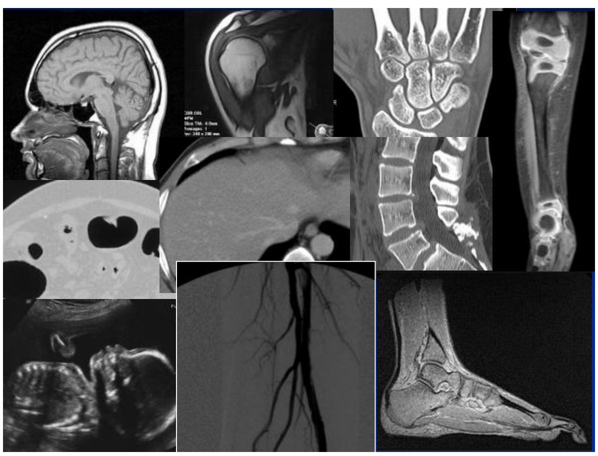
Artificial Intelligence for Computer-Aided Diagnosis in Medical Imaging

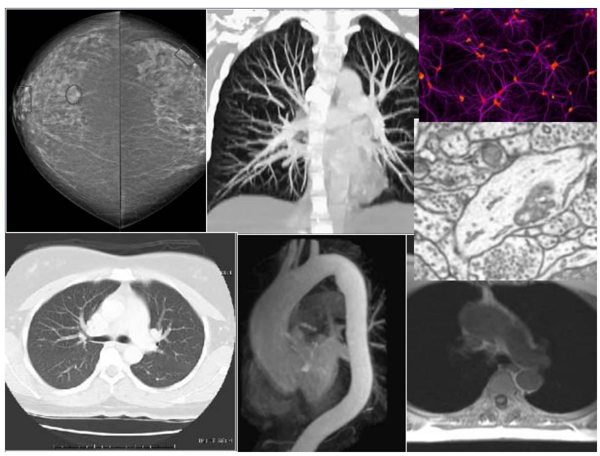
Jianming (Jimmy) Liang

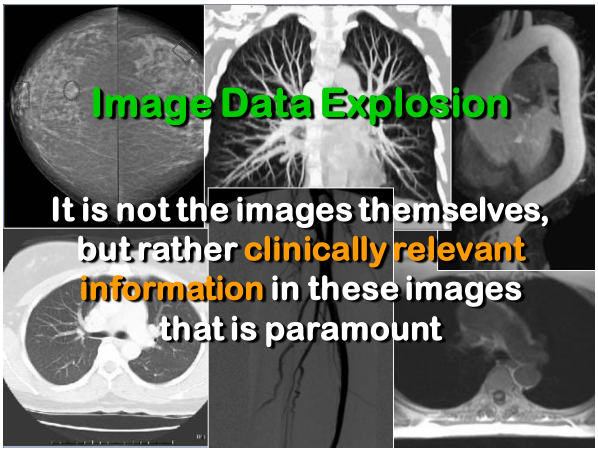
Arizona State University
Johnson Research Building, Mayo Clinic Arizona

jianming.liang@asu.edu

Disclosure: Co-Founder of IMANIN and VoxelCloud, and Consultant of VisionGate







Research Goal

Develop computer algorithms for gleaning clinically important information from images to support clinical decision making and facilitate precision medicine

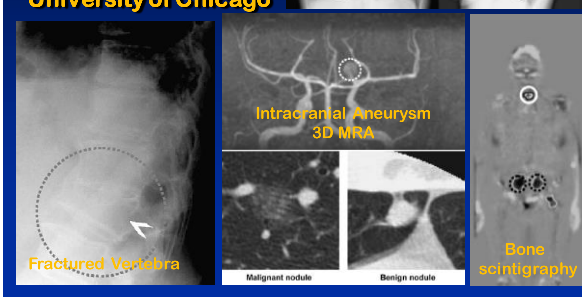
Computer-Aided Diagnosis (CAD) in Medical Imaging

Computer Aided Diagnosis (CAD)

CAD systems are not designed to replace physicians, but rather to enhance their capabilities through a computer-physician synergy

CAD: A Brief History (Doi, 2007)

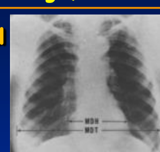
1980s: Kunio Doi at the University of Chicago

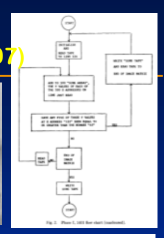


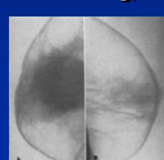
CAD: A Brief History (Doi, 2007)

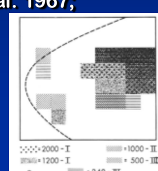
1960 – 70: Automated computer diagnosis

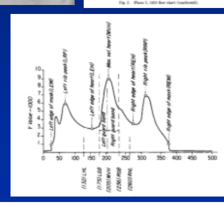
- Lodwick, et al. 1963;.
- Myers, et al. 1964;
- Winsbarg, et al. 1967;



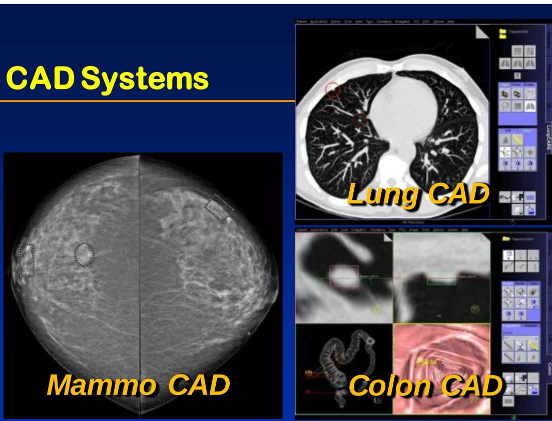




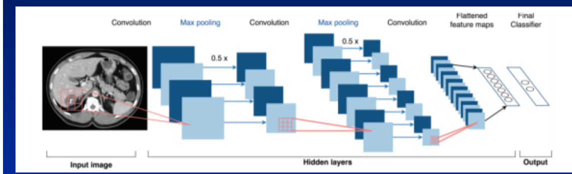




CAD Systems



Deep Learning

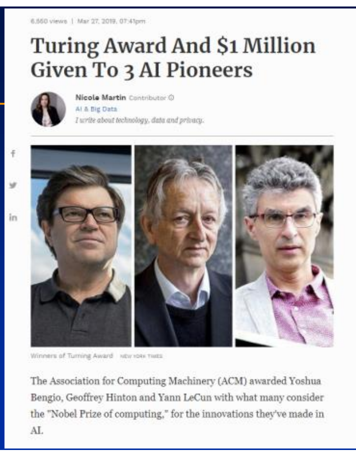


Chartrand, et al. Deep Learning: A Primer for Radiologists. Radiographics. 2017 Nov-Dec;37(7):2113-2131

Deep Learning

(Goodfellow, Bengio, Courville. 2016)

- Artificial Intelligence
  - Machine Learning
    - Representation Learning
      - Deep Learning



6,560 views | Mar 27, 2019, 07:41pm

Turing Award And $1 Million Given To 3 AI Pioneers

Nicole Martin Contributor
AI & Big Data
I write about technology, data and privacy.

Winners of Turning Award NEW YORK TIMES

The Association for Computing Machinery (ACM) awarded Yoshua Bengio, Geoffrey Hinton and Yann LeCun with what many consider the "Nobel Prize of computing," for the innovations they've made in AI.

Courtesy: NVIDIA (https://www.youtube.com/watch?v=YuyT2SDcYrU).

Deep Learning

Revolutionized computer vision, self-driving cars, speed understanding, and natural language processing

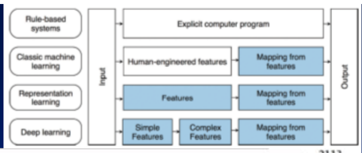
---

The greatest potential

Deep Learning in Healthcare

A revolution is coming to computer-aided diagnosis

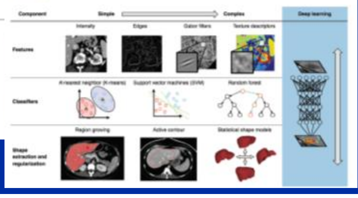
Deep Learning



2113

Deep Learning: A Primer for Radiologists[1]

Gabriel Chartrand, PhD
Phillip M. Cheng, MD, MS
Eugene Vorontsov, BASc Eng Sci
Michal Drozdzal, PhD
Simon Turcotte, MD, MSc
Christopher J. Pal, PhD
Samuel Kadoury, PhD
An Tang, MD, MSc



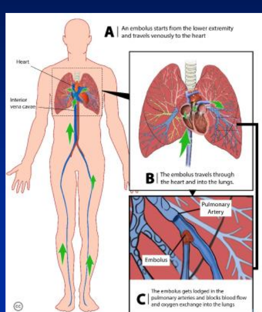
CRCHUM

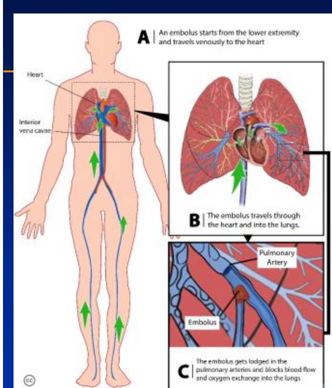
Three Systems

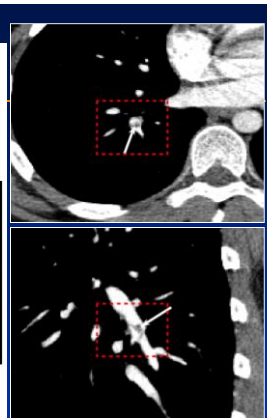
(Hybrid systems)

Project 1:

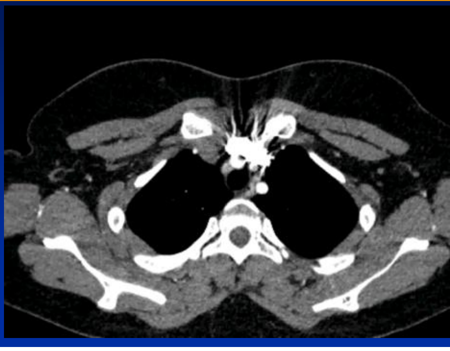
Pulmonary Embolism



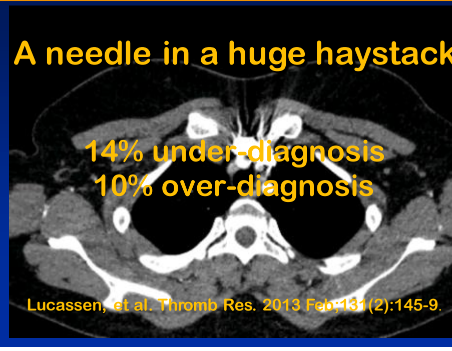




Reading CT Angiography



Reading CT Angiography



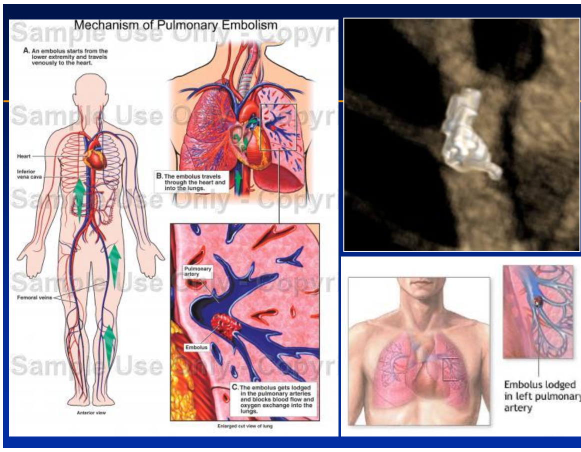
A CAD System for PE Detection

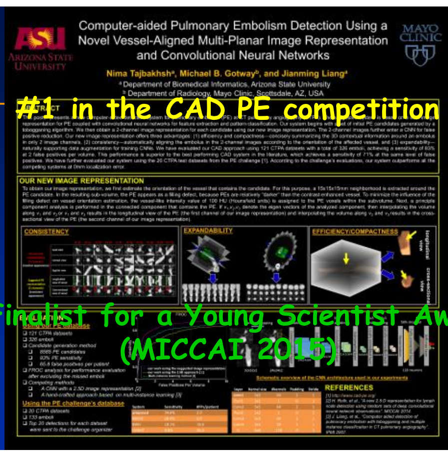
CT Scan

PE CAD

Markers

As a first reader, concurrent, second reader





#1 in the CAD PE competition

A Finalist for a Young Scientist Award (MICCAI 2015)

Project 2

Cardiovascular Disease

Cardiovascular Disease (CVD)

#1 killer in the US

- Every minute, one American dies
- 1/2 of the deaths occur suddenly
- 1/3 of the deaths occur before the age of 65

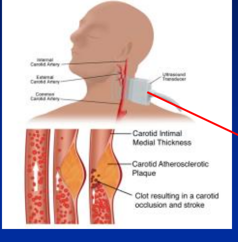
Preventive medicine

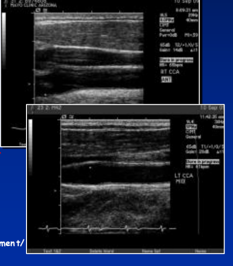
- CVD is largely preventable
- Efficacious therapies are available

Key: identify at-risk individuals before CVD events

CIMT: Carotid Intima-Media Thickness

Quantifying subclinical atherosclerosis





Source: http://dallasfamilymedical.com/heart-attack-stroke-risk-assessment/

No radiation. No needles. No pain. Affordable

CIMT: Carotid Intima-Media Thickness

Each patient has 4 videos

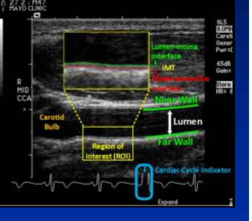
- Two on each side

Search the right frame

- From hundreds of frames within each video

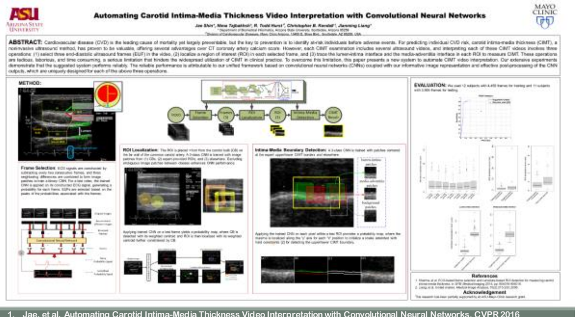
Find the right location

- Within the found frames



Measuring CIMT is tedious and time-consuming

Contribution 1: Fully Automating CIMT Video Analysis



1. Jae, et al, Automating Carotid Intima-Media Thickness Video Interpretation with Convolutional Neural Networks. CVPR 2016
2. Tajbakhsh, et al. Automatic interpretation of CIMT videos using convolutional neural networks. *Deep Learning for Medical Image Analysis*, Academic Press, 2017

Clinical Evaluation (preliminary)

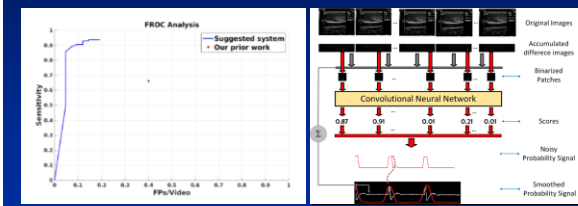
- 25 unseen subjects (100 CIMT videos)
- Two experts measure two times
- Automated measurement

Five measurements are not statistically distinguishable

CNNs have proven to be powerful in learning features, but to achieve a superior performance, it is critical to design meaningful image representations and post-process CNN's outputs.

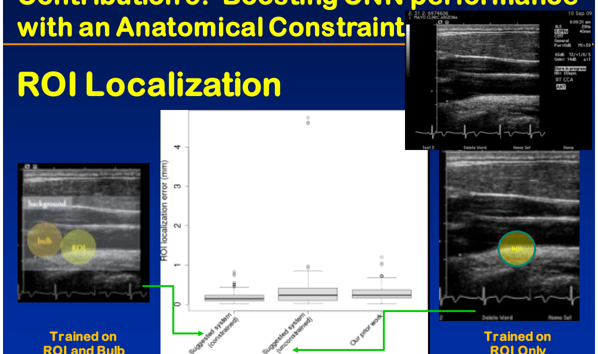
Contribution 2: Boosting CNN performance via effective pre- and post-processing

Frame Selection



Contribution 3: Boosting CNN performance with an Anatomical Constraint

ROI Localization

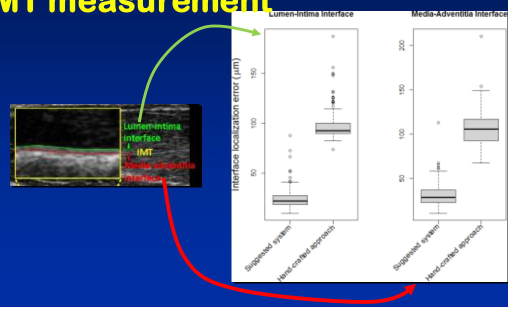


Trained on ROI and Bulb

Trained on ROI Only

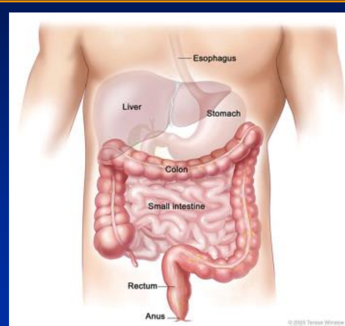
Contribution 4: Boosting CNN performance through Active Contours

IMT measurement



Project 3

Colon Cancer



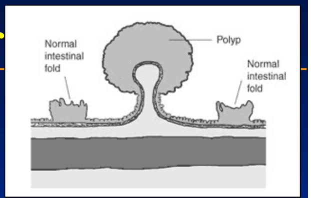
Colon Cancer

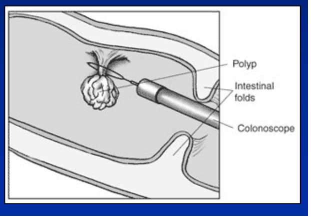
#2 leading cause of cancer death

both men and women

One of the most preventable

doctors can identify and remove the pre-cancerous growth: polyp with colonoscopy





Colonoscopy

Primary method for screening and preventing colon cancer

- contribute significantly to the decline of colon cancer

User-dependent procedure

- rely on colonopists' skills (diligence, attentiveness and thoroughness)

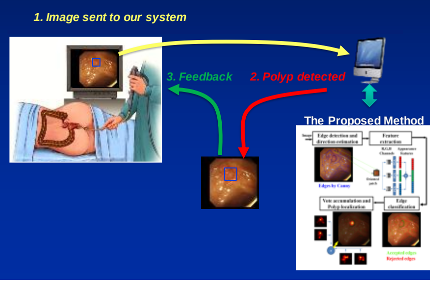
For every 5 polyps, ≈1 is missed

Reasons for missing polyps

1. Unreached polyps
   - incomplete colon examination
2. Reached but unrecognizable
   - rapid motion, too close
3. Recognizable but overlooked
   - inattentiveness

Polyps: Recognizable but overlooked

Automatically detecting polyps in colonoscopy videos

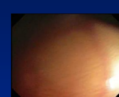


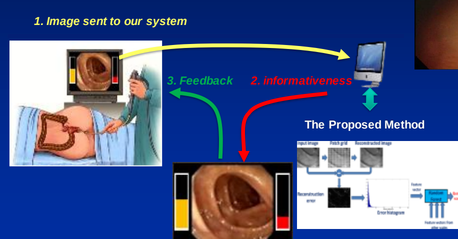
Detect Polyps:

Automatically alerting the physician to possible polyps

Polyps: Reached but unrecognizable

Automatically assessing informativeness of colonoscopy video frames

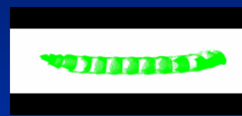


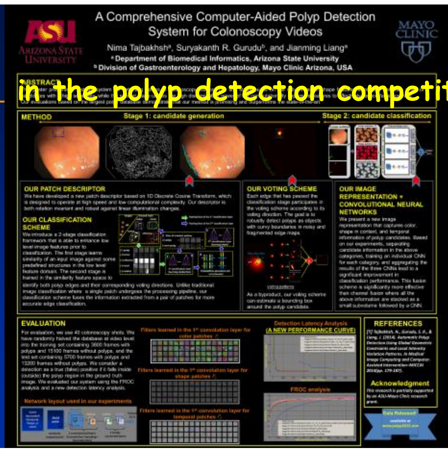


Monitor Video Quality:
Automatically monitoring the colonoscopic video quality

Polyps:
Unreached

Visualizing the colon in 3D with examined regions





#1 in the polyp detection competition

Other Projects

Classifying thyroid nodules based on ultrasound images
- The overall incidence of cancer in patients with thyroid nodules selected for the fine needle aspiration (FNA) is 9.2%–13.0%.
- Reducing biopsies (automatically determining malignancy)

Detecting, segmenting and classifying lung nodules
- Detecting and segmenting lung nodules at CT
- determining malignancy of lung nodules; reducing biopsies

Detecting, segmenting and classifying brain tumors
- Detecting and segmenting brain tumors at CT
- Classifying brain tumors into three types: 1p/19q, IDH, and TERT
- Reducing biopsies

Proton therapy for lung cancer
- Outlining tumors and at-risk organs
- Predicting the tumor response to proton therapy

Applications

↕

Methodologies

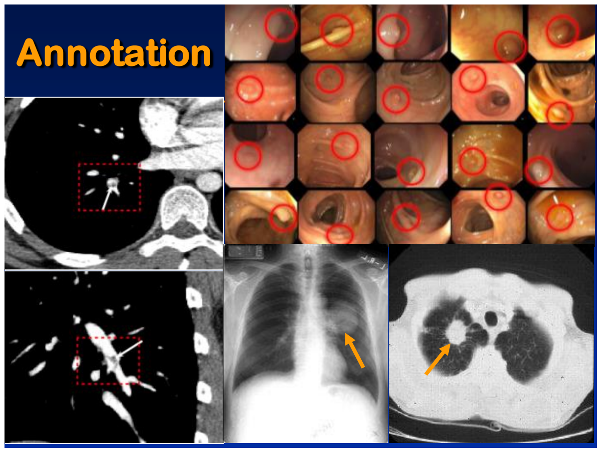
Methodologies
across diseases & modalities

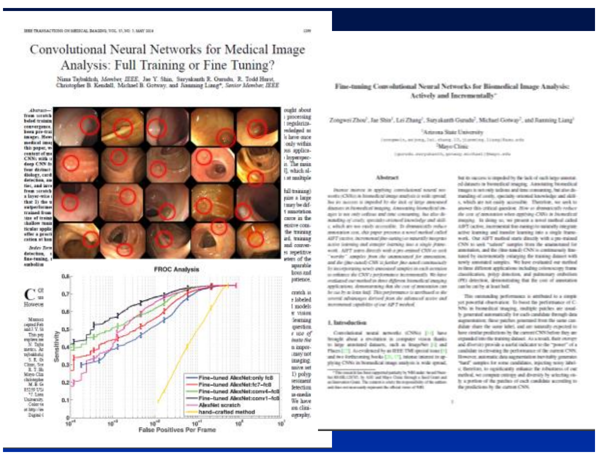
Deep Learning for Medical Imaging

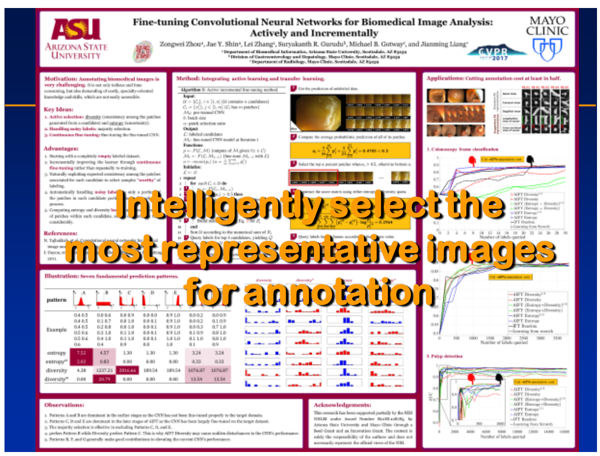
A Significant Disadvantage

Not enough annotation

Annotation







Active Fine-Tuning

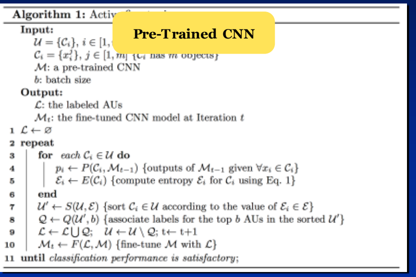
Algorithm 1: Active fine-tuning

Input:
- $\mathcal{U} = \{\mathcal{C}_i\}, i \in [1, n]$ {$\mathcal{U}$ contains n AUs}
- $\mathcal{C}_i = \{x_i^j\}, j \in [1, m]$ {$\mathcal{C}_i$ has m objects}
- $\mathcal{M}$: a pre-trained CNN
- b: batch size

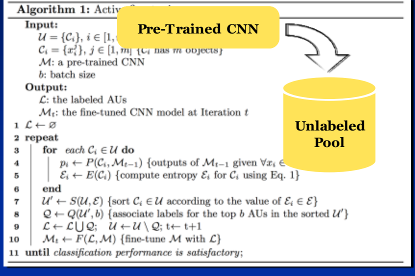
Output:
- $\mathcal{L}$: the labeled AUs
- $\mathcal{M}_t$: the fine-tuned CNN model at Iteration t

$\mathcal{L} \leftarrow \varnothing$
repeat
  for *each* $\mathcal{C}_i \in \mathcal{U}$ **do**
    $p_i \leftarrow P(\mathcal{C}_i, \mathcal{M}_{t-1})$ {outputs of $\mathcal{M}_{t-1}$ given $\forall x_i \in \mathcal{C}_i$}
    $\mathcal{E}_i \leftarrow E(\mathcal{C}_i)$ {compute entropy $\mathcal{E}_i$ for $\mathcal{C}_i$ using Eq. 1}
  end
  $\mathcal{U}' \leftarrow S(\mathcal{U}, \mathcal{E})$ {sort $\mathcal{C}_i \in \mathcal{U}$ according to the value of $\mathcal{E}_i \in \mathcal{E}$}
  $\mathcal{Q} \leftarrow Q(\mathcal{U}', b)$ {associate labels for the top b AUs in the sorted $\mathcal{U}'$}
  $\mathcal{L} \leftarrow \mathcal{L} \bigcup \mathcal{Q}$; $\mathcal{U} \leftarrow \mathcal{U} \setminus \mathcal{Q}$; t← t+1
  $\mathcal{M}_t \leftarrow F(\mathcal{L}, \mathcal{M})$ {fine-tune $\mathcal{M}$ with $\mathcal{L}$}
until *classification performance is satisfactory*;

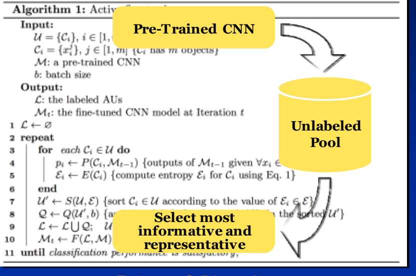
Active Fine-Tuning



Active Fine-Tuning

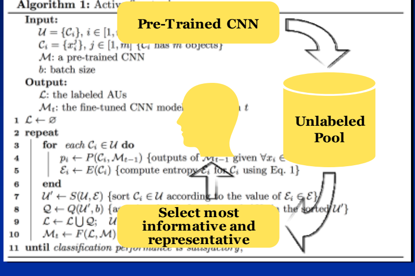


Active Fine-Tuning

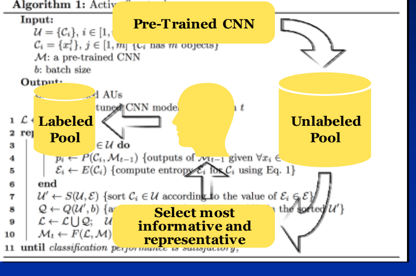


Entropy & Diversity

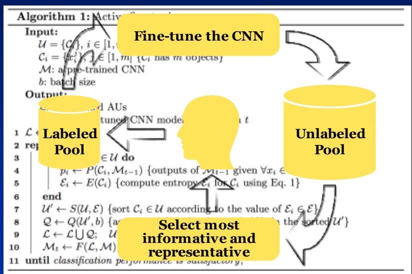
Active Fine-Tuning



Active Fine-Tuning

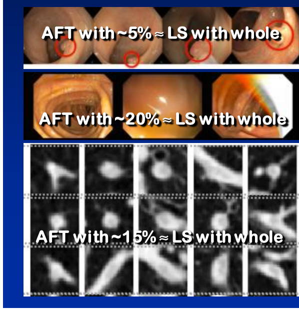


Active Fine-Tuning



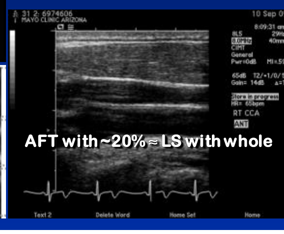
Active Fine-Tuning

Dramatically reduces the burden of annotation



AFT saves > 50% relative to FT

Quality beats Quantity



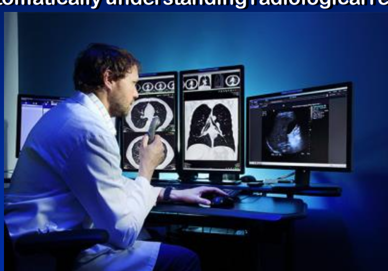
Deep Learning for Medical Imaging

A Significant Advantage

Plenty weakly labeled image data

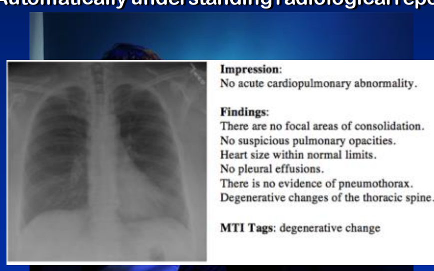
Methodological Research across diseases and modalities

2. Deep learning with weakly labeled data
   - Automatically understanding radiological reports



Methodological Research across diseases and modalities

2. Deep learning with weakly labeled data
   - Automatically understanding radiological reports



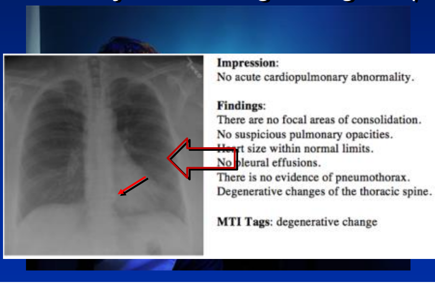
Impression:
No acute cardiopulmonary abnormality.

Findings:
There are no focal areas of consolidation.
No suspicious pulmonary opacities.
Heart size within normal limits.
No pleural effusions.
There is no evidence of pneumothorax.
Degenerative changes of the thoracic spine.

MTI Tags: degenerative change

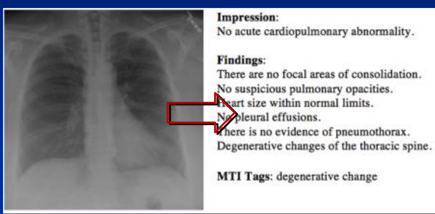
Methodological Research across diseases and modalities

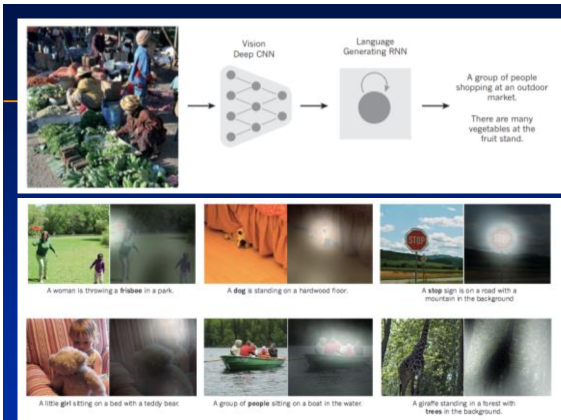
2. Deep learning with weakly labeled data
   - Automatically understanding radiological reports



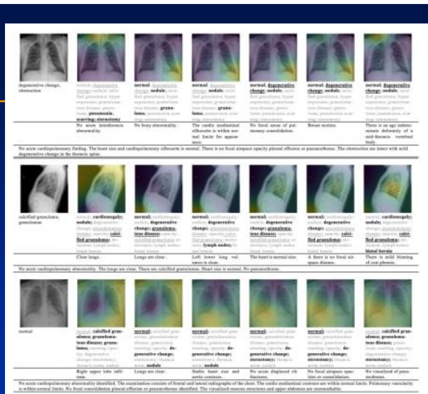
Methodological Research across diseases and modalities

3. Directly synthesizing radiological reports from biomedical images
   - Biomedical images → radiological reports





Y. LeCun, Y. Bengio and G. Hinton, Deep Learning, Nature, 521(7553), pp.436-444, 2015.



Baoyu Jing, Pengtao Xie, Eric Xing, 2018

Reinforcement learning

Flying through the colon

New Applications

Two Types of Tasks

1. Tasks that doctors have to do but do not really wants to do (low value, repetitive)
   - Tedious, laborious, and time consuming
   - CIMT video analysis; outlining the contours of the tumors and at-risk organs
2. Tasks that doctors really want to do but cannot do very well (high value)
   - Lack of knowledge and skills; require subvisual features
   - Determining the malignancy of tumor (benign or malignant) before biopsy or surgery; predicting the tumor response to radiation/chemo therapy

Domains

1. Radiotherapy
   - Outlining tumors and organs at-risk
   - Predicting the tumor response to radiation therapy
2. Chemotherapy
   - Predicting the tumor response to chemotherapy
3. Ultrasound
   - Ultrasounds are inexpensive and widely accessible
   - User-dependent; Difficult to interpret ultrasound images
4. Generic image segmentation
   - Tedious, laborious, and time consuming

Clinical Projects at CRCHUM

1. Automatically outlining tumors and organs at-risk in radiation therapy to relieve clinicians from the tedious, repetitive, laborious, time consuming, and error prone process, dramatically reducing patient turnaround times (in collaboration with Dr. Francois DeBlois and Dr. David Roberge at CRCHUM)
2. Predicting liver metastases response to chemotherapy to triage patients for chemotherapy and surgery, improving patient life quality (in collaboration with Dr. An Tang and Dr. Simon Turcotte at CRCHUM)
3. Deep learning for ultrasound imaging to simplify ultrasound operations, clarify ultrasound images, and amplify ultrasound portability, revolutionizing ultrasound imaging in clinical practice (in collaboration with Dr. Gilles Soulez, Dr. Guy Cloutier, and Dr. Samuel Kadoury at CRCHUM)
4. Accurately segmenting abdominal aortic aneurysm for precise diameter measurements, realizing stent graft customization (in collaboration with Dr. Gilles Soulez and Dr. Claude Kauffmann at CRCHUM)

Generative Models

Courtesy: NVIDIA (https://www.youtube.com/watch?v=Zc-ihT0DQg0).

Generative Models

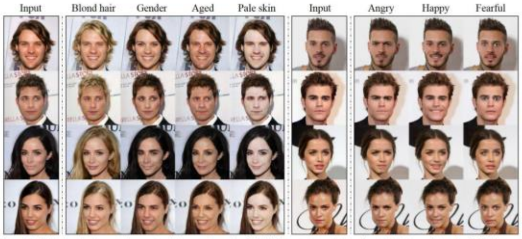
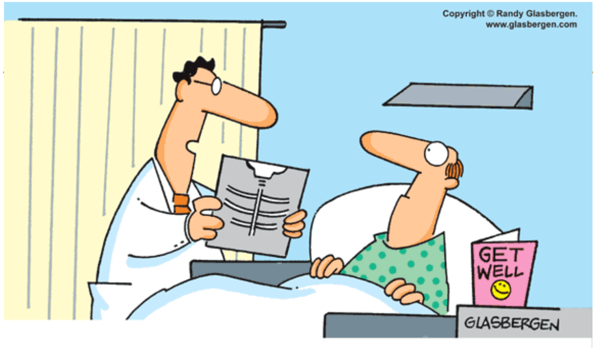


Figure 1. Multi-domain image-to-image translation results on the CelebA dataset via transferring knowledge learned from the RaFD dataset. The first and sixth columns show input images while the remaining columns are images generated by StarGAN. Note that the images are generated by a single generator network, and facial expression labels such as angry, happy, and fearful are from RaFD, not CelebA.

Yunjey Choi, et al. CVPR 2018.

Figure 1: Three source photos (top row) are each modified to match makeup styles in three reference photos (left column) to produce nine different outputs (3 × 3 lower right).

Huiwen Chang, et al. CVPR 2018



"Your x-ray showed a broken rib, but we fixed it with ~~Photoshop~~."
deep learning

"Your x-ray showed a broken rib, but we fixed it with ~~Photoshop~~."
deep learning

Train: diseased + normal images

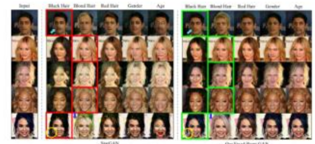
Test: any image → normal image

Detecting any and every disease

(even at early stage) in images

with only patient-level annotation

ICCV 2019



Learning Fixed Points in Generative Adversarial Networks:
From Image-to-Image Translation to Disease Detection and Localization

Md Mahfuzur Rahman Siddiquee[1], Zongwei Zhou[1,3], Nima Tajbakhsh[1], Ruibin Feng[1],
Michael B. Gotway[2], Yoshua Bengio[3], and Jianming Liang[1,3]
[1]Arizona State University; [2]Mayo Clinic; [3]Mila – Quebec Artificial Intelligence Institute

Fig. 1: [Better viewed on-line in color and zoomed in for details] Comparing our Fixed-Point GAN with StarGAN [illegible], the state of the art in multi-domain image-to-image translation, by translating images into five domains. Combining the domains may yield a same-domain (e.g., black to black hair) or cross-domain (e.g., black to blond hair) translation. For clarity, same-domain translations are framed in red for StarGAN and in green for Fixed-Point GAN. As illustrated, during cross-domain translations, and especially during same-domain translations, StarGAN generates artifacts: introducing a mustache (Row 1, Col. 2; light blue arrow), changing the face colors (Rows 2–5, Cols. 2–6), adding more hair (Row 5, Col. 2; yellow circle), and altering the background (Row 5, Col. 3; blue arrow). Our Fixed-Point GAN overcomes these drawbacks via fixed-point translation learning (see Sec. 3) and provides a framework for disease detection and localization with only image-level annotation (see Fig. 2).

Abstract

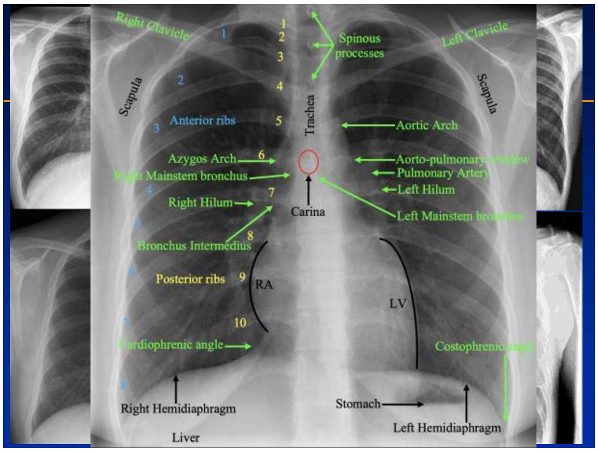
Generative adversarial networks (GANs) have ushered in a revolution in image-to-image translation. The development and proliferation of GANs raises an interesting question: can we train a GAN to remove an object, if present, from an image while otherwise preserving the image? Specifically, can a GAN "virtually heal" anyone by turning his medical image, with an unknown health status (diseased or healthy), into a healthy one, so that diseased regions could be revealed by subtracting those two images? Such a task requires a GAN to identify a minimal subset of target pixels for domain translation, an ability that we call fixed-point translation, which no GAN is equipped with yet. Therefore, we propose a new GAN, called Fixed-Point GAN, trained by (1) supervising same-domain translation through a conditional identity loss, and (2) regularizing cross-domain translation through revised adversarial, domain classification, and cycle consistency loss. Based on fixed-point translation, we further derive a novel framework for disease detection and localization using only image-level annotation. Qualitative and quantitative evaluations demonstrate that the proposed method outperforms the state of the art in multi-domain image-to-image translation and that it surpasses predominant weakly-supervised localization methods in both disease detection and localization. Implementation is available at https://github.com/jlianglab/Fixed-Point-GAN.

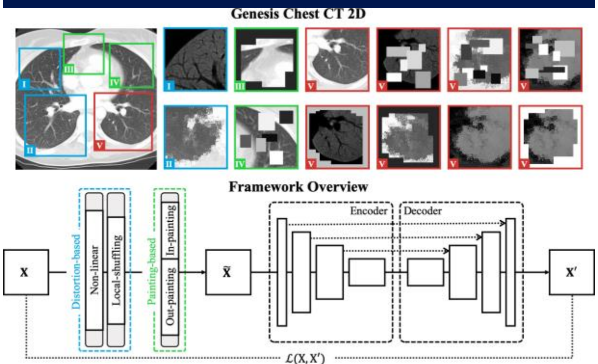
1

Deep Learning for Medical Imaging

Another Significant Advantage

Consistent, recurrent anatomy





MICCAI 2019

Models Genesis: Generic Autodidactic Models for 3D Medical Image Analysis

Zongwei Zhou[1], Vatsal Sodha[1], Md Mahfuzur Rahman Siddiquee[1], Ruibin Feng[1], Nima Tajbakhsh[1], Michael B. Gotway[2], and Jianming Liang[1]

[1] Arizona State University, Scottsdale, AZ 85259 USA
{zongweiz,vasodha,mrahmans,rfeng12,ntajbakh,jianming.liang}@asu.edu
[2] Mayo Clinic, Scottsdale, AZ 85259 USA
Gotway.Michael@mayo.edu

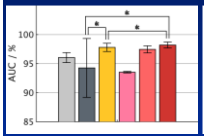
Abstract. Transfer learning from natural image to medical image has established as one of the most practical paradigms in deep learning for medical image analysis. However, to fit this paradigm, 3D imaging tasks in the most prominent imaging modalities (e.g., CT and MRI) have to be reformulated and solved in 2D, losing rich 3D anatomical information and inevitably compromising the performance. To overcome this limitation, we have built a set of models, called Generic Autodidactic Models, nicknamed Models Genesis, because they are created ex nihilo (with no manual labeling), self-taught (learned by self-supervision), and generic (served as source models for generating application-specific target models). Our extensive experiments demonstrate that our Models Genesis significantly outperform learning from scratch in all five target 3D applications covering both segmentation and classification.

Result 1:
Models Genesis outperform 3D models trained from scratch

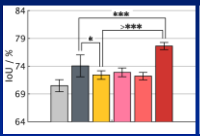
Task	Modality	Metric	Scratch (%)	Genesis (%)	*p*-value
Lung nodule false positive reduction	CT	AUC	94.25±5.07	**98.20±0.51**	0.0180
Lung nodule segmentation	CT	IoU	74.05±1.97	**77.62±0.64**	1.04e-4
PE false positive reduction	CT	AUC	79.99±8.06	**88.04±1.40**	0.0058
Liver segmentation	CT	IoU	74.60±4.57	**79.52±4.77**	0.0361
Brain tumor segmentation	MRI	IoU	90.16±0.41	**90.60±0.20**	0.0041

The statistical analyses are conducted between Scratch and Genesis.

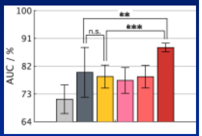
Result 2:
Models Genesis consistently top any 2D approaches



Lung nodule false positive reduction in 3D CT [LUNA-2016]

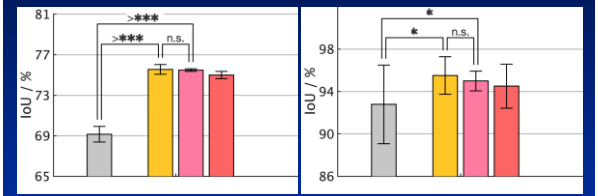


Lung nodule segmentation 3D CT [LIDC-IDRI]



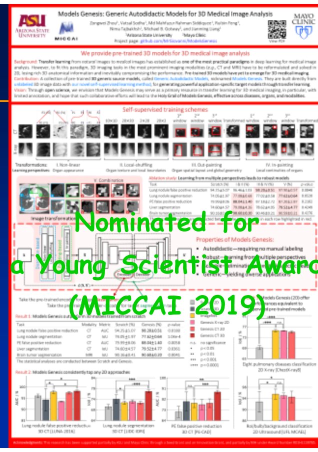
PE false positive reduction 3D CT [PE-CAD]

Result 3: Models Genesis (2D) offer performances equivalent to supervised pre-trained models



Eight pulmonary diseases classification
2D X-ray [ChestX-ray8]

RoI/bulb/background classification
2D Ultrasound [UFL MCAEL]



A Significant Challenge

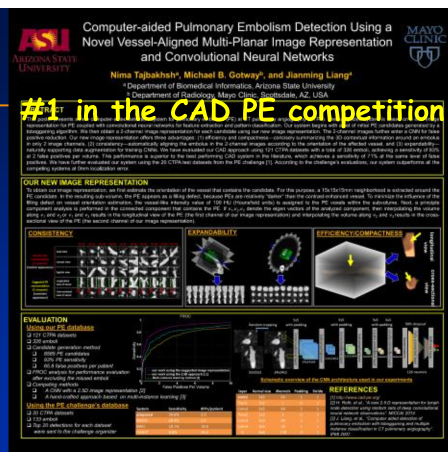
Image Data Explosion

A Manifestation of Big Data in Medical Imaging

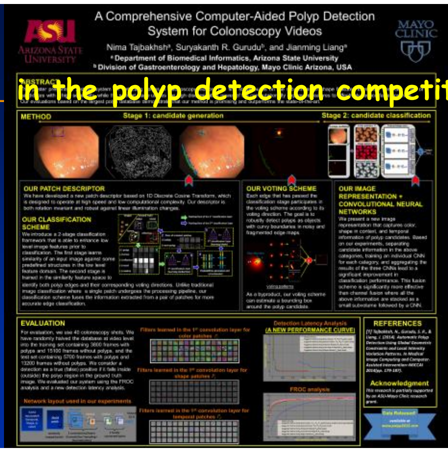
A Great Opportunity

Deep Learning

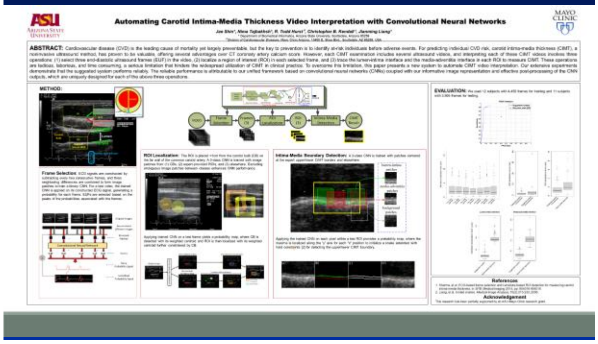
A revolution is coming to medical image interpretation



#1 in the polyp detection competition



#1 in making CIMT analysis automatic



Augmented Intelligence

Our systems are not designed to replace physicians, but rather to enhance their capabilities through a computer-physician synergy

Experts + Computer >> Experts

- Do what doctors do not wants to do
- Do what doctors cannot do well

Clinical Collaborators

Cardiology | Radiology | Gastroenterology

Acknowledgements

- NIH R01 (PE CAD)
- ABRC R01-like Grant (Proton Therapy)
- Mayo Discovery Translation (CIMT)
- ASU-Mayo Grant (Proton Therapy)
- Mayo Innovation Grant (Colonoscopy)
- ASU-Mayo Grant (Colonoscopy)
- Mayo CR 20 Program (CIMT)
- ASU-Mayo Grant (PE CAD)
- ASU-Mayo Grant (PE)

Thank You