The Artificial Intelligence in Medicine (AIM) INFN-CSN5 Project

Artificial Intelligence to become the next revolution in **medical diagnostics** and **therapy**.

- New image processing and data analysis strategies, including radiomics approaches, need to be developed and extensively validated.

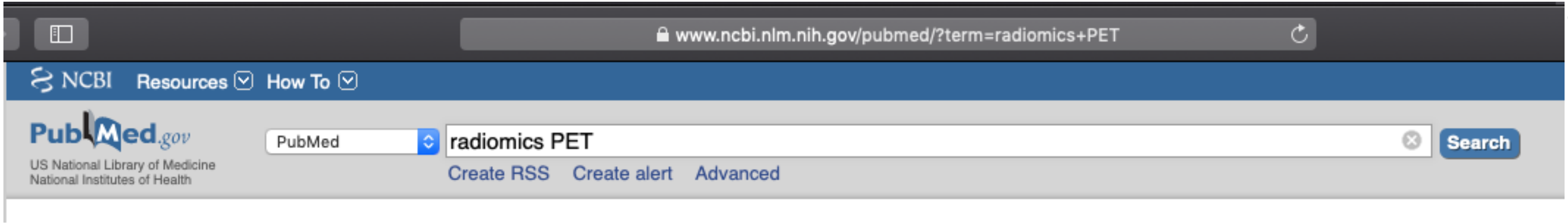
Resp. Naz. : A. Retico

Bari (S. Tangaro)
Bologna (D. Remondini)
Cagliari (P. Oliva)
Catania (M. Marrale)
Firenze (C. Talamonti)
Genova (A. Chincarini)
Pisa (M.E. Fantacci)

Objectives	Methods	Applications	
AIM1: Multicenter data harmonization	image processing; data filtering; feature extraction; feature classification; data harmonization; image classification; pattern recognition; radiomics; complex network analysis; network models; machine learning; deep learning	Reliability of multicenter studies in neuroimaging and in mammography.	MRI; RX
AIM2: Quantification		Quantification of radiotracer uptake in PET. Quantitative MRI methods.	MRI; PET; omics
AIM3: Predictive models		Radiomics and dosiomics in oncology. ML and DL for disease diagnosis	MRI; RX; RT dose; CT; omics

NEW: Analysis of lung CT in Covid-19

Long-standing collaboration with Italian & European centers (hospitals / IRCCS) and with international consortia for data sharing


www.ncbi.nlm.nih.gov/pubmed/?term=radiomics+PET
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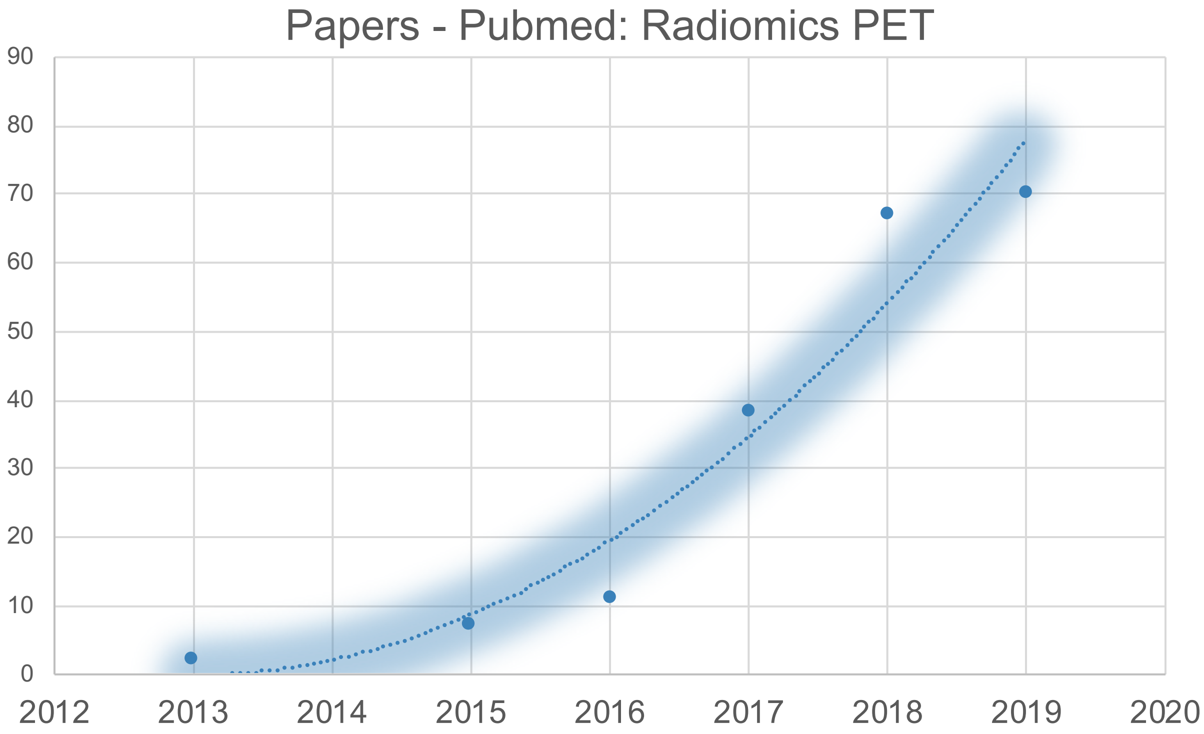
Papers - Pubmed: Radiomics PET
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2019
2020

Radiomics.....

Contents lists available at ScienceDirect
Physica Medica
journal homepage: http://www.physicamedica.com
ELSEVIER
Review paper

Beyond imaging: The promise of radiomics

Michele Avanzo [a,*], Joseph Stancanello [b], Issam El Naqa [c]

- Large-scale radiological image analysis and association with biological or clinical endpoints -> prognostic and/or predictive models
- “Radio” + “omics”
- Hypothesis: quantitative analysis of tumor through a radiomic features can provide valuable diagnostic, prognostic or predictive information
- Aim: develop diagnostic, predictive, or prognostic model to personalized medicine

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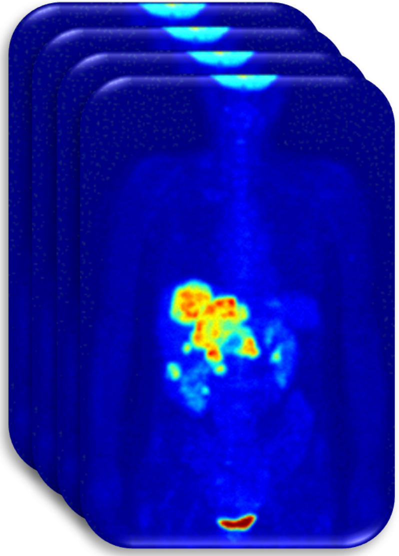
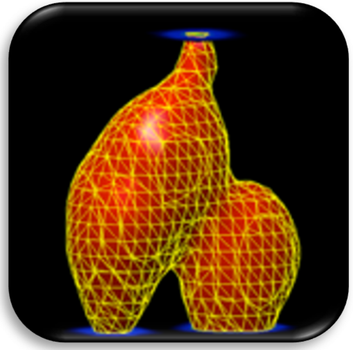
Radiomics: the flow chart

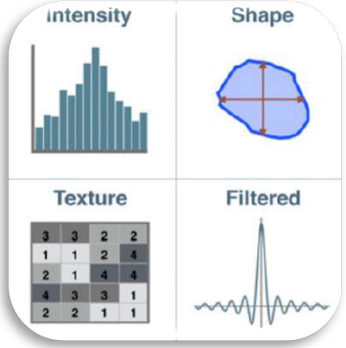
I. Imaging



II. Delineation



III. Features



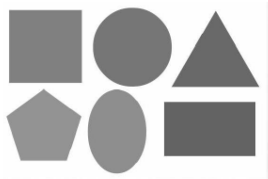
V. Model Building

Classifiers able to assign label or to predict the autcome:

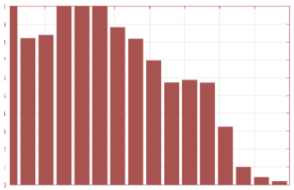
- Neural Networks
- Support Vector Machines
- Quantum-inspired Min Distance Classification
- Etc..

Radiomic features

Shape



Histogram (1^{st} Order)



Textural (2^{nd} order)

Higher order

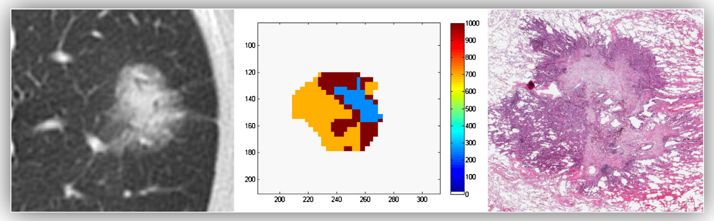
Radiomic features can be divided into 4 classes:

- ***Morphological***
    - information about the shape and physical characteristics features
    - ***surface area, surface-to-volume ratio, density, and mass***

- ***Statistical***
    - histogram features (i.e., *mean, median, std, kurtosis, skewness, entropy, uniformity, and variance*) and texture features

- Regional
    - tumor heterogeneity through subregional clustering

- Model-based
    - mathematical approaches (fractal alteration)



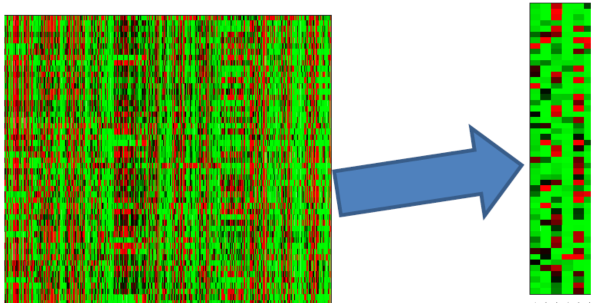
Radiomic Tools

- ePAD, Stanford University, doi.org/10.1016/B978-0-12-812133-7.00013-2
- PyRadiomics/Radiomics , Harvard Medical School *10.1158/0008-5472.CAN-17-0339*
- Texture Analysis Toolbox, Martin Vallières, https://github.com/mvallieres/radiomics/tree/master/TextureToolbox
- Quantitative Image Feature Engine (QIFE) Stanford University, 10.1007/s10278 017-0019-x
- IBEX: MD Anderson Cancer Center, doi: 10.1118/1.4908210.
- MaZda, Technical University of Lodz, Poland, doi:10.1016/j.nima.2012.09.006
- LifeX , Gustave Roussy, Parigi, 10.1158/0008-5472.CAN-18-0125

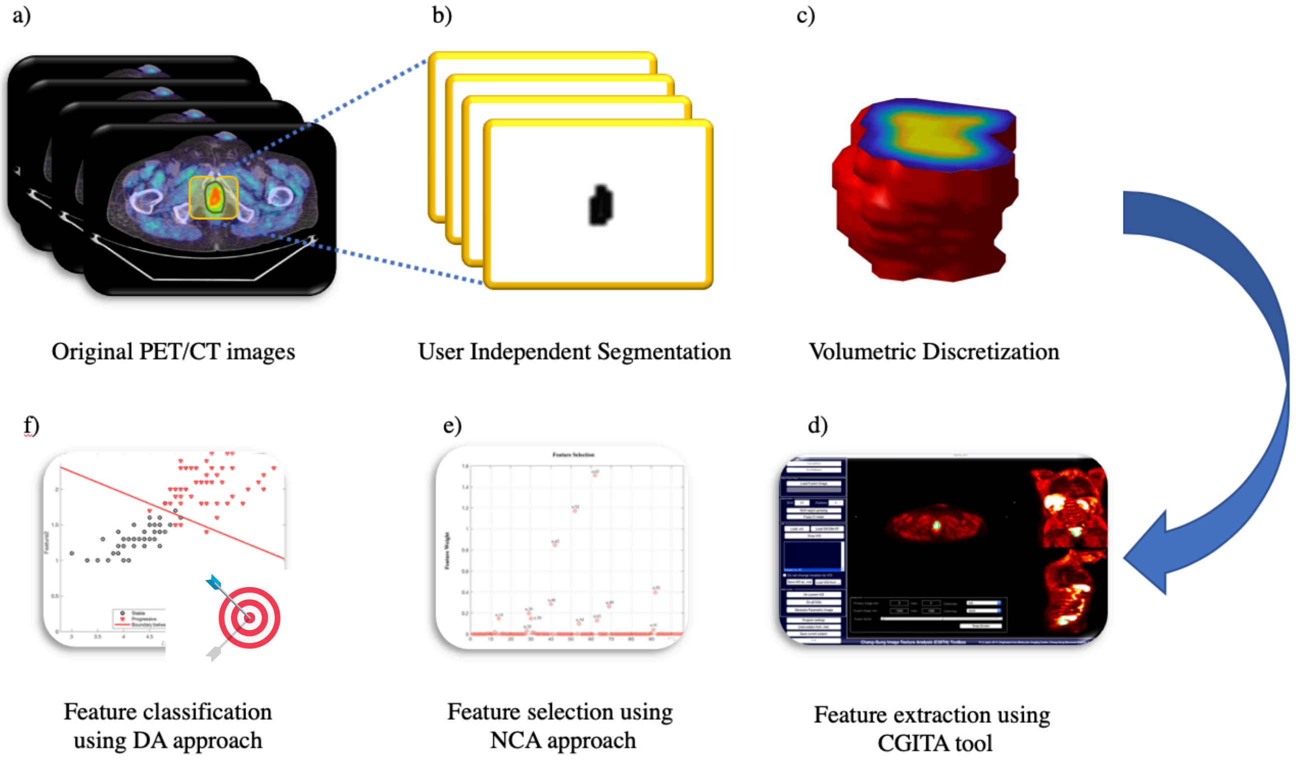
Feature Reduction

Feature selection, aiming to identify a subset of features among a possibly large set of features that are relevant for predicting a response, is an important preprocessing step in machine learning:

- **Minimum redundancy maximum relevance**
- **Principal Component Analysis**
- **Linear discriminant analysis**
- **Etc...**



Radiomic Work Flow



Idiopathic pulmonary fibrosis (IPF)

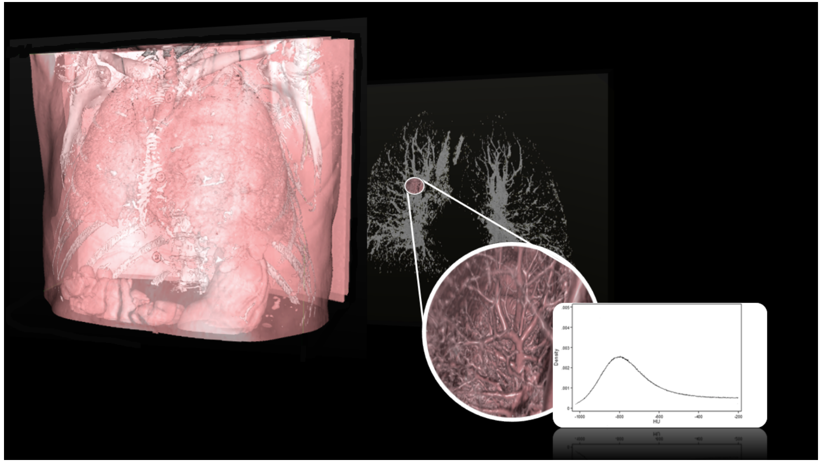
Catania

Con la fibrosi polmonare qui si «gioca d'anticipo»

Testi di **Elena Meli**

Una malattia che «indurisce» i polmoni, fino a renderli incapaci di scambiare l'ossigeno. Una progressione rapida e fatale nell'arco di tre, cinque anni al massimo. La fibrosi polmonare idiopatica è una patologia rara molto grave, contro cui si possono usare farmaci per rallentarne un po' il decorso ma che, spesso, viene diagnosticata tardi, perdendo tempo prezioso per l'intervento. «Per questo l'obiettivo del nostro progetto è individuare parametri clinici, biologici, molecolari e radiologici che possano costituire un pannello di marcatori per la diagnosi precoce ma possano aiutare anche a capire chi risponderà meglio alle terapie — spiega Carlo Vancheri del Centro di Riferimento Malattie Rare del Polmone dell'Università di Catania —. Coinvolgeremo più pazienti possibile, almeno una sessantina, impegnando medici, radiologi, fisici, biologi molecolari; capire quali elementi si associano a una progressione più rapida o a una miglior risposta alle cure consentirà di prescrivere a ciascun malato trattamenti più mirati, più efficienti e con minori effetti collaterali».

Roche per la Ricerca



A. Stefano, Gioè M, Russo G, Palmucci S, Torrisi SE, Bignardi S, et al.
Performance of Radiomics Features in the Quantification of Idiopathic Pulmonary Fibrosis from HRCT.
Diagnostics 2020, Vol 10, Page 306 2020; 10:306. https://doi.org/10.3390/DIAGNOSTICS10050306.

Palmucci, S.; Torrisi, S.E.; Falsaperla, D.; Stefano, A.; Torcitto, A.G.; Russo, G.; Pavone, M.; Vancheri, A.; Mauro, L.A.; Grassedonio, E.; et al.
Assessment of Lung Cancer Development in Idiopathic Pulmonary Fibrosis Patients Using Quantitative High-Resolution Computed Tomography: A Retrospective Analysis.
J. Thorac. Imaging 2019, 35, 115–122.

Torrisi, S.E.; Palmucci, S.; Stefano, A.; Russo, G.; Torcitto, A.G.; Falsaperla, D.; Gioè, M.; Pavone, M.; Vancheri, A.; Sambataro, G.; et al.
Assessment of survival in patients with idiopathic pulmonary fibrosis using quantitative HRCT indexes.
Multidiscip. Respir. Med. 2018, 13, 13–43.

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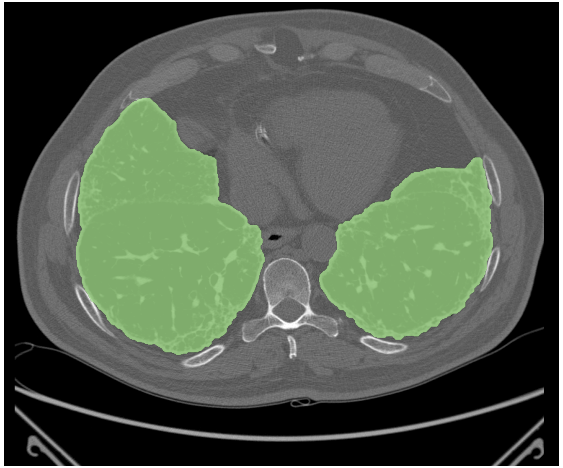

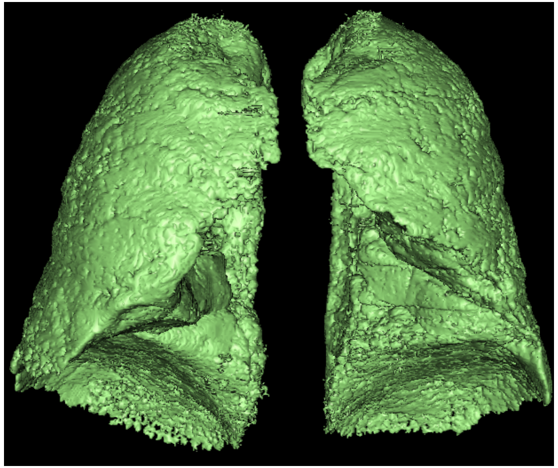

A. Stefano, et al.

Performance of Radiomics Features in the Quantification of Idiopathic Pulmonary Fibrosis from HRCT.

Diagnostics **2020**, Vol 10, Page 306 2020;10:306.

Our study assesses the diagnostic value of different features extracted from high resolution computed tomography (HRCT) images of 32 patients with idiopathic pulmonary fibrosis. These features are investigated over a range of HRCT lung volume measurements (in Hounsfield Units) for which no prior study has yet been published.

In particular, we provide a comparison of their diagnostic value at different HU thresholds, including corresponding pulmonary functional tests.

Results

The radiomics feature which provided the best results was the percentage of Normally attenuated Lung (NL%) at -200 HU, defined as the ratio between the whole lung volume and the NL (lung volume from −950 to −701 HU)

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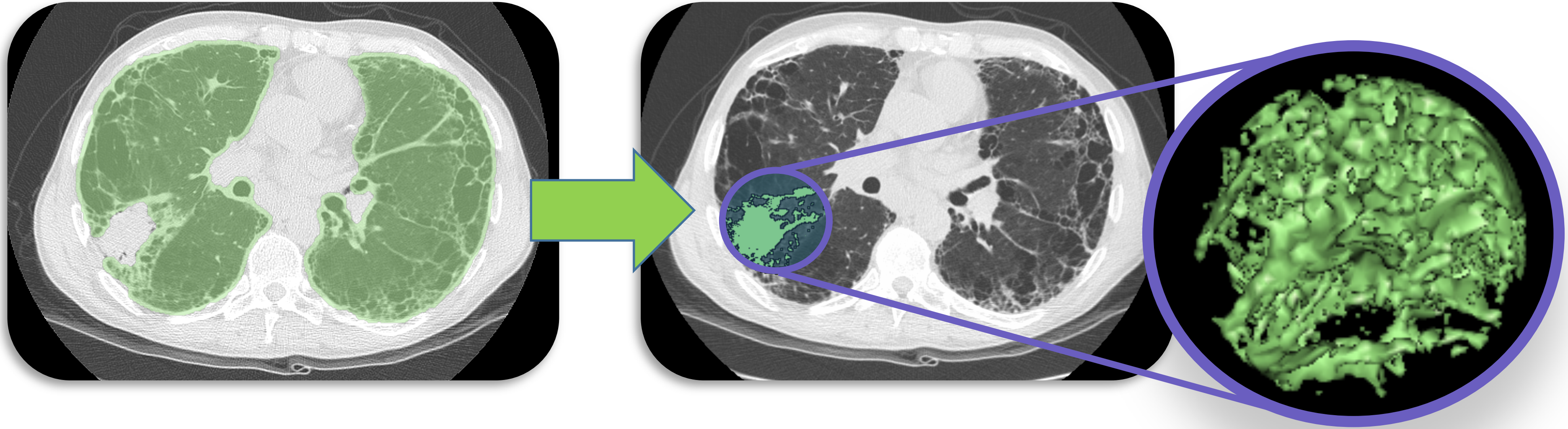
IPF and cancer

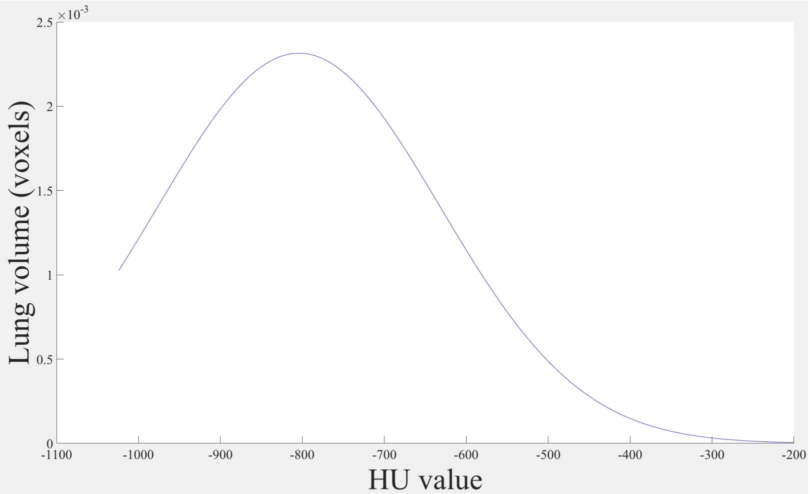
Palmucci, S.; et al.
Assessment of Lung Cancer Development in Idiopathic Pulmonary Fibrosis Patients Using Quantitative High-Resolution Computed Tomography: A Retrospective Analysis.
J. Thorac. Imaging 2019, 35, 115–122.



To investigate the diagnostic accuracy of Kurtosis, HAA (High Attenuation Area) and Fibrotic Area (FA) HRCT indexes in risk assessment of the development of lung cancer in IPF patients.

Results: Kurtosis, FA% and HAA% on Baseline HRCT provided limited diagnostic accuracy in risk assessment of Lung Cancer development in IPF patients.

Lung Cancer seems to develop in IPF patients who have lower kurtosis and skewness values during follow-up.



Torrisi, S.E.; et al.
Assessment of survival in patients with idiopathic pulmonary fibrosis using quantitative HRCT indexes.
Multidiscip. Respir. Med. **2018**, *13*, 13–43.

- 42 patients with a multidisciplinary team diagnosis of IPF according to 2011 ATS/ERS/JRS/LATA IPF guidelines
- Automatic lung parenchyma segmentation with user-friendly DICOM-based image processing software
- HRCT attenuation histogram, based on voxel density, was extracted
- **Follow-up time of 3 years**

Results

Kurtosis index and mean lung density value may provide an accurate estimate of survival in a population of IPF patients from the time of diagnosis

Oveview on *Radiomics* activity within INFN-CSN5

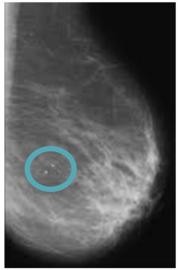
1998-2001 **CALMA**

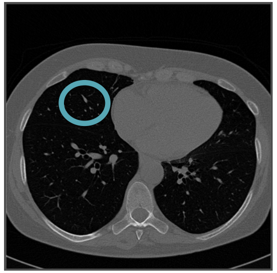
2002-2004 **GP-CALMA**

2005-2011 **MAGIC V**

INFN CSN5 funded projects on "Radiomics", 1998-today

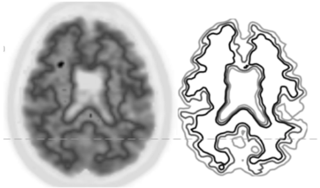
Istituto Nazionale di Fisica Nucleare





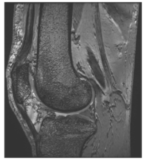
2011-2012 **SEVEN**

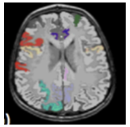
2012-2013 **M5L**

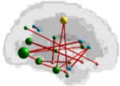


2012-2014 **MIND**

2013-2014 **TESLA**







2015-2017 **nextMR**

AIM

2019-2021

Brief and incomplete list of research achievements in lung CT data analysis

Vassallo L., Traverso A., Agnello M., Bracco C., Campanella D., Chiara G., Fantacci M.E., Lopez Torres E., Manca A., Saletta M., Giannini V., Mazzetti S., Stasi M., Cerello P., Regge D.	A cloud-based computer-aided detection system improves identification of lung nodules on computed tomography scans of patients with extra-thoracic malignancies	2019	European Radiology
Setio AAA, Traverso A, de Bel T, Berens MSN, Bogaard CVD, Cerello P, Chen H, Dou Q, Fantacci ME, Geurts B, Gugten RV, Heng PA, Jansen B, de Kaste MMJ, Kotov V, Lin JY, Manders JTMC, Sóñora-Mengana A, García-Naranjo JC, Papavasileiou E, Prokop M, Saletta M, Schaefer-Prokop CM, Scholten ET, Scholten L, Snoeren MM, Torres EL, Vandemeulebroucke J, Walasek N, Zuidhof GCA, Ginneken BV, Jacobs C.	Validation, comparison, and combination of algorithms for automatic detection of pulmonary nodules in computed tomography images: The LUNA16 challenge,	2017	Medical Image Analysis
Traverso A., Lopez Torres E., Fantacci M.E., Cerello P.	Computer-aided detection systems to improve lung cancer early diagnosis: State-of-the-art and challenges	2017	Journal of Physics: Conference Series
Traverso A., Torres E.L., Bracco C., Campanella D., Fantacci M.E., Regge D., Saletta M., Stasi M., Vassallo L., Cerello P.	90P: Clinical validation of the M5L lung computer-assisted detection system	2016	Journal of Thoracic Oncology
Lopez Torres E., Fiorina E., Pennazio F., Peroni C., Saletta M., Camarlinghi N., Fantacci M.E., Cerello P.	Large scale validation of the M5L lung CAD on heterogeneous CT datasets	2015	Medical Physics
Retico A.	Computer-aided detection for pulmonary nodule identification: Improving the radiologist's performance?	2013	Imaging in Medicine
Camarlinghi N., Gori I., Retico A., Bellotti R., Bosco P., Cerello P., Gargano G., Torres E.L., Megna R., Peccarisi M., Fantacci M.E.	Combination of computer-aided detection algorithms for automatic lung nodule identification	2012	International Journal of CARS
van Ginneken B., Armato S.G., de Hoop B., van Amelsvoort-van de Vorst S., Duindam T., Niemeijer M., Murphy K., Schilham A., Retico A., Fantacci M.E., Camarlinghi N., Bagagli F., Gori I., Hara T., Fujita H., Gargano G., Bellotti R., Tangaro S., Bolaos L., Carlo F.D., Cerello P., Cristian Cheran S., Lopez Torres E., Prokop M.	Comparing and combining algorithms for computer-aided detection of pulmonary nodules in computed tomography scans: The ANODE09 study	2010	Medical Image Analysis
Golosio B., Masala G.L., Piccioli A., Oliva P., Carpinelli M., Cataldo R., Cerello P., De Carlo F., Falaschi F., Fantacci M.E., Gargano G., Kasae P., Torsello M.	A novel multithreshold method for nodule detection in lung CT	2009	Medical Physics
Retico A., Fantacci M.E., Gori I., Kasae P., Golosio B., Piccioli A., Cerello P., De Nunzio G., Tangaro S.	Pleural nodule identification in low-dose and thin-slice lung computed tomography	2009	Computers in Biology and Medicine
Retico A., Delogu P., Fantacci M.E., Gori I., Preite Martinez A.	Lung nodule detection in low-dose and thin-slice computed tomography	2008	Computers in Biology and Medicine
Cascio D., Cheran S.C., Chincarini A., De Nunzio G., Delogu P., Fantacci M.E., Gargano G., Gori I., Masala G.L., Preite Martinez A., Retico A., Santoro M., Spinelli C., Tarantino T.	Automated detection of lung nodules in low-dose computed tomography	2007	Computer-Assisted Radiology and Surgery
Bellotti R., De Carlo F., Gargano G., Tangaro S., Cascio D., Catanzariti E., Cerello P., Cheran S.C., Delogu P., De Mitri I., Fulcheri C., Grosso D., Retico A., Squarcia S., Tommasi E., Golosio B.	A CAD system for nodule detection in low-dose lung CTs based on region growing and a new active contour model	2007	Medical Physics

Proposal for analysis of lung CT of patients with Covid-19

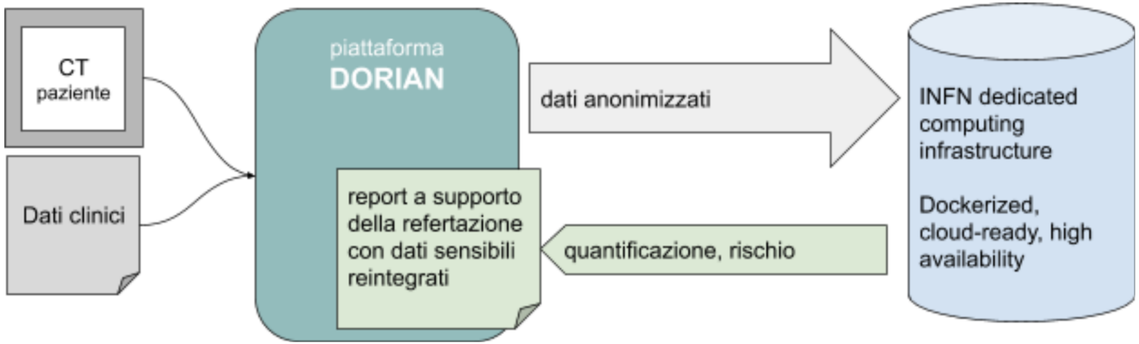
Proposal: **LQC** - Lung Quantification for COVID-19

Innova per l'Italia

LQC aims to extrapolate prognostic information, i.e. the probability of evolving in a clinically serious situation, through the use of AI on clinical data (blood, comorbidity, anamnestic) and lung CT images acquired at the baseline.

Objectives:

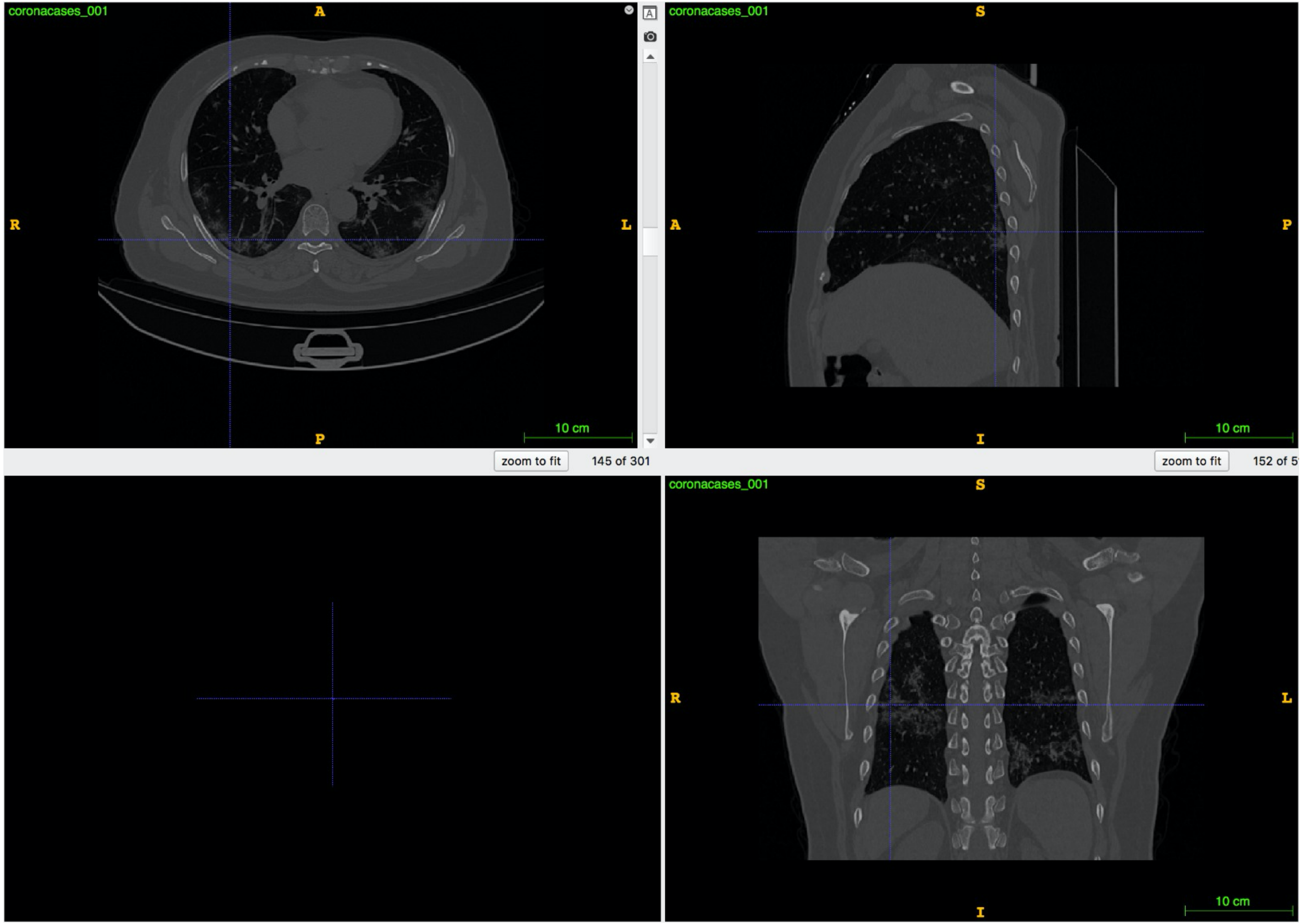
1. Quantitative and objective assessment of the lung areas affected by interstitial pneumonia (radiomic analysis)
2. Integration of clinical and epidemiological information with image analysis results to provide a single prognostic index that helps to prioritize patients and predict the need of intensive care.



Synergy with DORIAN
(A. Chincarini, INFN-TT)

DORIAN

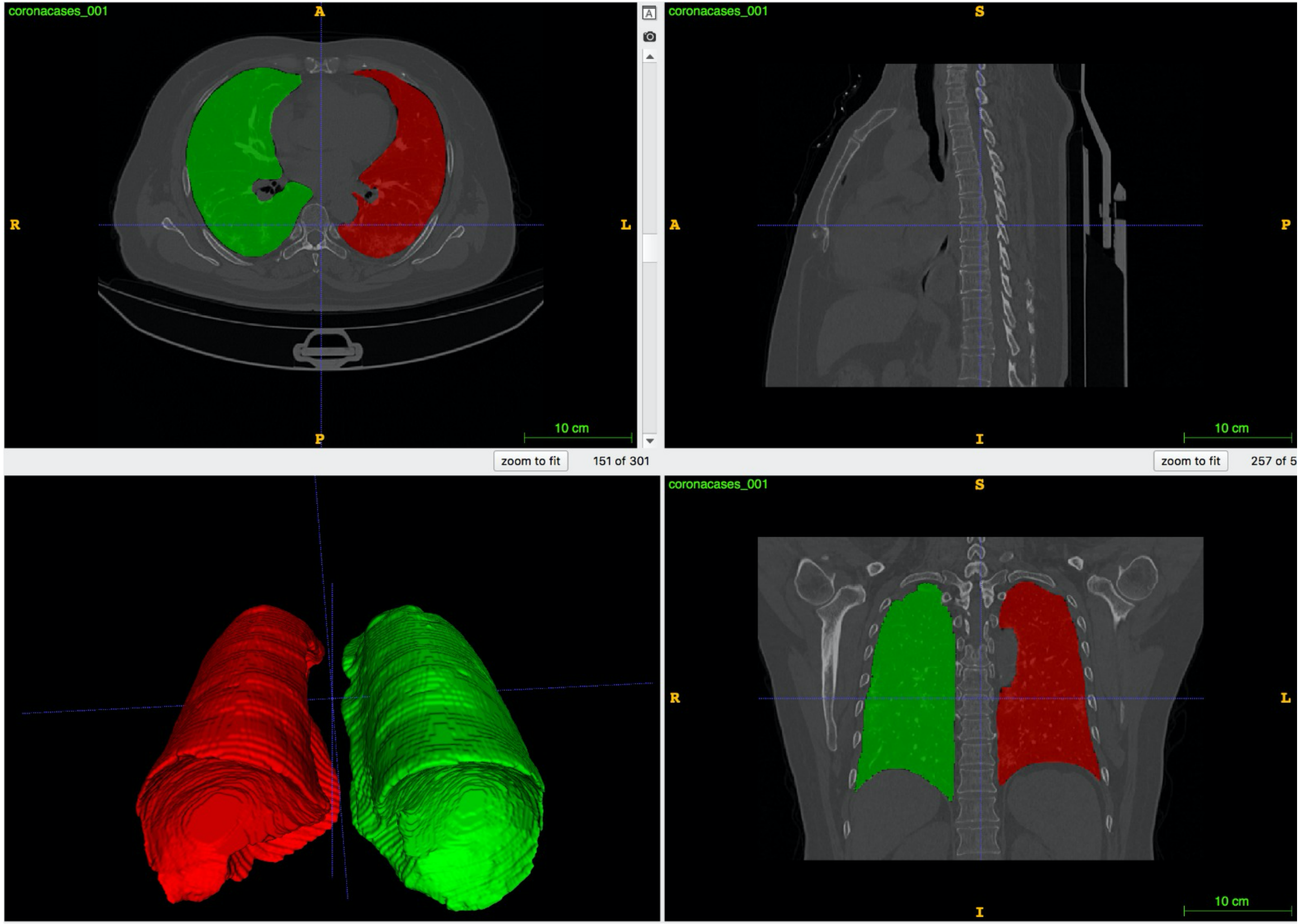
COVID-19 challenge: disease identification



Radiomics is a promising biomedical approach aiming to provide great volumes of quantitative features from medical images.

The first step in a radiomics workflow is the identification of the **region of interest** in the image in such a way as to avoid distortions in target feature extraction.

COVID-19: Training with a small HRCT dataset (32 pts)



We use an innovative and fast **deep learning algorithm** whose purpose is to tackle the real-time, three-dimensional, fully automated segmentation task of HRCT datasets.

Fondazione Ri.MED

IBFM

COVID-19 : Unsupervised Lung Segmentation for Radiomics Studies

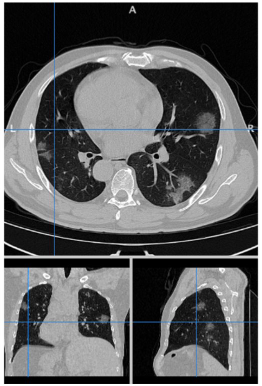
After automatic segmentation, we **extract radiomics features** and we use a novel feature selection approach to identify a relevant prognostic model to differentiate between patients with COVID-19 and other lung diseases (fibrosis, pneumonia, cancer, etc).

The AIM working group on lung CT analysis (AIM-Covid19-WG)

AIM1: Multicenter Data Harmonization

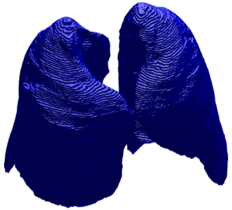
AIM2: Quantification

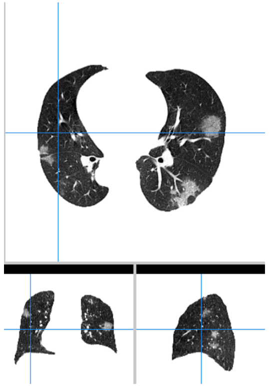
AIM3: Predictive Models



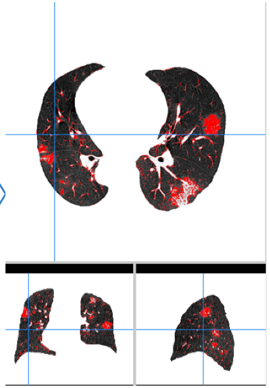
Classical algorithms for lung segmentation fail when lung appearance is strongly affected by interstitial pneumonia

Lung volume segmentation





Quantification of lung parenchyma affected by ground glass (GG) opacities



==> Deep learning segmentation methods need thousands of annotated cases to be “transferred” to accomplish this task

- Quantitative information on the amount of GG opacities and their distribution, possibly combined with clinical and epidemiological patient’s information, may be relevant to set up predictive models for patients’ stratification, prognosis prediction, etc.
- Even only pure quantification modules, once properly validated, could be valuable tools for clinicians to set up large-scale population studies

- **AIM-Covid19-WG** has collected interest by other INFN groups interested also in radiomics studies in a broad range (LNS, PV)
- Synergy with **ML_INFN** (T. Boccali)
- Open issues: ***access to large data samples***

INFN Istituto Nazionale di Fisica Nucleare

Società Italiana di Radiologia Medica e Interventistica

aifm Associazione Italiana di Fisica Medica – La Fisica Medica al servizio della salute

Three-parties scientific agreement

Joint EU proposal in preparation

AIM-Covid19-WG

- FTE
  - Giorgio Russo, 30%
  - Alessandro Stefano, 70%
- Request
  - Hardware, 1 GPU to be installed in a workstation – 2k€
  - Travels for internal meeting – 2k€