Radiomic and Beyond

Lights and Shadows of the standard machine learning approaches

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What learning means for humans

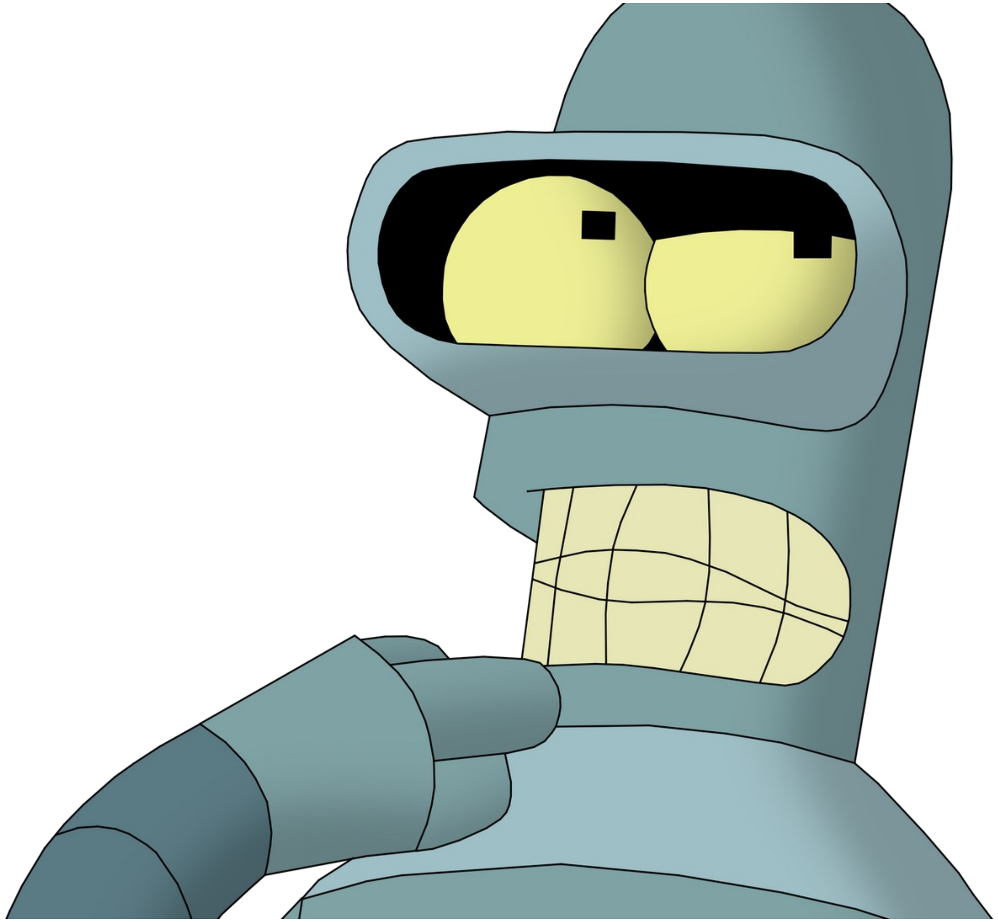
The human learning process is based on:

- Examples
- Trying (and re-trying)
- Mistakes
- Evaluation

Understanding the main features of the problem

What learning means for machines

The machine learning process is based on:

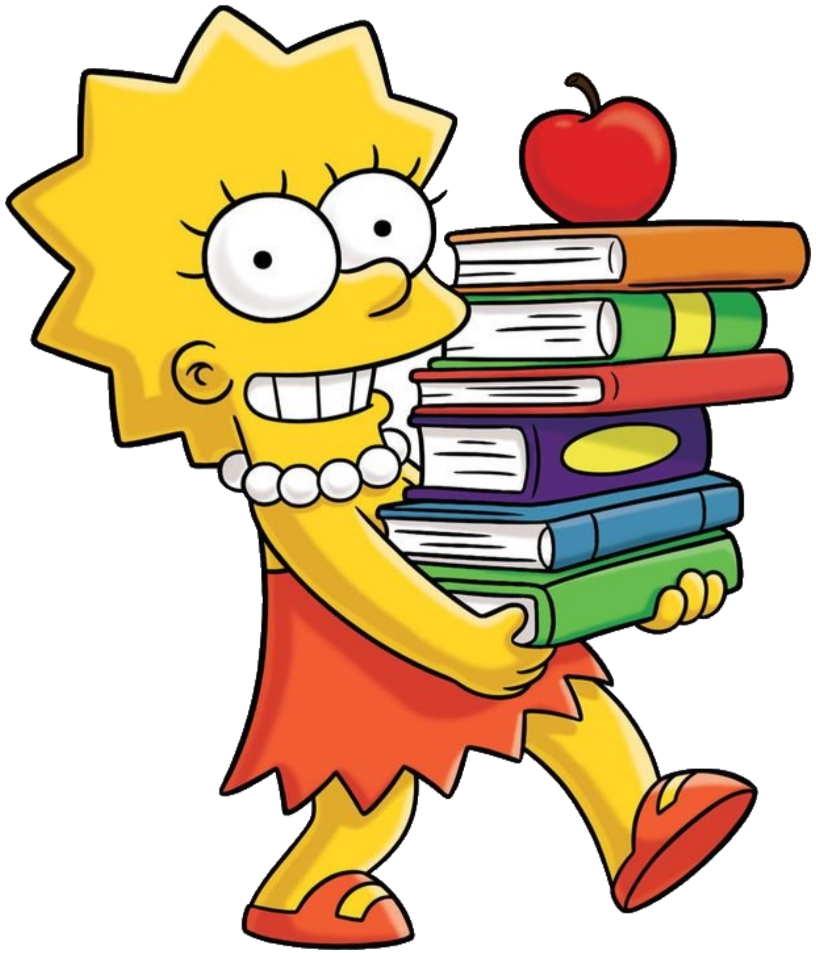


- Examples → multiple data
- Trying (and re-trying) → iterative process
- Mistakes → Error function
- Evaluation → Metric function

Understanding the main features of the problem

A simple example

Let's take a student who needs to study for a new exam

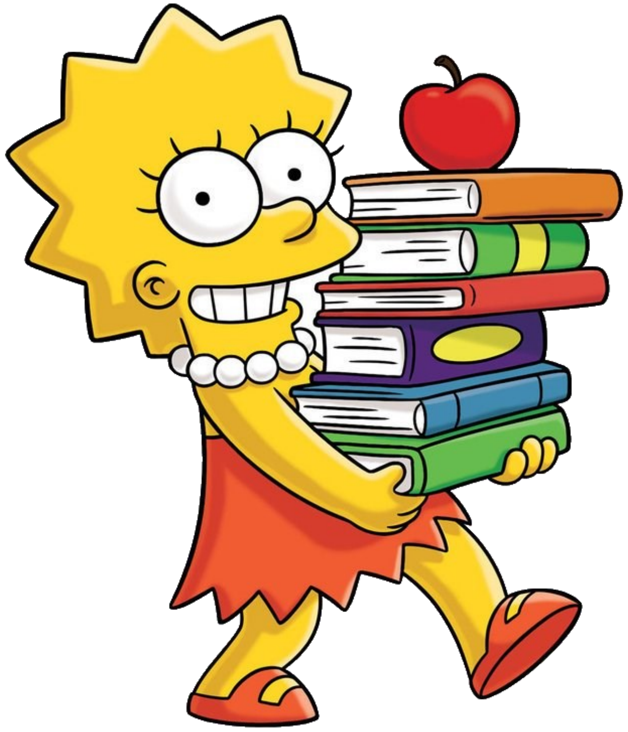


A simple example

What a **good** student does

- She studies the major part of the provided exercises, looking at the correct answers
- She keeps a small part of them to test its ability
- She finally checks if she has achieved the correct answer in the blind exercises

We provide to the student a series of exercises on which she can study

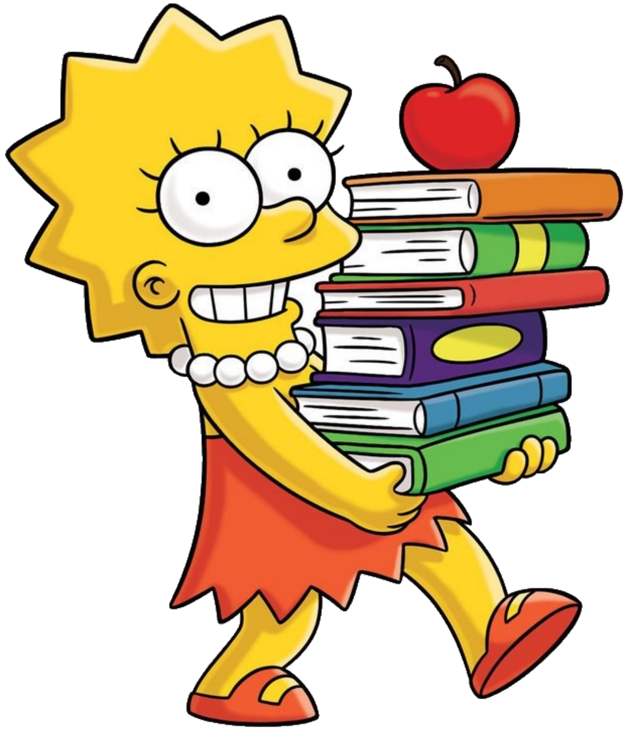


A simple example

What a **good** student **doesn't**

- She memorizes the entire set of the provided exercises
- She takes the correct answers using the entire set of available exercises
- She studies only one type of exercises since it should be the more likely for the exam

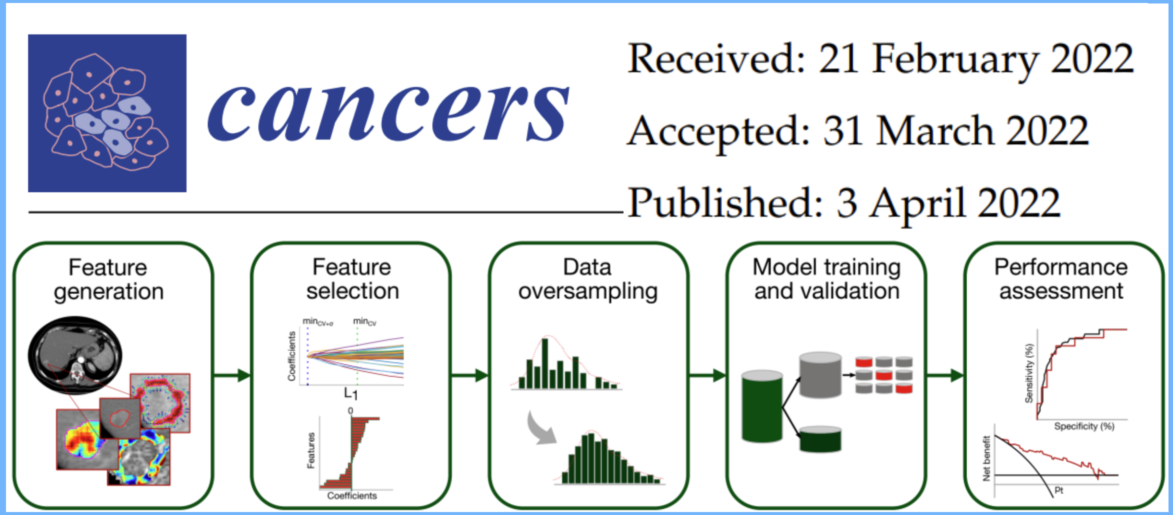
We provide to the student a series of exercises on which she can study



Real examples

The correct usage of the data is **fundamental** in any machine learning application

Example 1



Oversampling on the entire dataset

Real examples

The correct usage of the data is **fundamental** in any machine learning application

Example 2

[redacted] Cancer Imaging (2019) 19:60
https://doi.org/[redacted]

Cancer Imaging

RESEARCH ARTICLE Open Access

Data preprocessing

From … patient, 1044 sets of texture parameters were
extr… substitution to supplement some
text… missing individual
val… itive to MVI-
ne…
pling me… a
so that the ratio of th… 1:
1. Finally, we normalized the da… ea-
ture parameters were between (0, 1). The… of

Pre-processing on the entire dataset

methods, 21 methods were applied for radiomics research in our study. We divided the data into a training set and verification set. There were 148 patients in the training set and 58 patients in the verification set. Moreover, the train-

Real examples

The correct usage of the data is **fundamental** in any machine learning application

Example 3

European Journal of Radiology 145 (2021) 110013

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

ELSEVIER

RADIOLOGY

First, logistic regression analysis for predicting oncocytoma was performed using only the imaging derived parameters. A second model was constructed by adding the demographic parameters. Receiver Operating Characteristic (ROC) curves for both regression models were created and the area under the curve (AUC) was calculated. The optimal sensitivity and specificity were selected by maximizing the Youden's index (J = sensitivity + specificity-1). The ROC curves were compared using the DeLong method [29]. Standard errors (SE) and confidence intervals (CI) of AUC were calculated for comparison of the models

Model evaluation on the entire dataset

Real examples

The correct usage of the data is **fundamental** in any machine learning application

Example 4

cancers

Received: 23 June 2022
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Published: 25 July 2022

Abstract: *Background:* ChRCC and RO are two types of rarely occurring renal tumors that are difficult to distinguish from one another based on morphological features alone. They differ in prognosis, with

cross-validation. *Results:* The number of selected features with good model performance was 20, 40 and 6 for cohorts 1, 2 and combined, respectively. The best model performance in cohorts 1, 2 and combined had an excellent Area Under the Curve (AUC) of 1.00 ± 0.000, 1.00 ± 0.000 and 0.87 ± 0.073,

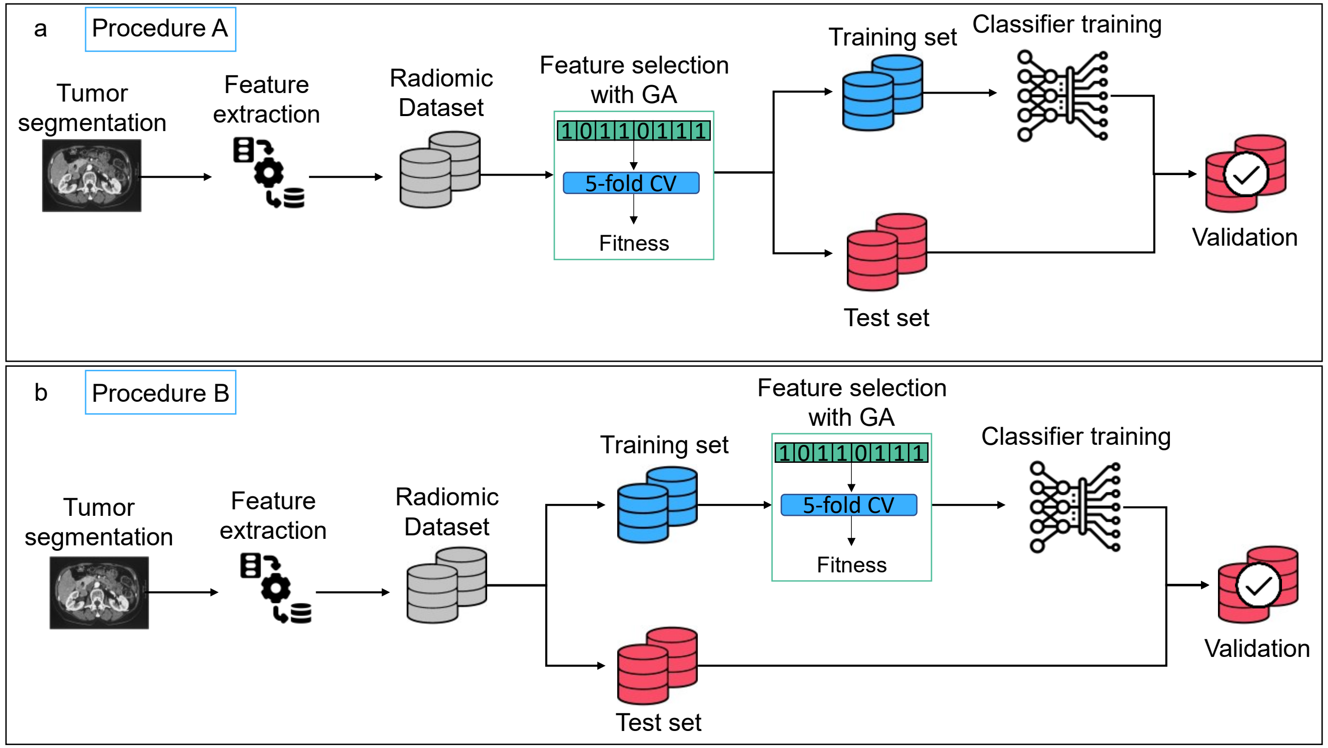
Renal cancer is no more an issue

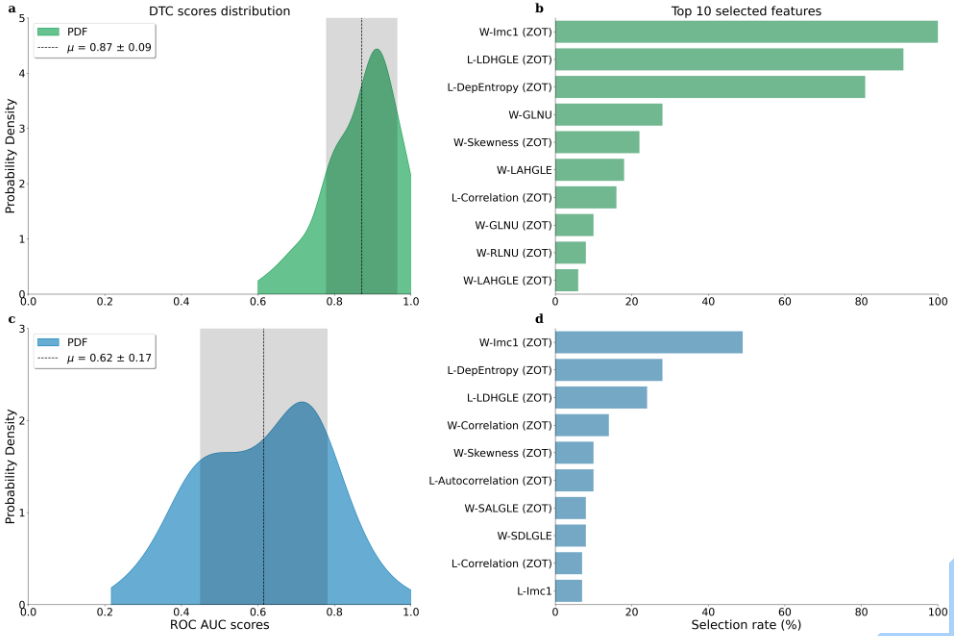
How can we check the correctness of our pipeline?

Carlini G. et al., *Journal of Personalized Medicine* (2023)

How can we check the correctness of our pipeline?

1. **Carefully** checking the steps of our pipeline
2. Testing our model on **new data**
3. Thinking about the **correctness** of the problem
4. Trying to **understand** what the model has learned

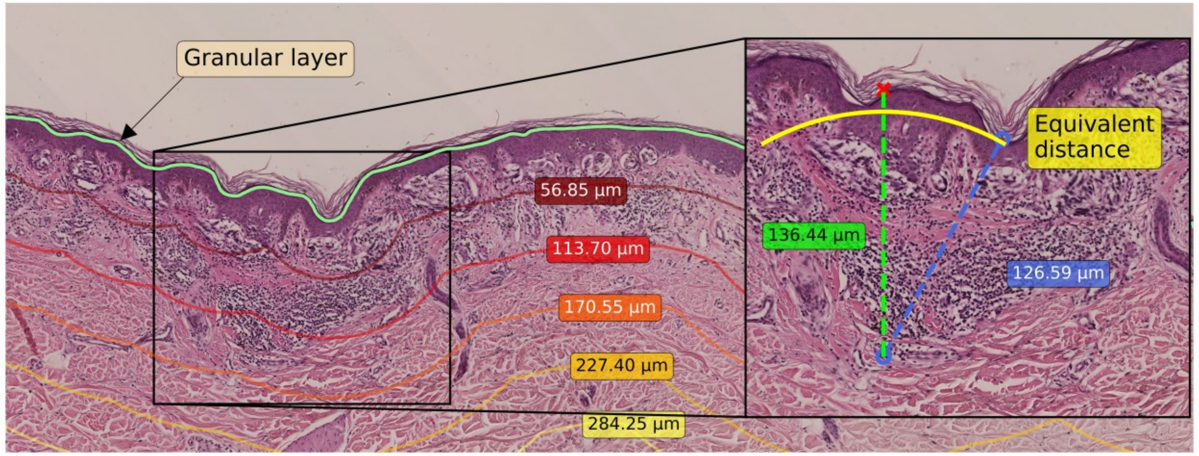




Thinking about the **correctness** of the problem

A real ill-posed problem example

Automated estimation of Breslow thickness in histopathological WSI of subjects affected by melanoma.



Curti et al., Breslow thickness: geometric interpretation, potential pitfalls , and computer automated estimation, *Pathology - Research and Practice* (2022)

university-based institutions in Italy. A recent study from the US reported that in the absence of a second opinion for pathologic interpretation of melanocytic skin lesions, 16.8% of cases would receive a reference-disconcordant diagnosis, resulting in 16,850 disconcordant diagnoses per 100,000 biopsies in the US each year with health care costs during the subsequent year estimated at $132,301,000 (95% CI,

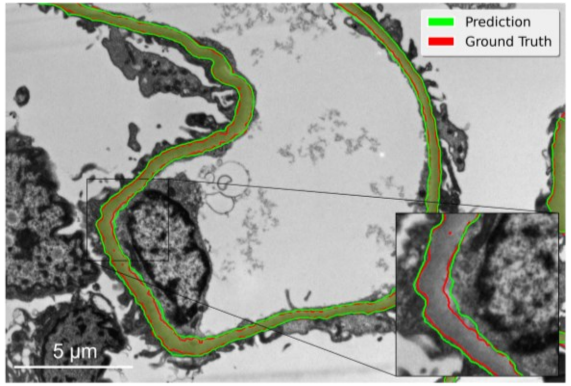
Curti et al., Advantages of manual and automatic computer-aided…, *Pathology - Research and Practice* (2022)

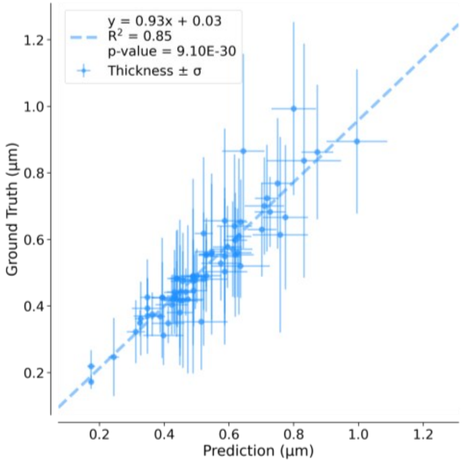
How to teach a machine to «replace» human intervention if human discord is so high?!

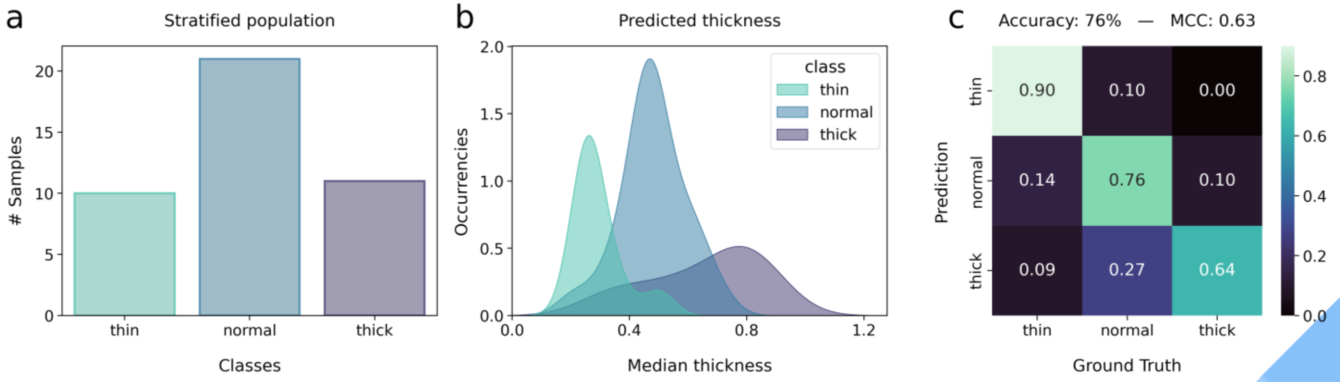
Thinking about the **correctness** of the problem

A real ill-posed problem example

Automated estimation of GBM thickness in TEM images for the renal transplant diagnosis.







Curti et al., Fully automated estimation of glomerular basement membrane thickness…, *Kidney International* **[Under review]**

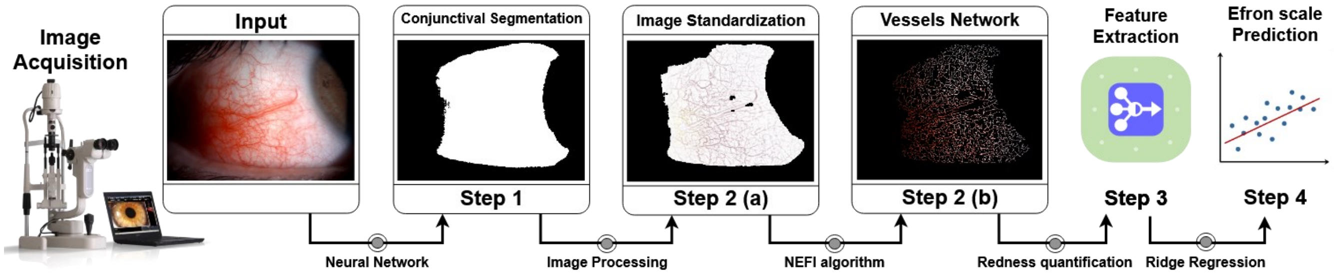
How to teach a machine to «replace» human intervention if human error is so high?!

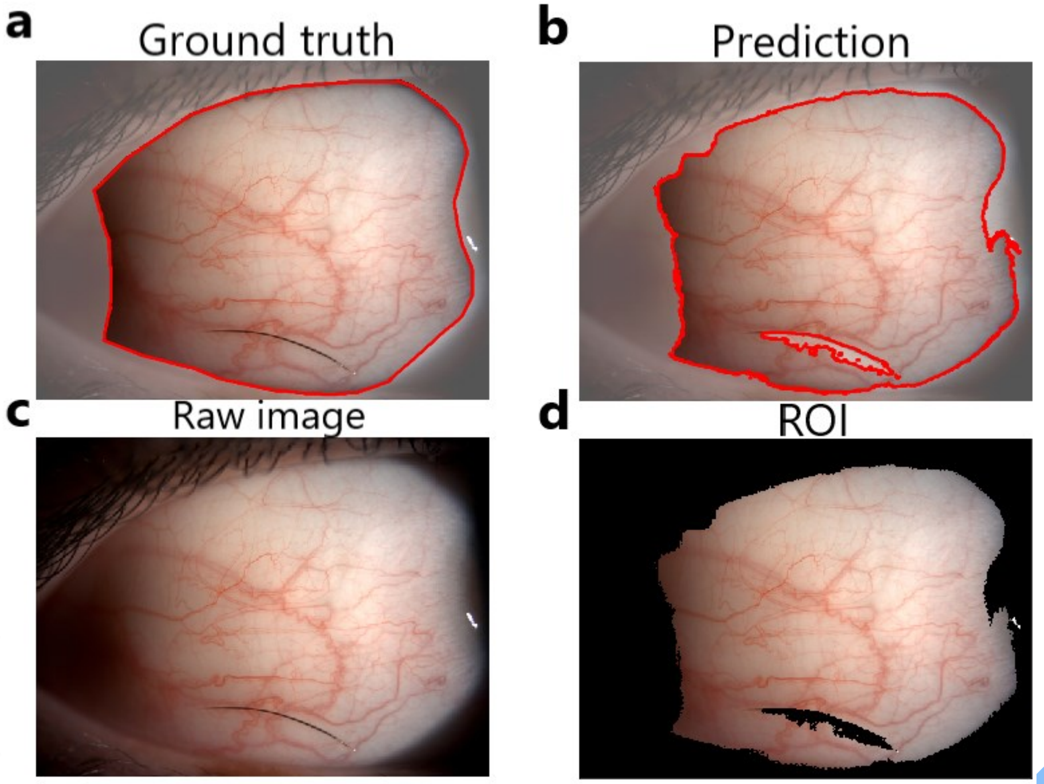
Curti N. et al., A fully automated pipeline for a robust…, *Applied Sciences* (2021)

Trying to **understand** what the model has learned

A real "simple" problem example

Fully automated estimation of conjunctival hyperemia in slit lamp images.

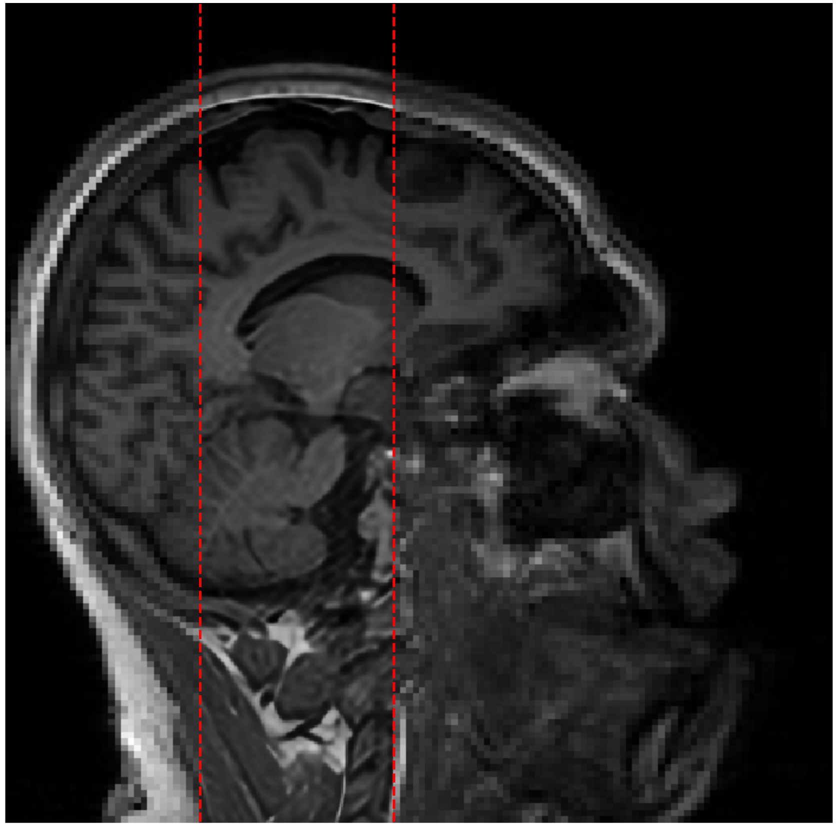




Trying to **understand** what the model has learned

A real "simple" problem example

Can a deep learning super resolution model be used on medical images without any kind of re-training or fine-tuning?



Fiscone C. et al., Generalizing the Enhanced-Deep-Super-Resolution neural network to brain MR..., *eNeuro* **[Under Review]**

If the problems are more difficult?

It is not always so simple to understand what a model has learned!

Especially when we work with High Dimensional datasets!

Radiomic Analysis

Radiomics – Machine Learning

Big Data Analysis
Large amount of information available from each image

Image processing
Several filters and image processing applied

Computer vision
Image features related to morphology and textures

Deep learning models
Valid input for machine learning pipelines and deep learning models

All the codes are open source

https://pyradiomics.readthedocs.io

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
- <u>Easy extraction of the results</u>

Vs

Cons

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

There are no alternatives!

Our Aim

Propose a **novel** approach to medical image **feature extraction**

Requirements

- Easy interpretation of the results
- Complementary information to Radiomic ones
- Simplify the morphological analysis
- Fast evaluation
- Compatible with standard clinical user interface

Medical Image Acquisition

Image Preprocessing

Image Feature Extraction

Radiomic Analysis + **New Technique**

Outcome prediction

Graphomic Analysis

The aim of the **graphomic** analysis is to leverage topology to extract a series of informative features

Image acquisition

Volume Segmentation

Volume Skeletonization

Skeleton-graph Extraction

Network-based features

This approach could be linked also to the *Extended Reeb Graph Theory* (Shinagawa et al., **1991**)

Graphomic Analysis

Image acquisition

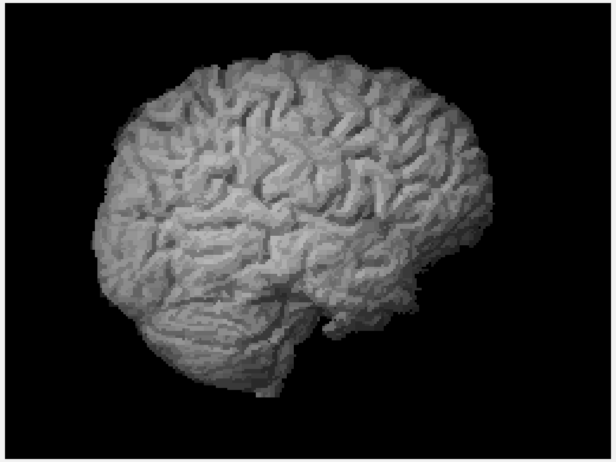
1

Medical Image acquisition in any standard formats

Volume Segmentation

2

Volume identification with arbitrary models

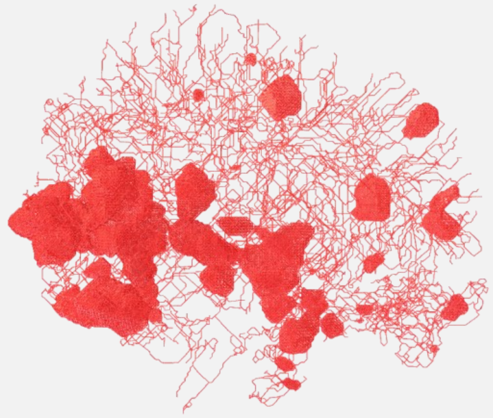


Graphomic Analysis

Volume Skeletonization

3

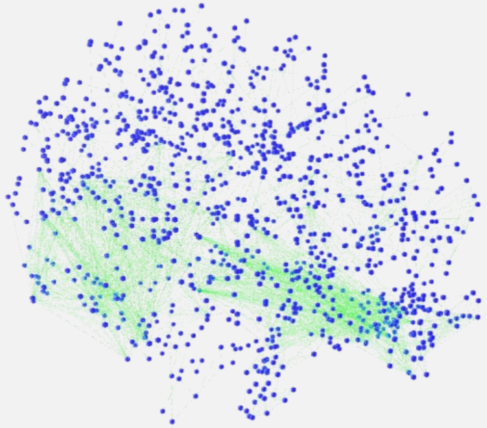
Volume simplification via skeletonization



Skeleton-graph Extraction

4

Skeleton graph extraction via custom algorithm



Graphomic Analysis

Network-based features

5

Graphomic feature extraction

Topology

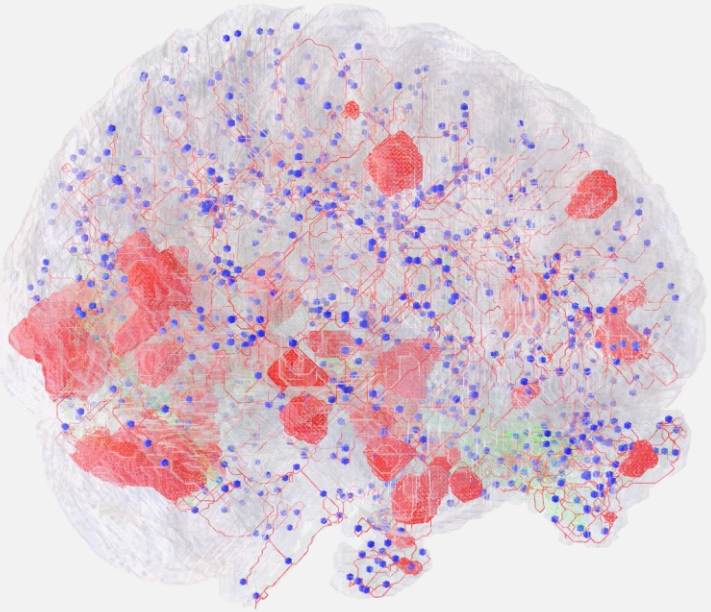
- Nodes
- Edges
- Weights
- Modularity
- Euler number
- Node type statistics
- etc.

Centrality

- Degree
- Betweenness
- Clustering
- Closeness
- Page-rank
- Harmonic
- etc.

Spatial

- Node density
- Fractal dim
- Shortest paths
- Eccentricity
- Node distances distribution
- etc.

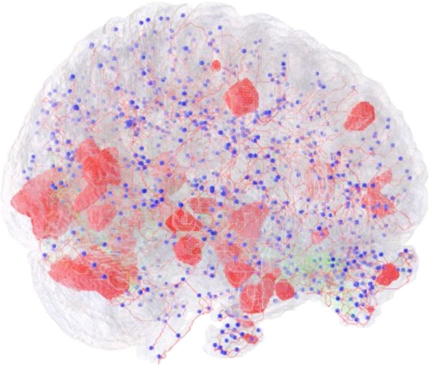


Graphomic Analysis

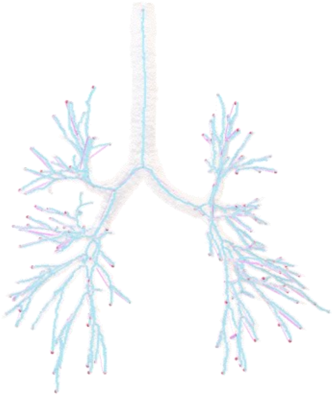
Graphomic analysis is totally independent from the image acquisition modality and **anatomical district**

Skeleton - bones -

Brain



Lung - airways -



Conclusion

Still Private

https://github.com/Nico-Curti/graphomic

Obtained results

- **Novel** approach to medical image analysis
- Toolkit ~~publicly available~~ for graphomic feature extraction
- Applicability to any **2D** and **3D** binary image/volume
- Fast extraction of the network-based features: $\sim$ **1** minute per patient
- **Easy explainability** of the results for clinical application

Future works

- **Validation** of the results with multiple datasets
- Extension of the graphomic approach to other relevant **medical** tasks
- Extension of the graphomic approach to other **machine learning** tasks

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