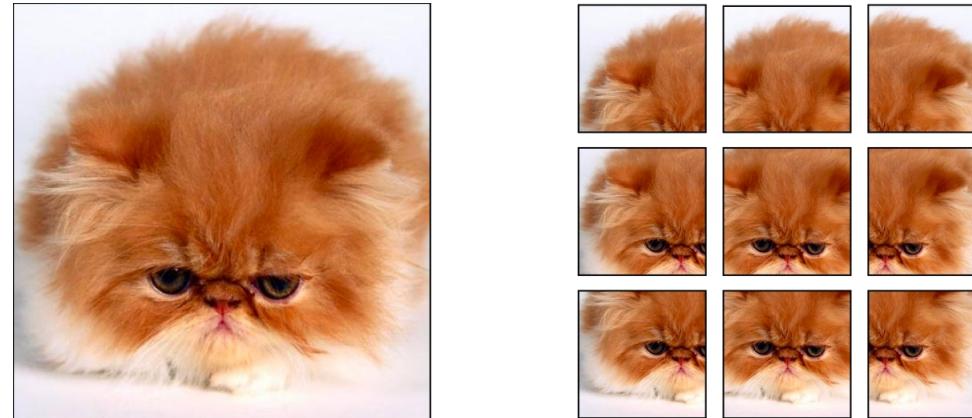
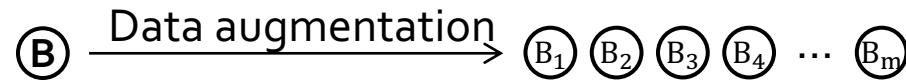
Summary





Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure, *diversity-based*



Introduction

Objective

Aim 1

Aim 2

Aim 3

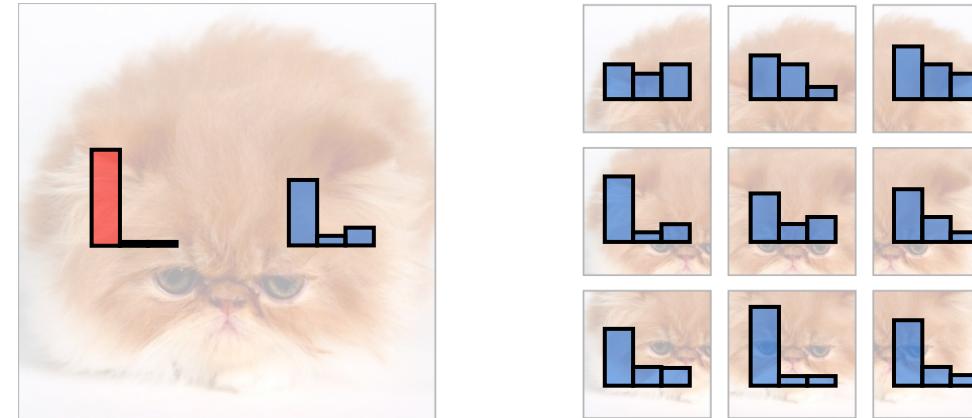
Summary

To train the deep model, many patches are usually generated via data augmentation; these patches generated from the same image share the *same label* (*cat*), and they are expected to have *similar predictions* by the current model.



Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure, *diversity-based*



Cross-entropy between
human labels and model
predictions

Consistency among
model predictions for
the same sample

Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary



Aim 1: Acquiring necessary annotation efficiently from human experts

Approach: “Human-in-the-loop” active learning procedure, *diversity-based*

Introduction

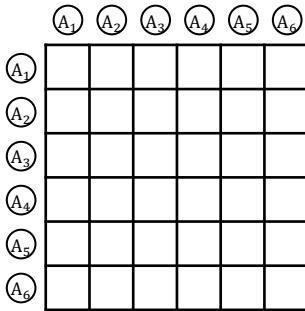
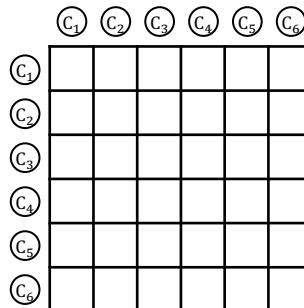
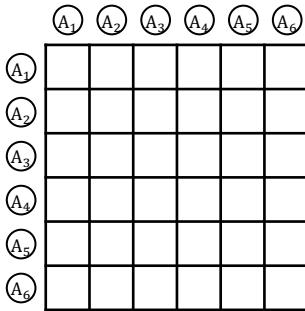
Objective

Aim 1

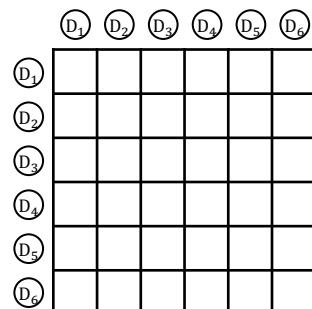
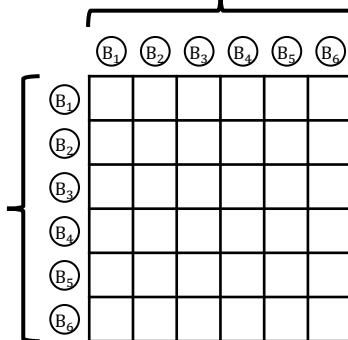
Aim 2

Aim 3

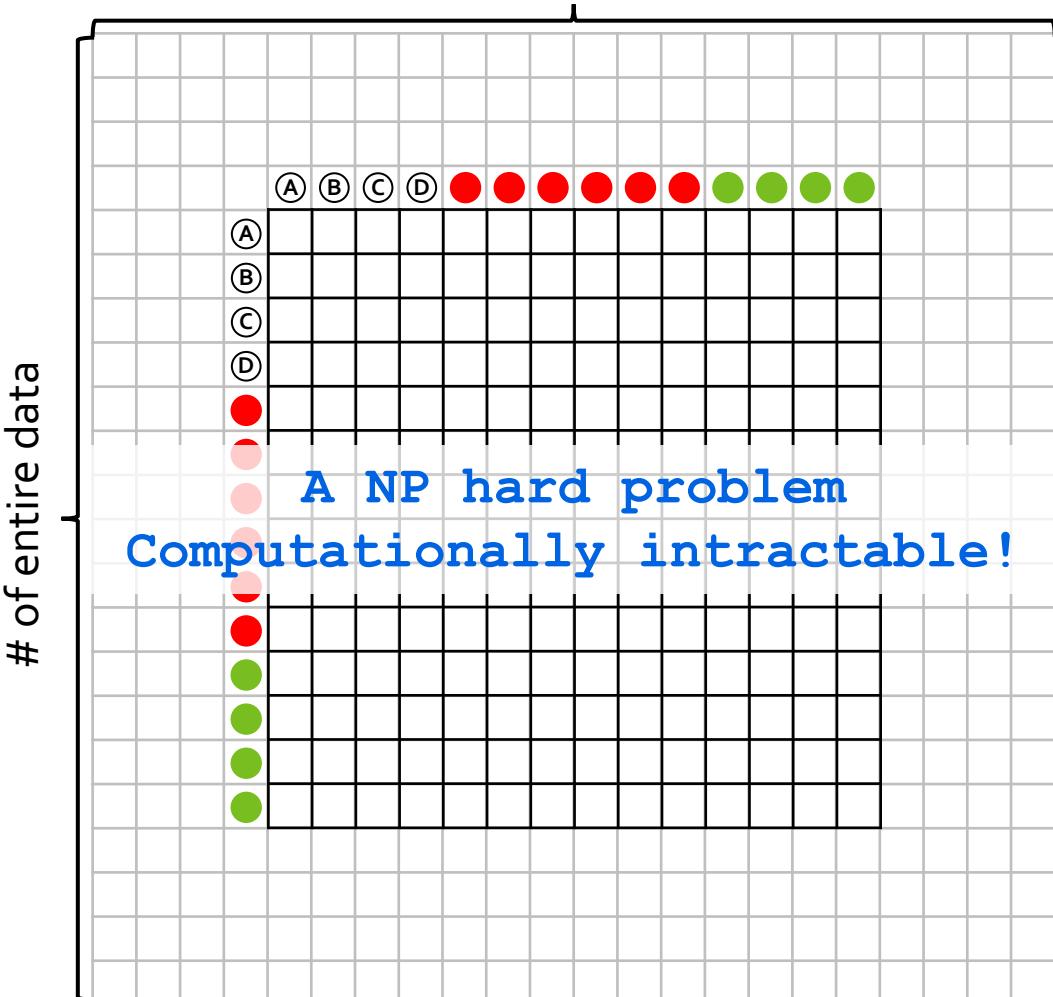
Summary



of augmentation



of entire data





Aim 1: Acquiring necessary annotation efficiently from human experts

Hypothesis: Wisely selecting important samples can reduce annotation cost

Introduction

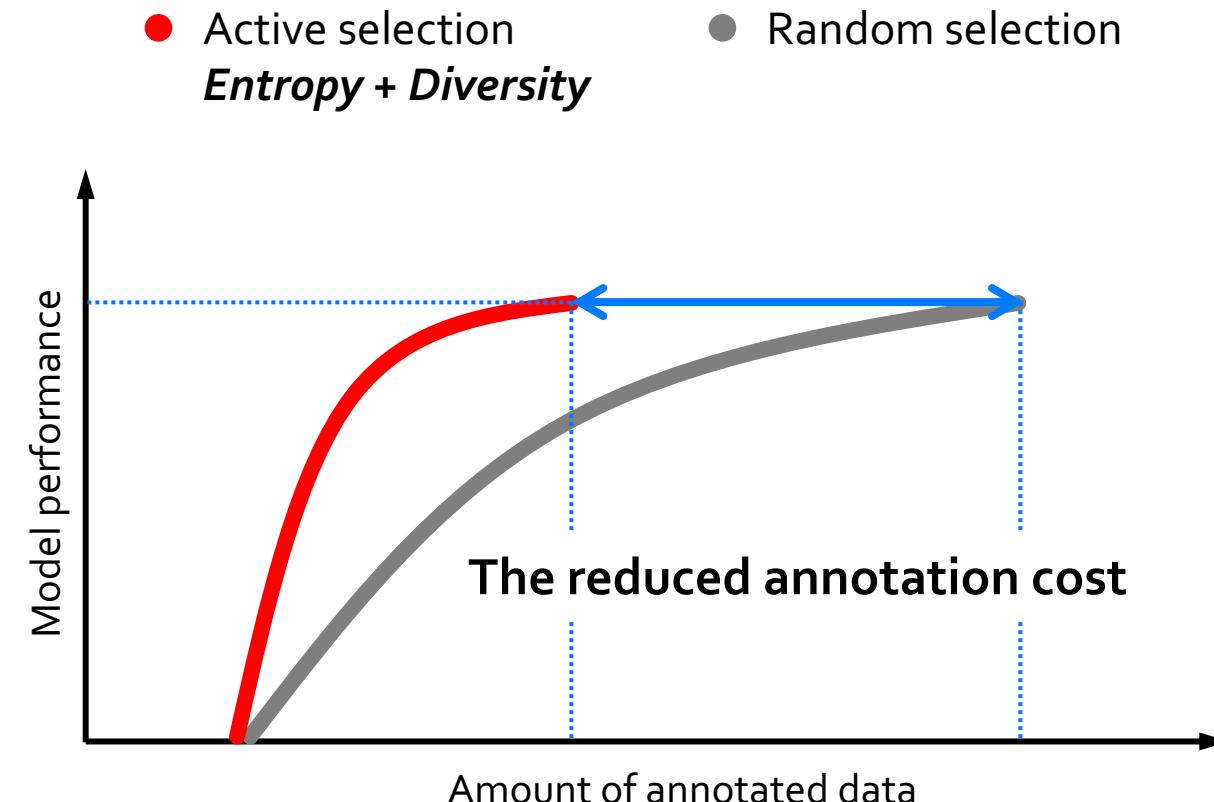
Objective

Aim 1

Aim 2

Aim 3

Summary





Aim 1: Acquiring necessary annotation efficiently from human experts

Contribution: Reduce annotation cost by over 80% compared with random selection

Introduction

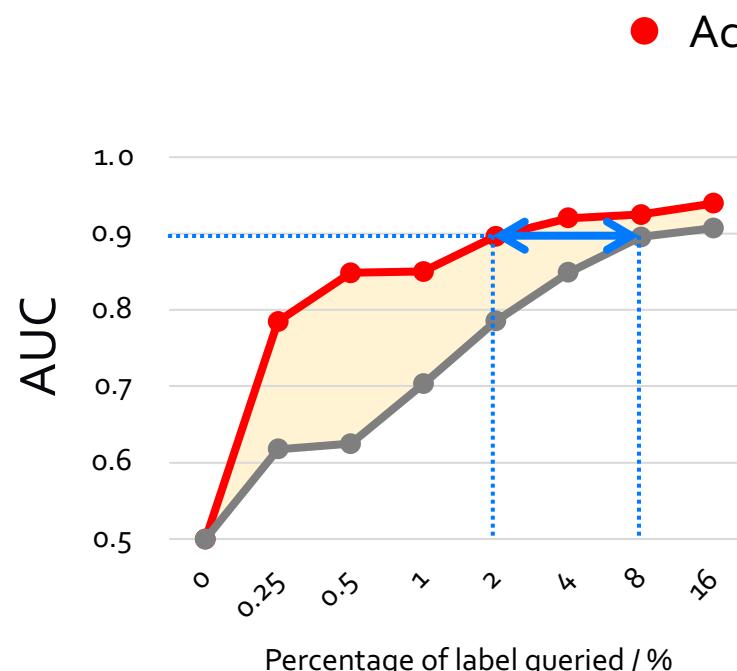
Objective

Aim 1

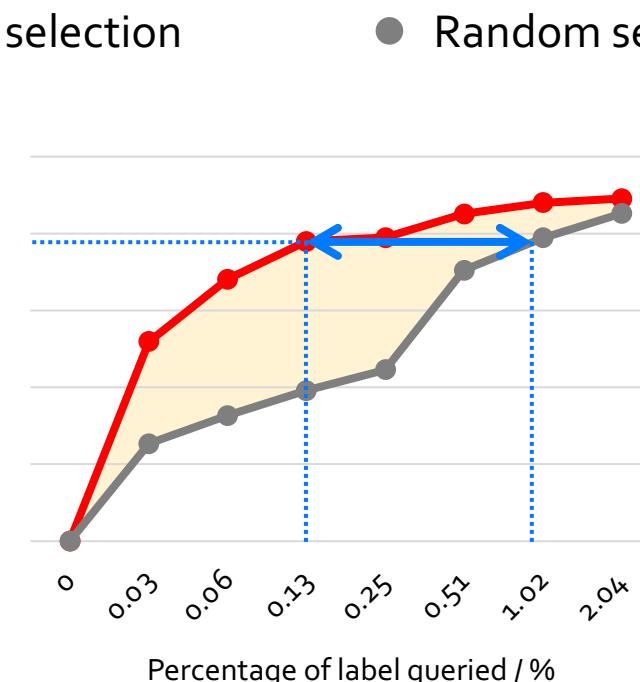
Aim 2

Aim 3

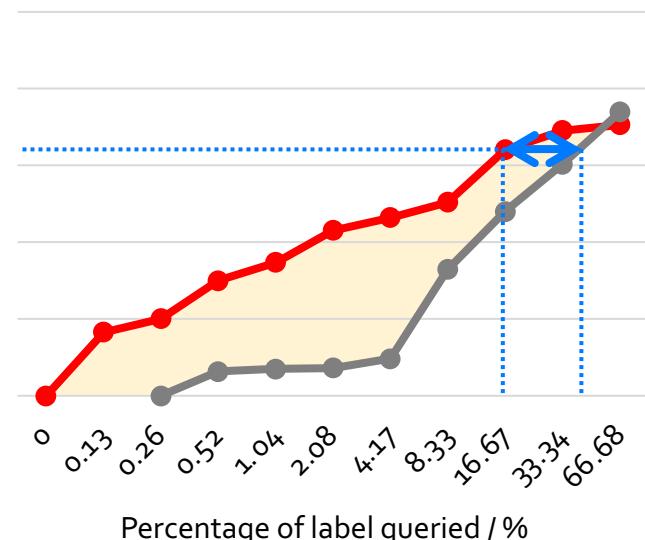
Summary



Colonoscopy Frame
Classification (-81.5%)



Polyp Detection
(-86.3%)



Pulmonary Embolism
Detection (-80.3%)

1. Zhou, Zongwei, et al. "Integrating active learning and transfer learning for carotid intima-media thickness video interpretation." Journal of digital imaging, 2019.
2. Zhou, Zongwei, et al. "Active, Continual Fine Tuning of Convolutional Neural Networks for Reducing Annotation Efforts." Medical Image Analysis , 2021.
3. Zhou, Zongwei, et al. "Fine-tuning convolutional neural networks for biomedical image analysis: actively and incrementally." CVPR, 2017.

Not All Data Is Created Equal

Publications for Aim 1:

- Z. Zhou, J. Shin, L. Zhang, S. Gurudu, M. Gotway, J. Liang, 2017. Fine-tuning Convolutional Neural Networks for Biomedical Image Analysis: Actively and Incrementally. *CVPR'17, one of only five papers in biomedical imaging accepted by CVPR'17.*
- Z. Zhou, J. Shin, S. Gurudu, M. Gotway, J. Liang, 2021. Active, Continual Fine Tuning of Convolutional Neural Networks for Reducing Annotation Efforts. *Medical Image Analysis.*
- Z. Zhou, J. Shin, R. Feng, R. Hurst, C. Kendall, J. Liang, 2019. Integrating Active Learning and Transfer Learning for Carotid Intima-Media Thickness Video Interpretation. *Journal of Digital Imaging.*
- L. Chen, Y. Bai, S. Huang, Y. Lu, B. Wen, A. Yuille, Z. Zhou. 2022. A Guide to Your First Choice: Addressing Cold Start Problem in Vision Active Learning. *NeurIPS HILL.*

Not All Data Is Created Equal

Clinical Impacts of Aim 1:

- An efficient “human-in-the-loop” procedure helps radiologists identify the *most important data*, therefore dramatically reducing the burden of annotation.
- The *continual learning capability* of deep models encourages data, label, and model reuse, significantly improving the training efficiency.



Aim 2: Utilizing existing annotation effectively from advanced architecture

Task: Enhance the architecture for modeling 1,000 annotated images

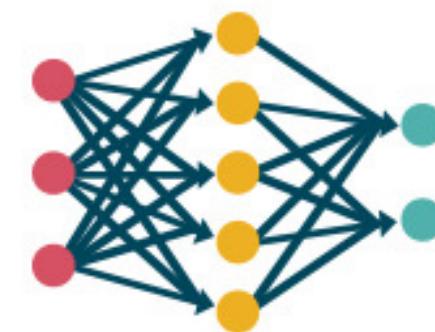
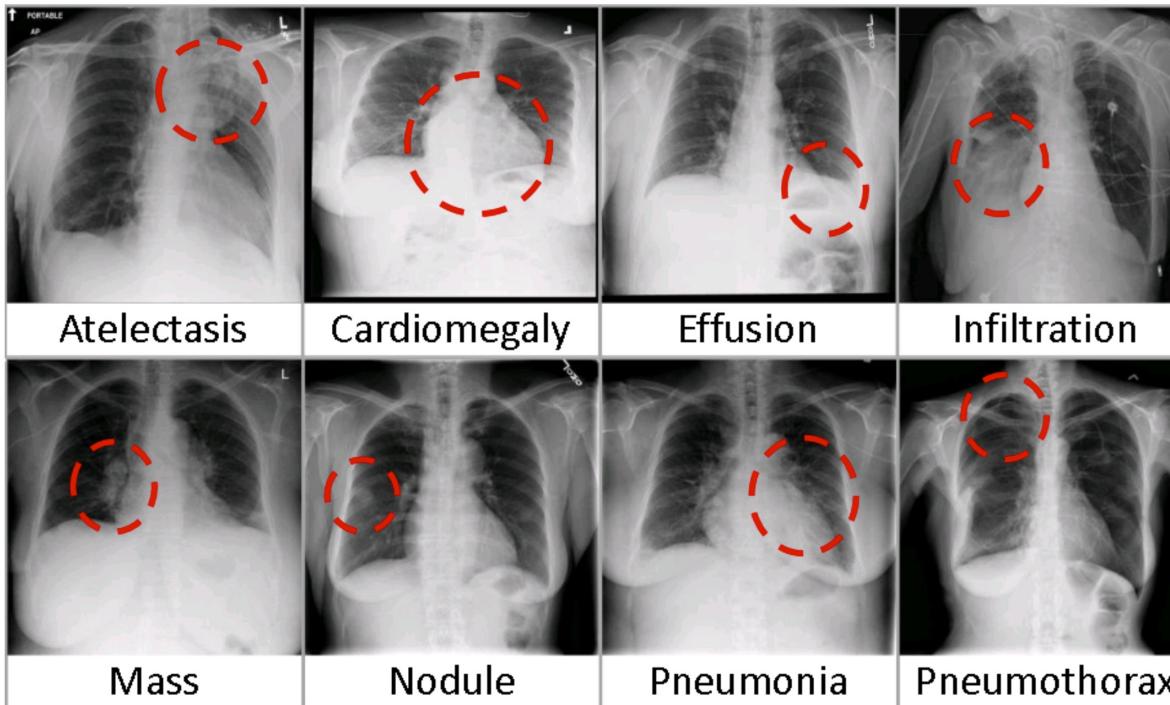
Introduction

Objective

Aim 1

Aim 2

Aim 3





Aim 2: Utilizing existing annotation effectively from advanced architecture

Segmentation: Partition an image into multiple segments to ease the analysis

Introduction

Objective

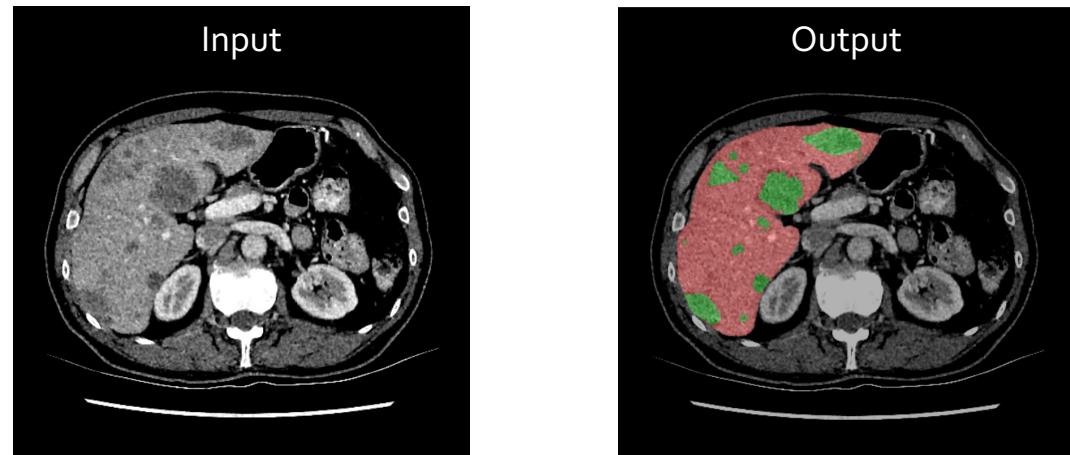
Aim 1

Aim 2

Aim 3

Summary

e.g., liver & lesion segmentation



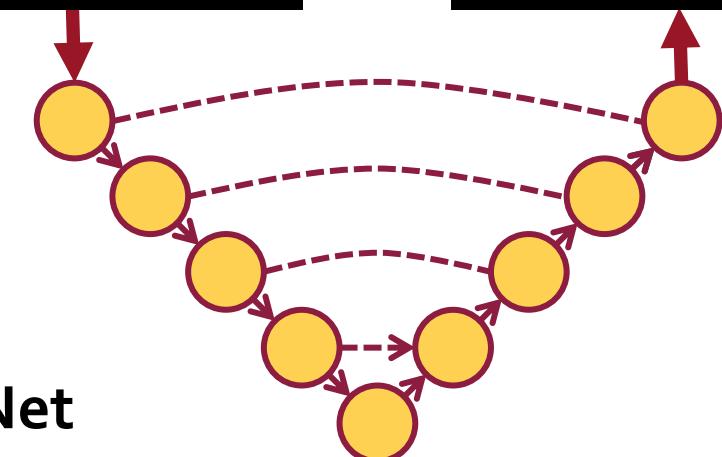
U-net: Convolutional networks for biomedical image segmentation

[O Ronneberger, P Fischer, T Brox - ... Conference on Medical image ..., 2015 - Springer](#)

... We demonstrate the application of the **u-net** to three different **segmentation** tasks. The first task is the **segmentation** of neuronal structures in electron microscopic recordings. An ...

[☆ Save](#) [⤓ Cite](#) [Cited by 51327](#) [Related articles](#) [All 30 versions](#)

U-Net





Aim 2: Utilizing existing annotation effectively from advanced architecture

Hypothesis: Multi-scale feature aggregation leads to powerful models

Introduction

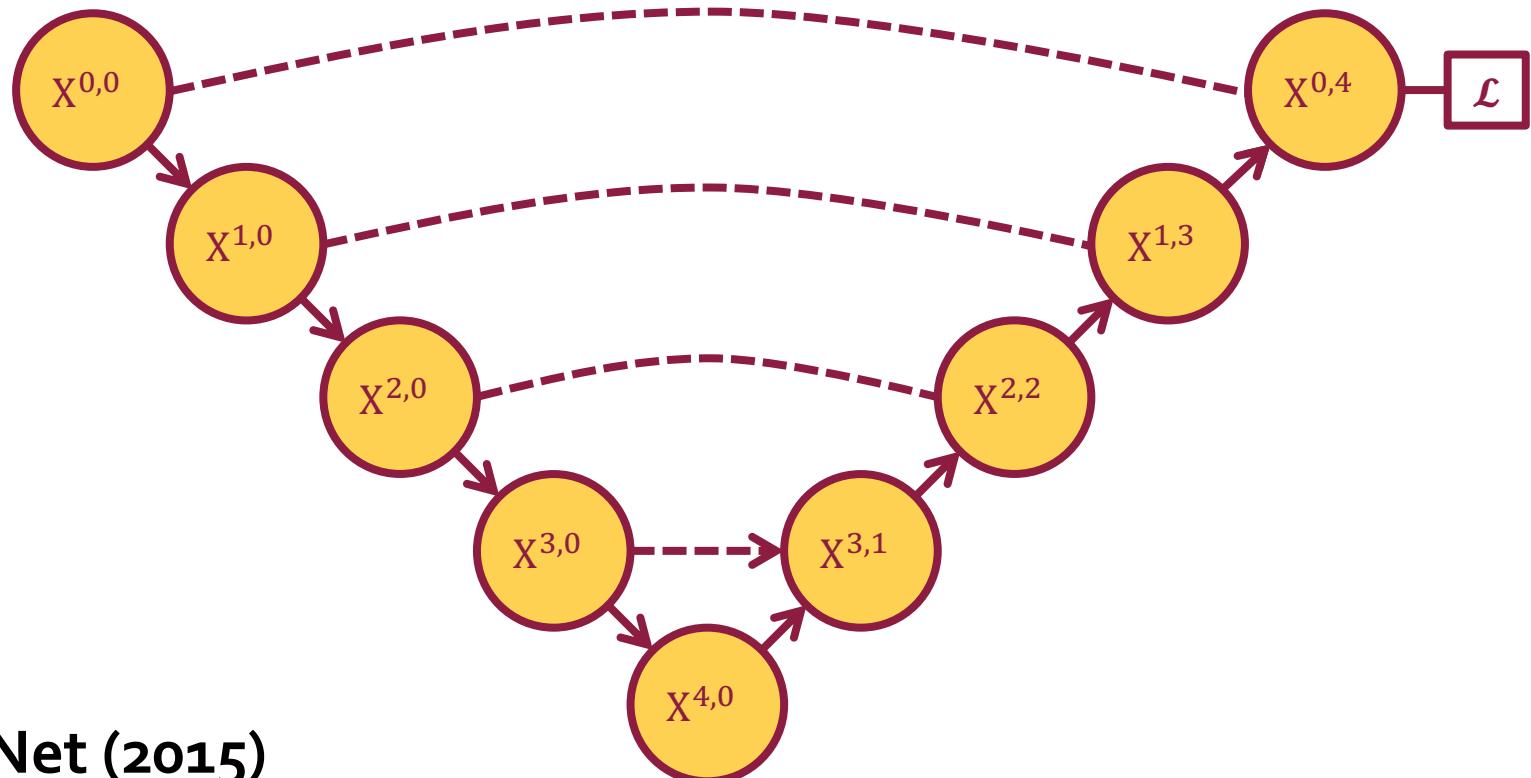
Objective

Aim 1

Aim 2

Aim 3

Summary



U-Net (2015)

1. Ronneberger, Olaf, et al. "U-net: Convolutional networks for biomedical image segmentation." MICCAI, 2015.



Aim 2: Utilizing existing annotation effectively from advanced architecture

Approach: Redesigned skip connections aggregate multi-scale features

Introduction

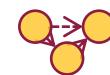
Objective

Aim 1

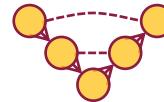
Aim 2

Aim 3

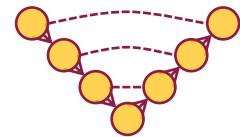
Summary



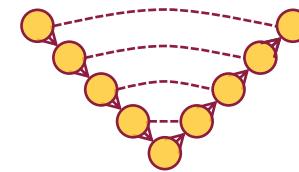
U-Net L^1



U-Net L^2

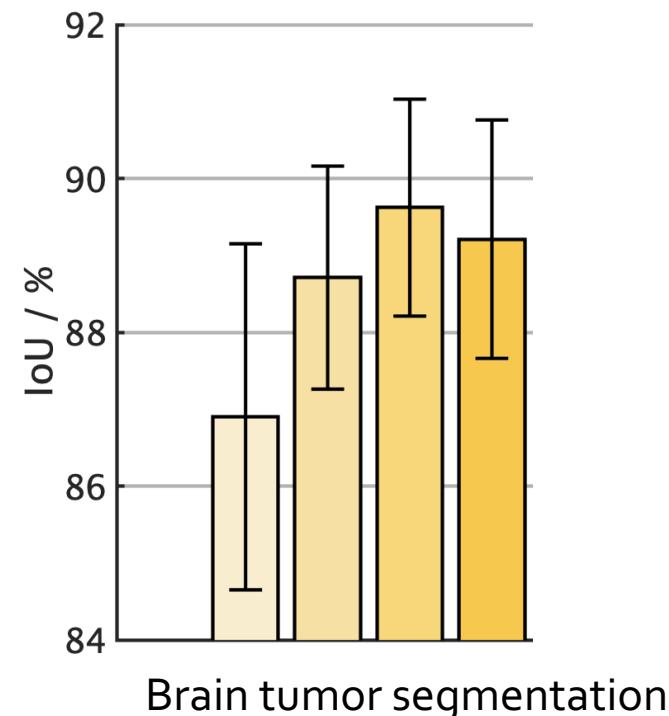
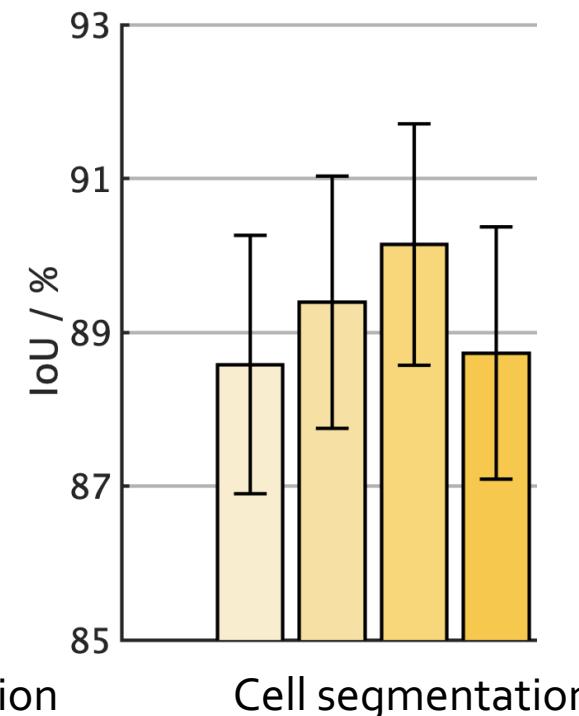
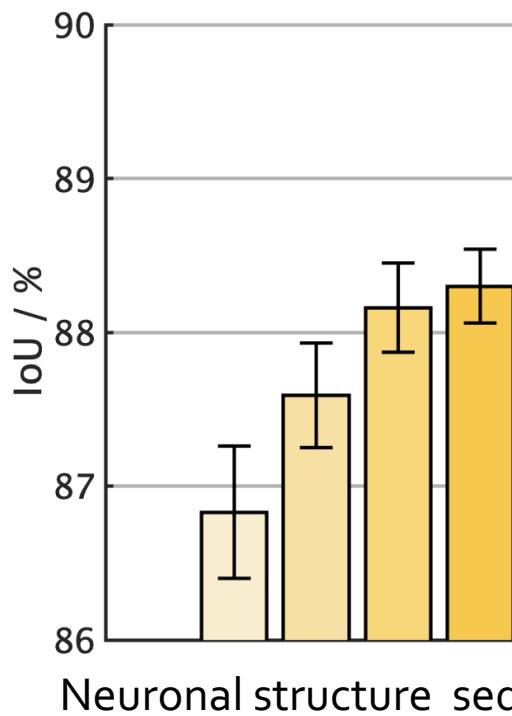


U-Net L^3



U-Net (L^4)

The best depth is unknown





Aim 2: Utilizing existing annotation effectively from advanced architecture

Approach: Redesigned skip connections aggregate multi-scale features

Introduction

Objective

Aim 1

Aim 2

Aim 3

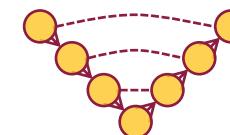
Summary



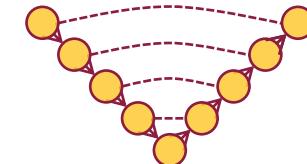
U-Net L¹



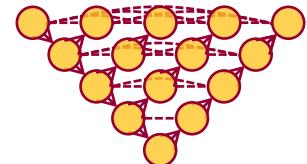
U-Net L²



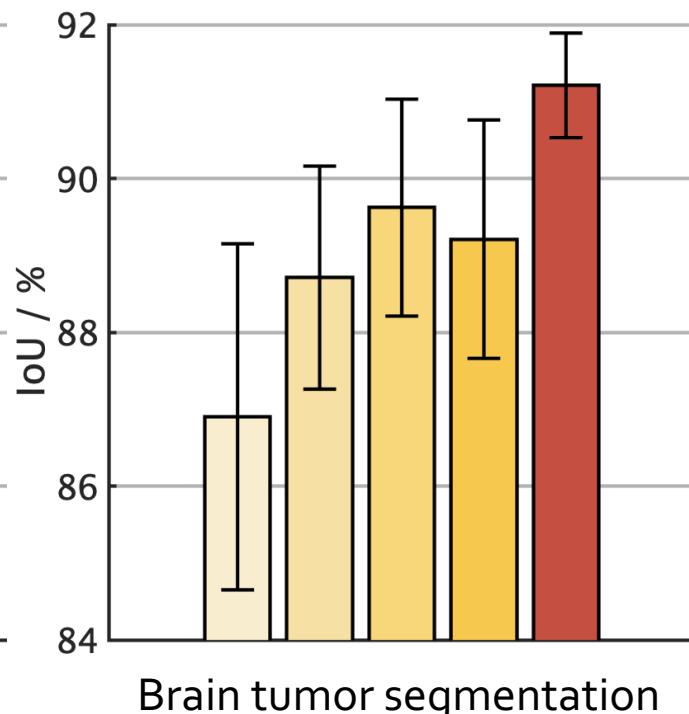
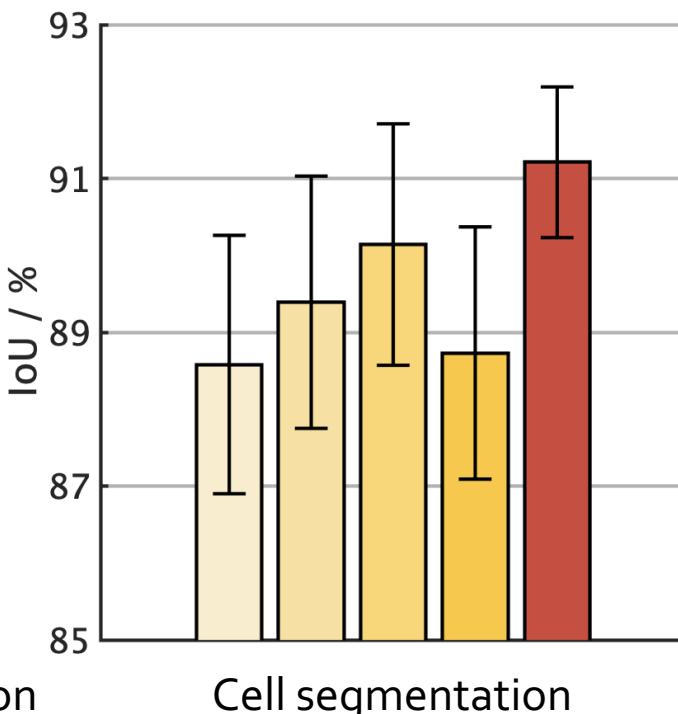
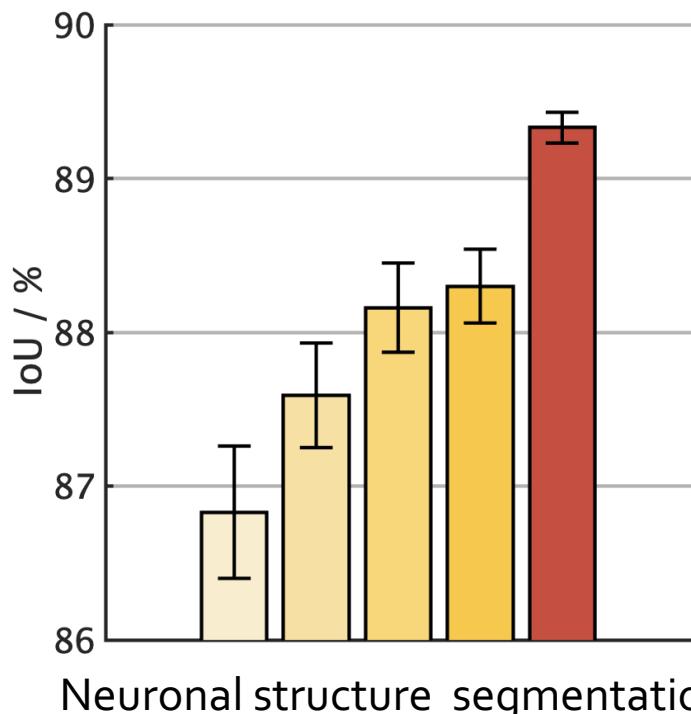
U-Net L³



U-Net (L⁴)



UNet++





Aim 2: Utilizing existing annotation effectively from advanced architecture

Approach: Redesigned skip connections aggregate multi-scale features

Introduction

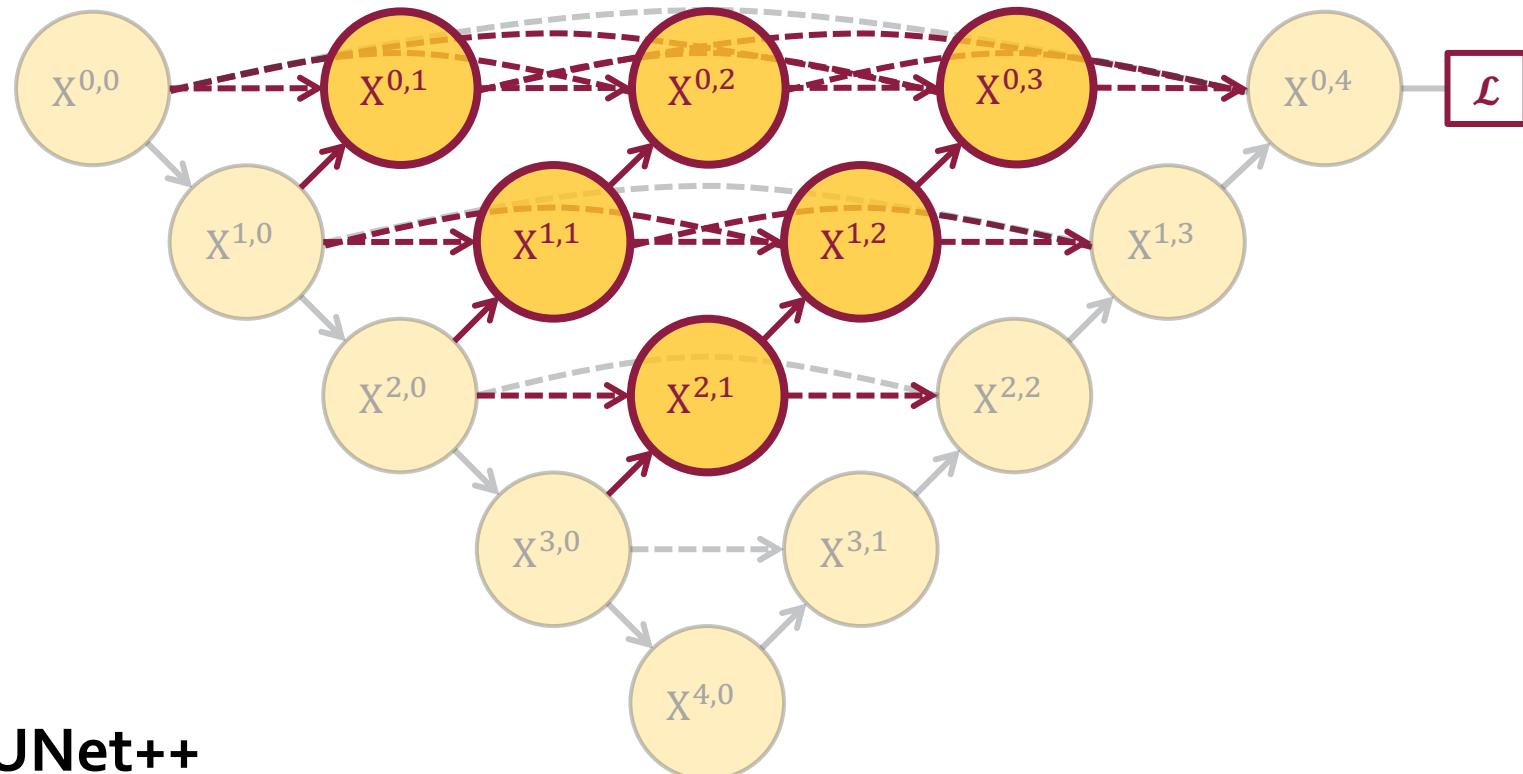
Objective

Aim 1

Aim 2

Aim 3

Summary



UNet++

1. Zhou, Zongwei, et al. "Unet++: A nested u-net architecture for medical image segmentation." DLMIA, 2018.
2. Zhou, Zongwei, et al. "Unet++: Redesigning skip connections to exploit multiscale features in image segmentation." TMI, 2019.



Aim 2: Utilizing existing annotation effectively from advanced architecture

Approach: Deep supervision stabilizes model training and enables model pruning

Introduction

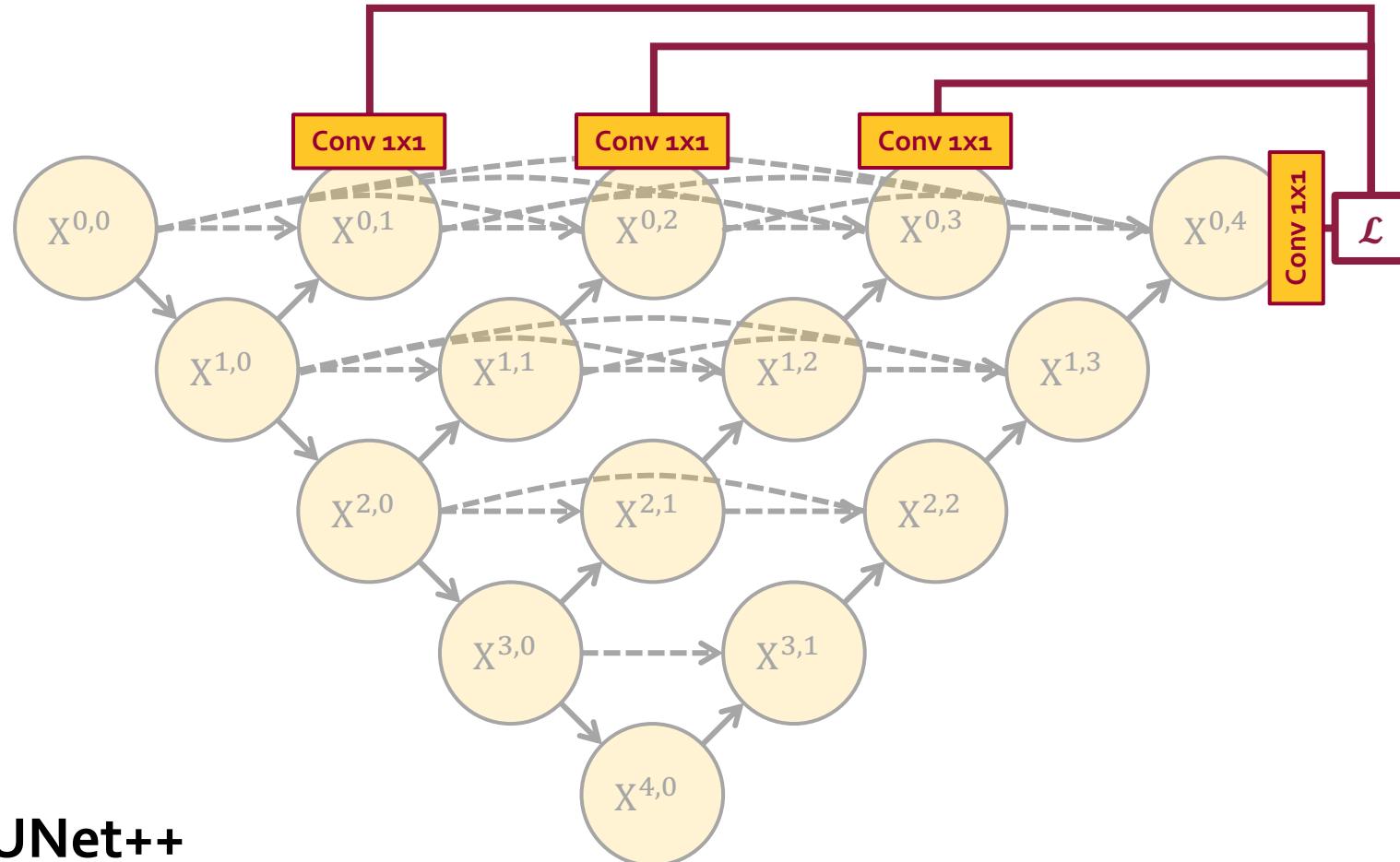
Objective

Aim 1

Aim 2

Aim 3

Summary



1. Zhou, Zongwei, et al. "Unet++: A nested u-net architecture for medical image segmentation." DLMIA, 2018.
2. Zhou, Zongwei, et al. "Unet++: Redesigning skip connections to exploit multiscale features in image segmentation." TMI, 2019.

Aim 2: Utilizing existing annotation effectively from advanced architecture

Approach: Deep supervision stabilizes model training and enables model pruning

Introduction

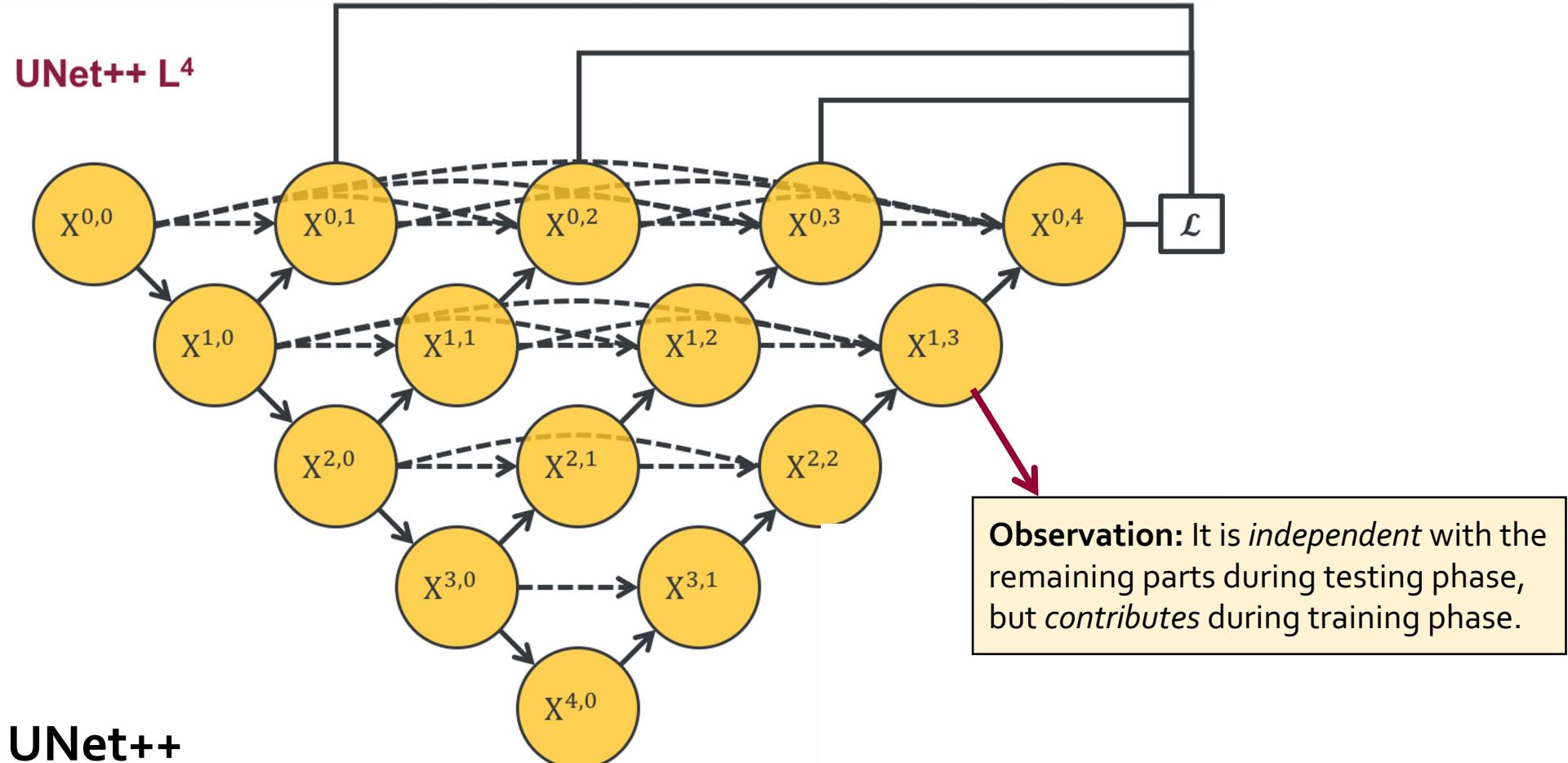
Objective

Aim 1

Aim 2

Aim 3

Summary



1. Zhou, Zongwei, et al. "Unet++: A nested u-net architecture for medical image segmentation." DLMIA, 2018.
2. Zhou, Zongwei, et al. "Unet++: Redesigning skip connections to exploit multiscale features in image segmentation." TMI, 2019.



Aim 2: Utilizing existing annotation effectively from advanced architecture

Contribution: UNet++ L² can process 2.4x more images than U-Net with similar accuracy.

Introduction

Objective

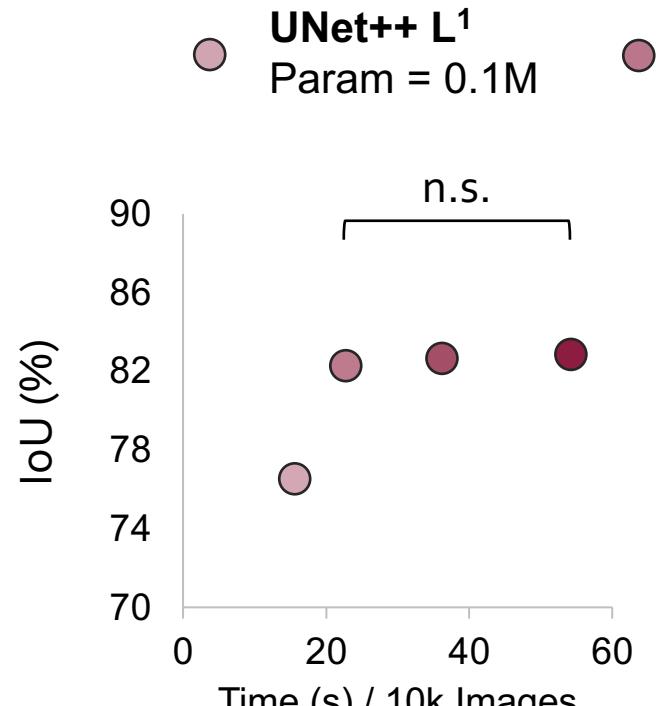
Aim 1

Aim 2

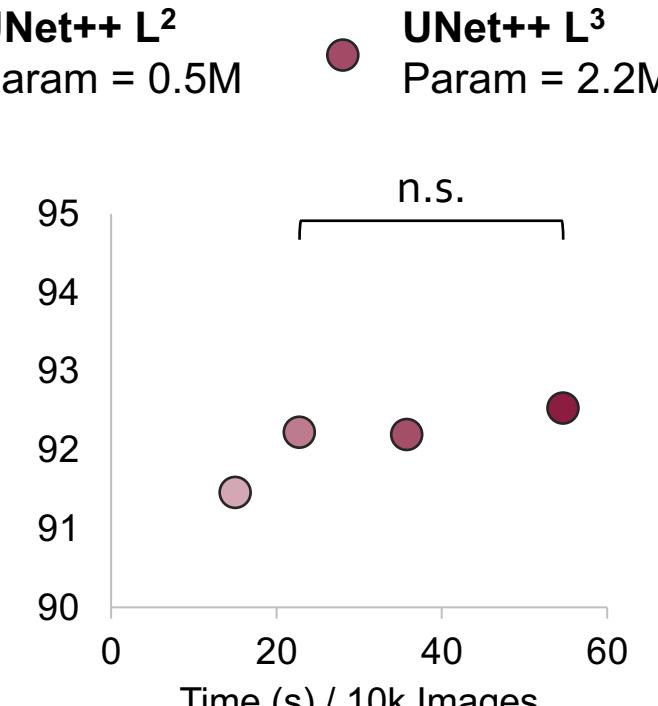
Aim 3

Summary

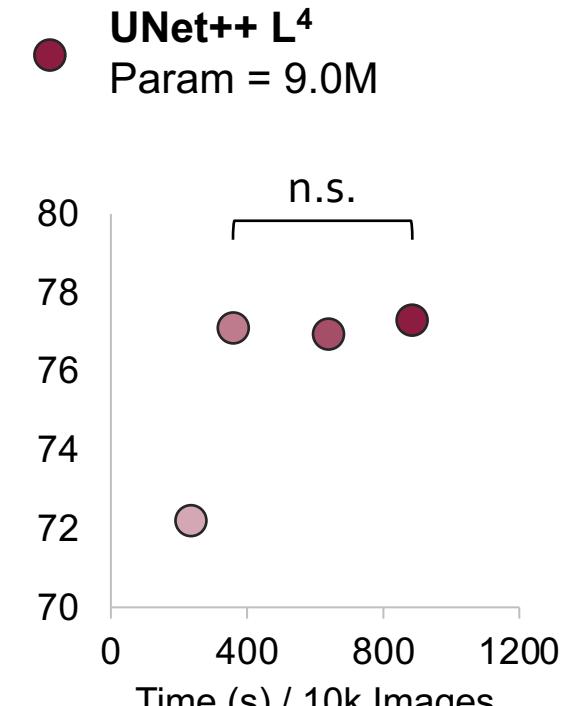
Reducing the memory footprint by 18 times!



Liver segmentation



Cell nuclei segmentation



Lung nodule segmentation

1. Zhou, Zongwei, et al. "Unet++: A nested u-net architecture for medical image segmentation." DLMIA, 2018.

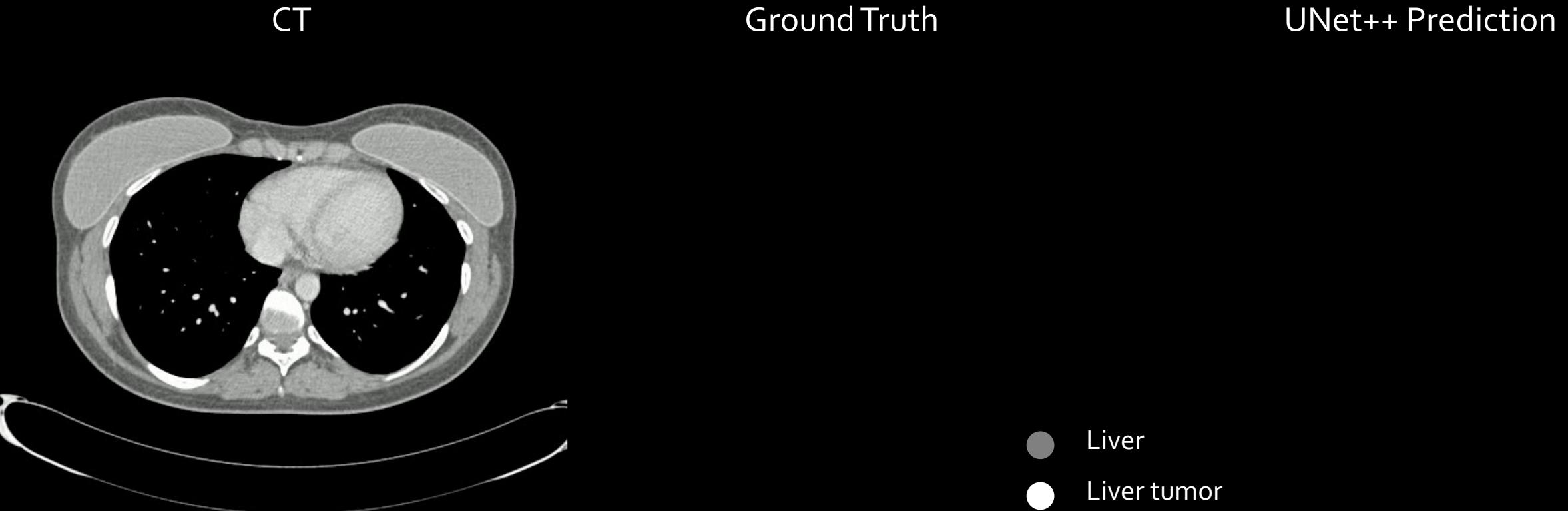
2. Zhou, Zongwei, et al. "Unet++: Redesigning skip connections to exploit multiscale features in image segmentation." TMI, 2019.

UNet++ can precisely detect tumors in CT scans



- I thank S. Bajpai for this experiment; the code can be found at <https://github.com/MrGiovanni/UNetPlusPlus/tree/master/pytorch>
- 1. Bajpai, Shivam. "Pre-Trained Models for nnUNet." Master diss., Arizona State University, 2021.
- 2. Zhou, Zongwei, et al. "Unet++: A nested u-net architecture for medical image segmentation." DLMIA, 2018.
- 3. Zhou, Zongwei, et al. "Unet++: Redesigning skip connections to exploit multiscale features in image segmentation." TMI, 2019.

UNet++ can detect very small tumors without predicting too many false positives



- I thank S. Bajpai for this experiment; the code can be found at <https://github.com/MrGiovanni/UNetPlusPlus/tree/master/pytorch>
- 1. Bajpai, Shivam. "Pre-Trained Models for nnUNet." Master diss., Arizona State University, 2021.
- 2. Zhou, Zongwei, et al. "Unet++: A nested u-net architecture for medical image segmentation." DLMIA, 2018.
- 3. Zhou, Zongwei, et al. "Unet++: Redesigning skip connections to exploit multiscale features in image segmentation." TMI, 2019.

43.9% → 58.1% (U-Net → UNet++)

Covid-19 segmentation (CT)
[Fan et al., IEEE TMI]

78.6% → 82.9% (U-Net → UNet++)

Fiber tracing (corneal confocal microscopy)
[Mou et al., MICCAI]

86.5% → 89.5% (U-Net → UNet++)

Spleen segmentation (MRI)
[Li et al., Computers & Graphics]

Intertwine the visual representation

Research Impacts of Aim 2: <https://github.com/MrGiovanni/UNetPlusPlus>

- We have made UNet++ open science to stimulate collaborations among the research community and to help translate the technology to clinical practice.

86.6% → 87.2% (U-Net → UNet++)

SegTHOR 2019 Challenge (CT)
[Zhang et al., IEEE TMI]

90.2% → 92.0% (U-Net → UNet++)

Optic Disc & Cup Segmentation (fundus image)
[Meng et al., MICCAI]

60.3% → 71.6% (U-Net → UNet++)

Ground-glass opacity segmentation (CT)
[Zheng et al., IEEE Access]

51.2% → 58.6% (U-Net → UNet++)

Esophagus segmentation (CT)
[Huang et al., IEEE Access]

63.7% → 66.3% (U-Net → UNet++)

Liver tumor segmentation (CT)
[Bajpai et al., Master Thesis]

90.7% → 91.6% (U-Net → UNet++)

Heart segmentation (MRI)
[Ji et al., MICCAI]

Unet++: A nested u-net architecture for medical image segmentation

Z Zhou, MM Rahman Siddiquee, N Tajbakhsh... - Deep learning in ..., 2018 - Springer

In this paper, we present UNet++, a new, more powerful architecture for medical image

☆ Save ⚡ Cite Cited by 2807 Related articles All 15 versions

Intertwine the visual representation

Publications for Aim 2:

- Z. Zhou, M. M. Rahman Siddiquee, N. Tajbakhsh, J. Liang, 2019. UNet++: Redesigning Skip Connections to Exploit Multi-Resolution Features in Image Segmentation. *IEEE Transactions on Medical Imaging, ranked among the most popular articles in IEEE TMI.*
- Z. Zhou, M. M. Rahman Siddiquee, N. Tajbakhsh, J. Liang, 2018. UNet++: A Nested U-Net Architecture for Medical Image Segmentation. *Deep Learn Med Image Anal Multimodal Learn Clin Decis Support.*

U.S. Patent

- US Patent 11,164,067, Systems, Methods, and Apparatuses for Implementing a Multi-resolution Neural Network for Use with Imaging Intensive Applications Including Medical Imaging

Intertwine the visual representation

Clinical Impacts of Aim 2:

- Image segmentation can help compute clinically more accurate and desirable *imaging bio-markers* or *precision measurement*.
- Model pruning has the potential to exert important impact on deploying CAD systems to *mobile devices* and *ordinary desktop/laptop PCs* in clinical practice.



Aim 3: Extracting generic knowledge directly from unannotated images

Task: Utilize 1,000,000 images without systematic annotation

Introduction

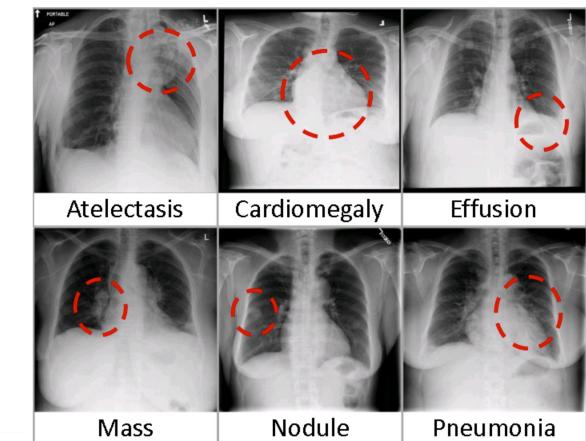
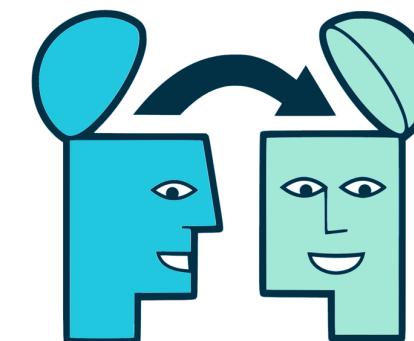
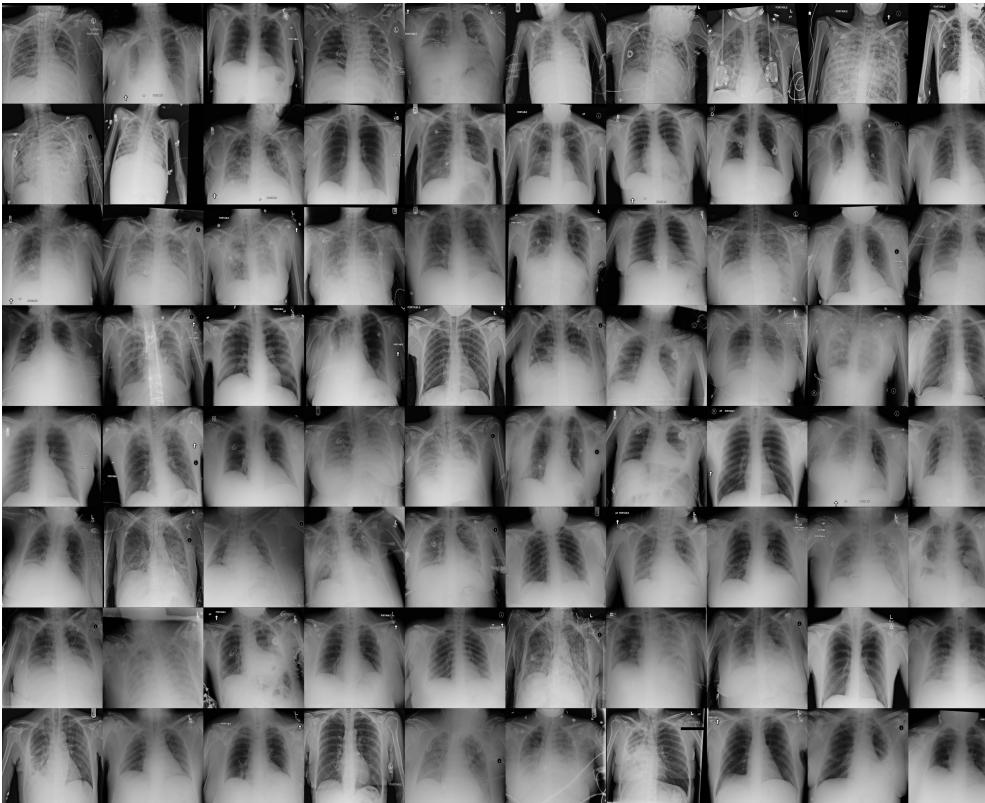
Objective

Aim 1

Aim 2

Aim 3

Summary





Aim 3: Extracting generic knowledge directly from unannotated images

Hypothesis: Generic models can be built upon consistent, recurrent anatomy

Introduction

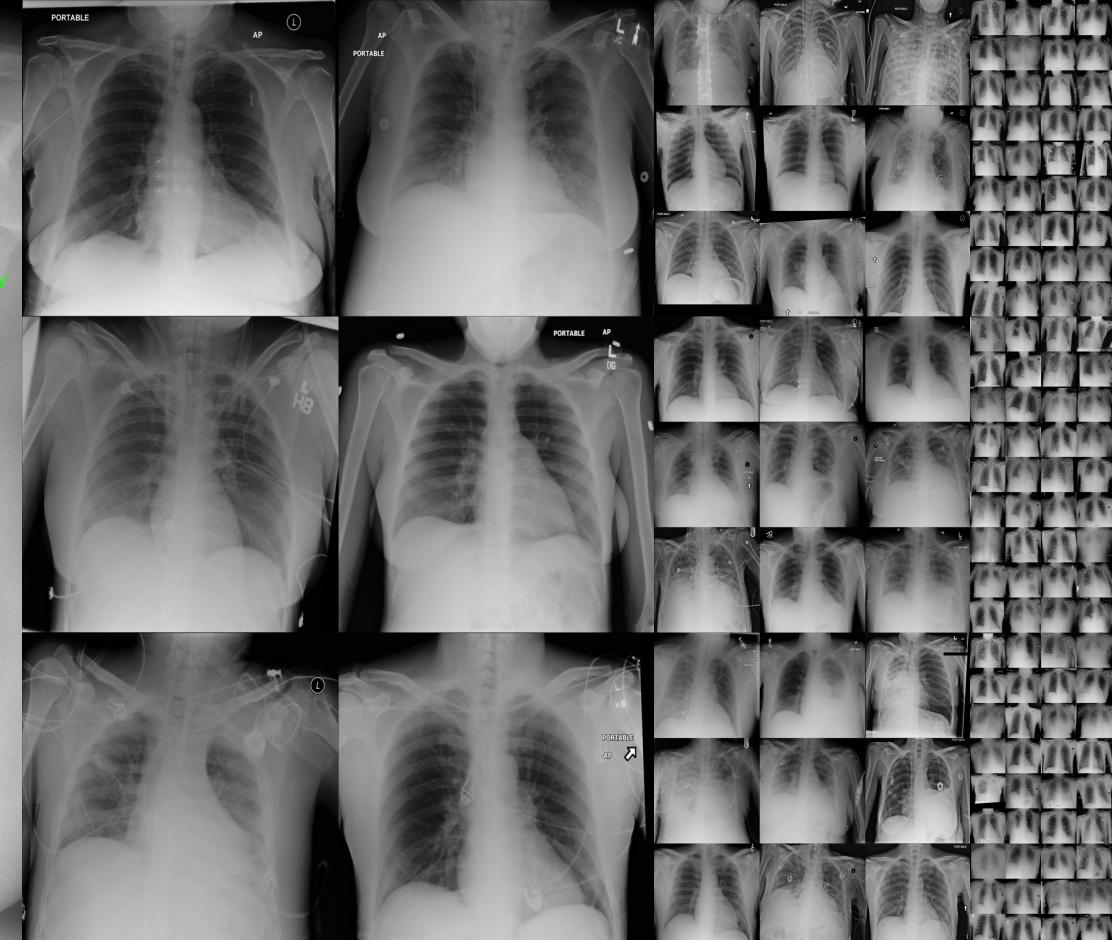
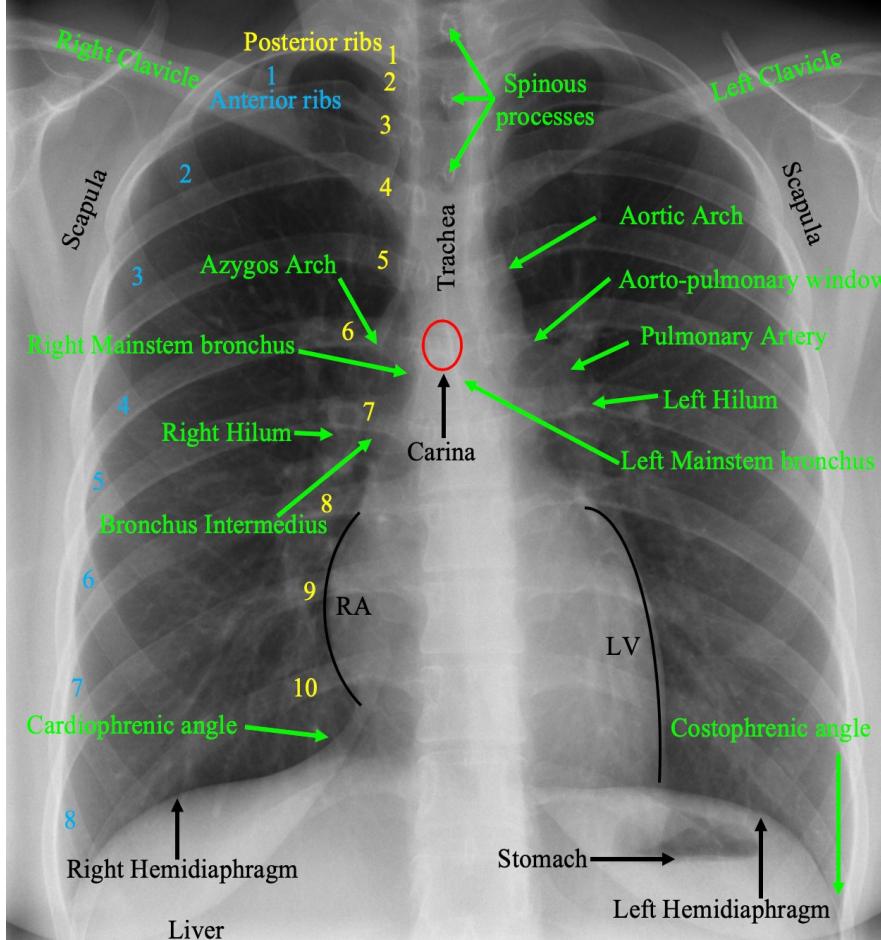
Objective

Aim 1

Aim 2

Aim 3

Summary



- I thank M. R. Hosseinzadeh Taher and M. Gotway for producing the left figure.



Aim 3: Extracting generic knowledge directly from unannotated images

Approach: Image restoration task helps model learn image representation

Introduction

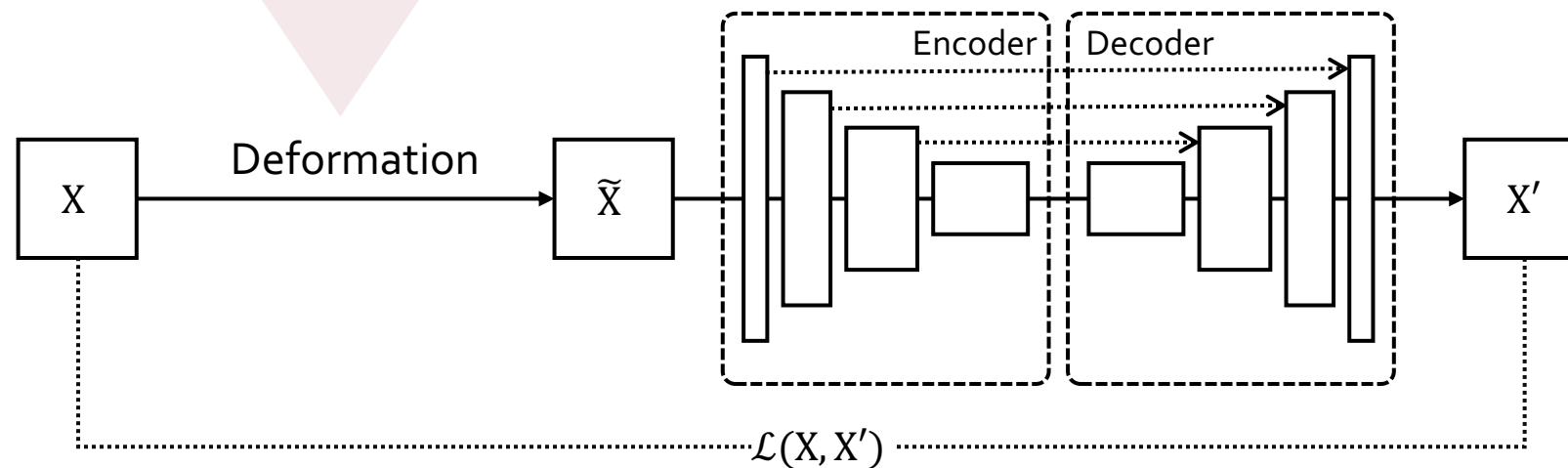
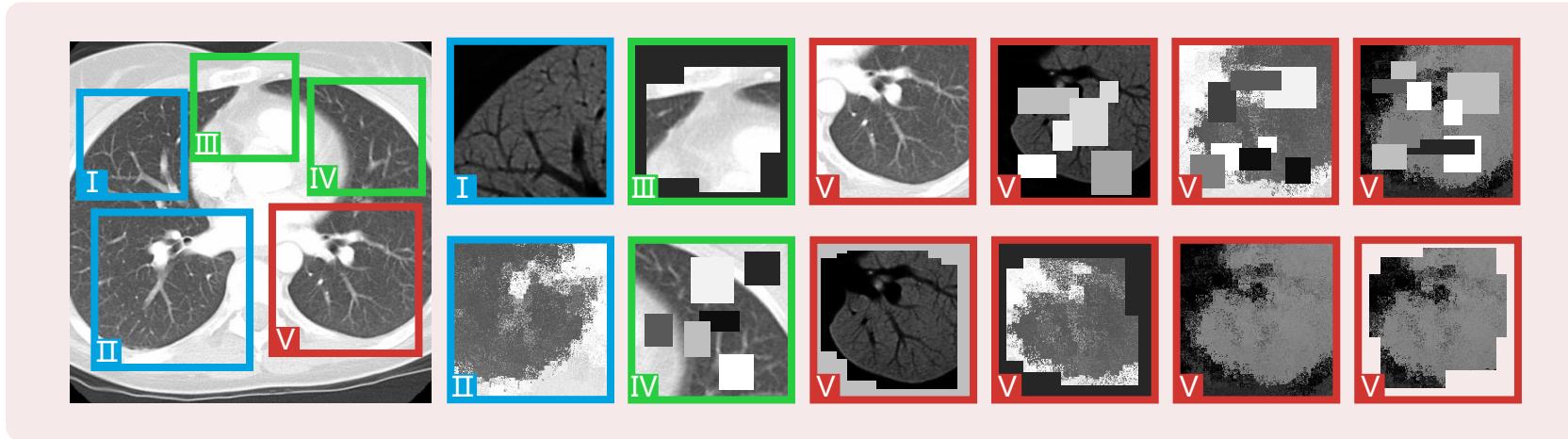
Objective

Aim 1

Aim 2

Aim 3

Summary

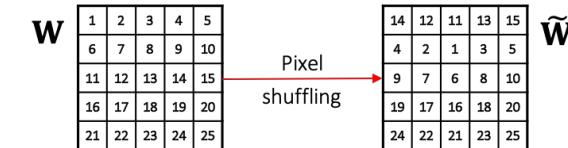
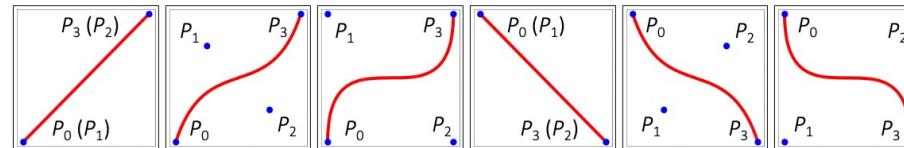




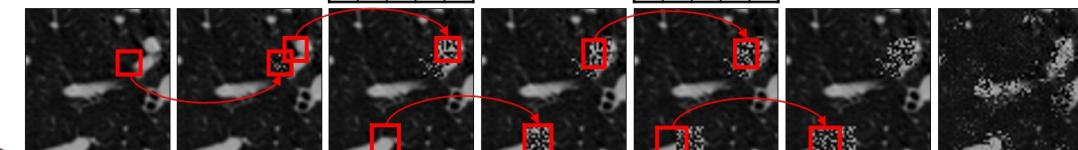
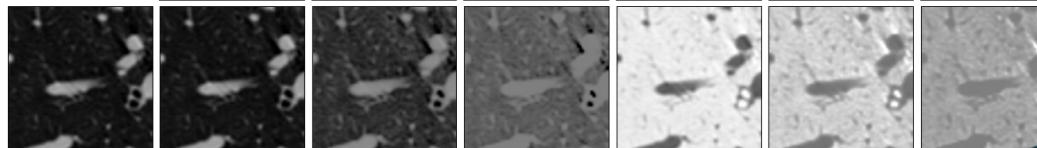
Aim 3: Extracting generic knowledge directly from unannotated images

Approach: Learning from multiple perspectives leads to robust models

Introduction



Objective



Aim 1

1. Learning organ appearance via
non-linear transformation



2. Learning organ texture and local
boundaries via **local pixel shuffling**

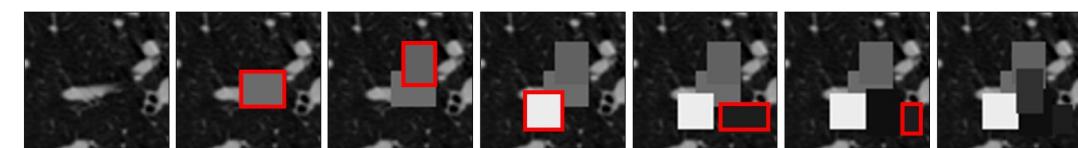
Aim 2

Aim 3

3. Learning organ spatial layout and
global geometry via **outer-cutout**



4. Learning local continuities
of organs via **inner-cutout**



Summary



Aim 3: Extracting generic knowledge directly from unannotated images

Contribution: Build generic pre-trained 3D models, named "Models Genesis"

Introduction

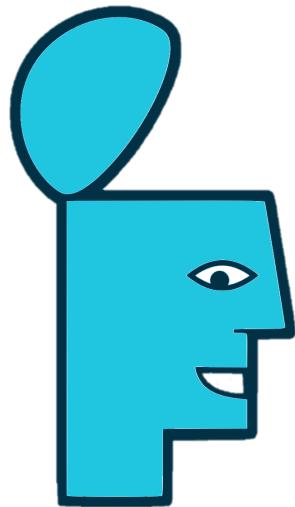
Objective

Aim 1

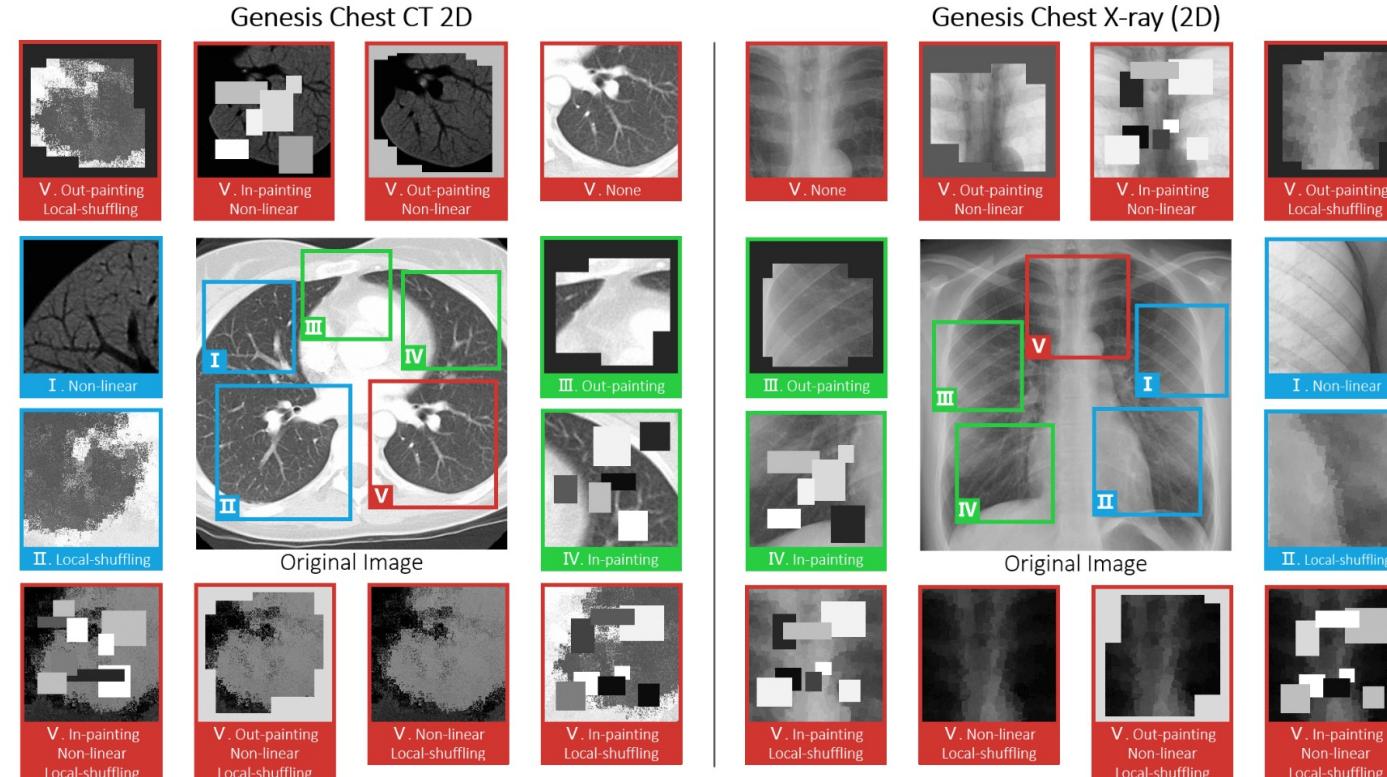
Aim 2

Aim 3

Summary



Models Genesis



1. Zhou, Zongwei, et al. "Models genesis: Generic autodidactic models for 3d medical image analysis." MICCAI, 2019.
2. Zhou, Zongwei, et al. "Models genesis." Medical image analysis, 2021.



Aim 3: Extracting generic knowledge directly from unannotated images

Contribution: Among the *first* endeavor for publicly available pre-trained 3D models

Introduction

[deepmind / kinetics-i3d](#) 240,000 annotated videos

[Watch](#) 52 [Unstar](#) 1.1k [Fork](#) 355

[Code](#) [Issues 68](#) [Pull requests 4](#) [Actions](#) [Projects 0](#) [Wiki](#) [Security](#) [Insights](#)

Objective

Convolutional neural network model for video classification trained on the Kinetics dataset.

[NifTK / NiftyNet](#) 90 annotated subjects

[Used by](#) 19 [Watch](#) 89 [Unstar](#) 1.1k [Fork](#) 365

[Code](#) [Issues 95](#) [Pull requests 3](#) [Actions](#) [Projects 3](#) [Wiki](#) [Security](#) [Insights](#)

Aim 1

An open-source convolutional neural networks platform for research in medical image analysis and image-guided therapy
<http://niftynet.io>

[Tencent / MedicalNet](#) 1,638 annotated subjects

[Unwatch](#) 43 [Unstar](#) 790 [Fork](#) 210

[Code](#) [Issues 28](#) [Pull requests 2](#) [Actions](#) [Projects 0](#) [Wiki](#) [Security](#) [Insights](#)

Aim 2

Many studies have shown that the performance on deep learning is significantly affected by volume of training data. The MedicalNet project provides a series of 3D-ResNet pre-trained models and relative code.

Summary

1. Carreira, Joao, et al. "Quo vadis, action recognition? a new model and the kinetics dataset." CVPR, 2017.
2. Gibson, Eli, et al. "NiftyNet: a deep-learning platform for medical imaging." Computer methods and programs in biomedicine, 2018.
3. Chen, Sihong, et al. "Med3d: Transfer learning for 3d medical image analysis." arXiv:1904.00625, 2019.



Aim 3: Extracting generic knowledge directly from unannotated images

Contribution: Models Genesis exceed publicly available pre-trained 3D models

Introduction

Objective	Pre-training	Approach	Target tasks				
			NCC ¹ (%)	NCS ² (%)	ECC ³ (%)	LCS ⁴ (%)	BMS ⁵ (%)
Aim 1	No	Random with Uniform Init	94.74±1.97	75.48±0.43	80.36±3.58	78.68±4.23	60.79±1.60
		Random with Xavier Init (Glorot and Bengio, 2010)	94.25±5.07	74.05±1.97	79.99±8.06	77.82±3.87	58.52±2.61
		Random with MSRA Init (He et al., 2015)	96.03±1.82	76.44±0.45	78.24±3.60	79.76±5.43	63.00±1.73
Aim 2	(Fully) supervised	I3D (Carreira and Zisserman, 2017)	98.26±0.27	71.58±0.55	80.55±1.11	70.65±4.26	67.83±0.75
		NiftyNet (Gibson et al., 2018b)	94.14±4.57	52.98±2.05	77.33±8.05	83.23±1.05	60.78±1.60
		MedicalNet (Chen et al., 2019b)	95.80±0.49	75.68±0.32	86.43±1.44	85.52±0.58 [†]	66.09±1.35
Aim 3	Self-supervised	De-noising (Vincent et al., 2010)	95.92±1.83	73.99±0.62	85.14±3.02	84.36±0.96	57.83±1.57
		In-painting (Pathak et al., 2016)	91.46±2.97	76.02±0.55	79.79±3.55	81.36±4.83	61.38±3.84
		Jigsaw (Noroozi and Favaro, 2016)	95.47±1.24	70.90±1.55	81.79±1.04	82.04±1.26	63.33±1.11
		DeepCluster (Caron et al., 2018)	97.22±0.55	74.95±0.46	84.82±0.62	82.66±1.00	65.96±0.85
		Patch shuffling (Chen et al., 2019a)	91.93±2.32	75.74±0.51	82.15±3.30	82.82±2.35	52.95±6.92
		Rubiks Cube (Zhuang et al., 2019)	96.24±1.27	72.87±0.16	80.49±4.64	75.59±0.20	62.75±1.93
Summary		Genesis Chest CT (ours)	98.34±0.44	77.62±0.64	87.20±2.87	85.10±2.15	67.96±1.29

¹NCC Lung nodule false positive reduction in CT images

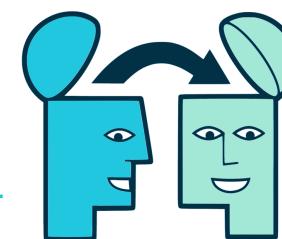
²NCS Lung nodule segmentation in CT images

³ECC Pulmonary embolism false positive reduction in CT images

⁴LCS Liver segmentation in CT images

⁵BMS Brain tumor segmentation in MR images

Genesis Chest CT



Target models

- I thank Z. Guo, F. Haghghi, M. R. Hosseinzadeh Taher, M. M. Rahman Siddiquee, and P. Zhang for their supports in experiments.
- Zhou, Zongwei, et al. "Models genesis: Generic autodidactic models for 3d medical image analysis." MICCAI, 2019.
- Zhou, Zongwei, et al. "Models genesis." Medical image analysis, 2021.



Aim 3: Extracting generic knowledge directly from unannotated images

Contribution: Models Genesis reduce annotation efforts by at least 30%

Introduction

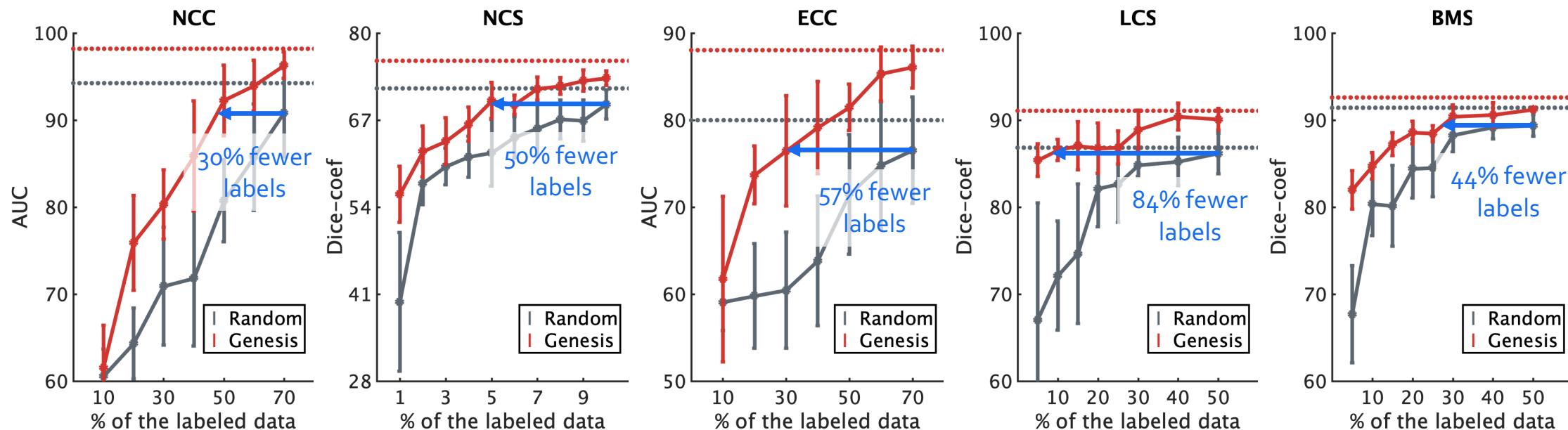
Objective

Aim 1

Aim 2

Aim 3

Summary



¹NCC Lung nodule false positive reduction in CT images

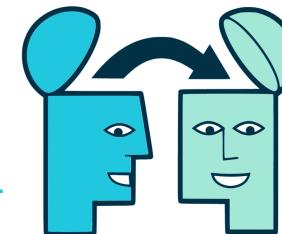
²NCS Lung nodule segmentation in CT images

³ECC Pulmonary embolism false positive reduction in CT images

⁴LCS Liver segmentation in CT images

⁵BMS Brain tumor segmentation in MR images

Genesis Chest CT



Target models

1. Zhou, Zongwei, et al. "Models genesis: Generic autodidactic models for 3d medical image analysis." MICCAI, 2019.

2. Zhou, Zongwei, et al. "Models genesis." Medical image analysis, 2021.



Aim 3: Extracting generic knowledge directly from unannotated images

Discussion: Extend to modality-oriented and organ-oriented models

Introduction

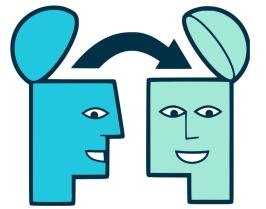
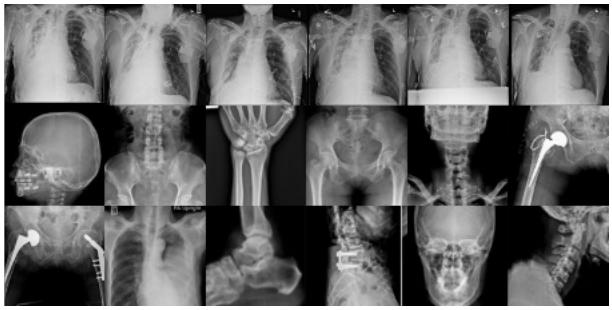
Objective

Aim 1

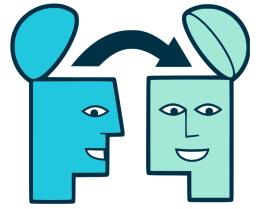
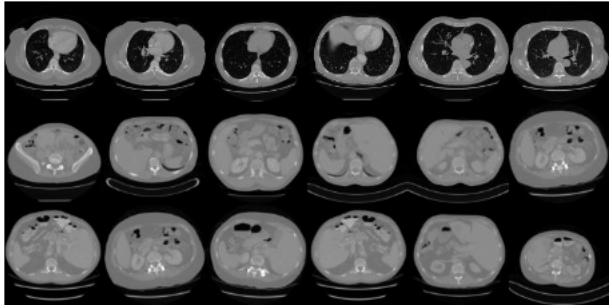
Aim 2

Aim 3

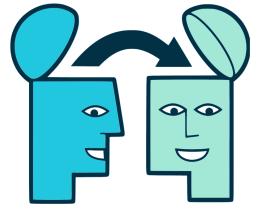
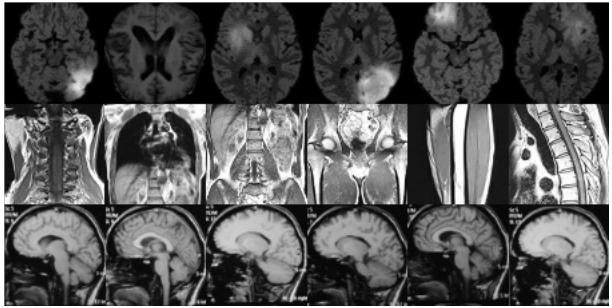
Summary



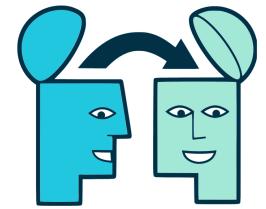
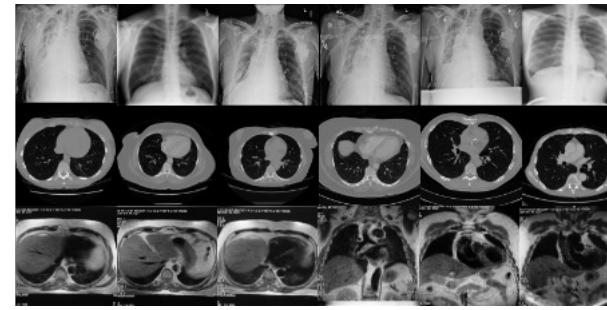
Genesis X-ray



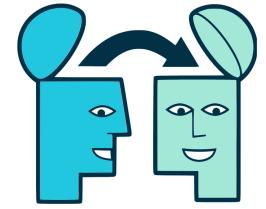
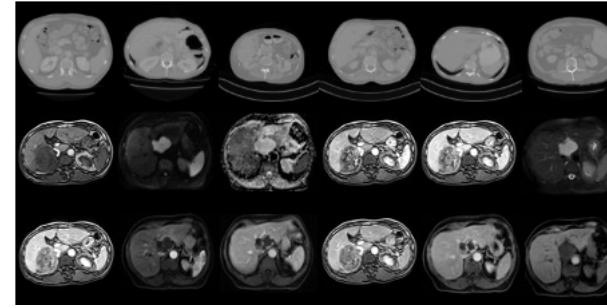
Genesis CT



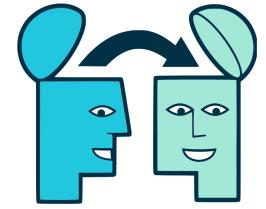
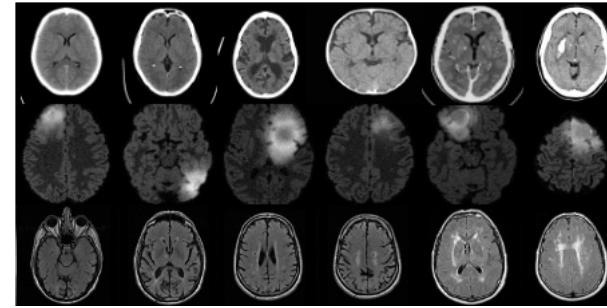
Genesis MRI



Genesis Lung



Genesis Liver



Genesis Brain

69.0% → 73.9% (Scratch → MG)

Prostate segmentation (MRI)

[Taleb et al., arXiv:1912.05396, 2019]

83.1% → 88.3% (Scratch → MG)

Lymph node classification (histology)

[Xu et al., BIBM, 2020]

72.3% → 85.8% (Scratch → MG)

Brain hemorrhage classification (CT)

[Zhu et al., arXiv:2012.07477, 2020]

Effective image features across diseases, organs, and modalities.

Research Impacts of Aim 3: <https://github.com/MrGiovanni/ModelsGenesis>

- We have made Models Genesis open science to stimulate collaborations among the research community and to help translate the technology to clinical practice.

67.0% → 74.5% (Scratch → MG)

Blood cavity segmentation (MRI)

[Zhang et al., arXiv:2010.06107, 2020]

67.8% → 69.3% (Scratch → MG)

13 organ segmentation (CT)

[Xie et al., arXiv:2011.12640, 2020]

90.0% → 95.0% (Scratch → MG)

Liver segmentation (CT&MRI)

[Taleb et al., arXiv:1912.05396, 2019]

77.5% → 92.5% (Scratch → MG)

COVID-19 classification (CT)

[Sun et al., arXiv:2012.06457, 2020]

76.0% → 77.5% (Scratch → MG)

Liver tumor segmentation (CT)

[Bajpai et al., Master Thesis, 2021]

74.0% → 79.3% (Scratch → MG)

Alzheimer's disease classification (MRI)

[Zhang et al., arXiv:2010.06107, 2020]

Effective image features across diseases, organs, and modalities.

Publications for Aim 3:

- Z. Zhou, V. Sodha, M. M. Rahman Siddiquee, R. Feng, N. Tajbakhsh, M. Gotway, J. Liang, 2019. Models Genesis: Generic Autodidactic Models for 3D Medical Image Analysis. *MICCAI'19, Young Scientist Award, Young Scientist Publication Impact Award Finalist*
- Z. Zhou, V. Sodha, J. Pang, M. Gotway, J. Liang, 2020. Models Genesis. *Medical Image Analysis, MedIA Best Paper Award.*

Effective image features across diseases, organs, and modalities.

Clinical Impacts of Aim 3:

- Instead of building a model from scratch (demanding numerous data and label acquisition), a *smaller dataset* can be used to efficiently fine-tune the existing model.
- Generic pre-trained models can serve as a *primary source of transfer learning* for many medical imaging applications, leading to accelerated training and improved performance.



Introduction

Objective

Aim 1

Aim 2

Aim 3

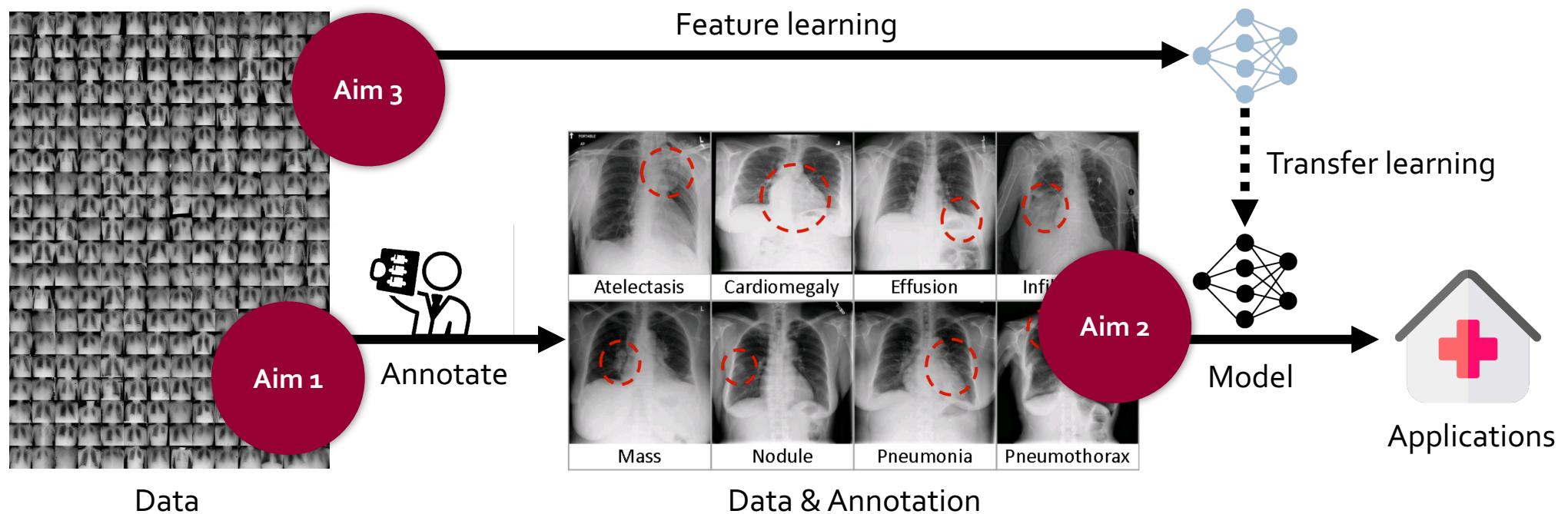
Summary

Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Aim 3: Extracting generic knowledge directly from unannotated images





Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary

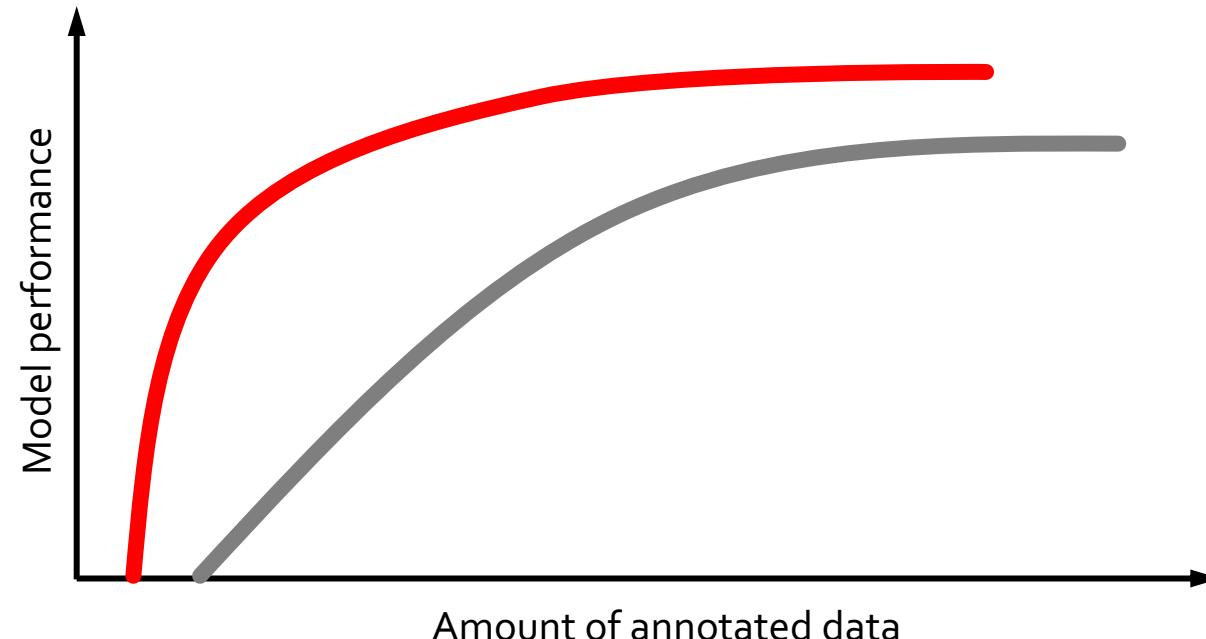
Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Aim 3: Extracting generic knowledge directly from unannotated images

Hypothesis: With a small part of the dataset annotated, we can deliver deep models that approximate or even outperform those that require annotating the entire dataset.





Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary

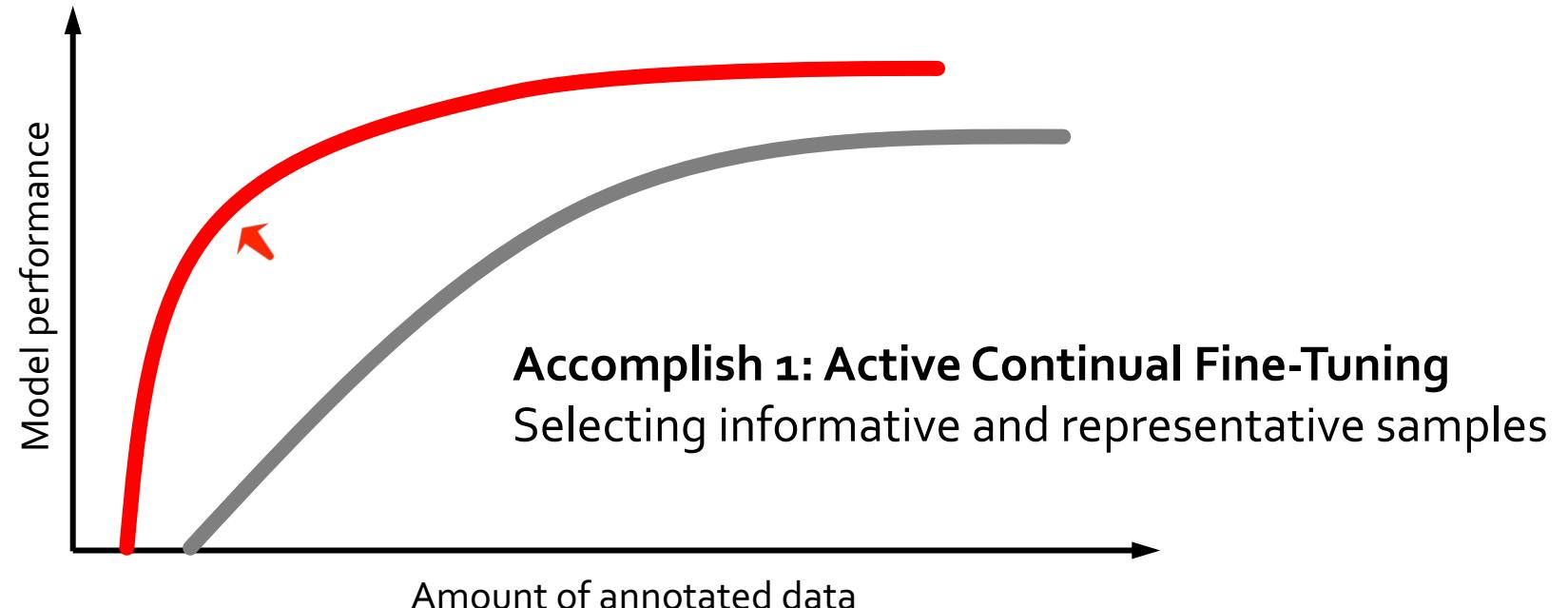
Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Aim 3: Extracting generic knowledge directly from unannotated images

Conclusion: With a small part of the dataset annotated, we can deliver deep models that approximate or even outperform those that require annotating the entire dataset. **Yes, we can!**





Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary

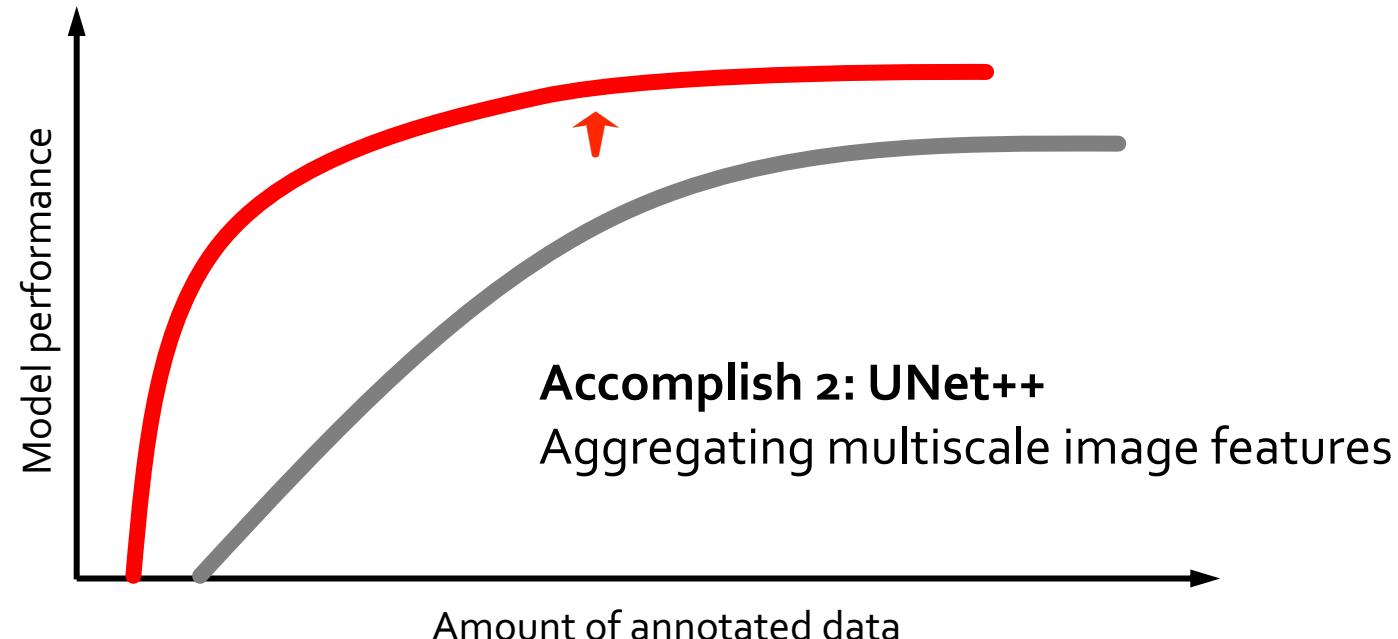
Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Aim 3: Extracting generic knowledge directly from unannotated images

Conclusion: With a small part of the dataset annotated, we can deliver deep models that approximate or even outperform those that require annotating the entire dataset. **Yes, we can!**





Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary

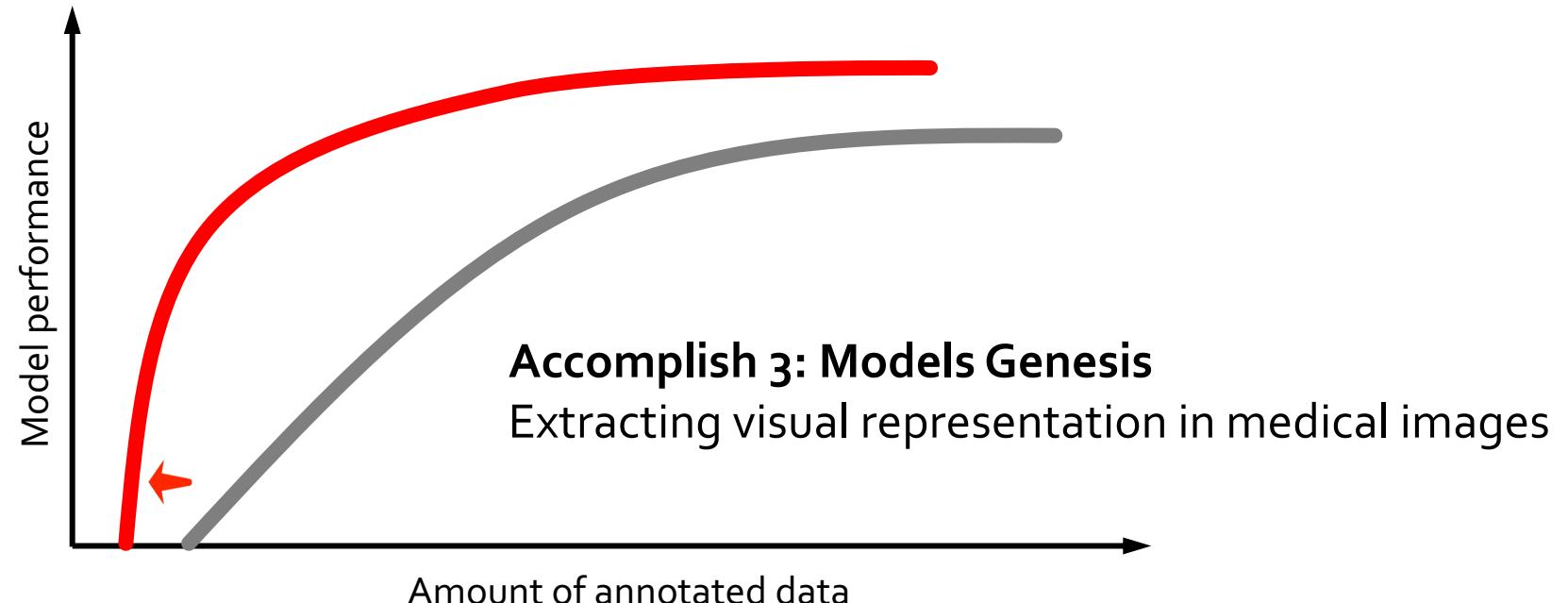
Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Aim 3: Extracting generic knowledge directly from unannotated images

Conclusion: With a small part of the dataset annotated, we can deliver deep models that approximate or even outperform those that require annotating the entire dataset. **Yes, we can!**





Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary

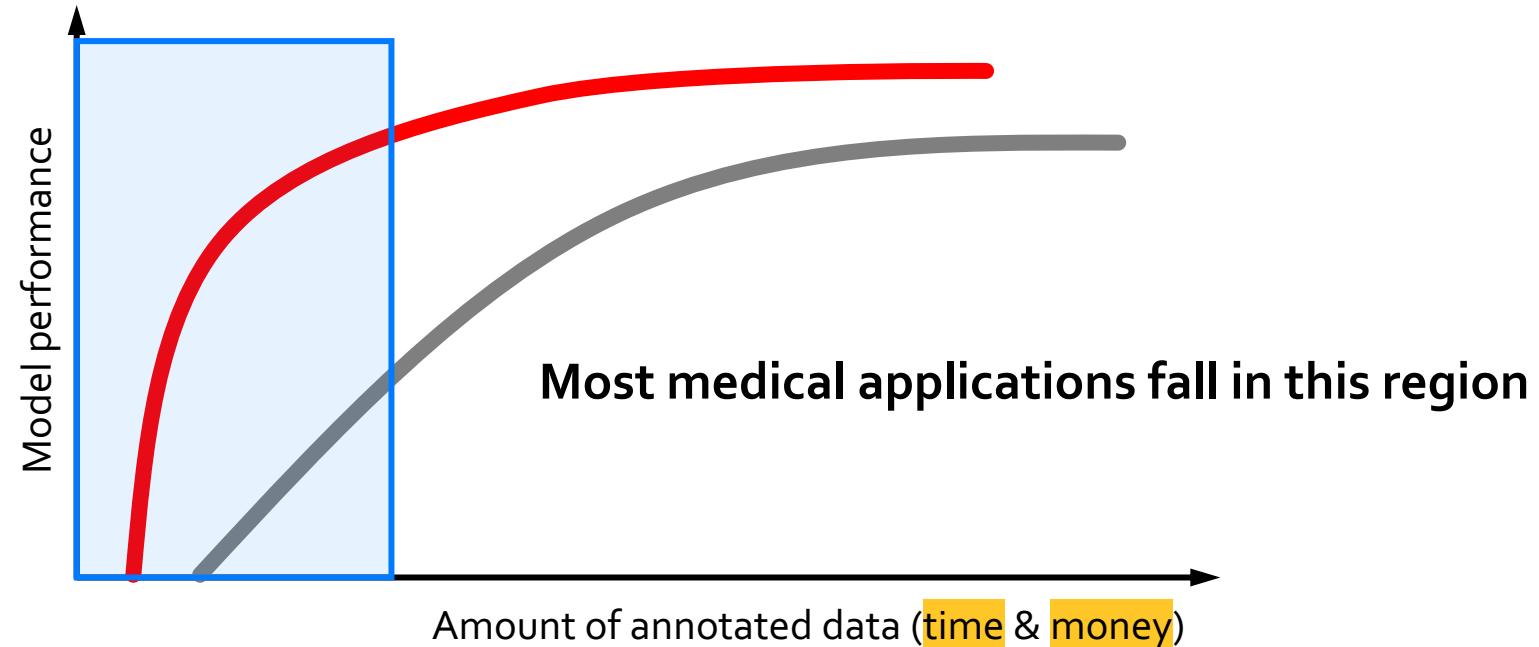
Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aim 1: Acquiring necessary annotation efficiently from human experts

Aim 2: Utilizing existing annotation effectively from advanced architecture

Aim 3: Extracting generic knowledge directly from unannotated images

Conclusion: With a small part of the dataset annotated, we can deliver deep models that approximate or even outperform those that require annotating the entire dataset. **Yes, we can!**





Introduction

Objective

Aim 1

Aim 2

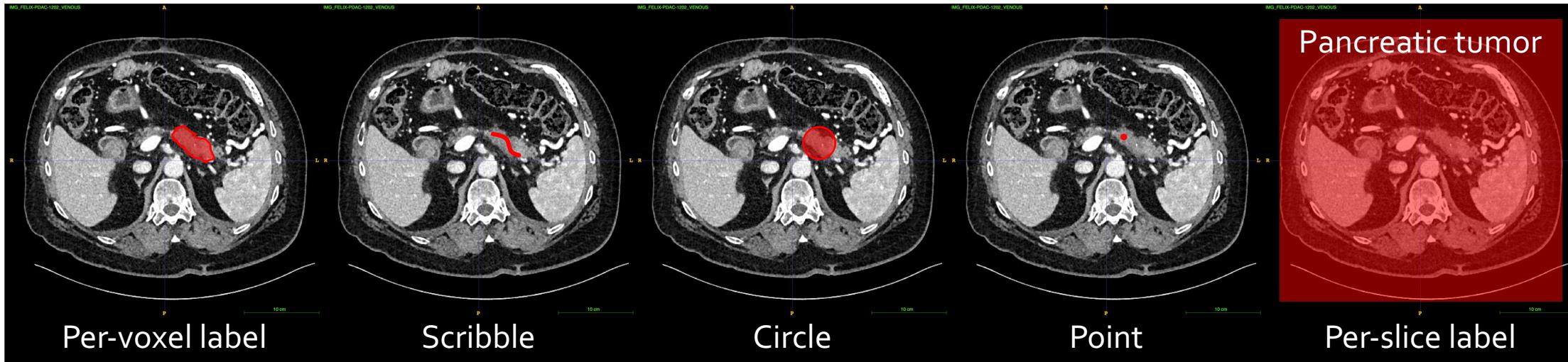
Aim 3

Summary

Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

Aims 1-3 (PhD): Reducing *detailed* annotation (per-voxel labels)

Aim Pro: Investigating *weak* annotation (scribble, circle, point, per-slice labels, etc.)



**15 human-year
to create**

Sensitivity = 92.4%
Specificity = 93.0%



**x10 faster
to create**

Sensitivity = 92.5%
Specificity = 91.3%

1. Yang, Shuojue et al. "Pancreatic Ductal Adenocarcinoma (PDAC) Detection Using Per-Slice Annotation." Radiological Society of North America (RSNA), 2022. (Oral Presentation)



Introduction

Objective

Aim 1

Aim 2

Aim 3

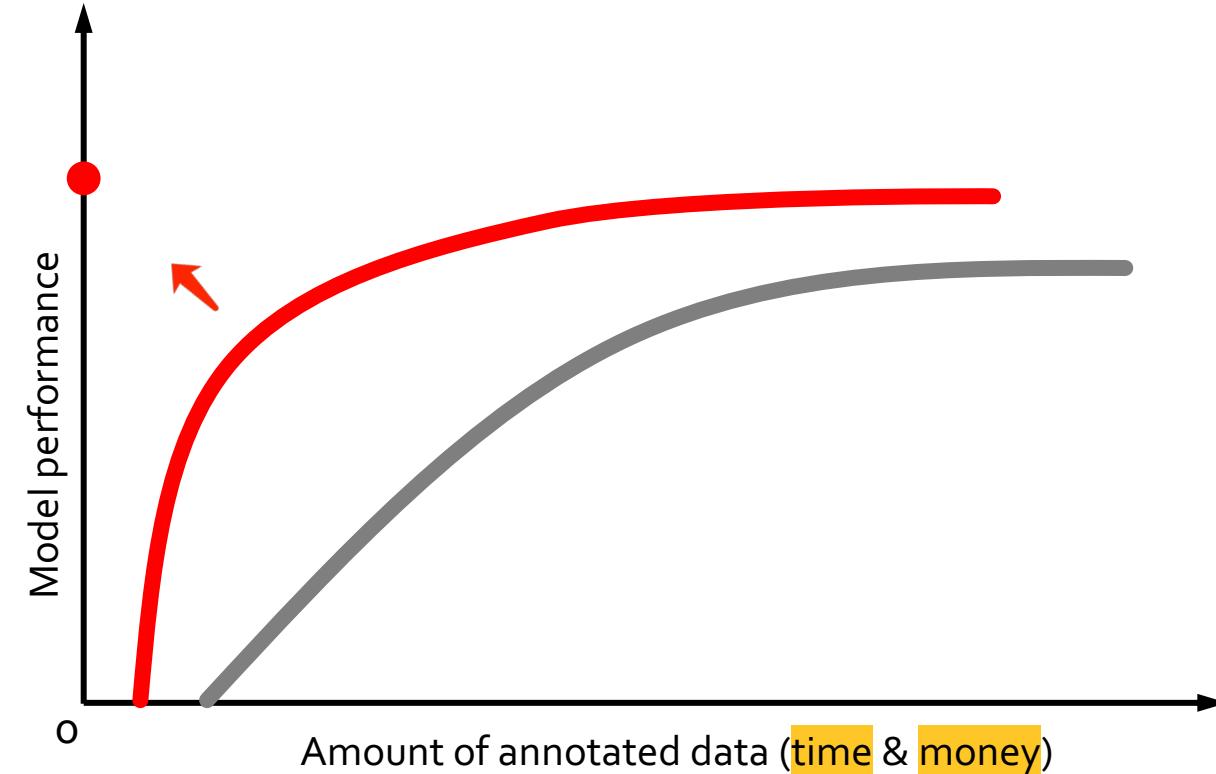
Summary

Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

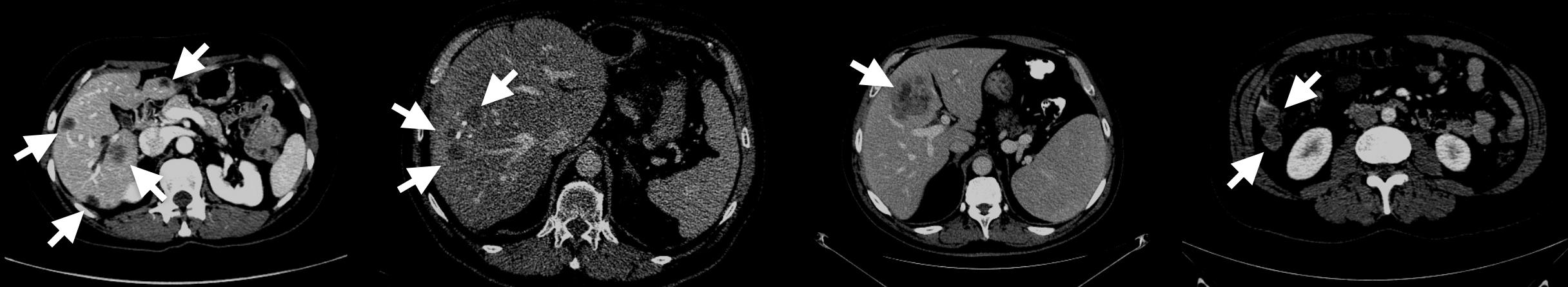
Aims 1-3 (PhD): Reducing *detailed* annotation (per-voxel labels)

Aim Pro: Investigating *weak* annotation (per-slice, points, scribbles, boxes, etc.)

Aim Pro Max: Exploring *ultra-weak* annotation (radiology reports, synthetic data, etc.)



Medical professionals with over 6-year experience cannot tell which are real and which are synthetic tumors

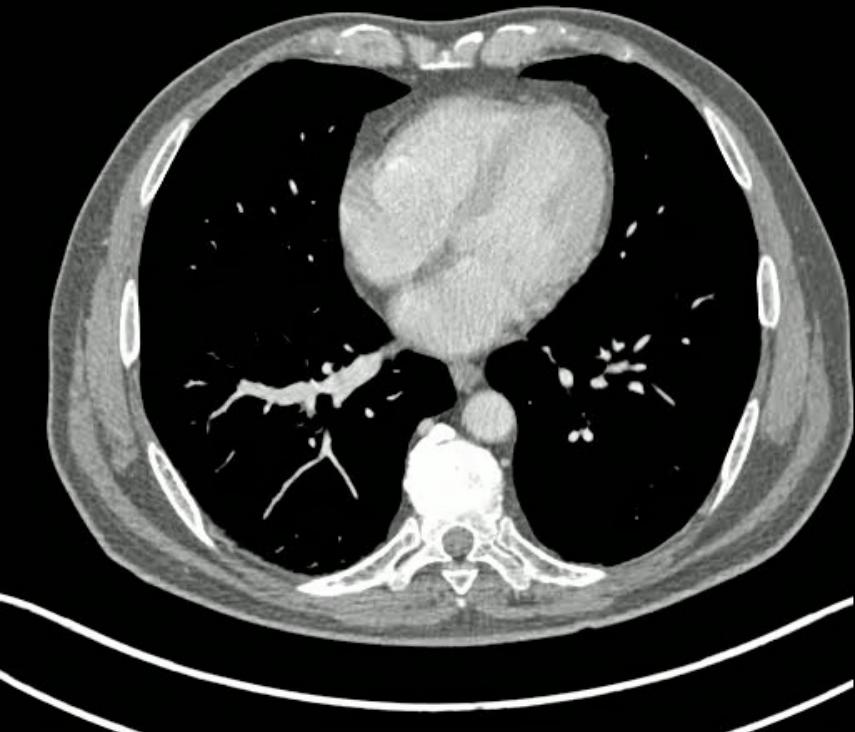


Can you?



Training AI on synthetic tumors performs almost as well as training it on real tumors.

CT



UNet++ prediction
trained on real tumors
with per-voxel annotation

UNet++ prediction
trained on synthetic tumors
with no annotation

- Liver
- Liver tumor



Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary

Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

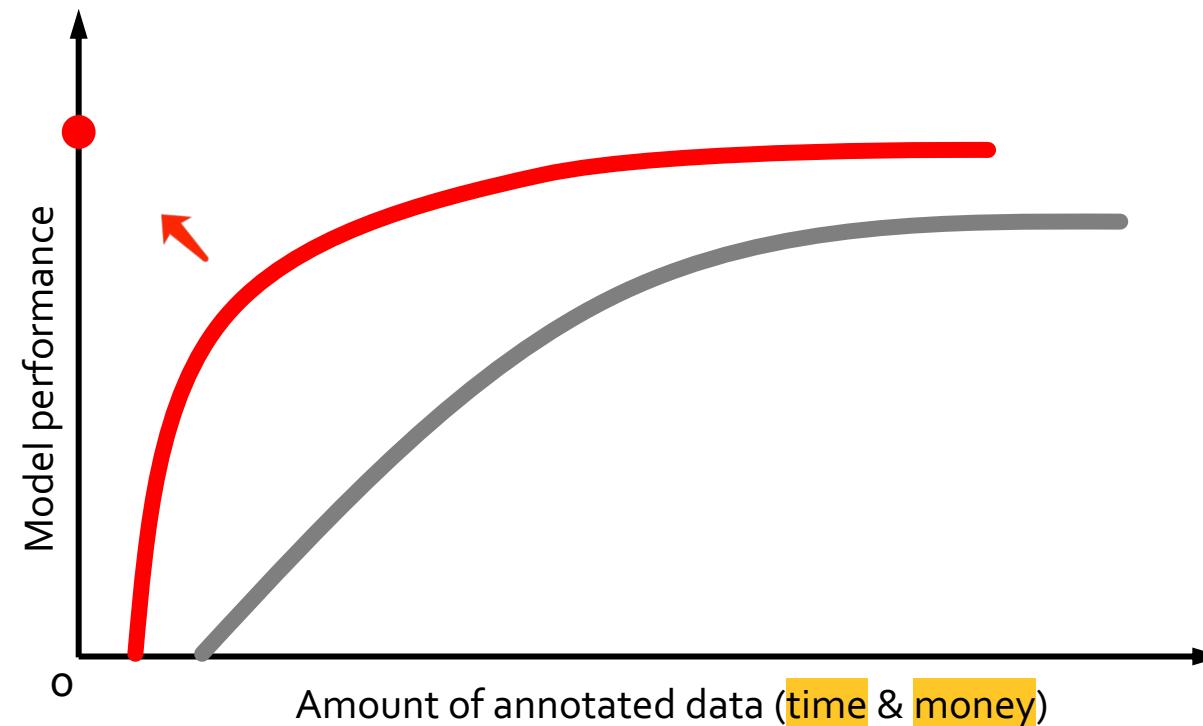
Aims 1-3 (PhD): Reducing *detailed* annotation (per-voxel labels)

Aim Pro: Investigating *weak* annotation (per-slice, points, scribbles, boxes, etc.)

Aim Pro Max: Exploring *ultra-weak* annotation (radiology reports, synthetic data, etc.)

I am actively looking for a faculty position to make this happen :)

- *Imaging Informatics, Computer Vision, Healthcare*





Introduction

Objective

Aim 1

Aim 2

Aim 3

Summary

Goal: Minimize manual annotation efforts for rapid, precise computer-aided diagnosis systems

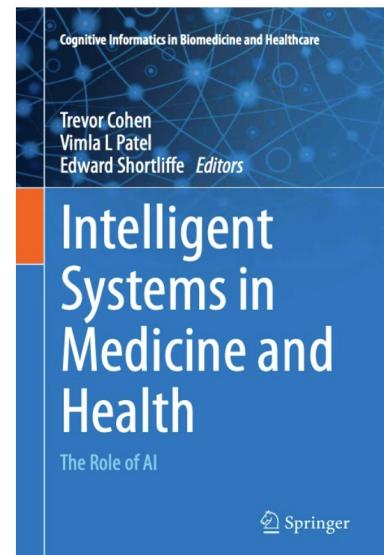
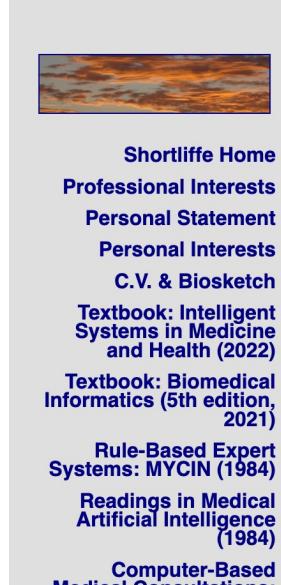
Aims 1-3 (PhD): Reducing *detailed* annotation (per-voxel labels)

Aim Pro: Investigating *weak* annotation (per-slice, points, scribbles, boxes, etc.)

Aim Pro Max: Exploring *ultra-weak* annotation (radiology reports, synthetic data, etc.)

Interpreting Medical Images: A book chapter that overviews AI in medical image interpretation

Edward H. Shortliffe, MD, PhD



Available as both an e-book and in hard copy
(671 pages)

Intelligent Systems in Medicine and Health:

The Role of AI

T.A. Cohen, V.L. Patel, and E.H. Shortliffe, Editors

Table of Contents

Front Matter

Dedication

Foreword by Bruce G. Buchanan

Preface and Acknowledgements

Table of Contents and Contributors

I. Introduction

1. Introducing AI in Medicine: A Cognitive Informatics Perspective

Trevor A. Cohen, Vimla L. Patel, and Edward H. Shortliffe

1. Zhou, Zongwei et al. "Interpreting Medical Images." In Cognitive Informatics in Biomedicine and Healthcare. Intelligent Systems in Medicine and Health: The Role of AI. T. Cohen, V. Patel and E. Shortliffe (eds.). Springer Nature, 2022.



THANK YOU

- Jianming Liang, Ph.D.
- Edward H. Shortliffe, M.D., Ph.D.
- Robert A. Greenes, Ph.D.
- Baoxin Li, Ph.D.
- Michael B. Gotway, M.D.
- Murthy Devarakonda, Ph.D.
- Alan L. Yuille, Ph.D.

Funding for research program supported by

- NIH R01 (R01HL128785)
- ASU-Mayo Grant
- Mayo Innovation Grant



Credit: Baymax!

Towards Annotation-Efficient Deep Learning for Computer-Aided Diagnosis

Zongwei Zhou

Postdoc, Department of Computer Science
Johns Hopkins University, Baltimore, MD
P: 1-(480)738-2575 | E: zzhou82@jh.edu