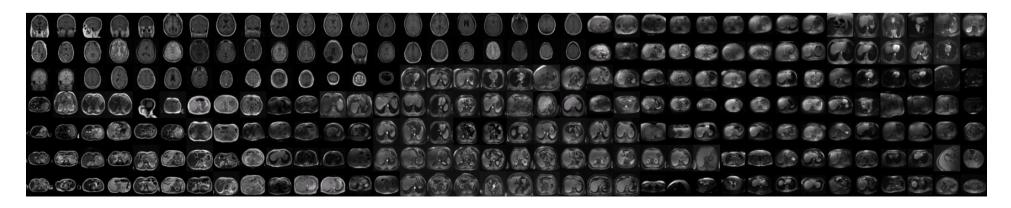




Towards Big Data, Weak Label and True Clinical Impact: Deep Label Discovery and Open-Ended Recognition (IWANN 2017, June 15th)

Le Lu, PhD, Staff Scientist, <u>le.lu@nih.gov</u>; NIH Clinical Center, Radiology and Imaging Sciences

3/7/17



The Partnership of the Future

Microsoft's CEO explores how humans and A.I. can work together to solve society's greatest challenges.



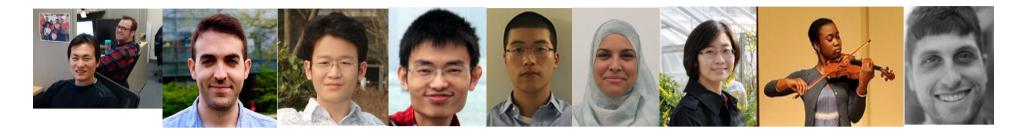
By Satya Nadella



From left, visually impaired Microsoft developer Saqib Shaikh stands next to CEO Satya

http://www.slate.com/ articles/technology/ future_tense/2016/06/ microsoft_ceo_satya_nad ella_humans_and_ai_can _work_together_to_solve_ society.html





Q1: Do deep learning and deep neural networks help in medical imaging or medical image analysis problems? (Yes)

- ✓ **Deep CAD:** Lymph node application package (52.9% \rightarrow 85%, 83%) and many CAD Applications
- ✓ Deep Segmentation → Precision Medicine in Radiology & Oncology: Pancreas segmentation application package (~53% → 81.14% in Dice Coefficient) and beyond (prostate segmentation, ...)
- Deep Lung (Interstitial Lung Disease) Application Package + DL Reading Chest X-ray;
 Pathological Lung Segmentation, ...
- ✓ Unsupervised category discovery using looped deep pseudo-task optimization (mapping large-scale radiology database with category meta-labels) → Learning from PACS!
- ✓ A large-scale Chest X-ray database (with NLP based annotation): Dataset and Benchmark
- Updates & Publications can be downloaded: <u>www.cs.jhu.edu/~lelu;</u> 3/7/<u>https://clinicalcenter.nih.gov/drd/staff/le_lu.html</u>



Perspectives

Why the previous or current computer-aided diagnosis (CADx) systems are not particularly successful yet? Integrating machine decisions is not easy for human doctors: Good doctors hate to use; bad doctors are confused and do not know how to use? --> Human-machine collaborative decision making process

Make machine decision more interpretable is very critical for the collaborative system --> learning mid-level attributes or embedding?

- Preventive medicine: what human doctors cannot do (in very large scales: millions of general population, at least not economical): → first-reader population risk profiling ...?
- Precision Medicine: a) new imaging biomarkers in precision medicine to better assist human doctors to make more precise decisions; b) patient-level similarity retrieval system for personalized diagnosis/therapy treatment: show by examples!



Three Key Problems (I)

Computer-aided Detection (CADe) and Diagnosis (CADx)

- Lung, Colon pre-cancer detection; Bone and Vessel imaging (6 years of industrial R&D at Siemens Corporation and Healthcare, 10+ product transfer; 13 conference papers in CVPR/ECCV/ICCV/MICCAI/WACV/CIKM, 12 US/EU patents, 27 Inventions)
- Lymph node, colon polyp, bone lesion detection using Deep CNN + Random View Aggregation (TMI 2016a; MICCAI 2014a)
- Empirical analysis on Lymph node detection and interstitial lung disease (ILD) classification using CNN (TMI 2016b)
- Non-deep models for CADe using compositional representation (MICCAI 2014b) and +mid-level cues (MICCAI 2015b); deep regression based multi-label ILD prediction (*in submission*); missing label issue in ILD (ISBI 2016); ISBI 2017 ...



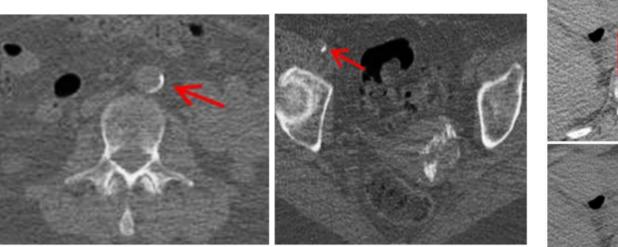
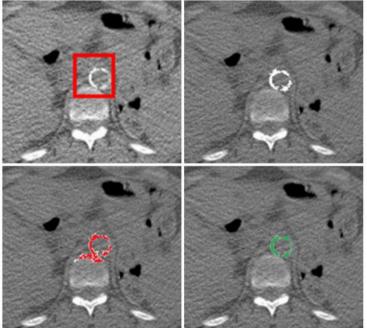
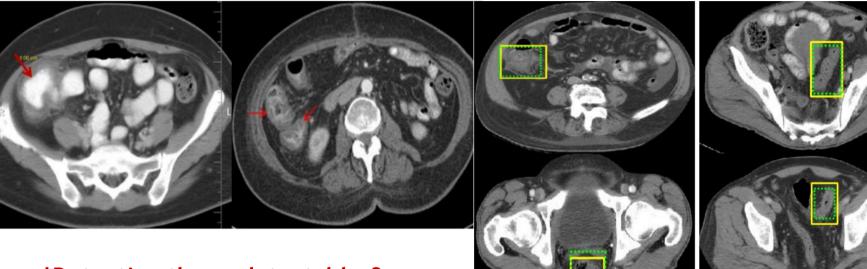


Figure 1. Examples of calcified plaques (red arrows) on abdominal (left) and pelvic (right) CT scans.



Atherosclerotic Vascular Calcification Detection and Segmentation on Low Dose Computed Tomography Scans ..., Liu et al., IEEE ISBI 2017 Oral





*Detecting the undetectables?

*Fitting in practical/real clinical settings in the wild??

COLITIS DETECTION ON COMPUTED TOMOGRAPHY USING REGIONAL CONVOLUTIONAL NEURAL NETWORKS, Liu et al., IEEE ISBI 2016



References: (Preventive CAD)

- 1. "A New 2.5D Representation for Lymph Node Detection using Random Sets of Deep Convolutional Neural Network Observations", MICCAI 2014
- 2. "2D View Aggregation for Lymph Node Detection using a Shallow Hierarchy of Linear Classifiers", MICCAI 2014
- 3. "Detection of Sclerotic Spine Metastases via Random Aggregation of Deep Convolutional Neural Network Classifications", (Oral), MICCAI Spine Imaging Workshop 2014
- 4. "Leveraging Mid-Level Semantic Boundary Cues for Computer-Aided Lymph Node Detection", MICCAI 2015
- 5. "Detection of sclerotic spine metastases via random aggregation of deep convolutional neural network classifications", Recent Advances in Computational Methods and Clinical Applications for Spine Imaging, Springer 2015
- 6. "An Analysis of Robust Cost Functions for Deep CNN in Computer-aided Diagnosis", MICCAI DLMIA workshop 2015
- 7. "Anatomy-specific Classification of Medical Images using Deep Convolutional Nets", IEEE ISBI 2015
- 8. "Improving Computer-aided Detection using Convolutional Neural Networks and Random View Aggregation", IEEE Trans. on Medical Imaging, May 2016
- "Deep Convolutional Neural Networks for Computer-Aided Detection: CNN Architectures, Dataset Characteristics and Transfer Learning", IEEE Trans. on Medical Imaging, May 2016
- 10. Three ISBI 2017 Orals ...



Where are we today?

USPSTF discourages thyroid cancer screening

Citing the lack of evidence for an overall benefit as well as the risk of harm from over-diagnosis and overtreatment, the U.S. Preventive Services Task Force (USPSTF) has finalized its recommendation against the use of screening with neck palpation or ultrasound for thyroid cancer in low-risk, asymptomatic adults.

NVIDIA hails Mayo Clinic AI initiative

- Building the second reader CAD may have a lot of issues going forward with the proper market appreciation and sound business acceptance. Over diagnosis/treatment? Do things where they really need an interpretable, trustworthy second opinion assistance.
 → highly intelligent AI-assist!
- Building the first reader CAD that may lead to a high-performance triage tool on 20~30 common diseases/cancers by one low-dose annual CT exam may be a meaningful solution, even game changer because this is what we cannot afford to do so (even recommended by ACA).
- ➤ However our current technologies on pathology detection, segmentation, parsing & reasoning are not ready yet. → too many false positives than we can afford! → growing opportunities & fast!



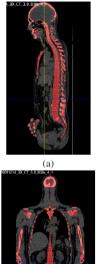
Three Key Problems (II)

Semantic Segmentation in Medical Image Analysis

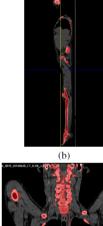
- "DeepOrgan" for pancreas segmentation (MICCAI 2015a) via scanning superpixels using multi-scale deep features ("Zoom-out") and probability map embedding.
- Deep segmentation on pancreas and lymph node clusters with Holisticallynested neural networks [Xie & Tu, 2015] as building blocks to learn unary (segmentation mask) and pairwise (labeling segmentation boundary) CRF terms + spatial aggregation or + structured optimization.
- The focus of three MICCAI 2016 papers since this is a much needed task → Small datasets; (de-)compositional representation is still the key. Scale up to thousands of patients if not more than that amount. Submissions to MICCAI 2017 → Effective and Efficient Precision Biomarkers, even predicting the future growth!
- ➤ Clinical Impacts: semantic segmentation can help compute clinically more accurate and desirable precision imaging bio-markers or measurements → precision imaging personalized treatment and therapy → less guess more doing ...

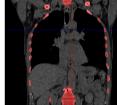


Results on PET-CT Patient Datasets (pathological ...)

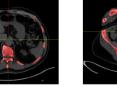


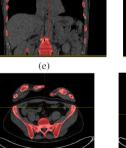
(d)

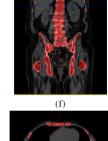




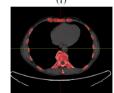


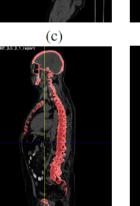




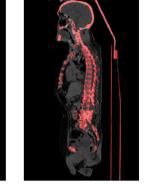


(C)





(a)



(b)



Towards whole Body precision measurements or computable precision imaging biomarkers



"Robust Whole Body 3D Bone Masking via Bottom-up Appearance Modeling and Context Reasoning in Low-Dose CT Imaging", Lu et al., **IEEE WACV 2016**

 \rightarrow

Bone Mineral Density (BMD) scores, Muscle/Fat volumetric measurements in whole body or arbitrary FOV imaging lung nodules, bone lesions, head-and-neck radiation sensitive organs, segmenting flexible soft anatomical structures for precision medicine, all clinically needed!

3/7/17



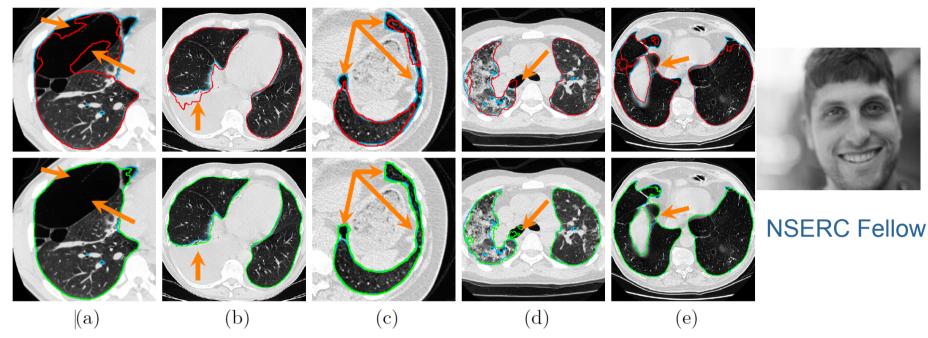


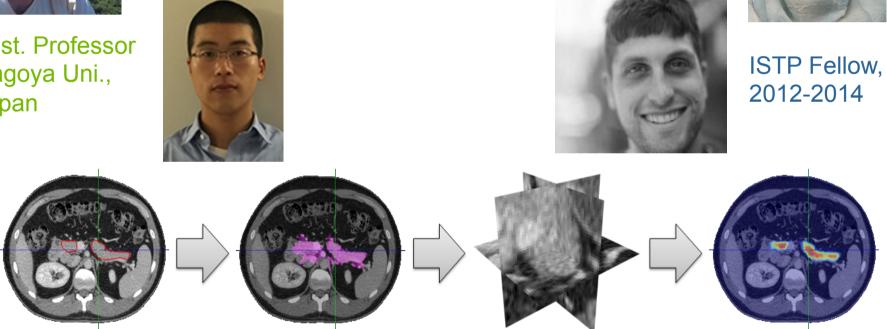
Fig. 2: Example masks of HNN and P-HNN, depicted in red and green, respectively. Ground truth masks are rendered in cyan. (a) HNN struggles to segment the pulmonary bullae, whereas P-HNN captures it. (b) Part of the pleural effusion is erroneously included by HNN, while left out of the P-HNN lung mask. (c) P-HNN is better able to capture finer details in the lung mask. (d) In this failure case, both HNN and P-HNN erroneously include the right main bronchus; however, P-HNN better captures infiltrate regions. (e) This erroneous ground-truth example, which was filtered out, fails to include a portion of the right lung. Both HNN and P-HNN capture the region, but P-HNN does a much better job of segmenting the rest of the lung.





A Roadmap of **Bottom-up Deep** Pancreas Segmentation: from Patch, Region, to Holistically-nested CNNs (HNN), P-HNN, Convolutional LSTM (context), ...

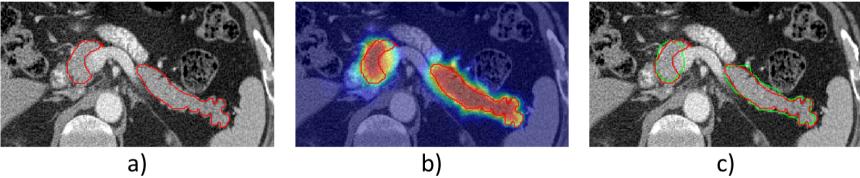
Asst. Professor Nagoya Uni., Japan



P-ConvNet



An Above-Average Example



a)



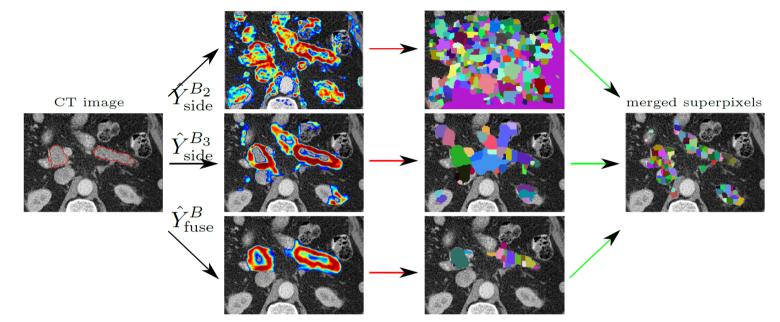


Fig. 2: "Multiscale Combinatorial Grouping" (MCG) [16] on three different scales of learned boundary predication maps from **HNN-B**: $\hat{Y}_{side}^{B_2}$, $\hat{Y}_{side}^{B_3}$, and \hat{Y}_{fuse}^{B} using the original CT image as input (shown with ground truth delineation of pancreas). MCG computes superpixels at each scale and produces a set of merged superpixel-based object proposals. We only visualize the boundary probabilities p > 10%.

Improved pancreas segmentation accuracy over previous state-ofthe-art work in Dice: from 68% to 84%; ASD: from 5~6mm to 0.7mm; computational time from 3 hours to >3 minutes!



References: (Precision Semantic Segmentation: Significant Ongoing Efforts ...)

- "DeepOrgan: Multi-level Deep Convolutional Networks for Automated Pancreas Segmentation", MICCAI 2015
- 2. "A Bottom-up Approach for Automatic Pancreas Segmentation Abdominal CT Scans", Oral, MICCAI Abdominal Imaging Workshop 2014
- "Spatial Aggregation of Holistically-Nested Networks for Automated Pancreas Segmentation", MICCAI 2016
- 4. Automatic Lymph Node Cluster Segmentation using Holistically-Nested Networks and Structured Optimization", MICCAI 2016
- 5. Pancreas Segmentation in MRI using Graph-based Decision Fusion on Convolutional Neural Networks", MICCAI 2016
- 6. "A Bottom-up Approach for Pancreas Segmentation Using Cascaded Superpixels and (Deep) Image Patch Labeling", IEEE Trans. Image Processing, Jan. 2017
- 7. "Spatial Aggregation of Holistically-Nested Convolutional Neural Networks for Automated Pancreas Localization and Segmentation", (in submission to IEEE TMI), CoRR abs/1702.00045, 2017
- 8. "Progressive and Multi-Path Holistically Nested Neural Networks for Pathological Lung Segmentation from CT Images", MICCAI 2017 (accepted)
- 9. "Improving Deep Pancreas Segmentation in CT and MRI Images via Recurrent Neural Contextual Learning and Direct Loss Function", MICCAI 2017 (accepted)
- 10. "High Precision Muscle Segmentation in MRI using Boundary-Preserving Convolutional Neural Networks", MICCAI 2017 (accepted)

11. 12. "Predicting (Future) Tumor Growth via Deep Neural Networks", MICCAI 2017 (accepted) 3/7/17



Three Key Problems (III)

Interleaved or Joint Text/Image Deep Mining on a Large-Scale Radiology Image Database → "large" datasets; weak labels (~216K 2D key images/ slices extracted from >60K unique patient studies)

- Interleaved Text/Image Deep Mining on a Large-Scale Radiology Image Database (IEEE CVPR 2015, a proof of concept study)
- Interleaved Text/Image Deep Mining on a Large-Scale Radiology Image Database for Automated Image Interpretation (its extension, JMLR, 17(107):1–31, 2016)
- Learning to Read Chest X-Rays: Recurrent Neural Cascade Model for Automated Image Annotation, (IEEE CVPR 2016)
- Unsupervised Category Discovery via Looped Deep Pseudo-Task Optimization Using a Large Scale Radiology Image Database, IEEE WACV 2017
- ChestX-ray8: Hospital-scale Chest X-ray Database and Benchmarks on Weakly-Supervised Classification and Localization of Common Thorax Diseases, IEEE CVPR 2017
- Clinical Impacts: eventually to build an automated mechanism to parse and learn from hospital scale PACS-RIS databases to derive semantics and knowledge ... has to be *deep learning* based since effective image features are very hard to be hand-crafted cross different diseases, imaging protocols and modalities.



References: (Big Data & Lung Imaging Informatics)

- 1. "Holistic Classification of CT Attenuation Patterns for Interstitial Lung Diseases via Deep CNNs", MICCAI DLMIA workshop 2015
- 2. "SEGMENTATION LABEL PROPAGATION USING DEEP CONVOLUTIONAL NEURAL NETWORKS AND DENSE CONDITIONAL RANDOM FIELD", IEEE ISBI, 2016
- 3. Multi-label Deep Regression and Unordered Pooling for Holistic Interstitial Lung Disease Detection", MICCAI-MLMI 2016.
- "Interleaved Text/Image Deep Mining on a Large-Scale Radiology Image Database", IEEE
 CVPR 2015
- 5. "Interleaved Text/Image Deep Mining on a Large-Scale Radiology Image Database for Automated Image Interpretation", **Journal of Machine Learning Research**, 2016
- 6. "Unsupervised Category Discovery via Looped Deep Pseudo-Task Optimization Using a Large Scale Radiology Image Database", arXiv:1603.07965, 2016
- 7. "Learning to Read Chest X-Rays: Recurrent Neural Feedback Model for Automated Image Annotation", IEEE **CVPR**, 2016
- 8. "Holistic Interstitial Lung Disease Detection using Deep Convolutional Neural Networks: Multi-label Learning and Unordered Pooling", in preparation, **arXiv:1701.05616**, 2017
- 9. "ChestX-ray8: Hospital-scale Chest X-ray Database and Benchmarks on Weakly-Supervised Classification and Localization of Common Thorax Diseases", IEEE **CVPR** 2017
- 10. "Unsupervised Joint Mining of Deep Features and Image Labels for Large-scale Radiology Image Categorization and Scene Recognition", ..., IEEE **WACV** 2017



Complexity & Composability



Q2: Are we at the edge of cracking radiology?



Data Science Bowl 2017

Can you improve lung cancer detection? \$1,000,000 · 1,972 teams · 25 days ago

Overview	Data	Kernels	Discussion	Leaderboard	More	Submit Predictions
Public Leader	board	Private	Leaderboard			
1 C C C C C C C C C C C C C C C C C C C				oximately 99% of ard reflects the fin		C Refresh

#	∆pub	Team Name 🛊 in the money	Kernel	Team Members	Score 🔞	Entries	Last
1		* grt123			0.39975	2	25d
2		★ Julian de Wit & Daniel Hammack		S	0.40117	2	1mo
3		* Aidence		M	0.40127	2	1mo
4		∗ qfpxfd		+5	0.40183	3	1mo
5		* Pierre Fillard (Therapixel)		5	0.40410	8	25d
6		∗ MDai		I	0.41630	2	1mo
7		* DL Munich		V 2 P 1	0.42752	2	1mo
8		* Alex Andre Gilberto Shize			0.43019	5	25d
9		∗ Deep Breath		+7	0.43872	2	1mo

*lssues/difficulties are beyond just datasets availability!

** There are many technical/methodological unknowns or challenges to tackle in application performance requirements, problem setups, label uncertainties and more importantly, proper image representations, Knowledge Ontology, handling long tail problems gracefully without too embarrassing breakdown, etc...

ARTIFICIAL INTELLIGENCE AND LIFE IN 2030

ONE HUNDRED YEAR STUDY ON ARTIFICIAL INTELLIGENCE | REPORT OF THE 2015 STUDY PANEL | SEPTEMBER 2016

PREFACE

The One Hundred Year Study on Artificial Intelligence, launched in the fall of 2014, is a longterm investigation of the field of Artificial Intelligence (AI) and its influences on people, their communities, and society. It considers the science, engineering, and deployment of AI-enabled computing systems. As its core activity, the Standing Committee that oversees the One Hundred Year Study forms a Study Panel every five years to assess the current state of AI. The Study



Panel reviews AI's progress in the years following the immediately prior report, envisions the potential advances that lie ahead, and describes the technical and societal challenges and opportunities these advances raise, including in such arenas as ethics, economics, and the design of systems compatible with human cognition. The overarching purpose of the One Hundred Year Study's periodic expert review is to provide a collected and connected set of reflections about AI and its influences as the field advances. The studies are expected to develop syntheses and assessments that provide expert-informed guidance for directions in

AI research, development, and systems design, as well as programs and policies to help ensure that these systems broadly benefit individuals and society.¹

The One Hundred Year Study is modeled on an earlier effort informally known as the "AAAI Asilomar Study." During 2008-2009, the then president of the Association for the Advancement of Artificial Intelligence (AAAI), Eric Horvitz, assembled a group of AI experts from multiple institutions and areas of the field, along with The overarching purpose of the One Hundred Year Study's periodic expert review is to provide a collected and connected set of reflections about AI and its influences as the field advances.

3/7/17

But several barriers have limited progress to date. Most hospital image archives have only gone digital over the past decade. More importantly, the problem in medicine is not to recognize what is in the image (is this a liver or a kidney?), but rather to make a fine-grained judgement about it (does the slightly darker smudge in the liver suggest a potentially cancerous tumor?). Strict regulations govern these high-stakes judgements. Even with state-of-the-art technologies, a radiologist will still likely have to look at the images, so the value proposition is not yet compelling. Also, healthcare regulations preclude easy federation of data across institutions. Thus, only very large organizations of integrated care, such as Kaiser Permanente, are able to attack these problems.

Still, automated/augmented image interpretation has started to gain momentum. The next fifteen years will probably not bring fully automated radiology, but initial forays into image "triage" or second level checking will likely improve the speed and costeffectiveness of medical imaging. When coupled with electronic patient record systems, large-scale machine learning techniques could be applied to medical image data. For example, multiple major healthcare systems have archives of millions of patient scans, each of which has an associated radiological report, and most have an associated patient record. Already, papers are appearing in the literature showing that deep neural networks can be trained to produce basic radiological findings, with high reliability, by training from this data.⁶⁴

⁶³ Sharecare, accessed August 1, 2016, https://www.sharecare.com.

⁶⁴ Hoo-Chang Shin, Holger R. Roth, Mingchen Gao, Le Lu, Ziyue Xu, Isabella Nogues, Jianhua Yao, Daniel Mollura, and Ronald M. Summers, "Deep Convolutional Neural Networks for Computer-aided Detection: CNN Architectures, Dataset Characteristics and Transfer Learning," *IEEE Transactions on Medical Imaging* 35, no. 5 (2016): 1285–1298.



Medical Dataset Availability is one of the Major Roadblocks and Helps are on the way!

- Database #1: Interleaved or Joint Text/Image Deep Mining on a Large-Scale Radiology Image Database -> "real PACS-large" datasets; "weak clinical annotations"
 - Interleaved Text/Image Deep Mining on a Large-Scale Radiology Image Database, IEEE CVPR 2015 (a proof of concept study)
 - Interleaved Text/Image Deep Mining on a Large-Scale Radiology Image Database for Automated Image Interpretation, JMLR, 17(107):1–31, 2016
 - Unsupervised Joint Mining of Deep Features and Image Labels for Large-scale Radiology Image Categorization and Scene Recognition, IEEE WACV, 2017
 - ...

...

- Clinical Goal: eventually to build an "automated programmable mechanism" to parse, extract and learn from hospital-scale PACS-RIS databases, to derive useful semantics and knowledge
 - Deep learning feature representation is a must since it is very hard to have effective hand-crafted image features cross different disease types, imaging protocols or modalities, if not at all impossible.
 - Algorithm innovations to facilitate learning from "big data, weak label" large-scale retrospective clinical database!





Unsupervised Joint Mining of Deep Features and Image Labels for Large-scale Radiology Image Categorization and Scene Recognition

Xiaosong Wang, Le Lu, Hoo-chang Shin, Lauren Kim, Hadi Bagheri, Isabella Nogues, Jianhua Yao and Ronald M. Summers

> Imaging Biomarkers and Computer-Aided Diagnosis Laboratory, Department of Radiology and Imaging Sciences, National Institutes of Health Clinical Center, Bethesda, MD 20892





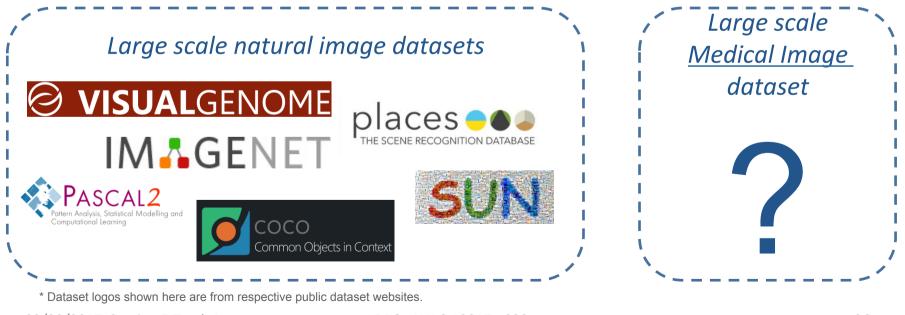
US Patent Application, 62/302,096





Motivation

- The availability of well-labeled data is the key for large scale machine learning, e.g., deep learning
- Labels for large medical imaging database are NOT available
- Conventional ways for collecting image labels are NOT applicable, e.g.
 - □ Google search followed by crowd-sourcing
 - □ Annotation on medical images requires professionals with clinical training



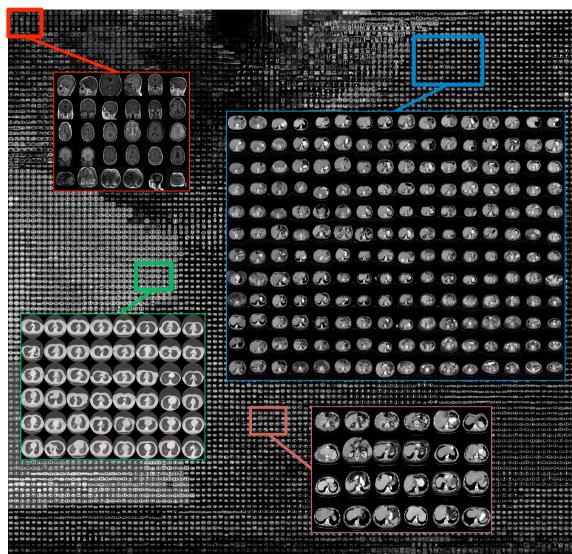
03/29/2017 Session 5 Track 1

LDPO - WACV 2017 - 039



Dataset

- A great treasure has been stored in our PACS system, i.e. images together with radiological reports.
- "Keyimage" dataset: 215,786 key images from 61,845 unique patient studies.
- Key images are significant one or more images in a study referenced in the linked radiological report.
- Key images are directly extracted from the DICOM file and resized as 256*256 bitmap images (.png).
- Their intensity ranges are rescaled using the default window settings stored in the DICOM header files.

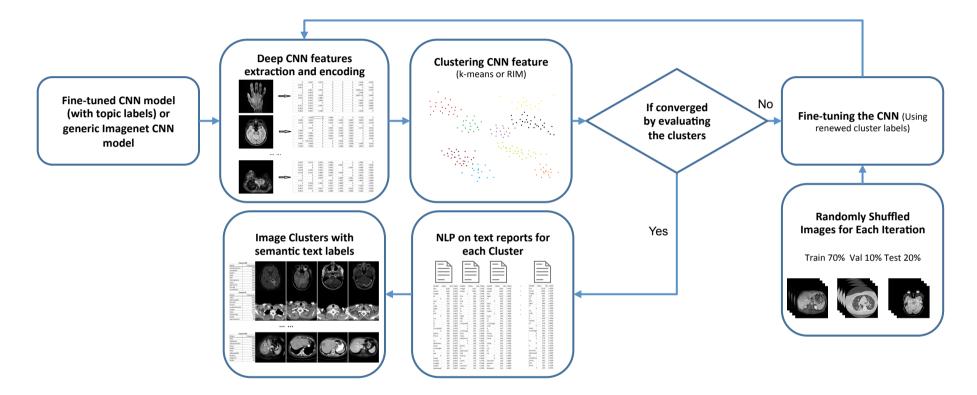


* 10000 random images from the dataset, using CNN FC7 features of images embedded with t-SNE



Unsupervised Categorization

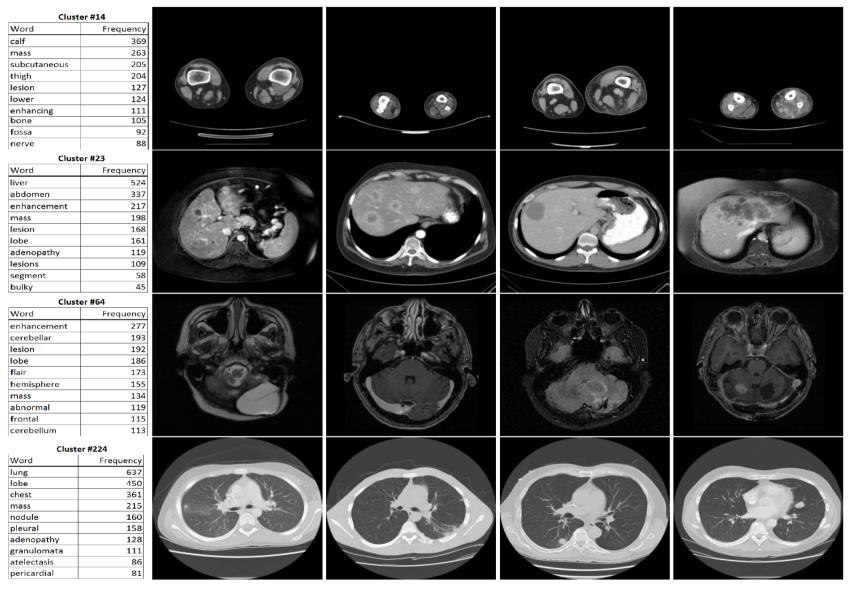
The proposed framework is designed towards automatic medical image annotation



• Hypothesized "convergence": better labels lead to better trained observable Convolutional Neural Network (CNN) models which consequently feed more effective deep image features to facilitate more meaningful clustering/labels.



Sample Categories





Experiment - CNN Setting

- The proposed framework is applicable to a variety of CNN models, by analyzing the CNN activations from layers of different depths.
- Encode the convolutional layer outputs in a form of dense pooling via Fisher Vector (FV) and Vector Locally Aggregated Descriptor (VLAD)
- Principal Component Analysis (PCA) is performed to reduce the dimensionality to 4096.

CNN model	Layer	Activations	Encoding	
AlexNet	Conv5	(13, 13, 256)	FV+PCA	
AlexNet	Conv5	(13, 13, 256)	VLAD+PCA	
AlexNet	FC7	4096	_	
GoogLeNet	Inception5b	(7, 7, 1024)	VLAD+PCA	
GoogLeNet Pool5		1024 —		



Experiment - Convergence

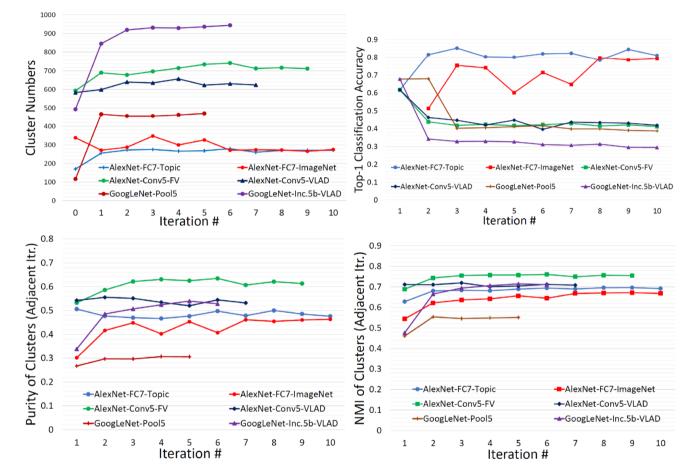
- Clustering via K-means only or over-fragmented K-means followed by Regularized Information Maximization (as an effective model selection method), are extensively explored and empirically evaluated.
- Two convergence measurements have been adopted, i.e., Clustering Purity and Normalized Mutual Information (NMI).
- Newly generated clusters are better in terms of

□ Visually more coherent and discriminative from instances from other clusters

- □ Balanced classes with approximately equivalent images per cluster
- □ The number of clusters is self-adaptive according to the nature of data
- □ Flexible to work with any clustering algorithm, no need to be differentiable or end-to-end trainable
- Our conceptually simple unsupervised deep clustering algorithm shows effectiveness for other computer vision or medical imaging problems



Quantitative Results



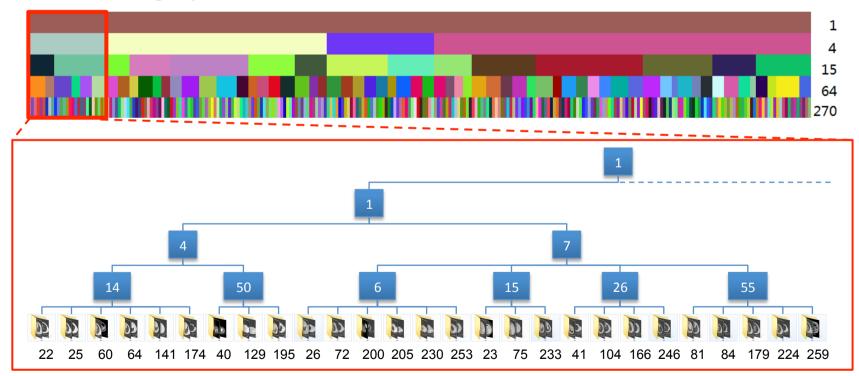
- The convergence of our categorization framework is measured and observed in the cluster-similarity measures, the CNN training classification accuracies and the self-adapted cluster number.
- AlexNet-FC7-Topic is preferred by two radiologists, which results in total 270 categories. The adopted FC7 feature is able to preserve the layout information of images.

03/29/2017 Session 5 Track 1



Hierarchical Category Relationship

• Hierarchical category relationships in a tree-like structure can be naturally formulated and computed from the final pairwise CNN classification confusion measures. The resulting category tree has (270, 64, 15, 4, 1) different class labels from bottom (leaf) to top (root). The random color coded category tree is shown below.





Application on Scene Recognition

- Images from the same scene category may share similar object patches but are different in overall setting, e.g. buildings all have windows but in different style.
- Integrate patch mining as a form of image encoding into our LDPO framework and perform the categorization and patch mining iteratively.



American Craftsman

Bedroom



Evaluation on Clustering Accuracy

- The purity and NMI measurements are computed between the final LDPO clusters and GT scene classes (purity becomes the classification accuracy against GT).
- We compare the LDPO scene recognition performance to those of several popular clustering methods.
- The state-of-the-art fully-supervised scene Classification Accuracies (CA) for each dataset are also provided.

Dataset	KM [57]	LSC [4]	AC [22]	EP [10]	MDPM [34]	LDPO-A-FC	LDPO-A-PM	LDPO-V-PM	Supervised
Clustering Accuracy (%)							CA(%)		
I-67 [44]	35.6	30.3	34.6	37.2	53.0	37.9	63.2	75.3	81.0[8]
B-25 [62]	42.1	42.6	43.2	43.8	43.1	44.1	59.2	59.5	59.1 [42]
S-15 [32]	65.0	76.5	65.2	73.6	63.4	73.1	90.1	84.0	91.6 [66]
	Normalized Mutual Information								
I-67 [44]	.386	.335	.359	-	.558	.389	.621	.759	-
B-25 [62]	.401	.403	.404	-	.424	.407	.588	.546	-
S-15 [32]	.659	.625	.653	-	.596	.705	.861	.831	-

* KM: k-means; AC: agglomerative clustering ; LSC: large-scale spectral clustering ; EP: ensemble projection + k-means; MDPM: mid-level discriminative patch mining + k-means



Evaluation on Learned Image Features and Initialization Settings

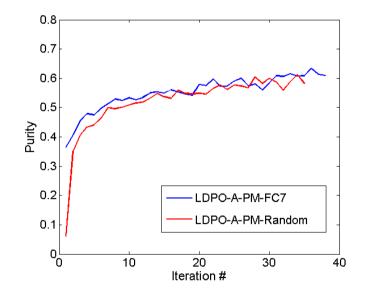
* Learned image representation:

- 1. Classification task on MIT-67, standard partition [44]
- 2. One-versus-all Liblinear classification on image features
- × LDPO-V-PM-LL does not improve upon purely unsupervised LDPO-V-PM. This may indicate that LDPO-PM image representation is sufficient to separate images from different classes.

Method	Accuracy (%)			
D-patch [53]	38.1			
D-parts [54]	51.4			
DMS [13]	64.0			
MDPM-Alex [34]	64.1			
MDPM-VGG [34]	77.0			
MetaObject [60]	78.9			
FC (VGG)	68.87			
CONV-FV (VGG) [8]	81.0			
LDPO-V-PM-LL	72.5			
LDPO-V-PM	75.3			

* Different initialization settings:

- 1. Random initialization
- 2. Image labels obtained from k-means clustering on FC7 features of an ImageNet pretrained AlexNet
- ✓ Both schemes ultimately converge to similar performance levels and it suggests that LDPO convergence is insensitive to the chosen initialization.



*Both results are computed using MIT Indoor-67 dataset.



Conclusion

- Now It is time to wake up the huge collection of clinical data sleeping in the PACS and put it to work!
- A novel looped deep pseudo-task optimization framework is presented for category discovery from a large-scale medical image database.
- Extracted categories are visually more coherent and semantically meaningful (manually verified by experienced radiologists)
- We systematically and extensively conduct experiments under different settings of the proposed framework to validate and evaluate its quantitative and qualitative performance on two different types of dataset → effectively applicable to other CAD problems by exploiting finer-grained category information in an unsupervised manner.
- The measurable "convergence" makes the ill-posed auto-annotation problem well constrained, at no human labeling cost → towards building radiology (anatomical & pathological) ontology image database!



Learning to Read Chest X-ray using Deep Neural Networks (a little more like humans' interpretation?) [Shin et al., IEEE CVPR 2016, US Patent Application: 62/302,084]

INVIDIA ACCELERATED COMPUTING Getting Started Downloads Training Ecosystem
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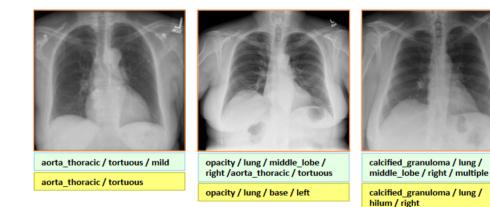
Detecting and Labeling Diseases in Chest X-Rays with Deep Learning

April 14, 2016

Researchers from the National Institutes of Health in Bethesda, Maryland are using NVIDIA GPUs and deep learning to automatically annotate diseases from chest x-rays.

Accelerated by Tesla GPUs, the team trained their convolutional neural networks on

a publicly available radiology dataset of chest x-rays and reports to describe the characteristics of a disease, such as location, severity and the affected organs.



Examples of annotation generations (light green box) compared to true annotations (yellow box) for input images in the test set.

Lung diseases killing 4 million people every year, in comparison to Nearly 1.3 million people die in road crashes each year!

Statistics from internet ...





ChestX-ray8: Hospital-scale Chest X-ray Database and Benchmarks on Weakly-Supervised Classification and Localization of Common Thorax Diseases

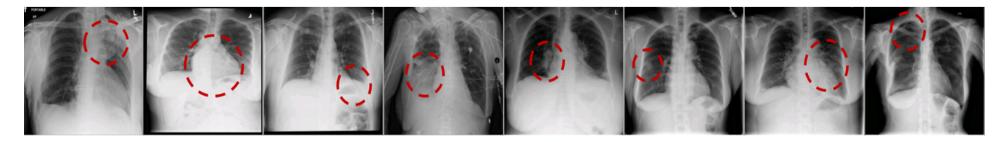
Xiaosong Wang¹, Yifan Peng², Le Lu¹, Zhiyong Lu², Mohammadhadi Bagheri¹, Ronald M. Summers¹

1 Department of Radiology and Imaging Sciences, Clinical Center 2 National Center for Biotechnology Information, National Library of Medicine National Institutes of Health, Bethesda, MD 20892



US Patent Application, 62/476,029







Motivation

- 1. Build a large-scale Chest X-rays dataset to facilitate the data-hungry deep learning paradigms
- 2. Critical/common disease patterns (predefined by radiologist)
- 3. Multiple labels (disease patterns) for images
- 4. Radiological report for each image
- 5. Small number of bounding boxes (outline the location of disease symptoms) for each disease category
- 6. Potential applications:
 - A. Disease detection/classification
 - B. Disease localization
 - C. Automatic radiological report generation

•••



Dataset 2#: A Hospital-scale Chest X-ray Dataset (Joint efforts by NIH-CC and NIH-NLM)







07/21/2017

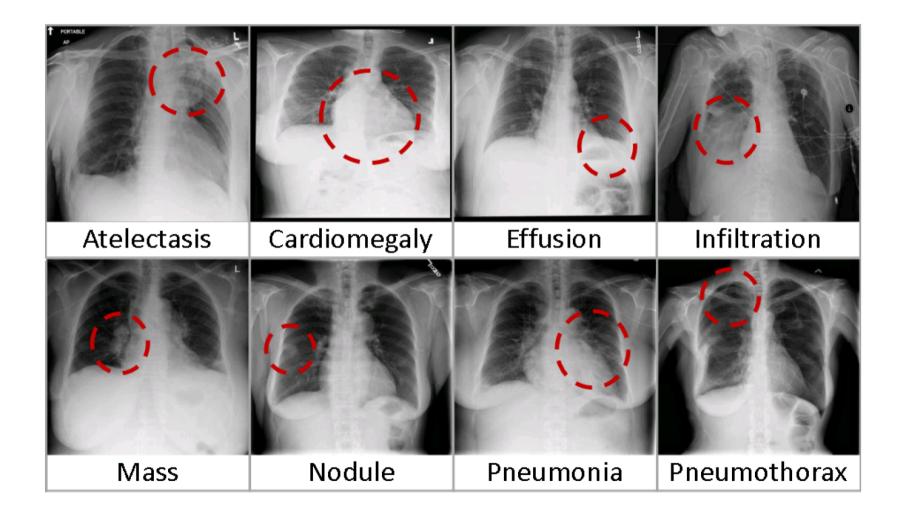


A Sample Entry

Image	Report	Label	Bounding Box (optional)
	findings: pa and lateral views of the chest demonstrate significantly improved bilateral lower lung field interstitial markings compatible with linear atelectasis. unchanged right 9th rib fracture peripherally. unchanged ossification left coracoacromial ligament. the cardiac and mediastinal contours are stable. impression: improved bilateral lower lung field linear atelectasis.	atelectasis	<pre>-<questions></questions></pre>



8 Common Thorax Diseases





Two-stage NLP of Radiology Reports

Stage 1: Pathology Detection

- DNorm is used to map every mention of keywords in a report to a unique concept ID in the Systematized Nomenclature of Medicine Clinical Terms (SNOMED-CT), a standardized vocabulary of clinical terminology for the electronic exchange of clinical health information.
- Another ontology-based approach, MetaMap, is adopted for the detection of Unified Medical Language System (UMLS) Metathesaurus.
- The results of DNorm and MetaMap are merged

Pneumonia	
C0032285	pneumonia
C0577702	basal pneumonia
C0578576	left upper zone pneumonia
C0578577	right middle zone pneumonia
C0585104	left lower zone pneumonia
C0585105	right lower zone pneumonia
C0585106	right upper zone pneumonia
C0747651	recurrent aspiration pneumonia
C1960024	lingular pneumonia
Pneumothorax	
C0032326	pneumothorax
C0264557	chronic pneumothorax
C0546333	right pneumothorax
C0546334	left pneumothorax

Sample SNOMED-CT concepts



Two-stage NLP of Radiology Reports

Stage 2: Removal of negation and uncertainty

- Rule out those negated pathological statements and uncertain mentions of findings and diseases
- Defined the rules on the dependency graph, by utilizing the dependency label and direction information between words, e.g.,

Rule	Example
Negation	
$no \leftarrow * \leftarrow DISEASE$	No acute pulmonary disease
$* \rightarrow prep_without \rightarrow DISEASE$	changes without focal airspace disease
clear/free/disappearance $\rightarrow prep_of \rightarrow DISEASE$	clear of focal airspace disease, pneumothorax, or pleural effusion
$* \rightarrow prep_without \rightarrow evidence \rightarrow prep_of \rightarrow DISEASE$	Changes without evidence of acute infiltrate
$no \leftarrow neg \leftarrow evidence \rightarrow prep_of \rightarrow DISEASE$	No evidence of active disease
Uncertainty	·
cannot $\leftarrow md \leftarrow$ exclude	The aorta is tortuous, and cannot exclude ascending aortic aneurysm
$concern \rightarrow prep_for \rightarrow *$	There is raises concern for pneumonia
could be/may be/	which could be due to nodule/lymph node
difficult \rightarrow <i>prep_to</i> \rightarrow exclude	interstitial infiltrates difficult to exclude
$may \leftarrow md \leftarrow represent$	which may represent pleural reaction or small pulmonary nodules
suggesting/suspect/ $\rightarrow dobj \rightarrow DISEASE$	Bilateral pulmonary nodules suggesting pulmonary metastases



Two-stage NLP of Radiology Reports

Stage 2: Removal of negation and uncertainty

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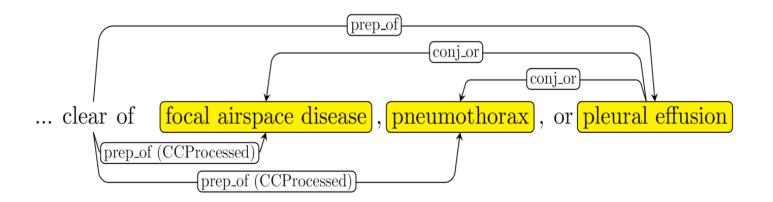




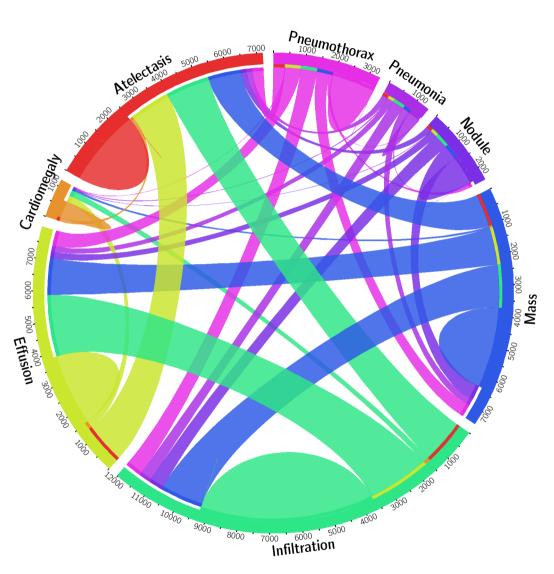
Image preparation

- 1. Select frontal view images only
- 2. Convert to 8-bit RBG images by using default window level and width
- 3. Resize image to 1024 * 1024
- 4. Totally 108,948 frontal view chest X-ray images of 32,717 unique patients. This is about 27 times of the previously available largest frontal view chest x-ray database OPENi.



Disease Category Statistics

Item #	OpenI	Ov.	ChestX-ray8	Ov.
Report	2,435	-	108,948	-
Annotations	2,435	-	-	-
Atelectasis	315	122	5,789	3,286
Cardiomegaly	345	100	1,010	475
Effusion	153	94	6,331	4,017
Infiltration	60	45	10,317	4,698
Mass	15	4	6,046	3,432
Nodule	106	18	1,971	1,041
Pneumonia	40	15	1,062	703
Pneumothorax	22	11	2,793	1,403
Normal	1,379	0	84,312	0





Evaluation of Disease Labeling

OPEN

Item #	OpenI	Ov.	ChestX-ray8	Ov.
Report	2,435	-	108,948	-
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Pneumonia	40	15	1,062	703
Pneumothorax	22	11	2,793	1,403
Normal	1,379	0	84,312	0

Disease	MetaMap	Our Method	
Disease	P/ R/ F	P/ R/ F	
Atelectasis	0.95 / 0.95 / 0.95	0.99 / 0.85 / 0.91	
Cardiomegaly	0.99 / 0.83 / 0.90	1.00 / 0.79 / 0.88	
Effusion	0.74 / 0.90 / 0.81	0.93 / 0.82 / 0.87	
Infiltration	0.25 / 0.98 / 0.39	0.74 / 0.87 / 0.80	
Mass	0.59 / 0.67 / 0.62	0.75 / 0.40 / 0.52	
Nodule	0.95 / 0.65 / 0.77	0.96 / 0.62 / 0.75	
Normal	0.93 / 0.90 / 0.91	0.87 / 0.99 / 0.93	
Pneumonia	0.58 / 0.93 / 0.71	0.66 / 0.93 / 0.77	
Pneumothorax	0.32 / 0.82 / 0.46	0.90 / 0.82 / 0.86	
Total	0.84 / 0.88 / 0.86	0.90/0.91/0.90	

Table 2. Evaluation of image labeling results on OpenI dataset. Performance is reported using P, R, F1-score.

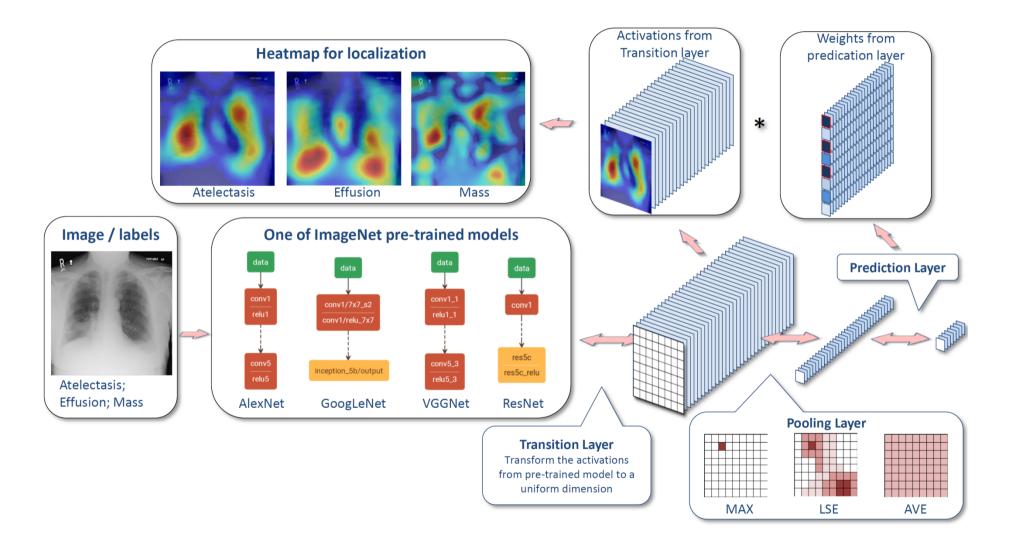


Weakly-Supervised Classification and Localization of Common Thorax Diseases





Framework Overview





Multi-label Setting

• We define a 8-dimensional label vector

 $\mathbf{y} = [y_1, ..., y_c, ..., y_C], y_c \in \{0, 1\}, C = 8$

- *y_c* indicates the presence with respect to according pathology in the image
- A all-zero vector represents the status of "Normal".
- This definition transits the multi-label classification problem into a regression-like loss setting



Transition Layer

- A variety of CNN networks are adopted and integrated into the proposed framework, e.g. GoogLeNet and ResNet
- Transform the activations from $S \times S \times D, S \in \{8, 16, 32\}$ uniform dimension of output
- Pass down the weights from pre-trained DCNN models in a standard form, which is critical for using this layers' activations to further generate the heatmap in pathology localization step



Multi-label Classification Loss Layer

- We first experiment 3 standard loss functions for the regression task instead of using the softmax loss for traditional multi-class classification model, i.e., Hinge Loss (HL), Euclidean Loss (EL) and Cross Entropy Loss (CEL)
- The model has difficulty learning positive because of onehot-like image labeling strategy (sparse image labels) and the unbalanced numbers of pathology and "Normal" classes.
- Positive/negative balancing, e.g.

$$L_{W-CEL}(f(\vec{x}), \vec{y}) = \beta_P \sum_{y_c=1}^{\infty} -\ln(f(x_c)) + \beta_N \sum_{y_c=0}^{\infty} -\ln(1 - f(x_c)),$$

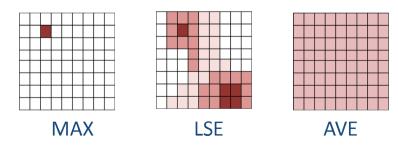


Global Pooling Layer

- The pooling layer plays an important role that chooses what information to be passed down [Zhou et al., 2016].
- Besides the conventional max pooling and average pooling, we also utilize the Log-Sum-Exp (LSE) pooling, which is defined as

$$x_p = \frac{1}{r} \cdot \log \left[\frac{1}{S} \cdot \sum_{(i,j) \in \mathbf{S}} exp(r \cdot x_{ij}) \right] \quad \begin{aligned} x_p = x^* + \frac{1}{r} \cdot \log \left[\frac{1}{S} \cdot \sum_{(i,j) \in \mathbf{S}} exp(r \cdot (x_{ij} - x^*)) \right] \\ \text{where } x^* = max\{|x_{ij}|, (i,j) \in \mathbf{S}\}. \end{aligned}$$

• By controlling the hyper-parameter r, the pooled value ranges from the maximum in S (when r -> 1) to average (r -> 0).





Disease Localization Results - Atelectasis

Radiology report	Keyword	Localization Result
findings include: 1. left basilar at- electasis/consolidation. 2. prominent hilum (mediastinal adenopathy). 3. left pic catheter (tip in atriocaval junc- tion). 4. stable, normal appearing car- diomediastinal silhouette. impression: small right pleural ef- fusion otherwise stable abnormal study including left basilar infil- trate/atelectasis, prominent hilum, and position of left pic catheter (tip atriocaval junction).	Effusion; Infiltration; Atelectasis	



Disease Localization Results - Cardiomegaly

Radiology report	Keyword	Localization Result
findings include: 1. cardiomegaly (ct ratio of 17/30). 2. otherwise normal lungs and mediastinal contours. 3. no evidence of focal bone lesion. dictat- ing	Cardiomegaly	



Disease Localization Results - Effusion

Radiology report	Keyword	Localization Result
findings: no appreciable change since XX/XX/XX. small right pleural effusion. elevation right hemidiaphragm. diffuse small nodules throughout the lungs, most numerous in the left mid and lower lung. impression: no change with bilateral small lung metastases.	Effusion; Nodule	



Disease Localization Results - Infiltration

Radiology report	Keyword	Localization Result
findings: port-a-cath reservoir re- mains in place on the right. chest tube remains in place, tip in the left apex. no pneumothorax. diffuse patchy in- filtrates bilaterally are decreasing. impression: infiltrates and effusions decreasing.	Infiltration	



Disease Localization Results - Mass

Radiology report	Keyword	Localization Result
findings: right internal jugular catheter remains in place. large metastatic lung mass in the lateral left upper lobe is again noted. no in- filtrate or effusion. extensive surgical clips again noted left axilla. impression: no significant change.	Mass	



Disease Localization Results - Pneumonia

Radiology report	Keyword	Localization Result
findings: unchanged left lower lung field infiltrate/air bronchograms. un- changed right perihilar infiltrate with obscuration of the right heart bor- der. no evidence of new infiltrate. no evidence of pneumothorax the car- diac and mediastinal contours are sta- ble. impression: 1. no evidence pneumothorax. 2. unchanged left lower lobe and left lingular consoli- dation/bronchiectasis. 3. unchanged right middle lobe infiltrate	Pneumonia; Infiltration	



Disease Localization Results - Pneumothorax

Radiology report	Keyword	Localization Result				
findings: frontal lateral chest x-ray performed in expiration. left apical pneumothorax visible. small pneu- mothorax visible along the left heart border and left hemidiaphragm. pleu- ral thickening, mass right chest. the mediastinum cannot be evaluated in the expiration. bony structures intact. impression: left post biopsy pneu- mothorax.	Mass; Pneumothorax	The results of the re				

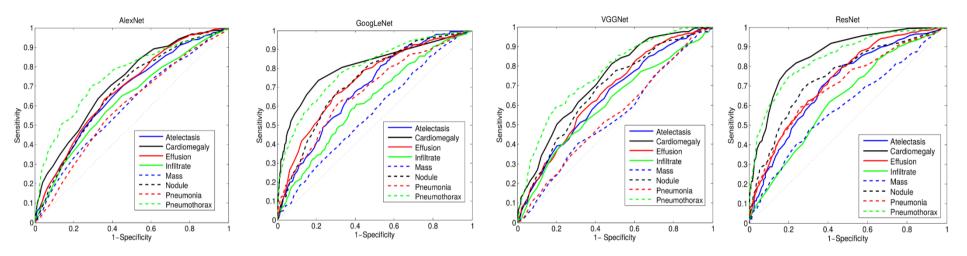


Experiment Setting

- 108,948 frontal-view X-ray images, 24,636 images contain one or more pathologies + 10,000 images of "Normal"
- Randomly shuffled the dataset into three subgroups: i.e. training (70%), validation (10%) and testing (20%)
- Multi-label CNN architecture is implemented using Caffe framework
- The ImageNet pre-trained models, i.e., AlexNet, GoogLeNet, VGGNet-16 and ResNet-50 are obtained from the Caffe model zoo
- Due to the large image size and the limit of GPU memory, reduce the image batch size while increasing the iter size to accumulate the gradients. We set batch size * iter size = 80



Multi-label Disease Classification Results



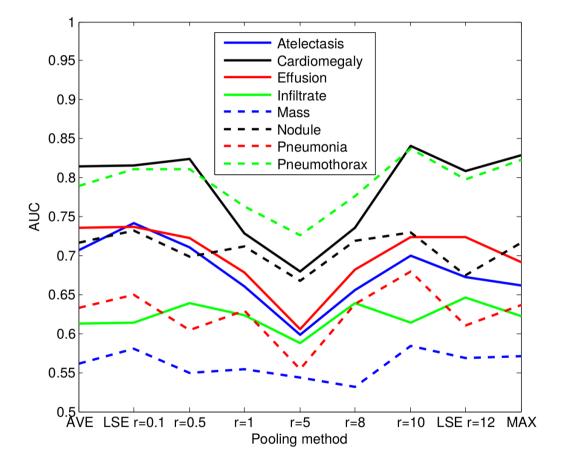
Setting	Atelectasis	Cardiomegaly	Effusion	Infiltration	Mass	Nodule	Pneumonia	Pneumothorax
Initialization with different pre-trained models								
AlexNet	0.6458	0.6925	0.6642	0.6041	0.5644	0.6487	0.5493	0.7425
GoogLeNet	0.6307	0.7056	0.6876	0.6088	0.5363	0.5579	0.5990	0.7824
VGGNet-16	0.6281	0.7084	0.6502	0.5896	0.5103	0.6556	0.5100	0.7516
ResNet-50	0.7069	0.8141	0.7362	0.6128	0.5609	0.7164	0.6333	0.7891
Different multi-label loss functions								
CEL	0.7064	0.7262	0.7351	0.6084	0.5530	0.6545	0.5164	0.7665
W-CEL	0.7069	0.8141	0.7362	0.6128	0.5609	0.7164	0.6333	0.7891

Table 3. AUCs of ROC curves for multi-label classification in different DCNN model setting.

Note that the above Multi-label disease classification results have been noticeably improved since the CVPR deadline in Nov. 2016.



Different Spatial Pooling Strategies



- The hyper-parameter r in LSE pooling varies in { 0.1, 0.5, 1, 5, 8, 10, 12}
- LSE pooling behaves like a weighed pooling method or a transition scheme between average and max pooling under different r values



Disease Localization Results – IoBB*

T(IoBB)	Atelectasis	Cardiomegaly	Effusion	Infiltration	Mass	Nodule	Pneumonia	Pneumothorax
T(IoBB) = 0.1								
Acc.	0.7277	0.9931	0.7124	0.7886	0.4352	0.1645	0.7500	0.4591
AFP	0.0823	0.0487	0.0589	0.0426	0.0691	0.0630	0.0691	0.0264
T(IoBB) = 0.25 (Two times larger on both x and y axis than ground truth B-Boxes)								
Acc.	0.5500	0.9794	0.5424	0.5772	0.2823	0.0506	0.5583	0.3469
AFP	0.1666	0.1534	0.1189	0.0914	0.0975	0.0741	0.1250	0.0487
T(IoBB) = 0.5								
Acc.	0.2833	0.8767	0.3333	0.4227	0.1411	0.0126	0.3833	0.1836
AFP	0.2703	0.2611	0.1859	0.1422	0.1209	0.0772	0.1768	0.0772
T(IoBB) = 0.75								
Acc.	0.1666	0.7260	0.2418	0.3252	0.1176	0.0126	0.2583	0.1020
AFP	0.3048	0.3506	0.2113	0.1737	0.1310	0.0772	0.2184	0.0873
T(IoBB) = 0.9								
Acc.	0.1333	0.6849	0.2091	0.2520	0.0588	0.0126	0.2416	0.0816
AFP	0.3160	0.3983	0.2235	0.1910	0.1402	0.0772	0.2317	0.0904

*Intersection over the detected B-Box area ratio (IoBB) (similar to Area of Precision or Purity)



Future work - Challenges

• Improving image labeling accuracy

- Disease category
- NLP technique
- Annotate reports for evaluation
- Improving multi-label classification accuracy
 - Other CNN architecture, e.g. classic layer setting
 - More accurate image labels lead to more effective learning
 - LSTM text-assisted end-to-end deep training
- Improving localization accuracy
 - Better bounding box generation method
 - integrate text info. by adopting attention model & location information



(d)

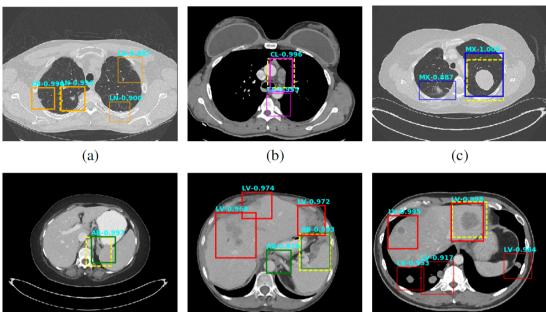


Fig. 4. Six sample detection results are illustrated with the annotation lesion patches as yellow dashed boxes. The outputs from our proposed detection framework are shown in colored boxes with LiVer lesion (LV) in Red, Lung Nodule (LN) in Orange, ABdomen lesion (AB) in Green, Chest Lymph node (CL) in magenta and other MiXed lesions (MX) in blue. (a) Four lung lesions are all correctly detected; (b) Two lymph nodes in mediastinum is presented; (c) A Ground Glass Opacity (GGO) and a mass are detected in the lung; (d) An adrenal nodule; (e) Correct detections on both the small abdomen lymph node nearly aorta but also other metastases in liver and spleen; (f) Two liver metastasis are correctly detected. Three lung metastases are detected but erroneously classified as liver lesions .

(e)

(f)

Runtime of 88ms to label a testing 512x512 slice on a single Titan-X GPU, → ~1 minute to read a 700 slice Chest/Abdomen CT scan!

A new CAD paradigm via mining ultra-large scale retrospective clinical datasets with weak annotations: \rightarrow universal, multipurpose deeply trainable CAD systems, almost effortlessly from the workload perspective required for radiologists or human annotators. (Patent Pending) Database #3?





The day of "big data, weak label, true clinical impacts" seems coming faster than what we all have realized, just a few months ago. Thanks to Deep Learning developments in Computer Vision, MICCAI and "Open Science Initiative!"

So get prepared! Exciting days are yet to come ...



Le Lu Yefeng Zheng Gustavo Carneiro Lin Yang *Editors*

Deep Learning and Convolutional Neural Networks for Medical Image Computing

Precision Medicine, High Performance and Large-Scale Datasets



Deep Learning for Medical Image Analysis

Edited by S. Kevin Zhou Hayit Greenspan Dinggang Shen





You are cordially invited to be part of the force!



WE WANT YOU!



Medical Computer Vision and Health Informatics Workshop (CVPR 2017), July 26th (Full Day)

Le Lu (National Institutes of Health Clinical Center, USA) Tal Arbel (Associate Professor, McGill University, Canada) Leo Grady (HeartFlow, Inc. Redwood City, CA, USA) Bjoern Menze (Technical University of Munchen, Germany) Georg Langs (Medical University of Vienna & MIT, Austria)

Confirmed Speakers (and growing ..., We are preparing up to 16 high quality talks of 30 minutes each):

Prof. Jiebo Luo (University of Rochester)
 Prof. Chunhua Shen (University of Adelaide)
 Prof. Greg Hager (Johns Hopkins University)
 Prof. Pascal Fua (EPFL)
 Prof. Nikos Paragios (Ecole Centrale Paris)
 Dr. Dale Webster, Dr. Martin Stumpe (Google Research)
 Dr. Xiaosong Wang (NIH Clinical Center)
 Prof. Junzhou Huang (UT Arlington)
 Prof. Lin Yang (University of Florida)
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 Mr. Andre Esteva (Stanford University)

1, Prof. Daniel Rueckert (Imperial College London)

**Bridging CVPR, ICCV, MICCAI, ECCV, NIPS, ISBI, RSNA, GTC ... to solve important medical (imaging) diagnosis problems for the life-saving mission!





THANK YOU!



Scan to download the Key Radiology Image and Chest X-ray datasets via Google Cloud (free to everyone!)

https://console.cloud.google.com/storage/gcspublic-data--nih

Acknowledgement

- This work is supported by the Intramural Research Program of the National Institutes of Health Clinical Center and National Library of Medicine.
- We thank Nvidia corporation for the GPU donation.



National Institutes of Health Turning Discovery Into Health







Thank you & our amazing trainees, collaborators, Industrial partnerships!



Department of Radiology and Imaging Sciences National Institutes of Health Clinical Center Bethesda, Maryland 20892-1182

Contacts: le.lu@nih.gov; rms@nih.gov

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