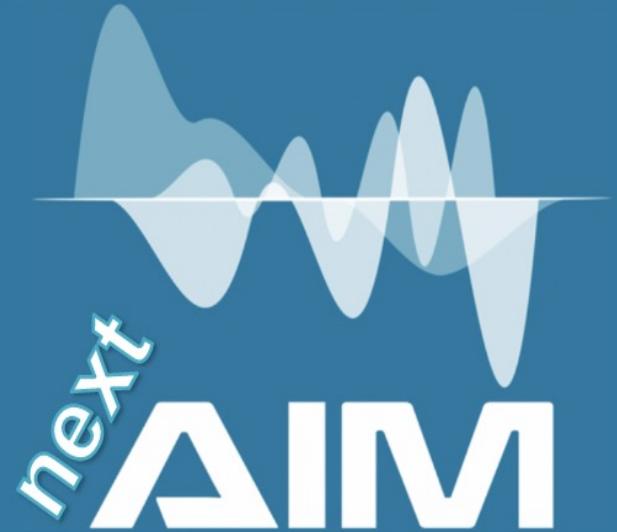


Artificial
Intelligence in
Medicine



RADIOMICS AND DEEP LEARNING ANALYSIS OF CT AND PATIENTS' DATA IN COVID-19

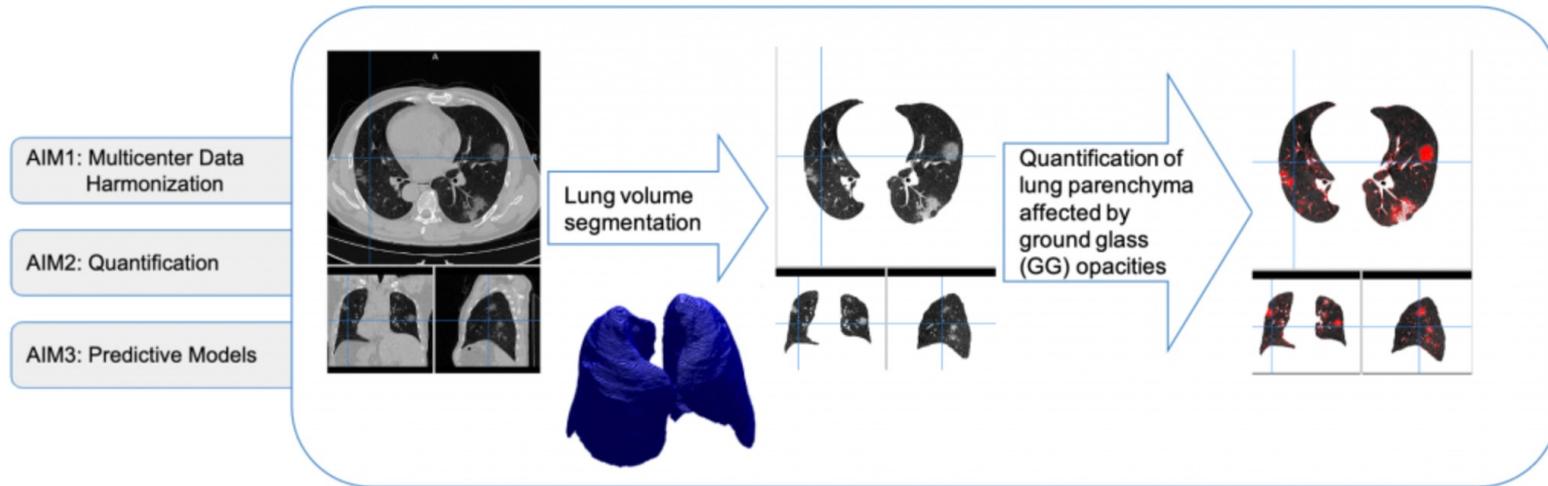
C. Scapicchio for the Covid19-WG



Outline

- AIM - Covid19-WG
- A new quantification system: LungQuant
- Evaluation of the quantification SW and the collaboration with the clinicians
- STOIC Challenge
- CRX Challenge
- Progetto AI ASST Niguarda – UNIMI Dip. Fisica

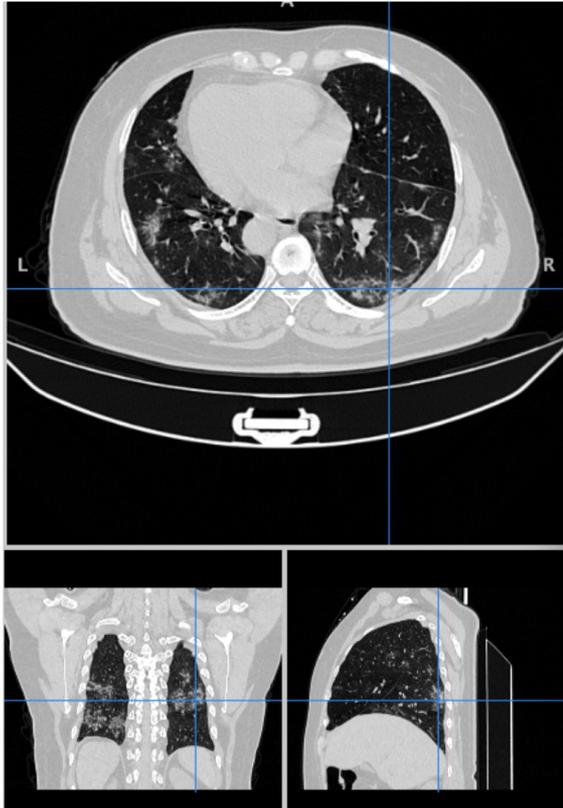
AIM - Covid19-WG [PI,MI,PV,GE,FI,PA,CA]



Quantitative information on the amount of GG opacities and their distribution, possibly combined with clinical and epidemiological patient's information.

ML predictive models of disease evolution to favor a correct prognosis/therapy.

AIM - Covid19-WG [PI,MI,PV,GE,FI,PA,CA]



Lung CT of patients affected by Covid-19 pneumonia.

Sign of progressing critical illness:

- ground glass opacities (GGO)
- rounded opacities
- consolidations

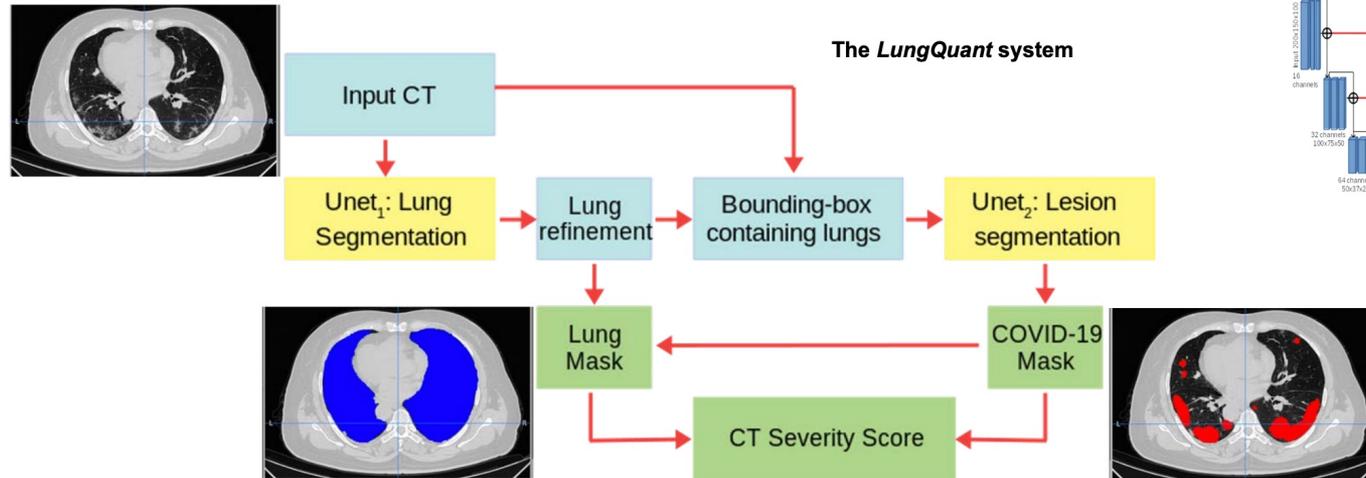
The radiographic presentation is similar to that of other influenza-associated pneumonias.

Techniques for distinguishing between these differently originated pneumonias are required.

A new quantification system: LungQuant

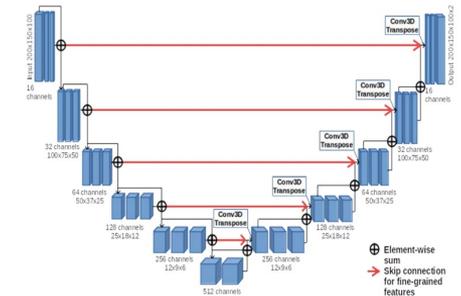
A cascade of two trained U-nets for Lung and Covid lesion segmentation provides:

- Lung mask
- Lesion mask



Input (3D, 16-bit data): CT
data resampled to
200x150x100 arrays

Target: 200x150x100
arrays; 2-bit data



An index of severity of lung involvement is provided:

CT-Severity Score (CT-SS): **1** (<5%), **2** (5%-25%), **3** (25%-50%), **4** (50%-75%), **5** (>75%)

Lizzi F, Agosti A, Brero F, Cabini RF, Fantacci ME, Figini S, et al. Quantification of pulmonary involvement in COVID-19 pneumonia by means of a cascade of two U-nets: training and assessment on multiple datasets using different annotation criteria. *Int J Comput Assist Radiol Surg* 2021. <https://doi.org/10.1007/s11548-021-02501-2>.

A new quantification system

We used only **public datasets** with annotations
(in part collected for other clinical purposes)

DATASETS	Clinical motivation	Number of cases	Lung mask	Lesion mask	CT-SS
COVID-19-Challenge [1]	COVID-19 pandemic	199	No	Yes	No
MosMed [2]	COVID-19 pandemic	1110	Yes, only for 91 CTs (made in house)	Yes, only for 50 CTs	Yes
TCIA-Plethora [3]	Lung/pleura diseases	402	Yes	No	No
TCIA-LCTSC Lung segmentation [3]	Lung cancer	60	Yes	No	No
COVID-19-CT-Seg Benchmark [4]	COVID-19 pandemic	10	Yes	Yes	Yes

Metrics	Lung segmentation			
	vDSC	sDSC (1 mm)	sDSC (5 mm)	sDSC (10 mm)
<i>Lung Quant</i> (U-net ₂ ^{60%})	0.96 ± 0.01	0.66 ± 0.09	0.95 ± 0.02	0.98 ± 0.01
<i>Lung Quant</i> (U-net ₂ ^{90%})	0.95 ± 0.01	0.65 ± 0.09	0.95 ± 0.02	0.98 ± 0.01
Infection Segmentation				
<i>Lung Quant</i> (U-net ₂ ^{60%})	0.62 ± 0.09	0.29 ± 0.06	0.75 ± 0.11	0.90 ± 0.09
<i>Lung Quant</i> (U-net ₂ ^{90%})	0.66 ± 0.13	0.36 ± 0.13	0.76 ± 0.18	0.87 ± 0.13

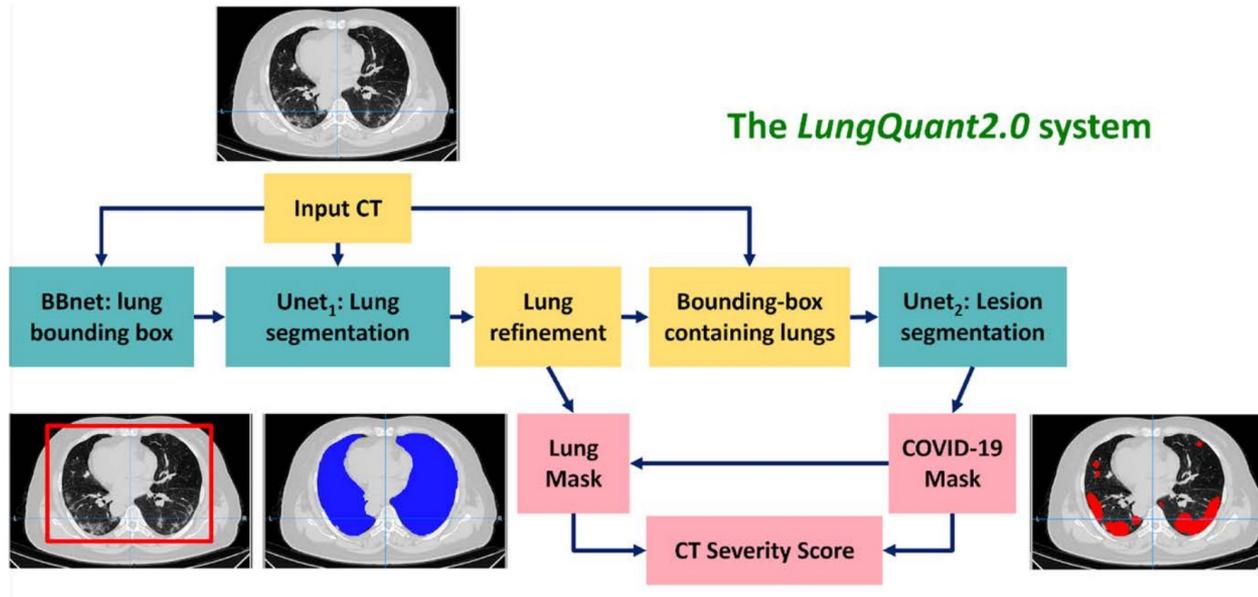
Table 5 Performances of the *Lung Quant* system on the independent COVID-19-CT-Seg test dataset. The vDSC and sDSC computed between the lung and lesion reference masks and those predicted by the *LunQuant* system are reported

Lizzi F, Agosti A, Brero F, Cabini RF, Fantacci ME, Figini S, et al. Quantification of pulmonary involvement in COVID-19 pneumonia by means of a cascade of two U-nets: training and assessment on multiple datasets using different annotation criteria. *Int J Comput Assist Radiol Surg* 2021. <https://doi.org/10.1007/s11548-021-02501-2>.

Lizzi F, Brero F, Cabini RF, Fantacci ME, Piffer S, Postuma I, et al. Making data big for a deep-learning analysis: Aggregation of public COVID-19 datasets of lung computed tomography scans. *Proc 10th Int Conf Data Sci Technol Appl DATA 2021* 2021:316–21. <https://doi.org/10.5220/0010584403160321>.

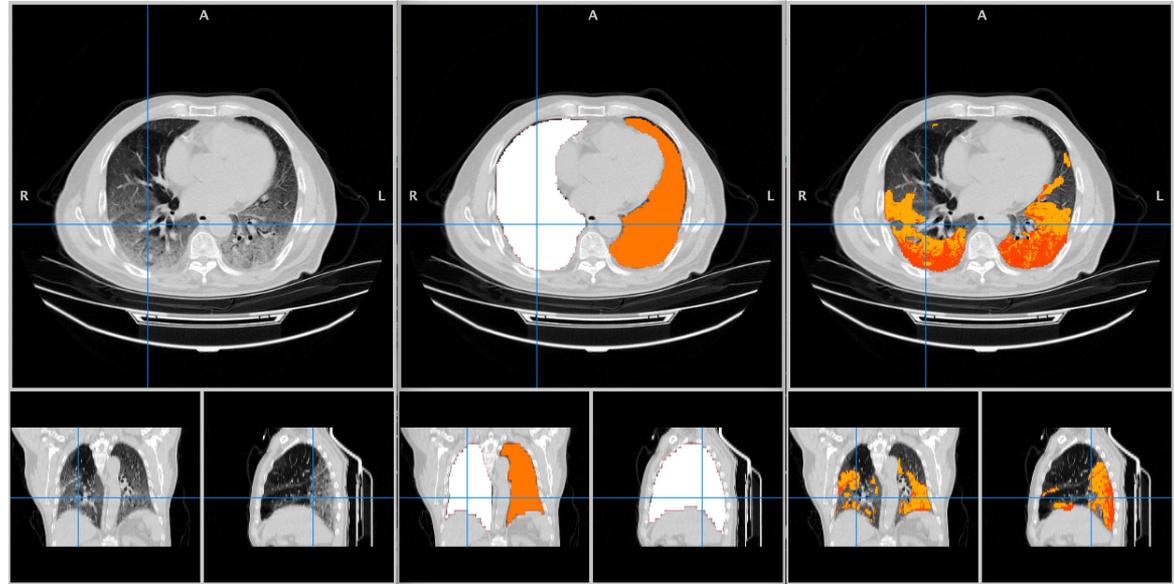
A new quantification system – Last version

- A network for lung bounding box prediction upstream of the entire pipeline.
- A function separating right and left lung.
- A threshold to distinguish consolidation from GGO.



A new quantification system – Last version

Output of the last
version of LungQuant



table_results

ID	lung_volume_mm3	lesions_volume_mm3	Lesions_to_Lung_ratio	CTSS	consolidation_vol	ground_glass_vol	ground_glass_R_ratio	ground_glass_L_ratio	consolidation_R_ratio	consolidation_L_ratio
0 volume-covid19-A-0041	6354312.42	305574.50	0.04	1	15576.48	311896.54	0.01	0.08	0.02	0.00
0 volume-covid19-A-0319	4396079.51	514796.34	0.11	2	50270.53	929051.62	0.27	0.15	0.01	0.01
0 volume-covid19-A-0120	3378643.30	48209.30	0.01	1	6962.34	82493.92	0.00	0.04	0.00	0.00
0 volume-covid19-A-0003	2778919.56	413522.35	0.14	2	45464.49	736089.43	0.02	0.43	0.00	0.02
0 volume-covid19-A-0251	4230179.70	560512.83	0.13	2	25525.16	1069975.33	0.16	0.32	0.00	0.01

Evaluation of the quantification SW

Study Design

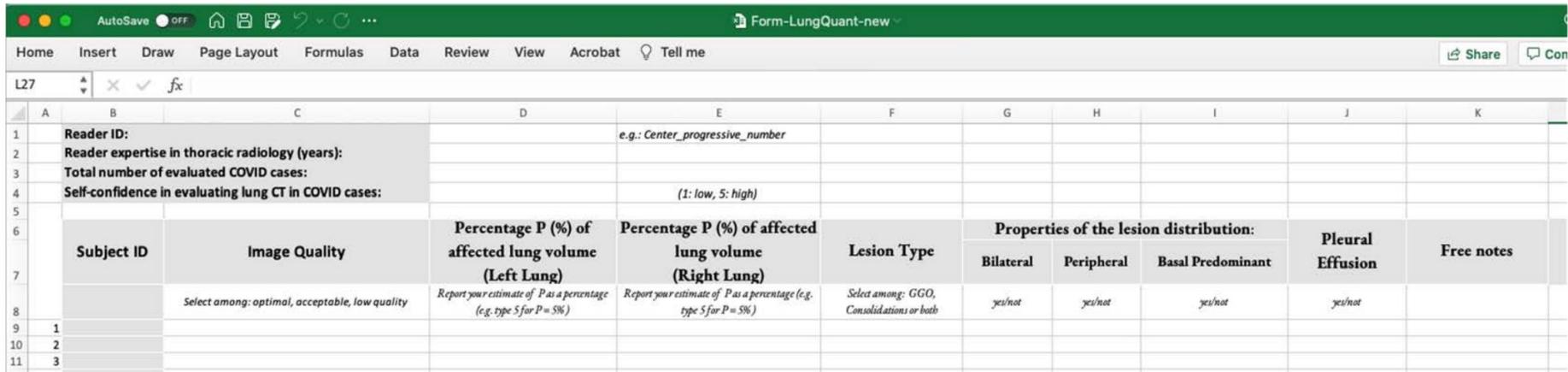
A multicenter study (5 clinical centers involved in AIM: PI, MI, PV, FI, PA) to validate and assess the accuracy of the automatic quantification algorithm (*LungQuant*).

The procedure could directly retrace the approach proposed in:

Chincarini, A., Peira, E., Morbelli, S., Pardini, M., Bauckneht, M., Arbizu, J., ... Nobili, F. (2019). "Semi-quantification and grading of amyloid PET: A project of the European Alzheimer's Disease Consortium (EADC)". *NeuroImage: Clinical*, 23(April), 101846. <https://doi.org/10.1016/j.nicl.2019.101846>

It involves 14 expert readers, who were asked to review 120 Lung CT, in COVID-19 public collection available on TCIA: <https://wiki.cancerimagingarchive.net/display/Public/CT+Images+in+COVID-19#702271074dc5f53338634b35a3500cbcd18472e0>, selected among the images not used for the training of the segmentation system, and to fill a form providing the evaluation of each case.

Evaluation of the quantification SW



Form-LungQuant-new										
Home Insert Draw Page Layout Formulas Data Review View Acrobat Tell me										
L27										
e.g.: Center_progressive_number										
(1: low, 5: high)										
Subject ID	Image Quality	Percentage P (%) of affected lung volume (Left Lung)	Percentage P (%) of affected lung volume (Right Lung)	Lesion Type	Properties of the lesion distribution:			Pleural Effusion	Free notes	
	Select among: optimal, acceptable, low quality	Report your estimate of P as a percentage (e.g. type 5 for P= 5%)	Report your estimate of P as a percentage (e.g. type 5 for P= 5%)	Select among: GGO, Consolidations or both	Bilateral	Peripheral	Basal Predominant	yes/not		
1					yes/not	yes/not	yes/not	yes/not		
2										
3										

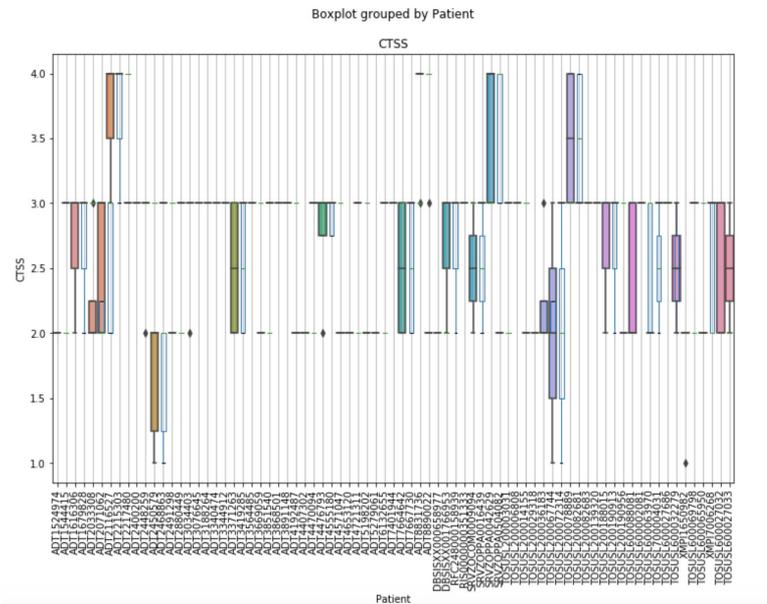
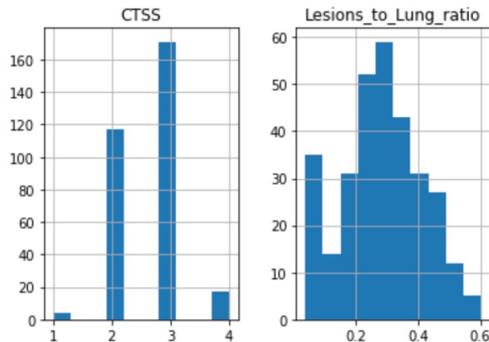
Expected outcome

- Sample homogeneity and data model
- Readers concordance
- Evaluation latitude
- Classification performance
- Scan quality/asymmetry effect
- Future studies : CT image reading with software aid [i.e. new reading with quantitative support]

Collaboration with the clinicians

Local collaborations for each centre to:

- Validate the quantification algorithm and assess its usefulness for clinical trials.
- Develop predictive models for pathology evolution it is necessary to jointly analyze samples of subjects for which clinical information is available in addition to the CT data.
- Obtain private datasets: Pavia, Pisa, Palermo.

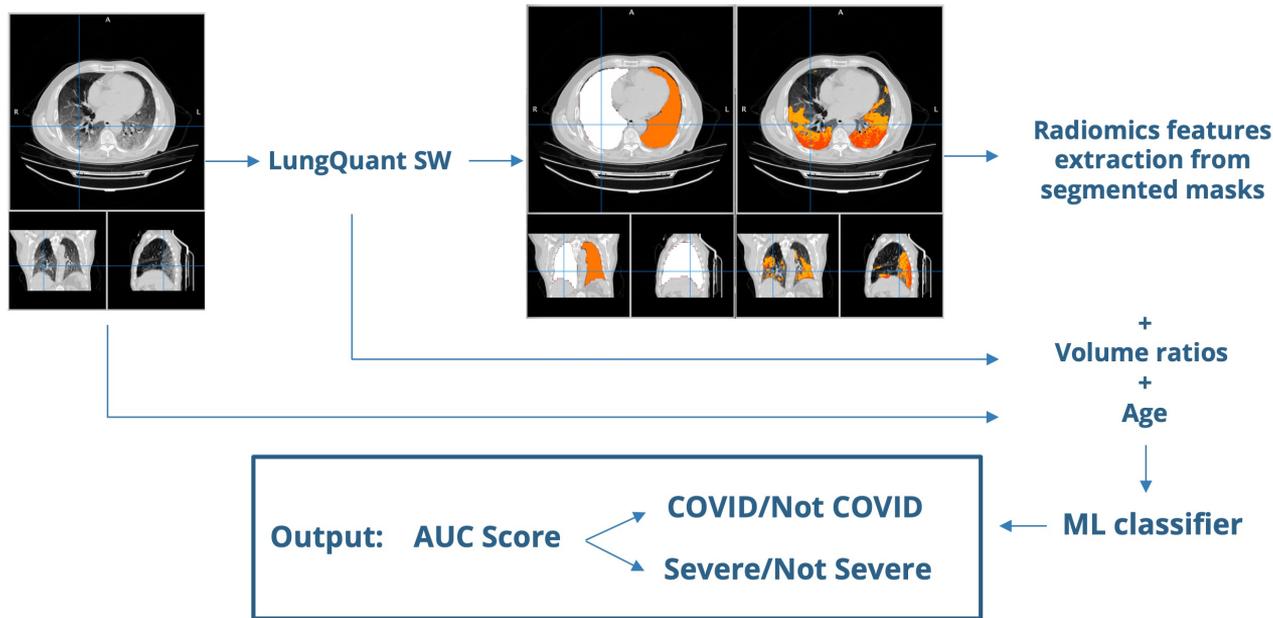


STOIC Challenge



The focus of the challenge is the prediction of severe COVID-19, defined as intubation or death within one month from the acquisition of the CT scan (AUC, primary metric). COVID19 positivity will be assessed as a secondary metric in the leaderboard.

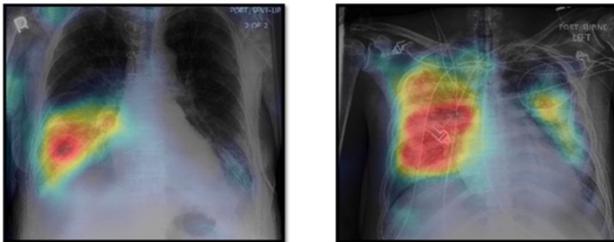
Can you predict from a CT scan who will develop severe COVID-19?



CRX Challenge

covidcxr - Hackathon

Artificial Intelligence for Covid-19 prognosis: aiming at accuracy and explainability



Aims at designing solutions based on machine learning and data science to formulate a Covid-19 prognosis from early chest X-ray images and clinical data.

Input data	Approach	Accuracy
Clinical data	ML	0.734 ± 0.044
	DL	0.663 ± 0.016
	Handcrafted	0.625 ± 0.083
CXr images	Hybrid	0.693 ± 0.053
	End-to-end	0.705 ± 0.010
	Handcrafted	0.752 ± 0.067
Clinical data and CXr images	Hybrid	0.743 ± 0.061
	End-to-end	0.709 ± 0.005

Soda, Paolo, et al. "AlforCOVID: predicting the clinical outcomes in patients with COVID-19 applying AI to chest-X-rays. An Italian multicentre study." *Medical image analysis* 74 (2021): 102216.

CRX image



Clinical features

Age
Sex
Body Temperature (°C)
Cough
Dyspnea
WBC
CRP
Fibrinogen
LDH
D-dimer
O2
PaO2
SaO2
pH
Cardiovascular Disease
Respiratory Failure

+



CNN



outcome

↓
Explainability

Progetto AI ASST GOM Niguarda – UNIMI Dip. Fisica

**Luca Berta, Giulia Zorzi, Cristina Lenardi, Cristina De Mattia,
Marco Felisi, Paola Enrica Colombo, Alberto Torresin**

Breve sintesi

- **Esperienza maturata «sul campo»**

1. **Definizione Quesito Clinico:**

- a) **Classificazione pazienti COVID-19 vs H1N1 (Polmoniti virali)**

- b) **analisi in pazienti Terapia Intensiva per prognosi**

2. **Sviluppo Metriche Quantitative per CT polmone**

3. **Datalake per raccolta sistematica immagini/dati clinici**

4. **Validazione segmentazioni automatiche**

5. **Flowchart per estrazione automatica di features e modellizzazione AI**

- **I software aziendali AI**

- **Scuola Europea di AI**

Analisi quantitativa del polmone: il primo lavoro

Anesthesiology
69:824-832, 1988

Relationships Between Lung Computed Tomographic Density, Gas Exchange, and PEEP in Acute Respiratory Failure

Gianluigi Gattinoni, M.D.,* Antonio Pesenti, M.D.,† Michela Bombino, M.D.,‡ Simone Baglioni, M.D.,‡
Simone Rivolta, M.D.,‡ Francesca Rossi, M.D.,‡ Gianpiera Rossi, M.D.,§ Roberto Fumagalli, M.D.,§
Roberto Marcolin, M.D.,¶ Daniele Mascheroni, M.D.,¶ Alberto Torresin, Ph.D.**

Anesthesiology
V 69, No 6, Dec 1988

CT SCAN IN ARF

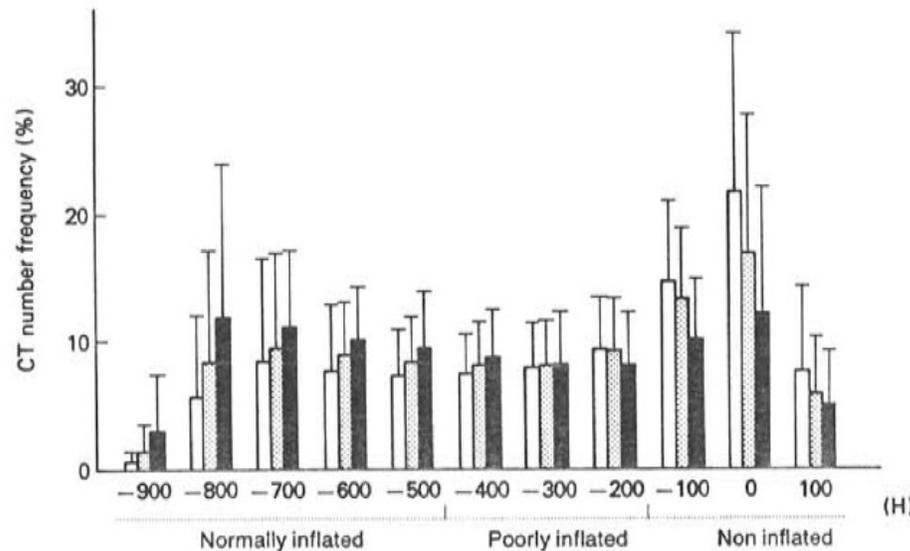


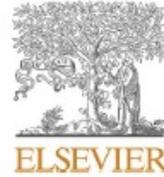
FIG. 4. Frequency distribution of CT numbers in 11 compartments each comprising 100 Hounsfield Units (H) at 5 cm H₂O PEEP (white columns), at 10 cm H₂O PEEP (dashed columns), and 15 cm H₂O PEEP (black columns); normally inflated, poorly inflated, and non-inflated compartments are also indicated (n = 22).

Twenty-two patients with acute respiratory failure underwent lung computed tomography (CT) and physiological measurements at 5, 10, and 15 cm H₂O positive end-expiratory pressure (PEEP) to investigate the relationship between morphology and function. Lung densities were primarily concentrated in the dependent regions. From the frequency distribution of CT numbers (difference in x-ray attenuation between water and lung) and lung gas volume measurements the authors obtained a quantitative estimate of normally inflated, poorly inflated, and non-inflated lung tissue weight. This estimated average lung weight was increased twofold above normal and excess lung weight correlated with the mean pulmonary artery pressure ($P < 0.01$). Venous admixture correlated with the non-inflated tissue mass ($P < 0.01$). Increasing PEEP caused progressive clearing of radiographic densities and increased the mass of normally inflated tissue (anatomic recruitment), while reducing venous admixture. The cardiac index decreased after increasing PEEP while oxygen delivery was unchanged. The authors conclude that CT scan lung density and oxygen exchange efficiency are correlated; the main

Analisi quantitativa del polmone: evoluzione

Physica Medica 82 (2021) 28–39

- Sviluppo metriche quantitative:



Contents lists available at [ScienceDirect](#)

Physica Medica

journal homepage: www.elsevier.com/locate/ejmp



Original paper

A patient-specific approach for quantitative and automatic analysis of computed tomography images in lung disease: Application to COVID-19 patients

L. Berta^a, C. De Mattia^a, F. Rizzetto^c, S. Carrazza^c, P.E. Colombo^{a,c}, R. Fumagalli^{b,f}, T. Langer^{b,f}, D. Lizio^a, A. Vanzulli^{d,e}, A. Torresin^{a,c,*}

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^c Department of Physics, Università degli Studi di Milano and INFN Sezione di Milano, via Giovanni Celoria 16, Milan 20133, Italy

^d Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, via Festa del Perdono 7, Milan 20122, Italy

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^f Department of Anaesthesia and Intensive Care Medicine, ASST Grande Ospedale Metropolitano Niguarda, Piazza Ospedale Maggiore 3, Milan 20162, Italy

ARTICLE INFO

Keywords:

Quantitative imaging
Computed tomography
QCT
Image analysis
Radiomic
COVID-19

ABSTRACT

Purpose: Quantitative metrics in lung computed tomography (CT) images have been widely used, often without a clear connection with physiology. This work proposes a patient-independent model for the estimation of well-aerated volume of lungs in CT images (WAVE).

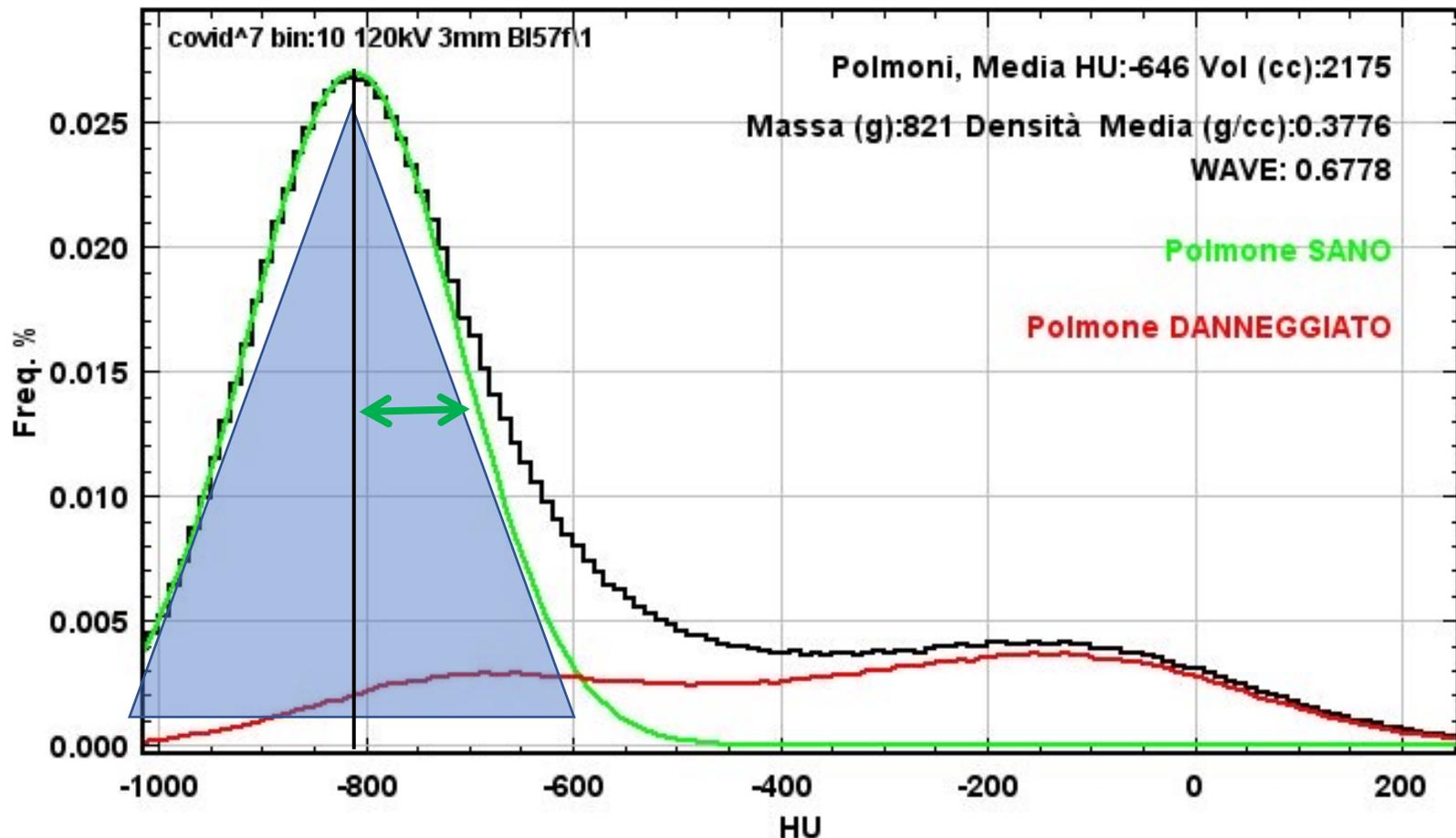
Methods: A Gaussian fit, with mean ($\mu.f$) and width ($\sigma.f$) values, was applied to the lower CT histogram data points of the lung to provide the estimation of the well-aerated lung volume (WAVE.f). Independence from CT reconstruction parameters and respiratory cycle was analysed using healthy lung CT images and 4DCT acquisitions. The Gaussian metrics and first order radiomic features calculated for a third cohort of COVID-19 patients were compared with those relative to healthy lungs. Each lung was further segmented in 24 sub-regions and a new biomarker derived from Gaussian fit parameter $\mu.f$ was proposed to represent the local density changes.

Results: WAVE.f resulted independent from the respiratory motion in 80% of the cases. Differences of 1%, 2% and up to 14% resulted comparing a moderate iterative strength and FBP algorithm, 1 and 3 mm of slice thickness and different reconstruction kernel. Healthy subjects were significantly different from COVID-19 patients for all the metrics calculated. Graphical representation of the local biomarker provides spatial and quantitative information in a single 2D picture.

Conclusions: Unlike other metrics based on fixed histogram thresholds, this model is able to consider the inter- and intra-subject variability. In addition, it defines a local biomarker to quantify the severity of the disease, independently of the observer.

Modello «Gaussiano» per l'analisi del Polmone

3D



Parenchima Sano
(Tessuto omogeneo)

Parenchima Non-Sano
(Densità maggiore)

Volume ben Aerato
(Funzione Gaussiana)

$$f(x) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$$

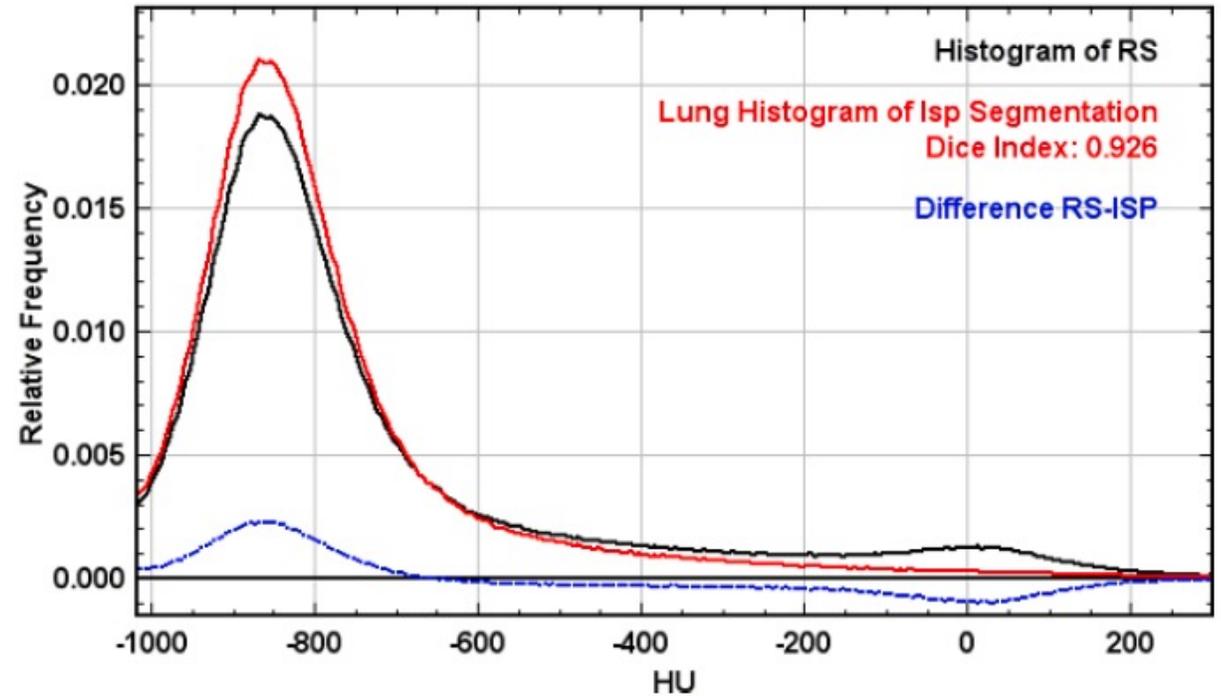
Valutazione/Validazione segmentazioni per estrazione automatica features



Original paper

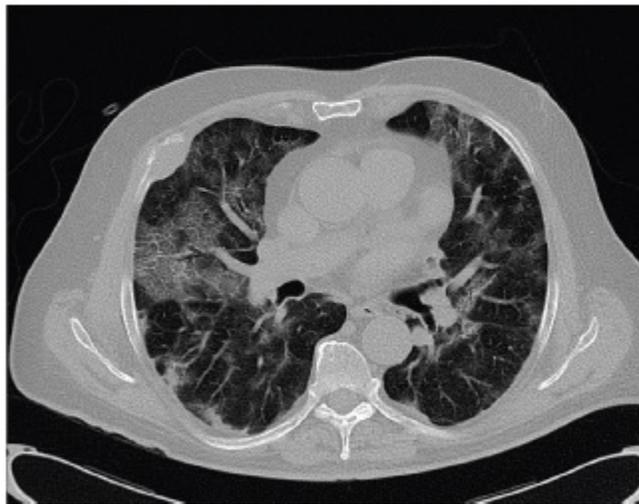
Automatic lung segmentation in COVID-19 patients: Impact on quantitative computed tomography analysis

L. Berta^a, F. Rizzetto^{b,c}, C. De Mattia^a, D. Lizio^a, M. Felisi^a, P.E. Colombo^a, S. Carrazza^{d,e}, S. Gelmini^d, L. Bianchi^{b,c}, D. Artioli^b, F. Travaglini^b, A. Vanzulli^{b,f}, A. Torresin^{a,d,*}, on behalf of the Niguarda COVID-19 Working Group

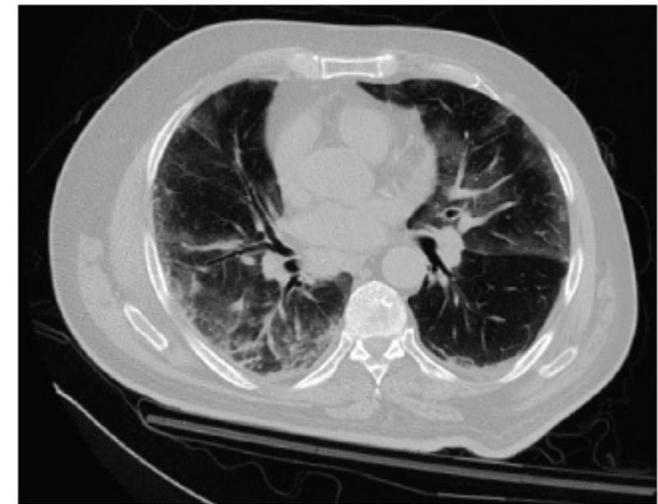


Quesito Clinico 1: CLASSIFICATORE COVID vs NON COVID (sul campo)

COVID



no-COVID



H1N1 vs COVID19

OBIETTIVI PROGETTO NIGUARDA

IN ATTUALE SVILUPPO:

- **CLASSIFICATORE COVID vs NON COVID (sul campo)**

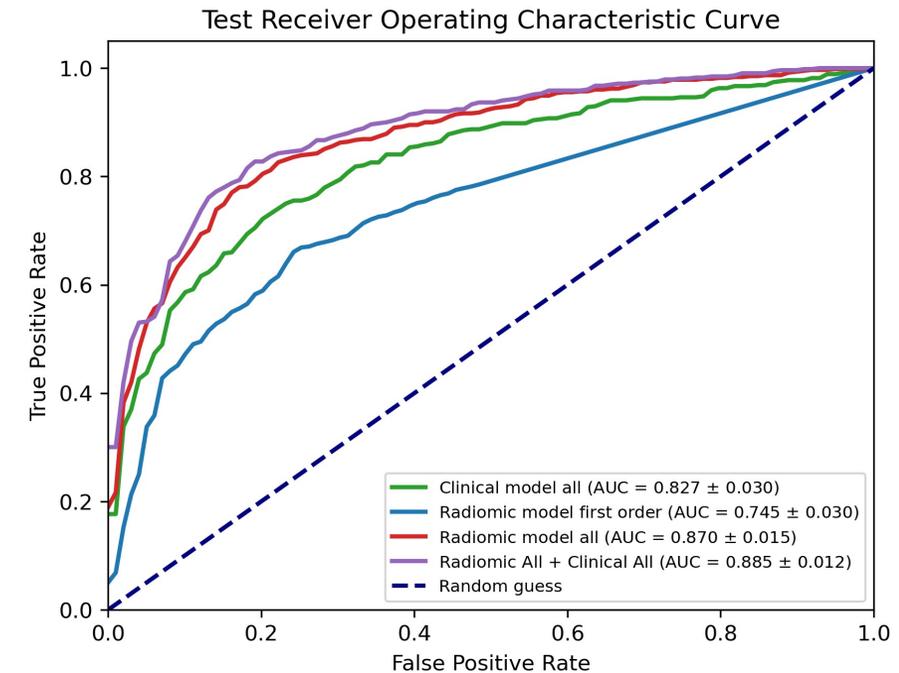
Differenziare nei pazienti in ingresso la polmonite COVID19 da altre patologie polmonari con caratteristiche simili

Dataset: 1028 patients with viral pneumonia (M=67%, F=33%)

- **646 with COVID-19 disease**
- **382 positive to H1N1 infections**

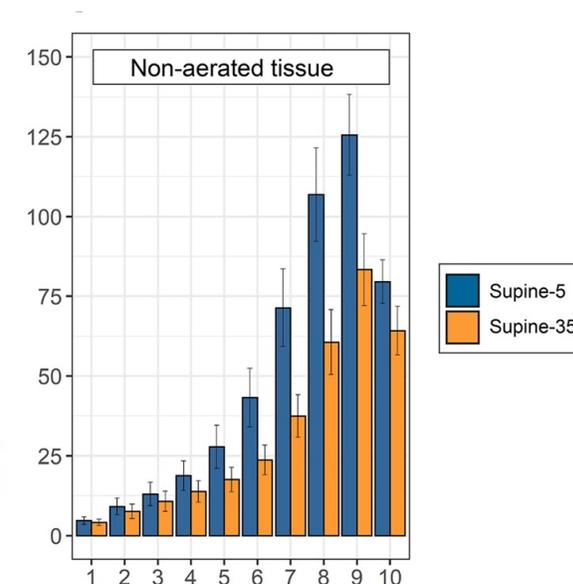
	Sex/Age	Total Lung			Lung Subdivision	Tot Features	AUC
		QM	RF1	RF2	QM		
Model 1	2	20				22	0.759
Model 2	2	20				80	0.827
Model 3	2		18			20	0.745
Model 4	2		18	120		140	0.87
Model 5	2	20	18	120	80	240	0.885

- QM= Quantitative metrics from Gaussian Model for aerated lung
- RF= Radiomic Features calculated with Pyradiomics of 1° and 2° orders



Quesito Clinico 2: PROGNOSI PAZIENTI IN TERAPIA INTENSIVA (work in progress)

- Predire efficacia della pronazione per un miglior management del paziente
- Analisi di metriche di imaging (standard-storiche e personalizzate)
- Correlazione con dati clinici



I software aziendali AI

- **Molteplici soluzioni AI prodotte dalle aziende e proposte ai clinici «in scatola chiusa»**
- **Qualità del SW originale: avere informazioni su come costruito il modello (training and validation tests, sensibilità, specificità, ROC, protocolli di acquisizione – FBP _Iterative recon -, spessor strati, dose....)**
- **Ruolo dei fisici**

ESMPE (di EFOMP) per AI

- **WG europeo per formazione di una scuola per MPE su AI (Chiar: F. Zanca, A.Torresin)**
 - **Preparazione di corsi on line (E-learning platform di EFOMP - <https://e-learning.efomp.org/login/index.php>) per i requisiti di base**
 - **Corso *live* (ottobre-novembre 2022)**