CV & DL for COVID-19

Università degli Studi Cagliari

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Update: 31/03/2021 – Update on Lung Analysis Activities

History of the Updates

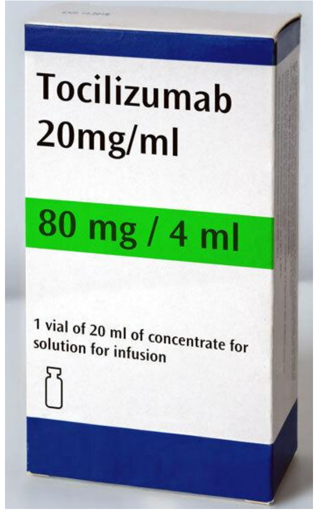
- 04/02/2021: Project Creation
- 08/02/2021: Found new solutions for lung analysis **[LP]**
- 22/02/2021: First results with CycleGan against U-NET on AiForCovid lung data **[LP]**
- 25/02/2021: Second tranche of results of SegGanV2 against U-Net on AiForCovid lung data **[LP]**
- 03/03/2021: Results on approach on Cycle-consistent GAN **[LP]**
- 31/03/2021: Added results on Solutions 4 2.1 **[LP]**

The COVID-19 disease

- Recent epidemiological data on the spread of the virus indicate an extremely worrying scenario:
    - 53 mln people have been infected
    - 1,3 mln people have died

What’s next?

- The first responses of the medical and scientific community has considered the use of certain drugs, able to slow the decline of symptoms, so as to give breathing space to intensive therapies.
- The latter have been the true Achilles heel of health care system(both Italian and international)
- Reason: especially in the early stages of the epidemic, even in the presence of mild symptoms, it tended to hospitalize in the ICU all COVID positives.
    - In a short time, the ICUs became saturated and COVID positives with serioous symptoms were without adequate care to combat the virus.

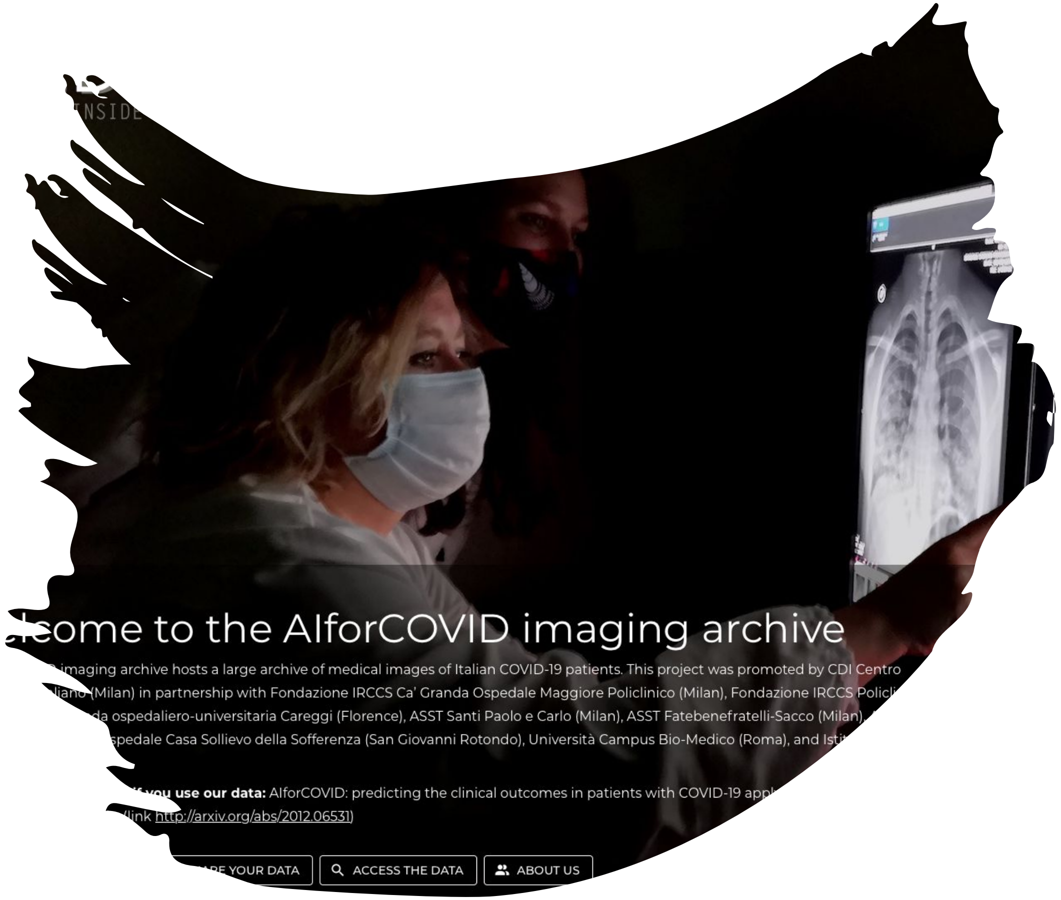


What is failure?

- Community responses were driven by the need to offer the best of care to all
  - It is simple, in hindsight, to make the assessments of the case
- But experience can be useful to learn from mistakes
- What was missing was a criterion for assessing the severity of the disease on the individual patient.
  - This decision must be taken on the basis of precise data and detailed information.

AIforCOVID imaging archive*

- In this regard, a database of data and images has been created to support research on COVID. The data were collected by the CDI (Centro Diagnostico Italiano) based in Milan, in collaboration with other Italian foundations and hospitals **
- https://aiforcovid.radiomica.it
- The archive contains images of CXR and medical records of about 820 patients.



**CDI Centro Diagnostico Italiano (Milan), Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico (Milan), Fondazione IRCCS Policlinico San Matteo (Pavia)
Azienda ospedaliero-universitaria Careggi (Florence), ASST Santi Paolo e Carlo (Milan), ASST Fatebenefratelli-Sacco (Milan)
ASST Ospedale San Gerardo (Monza), Ospedale Casa Sollievo della Sofferenza (San Giovanni Rotondo), Università Campus Bio-Medico (Roma)
Istituto Italiano di Tecnologia (Genova).

Reference Paper

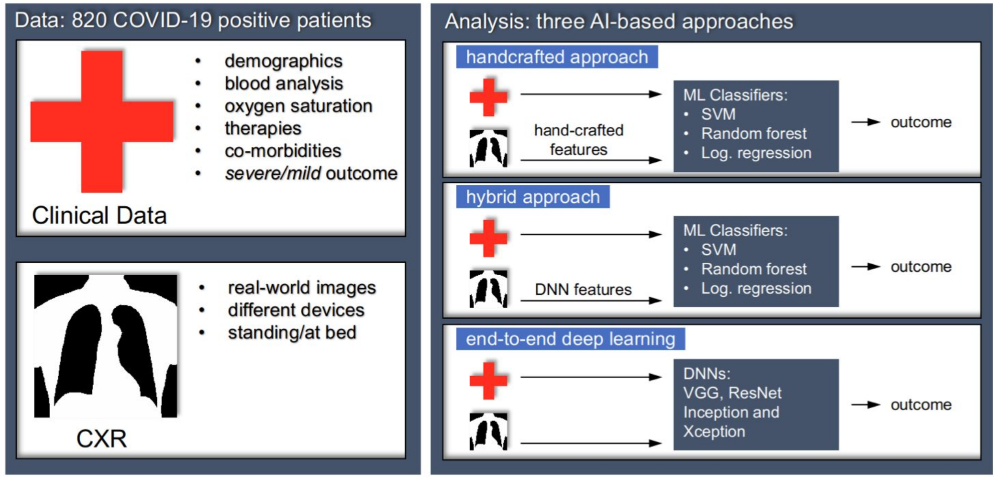
- This paper can be downloaded (al momento ancora unpublished) here -> http://arxiv.org/abs/2012.06531
- Currently, it may be considered as a benchmark for our studies

AIforCOVID: predicting the clinical outcomes in patients with COVID-19 applying AI to chest-X-rays. An Italian multicentre study.

A Preprint

The data and the approach

- Data
  - CXR (Chest X-Ray)
  - Complete Medical Records
- Classification purpose
  - Prognosis of the patient
    - *Mild*
    - *Severe*
- Preliminary approaches
  - *Handcrafted*
  - *Hybrid*
  - *End-to-End DL*



Medical record

Name	Description	Overall-population	Mild-group (A)	Severe-group (B)	A vs B p-value	Missing data (%)
Active cancer in the last 5 years	Patient had active cancer in the last 5 years (% reported)	7%	5%	8%	<0.05†	1.4
Age	Patient's age (years)	64; 54-77	60; 49-72	70; 60-79	<0.001*	0
Atrial Fibrillation	Patient had atrial fibrillaton (% reported)	9%	5%	11%	<0.01 †	2.2
Body temperature (°C)	Patients temperature at admission (in °C)	38; 37-38	38; 37-38	38; 37-38	0.171	8.8
Cardiovascular Disease	Patient had cardiovascular diseases (% reported)	35%	23%	40%	<0.001†	1.7
Chronic Kidney disease	Patient had chronic kidney disease (% reported)	6%	4%	9%	<0.01†	1.4
COPD	Chronic obstructive pulmonary disease (% reported)	7%	4%	10%	<0.01†	1.4
Cough	Cought (%yes)	54%	59%	50%	<0.05†	0.5
CRP	C-reactive protein concentration (mg/dL)	57; 24-119	42; 17-75	103; 48-163	<0.001*	3.5
Days Fever	Days of fever up to admission (days)	3; 2-4	3; 2-4	3; 2-3	0.289	10.96
D-dimer	D-dimer amount in blood	632; 352-1287	549; 262-909	820; 438-2056	<0.001*	77.6
Death+	Death of patient occurred during hospitalization for any cause	168	0	168	-	-
Dementia	Patient had dementia (% reported)	4%	3%	6%	0.087	1.8
Diabetes	Patient had diabetes (% reported)	16%	10%	21%	<0.001†	1.4
Dyspnea	Patient had intense tightening in the chest, air hunger, difficulty breathing, breathlessness or a feeling of suffocation (%yes)	50%	37%	62%	<0.001†	0.4
Fibrinogen	Fibrinogen concentration in blood (mg/dL)	607; 513-700	550; 473-658	615; 549-700	<0.001*	73.6
Glucose	Glucose concentration in blood (mg/dL)	110; 96-130	104; 93-121	114; 101-139	<0.001*	20.6
Heart Failure	Patient had heart failure (% reported)	2%	1%	3%	0.157	2.3
Hypertension	Patient had high blood pressure (% reported)	46%	38%	54%	<0.001†	1.4
INR	International Normalized Ratio	1.13; 1.07-1.25	1.11; 1.06-1.20	1.15; 1.08-1.28	0.004*	28.8
Ischemic Heart Disease	Patient had ischemic heart disease (% reported)	15%	11%	18%	<0.01†	18.3
LDH	Lactate dehydrogenase concentration in blood (U/L)	320; 249-431	271; 214-323	405; 310-527	<0.001*	24.6
O_2 (%)	Oxygen percentage in blood (%)	95; 90-97	96; 94-98	92; 87-96	<0.001*	16.5
Obesity	Patient had obesity (% reported)	9%	6%	11%	0.058	36.1
$PaCO_2$	Partial pressure of carbon dioxide in arterial blood (mmHg)	33; 30-36	34; 30-37	33; 30-35	0.116	15.4
PaO_2	Partial pressure of oxygen in arterial blood (mmHg)	69; 59-80	73; 67-81	64; 54-76	<0.001*	15.3
PCT	Platelet count (ng/mL)	0.19; 0.09-0.56	0.09; 0.05-0.26	0.28; 0.13-0.72	<0.001*	71.8
pH	Blood pH	7; 7-7	7; 7-7	7; 7-7	<0.001*	17.3
Position+	Patient position during chest x-ray (%supine)	78%	68%	87%	<0.001†	0
Positivity at admission	Positivity to the SARS-CoV-2 swab at the admission time (% positive)	95%	94%	96%	0.142	4.7
Prognosis	Patient outcome, see section 2 (% cases)	-	46.8%	53.2%	0.468†	0.0
RBC	Red blood cells count (10^9/L)	4.65; 4.26-5.07	4.70; 4.34-5.11	4.59; 4.13-5.03	<0.001*	3.0
Respiratory Failure	Patient had respiratory failure (% reported)	1%	100%	2%	0.131	19.0
SaO_2	arterial oxygen saturation (%)	95; 91-97	96; 94-98	92;87-96	<0.001*	59.2
Sex	Patient's sex (%males)	68%	59%	75%	<0.001†	0
Stroke	Patient had stroke (% reported)	4%	3%	4%	0.447	2.3
Therapy Anakinra+	Patient was treated with Anakinra (%yes)	100%	0%	0%	-	10.8
Therapy anti-inflammatory+	Patient was treated with anti-inflammatory drugs therapy (%yes)	55%	53%	57%	0.243	13.5
Therapy antiviral+	Patient was treated with antiviral drugs (%yes)	47%	44%	50%	0.129	10.7
Therapy Eparine+	Patient was treated with eparine (no; yes; prophylactic treatment; therapeutic treatment)	56.6%; 11.5%; 28%; 3.9%	73.3%; 8.3%; 17.2%; 1.1%	39.9%; 14.7%; 38.8%; 6.6%	<0.001†	13.4
Therapy hydroxychloroquine+	Patient was treated with hydroxychloroquine (%yes)	59%	56%	62%	0.118	11.6
Therapy Tocilizumab+	Patient was treated with Tocilizumab (%yes)	9%	2%	15%	<0.001†	12.4
WBC	White blood cells count (10^9/L)	6.30; 4.73-8.42	5.58; 4.32-7.17	7.10; 5.25-9.80	0.012*	0.7

Table 4: Best recognition performance attained by each of the learning methods when the experiments were executed according to the 10-fold cross-validation (20 repetitions). In the second column, ML and DL stands for Machine-Learning and Deep Learning, respectively. The last column reports the learners providing the results shown here.

Input data	Approach	Accuracy	Sensitivity	Specificity	Learner
Clinical data	ML	$.757 \pm .008$	$.760 \pm .007$	$.754 \pm .011$	SVM
	DL	$.684 \pm .019$	$.753 \pm .020$	$.654 \pm .012$	MLP
CXR images	Handcrafted	$.658 \pm .015$	$.676 \pm .016$	$.638 \pm .019$	LGR
	Hybrid	$.728 \pm .038$	$.769 \pm .072$	$.680 \pm .076$	VGG-11 + RF
	End-to-end	$.742 \pm .010$	$.748 \pm .019$	$.738 \pm .013$	Resnet50
Clinical data and CXR images	Handcrafted	$.755 \pm .007$	$.758 \pm .008$	$.753 \pm .013$	SVM
	Hybrid	$.769 \pm .054$	$.788 \pm .064$	$.747 \pm .059$	GoogleNet + SVM
	End-to-end	$.748 \pm .008$	$.745 \pm .017$	$.751 \pm .015$	Resnet50 + MLP

Table 5: Best recognition performance attained by each of the learning methods when the experiments were executed according to the LOCO cross-validation. In the second column, ML and DL stands for Machine-Learning and Deep Learning, respectively. The last column reports the learners providing the results shown here.

Input data	Approach	Accuracy	Sensitivity	Specificity	Learner
Clinical data	ML	$.734 \pm .044$	$.699 \pm .158$	$.795 \pm .136$	SVM
	DL	$.663 \pm .016$	$.709 \pm .032$	$.644 \pm .018$	MLP
CXR images	Handcrafted	$.625 \pm .083$	$.641 \pm .159$	$.644 \pm .200$	SVM
	Hybrid	$.693 \pm .053$	$.806 \pm .161$	$.549 \pm .213$	Vgg11 + SVM
	End-to-end	$.705 \pm .010$	$.720 \pm .011$	$.696 \pm .015$	Resnet50
Clinical data and CXR images	Handcrafted	$.752 \pm .067$	$.711 \pm .165$	$.824 \pm .154$	LGR
	Hybrid	$.743 \pm .061$	$.769 \pm .189$	$.685 \pm .155$	GoogleNet + LGR
	End-to-end	$.709 \pm .005$	$.734 \pm .018$	$.696 \pm .009$	Resnet50 + MLP

The obtained preliminary results

Activities(1° draft)*

1. Lung Segmentation (CXR)
2. Prognosis Classification (CXR)
3. Data Correlation and Dimensionality reduction (med. record)
4. Heterogeneous data fusion (CXR & med. record)
5. Data weighting (med. record)
6. Data Classification (med. record)
7. Prognosis Classification (med. record)
8. Prognosis Classification with heterogenoues data fusion.

Activity 1. Lung analysis

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CV & DL for COVID-19

Lung Analysis

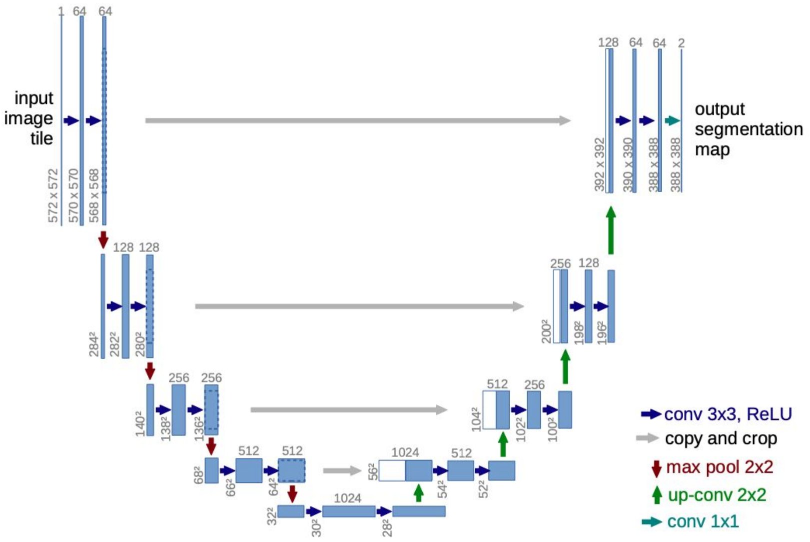
- Dataset
  - Open-i service of the National Library of Medicine
    - https://openi.nlm.nih.gov/gridquery?sub=x&m=1&n=100&it=xg
  - Montgomery County CXR set (MC) [IMGS e MASKS]
    - https://academictorrents.com/download/ac786f74878a5775c81d490b23842fd4736bfe33.torrent
    - Ref1:https://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=6663723
    - Ref2: https://ieeexplore.ieee.org/stamp/stamp.jsp?arnumber=6616679
  - JSRT Dataset
    - http://db.jsrt.or.jp/eng.php [redacted]
    - Ref1: https://www.ajronline.org/doi/10.2214/ajr.174.1.1740071
    - Le maschere di segmentazione di questo dataset sono le seguenti:
      - SCR Database (database che contiene SOLO le maschere di segmentazione per JSRT)
        - http://www.isi.uu.nl/Research/Databases/SCR/
        - Ref1: https://core.ac.uk/reader/13706045?utm_source=linkout

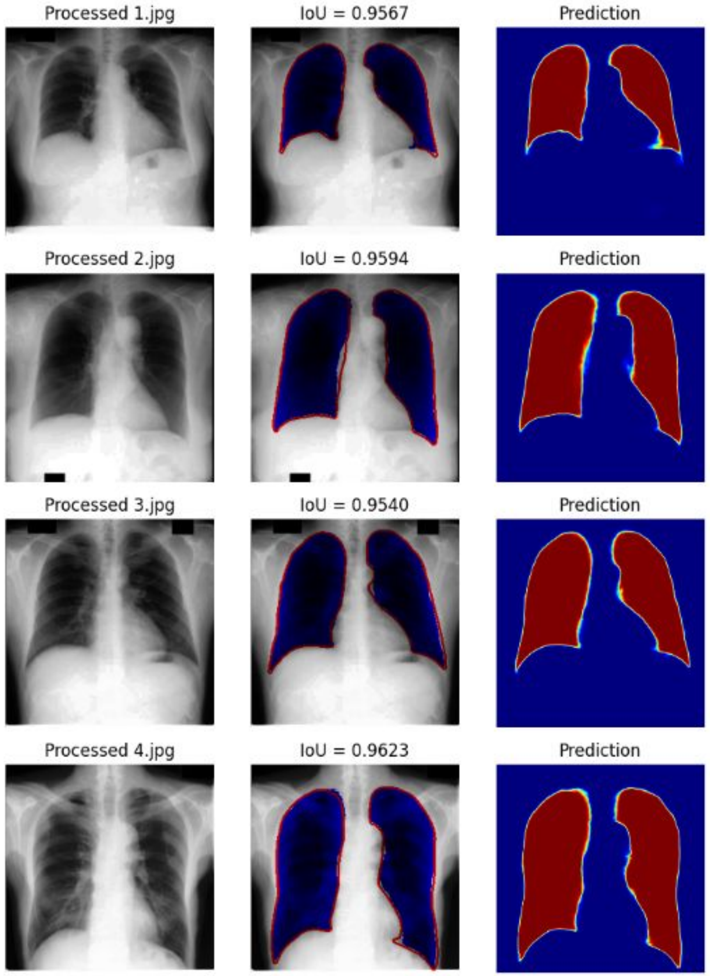
Lung Analysis (cont.)

- Chest X-Ray Images (Pneumonia)
  - https://www.kaggle.com/paultimothymooney/chest-xray-pneumonia
  - http://www.cell.com/cell/fulltext/S0092-8674(18)30154-5
  - The dataset is organized into 3 folders (train, test, val) and contains subfolders for each image category (Pneumonia/Normal). There are 5,863 X-Ray images (JPEG) and 2 categories (Pneumonia/Normal).
  - Chest X-ray images (anterior-posterior) were selected from retrospective cohorts of pediatric patients of one to five years old from Guangzhou Women and Children's Medical Center, Guangzhou. All chest X-ray imaging was performed as part of patients' routine clinical care.
  - For the analysis of chest x-ray images, all chest radiographs were initially screened for quality control by removing all low quality or unreadable scans. The diagnoses for the images were then graded by two expert physicians before being cleared for training the AI system. In order to account for any grading errors, the evaluation set was also checked by a third expert.

Lung Segmentation (state of the art)

- Lung Segmentation
- For the segmentation of the lungs, U-NET has been used

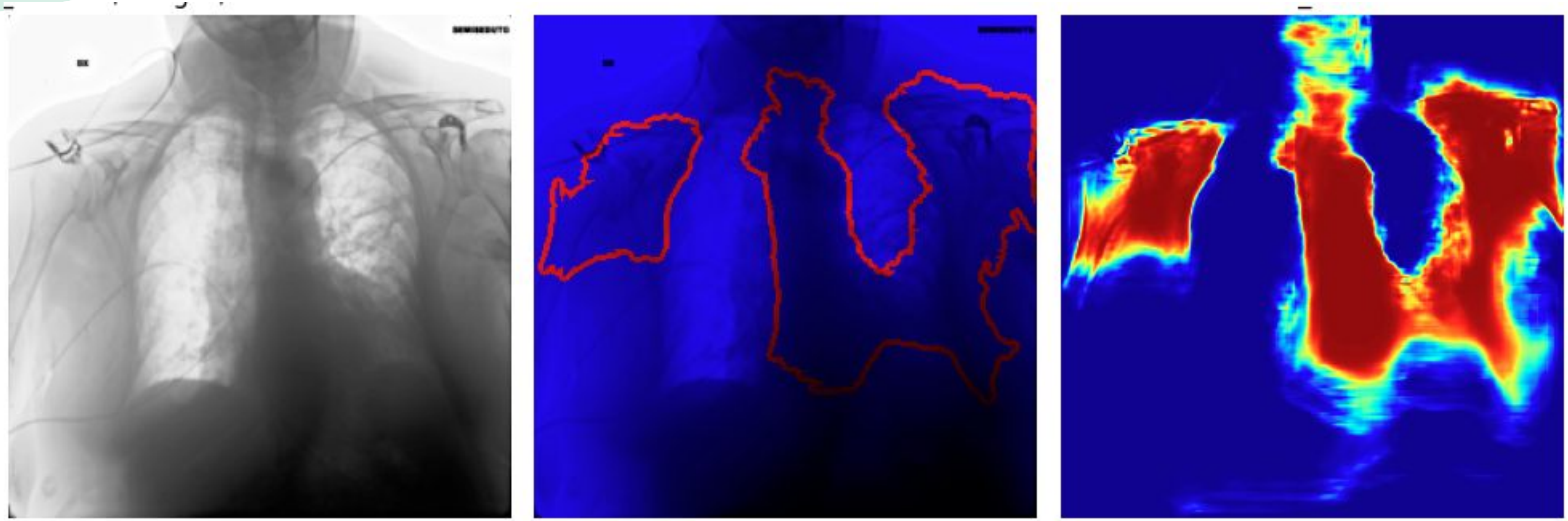




U-NET REPO: https://github.com/imlab-uiip/lung-segmentation-2d
U-NET Explanation: https://lmb.informatik.uni-freiburg.de/people/ronneber/u-net/
U-NET PAPER: https://arxiv.org/pdf/1505.04597.pdf

Issues in Lung Segmentation

on AiForCovid dataset

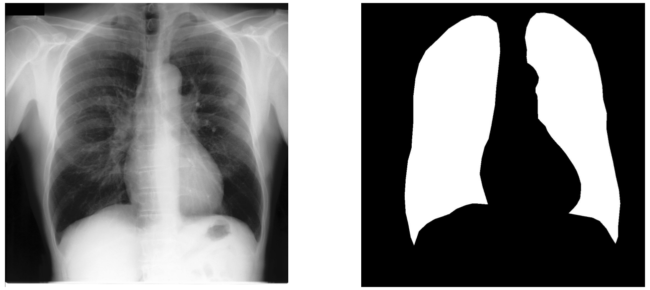


How to overcome such issues?

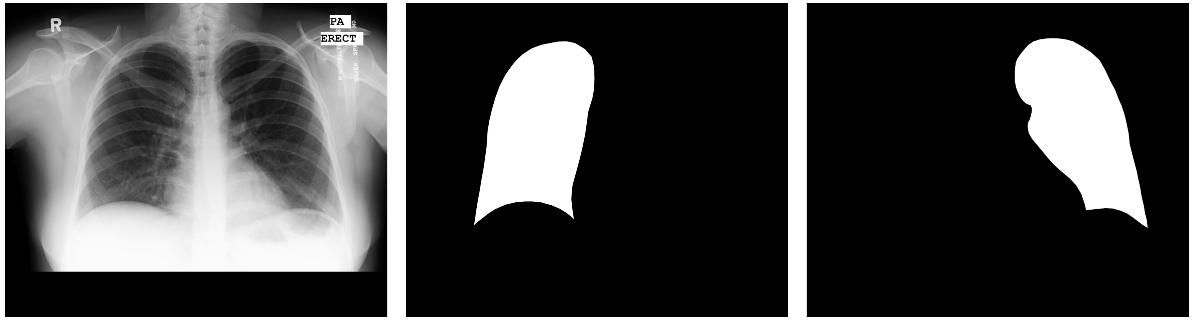
Reason??

Training images

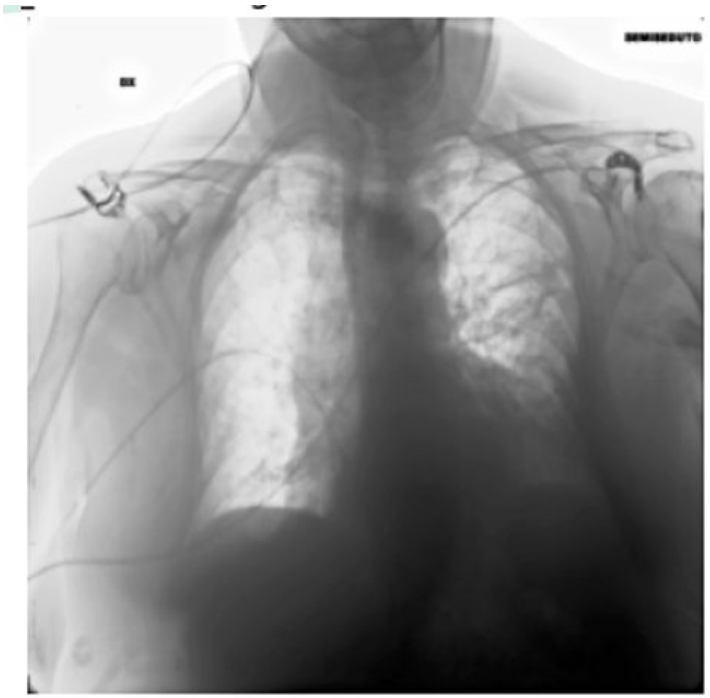
JSRT dataset



Montgomery dataset



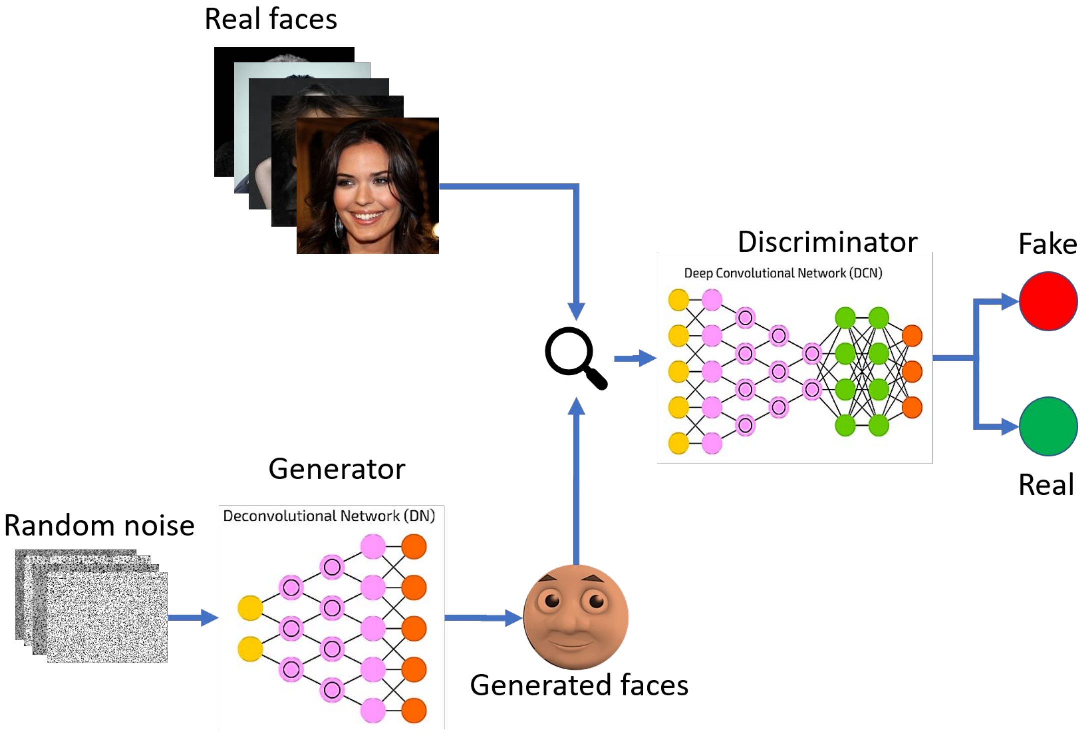
Testing images



Potential Solutions

Using GANs to generate custom images

- Generative Adversarial Networks
  - https://arxiv.org/pdf/1406.2661

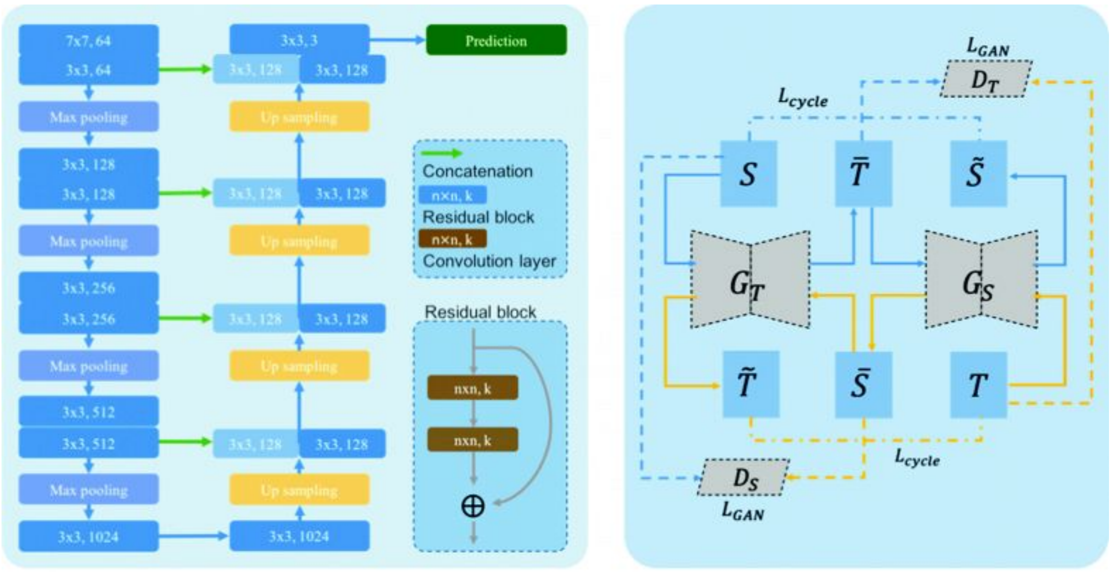


Is it possible to modify such kind of images…

… and turn them in something like this?

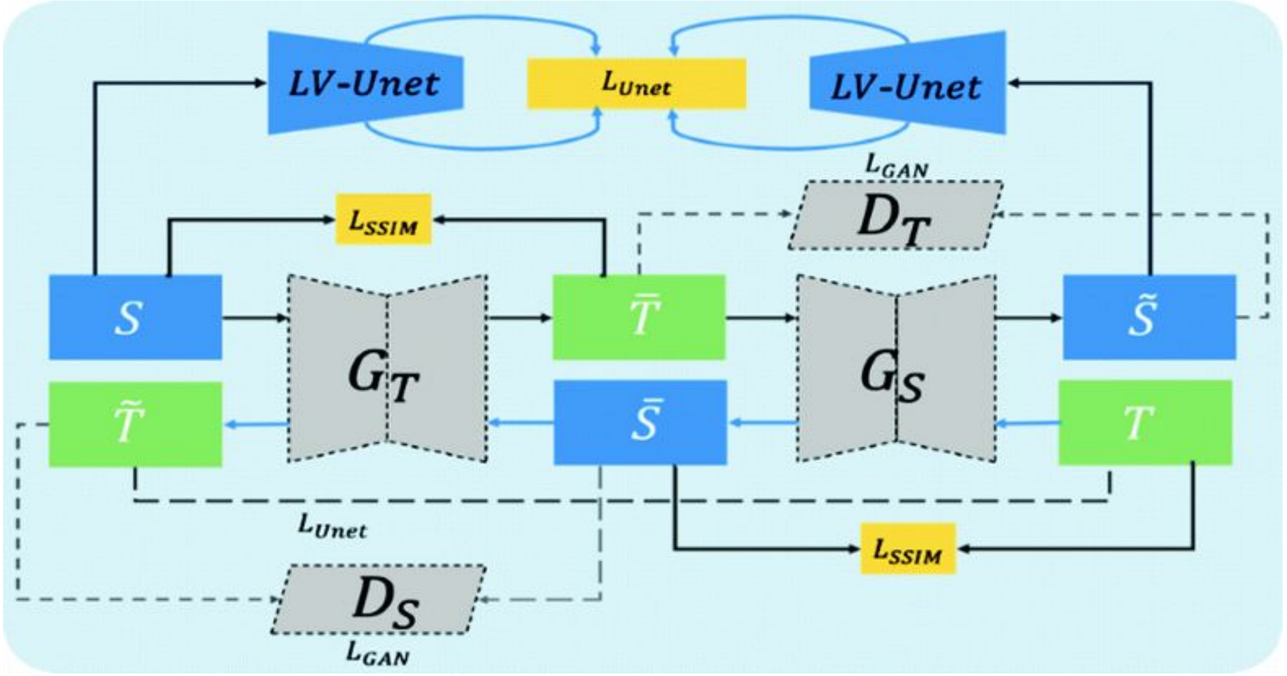
The Domain Shift Problem of Medical Image Segmentation and Vendor-Adaptation by Unet-GAN

https://link.springer.com/chapter/10.1007/978-3-030-32245-8_69



(a)

(b)



Update: 08/02/2021 Thanks to Leonardo Piano

CycleGAN for Segmenting XRays

https://www.kaggle.com/kmader/cyclegan-for-segmenting-xrays

- Here we try an experiment to see if we can take unpaired (they happen to be paired in this dataset but we ignore that) images of chest x-rays and segmentations of lungs and learn a forward (X-Ray→→ Lungs) and reverse (Lungs →→ X-ray) mapping using the CycleGAN approach.
- The basic idea is we have generators for both of the mappings with a U-Net style architecture (which forces them to learn something from the original pixels). We then have discriminators which determine if the images we have created are real or fake. Finally we have the cycle-consistent loss of using both the forward and backward back-to-back which should give us the original images.
- If this works well it could be applied to lots of issues where paired training data are not available. It should also produce more 'realistic' segmentations since the discriminator is actively trying to determine if the image output is discernible real data.
- https://www.kaggle.com/paultimothymooney/chest-xray-pneumonia
- http://www.cell.com/cell/fulltext/S0092-8674(18)30154-5

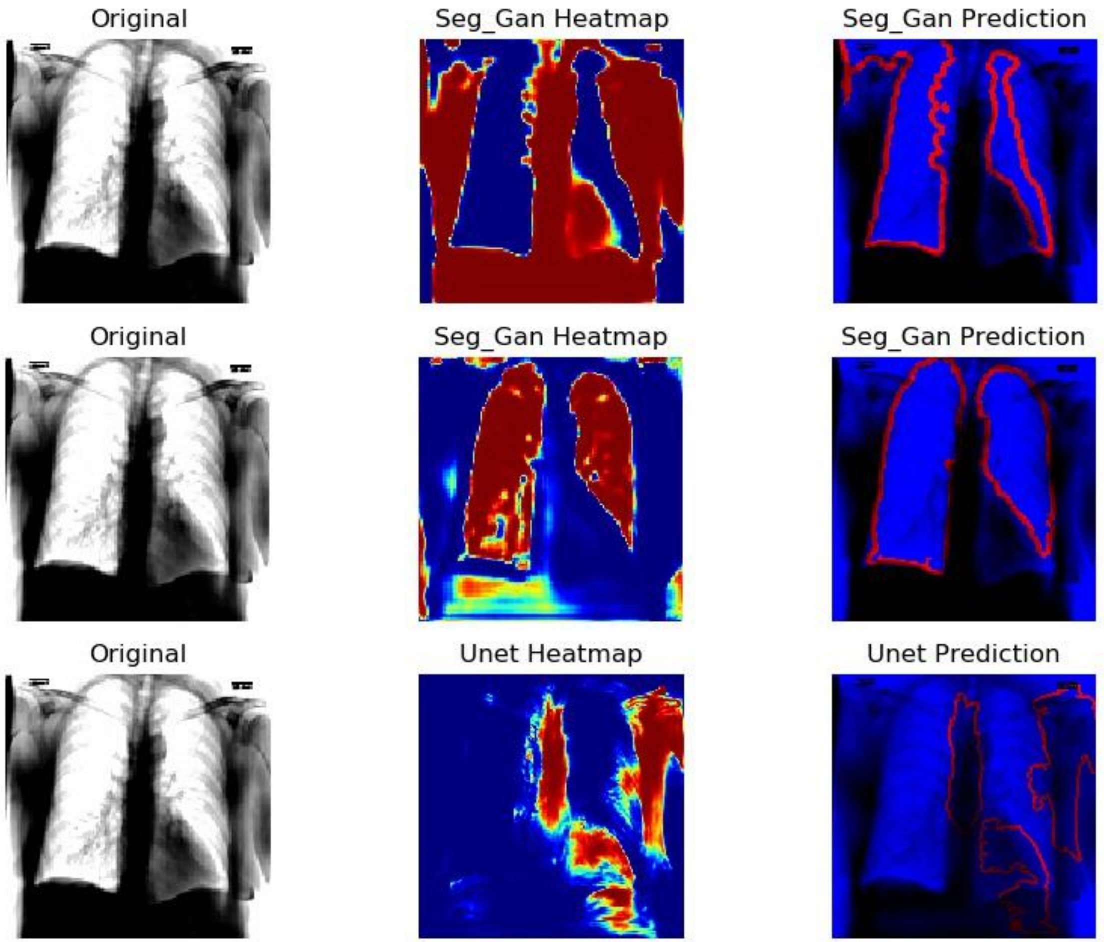
Update: 08/02/2021 Thanks to Leonardo Piano

Preliminary Results for Solution 3: Unpaired Masks-Images Segmentation

SegGan: CycleGan with Generator Backbone U-NET

SegGanV2: SegGan w/ image normalization (0-mean, 1-stdev)

U-NET: state of the art



Consideration: The SegGanV2 achieves better than U-NET and SegGan. Now two paths can be walked:
- Make some hyperparameter tuning, so to try and improve further SegGanV2
- Try with StarGan series of GAN.

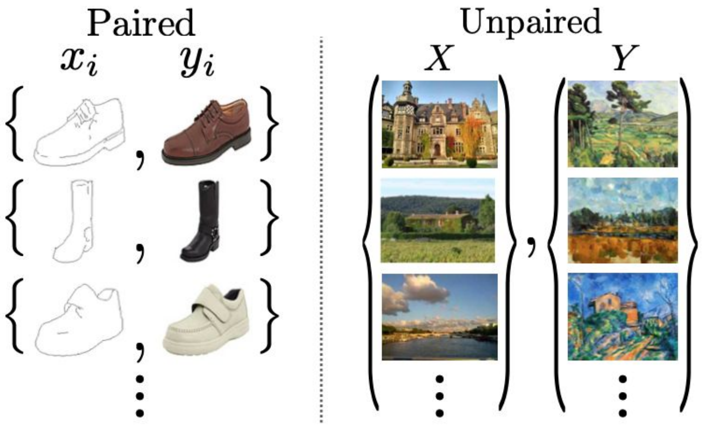
We decided for the second. However, if things go better with StarGan, the further improvement should regard the tuning of the Hyperparameters of the StarGan. Finally the all of three nets must be executed on SOTA datasets so to obtain some quantitative results.

Update: 25/02/2021 Thanks to Leonardo Piano

Unpaired Image-to-Image Translation using Cycle-Consistent Adversarial Networks

https://openaccess.thecvf.com/content_ICCV_2017/papers/Zhu_Unpaired_Image-To-Image_Translation_ICCV_2017_paper.pdf

- This solution considers unpaired training data: in particular the system captures special characteristics of one image collection and figures out how these characteristics can be translated into an other image collections, in absence of any paired training examples



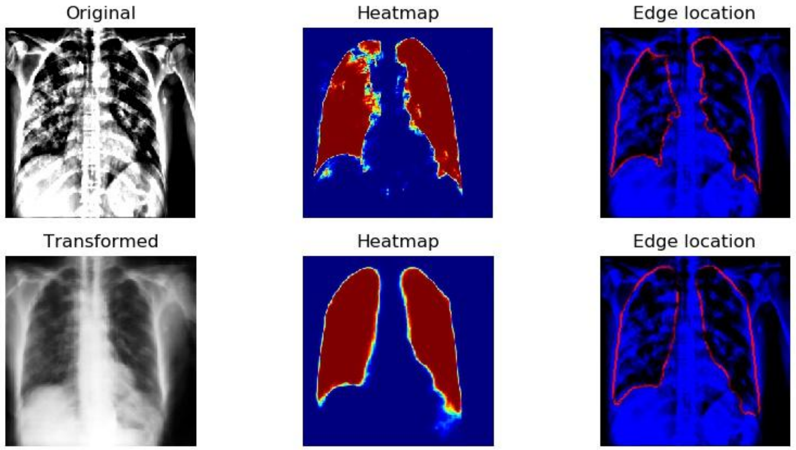
- Two application modes will be investigated

1. Swapping the domain of AiForCOVID lung images into the images used for training U-NET
2. From lung images provided with GT, try to produce masks for AiForCOVID lung imgs

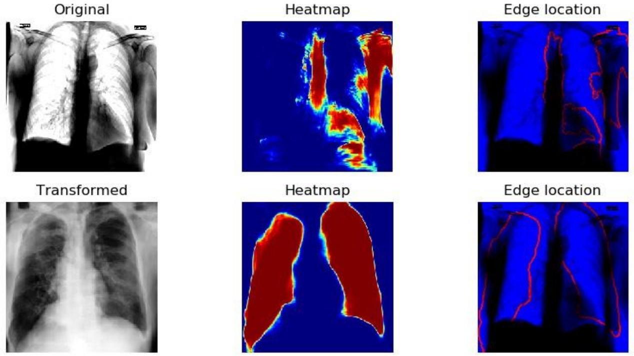
Update: 25/02/2021 Thanks to Leonardo Piano

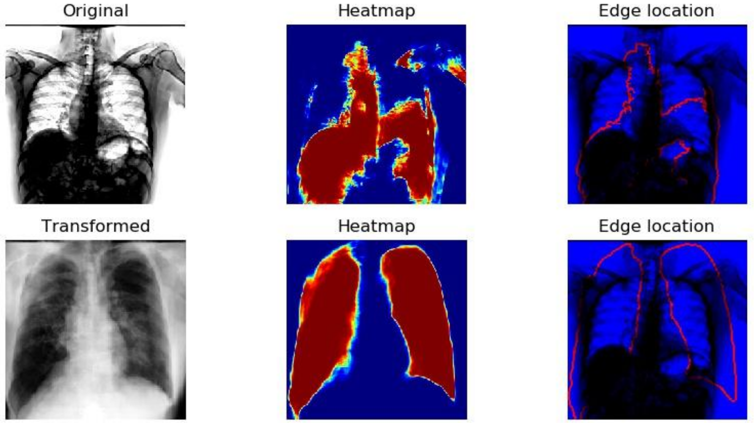
Swapping the domain of AiForCOVID lung images into the images used for training U-NET

- E solution explored has highlighted a twofold result:
  - a good one, in which the image is correctly btransformed in the domain of the images used for U-NET. In these cases, the segmentation is quite good.
  - A bad one, in which the Net actually overfits on the images used for training U-NET. This means that the transformed image is not similar to the original one, but it becomes equal to those of the source dataset.



GOOD





BAD

Update: 25/02/2021 Thanks to Leonardo Piano

From lung images provided with GT, try to produce masks for AiForCOVID lung imgs (Unpaired)

We trained the CycleGan (Unpaired) with pix2pix arch.
- Training AiForCovid (X)
- Mask from JSRT&Montgomery (Y)

Test on all JSRT

- IoU Bassissimo % (w/o 255-Image)
- **IoU 66 % (w 255-Image)**
- **Dice 79 %**

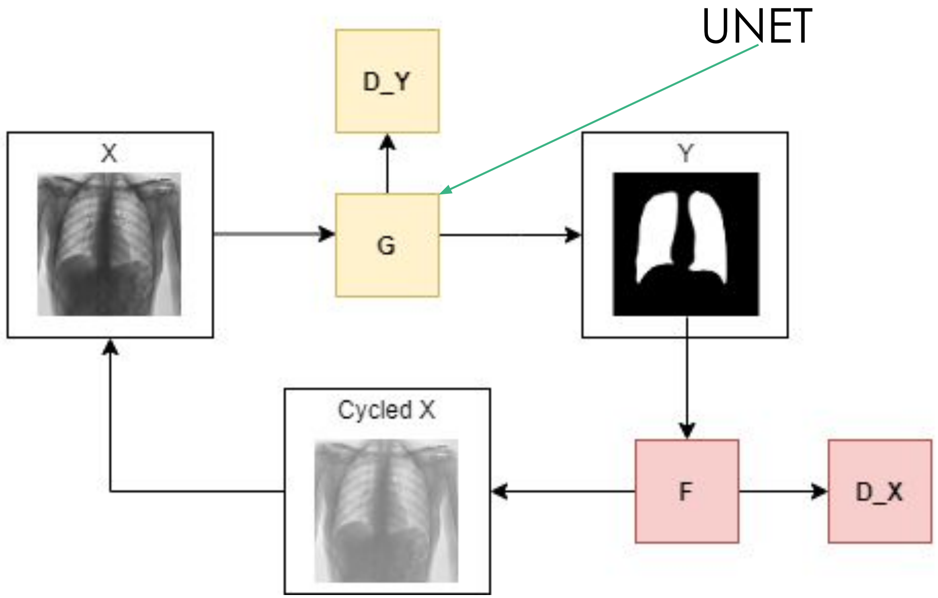
https://towardsdatascience.com/metrics-to-evaluate-your-semantic-segmentation-model-6bcb99639aa2

Generator G learn to transform image X to image Y. (G:X->Y)

Generator F learns to transform image Y to image X. (F:Y->X)

Discriminator D_X learns to differentiate between image X and generated image X (F(Y)).

Discriminator D_Y learns to differentiate between image Y and generated image Y (G(X)).



We trained the Cycle from Kaggle (U-NET as Generator) (Unpaired)
- Training AiForCovid (X)
- Mask from JSRT&Montgomery (Y)

Test on all JSRT

- IoU Bassissimo (w/o 255-Image)
- **IoU 53% (w 255-Image)**
- **Dice 69 %**

Update: 25/02/2021 Thanks to Leonardo Piano

From lung images provided with GT, try to produce masks for AiForCOVID lung imgs(Paired) UNET

We notice how the color variations in the radiography led Unet to no longer distinguish between background and foreground.
We then decide to increase the variability of the training images feeding to the network both original and inverted images.

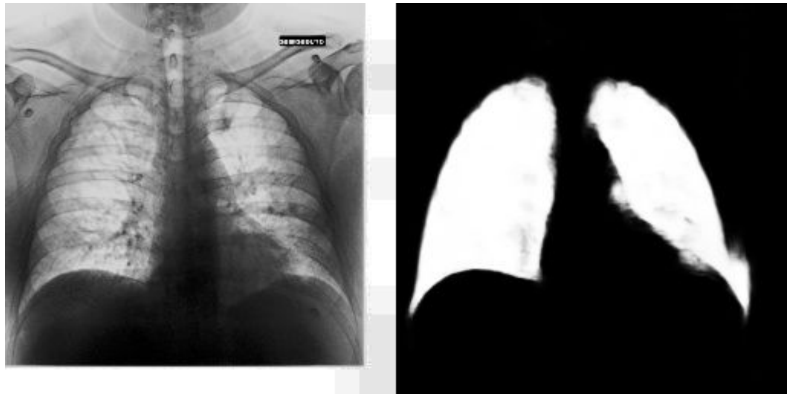
Training Sets
-JSRT
-JSRT + MONTGOMERY

Training Parameters
Batch size = 8
Image resolution (256x256)
Epochs = 70

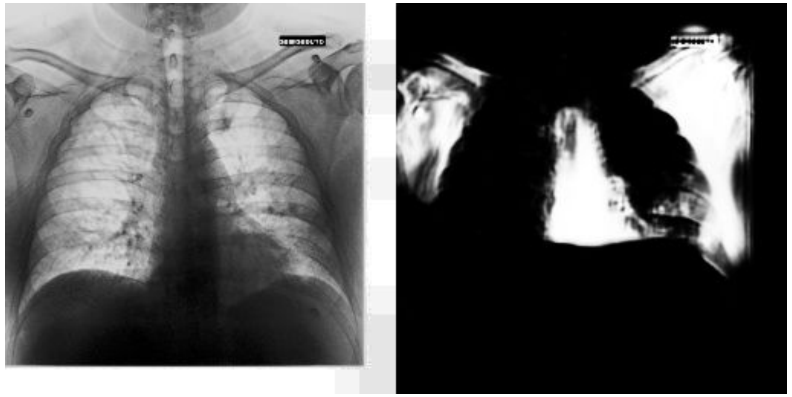
Test on the SHENZEN Dataset (566 crx with masks)

Metrics	JSRT	JSRT + MONTGOMERY
Iou	**90.4%**	**88%**
Dice	**94 %**	**93%**

Unet Trained on JSRT adding inverted images



Unet Trained on JSRT without inverted images

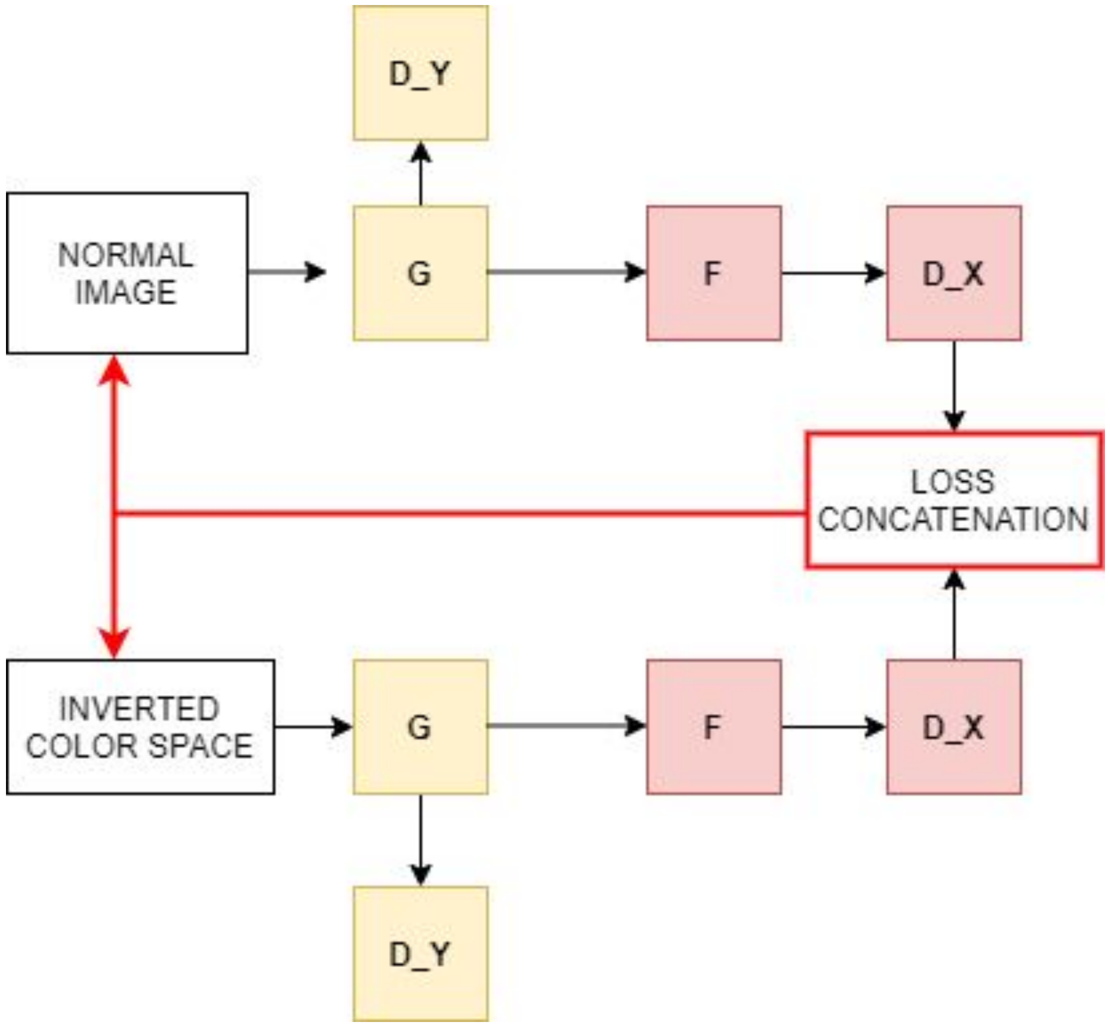


Update: 31/03/2021 Thanks to Leonardo Piano

- 1-----------------------------------
- Resnet al posto di UNet nel generatore della CycleGan
- Alleniamo con JSRT e Testiamo con Montgomery
- Alleniamo U-NET con JSRT e Testiamo con Montgomery

- 2-----------------------------------
- La cyclegan allenata con JSRT (in entrambe gli spazi di colore) e testata su montgomery
- U-NET allenata con JSRT (in entrambe gli spazi di colore) e testata su Montgomery

- e Viceversa (allenare su Montgomery e testare su JSRT)



Solution 5: Using StarGan – Updates will follow

StarGan

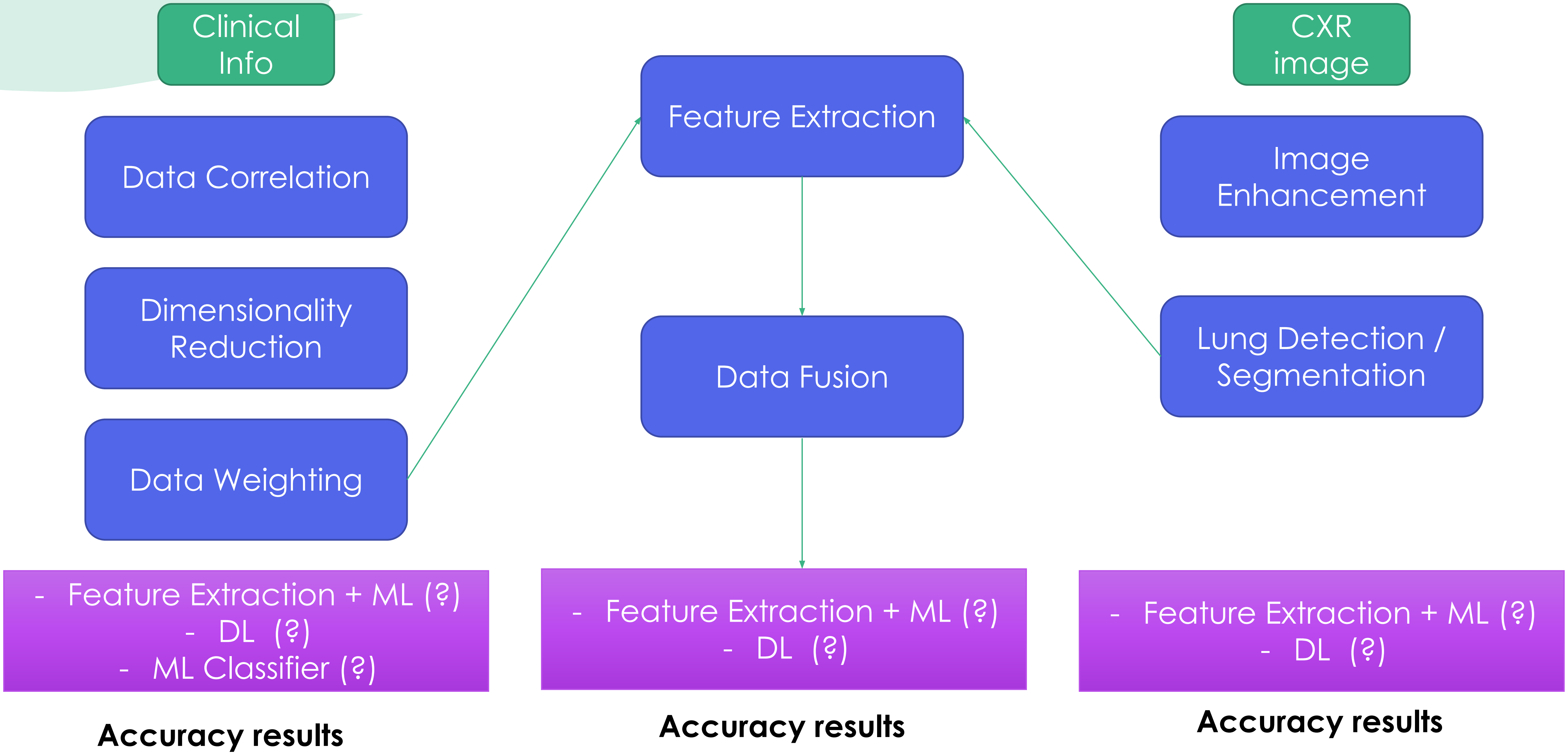
https://openaccess.thecvf.com/content_cvpr_2018/papers/Choi_StarGAN_Unified_Generative_CVPR_2018_paper.pdf

StarGanV2

https://openaccess.thecvf.com/content_CVPR_2020/papers/Choi_StarGAN_v2_Diverse_Image_Synthesis_for_Multiple_Domains_CVPR_2020_paper.pdf

- According to what Leonardo says, with stargan both image domain translation and mask generation is possible.
- Updates will follow.

Final Objective of the research project



For questions about the project

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