Deep Learning in Medical Imaging[1]

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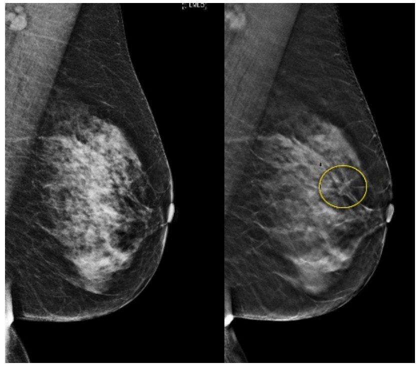
Agenda

- Medical Data Acquisition
- Neural Networks History
- Medical Applications
- Network Exploration
- Summary

Medical Data Acquisition

Medical Imaging – Modality

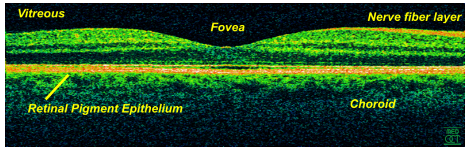
- Computer Tomography (CT)
- Magnet Resonance Imaging (MRI)
- Positron Emission Tomography (PET)/CT
- Histological Images
- Flow Cytometry, Biomarkers
- Ultrasound
- X-Ray



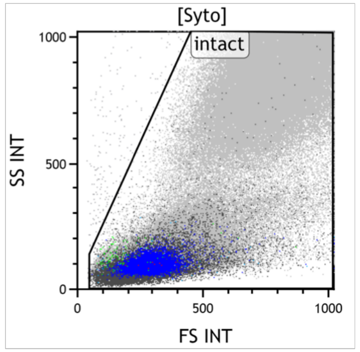
X-Ray Mammography
http://img.medscapestatic.com/pi/meds/ckb/35/15935.jpg

CT Images
Roth et al. ISBI 2015

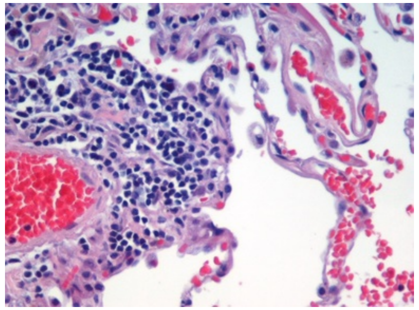
First X-Ray - Roentgen



OCT
https://upload.wikimedia.org/wikipedia/commons/2/2d/Retina-OCT800.png

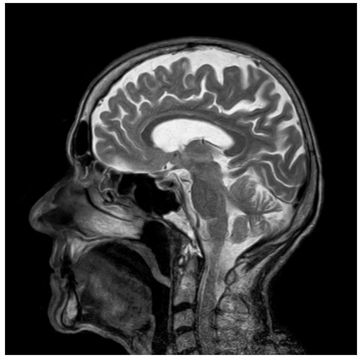


Flow Cytometry



Histological Image
https://en.wikipedia.org/wiki/File:Emphysema_H_and_E.jpg

Ultrasound
https://en.wikipedia.org/wiki/Ultrasound#/media/File:CRL_Crown_rump_lengh_12_weeks_ecografia_Dr._Wolfgang_Moroder.jpg



MRI
https://pixabay.com/de/mri-magnetresonanzr%C3%B6ntgen-sch%C3%A4del-782459/

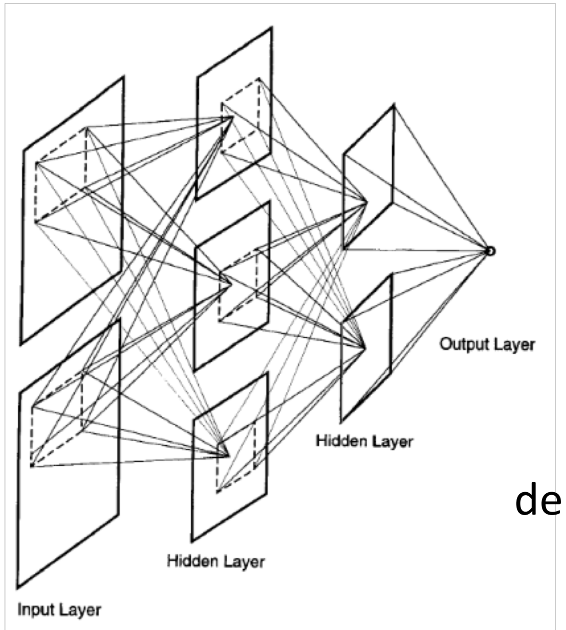
Medical Imaging - Challenges

- Subject specific variances
- Small study populations/datasets
- Developmental differences
- Heterogeneity of pathology
- Treatment response
- Annotation needs experts

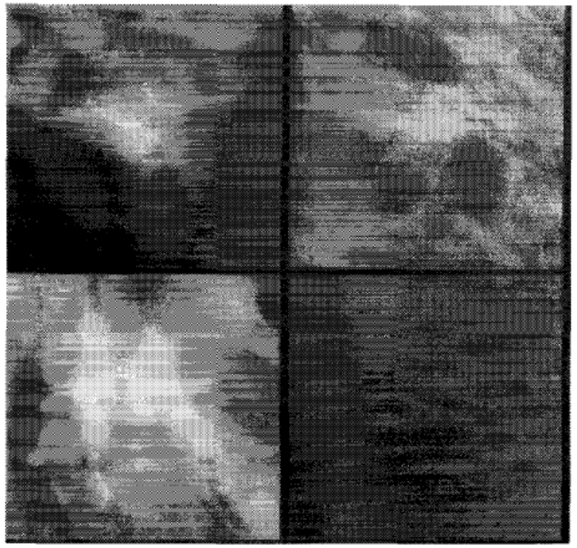
Neural Networks History

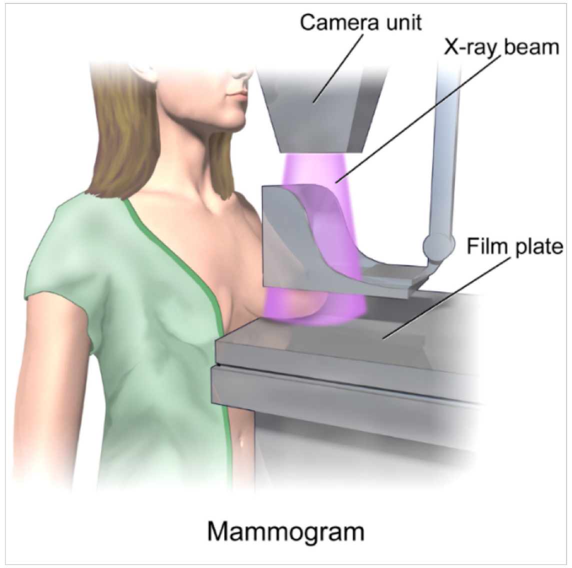
Neural Networks in Medical Imaging in the Past

- Convolution Neural Network (CNN)
  - Lung nodule detection 1993 [2], micro calcification mammography 1995 [3]
  - Classification of breast tissue 1996 [4]



Sahiner et al. 1996 [4]





Blausen.com staff. "Blausen gallery 2014". *Wikiversity Journal of Medicine*. DOI:10.15347/wjm/2014.010. ISSN 20018762.

Neural Networks in Medical Imaging in the Past

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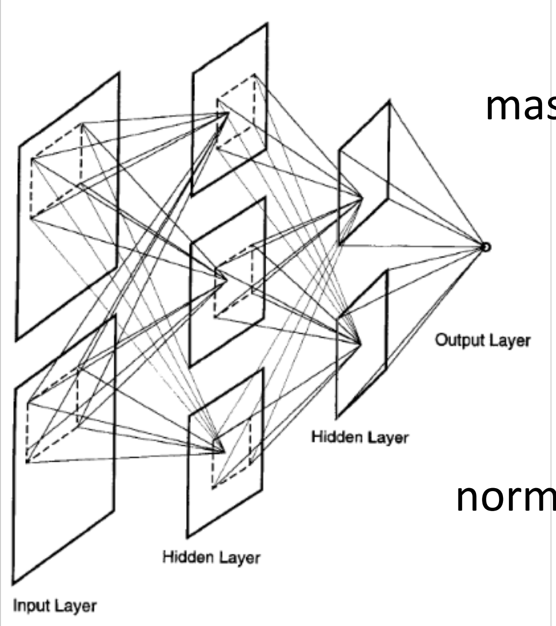


Sahiner et al. 1996 [4]

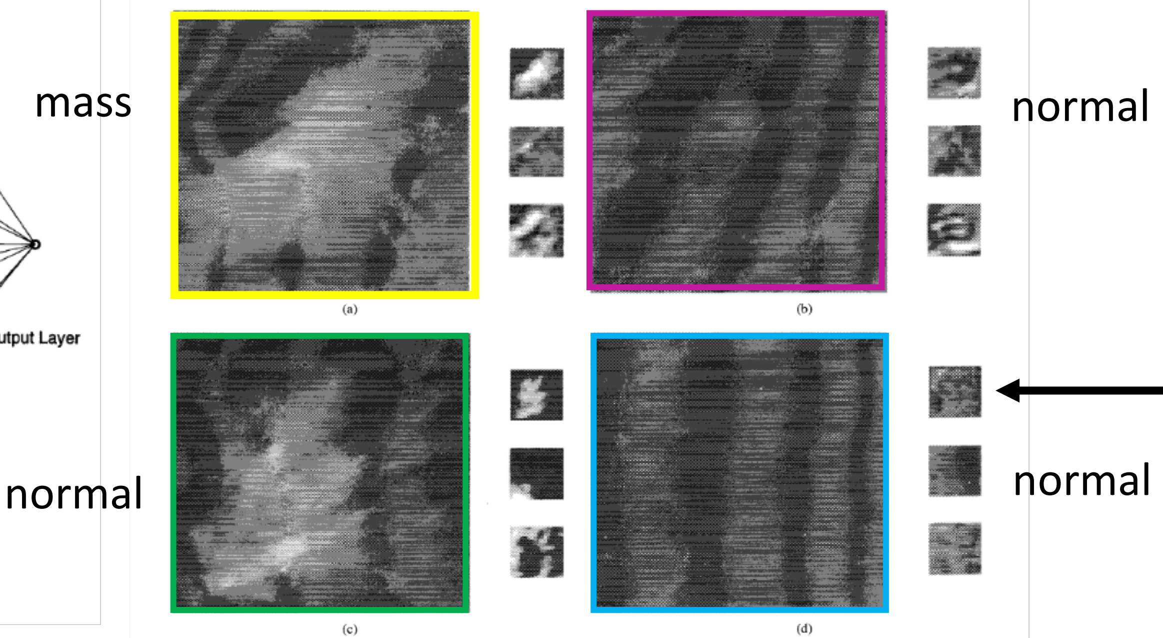
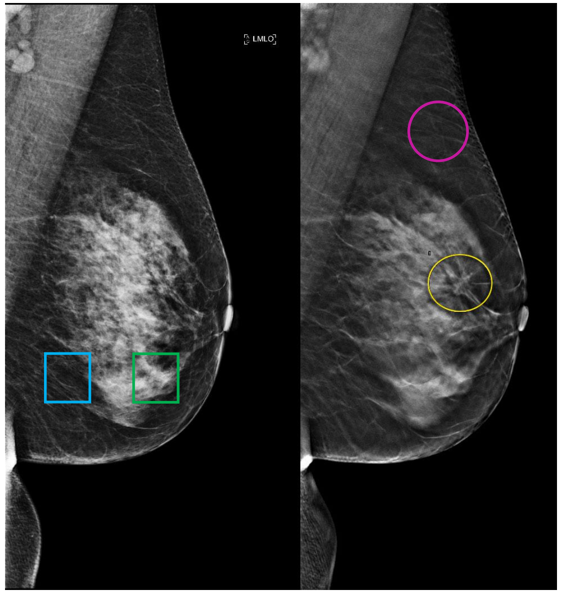


Fig. 11. Background corrected image, subsampled image, GLDS mean texture-image at $d_0 = 4$, and SGLD correlation texture-image at $d_0 = 16$ for (a) a mass ROI, as shown in Fig. 4(b), and (b)-(d) three nonmass ROI's extracted from the same mammogram.



http://img.medscapestatic.com/pi/meds/ckb/35/15935.jpg

Neural Networks in Medical Imaging Today

- Deep CNN
  - „Computationally expensive“ – acceleration using GPU
  - Highly parallelizable
  - Deep architecture for feature extraction

- Deep CNN Training
  - Large amount of training data and labels
  - Large computational and memory resources
  - Overfitting and convergence as possible complication

Neural Networks in Medical Imaging Today

- Supervised
  - Annotation required
  - Majority of works are supervised CNNs
  - Dimensionality of input data (2D, 2.5D, 3D)
  - Application: Segmentation, detection and labeling
- Unsupervised
  - No annotation required
  - Large computational and memory resources
  - Overfitting and convergence as possible complication
  - Application: Image encoding, representation and preprocessing

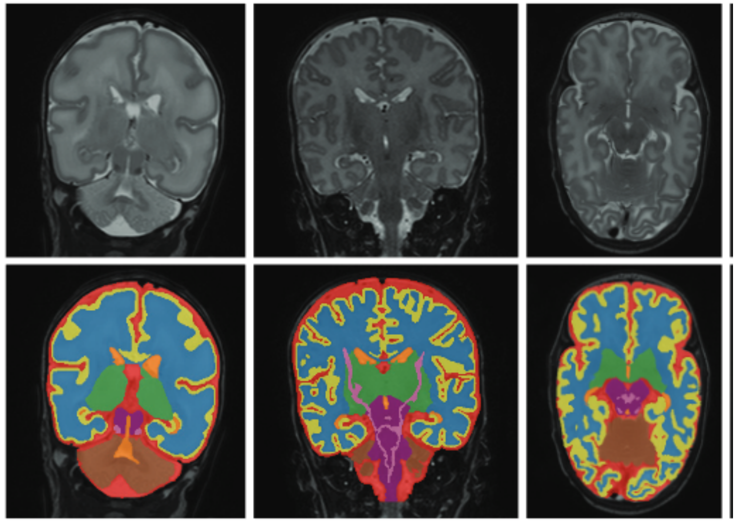


Image from Moeskops et al. [9]

Can deep networks be used effectively for medical tasks?

How can we use the training data most efficiently?

Medical Applications

Medical Applications

- Computer Aided Diagnosis
- Segmentation and Shape Modelling
- Classification
- Anomaly Detection
- Image Registration
- Action Recognition

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Medical Applications – Computer Aided Diagnosis

- 2D CNN
  - 2D Patch of image data centered on the location of pathology
  - Setio et al. [5] pulmonary nodules, 3D CT scans of chest

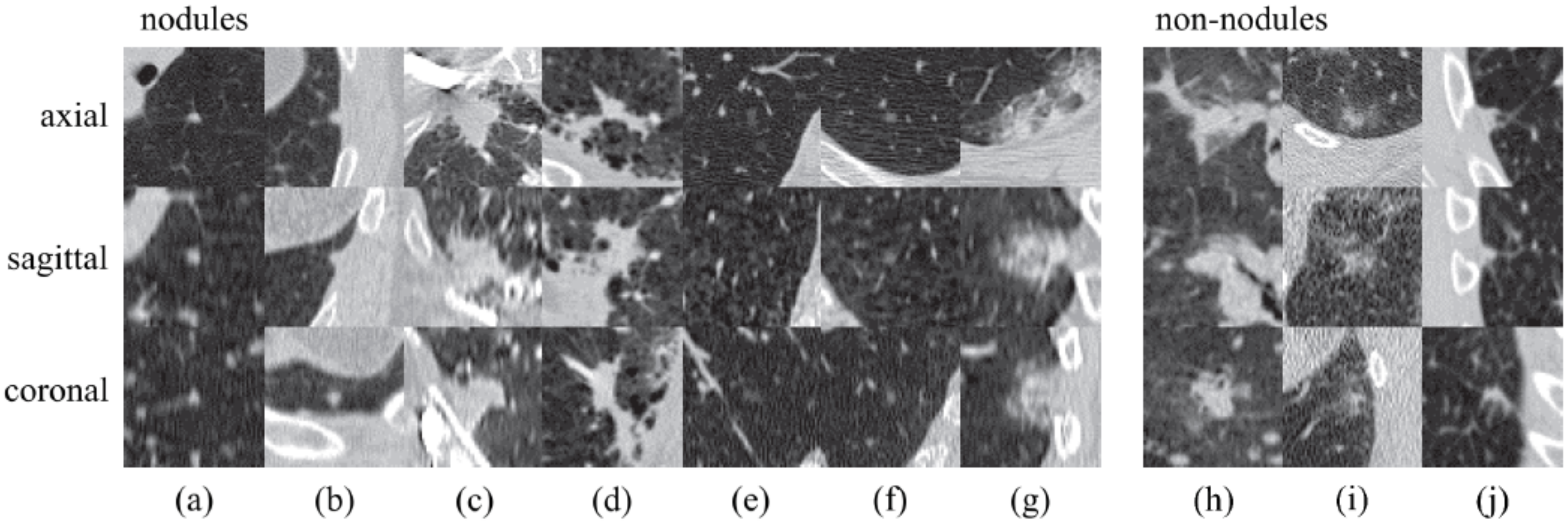


Image taken from Setio et al. [5]

Setio et al. [5], Detection of pulmonary nodules

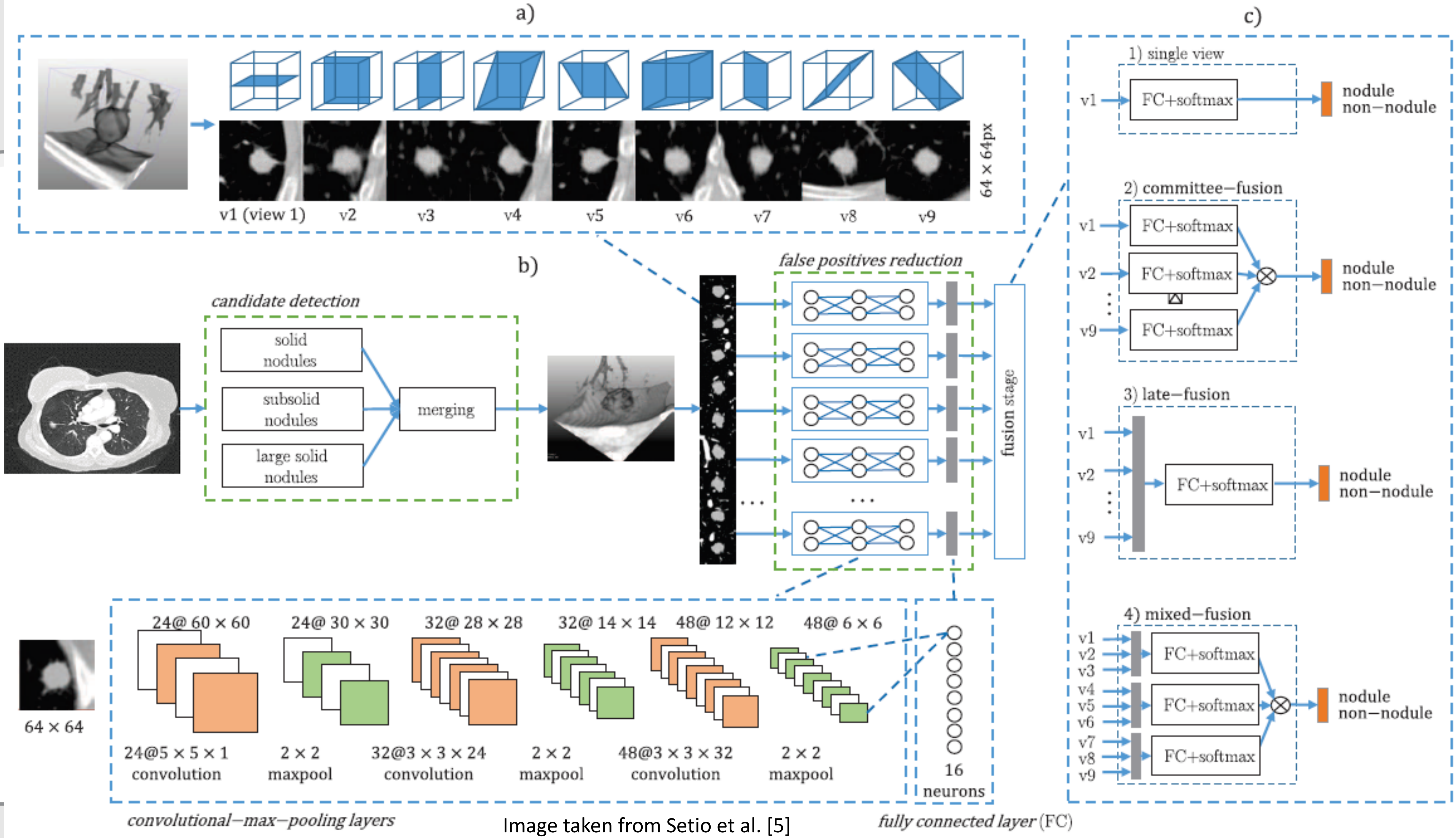
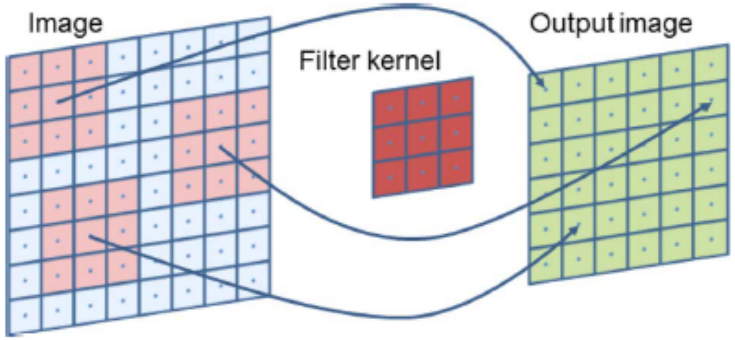


Image taken from Setio et al. [5]

Medical Applications – Computer Aided Diagnosis

- 2.5 D CNN
  - 3 orthogonal directions
  - 100 randomly rotated views
  - 13 – 14% increase of sensitivity



Images taken from Roth et al. [6]

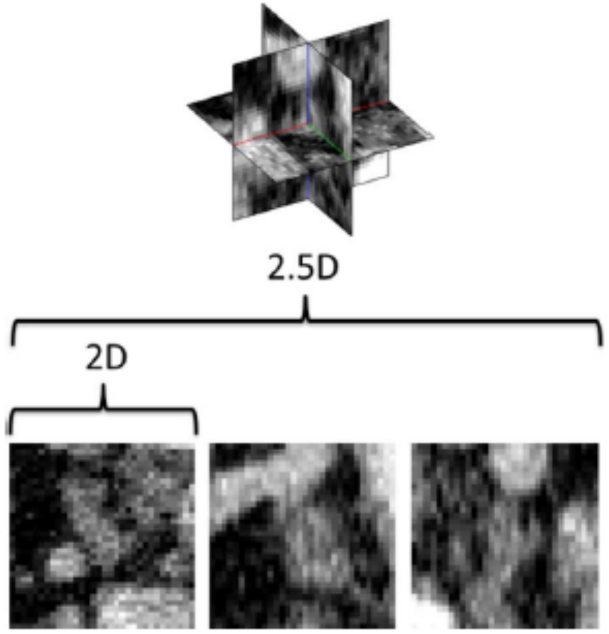
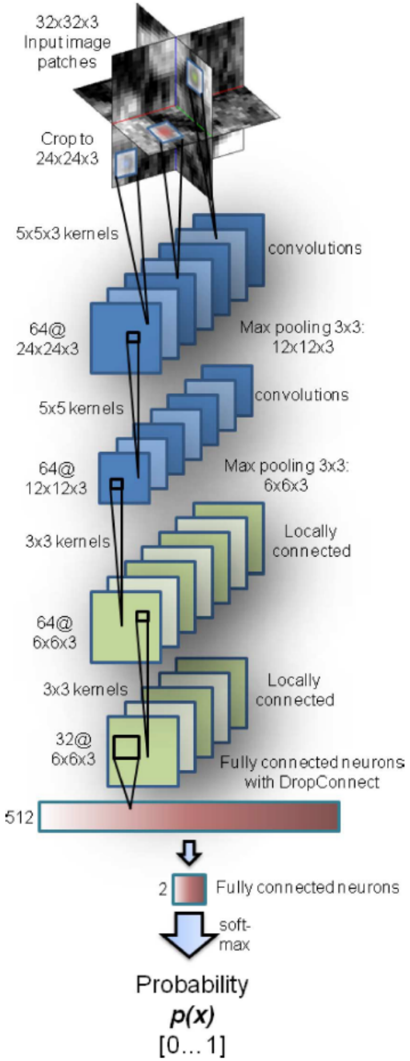


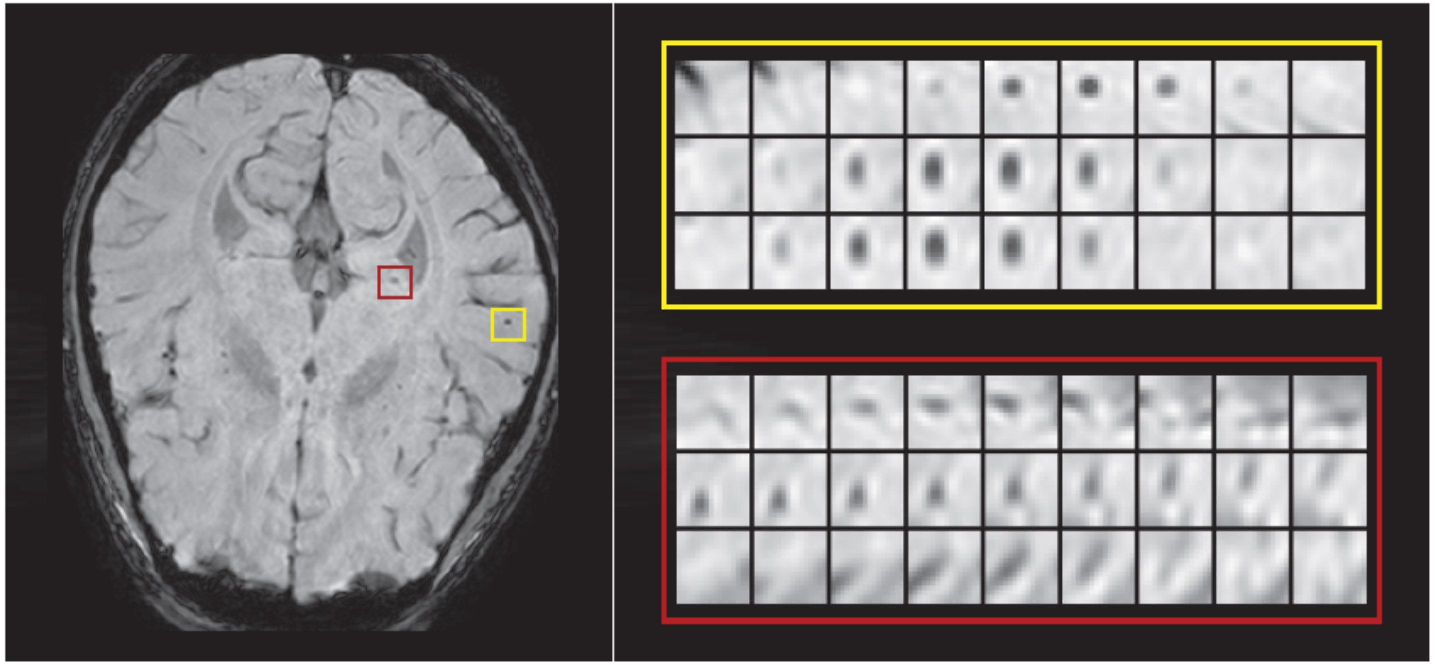
Fig. 4. CADe locations can be either observed as 2D image patches or using a 2.5D approach, that samples the image using three orthogonal views. Here, a lymph node in CT is shown as the input to our method.

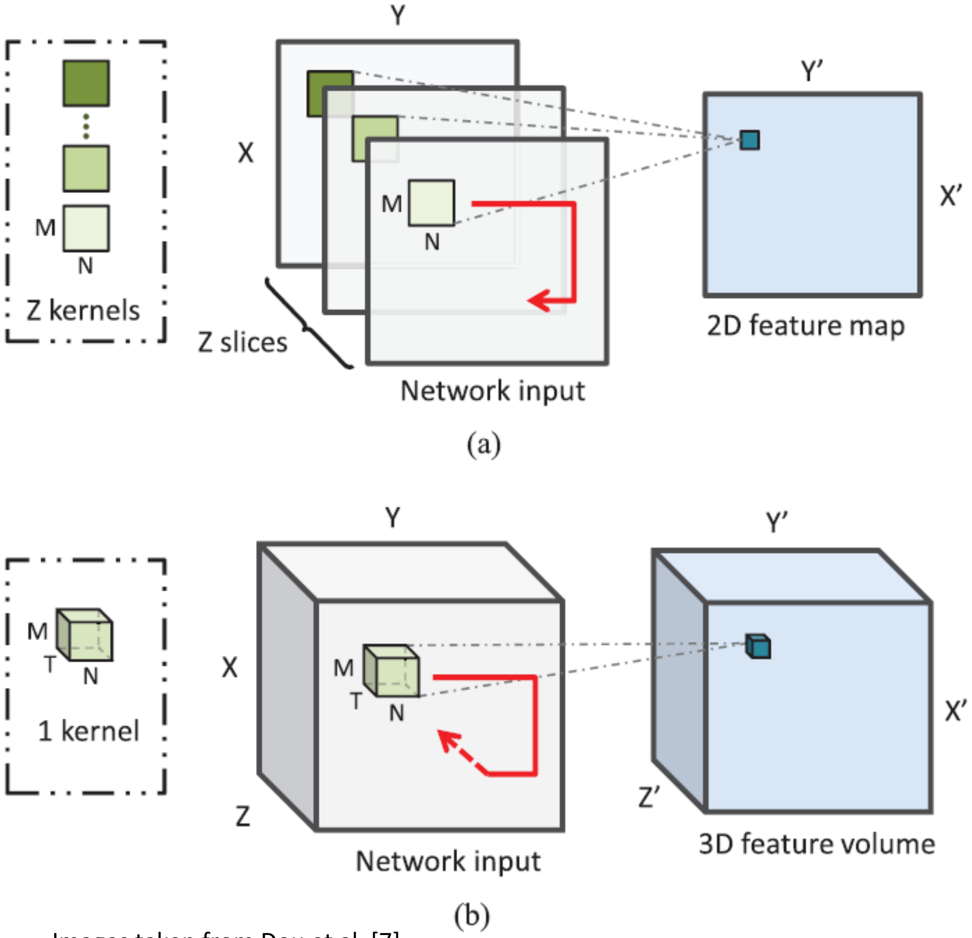


Roth et al. [6] colonic polyps, spine metastasis, enlarged lymphnodes from CT

Medical Applications – Pathology Detection

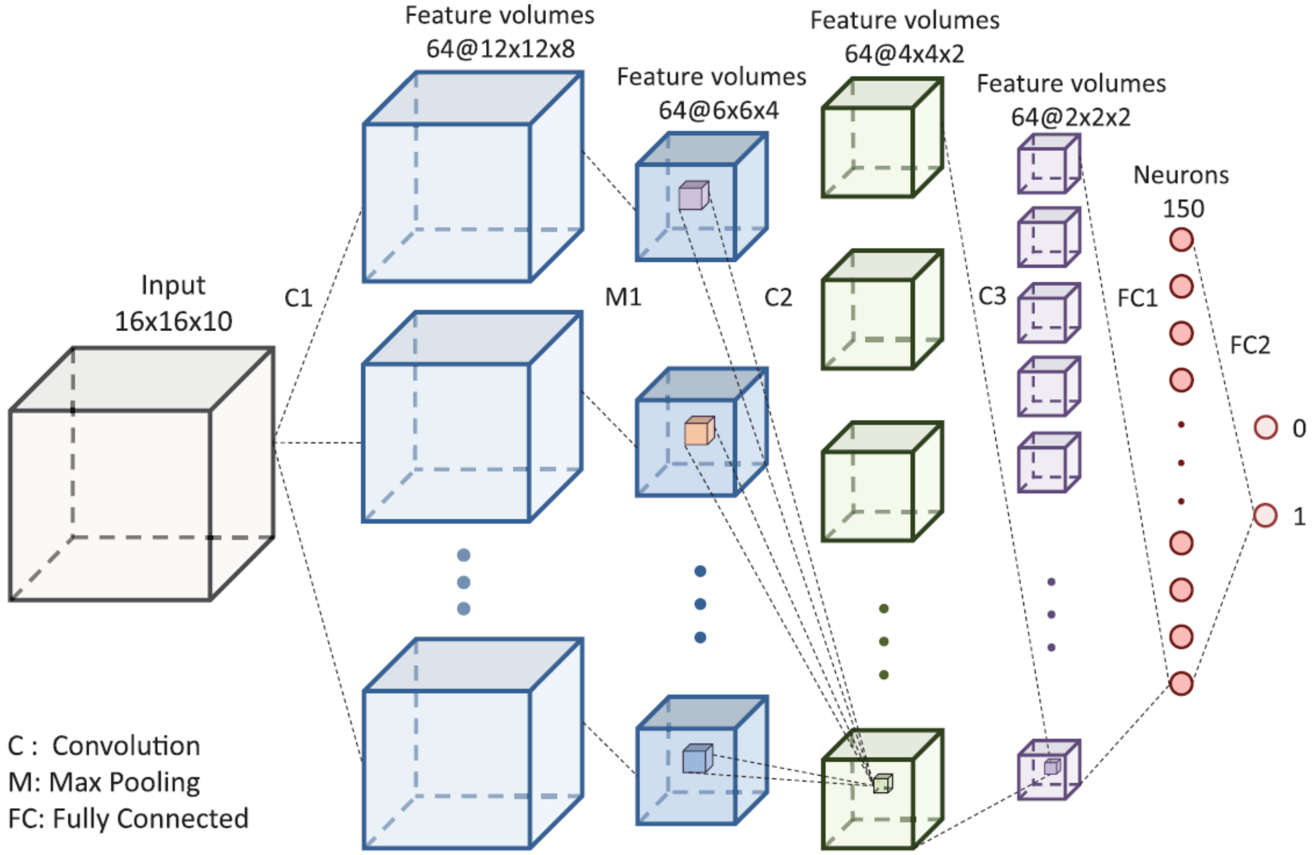
- 3D CNN

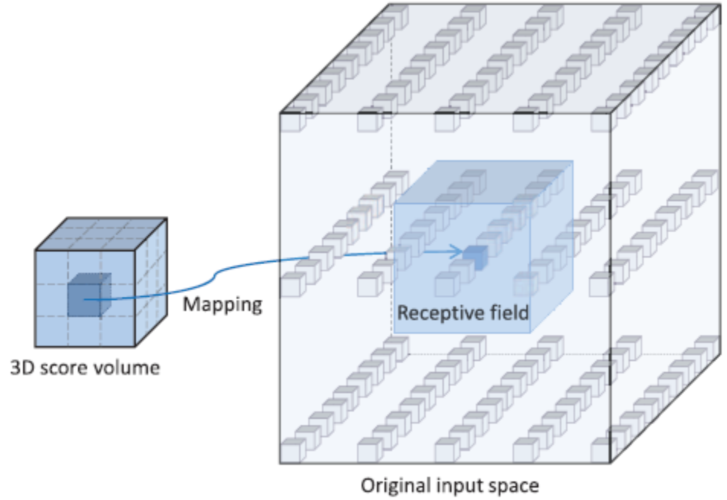


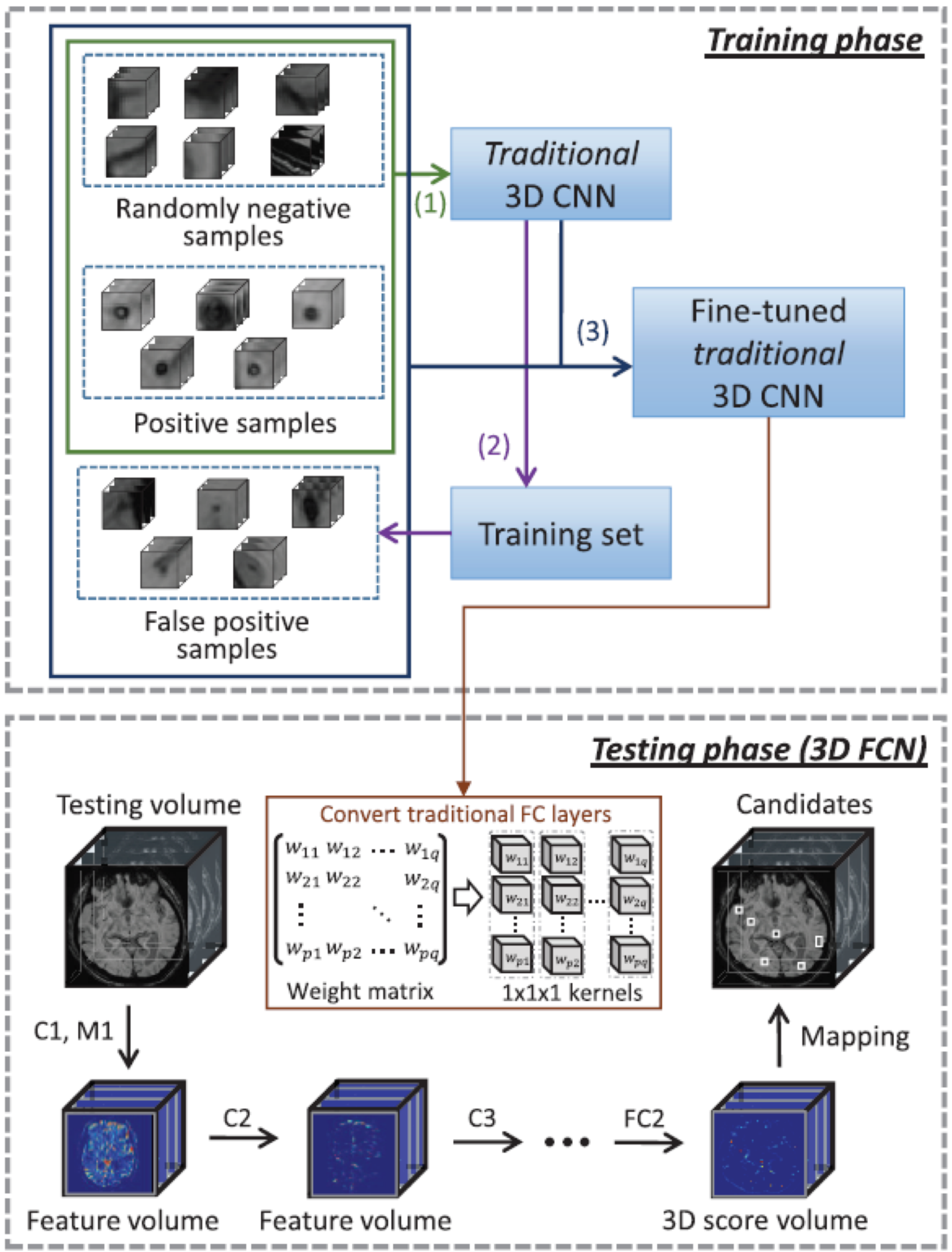


Dou et al. [7] cerebral microbleeds MRI scans

Images taken from Dou et al. [7]







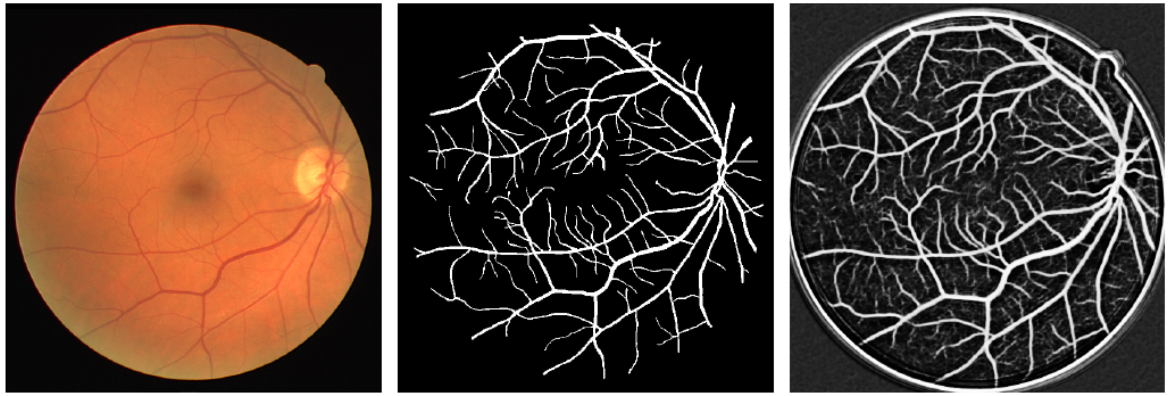
Images taken from Dou et al. [7]

Medical Applications

- Computer Aided Diagnosis
- Segmentation and Shape Modelling
- Classification
- Anomaly Detection
- Image Registration
- Action Recognition

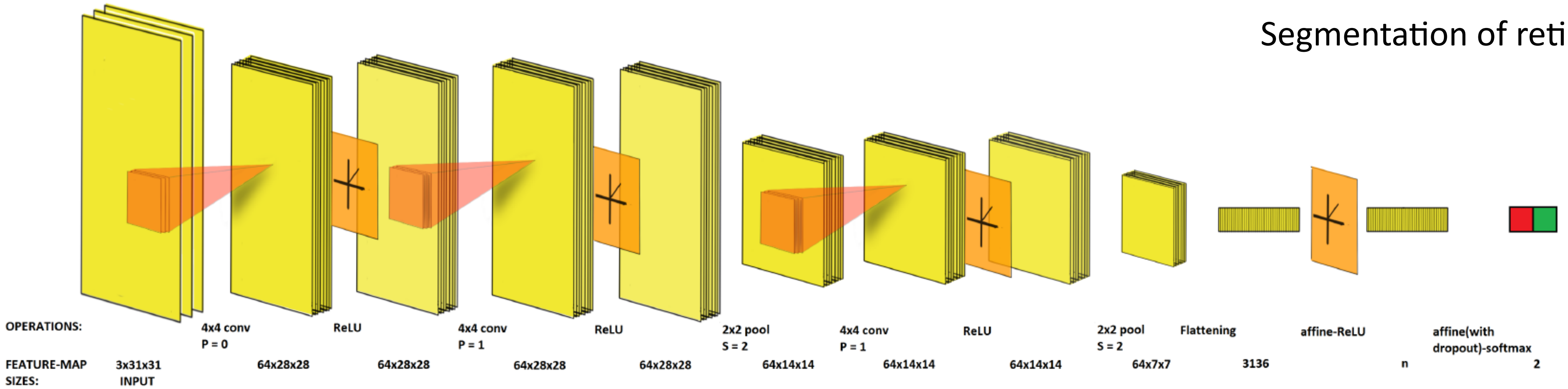
Medical Application- Segmentation

- Ensemble of Deep CNNs, 3D patches
- DRIVE database 40 images, 60k patches
- Independent training



(a) Fundus image (b) Ground truth (c) Detected vessels

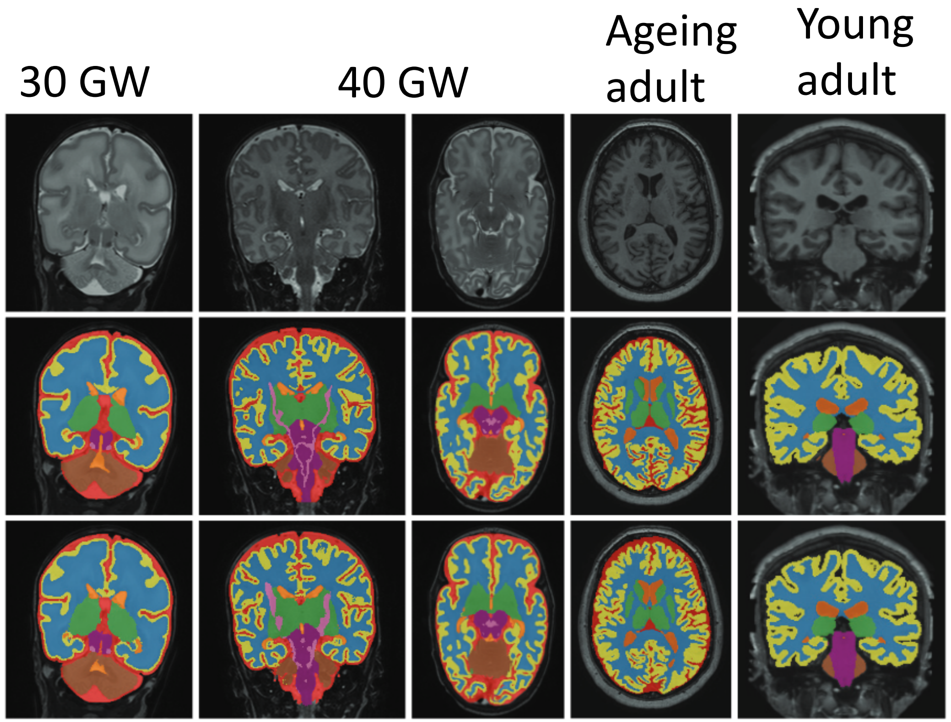
Segmentation of retinal vessels

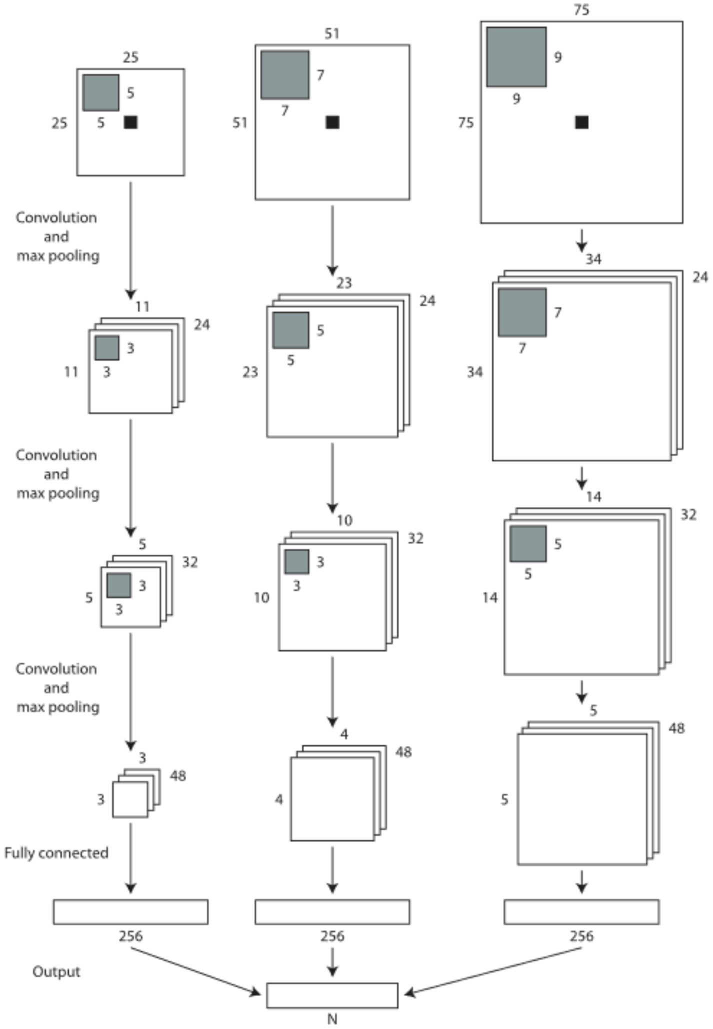


Maji 2016 [8] arXiv Retinal Vessel Detection

Medical Application - Segmentation

- Multi-Scale CNN
- 22 neonatal
- 20 ageing adults
- 15 young adults





Moeskops et al. [9] Brain segmentation

Single soft max layer

Medical Application - Segmentation

- Multi-Scale CNN

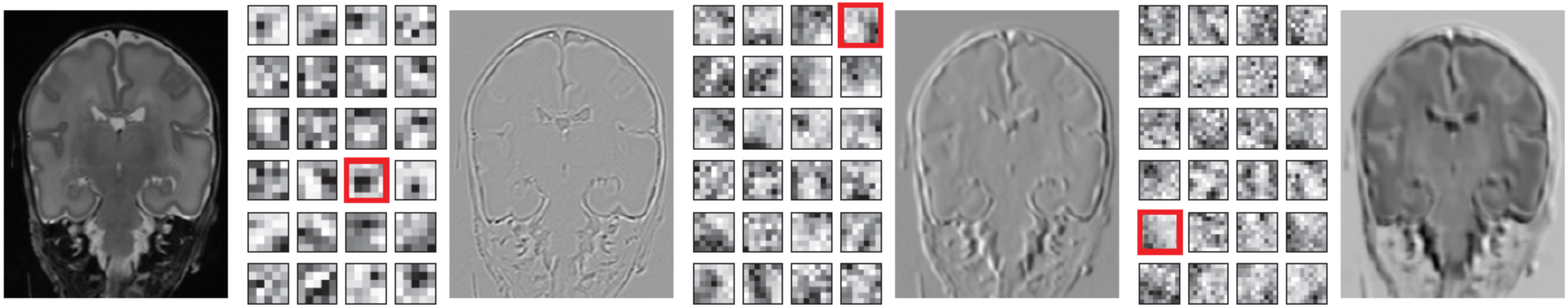
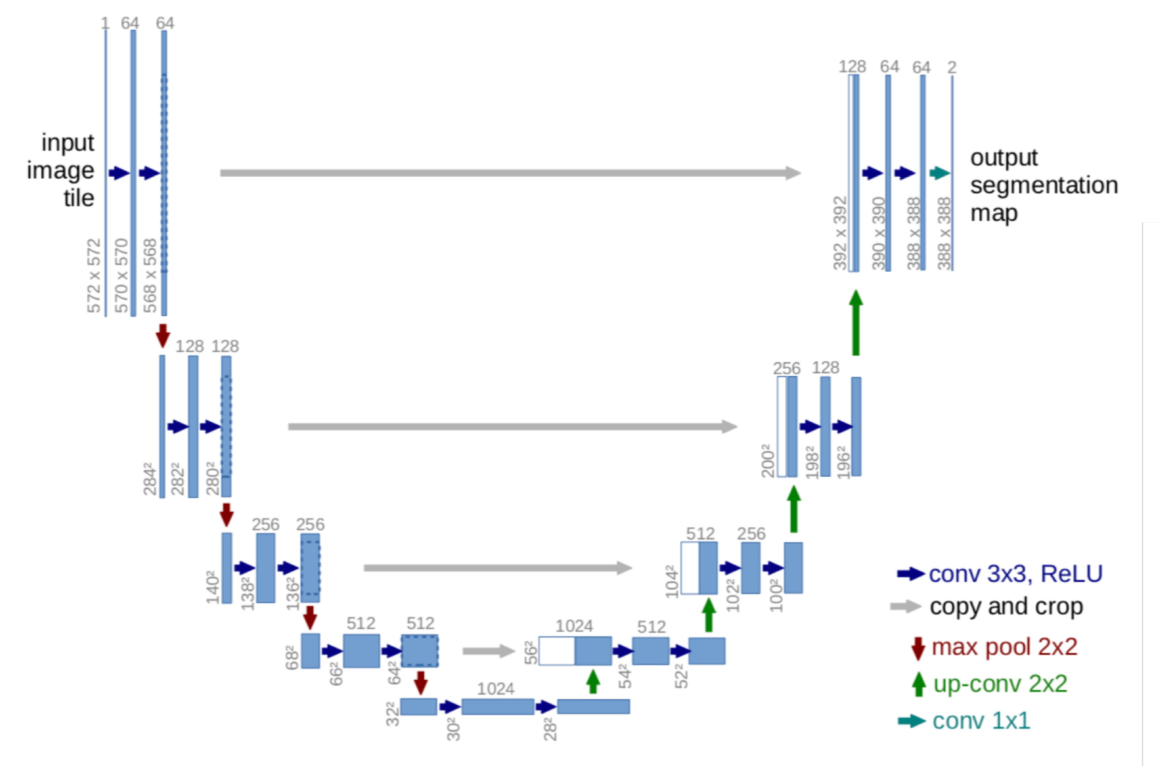


Fig. 2. Trained convolution kernels in the first layer after 10 epochs using the 5 training images acquired at 30 weeks PMA, and the kernels indicated in red applied to a test image. From left to right: the T_2-weighted test image, the kernels of 5×5 voxels, the image convolved with the indicated 5×5 kernel, the kernels of 7×7 voxels, the image convolved with the indicated 7×7 kernel, the kernels of 9×9 voxels, and the image convolved with the indicated 9×9 kernel.

Moeskops et al. [9] Brain segmentation

Medical Application - Segmentation

- U-NET



- Contracting path – context capturing
- Expanding path – precise localization
- Training 30 images 512x512 pixels
- Data Augmentation

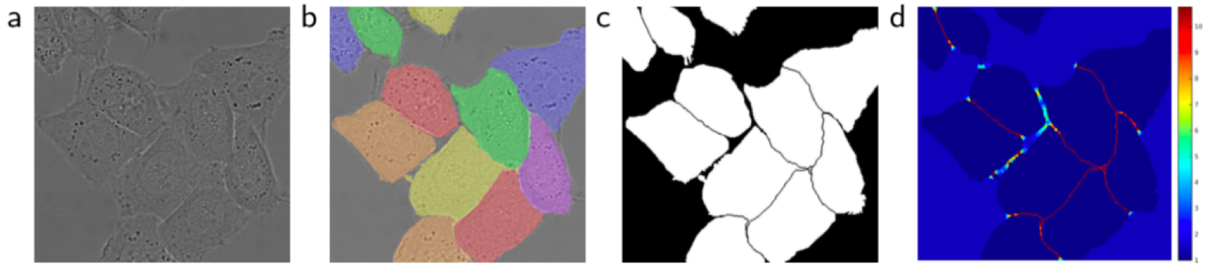


Fig. 3. HeLa cells on glass recorded with DIC (differential interference contrast) microscopy. (**a**) raw image. (**b**) overlay with ground truth segmentation. Different colors indicate different instances of the HeLa cells. (**c**) generated segmentation mask (white: foreground, black: background). (**d**) map with a pixel-wise loss weight to force the network to learn the border pixels.

Ronneberger et al. [18] MICCAI 2016, http://lmb.informatik.uni-freiburg.de/people/ronneber/u-net

Medical Application - Segmentation

- Cascaded U-NET + 3D CRF
- Liver lesion segmentation
- Class balancing

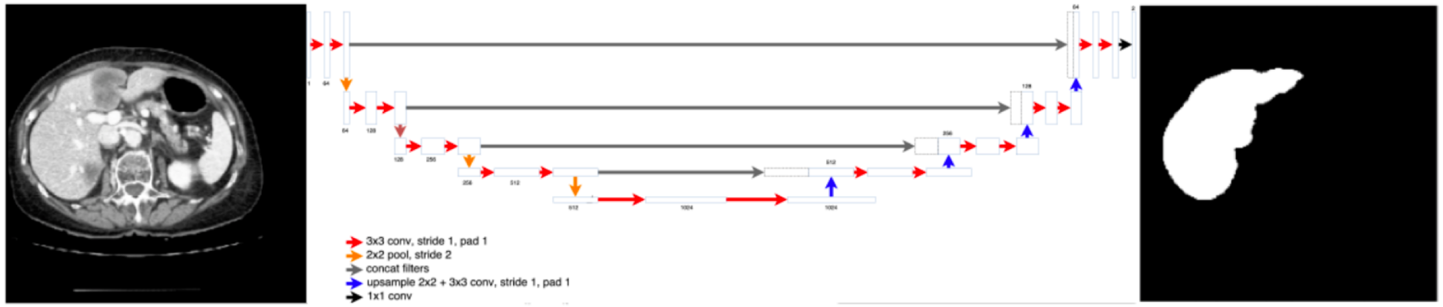


Figure 5: Step 1 of Cascaded FCN: The first U-Net learns to segment livers from a CT slice.

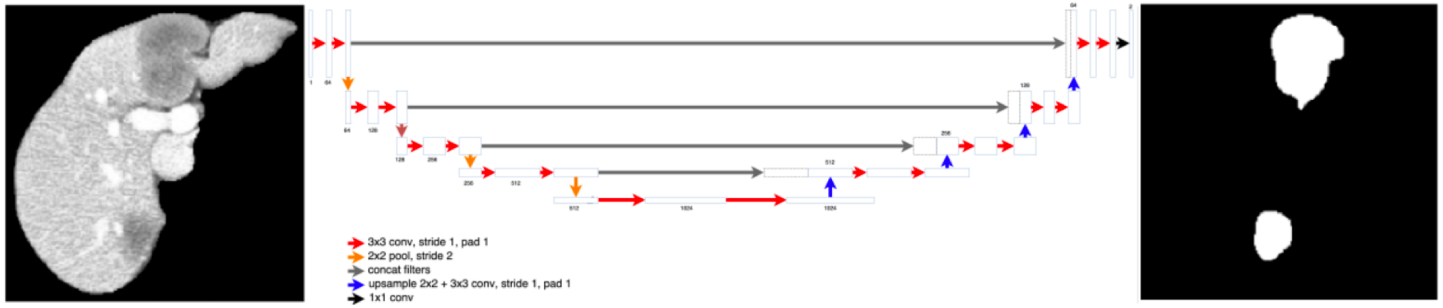


Figure 6: Step 2 of Cascaded FCN: The second U-Net learns to segment lesions from a liver segmentation mask segmented in step 1 of the cascade

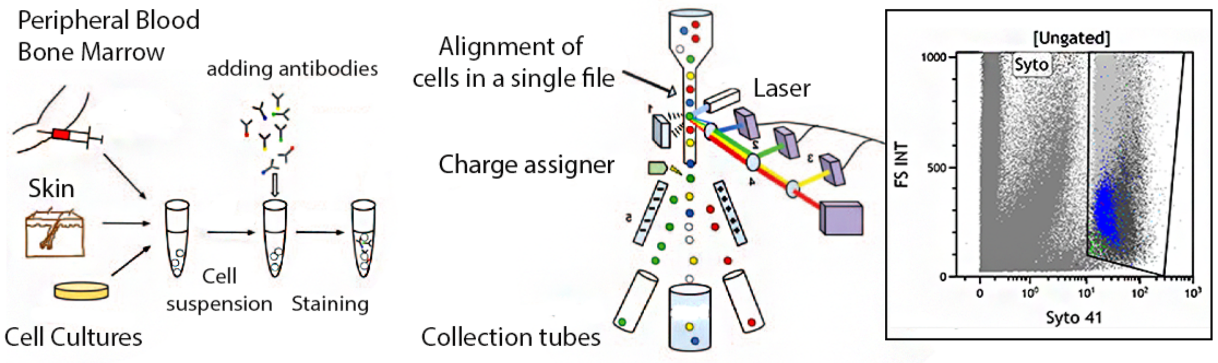
Christ et al. [19] 2017, https://github.com/IBBM/Cascaded-FCN

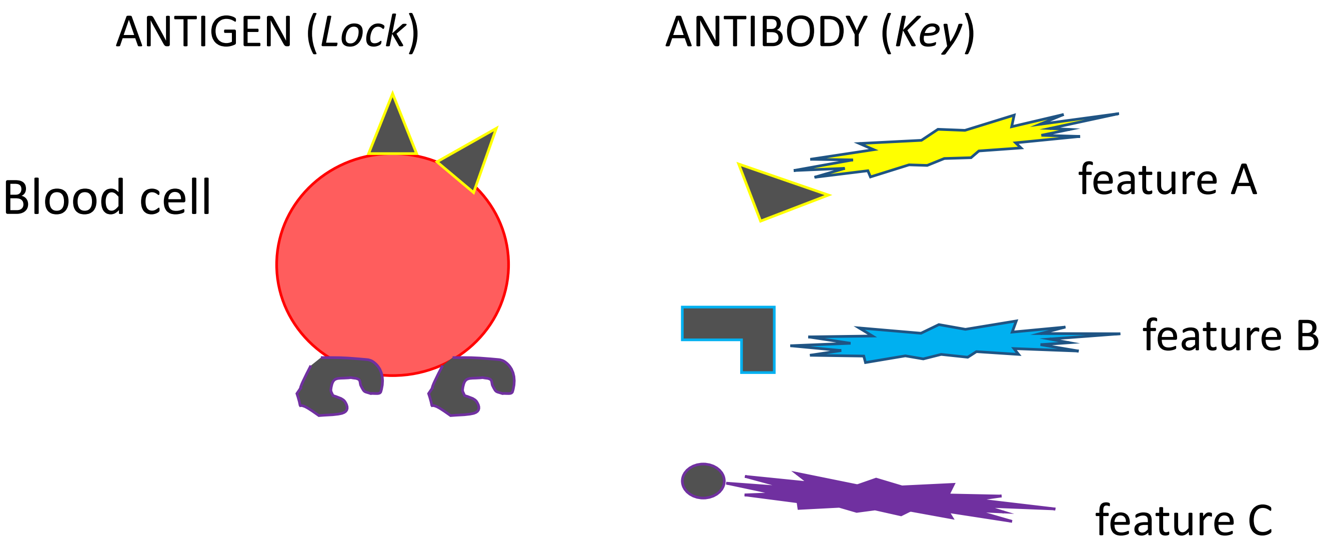
Medical Application

- Computer Aided Diagnosis
- Segmentation and Shape Modelling
- Classification
- Anomaly Detection
- Image Registration
- Action Recognition

Medical Application - Classification

- Stacked layout of Auto-Encoders (SAE)
- Cell type specific antigen pattern
- 10^6 cells per patients
- 10 features





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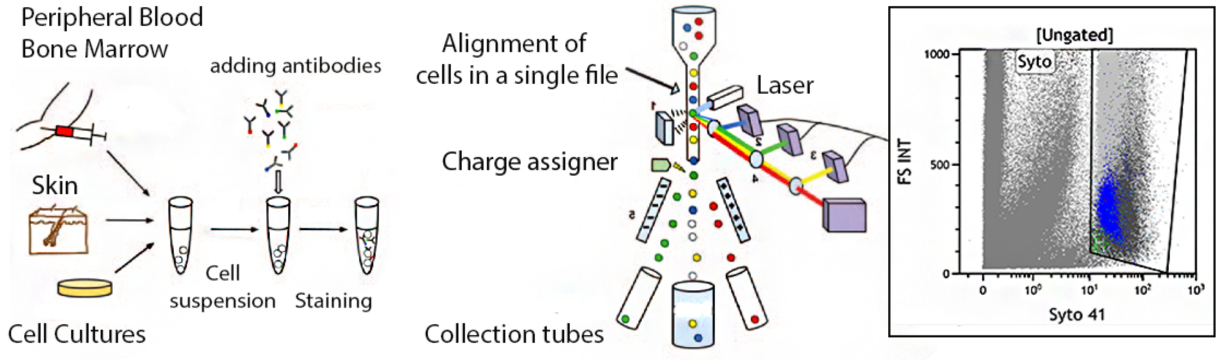

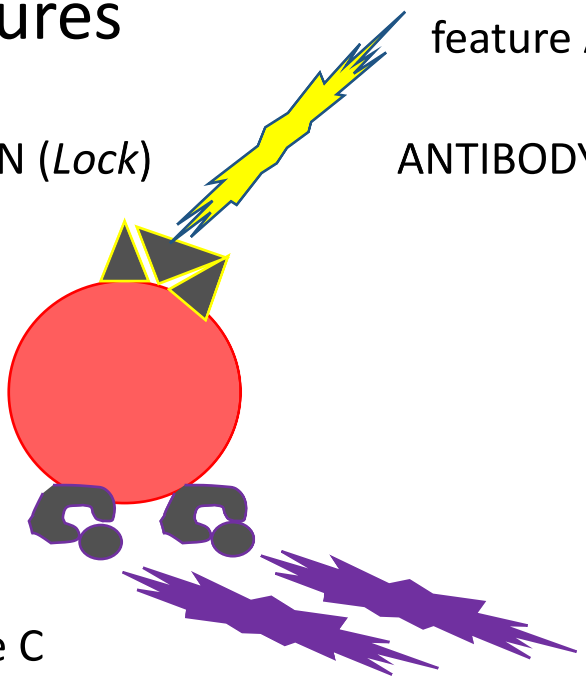

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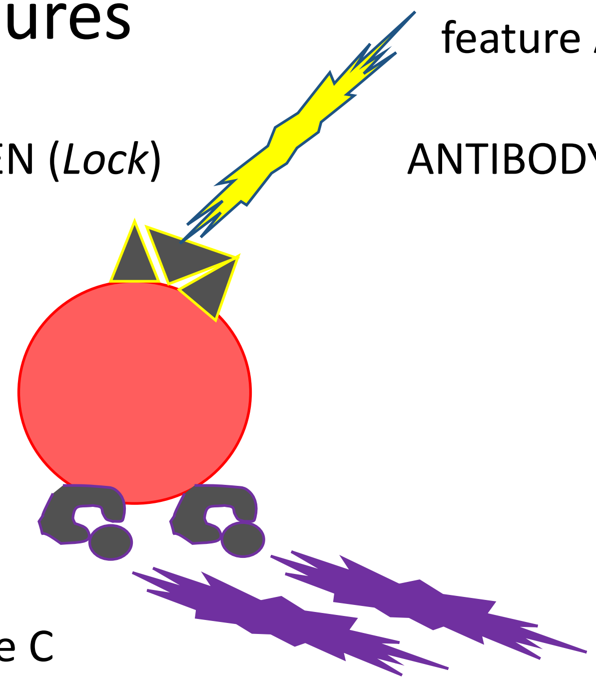

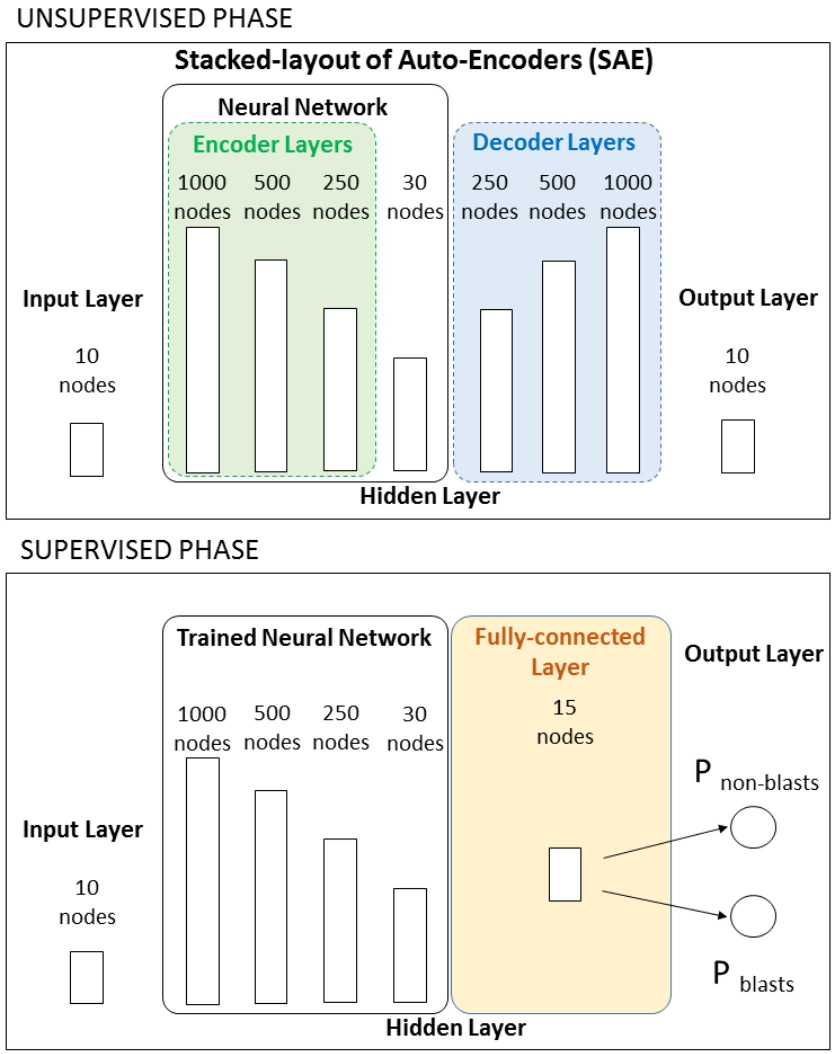

Licandro et al. CBMI 2016

Medical Applications

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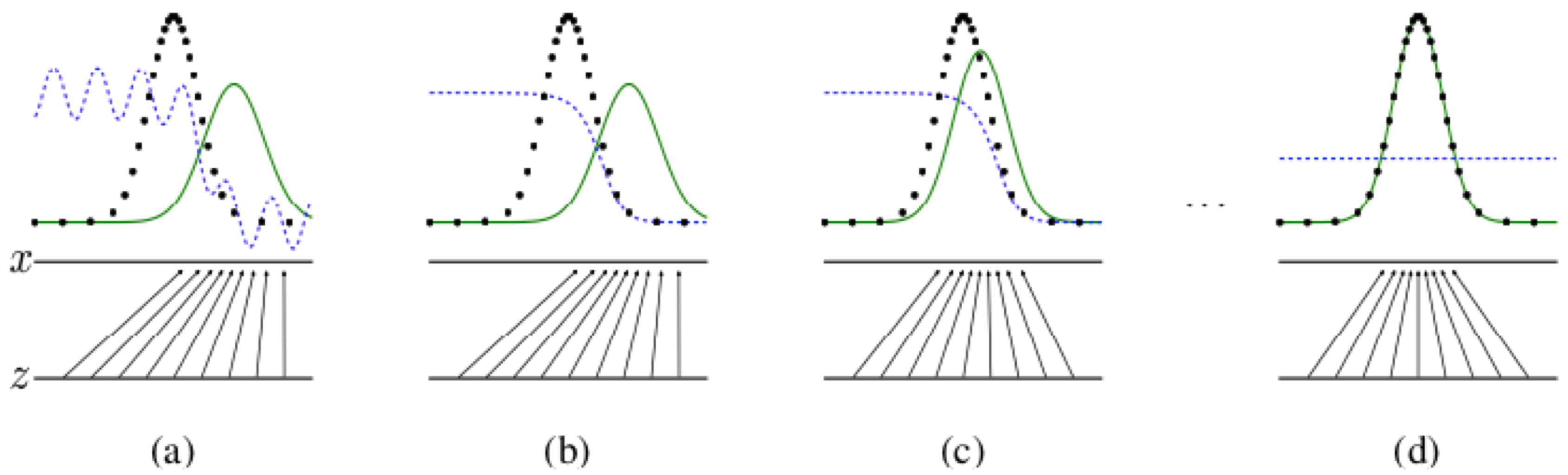
Medical Application – Anomaly Detection

- Generative Adversarial Network (GAN)
  - Unsupervised learning
  - Generator (DNN) – learn mapping from latent space to data distribution
  - Discriminator (CNN) – discriminate between true & generated data



Data generating distribution

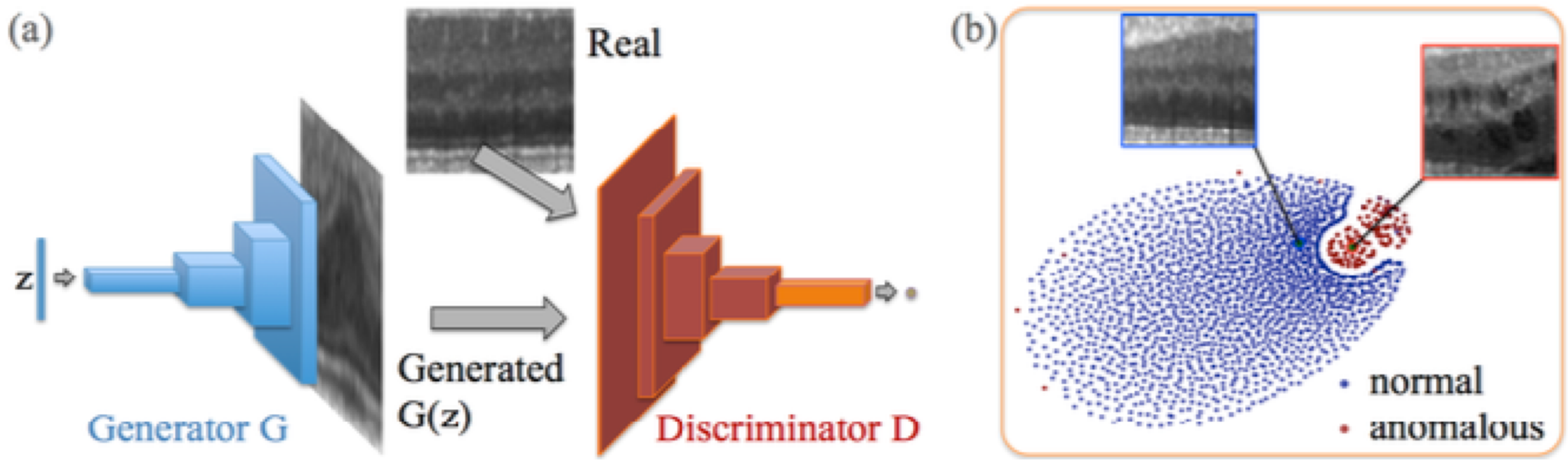
Generative distribution

Discriminative distribution

I.J. Goodfellow et al. 2014, Generative Adversarial Network, arXiv:1406.2661v1

Medical Application – Anomaly Detection

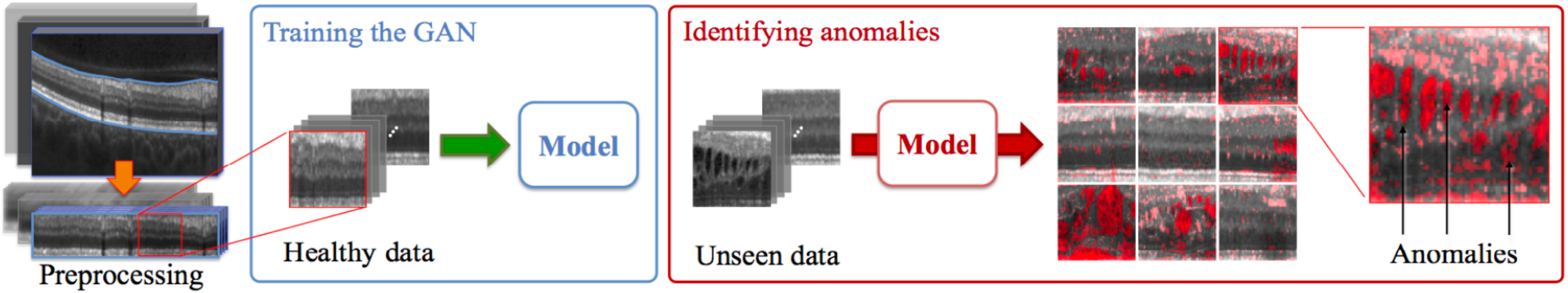
- Generative Adversarial Network (GAN) for anomaly detection

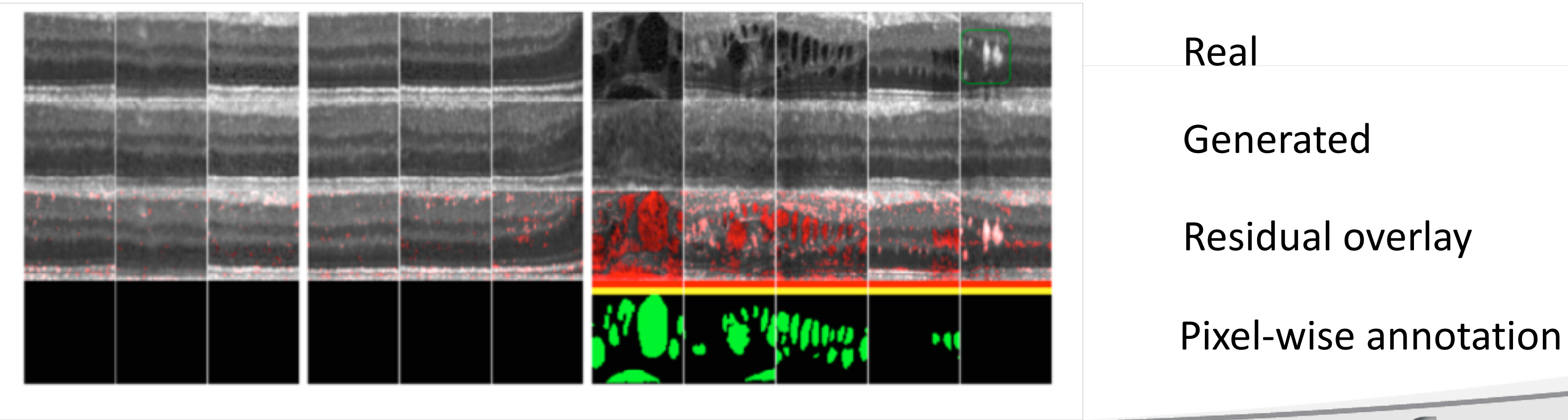


Schlegl T. et al. IPMI 2017 [19]

Medical Application – Anomaly Detection

- Generative Adversarial Network (GAN) for anomaly detection





Schlegl T. et al. IPMI 2017 [19]

Medical Applications

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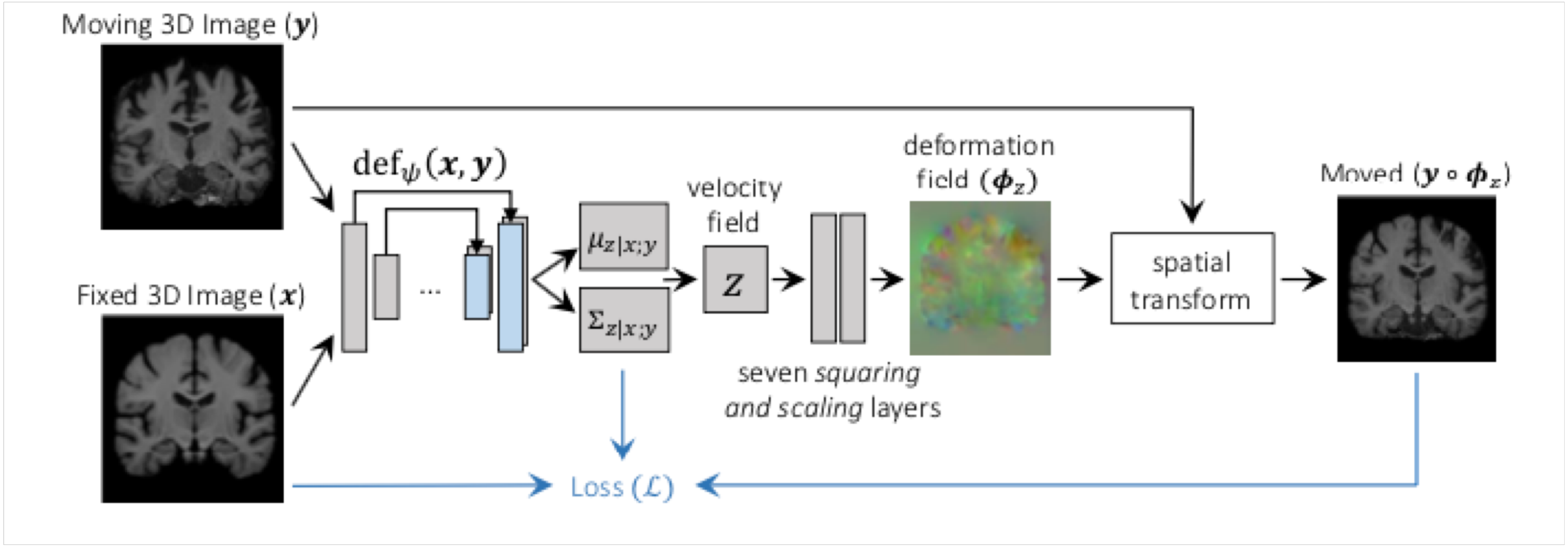
Medical Application- Registration

- Unsupervised Deep Learning for Image Registration



A. Dalca. et al. 2018 arXiv:1805.04605 [20], https://github.com/voxelmorph/voxelmorph.

Medical Application

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Medical Application - Action Recognition

- Recognizing Surgical Activities using RNN
  - Kinematic signals over time (position, velocity, gripper angle)
  - Joint segmentation and classification of surgical activity (10 gestures)
  - JIGSAWS, MISTIC public benchmark surgical activity dataset (*da Vinci)*

DiPietro et al. [11]

SURGICAL ROBOT *Da Vinci* - http://www.robocatz.com/images/News-Da-Vinci-Surgical-Robot-5.jpg

Medical Applications- Action Recognition

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  - Kinematic signals over time (position, velocity, gripper angle)
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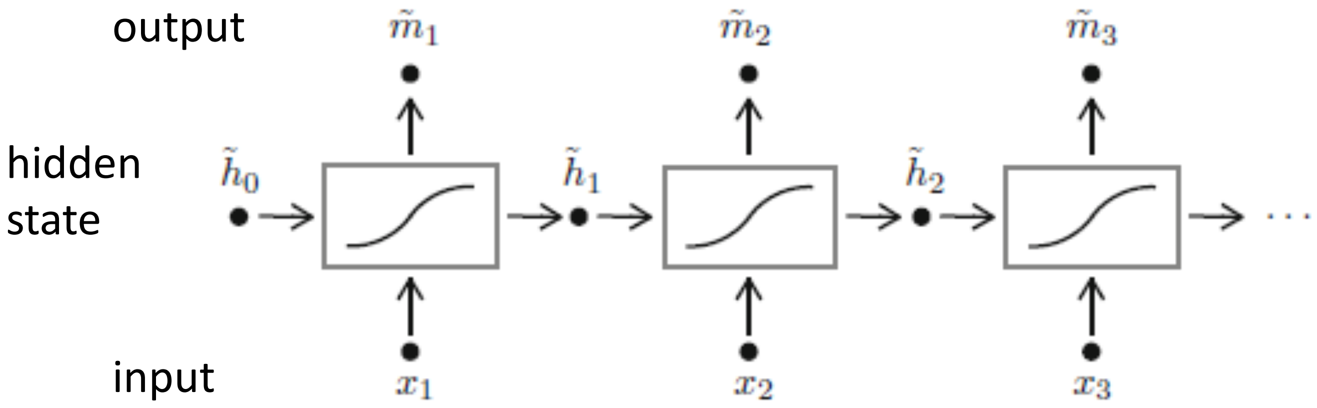
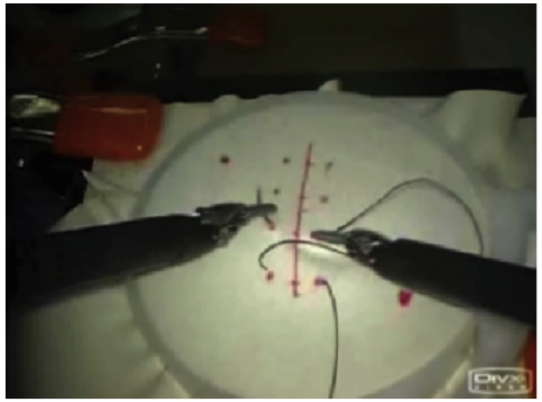


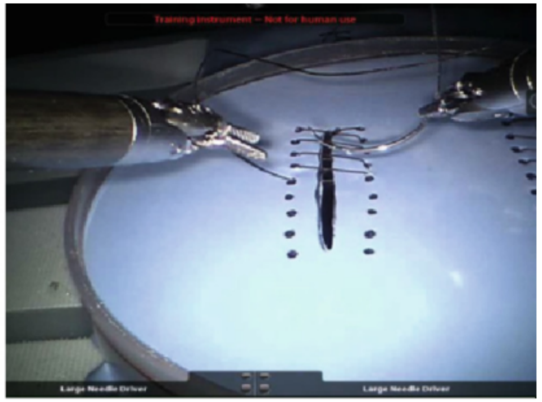
(a) A recurrent neural network.

DiPietro et al. [11]

Images taken from [11] – JIGSAWS and MISTIC datasets



4-throw suturing task



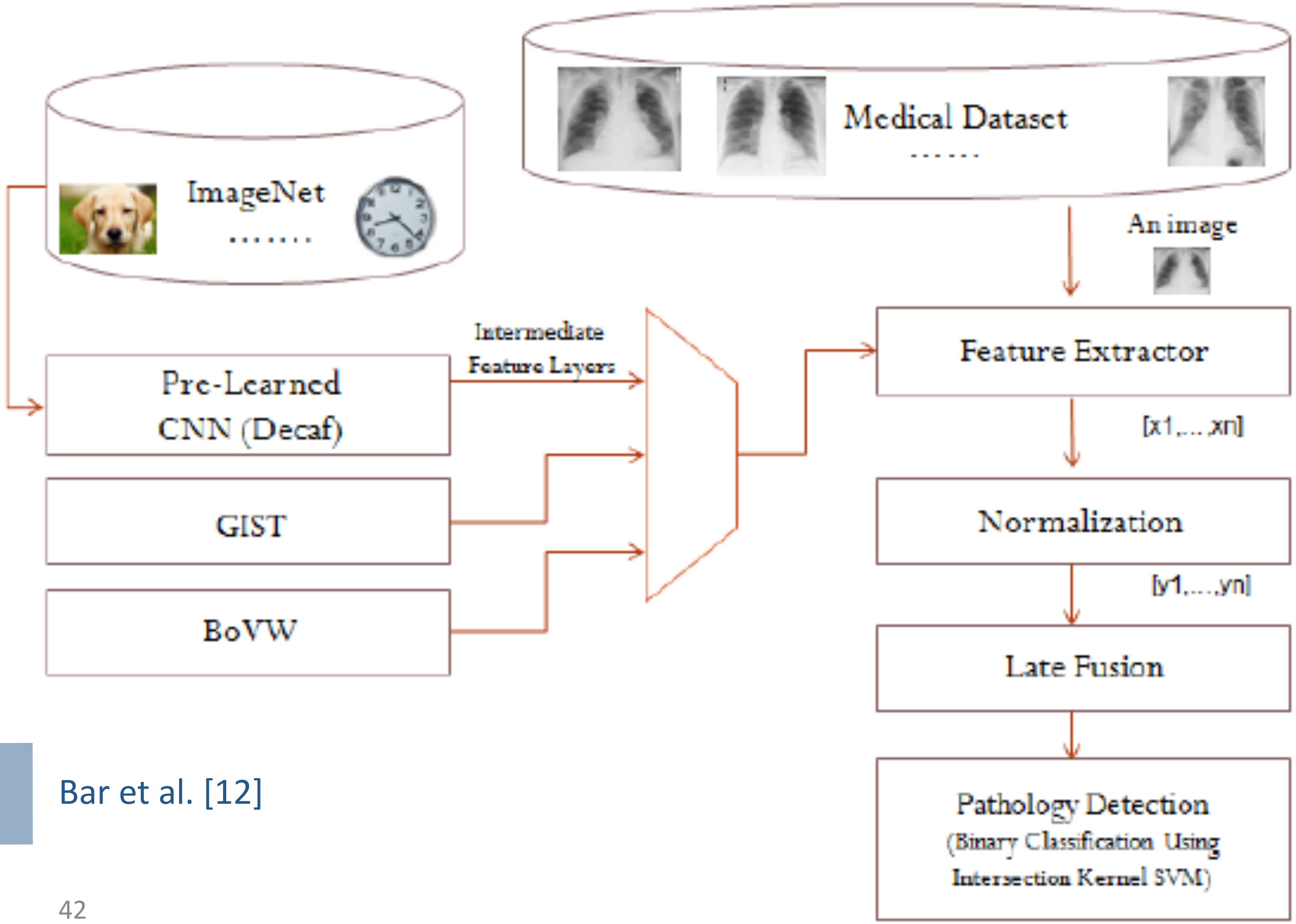
What can we do in cases where data are not available?

What are the key components to use deep CNNs in medical imaging applications?

Transfer Learning

- Supervised pre-trained CNN models used for a new medical task
- Data for pre-training
  - Different medical domain
  - Natural image dataset (e.g. ImageNet)
- Output extracted from layers considered as features
- Input to pattern classifier

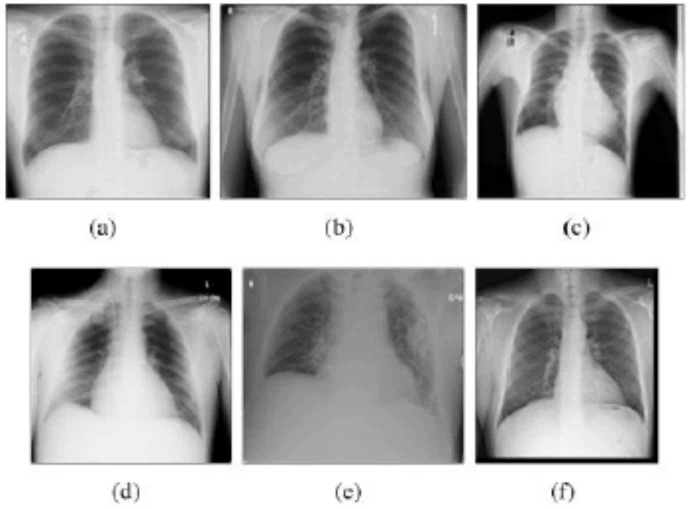
Transfer Learning



443 chest x-ray

Healthy

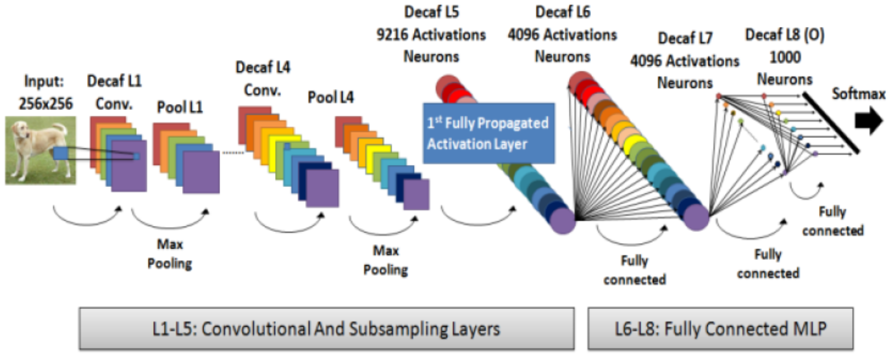
Enlarged heart



Decaf pre-trained CNN model

Subset of image from ImageNet

>1M images, >1K categories



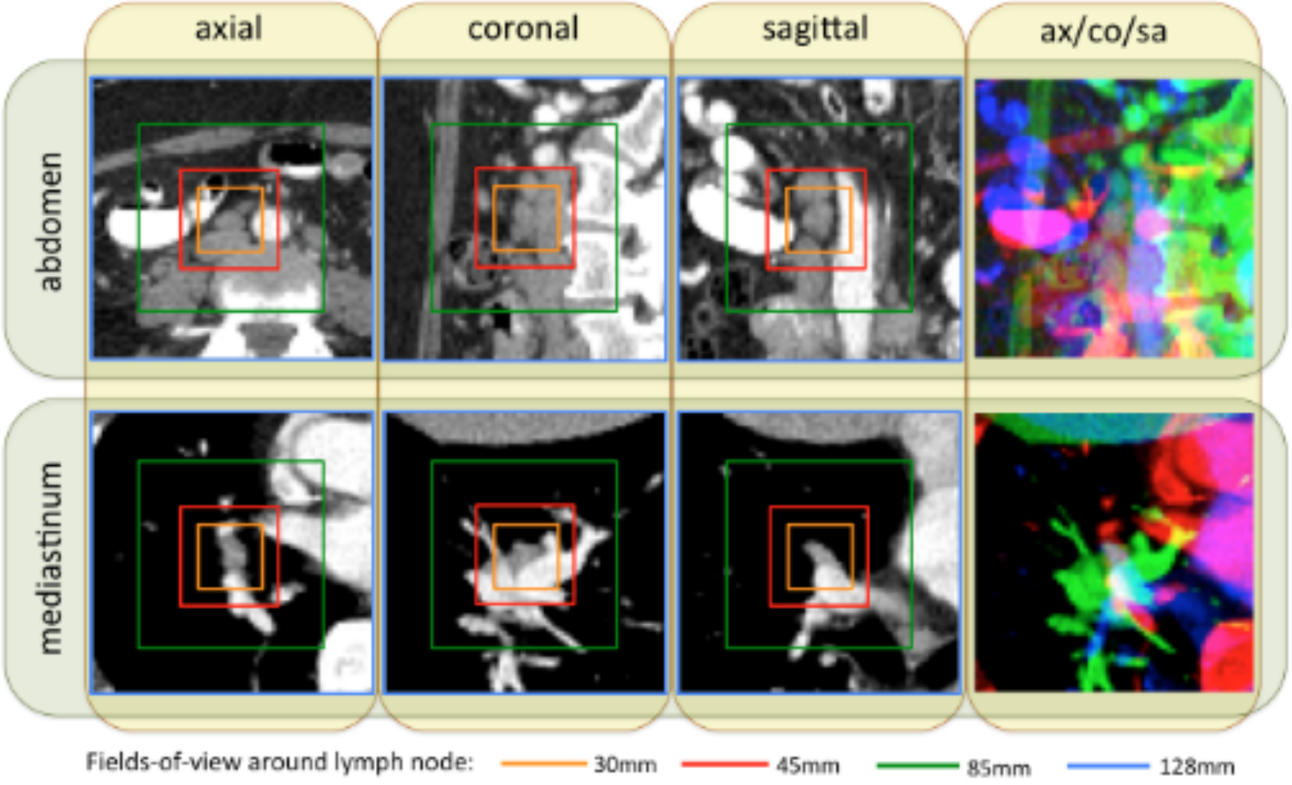
Bar et al. [12]

Fine-Tuning

- Medium sized dataset exists for the task
- Pre-trained CNN used as initialization of the network
- Input of subsequent supervised training
- Deep fine-tuning, shallow fine-tuning Tajbakhsh et al. [13]

Fine-Tuning

- Thoraco-abdominal lymph node detection
- ImageNet pre-trained
- CifarNet, AlexNet, GoogLeNet
- Preprocessing of input
- Adaptations
  - Pooling parameters
  - Filtersize
  - Stride parameters



Shin et al. [17]

Are there alternative methods for acquiring and annotating data?

Expert vs. Non-Expert

- Annotation
  - Cost intensive
  - Time consuming
  - Lack of publicly available ground-truth data

- Crowdsourcing - Non Experts
  - Noisy annotations of single non experts
  - Disagreement between users
  - CNN – learning input from the crowds
  - Aggregation layer added
  - Crowd of nonprofessional, inexperienced users can perform as well as the medical experts [14, 15, 16]

Publicly available medical datasets

- VISCERAL http://visceral.eu/
- The Cancer Imaging Archive http://www.cancerimagingarchive.net
- Ongoing benchmark studies and challenges
  - http://www.grand-challenge.org
  - Precise definition of task to be solved is given
  - Evaluation metrics are defined
  - Standardized and fair comparison
- https://www.kaggle.com/c/diabetic-retinopathy-detection

Summary

- Evolution of Deep Learning in Medicine
- 2D/2.5D/3D CNN, Stacked Auto Encoder, Recurrent Neural Nets
- Unsupervised Anomaly Detection, Registration
- Accuracy of result important
- Most approaches are supervised
- Alternative to experts - crowdsourcing
- Transfer learning and training
- Trend towards BigData, challenges at conferences, public data sets

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