

Departamento de Eletrónica, Telecomunicações e
Informática

Complements of Machine Learning

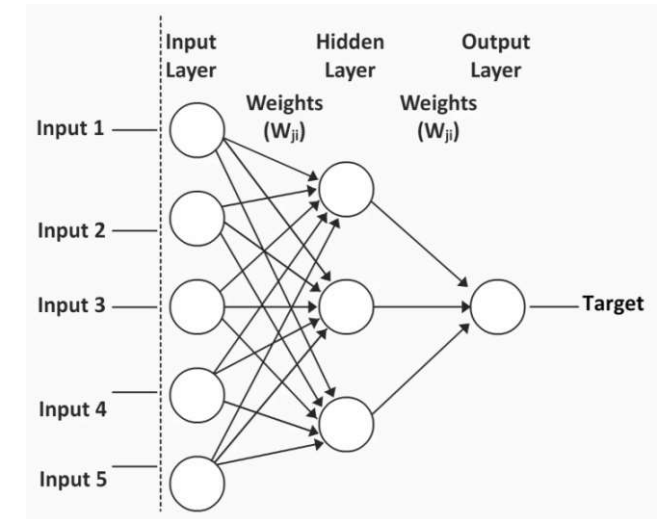
LECTURE 7 : Deep Learning for Medical Imaging
Petia Georgieva
(petia@ua.pt)

Outline

- **Healthcare applications: medical imaging**
- **Data pre-processing**
- **AI architecture – CNN Dense Net**
- **Explainable AI (XAI) – Grad CAM method**

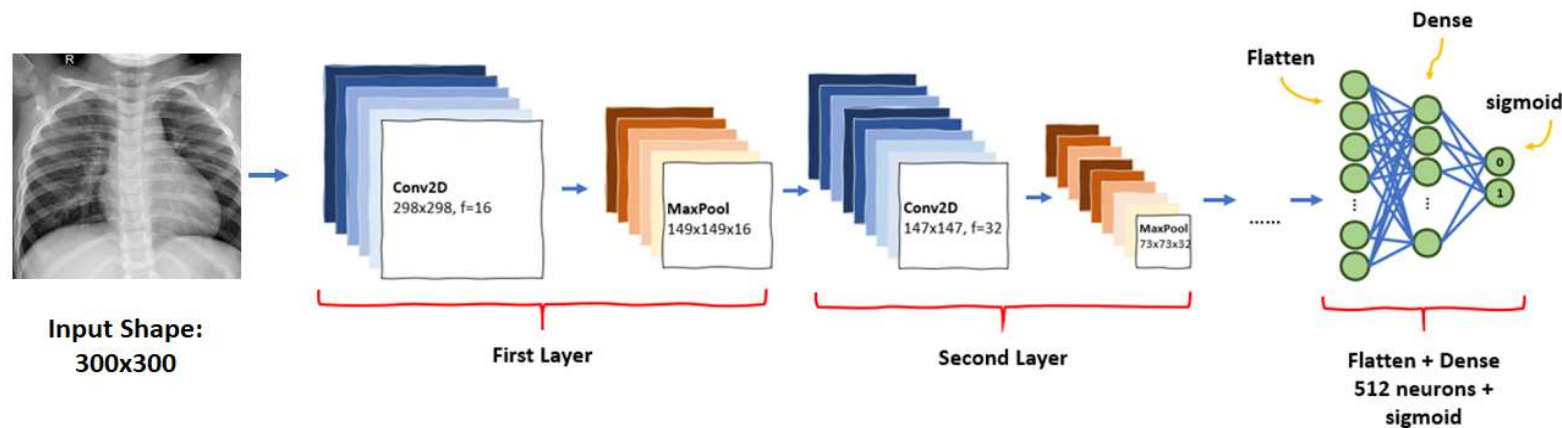
Image Processing

In the past: Transform 3D (RGB) image into a pixel vector $x \Rightarrow$ train NN model to detect a pathology (1, 0)

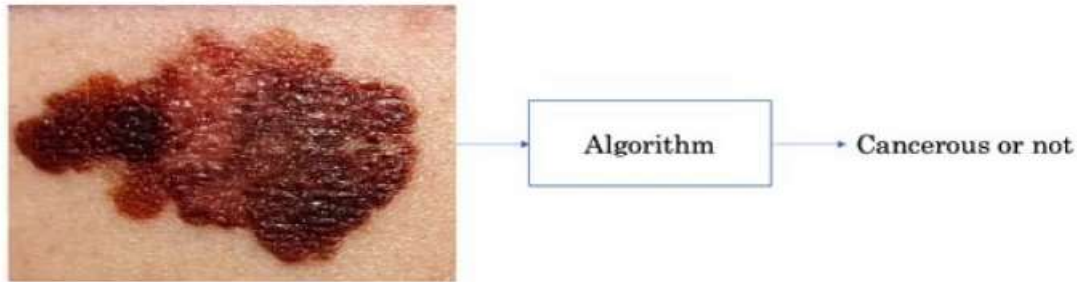


Currently: Conv NN

Pneumonia Detection using Convolutional Neural Network (CNN)

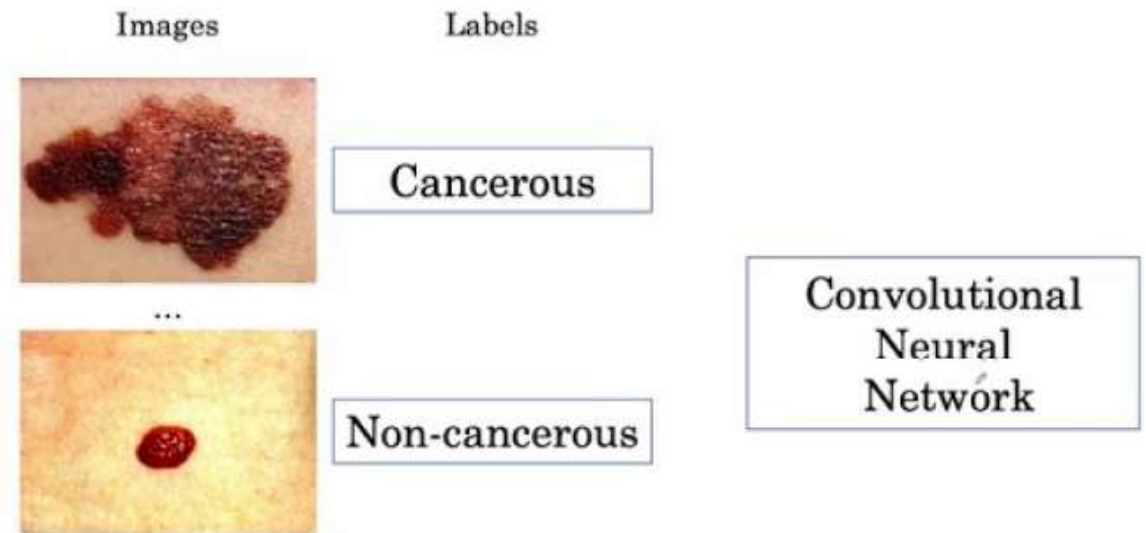


Dermatology



Skin cancer diagnosis problem:

Set of labeled images => train DL model (e.g. CNN)



Ophthalmology



→ Diabetic Retinopathy (DR)

Retinal Fundus Photos

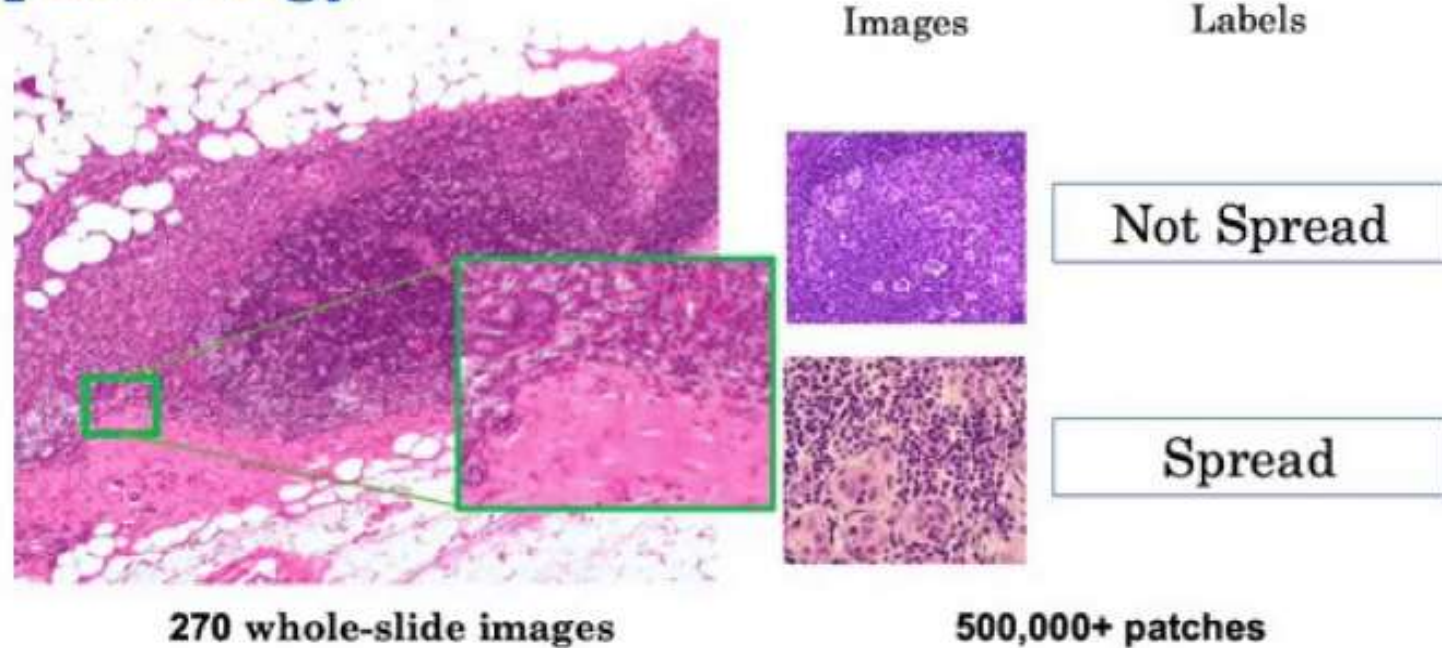
Diabetic retinopathy problem:

Set of labeled images => train DL model (e.g. CNN)



Histopathology

Histopathology



Microscopic tissue images to determine if cancer has spread:

Large resolution digital images (100 000 x 100 000 pixels) => extract several patches (brake down large image into smaller images) , magnify and label them => train DL model.

Lab work: Chest X-ray images



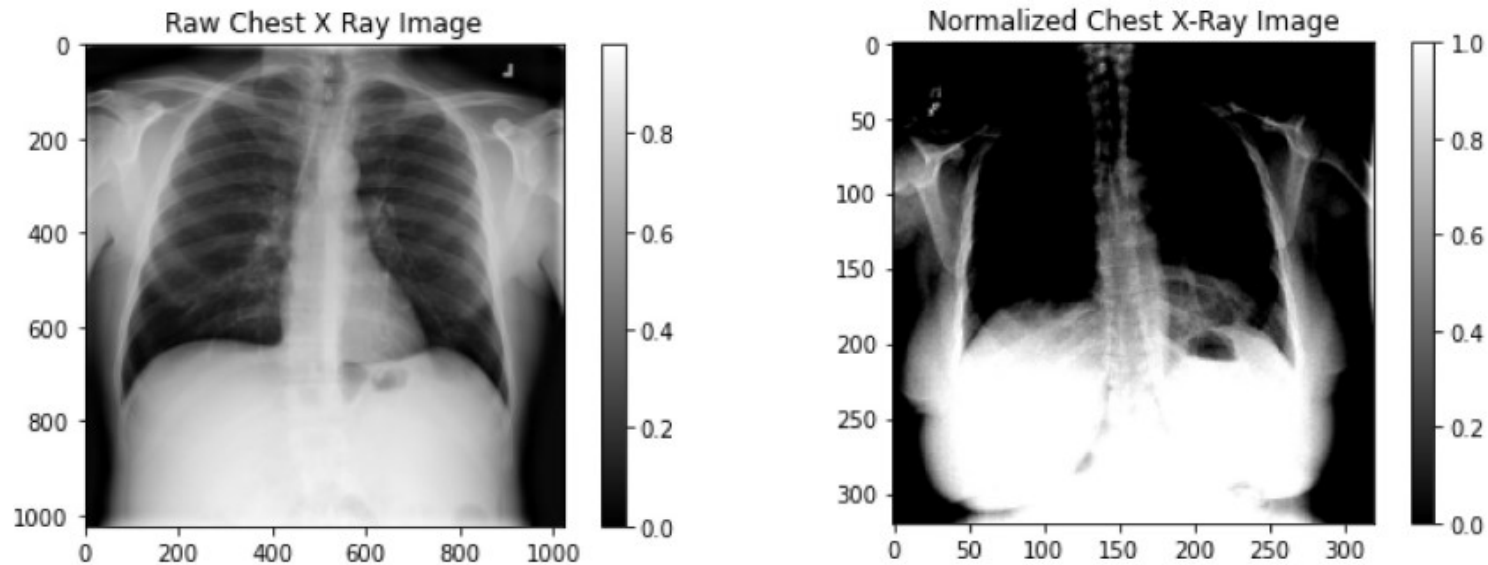
```
['Cardiomegaly',  
'Emphysema',  
'Effusion',  
'Hernia',  
'Infiltration',  
'Mass',  
'Nodule',  
'Atelectasis',  
'Pneumothorax',  
'Pleural_Thickening',  
'Pneumonia',  
'Fibrosis',  
'Edema',  
'Consolidation']
```

Detect different (14) pathologies :

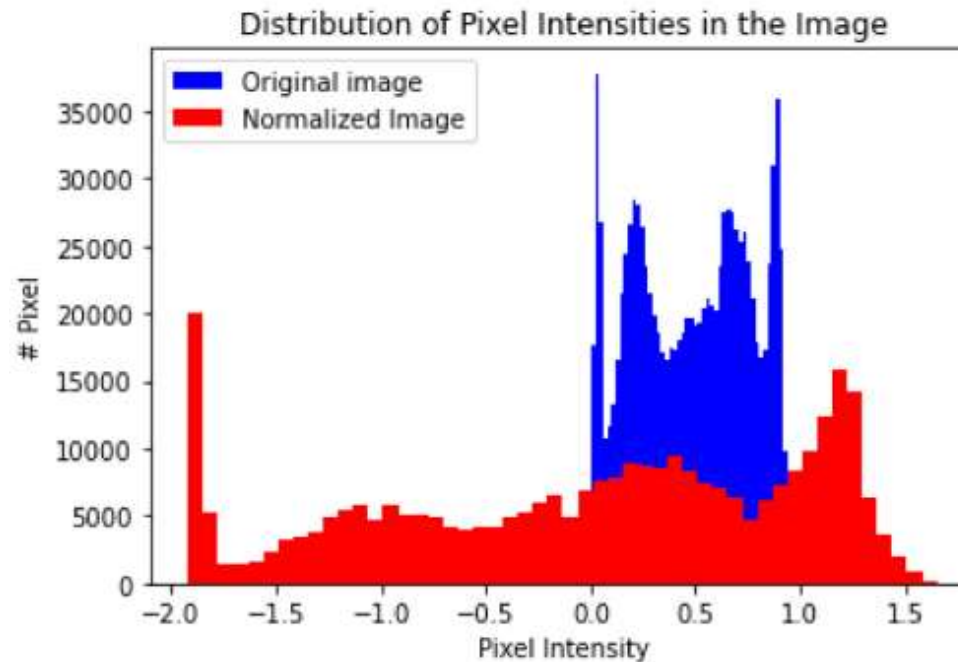
Binary classification => pathology (1) or normal (0) with DenseNet (DL model)

Chest X-ray - one of the most common diagnostics imaging procedure critical for detection of pneumonia, lung cancer, etc.

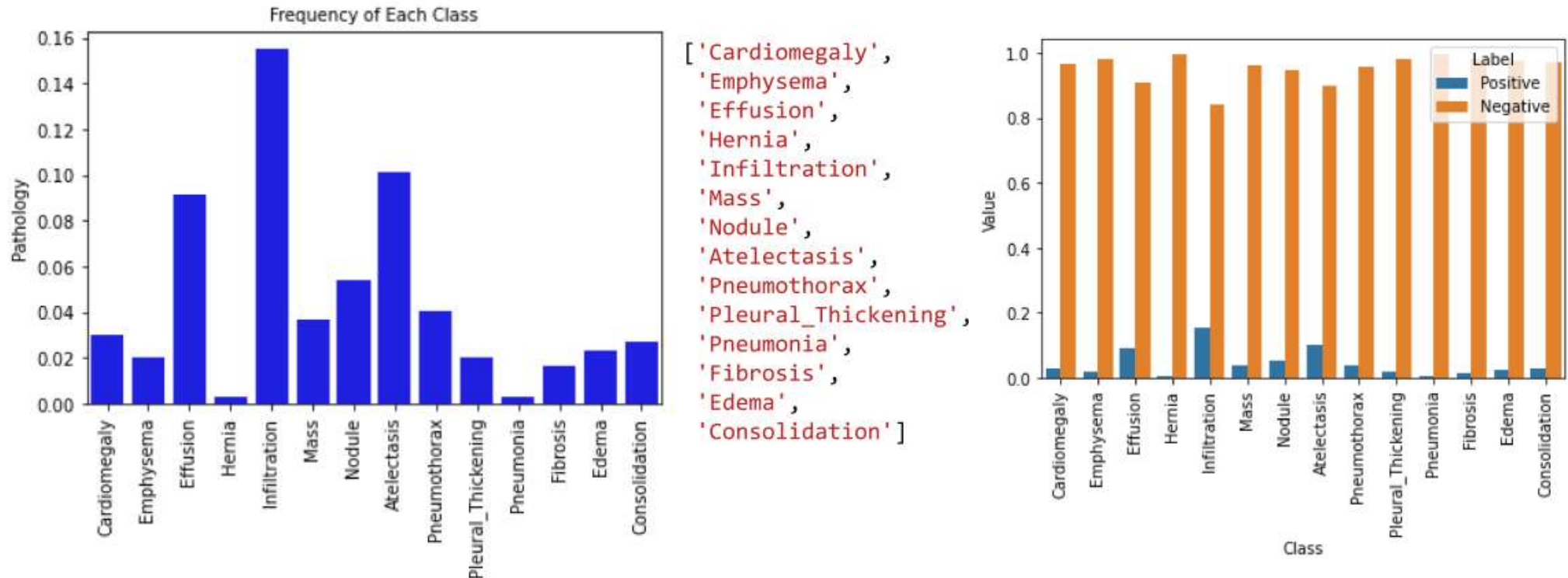
Image normalization



Standardize the pixel distribution: mean =0, std=1



Unbalanced data



The contribution of positive class is much lower than that of the negative class.

$w_p = \# \text{ of negative examples} / N$

$w_n = \# \text{ of positive examples} / N$

$w_p \gg w_n \Rightarrow \text{Weighted Binary cross-entropy Loss}$

$$\mathcal{L}_{cross-entropy}^w(x) = -(w_p y \log(f(x)) + w_n (1 - y) \log(1 - f(x)))$$

Unbalanced data

Solution 1: Re-sampling methods (under-sampling, oversampling)

Examples

P1 Normal
P2 Normal
P3 Normal
P4 Mass
P5 Normal
P6 Normal
P7 Mass
P8 Normal

Normal
P1, P2, P3, P5,
P6, P8

Mass
P4, P7

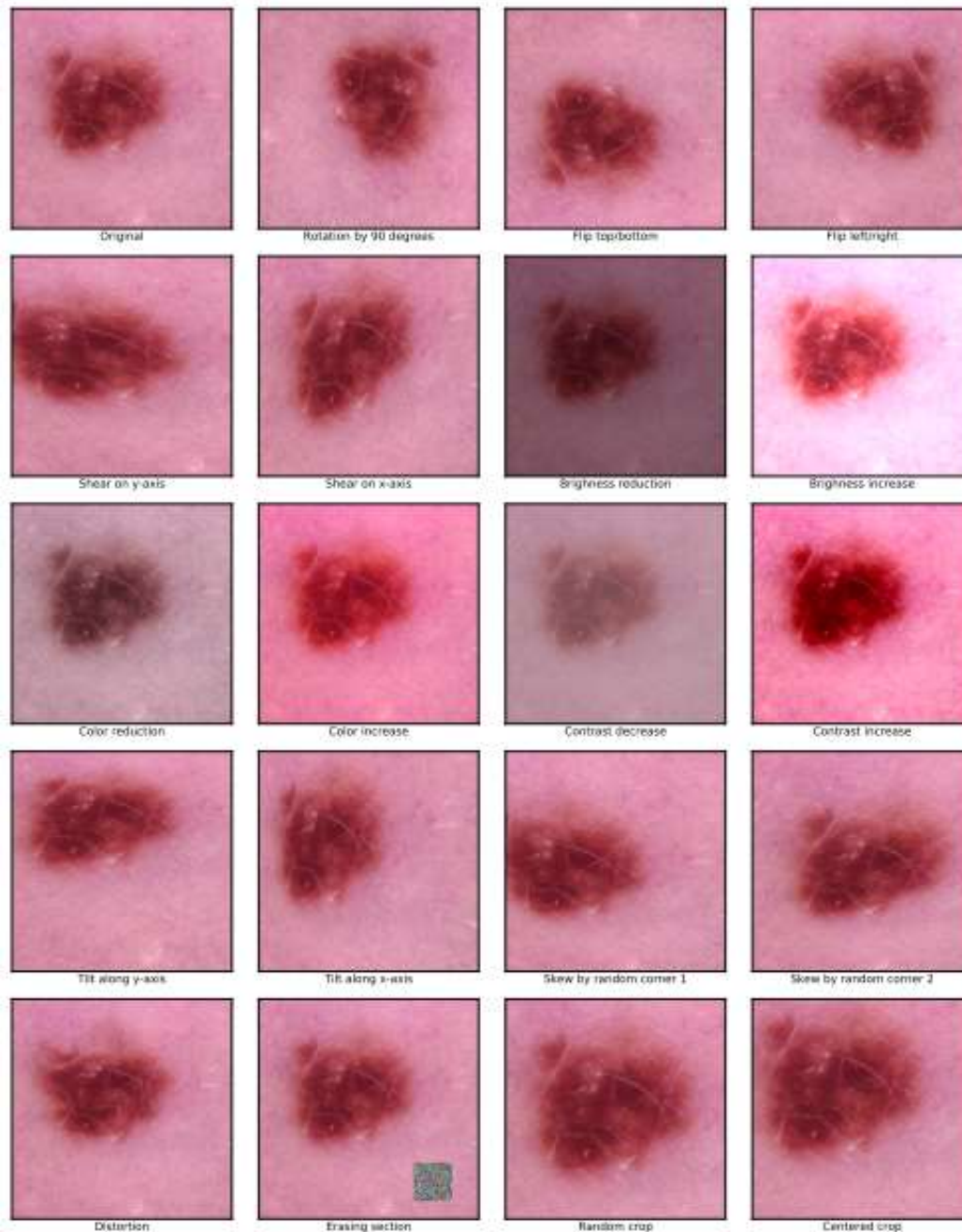
Sample 4

Sample 4

Re-Sampled

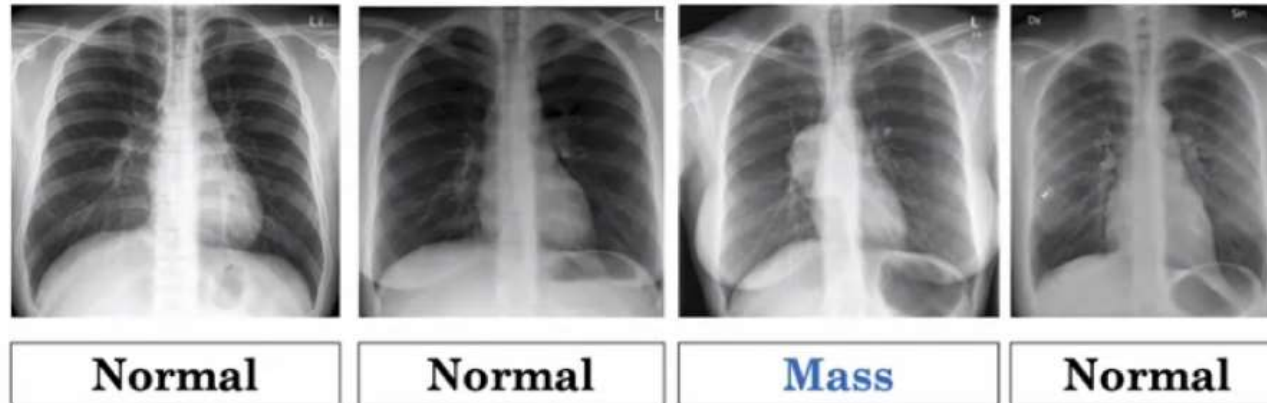
P3 Normal
P6 Normal
P1 Normal
P8 Normal
P7 Mass
P4 Mass
P7 Mass
P4 Mass

Solution 2: Data Augmentation



- Horizontal flips;
- Vertical flips;
- 90° rotations;
- Randomly increase or decrease contrast;
- Randomly increase or decrease brightness;
- Randomly increase or decrease color intensity;
- Randomly erase a small section of the image;
- Shears on x or y axis with 20 degrees to the left/right or top/down, respectively.

Unbalanced data



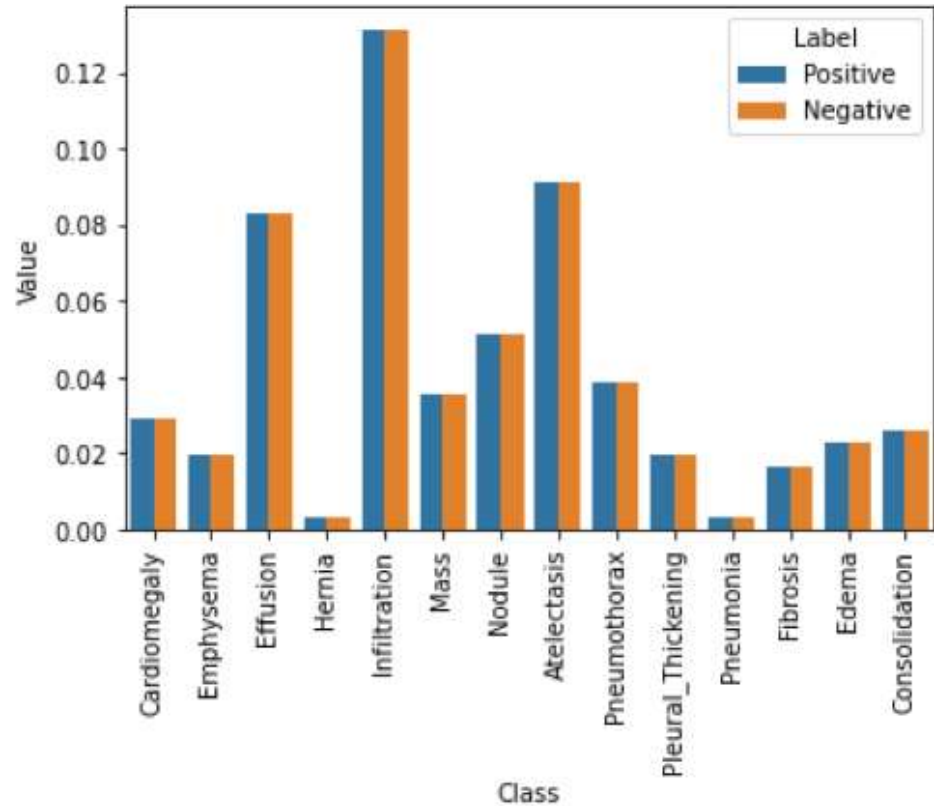
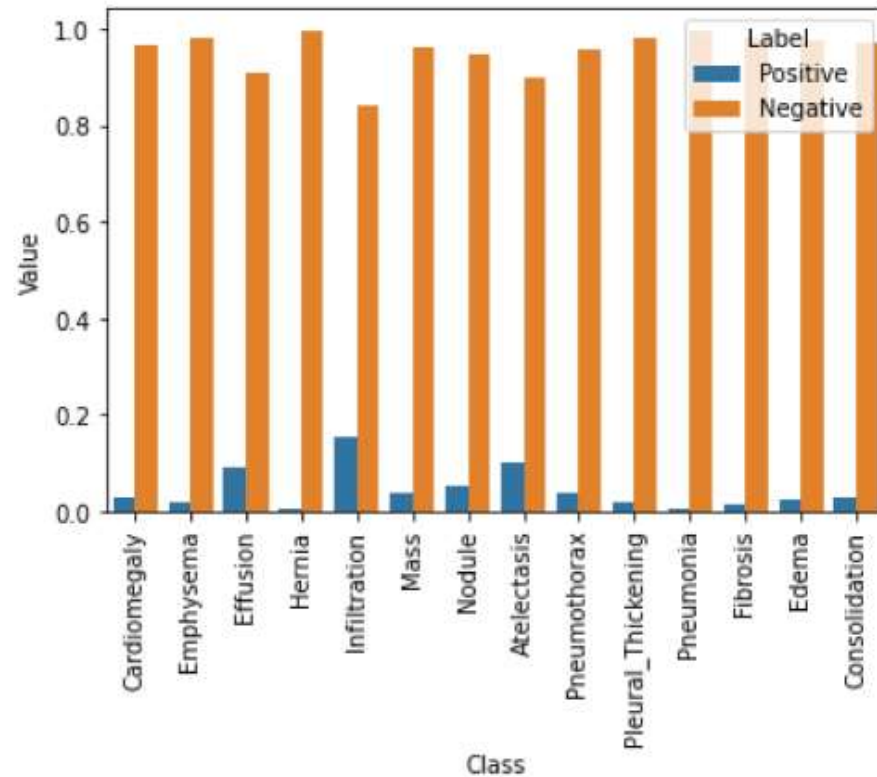
Solution 3: Weighted Binary Cross Entropy Loss

Weights:

$$w_p = \frac{\text{num negative}}{\text{num total}} \quad w_n = \frac{\text{num positive}}{\text{num total}}$$

$$\mathcal{L}_{cross-entropy}^w(x) = -(w_p y \log(f(x)) + w_n (1 - y) \log(1 - f(x))).$$

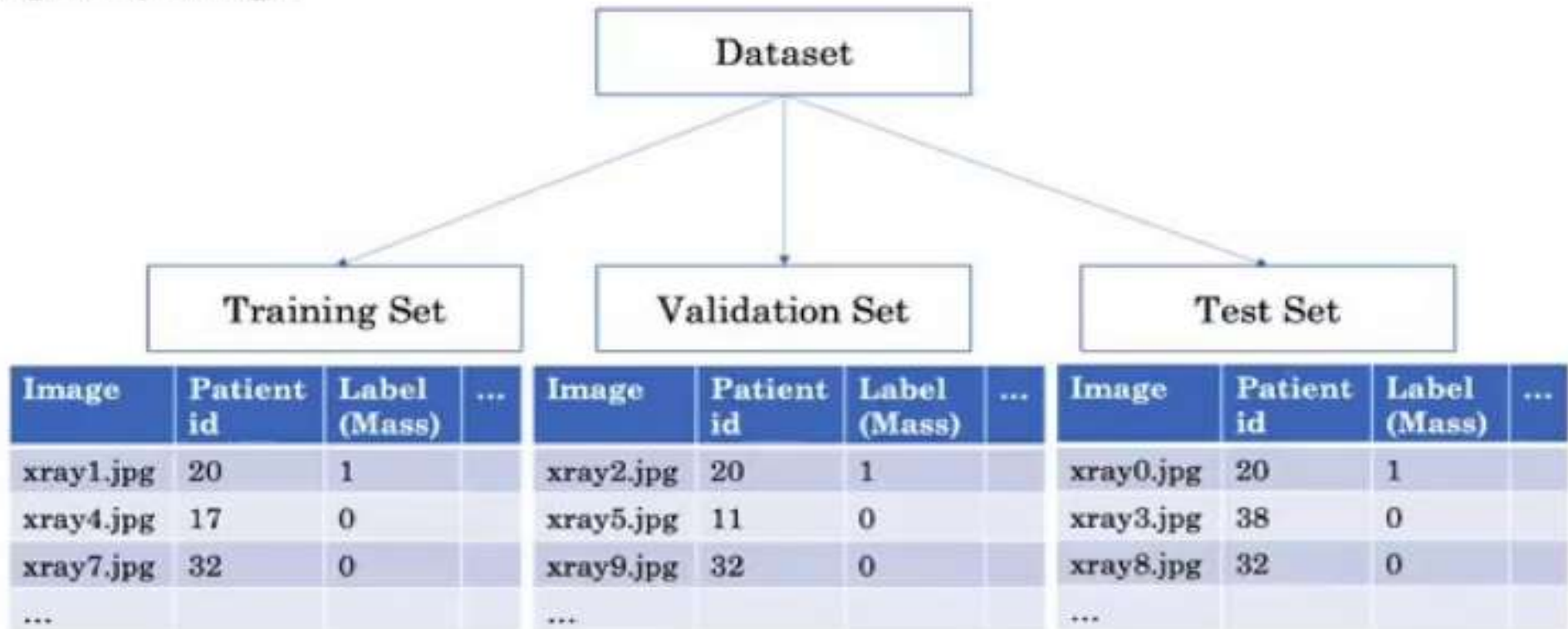
Weighted Binary cross-entropy Loss



$$\mathcal{L}_{cross-entropy}^w(x) = -(w_p y \log(f(x)) + w_n (1 - y) \log(1 - f(x)))$$

Patient Overlap

Split By Image

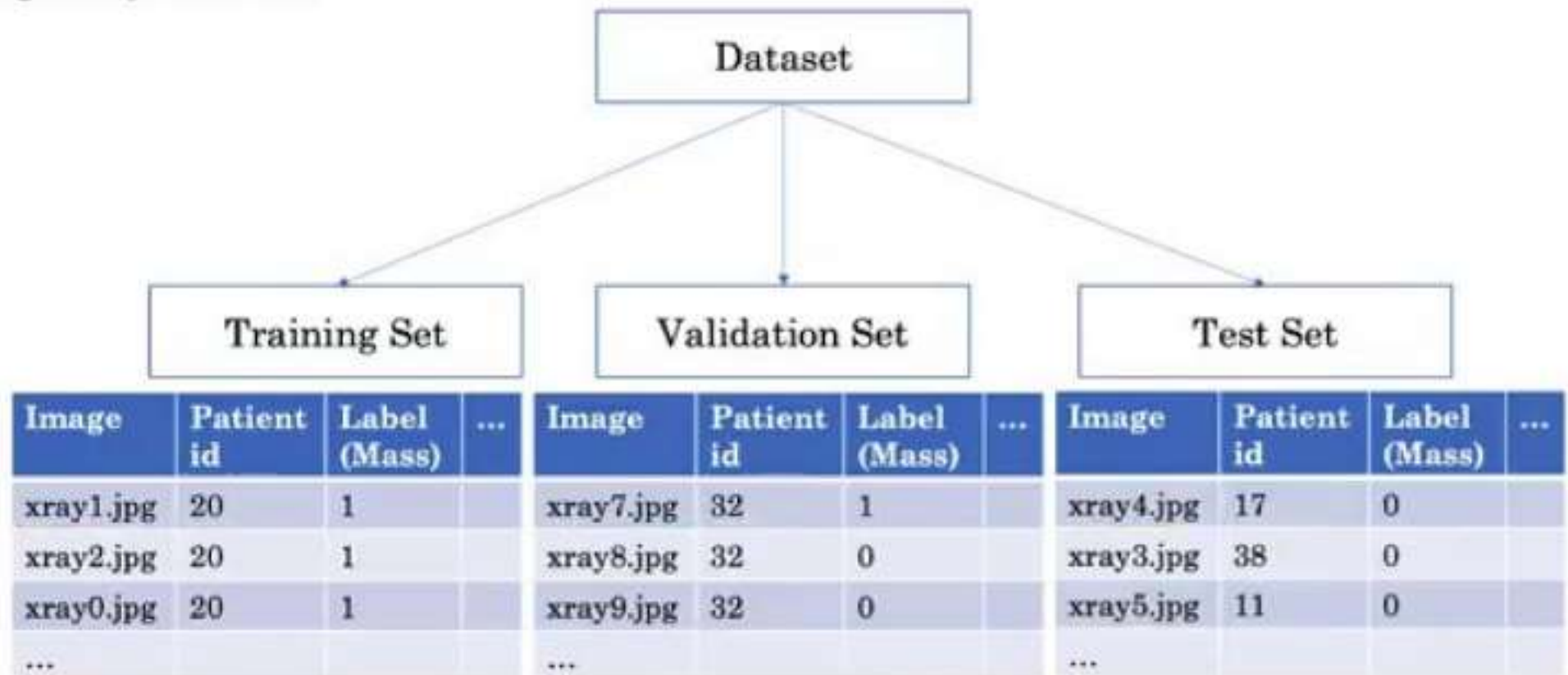


Patient Overlap

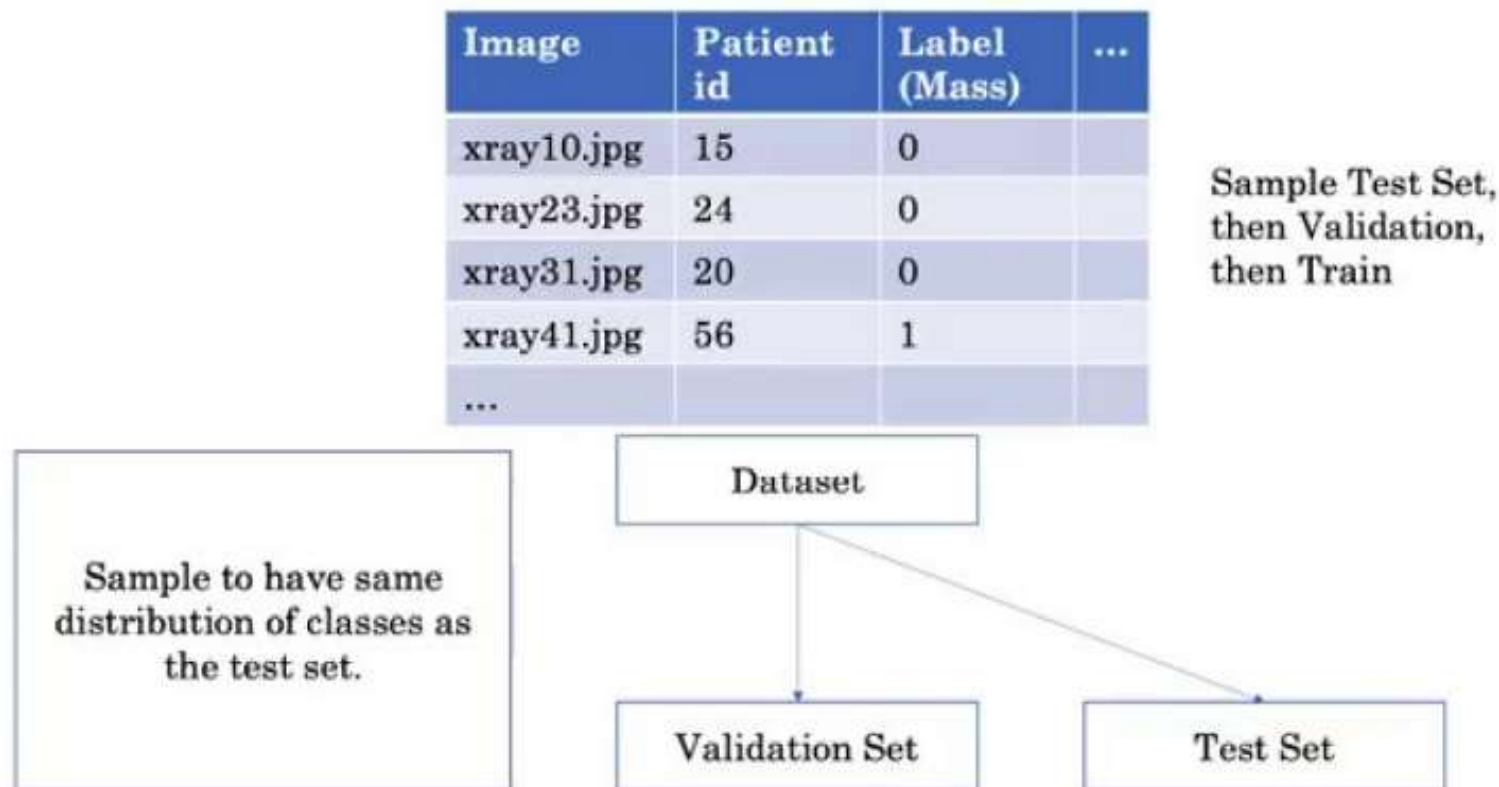
Patient Overlap

Solution: Ensure that a patient's x-ray image occurs only once in any of the data sets. This can be achieved by dividing the images by patient resulting into same patient's images will be present in one set only.

Split By Patient



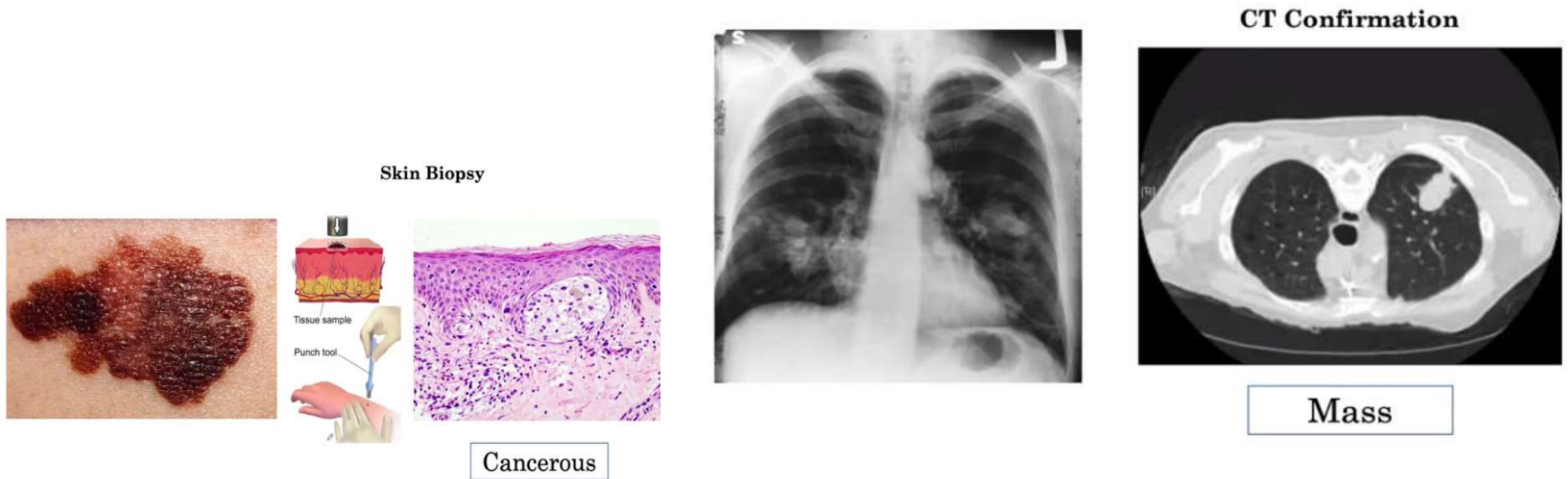
Set Sampling



In medical field we usually have a small data set therefore clever test and validation data sampling is required. If we randomly split, diseased examples might be absent in one of the subsets.

Solution: Sample equal % of examples of minority class for both test and validation data set, the rest goes in train set.

Ground Truth



How to determine the correct label for an example ?

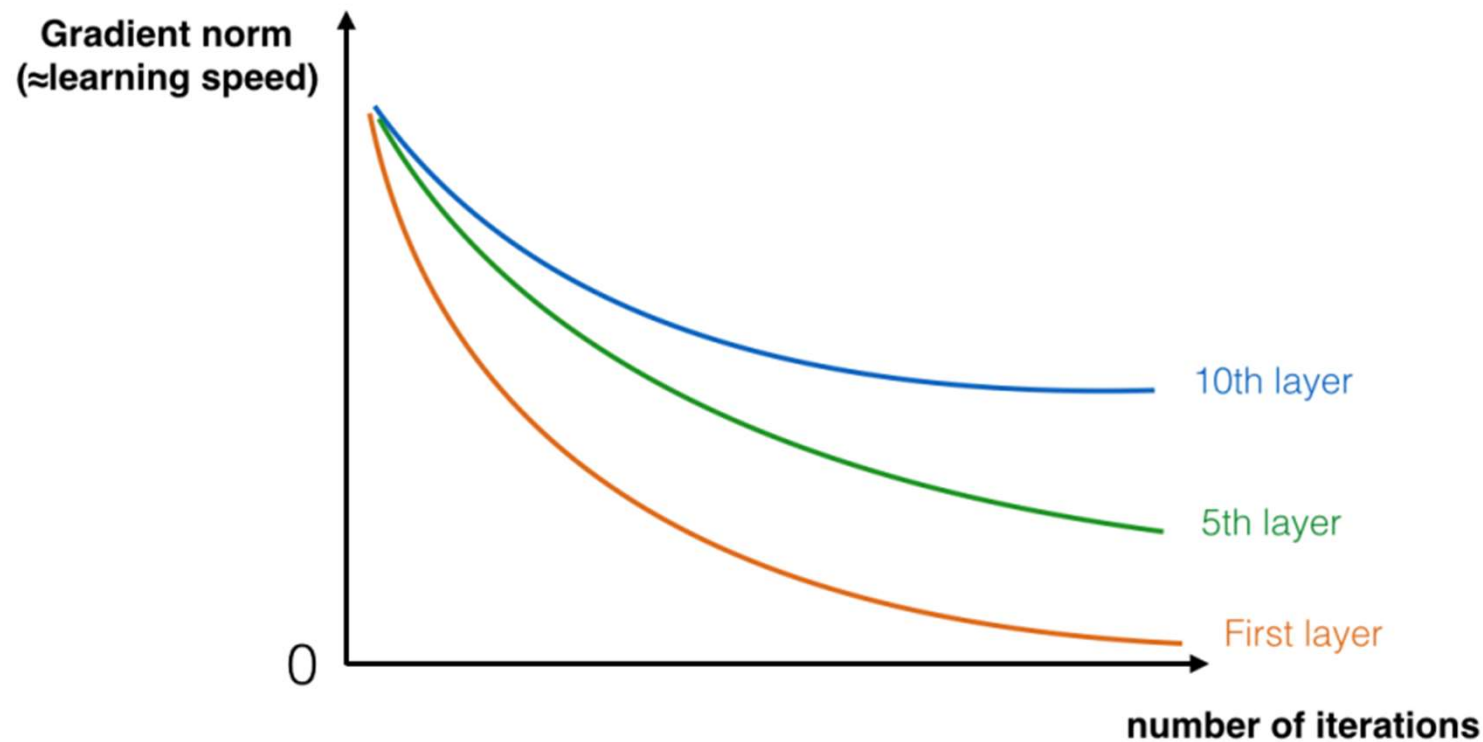
The label is called *Ground Truth* in ML or *Reference Standard* in medical community.

In medical labelling there may happen disagreement between experts !!!

Solution 1: Use consensus voting - group of experts take majority vote.

Solution 2: Add other exams to confirm the results.

Vanishing gradient



Very deep NNs are difficult to train because of vanishing or exploding gradient issues.

During training, the magnitude of the gradient for the shallower (the first) layers tends to 0 very rapidly as training proceeds.

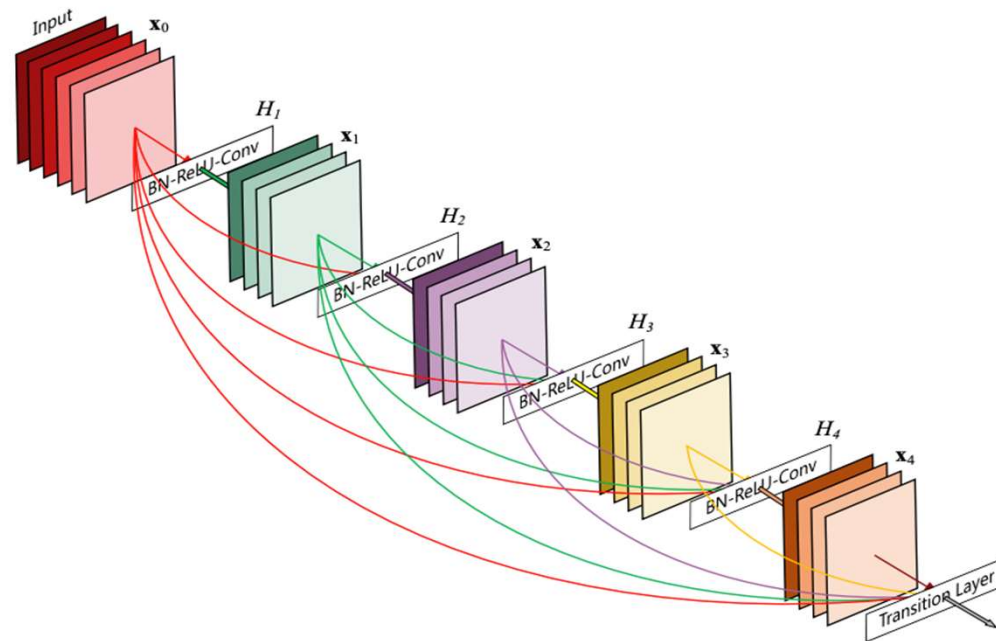
DenseNet

DenseNet is a deep CNN divided into blocks with several conv layers. Each layer is connected to the next layers in the same block.

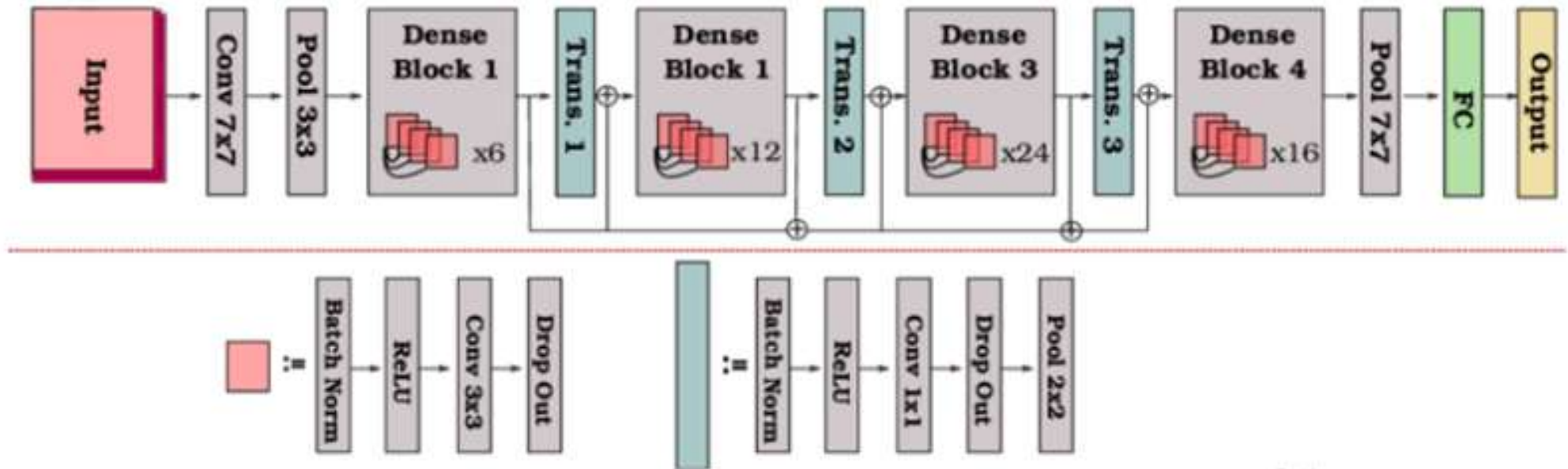
The first layer is connected to the 2nd, 3rd, 4th etc in the same block.

The second layer is connected to the 3rd, 4th, 5th etc. in the same block.

Fig. One block of DenseNet



DenseNet

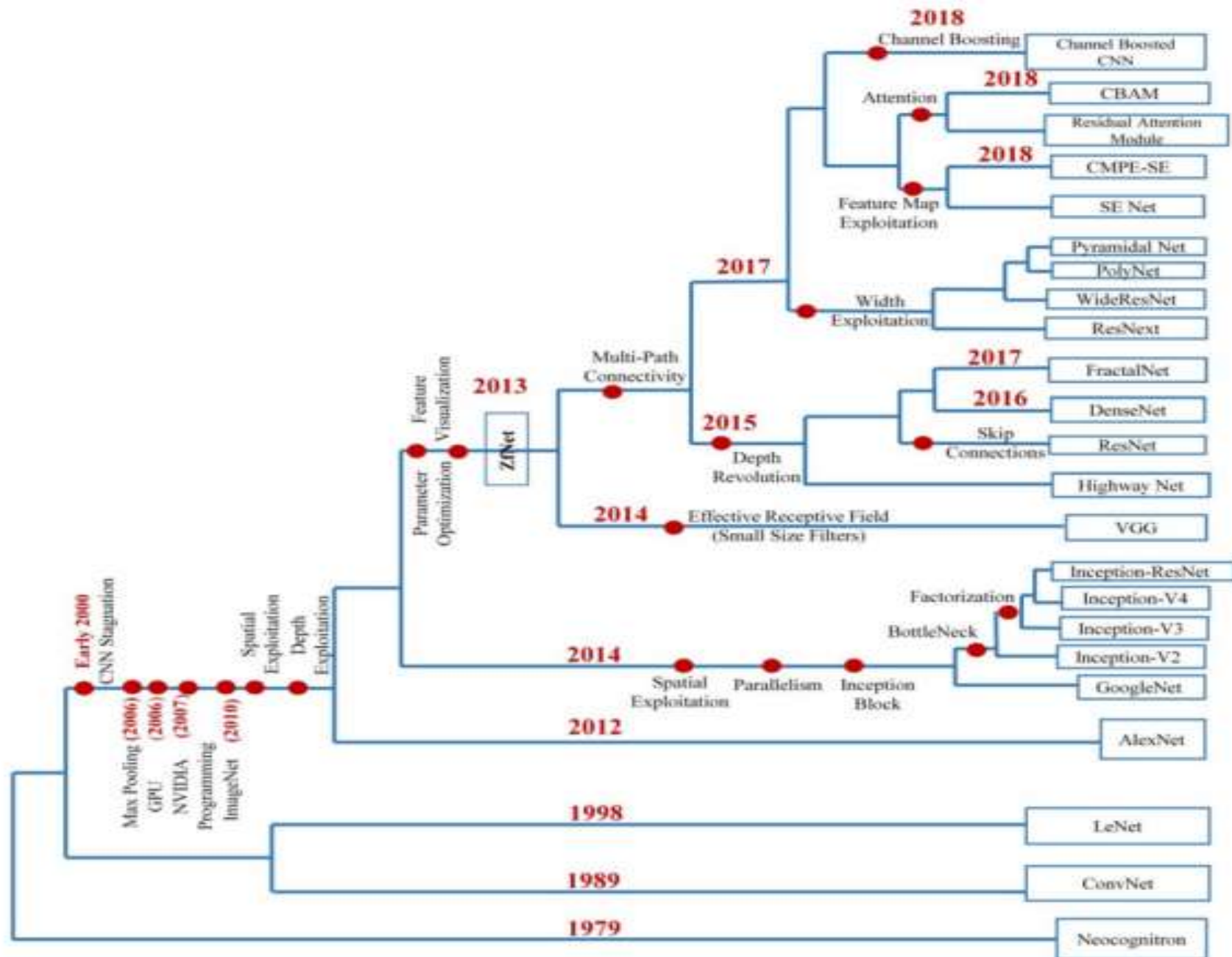


DenseNet aims to improve the problem with vanishing gradient in DNN. Due to the long sequence of layers, the gradients of the errors (computed at the output) vanish before reaching the initial payers.

DenseNet family

Layers	Output Size	DenseNet-121	DenseNet-169	DenseNet-201	DenseNet-264
Convolution	112×112	7×7 conv, stride 2			
Pooling	56×56	3×3 max pool, stride 2			
Dense Block (1)	56×56	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 6$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 6$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 6$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 6$
Transition Layer (1)	56×56	1×1 conv			
	28×28	2×2 average pool, stride 2			
Dense Block (2)	28×28	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 12$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 12$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 12$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 12$
Transition Layer (2)	28×28	1×1 conv			
	14×14	2×2 average pool, stride 2			
Dense Block (3)	14×14	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 24$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 32$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 48$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 64$
Transition Layer (3)	14×14	1×1 conv			
	7×7	2×2 average pool, stride 2			
Dense Block (4)	7×7	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 16$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 32$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 32$	$\begin{bmatrix} 1 \times 1 \text{ conv} \\ 3 \times 3 \text{ conv} \end{bmatrix} \times 48$
Classification Layer	1×1	7×7 global average pool			
		1000D fully-connected, softmax			

Evolution of deep architectures



Explainable AI (XAI) – Grad CAM method

EXPLAINABLE AI – general view

XAI is especially important in areas where someone's life could be immediately affected.

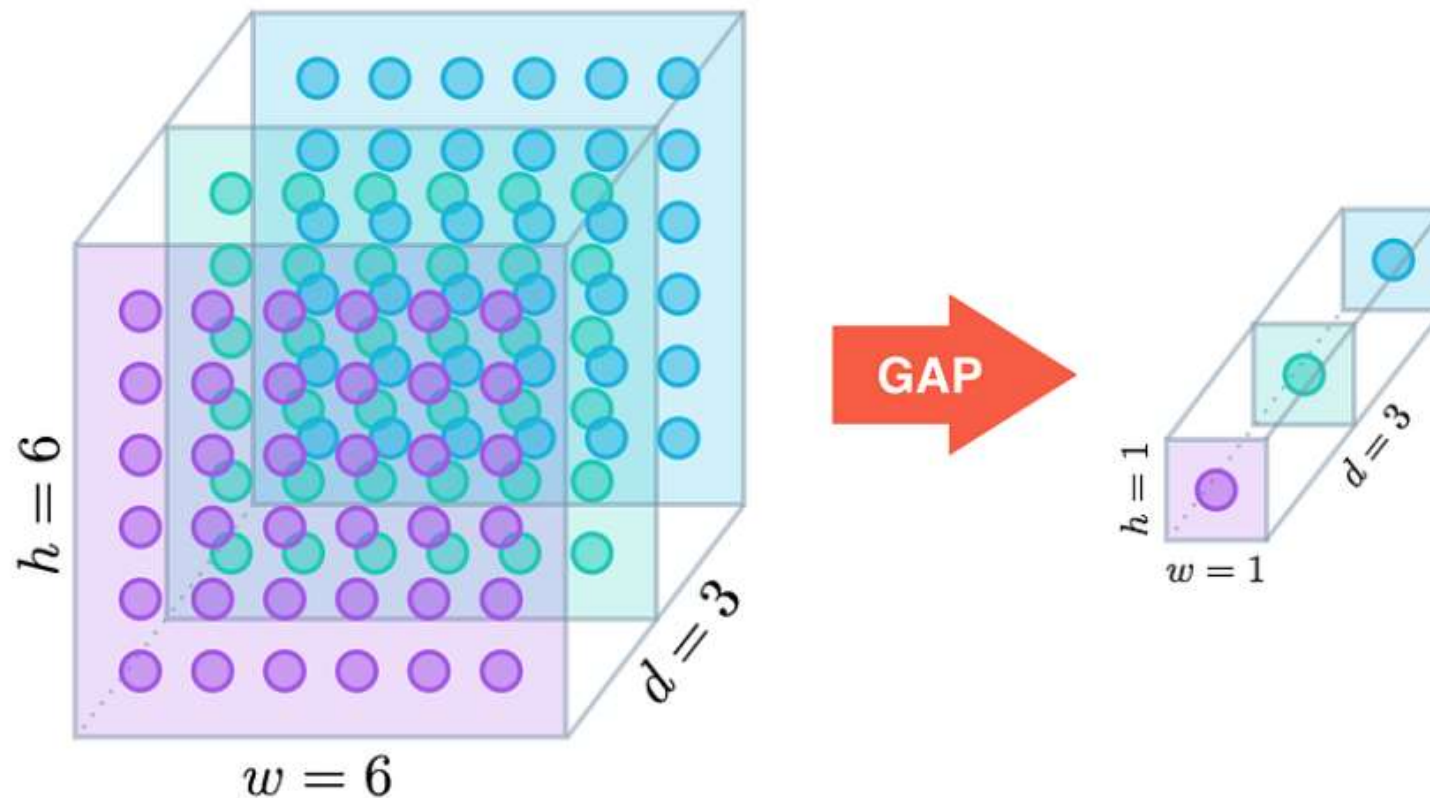
- Healthcare.** XAI systems for patient diagnosis can help build trust between doctor and system, as the doctor can understand how the AI system reaches a diagnosis.

- Financial.** XAI is used to approve or deny financial claims such as loans or mortgage applications, as well as to detect financial fraud.

- Autonomous vehicles.** XAI is used in autonomous vehicles to explain driving-based decisions, especially those that revolve around safety. If a passenger can understand how and why the vehicle is making its driving decisions, they can feel safer knowing what scenarios the vehicle can or can't handle well.

Simplified XAI: Feature importance; Feature selection

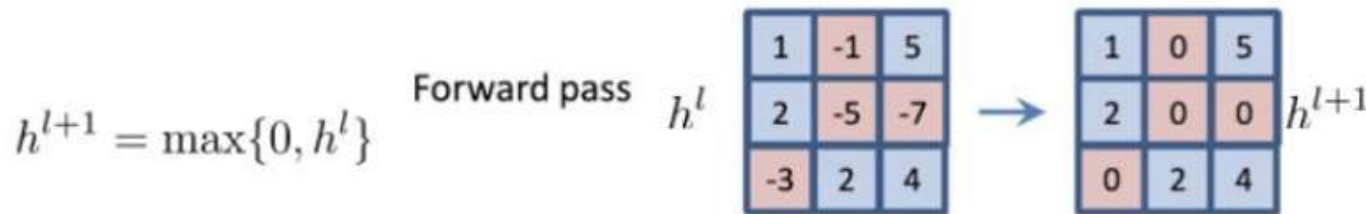
XAI: Global Average Pooling (GAP)



GAP layers perform a more extreme type of dimensionality reduction than max pooling layers, where a tensor with dimensions $h \times w \times d$ is reduced in size to have dimensions $1 \times 1 \times d$. GAP layers reduce each $h \times w$ feature map to a single number by taking the average of all hw values.

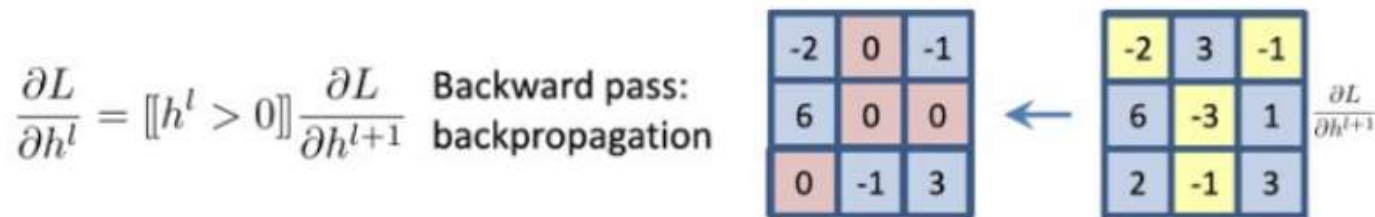
<https://medium.com/@chinesh4/generalized-way-of-interpreting-cnns-a7d1b0178709>

XAI: Guided Backpropagation



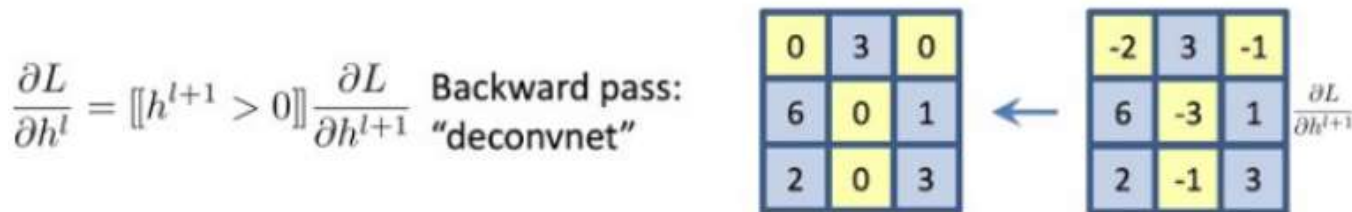
Relu Forward Pass:

flow forward values > 0



Relu Backward Pass:

flow values, where value > 0 in filter h^l during forward prop.



Deconvolution for Relu:

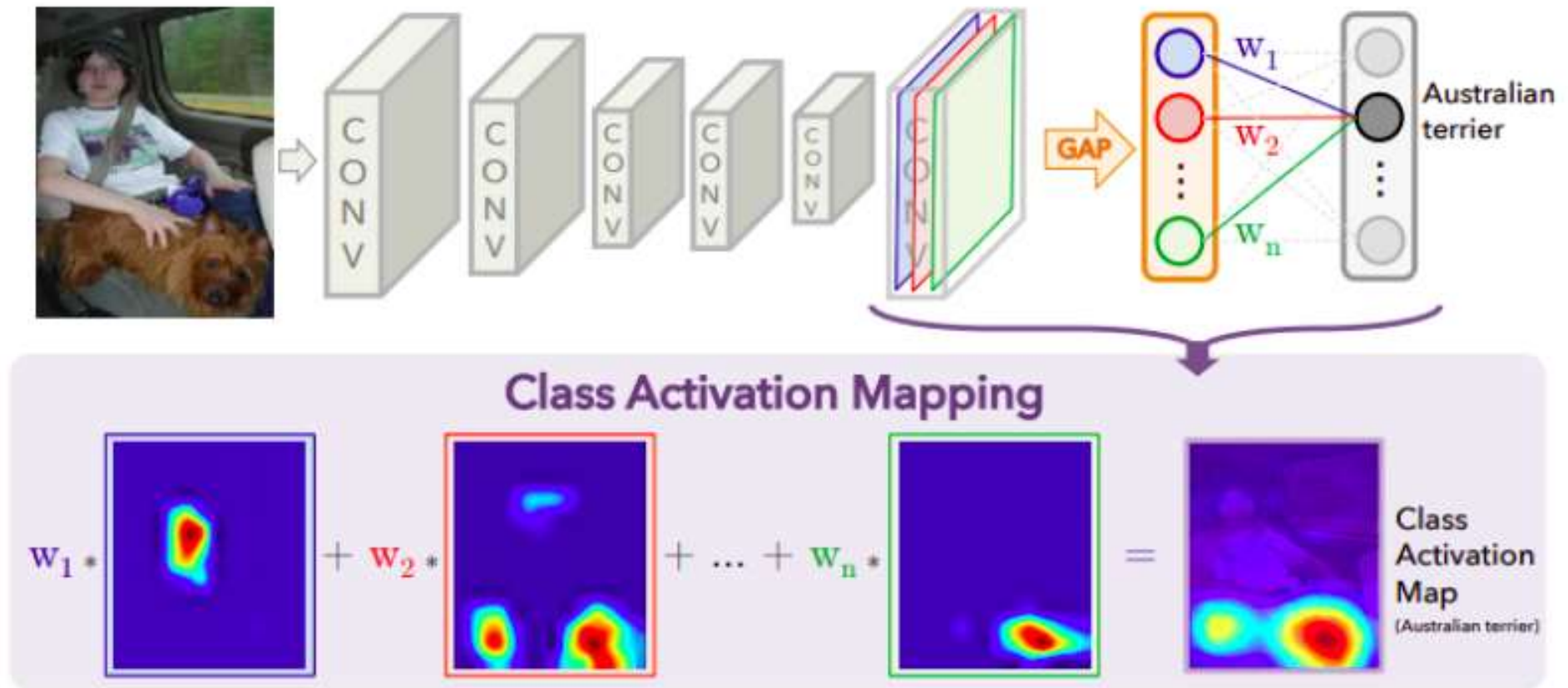
flow values backward, where value in the filter > 0 .



Guided Backpropagation:

intersection of the concept of Backward pass & deconvolution.

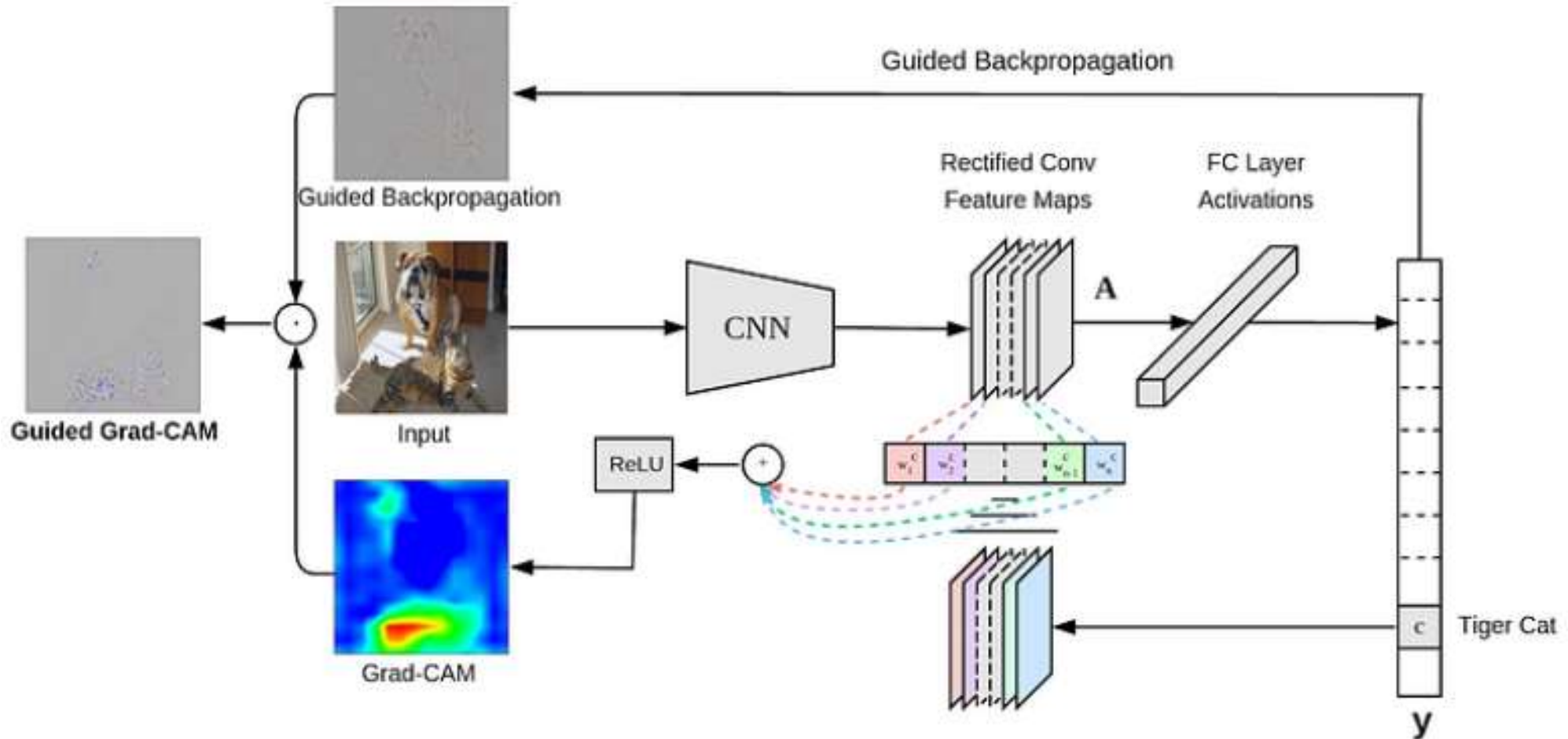
XAI: Class Activation Mapping (CAM)



Modify the base CNN architecture: remove fully-connected (FC) layers, softmax layer takes as input the Global-Average-Pooled (GAP) conv feature maps from the last Conv layer, and outputs the probability for each class.

CAM is upsampled by Bi-Linear Interpolation and superimposed on the input image to show the regions which the CNN model is looking at.

XAI: Grad CAM — Gradient-weighted Class Activation Mapping



Grad-Cam uses both CAM & gradient information flowing into the last conv layer of the CNN to understand the impact of each neuron for a decision of one class. Grad-CAM is upsampled to the input image resolution using bilinear interpolation. It creates coarse heatmap.

Guided Grad-CAM combines Guided Backpropagation and Grad-CAM via element-wise multiplication to get high resolution visualization (fine-grained information of the pixel activation).

Published work with students

Paper: COVID-19 detection through X-Ray chest images

Diego Hernandez, Rodrigo Pereira, P. Georgieva

2020 Int Conf of Automatics and Informatics

Proof of concept: COVID-19 infected patients can be detected based on their X-ray chest images.

Our strategy:

- 1) (Binary classification). Use a large data set of not COVID-19 X-ray chest images (ChexPert) and train a **custom CNN (Model 1)**. Then, fine tune the model with the small COVID-19 data.
- 2) (Binary classification). Import **pre-trained deep learning models** and fine tune them with the COVID-19 data. Here we designed and tuned two models based on ResNet50 (**Model 2**) and VGG16 (**Model 3**), respectively.
- 3) Multi-class scenario (healthy, pneumonia, Covid19) -
Model 4 based on DenseNet121 architecture.

Data Sets

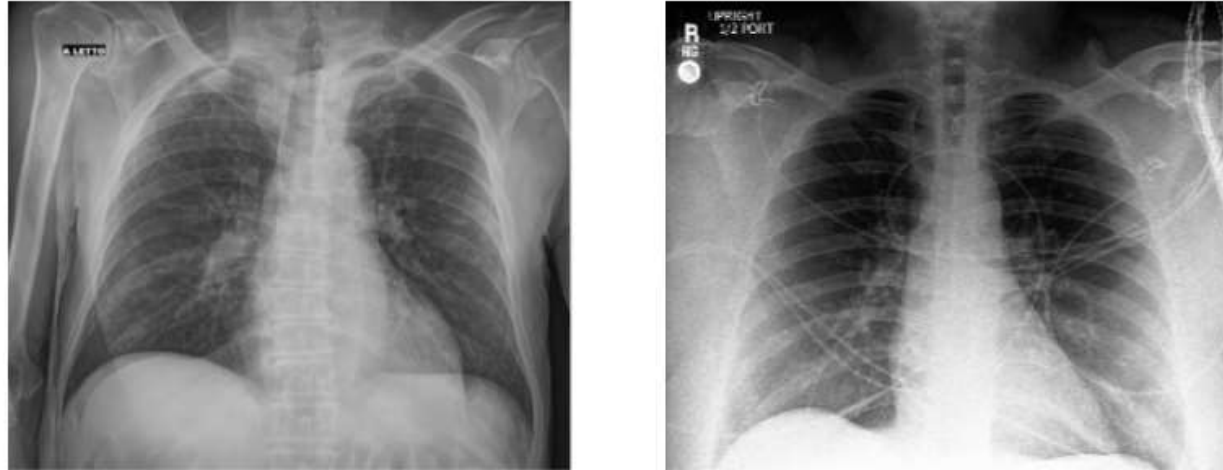
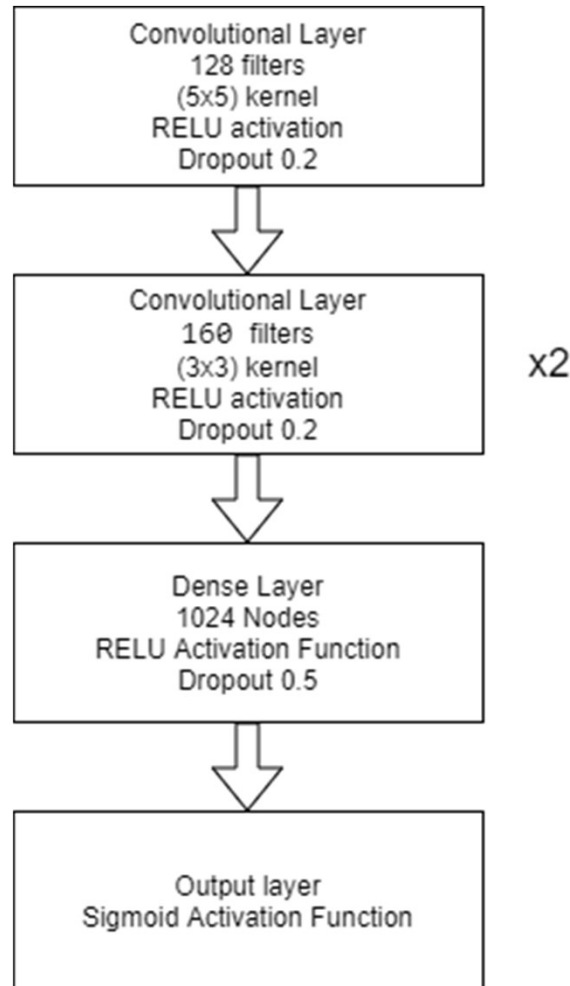


Fig. 1. Dataset 1 samples: X-Ray images of covid19 infected patient (left image) and healthy patient (right image)

Pathology	Positive (%)	Uncertain (%)	Negative (%)
No Finding	16627 (8.86)	0 (0.0)	171014 (91.14)
Enlarged Cardiom.	9020 (4.81)	10148 (5.41)	168473 (89.78)
Cardiomegaly	23002 (12.26)	6597 (3.52)	158042 (84.23)
Lung Lesion	6856 (3.65)	1071 (0.57)	179714 (95.78)
Lung Opacity	92669 (49.39)	4341 (2.31)	90631 (48.3)
Edema	48905 (26.06)	11571 (6.17)	127165 (67.77)
Consolidation	12730 (6.78)	23976 (12.78)	150935 (80.44)
Pneumonia	4576 (2.44)	15658 (8.34)	167407 (89.22)
Atelectasis	29333 (15.63)	29377 (15.66)	128931 (68.71)
Pneumothorax	17313 (9.23)	2663 (1.42)	167665 (89.35)
Pleural Effusion	75696 (40.34)	9419 (5.02)	102526 (54.64)
Pleural Other	2441 (1.3)	1771 (0.94)	183429 (97.76)
Fracture	7270 (3.87)	484 (0.26)	179887 (95.87)
Support Devices	105831 (56.4)	898 (0.48)	80912 (43.12)

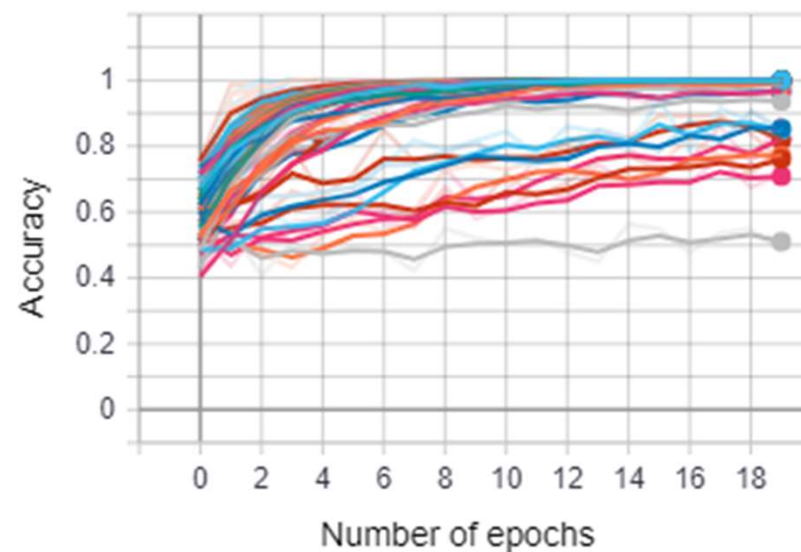
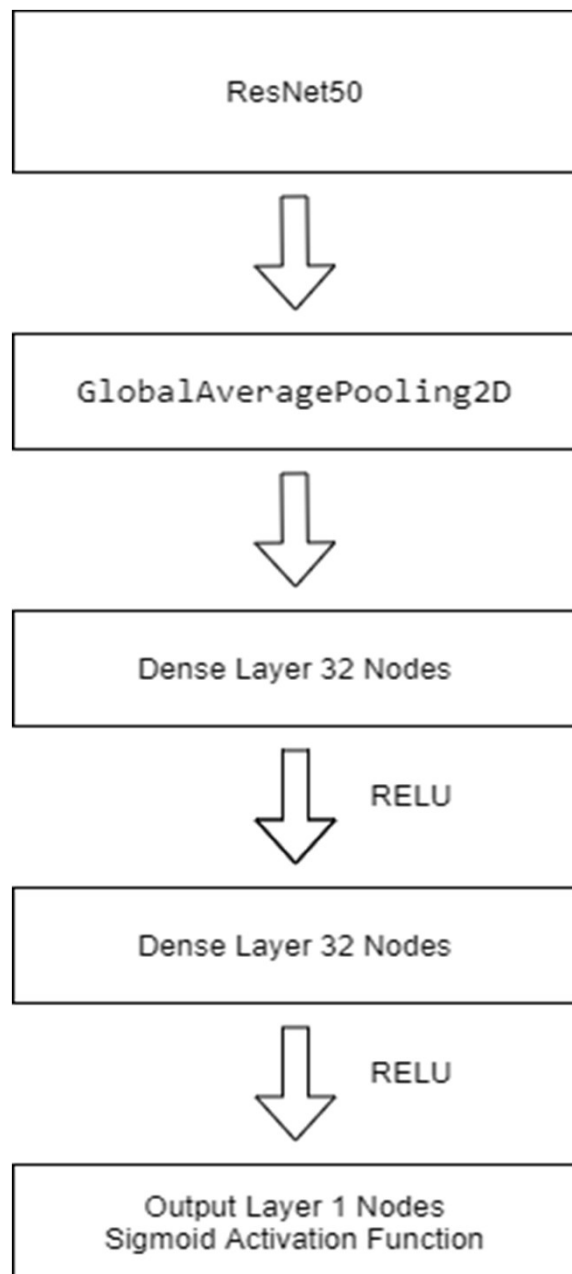
Fig. 2. Dataset 2: Chexpert meta data

Model 1 (binary classification scenario): Custom End-to-End trained CNN



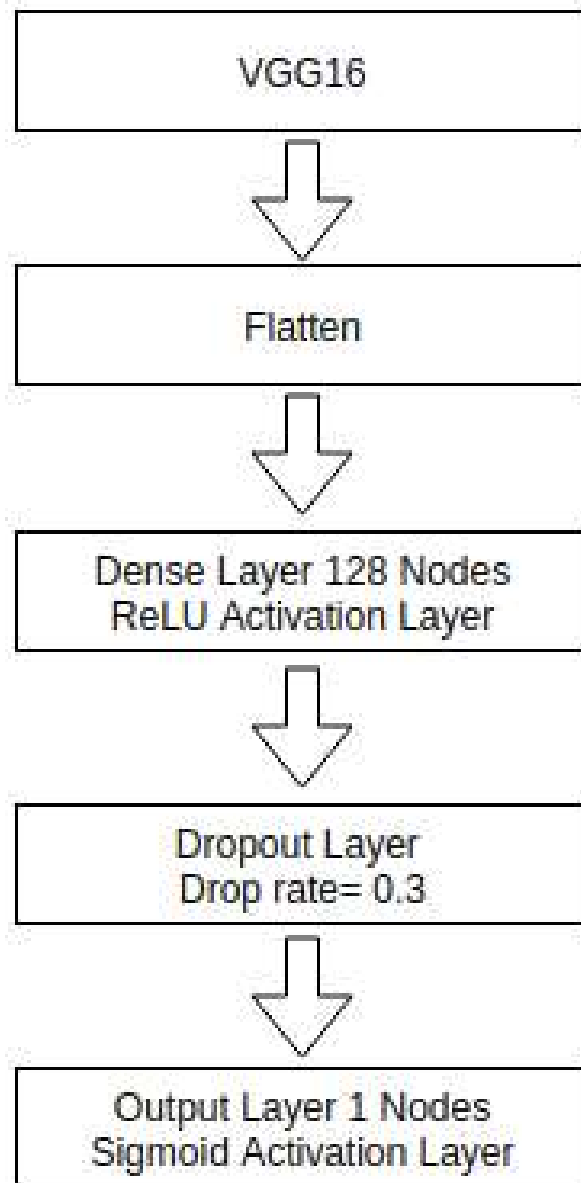
Model	Accuracy	Precision	Recall	F1 Score
Model 1 (Custom CNN)	0.68	0.67	0.63	0.65

Model 2: ResNet50 + fine tuning (ResNet50+)



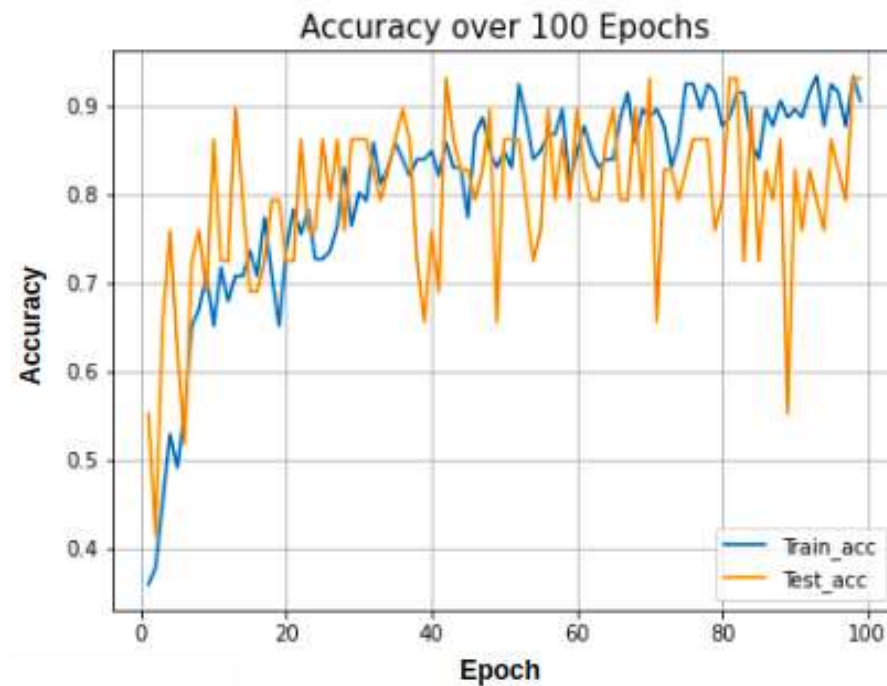
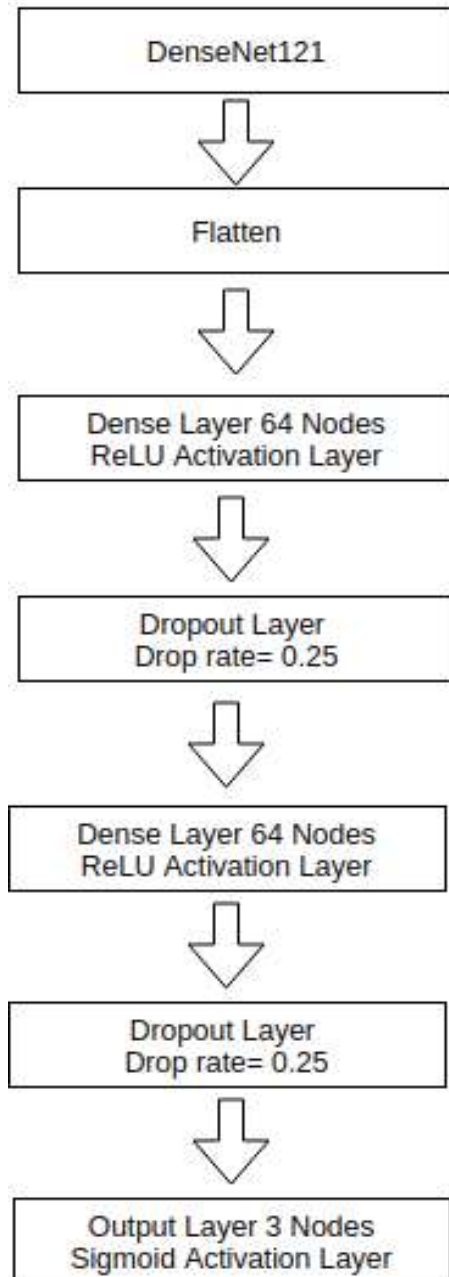
Model	Accuracy	Precision	Recall	F1 Score
Model 1 (Custom CNN)	0.68	0.67	0.63	0.65
Model 2 (ResNet50+)	0.9063	0.90	0.9167	0.9072

Model 3: VGG16 + fine tuning ((VGG16+))



Model	Accuracy	Precision	Recall	F1 Score
Model 1 (Custom CNN)	0.68	0.67	0.63	0.65
Model 2 (ResNet50+)	0.9063	0.90	0.9167	0.9072
Model 3 (VGG16+)	0.8229	0.8039	0.8541	0.8282

Model 4 (multi-class scenario): DenseNet121 + fine tuning



MODEL PERFORMANCE METRICS ON TEST DATA

Model	Accuracy	Precision	Recall	F1 Score
Model 1 (Custom CNN)	0.68	0.67	0.63	0.65
Model 2 (ResNet50+)	0.9063	0.90	0.9167	0.9072
Model 3 (VGG16+)	0.8229	0.8039	0.8541	0.8282
Model 4 (DenseNet121+)	0.834	0.89	0.67	0.7619

Transfer learning - more favourable performance

Proof of concept hypothesis that COVID-19 infected patients can be detected based on their X- ray chest images is confirmed.

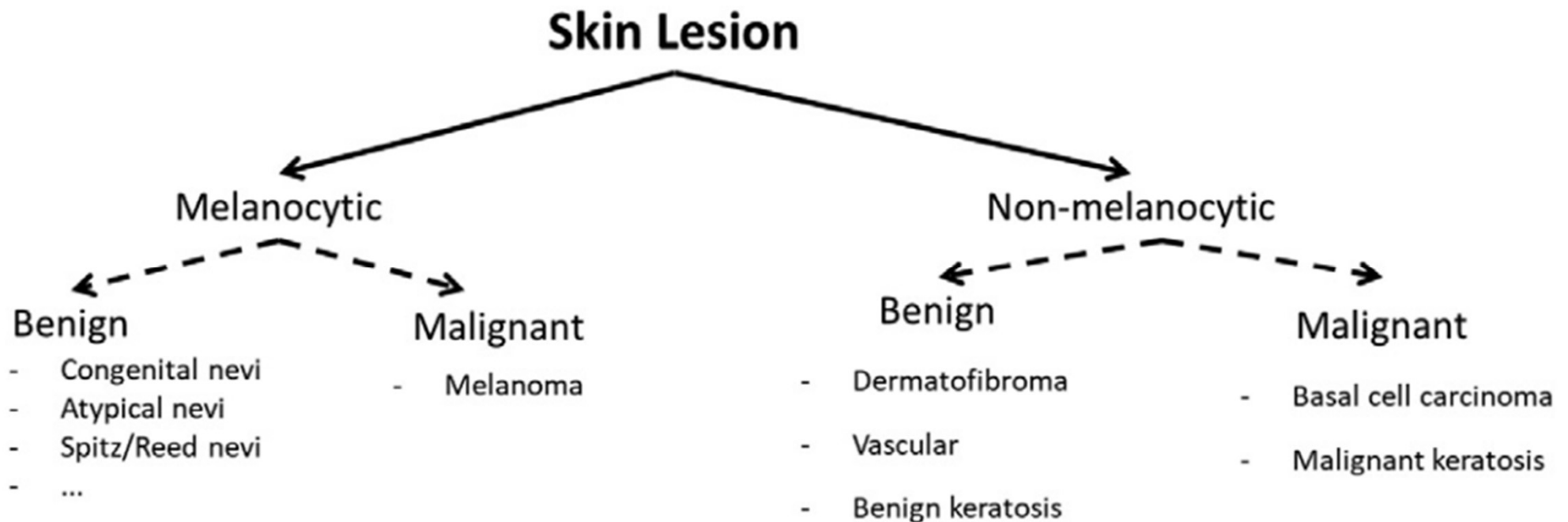
Promising study opens a new way to test and detect COVID-19 infected patients.

Paper: Automated Diagnosis of Skin Lesions

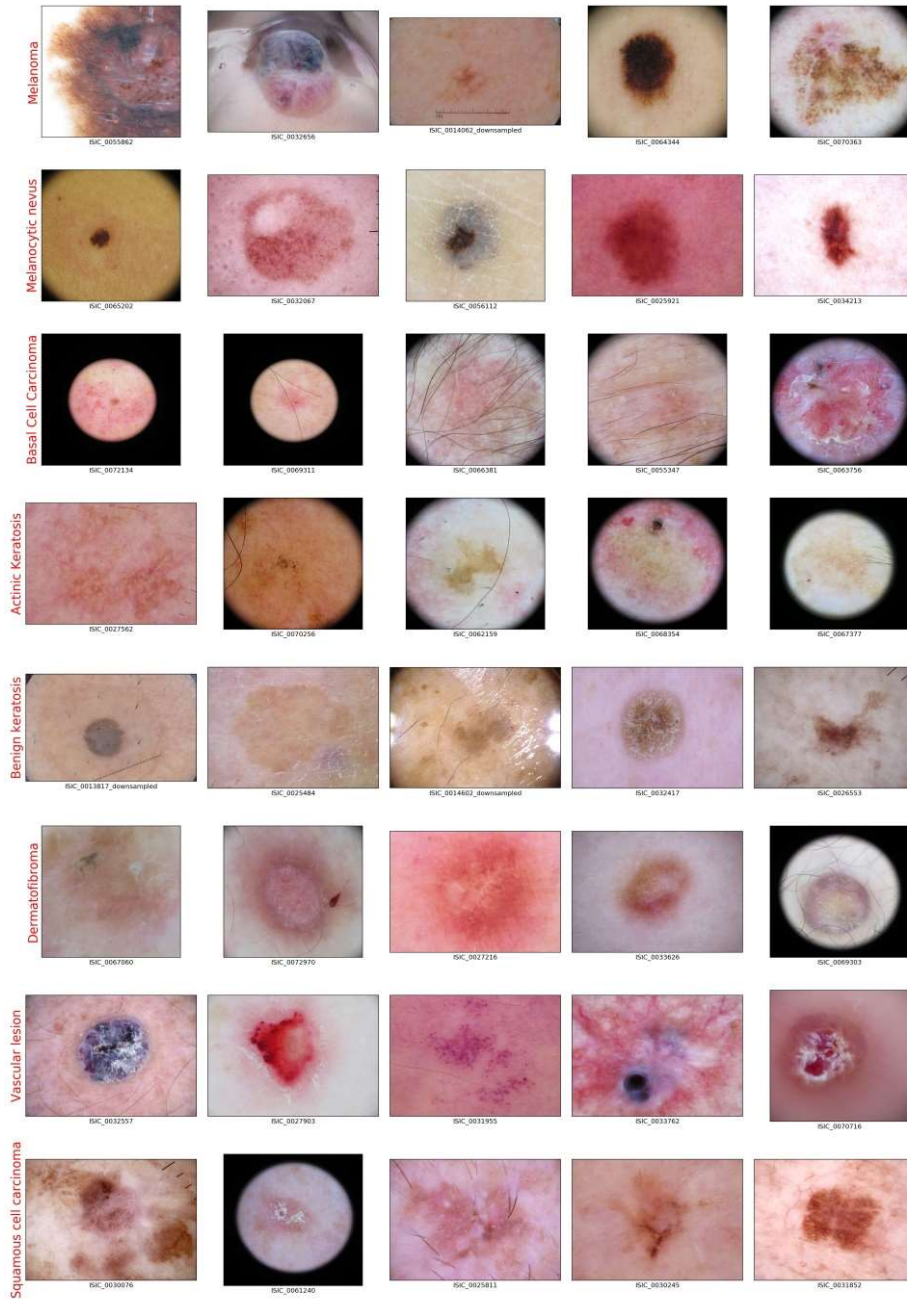
Fabio Santos, Filipe Silva, P. Georgieva

2020 IEEE Conf on Intelligent Systems

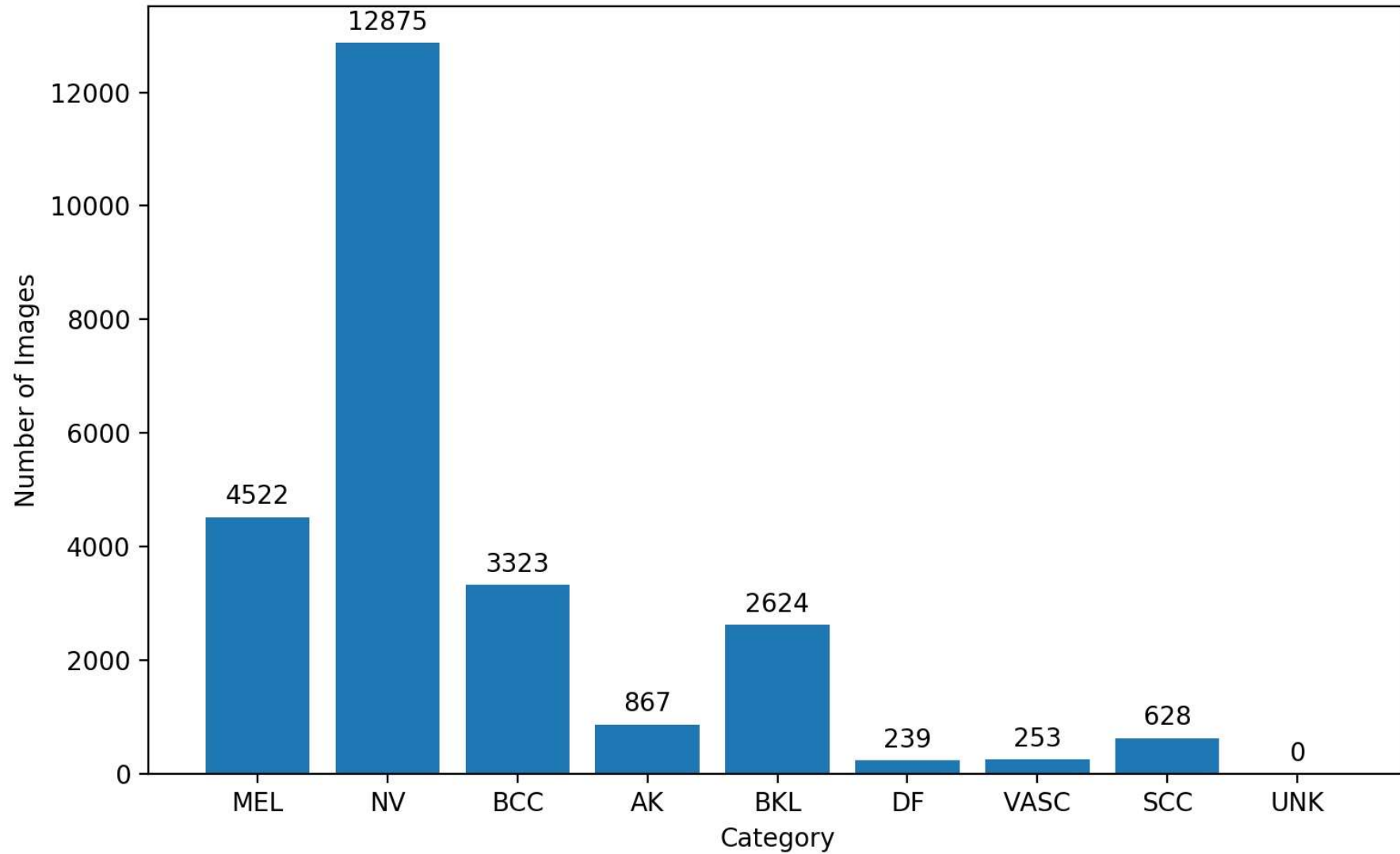
Goal: Detect 8 skin lesions categories



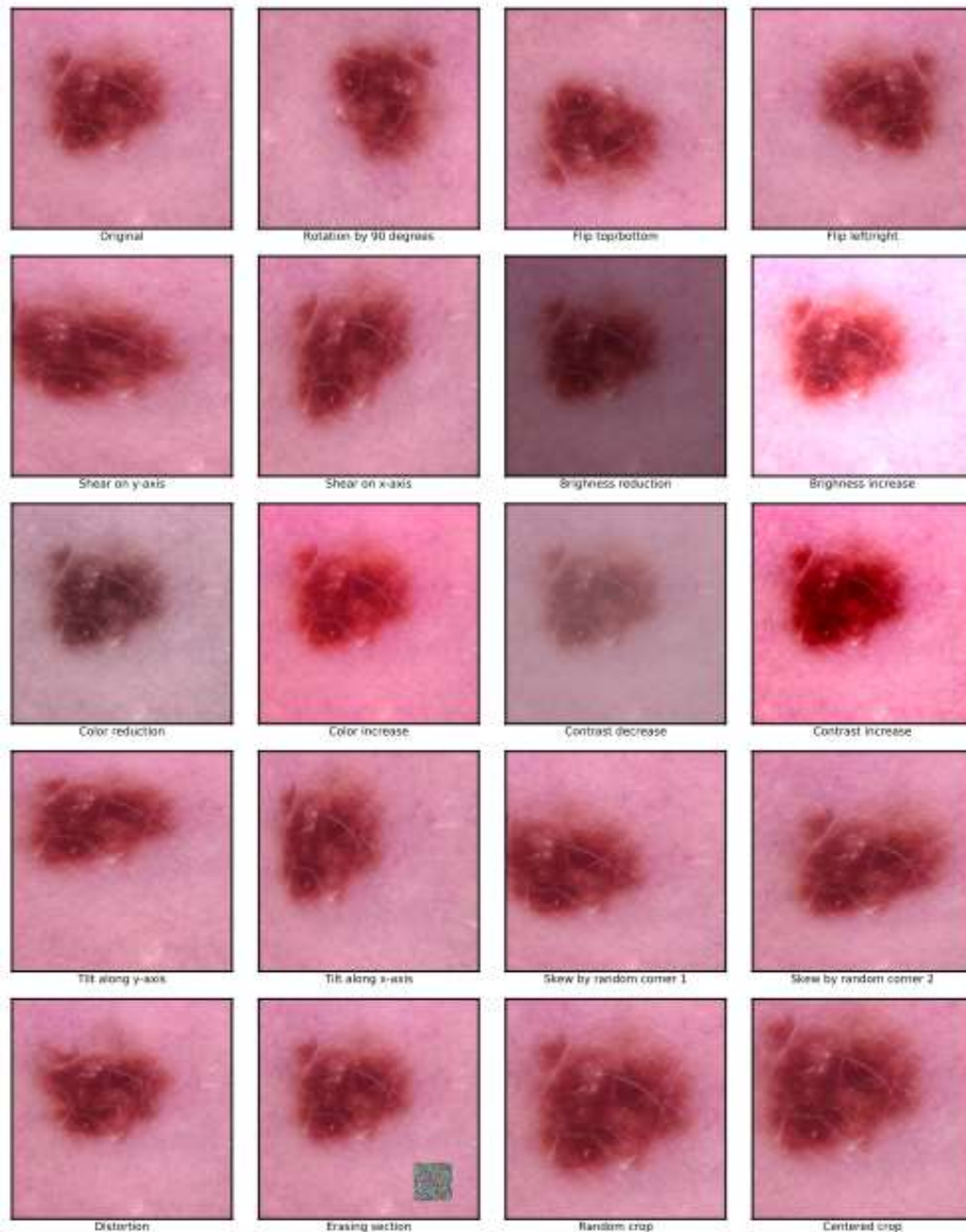
Data: <https://challenge.isic-archive.com/> International Skin Imaging Collaboration (ISIC)



Data Distribution



Data Augmentation



- Horizontal flips;
- Vertical flips;
- 90° rotations;
- Randomly increase or decrease contrast;
- Randomly increase or decrease brightness;
- Randomly increase or decrease color intensity;
- Randomly erase a small section of the image;
- Shears on x or y axis with 20 degrees to the left/right or top/down, respectively.

DenseNet201

