

# Improved interpretability with DNetPRO classifier applied to radiomics data

*with*

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Daniel Remondini

27/09/2024

## Contacts

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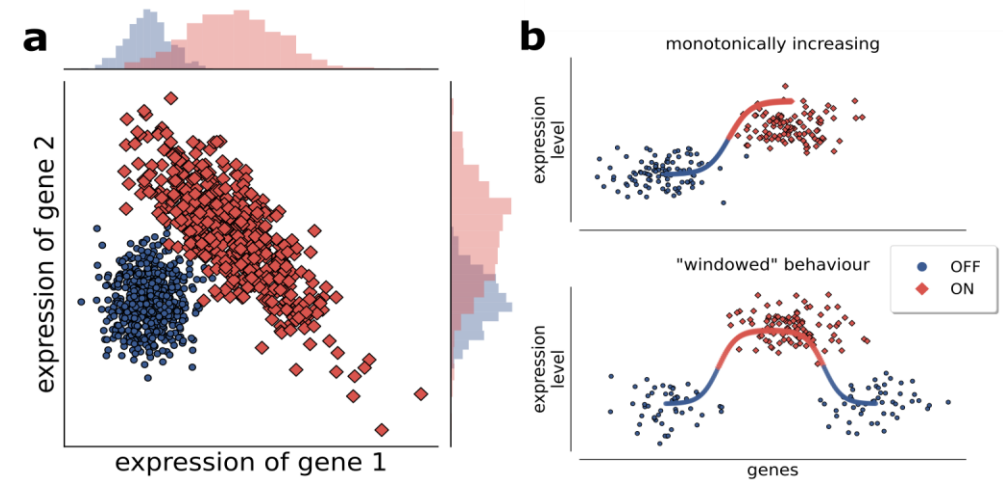
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## DNetPRO: A network approach for low-dimensional signatures from high-throughput data

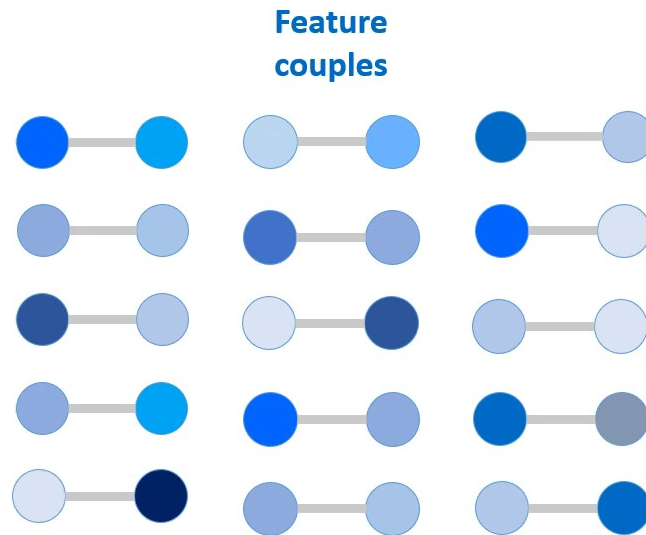
- High-throughput data ( $10^3 - 10^5$  variables)
- Looking for low-dimensional set of observables
- **Gene** or **Protein** expression by an up/down regulation
- Features selection is a critical step
- Exploration of all feature space is an NP-hard problem
- Few samples available
- Ill-posed problem



Methods that select variables for multi-dimensional signatures based on single-variable performance can have limits in predicting higher-dimensional signature performance. As shown in the Fig. a, in which both variables taken singularly perform poorly, but their performance becomes optimal in a 2-dimensional combination, in terms of linear separation of the two classes.



## DNetPRO: A network approach for low-dimensional signatures from high-throughput data





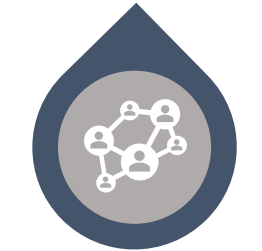
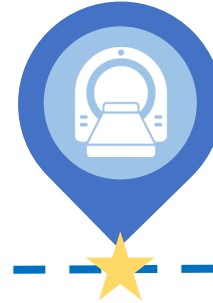
**2019**  
**Cytokines**  
Alzheimer Disease



**2022**  
**TCGA**  
*Method Release*



**2024**  
**Radiomic**  
*MRI & CT samples*



**2018**  
**No Med App**  
Traffic



**2020**  
**Veterinary**  
mRNA samples

2 years

Application to  
Radiomic Data

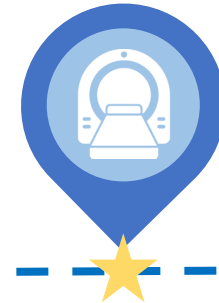
2018



**2019**  
**Cytokines**  
 Alzheimer Disease



**2024**  
**Radiomic**  
 MRI & CT samples



**2018**  
**No Med App**  
 Traffic



**2020**  
**Veterina**  
 mRNA sampl

Mizzi et al. *EPJ Data Science* (2018) 7:44  
<https://doi.org/10.1140/epjds/s13688-018-0168-2>

**EPJ Data Science**  
 a SpringerOpen Journal

**EPJ.org**

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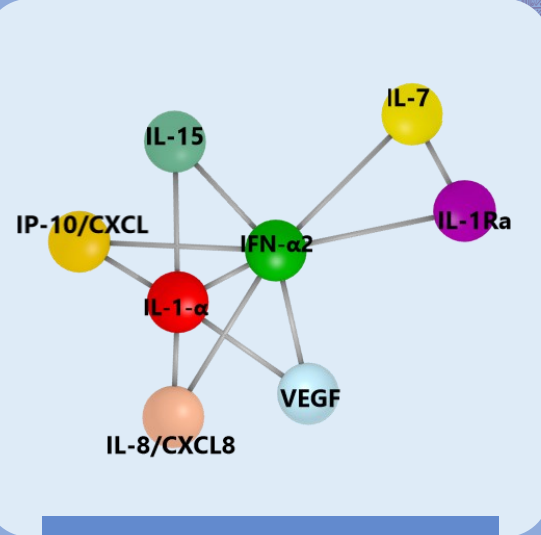
**Unraveling pedestrian mobility on a road network using ICTs data during great tourist events**

Chiara Mizzi<sup>1</sup>, Alessandro Fabbri<sup>1</sup>, Sandro Rambaldi<sup>1</sup>, Flavio Bertini<sup>1</sup>, Nico Curti<sup>1</sup>, Stefano Sinigardi<sup>1</sup>, Rachele Luzi<sup>1</sup>, Giulia Venturi<sup>1</sup>, Micheli Davide<sup>2</sup>, Giuliano Muratore<sup>2</sup>, Aldo Vannelli<sup>2</sup> and Armando Bazzani<sup>1\*</sup>

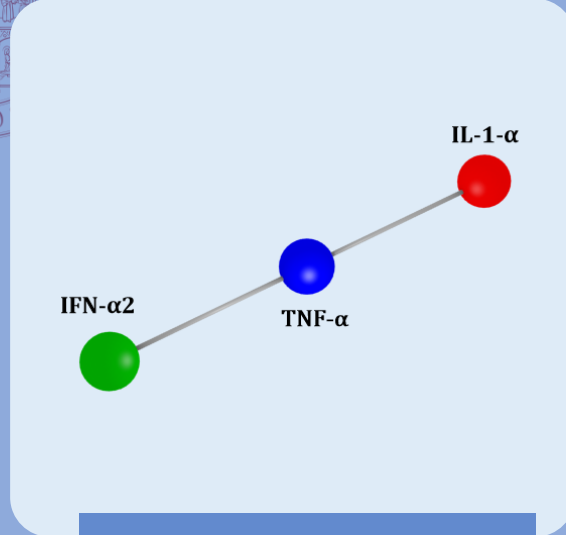
**Application to Radiomic Data**

2019

2019  
Cytokines  
Alzheimer Disease

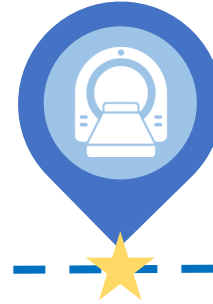


Signature CTL vs MCI



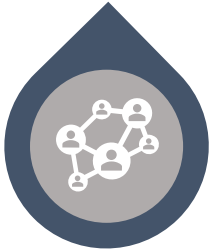
Signature CTL vs AD

2024  
Radiomic  
MRI & CT samples



Application to  
Radiomic Data

2018  
No Med App  
Traffic



2020  
Veterinar  
mRNA samp



Observational Study > J Alzheimers Dis. 2019;72(3):911-918. doi: 10.3233/JAD-190480.

### Cognitive Decline and Alzheimer's Disease in Old Age: A Sex-Specific Cytokine Signature

Virginia Boccardi<sup>1</sup>, Lucia Paolacci<sup>1</sup>, Daniel Remondini<sup>2</sup>, Enrico Giampieri<sup>2</sup>, Giulia Poli<sup>3</sup>, Nico Curti<sup>2</sup>, Roberta Cecchetti<sup>1</sup>, Alfredo Villa<sup>4</sup>, Carmelinda Ruggiero<sup>1</sup>, Stefano Brancorsini<sup>3</sup>, Patrizia Mecocci<sup>1</sup>

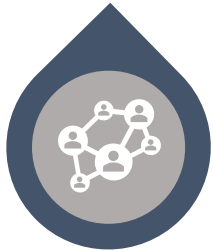
Affiliations + expand

PMID: 31658056 DOI: 10.3233/JAD-190480

**2019**  
**Cytokines**  
Alzheimer Disease



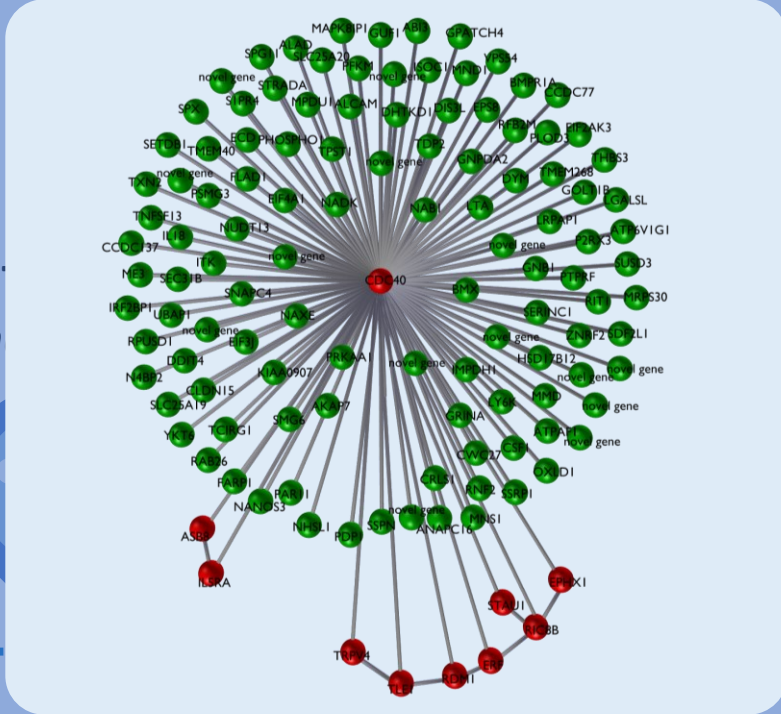
**2018**  
No Med App  
Traffic



**2020**  
Veterinary  
mRNA samples



**2020**



**2024**  
**Radiomic**  
MRI & CT samples



Application to  
**Radiomic Data**



Article

**Combinatorial Discriminant Analysis Applied to RNAseq Data Reveals a Set of 10 Transcripts as Signatures of Exposure of Cattle to *Mycobacterium avium* subsp. *paratuberculosis***

Michela Malvisi <sup>1,2,†</sup>, Nico Curti <sup>3,†</sup>, Daniel Remondini <sup>3,\*,†</sup>, Maria Grazia De Iorio <sup>2</sup>, Fiorentina Palazzo <sup>4</sup>, Gustavo Gandini <sup>2</sup>, Silvia Vitali <sup>3</sup>, Michele Polli <sup>2</sup>, John L. Williams <sup>5</sup> and Giulietta Minozzi <sup>2,\*,†</sup>

2022

mRNA

DDA	0.673	0.565	0.658	0.618
KNN	0.721	0.579	0.607	0.617
DA	0.713	0.589	<b>0.710</b>	<b>0.640</b>
LR	0.697	0.589	0.668	0.604
NC	0.670	0.594	0.615	0.612
PLS	0.713	0.589	0.671	<b>0.640</b>
RF	0.733	0.569	0.633	0.619
SVM	0.725	0.608	0.658	0.626
DNetPRO (procedure A)	<b>0.739</b>	<b>0.666</b>	0.641	0.589
DNetPRO (procedure B)	0.724	0.637	0.616	0.586
	KIRC	GBM	LUJC	OV

miRNA

DDA	0.682	0.566	0.543	0.586
KNN	0.568	0.536	0.551	0.582
DA	0.677	0.534	0.523	0.605
LR	0.657	0.561	0.510	0.594
NC	0.670	0.539	<b>0.487</b>	0.584
PLS	0.677	0.534	0.523	0.605
RF	0.692	0.561	<b>0.477</b>	0.589
SVM	0.621	0.564	0.531	<b>0.625</b>
DNetPRO (procedure A)	<b>0.738</b>	<b>0.620</b>	0.598	0.609
DNetPRO (procedure B)	0.700	0.599	<b>0.628</b>	0.569
	KIRC	GBM	LUJC	OV

RPPA

DDA	0.714	0.671	0.578
KNN	0.683	0.643	0.595
DA	0.667	0.620	0.575
LR	0.652	0.645	0.618
NC	0.707	0.671	0.599
PLS	0.667	0.620	0.589
RF	0.664	0.643	0.546
SVM	0.721	<b>0.696</b>	0.625
DNetPRO (procedure A)	<b>0.734</b>	0.615	<b>0.660</b>
DNetPRO (procedure B)	0.563	0.620	0.567
	KIRC	LUJC	OV



2019  
Cytokine  
Alzheimer Di



2024  
omic  
T samples

# scientific reports

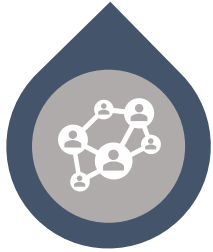
OPEN

## A network approach for low dimensional signatures from high throughput data

Nico Curti<sup>1,2,4</sup>, Giuseppe Levi<sup>1,2,4</sup>, Enrico Giampieri<sup>2,3</sup>, Gastone Castellani<sup>2,3</sup> & Daniel Remondini<sup>1,2</sup>

Check for updates

Application to  
omic Data



2018  
No Med App  
Traffic

mR



2022

Python  
latest

Search docs

CONTENTS:

- Theory
- Installation guide
- C++ API
- Python API
- References

Docs » Welcome to DNetPRO algorithm's documentation!

[Edit on GitHub](#)

## Welcome to DNetPRO algorithm's documentation!

Official implementation of the DNetPRO algorithm published on [BioRxiv](#) by Curti et al. The *DNetPRO* algorithm produces multivariate signatures starting from all the couples of variables analyzed by a Discriminant Analysis. The method is particularly designed to gene-expression data analysis and it was tested against the most common feature selection techniques. In the current implementation the *DNetPRO* object is totally equivalent to a *scikit-learn* feature-selection method and thus it provides the member functions *fit* (to train your model) and *predict* (to test a trained model on new samples). The combinatorial evaluation is performed using a C++ version of the code wrapped using *Cython*.

2019  
Cytokine  
Alzheimer Di



2024  
omic  
T samples

## scientific reports

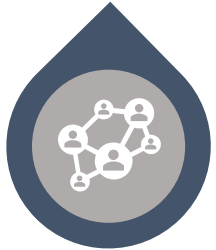
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# A network approach for low dimensional signatures from high throughput data

Nico Curti<sup>1,2,4</sup>, Giuseppe Levi<sup>1,2,4</sup>, Enrico Giampieri<sup>2,3</sup>✉, Gastone Castellani<sup>2,3</sup> & Daniel Remondini<sup>1,2</sup>

Check for updates

Application to  
omic Data



2018  
No Med App  
Traffic

V  
mR

# Radiomic Analysis



**Radiomic Analysis** is becoming a **standard practice** in many medical applications

Number of publications per year since 1967.

Huang et al.,  
*Nature Reviews*, 2023



## Pros

- Multiple features
- Easy to use
- Integration with other software
- Use of Anatomical image information
- Easy extraction of the results

Vs

## Cons

- Multi-dimensional analyses
- Ill-posed problems
- Large noise sources
- Biases and batch effects in multi-center studies
- Hard interpretation of the results

# PET/CT Recurrent Rectal Cancer



1 hospital – IRCCS Sant’Orsola – Malpighi Bologna



44 patients – radical resection – primary rectal adenocarcinoma



PET/CT dataset – manual segmentation of lesions performed by expert radiologists

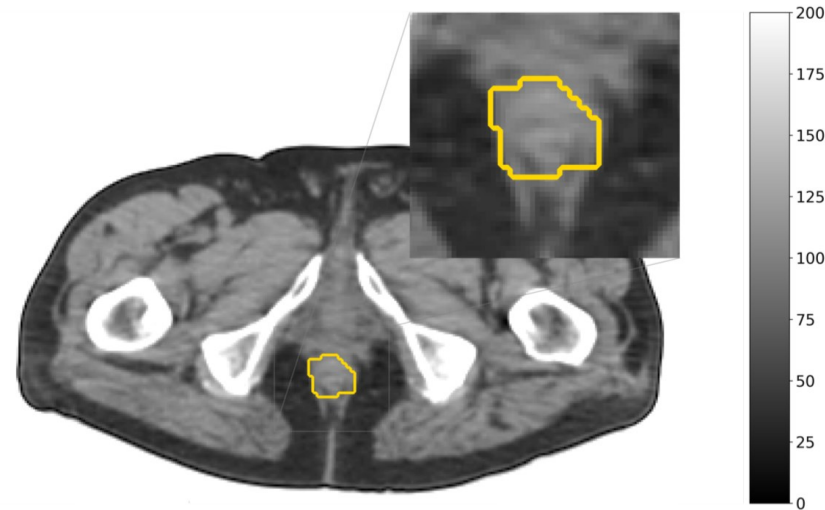


Full set of radiomic features – Original, Wavelet, and LoG

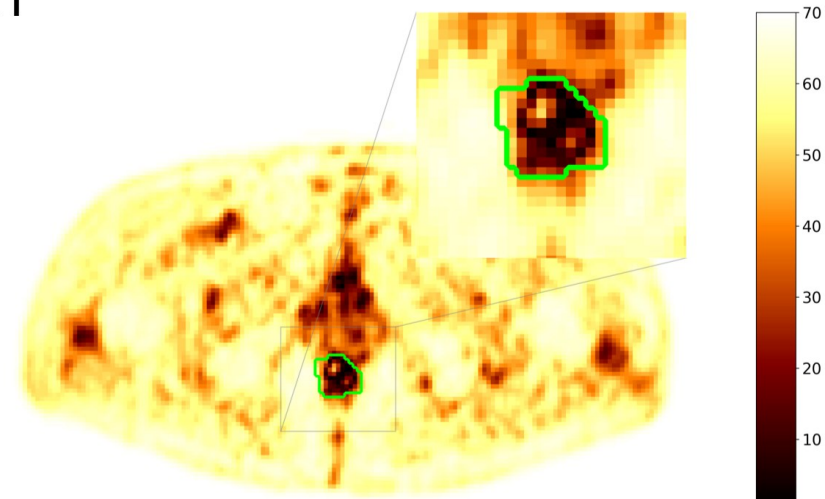


Classification pipeline – Locally Recurrent Rectal Cancer (LRR) vs NO LRR

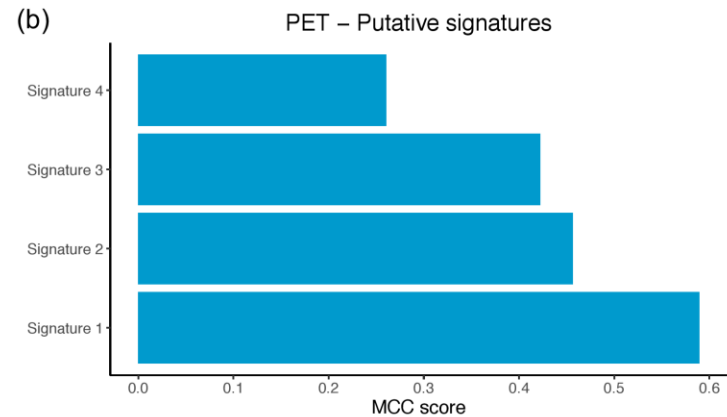
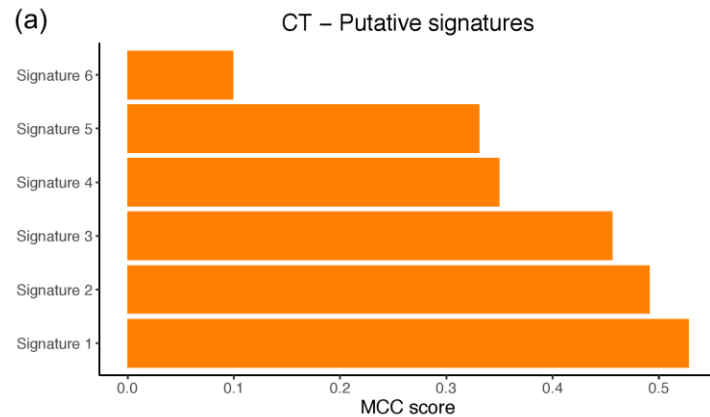
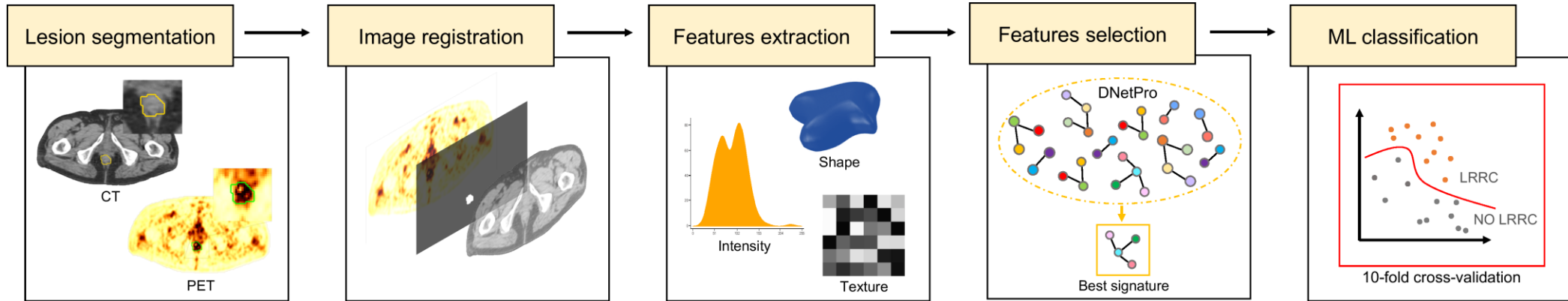
a) CT



b) PET



# PET/CT LRRC - DNetPRO



## Signature legend

### CT

- Signature 1 = {Entropy, LargeDependenceEmphasis}
- Signature 2 = {Entropy, Kurtosis, Mean, Range, LargeDependenceEmphasis}
- Signature 3 = {Entropy, Mean}
- Signature 4 = {Entropy}
- Signature 5 = {Entropy, Kurtosis, Mean, Range, TotalEnergy, SumAverage, SumEntropy, SumSquares, GrayLevelVariance, LargeDependenceEmphasis}
- Signature 6 = {GrayLevelVariance}

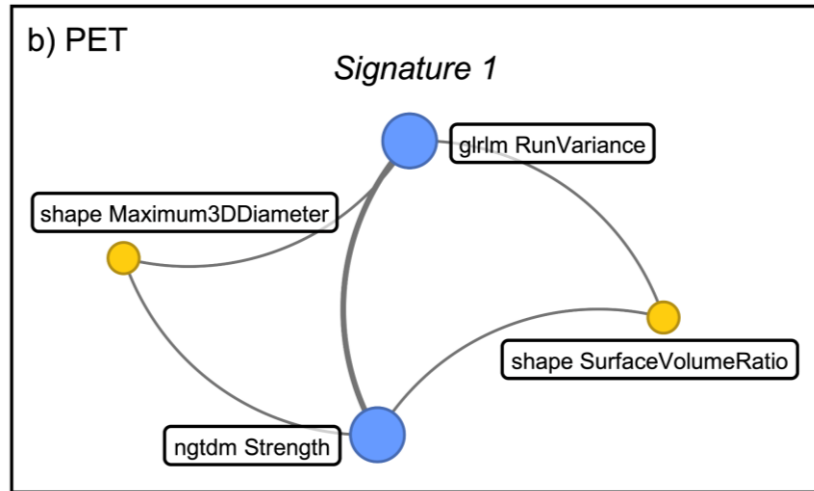
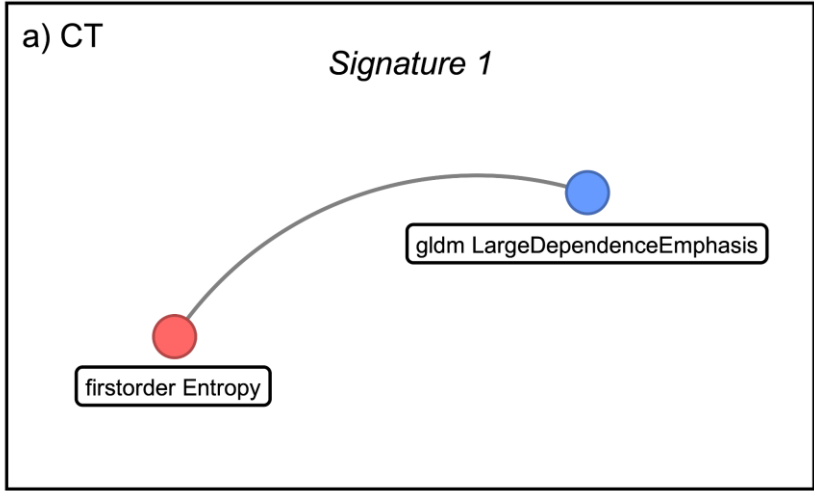
### PET

- Signature 1 = {RunVariance, Strength, Maximum3DDiameter, SurfaceVolumeRatio}
- Signature 2 = {Strength}
- Signature 3 = {ShortRunEmphasis, Strength}
- Signature 4 = {RunEntropy, ShortRunHighGrayLevelEmphasis}

# PET/CT LRRC - DNetPRO



**Under Review**



Identification of PET/CT radiomic signature for locally recurrent rectal cancer classification

Sara Dalmonte<sup>a,b,\*</sup>, Maria Adriana Coccozza<sup>c,\*</sup>, Dajana Cuicchi<sup>d</sup>, Daniel Remondini<sup>e</sup>, Lorenzo Faggioni<sup>k,1</sup>, Paolo Castellucci<sup>f,1</sup>, Andrea Farolfi<sup>f</sup>, Emilia Fortunati<sup>f</sup>, Alberta Cappelli<sup>c</sup>, Riccardo Biondi<sup>g</sup>, Arrigo Cattabriga<sup>c</sup>, Gilberto Poggioli<sup>d</sup>, Stefano Fanti<sup>f</sup>, Gastone Castellani<sup>h,\*\*</sup>, Francesca

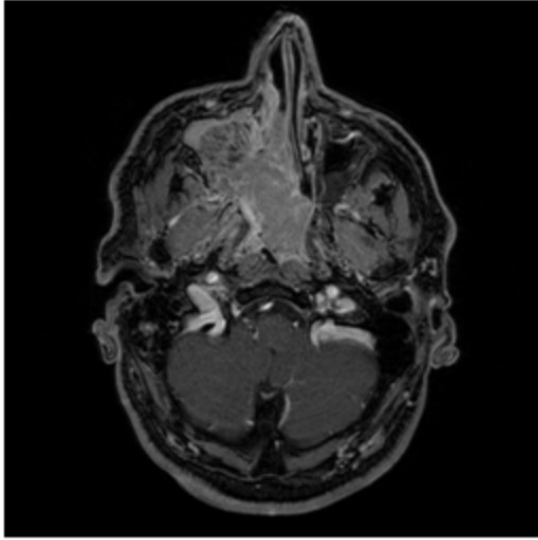
Features	Sensitivity	Specificity	BAS	MCC
CT	0.80	<b>0.82</b>	<b>0.81</b>	<b>0.61</b>
PET	<b>0.93</b>	0.61	0.77	0.52
CT + PET	0.80	0.75	0.77	0.53

Table 2: Results of the SVC model trained in a 10-fold cross-validation with selected CT, PET, and CT+PET features.

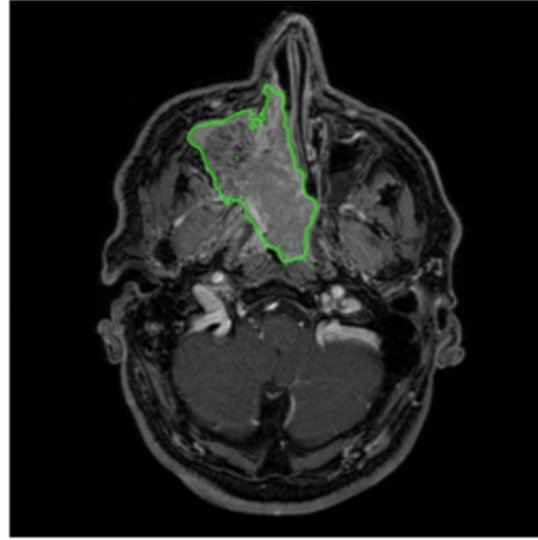
# MRI Sinonasal tumors



Original MRI  
(slice 107)



Ground Truth  
Tumor mask overlay



2 hospitals – Como & Varese centres  
New collaborations !!



145 patients – sinonasal tumor – multiple tumor classes grouped as Malignant vs Benign



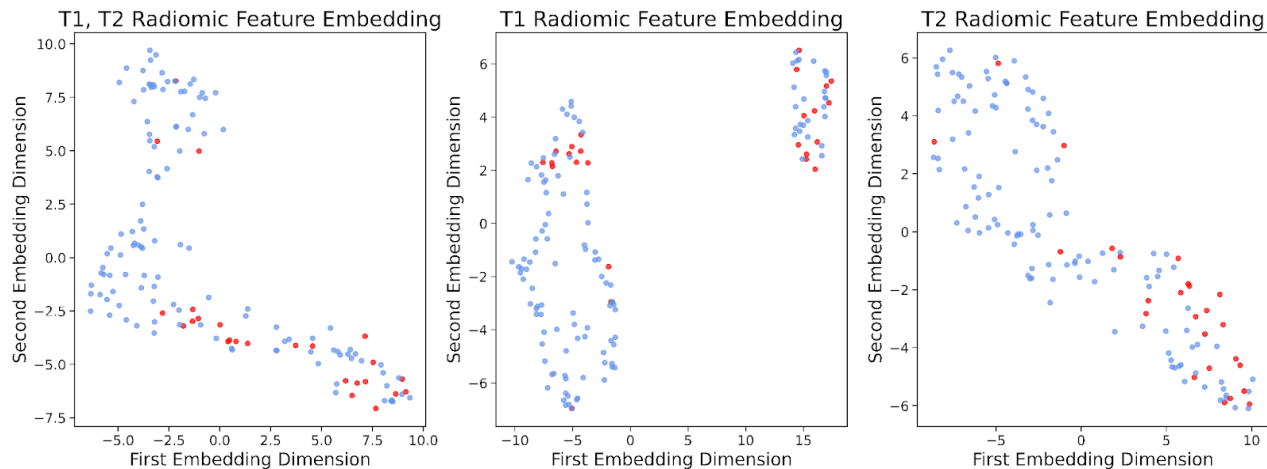
T1w & T2w – manual segmentation of lesions performed by expert radiologists



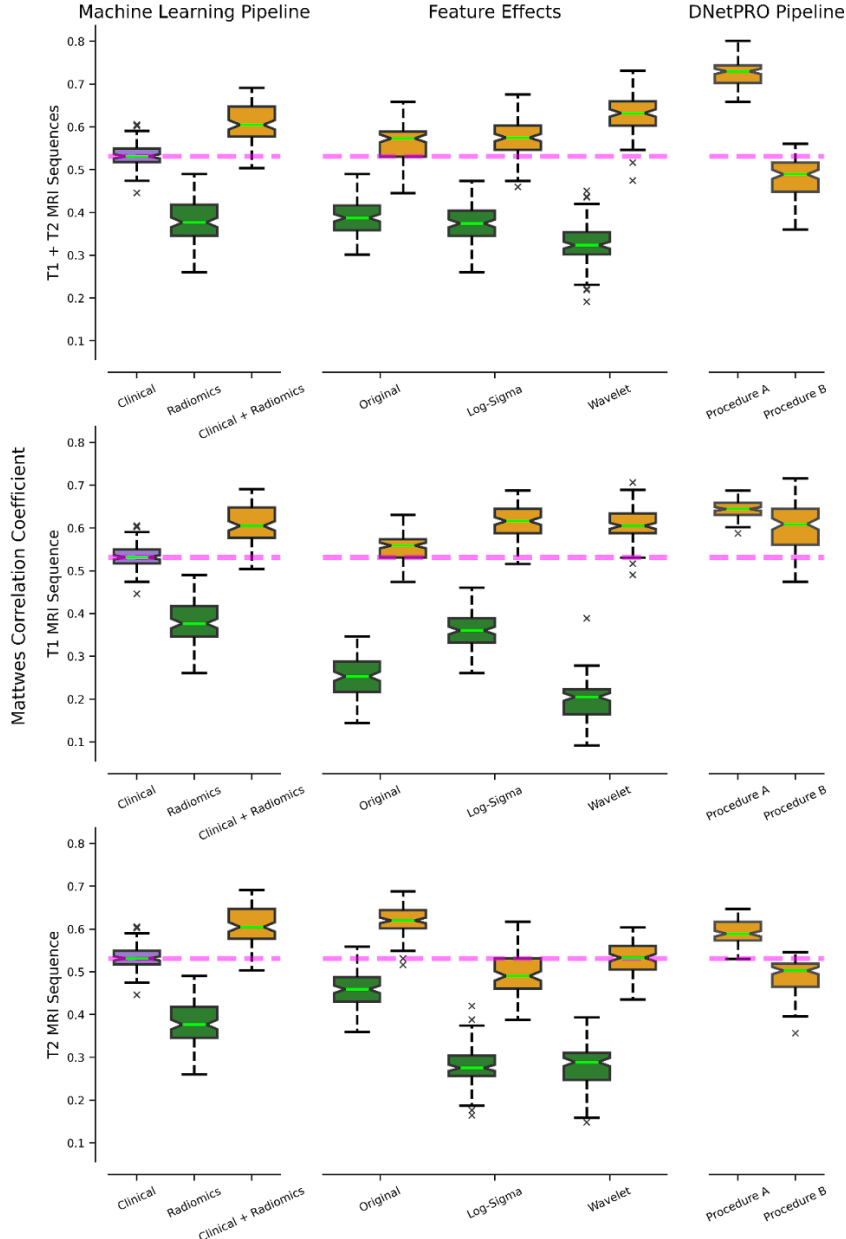
Full set of radiomic features – Original, Wavelet, and LoG



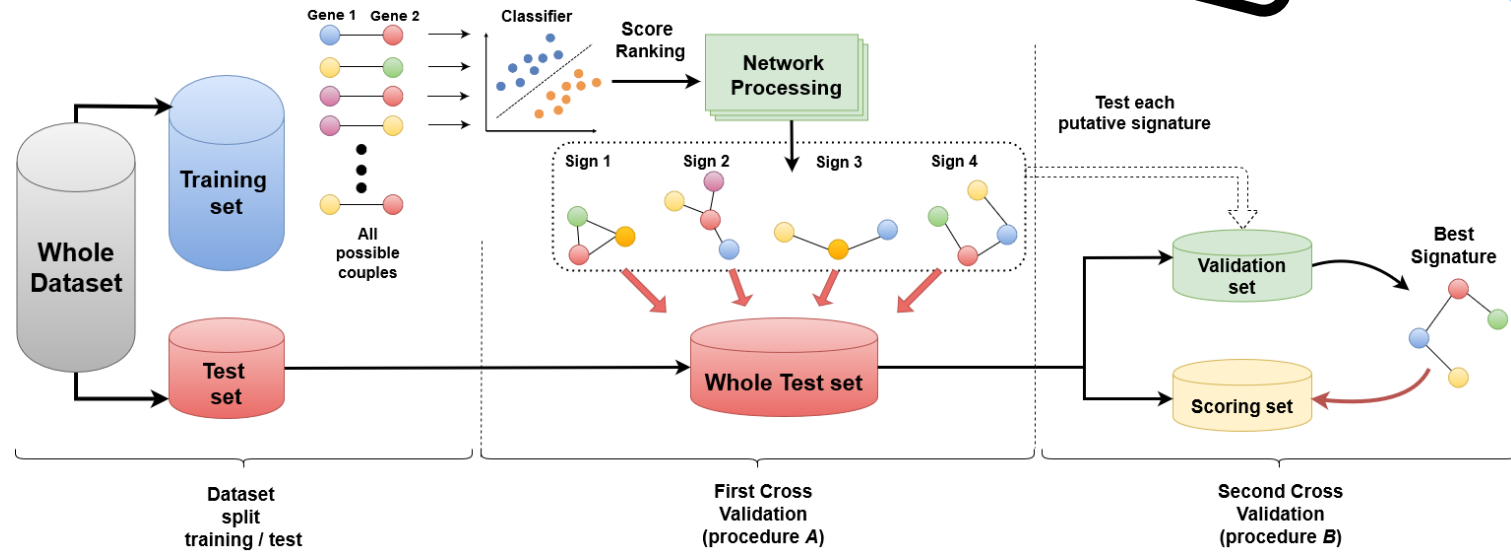
Classification pipeline – Malignant vs Benign Tumors



# Sinonasal MRI - DNetPRO



**Preliminary Results**





## Preliminary Results & Conclusions

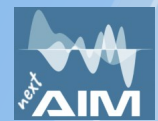


- **DNetPRO** as **Novel** approach to feature selection in AIM
- **Publicly available** code in multiple languages
- Applicability to different kind of samples (**new in Radiomics!**)
- Computationally efficient on ill-posed like problems
- Possibility to extract multiple (or just one) signatures
- **Easy Explainability** of the results for biomedical (and clinical) applications
- We are currently developing **web (server) interface** for public usages



<https://github.com/Nico-Curti>





Nico Curti, Sara Dalmonte, Riccardo Biondi,  
Daniel Remondini

**Thank you for  
Your attention**

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