RADIOMICS ANALYSIS OF 11C-METHIONINE PET/CT IMAGES THROUGH A MACHINE LEARNING APPROACH

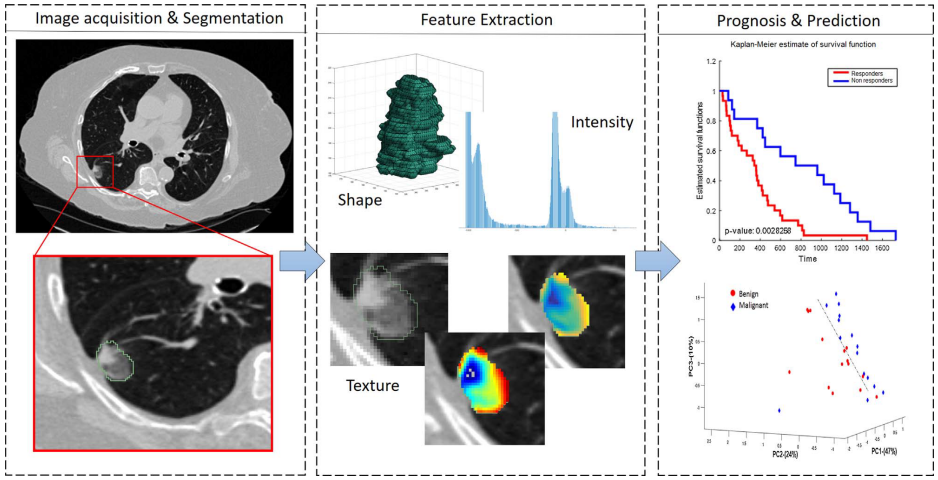
Selene Richiusa

Alessandro Stefano, Albert Comelli, Maria Gabriella Sabini, Gaetano Savoca, Sebastiano Cosentino, Massimo Ippolito, Giorgio Russo

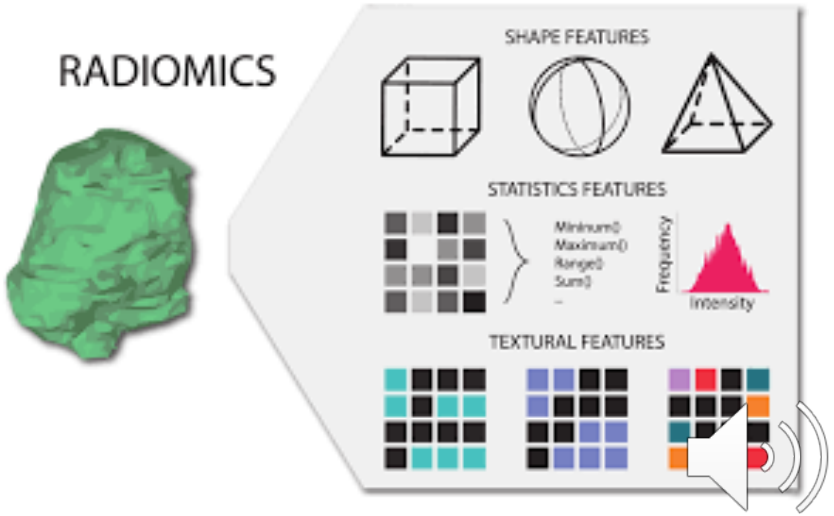
INTRODUCTION
DEFINITION OF RADIOMICS:

Radiomics is a new multi-disciplinary science that aims to quantitatively analyze a diagnostic image, through the extraction of features with a statistical and informatic approach, to provide information on the pathophysiology of the underlying tumor, which cannot be qualitatively appreciated by the human eye.

WORKFLOW IN RADIOMICS



CATEGORIES OF FEATURES

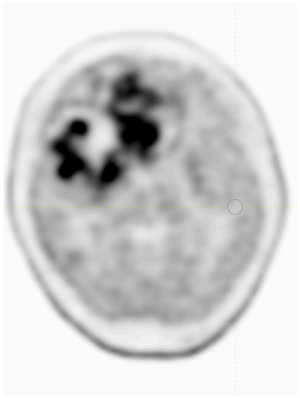


Radiomics and radiogenomics in lung cancer: A review for the clinician

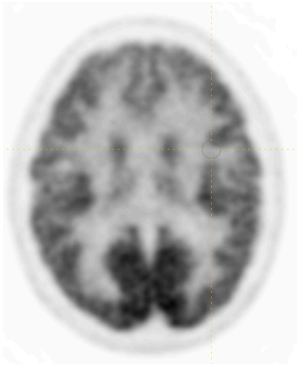
Rajat Thawani[a,b,*,1], Michael McLane[b,1], Niha Beig[b], Soumya Ghose[b], Prateek Prasanna[b], Vamsidhar Velcheti[c], Anant Madabhushi[b]

AIM OF THE RESEARCH

Is to identify a relevant prognostic model concerning a real clinical problem, in a dataset of 56 patients with brain tumors underwent 11C-methionine-PET exams, to discriminate between low- and high-grade tumors.



11C-MET



18F-FDG

OSPEDALE CANNIZZARO CATANIA
AZIENDA OSPEDALIERA PER L'EMERGENZA

Data Acquisition: The images presenting the required conditions was acquired by different Tomographs:

Tomographs	Number of images	LOW GRADE "0"	HIGH GRADE "1"
ALL	56	17	39
GE DISCOVERY 690	32	9	23
Siemens BIOGRAPH HORIZON	24	8	1[illegible]

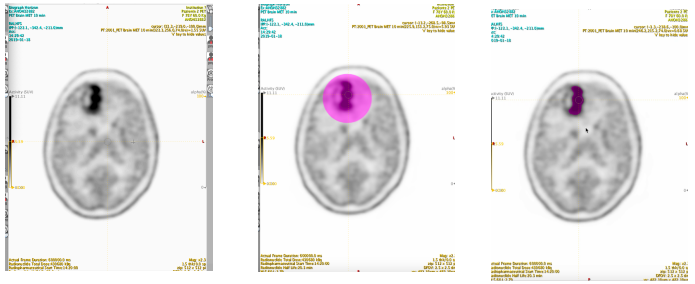
EXPERIMENTAL METHOD

LifeX Software:

Local Image Features Extraction
— LIFEx —

C. Nioche, F. Orlhac, I. Buvat

LIFEx version 6.nn,
Last update of document: 2019/12/26



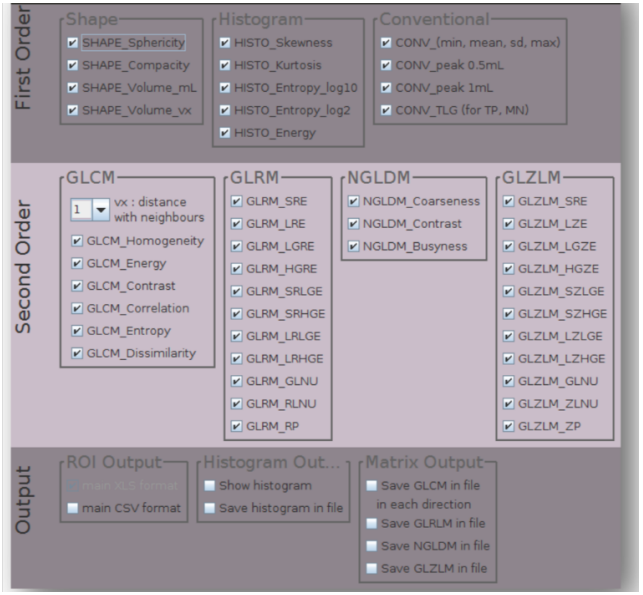
- Visualization of the image:

Pre-processing:
0-64 intensities / 0-20 SUV

- Segmentation of the volume of interest:

Threshold method = $\begin{cases} tumor & if \quad f(x,y) \geq T \\ non\ tumor & if \quad f(x,y) < T \end{cases}$

T = 40% SUVmax



- Extraction of features (44):

4 Shape features
4 Conventional features
5 Histogram features
31 Textural features

- The files acquired for each patient were two:

1. The extraction of features from the segmented volume (Threshold ROI).
2. A ROI of 81 voxels was designed on the SUV max, to eliminate dependence on the segmented volume (Fixed ROI).

	FEATURE-1	FEATURE-2	....	FEATURE-m
PATIENT-1				
PATIENT-2				
...				
PATIENT-n				

Y
0
0

'X' matrix:
n rows (patients)
m columns (features)

'Y' vector:
1 = high grade
0 = low grade

DATA ANALYSIS

Proposed Method of Features Selection

1. For each column of matrix X, calculate the point biserial correlation (pbc) index between variables x (features) and dichotomic variable y.

$\bar{x}_1$, *be the corresponding averages the values of* x *which are paired with* $y = 1$ (n_1)
$\bar{x}_0$, be the corresponding averages the values of x which are paired with $y = 0$ (n_0)
$\bar{x}$ the total average (n)

$$pbc = \frac{\sqrt{\frac{n_1 n_0}{n}}(\bar{x}_1 - \bar{x}_0)}{\left[\sum_{i=0}^{1}\sum_{j=1}^{n_i}(x_{ij} - \bar{x})^2\right]^{1/2}}$$

2. Sort the X columns in descending order of absolute value of point biserial correlation index

3. Start a WHILE-DO cycle, and it is done a logistic regression analysis, through function 'FITGLM' in Matlab, where one of the outputs is the p-value:

WHILE (p-value decreases)
Add regressor column and perform logistic regression
DO
Add last regressor column

Relevant Features

TOMOGRAPH	FEATURES	p-VALUE
ALL	NGLDM	0.1615
	Busyness	0.3207
	GLZLM LZLGE	
GE	GLRLM LRLGE	0.05
	GLZLM LZLGE	0.137
SIEMENS	HISTO Skewness	0.0136
	CONV SUV	0.0136

Fixed ROI

TOMOGRAPH	FEATURES	p-VALUE
ALL	SHAPE Sphericity	0.0314
	SHAPE Compacity	0.0215
	HISTO Kurtosis	0.0232
GE	GLRLM LRLGE	0.0481
	GLRLM LGRE	0.117
SIEMENS	GLCM Correlation	0.00036
	SHAPE Compacity	0.0014

Threshold ROI

DATA ANALYSIS

Machine Learning Model: Discriminant Analysis

- Classification: the process of predicting a qualitative response Y, starting from a set of predictors X
- Supervised learning: use labeled data (to map the data to the desired output classification)

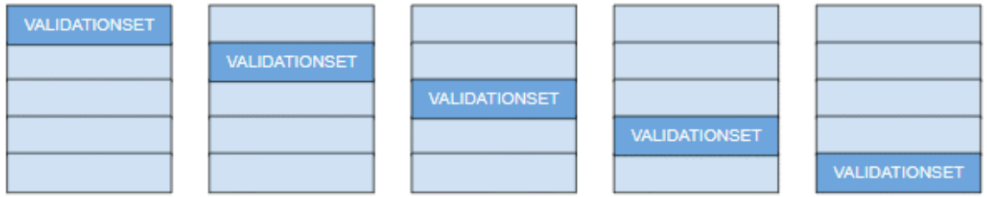
Training set:
a set of examples, represented as a pair of an input vector (features) and a desired output value (target or category label).

Classifier: the classification algorithm analyzes the training data and infers a hypothesis (function), which can be used to predict new outputs. In matlab the function "mdl = fitcdiscr(X,Y)" returns a discriminant analysis classifier based on the input variables X and response Y.

Validation set:
The performance of a model is estimated on a validation sample

Each time, one of the k subsets is used as the validation set, and the other k-1 subsets are put together to form a training set.
This step is useful in the case of a small amount of data.

K-fold Cross Validation



K=5

DATA ANALYSIS

Performance Evaluation

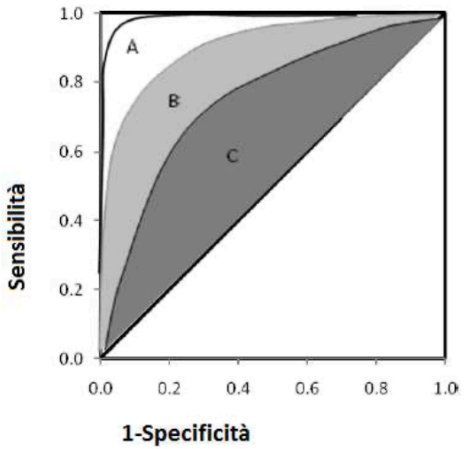
y = observed value
$\hat{y}$ = predicted value

$$
\begin{aligned}
&if \quad y = 0 \quad and \quad \hat{y} = 0 \quad \Leftrightarrow \quad correct \quad prediction, true \quad negative(TN)\\
&if \quad y = 1 \quad and \quad \hat{y} = 1 \quad \Leftrightarrow \quad correct \quad prediction, true \quad positive(TP)\\
&if \quad y = 0 \quad and \quad \hat{y} = 1 \quad \Leftrightarrow \quad false \quad positive(FP)\\
&if \quad y = 1 \quad and \quad \hat{y} = 0 \quad \Leftrightarrow \quad false \quad negative(FP)
\end{aligned}
$$

$$Sensitivity = \frac{TP}{TP + FN} \qquad Specificity = \frac{TN}{TN + FP} \qquad Accuracy = \frac{TP + TN}{TP + FP + FN + TN}$$

ROC CURVE:
Receiver Operating Characteristics

AUC INDEX (Area under the Curve):
is the area of the surface enclosed between the ROC curve and the bisector of the first quadrant (case of the random classifier).



AUC = 0.5 non-informative

AUC > 0.7 significant value

AUC = 1.0 perfect

RESULTS

Threshold ROI

TOMOGRAPH	SENSITIVITY	SPECIFICITY	ACCURACY Error
ALL	52.44 %	76.62 %	70.31 % 29.69%
GE	71.76 %	83.76 %	80.51 % 19.49%
SIEMENS	86.67 %	84.86 %	84.98 % 15.02%

Fixed ROI

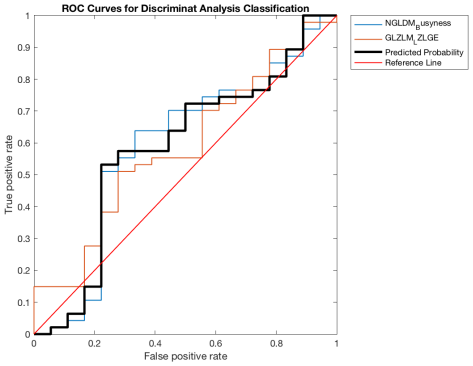
TOMOGRAPH	SENSITIVITY	SPECIFICITY	ACCURACY Error
ALL	41.17 %	63.60 %	57.25 % 42.75%
GE	28.52 %	88.47 %	71.64 % 28.36%
SIEMENS	76.67 %	71.81 %	72.88 % 27.12%

1. Our workflow achieves, using an innovative feature selection method, good performance, in terms of accuracy, which is greater than 70.31% and specificity, which is greater than 71.81% , in all cases except when we consider both scanners using the fixed ROI.

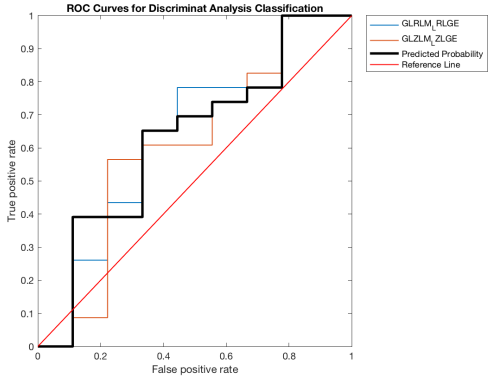
2. Higher performance values are found for the data set of threshold ROI. We can conclude that there are no particular advantages in using a homogeneous region of interest (e.g. fixed ROI) rather than a variable ROI among patients (e.g. thresholding method).

RESULTS

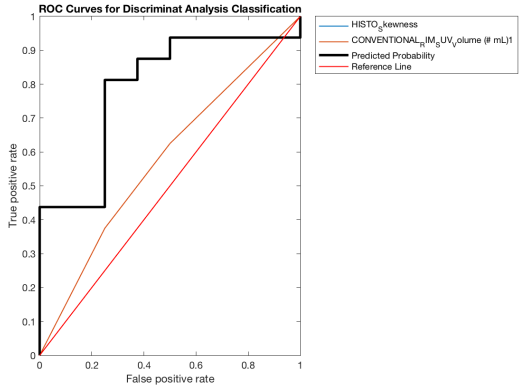
ROC CURVE - FIXED ROI



TOMOGRAPH	AUC (95%CI)
ALL	58.51% 41.75/75.27 %

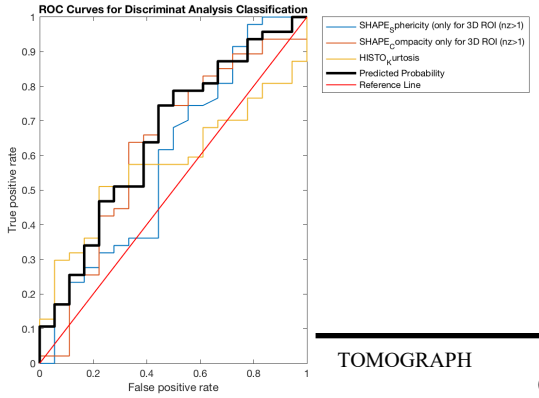


TOMOGRAPH	AUC (95%CI)
GE	62.80% 39.15/86.45%

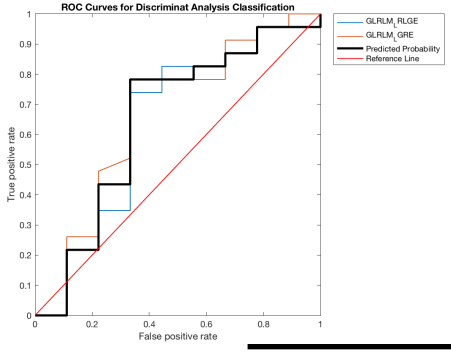


TOMOGRAPH	AUC (95%CI)
SIEMENS	78.91% 58.80/99.01%

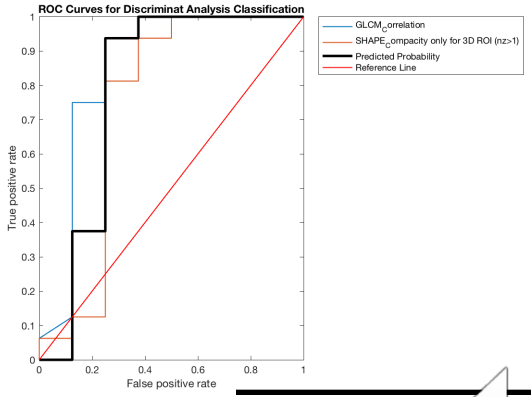
ROC CURVE – THRESHOLD ROI



TOMOGRAPH	AUC (95%CI)
ALL	64.13% 49.76/80.50%



TOMOGRAPH	AUC (95%CI)
GE	65.73% 40.04/89.43%



TOMOGRAPH	AUC (95%CI)
SIEMENS	78.91% 51.96/105.85%

CONCLUSIONS

- Low-performance values are noted for the AUC (< 78.91%): The main cause is the low number of patients. In addition, the patient dataset is unbalanced. For better performance, a machine learning algorithm should work with the same number of "objects" for both classes. The group that shows the most symmetry is the one related to Siemens, in fact, in all the results we notice higher values.

Tomographs	Number of images	LOW GRADE "0"	HIGH GRADE "1"
ALL	56	17	39
GE DISCOVERY 690	32	9	23
Siemens BIOGRAPH HORIZON	24	8	16

- In all cases lower values are noticed when the scanners are united in the same group "ALL". This is a particular limitation: radiomics features are affected by acquisition parameters, reconstruction algorithm, slice thickness, voxel size, thus hampering multicenter studies.

Radiomics is a new discipline and for this reason it needs standardization and future studie