CRO
AVIANO

Methods for radiomics analysis

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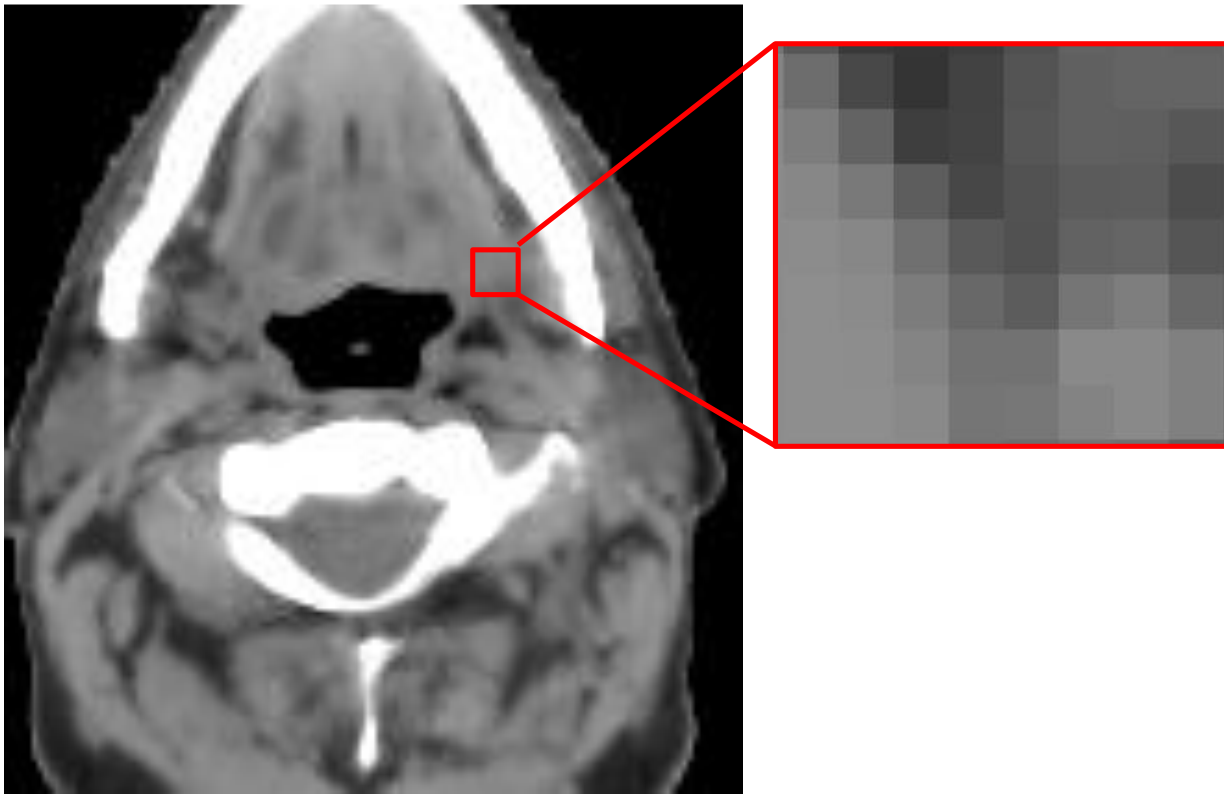
“Images are more than pictures, they are data”

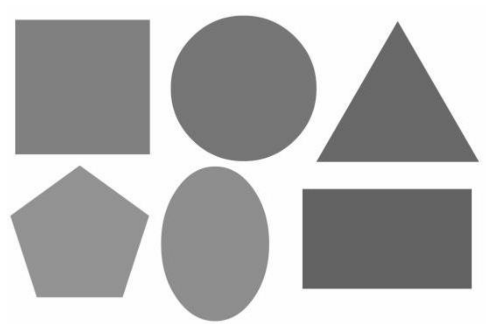


1	3	4	5	3	2	2	1
1	2	3	4	3	3	2	3
1	1	2	3	3	3	3	4
1	1	1	2	2	2	2	3
1	1	0	1	1	1	1	2
0	0	0	1	2	0	0	1
0	0	0	0	0	0	0	1
0	0	0	0	0	0	0	0

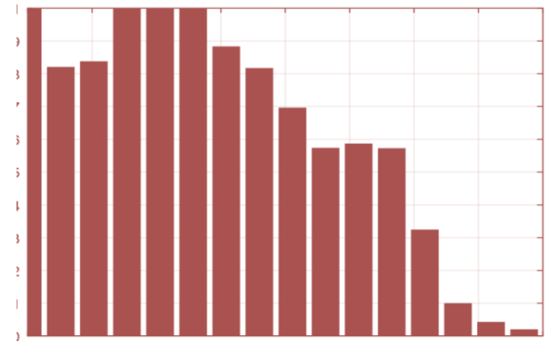
Gillies, Radiology 2016;278:563-577.

Radiomic features

Shape



Histogram (1st Order)



Textural (2nd order)

Higher order

Avanzo et al. Phys Med 38 (2017) 122-139

Radiomic features

Shape

$$compactness\ 2 = 36\pi \frac{A^2}{V^3}$$

Histogram (1st Order)

$$kurtosis = \frac{\frac{1}{N}\sum_i \left(X(i) - \bar{X}\right)^4}{\left(\frac{1}{N}\sum_i \left(X(i) - \bar{X}\right)^2\right)^2}$$

$$entropy = \sum_i \left(P(i)\log_2 P(i)\right)$$

Textural (2nd order)

$$autocorrelation = \sum_{i.j} i * j * P(i, j)$$

$$cluster\ shade = \sum_{i.j} (i + j - 2\mu)^3 * P(i, j)$$

Higher order

$$coarseness = \frac{1}{\varepsilon + \sum_i P(i)s(i)}$$

Avanzo et al. Phys Med 38 (2017) 122-139

Textural features

- The gray-level co-occurrence matrix (GLCM) is a matrix whose row and column numbers represent gray values, and the cells contain the number of times corresponding gray values are in a certain relationship (angle, distance).

Test image

1	1	2	2
1	1	2	2
1	3	3	3
3	3	4	4

GLCM 0°

4	2	1	0
2	4	0	0
1	0	6	1
0	0	1	2

GLCM 90°

6	0	2	0
0	4	2	0
2	2	2	2
0	0	2	0

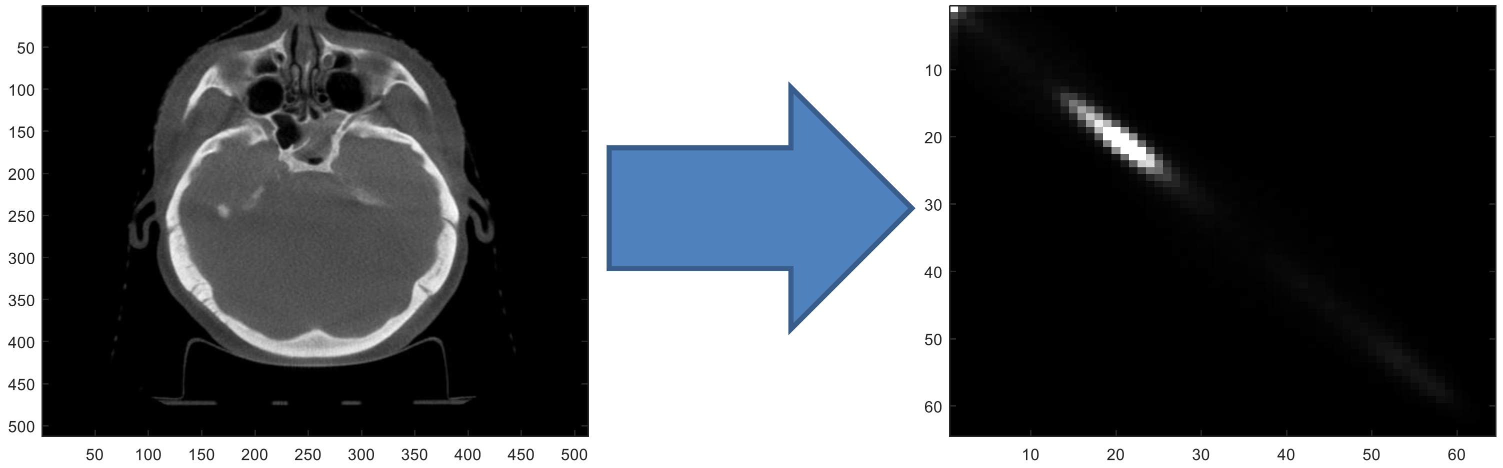
GLCM 135°

2	1	3	0
1	2	1	0
3	1	0	2
0	0	2	0

GLCM with distance one pixel along directions 0°, 90°, 135°

Textural features

- The gray-level co-occurrence matrix (GLCM) is a matrix whose row and column numbers represent gray values, and the cells contain the number of times corresponding gray values are in a certain relationship (angle, distance).



$$autocorrelation = \sum_{i,j} i * j * P(i, j)$$

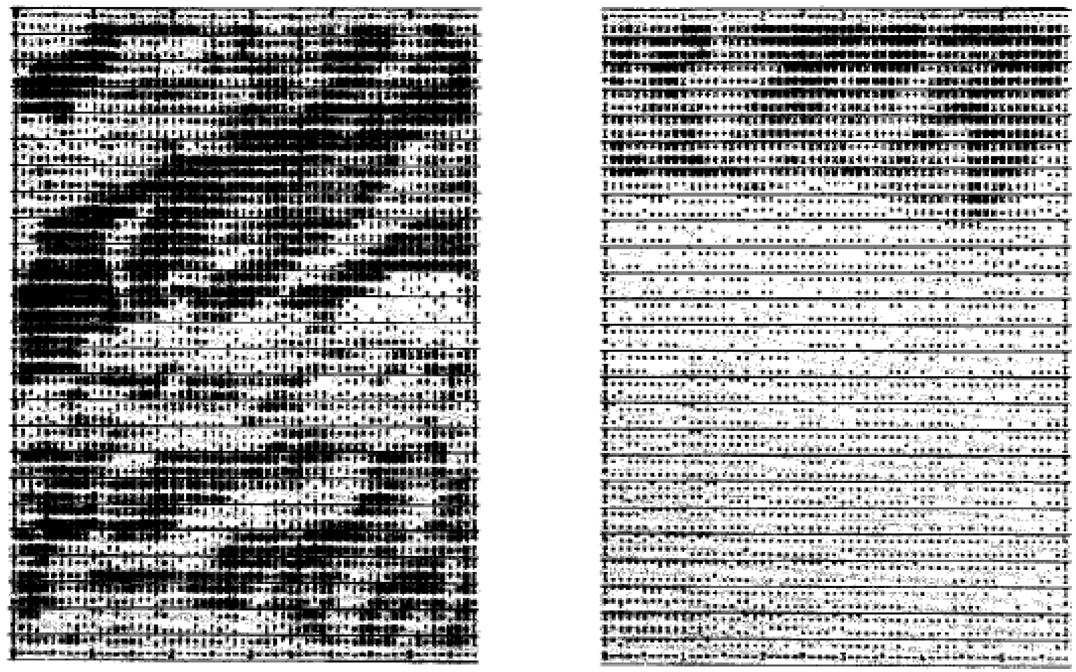
represents the correlation of the image along the specified direction

$$cluster\ shade = \sum_{i,j} \left(i + j - 2\mu\right)^3 * P(i, j)$$

P(i,j) = element of GLCM, μ = average of GLCM

When were features born?

- GLCM



	Grassland			Water Body		
Angle	ASM	Contrast	Correlation	ASM	Contrast	Correlation
0°	.0128	3.048	.8075	.1016	2.153	.7254
45°	.0080	4.011	.6366	.0771	3.057	.4768
90°	.0077	4.014	.5987	.0762	3.113	.4646
135°	.0064	4.709	.4610	.0741	3.129	.4650
Avg.	.0087	3.945	.6259	.0822	2.863	.5327

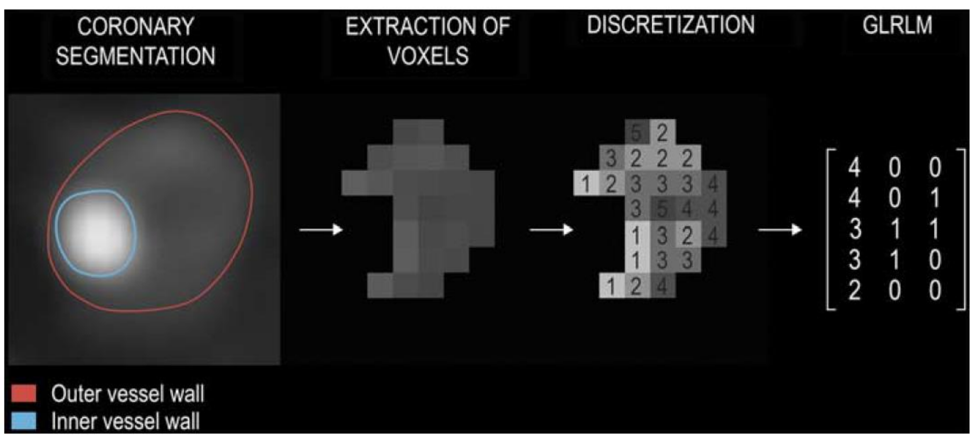
(a) (b)

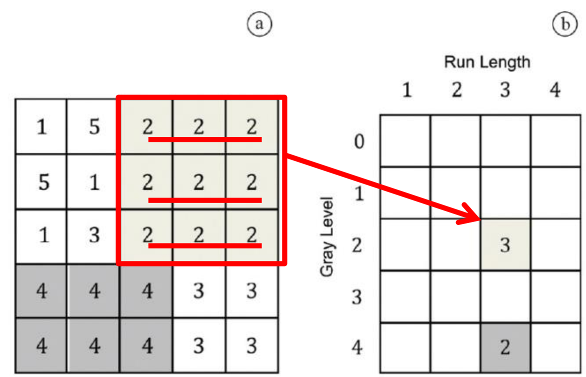
Fig. 4. Textural features for two different land-use category images.

Haralick 1973

Textural features

- Gray Level Run Length Matrix (GLRLM) is a two-dimensional matrix in which each element describes the number of times j a gray level i appears consecutively in the direction specified





. GLRLM matrix calculation for θ = 0°. (a) ROI 5×5; (b) Occurrences of gray levels with run length of k = 3.

Wanderley Rev. Bras. Eng. Bioméd 30 (1) 17-26, 2014; Journal of Thoracic Imaging · March 2017

Higher order variables

- In the neighborhood gray-tone difference matrix (NGTDM), the ith entry is a summation of the differences between all pixels with gray-tone i and the average value of their surrounding neighbors

Image

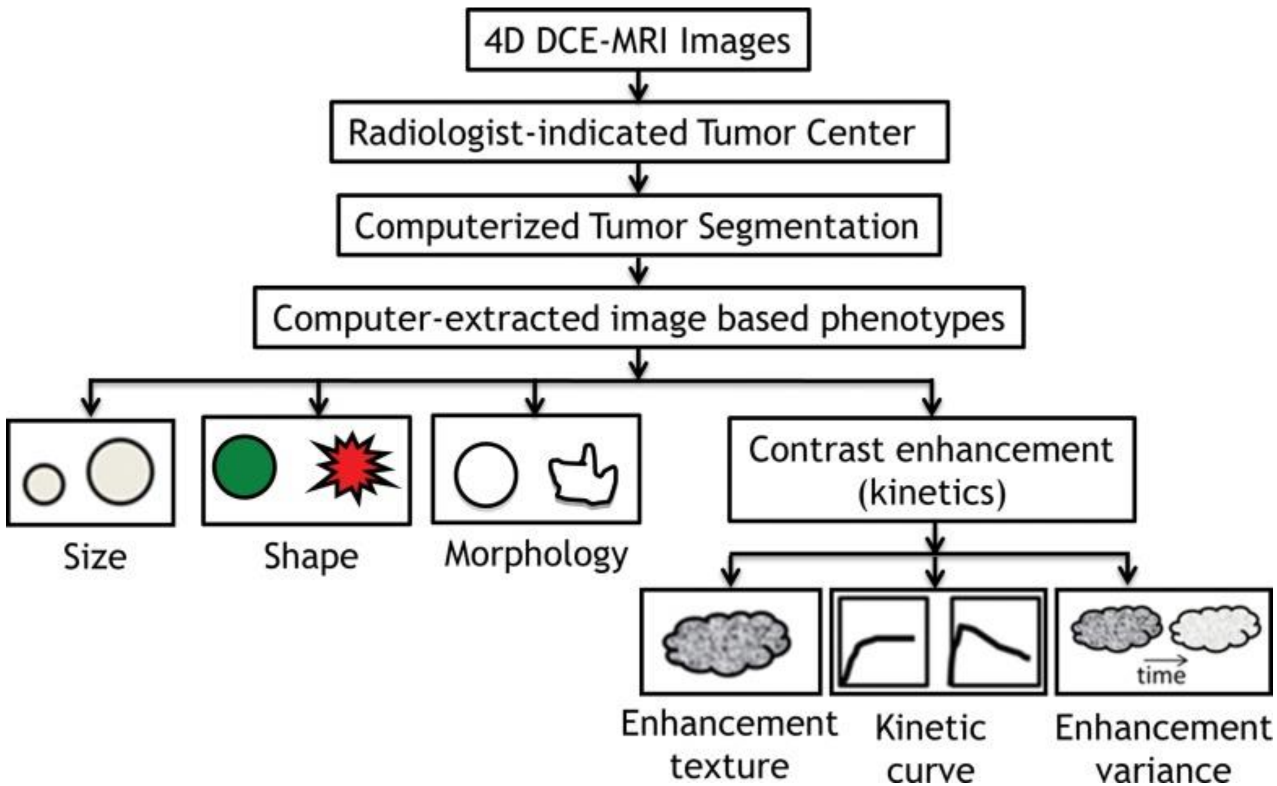
3	2	0	1	0
1	**2**	**1**	**3**	0
3	**1**	**0**	**2**	3
1	**2**	**3**	**0**	3
0	0	0	0	1

NGTMD

j	*S(j)*
0	3.25
1	1.00
2	2.00
3	4.25

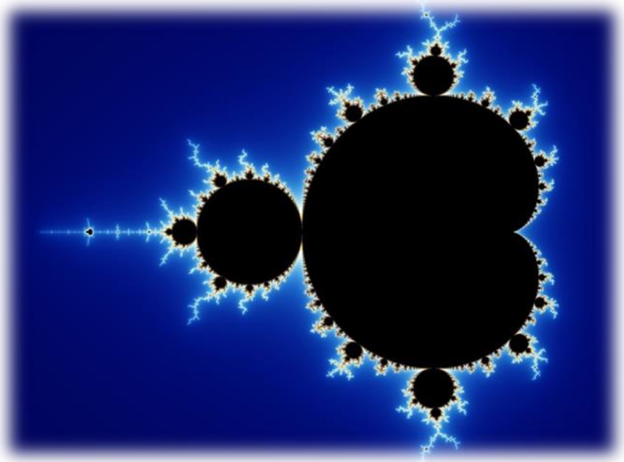
Kynetic variables

- Pharmacokinetics (uptake rate of contrast agent, washout…)
- Evolution in time of radiomic features in 4D DCE-MRI



Other features

Fractal

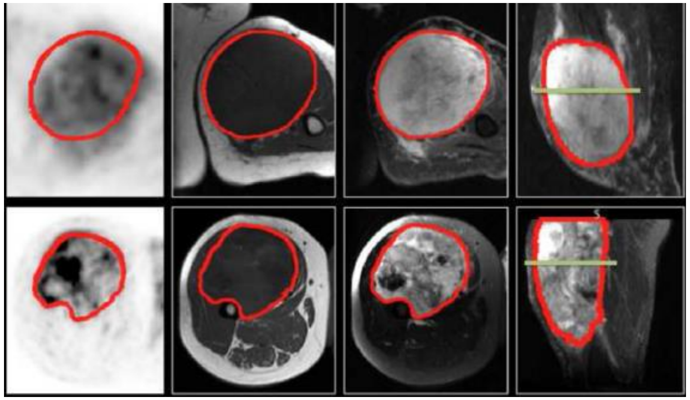


Hausdorff's fractal dimension refers to self-repeating textures of a pattern as one magnifies the feature:

$$D_0 = -\lim_{\varepsilon \to 0}(\log_{\varepsilon} N(\varepsilon)) = \lim_{\varepsilon \to 0} \frac{\log(N(\varepsilon))}{\log(\varepsilon^{-1})}$$

where N(ε) is the number of ε × ε squares needed to cover the 2D area.

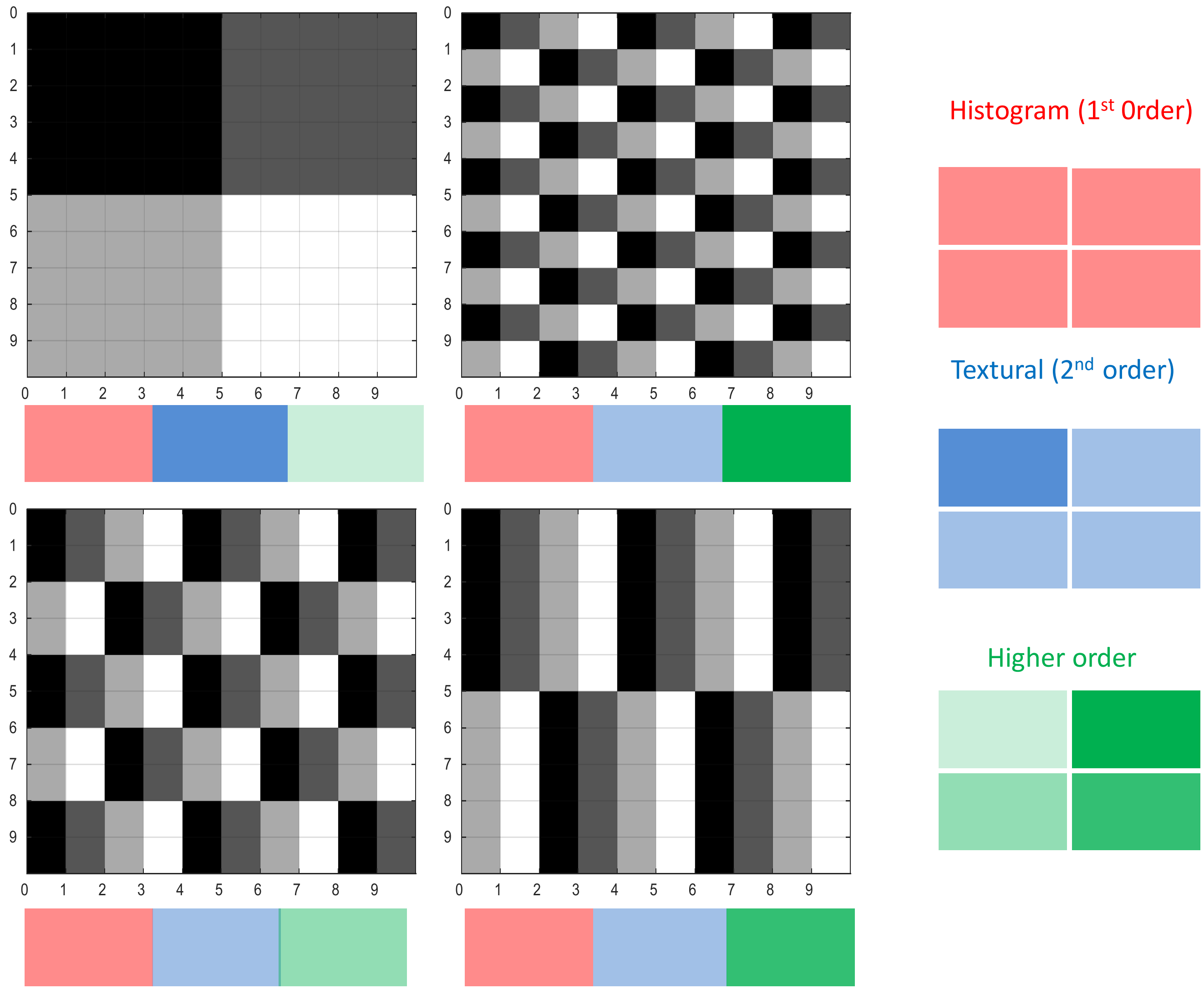
Fusion



Vallieres, Phys. Med. Biol. **60** (2015) 5471

Wavelet discrete trasform can be used to fuse images. The weight of wavelet bands in fusion can be used as a feature

Radiomic features



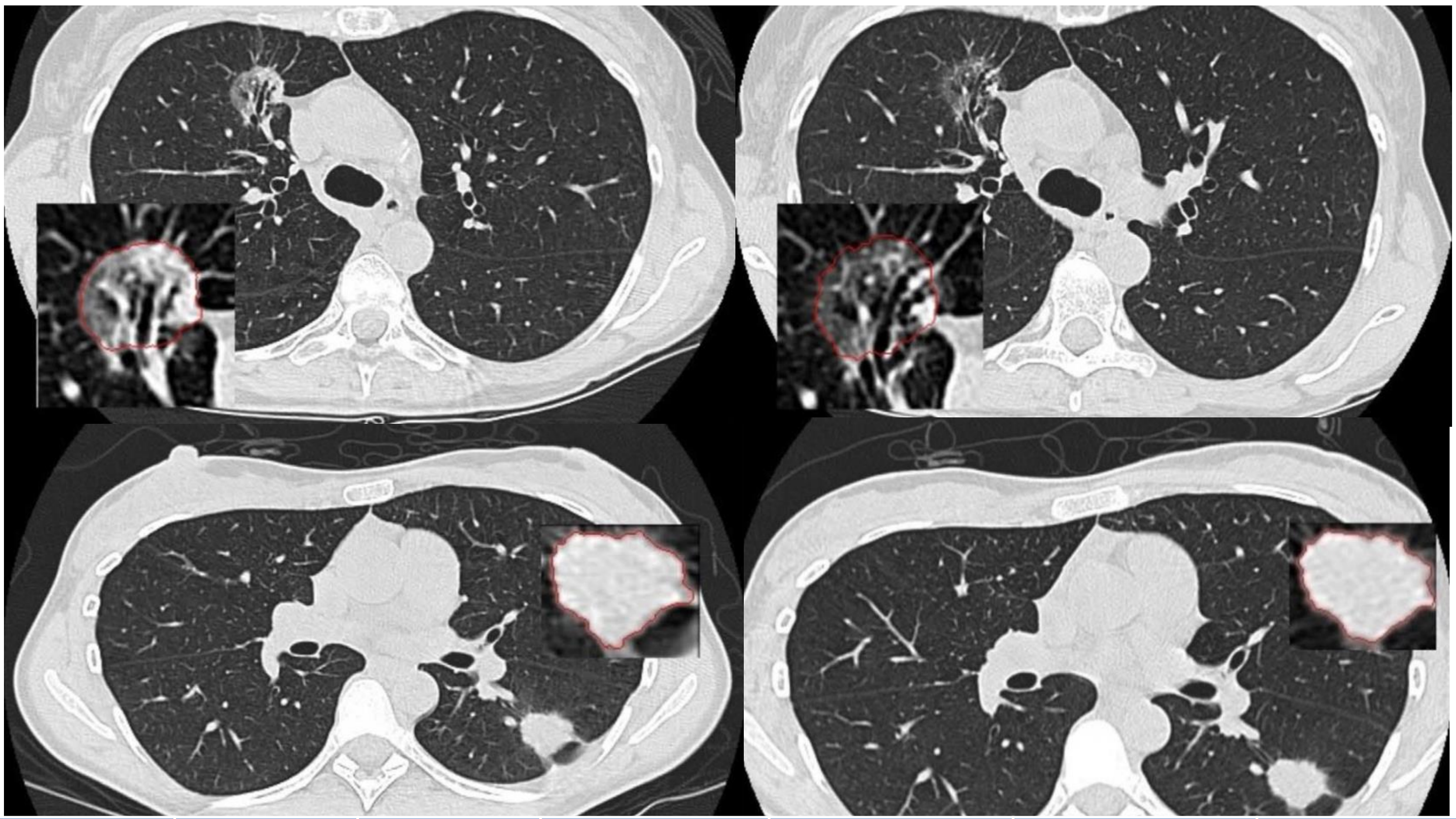
Aerts et al. Sci Rep 6 (2016) 33860

Radiomic features vs EGF mutation status

pre-RT post-RT

EGF +

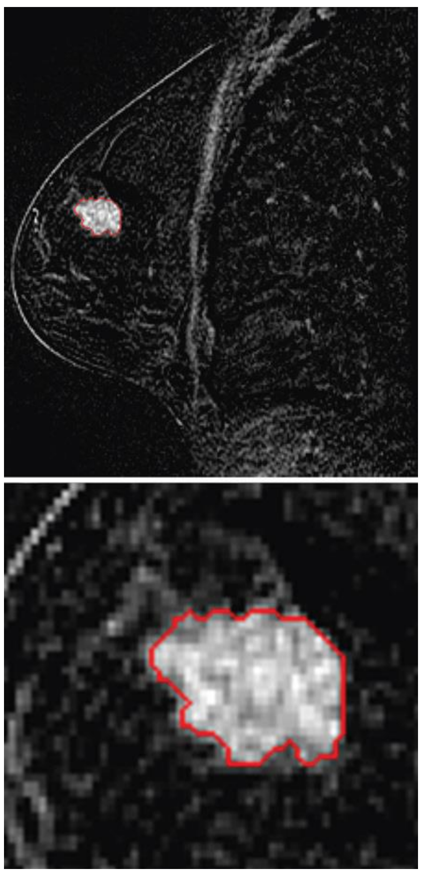
Wildtype

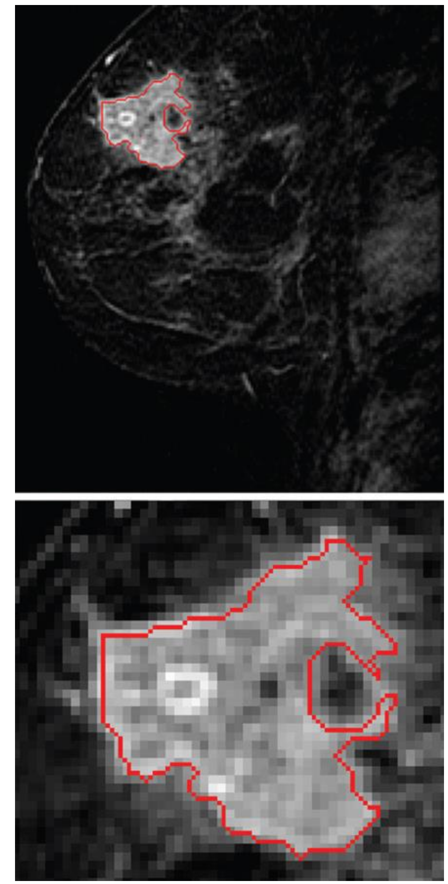


EGFR status	CT acquisition	Volume	Radius_Std	Shape_SI6	Gabor_Energy-dir135-w3	Gabor_Energy-dir45-w9	Laws_Energy-10	Laws_Energy-13
EGFR positive	Baseline (Fig 1-a)	7766.5	1.522	0.145	5337.9	419770.4	475.2	1369.6
	Followup (1-b)	7195.8	1.657	0.151	4043.5	327365.1	512.0	1352.9
	Change	**-570.6**	**0.135**	**0.006**	**-1294.4**	**-92405.3**	**36.8**	**-16.6**
Wild type	Baseline (Fig 1-c)	3502.4	1.422	0.173	11601.7	419578.9	367.7	353.9
	Followup (1-d)	4522.8	1.251	0.165	10605.5	361191.5	326.3	349.3
	Change	**1020.4**	**-0.171**	**-0.009**	**-996.2**	**-58387.4**	**-41.5**	**-4.5**

Breast Cancer

ER, PR, positive, HER2 negative, stage II invasive breast cancer, good prognosis.



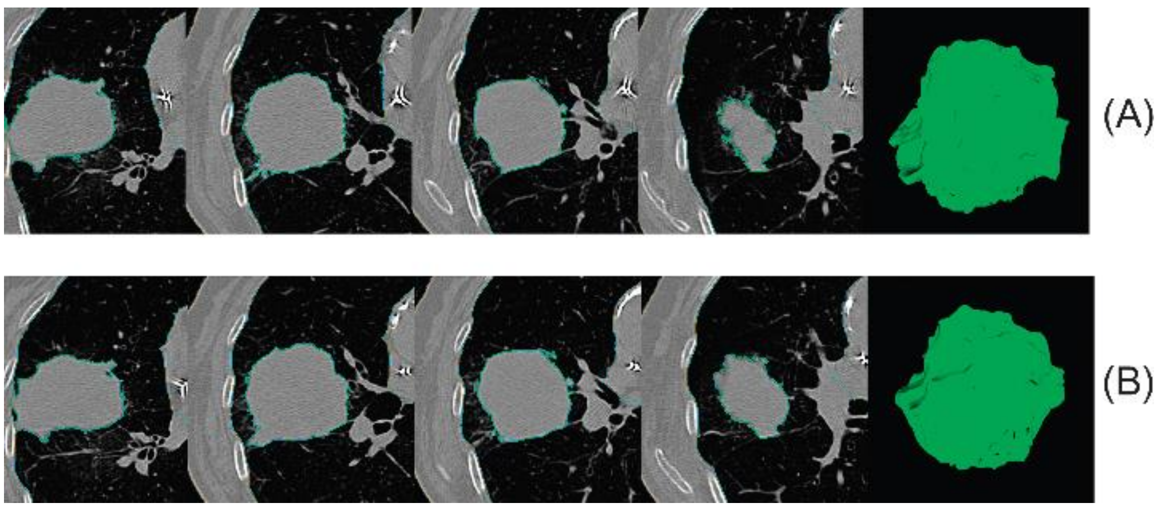


ER, PR, HER2 negative, stage II invasive breast , poor prognosis

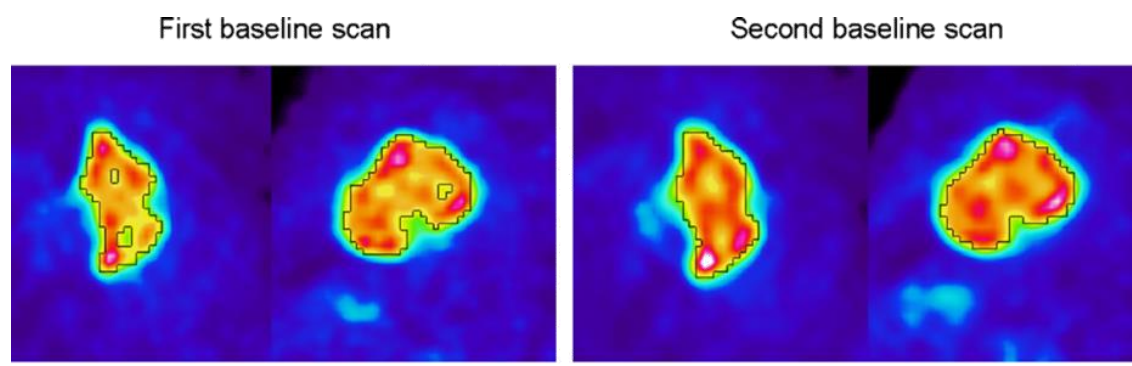
Radiology November 2016; 281(2): 382–391.

Reproducibility (Test-retest)

- Measured from repeated measurements on same conditions



93(42.4%) over 219 features were stable (Concordance Correlation Coefficient above 0.85) respectively in the RIDER dataset



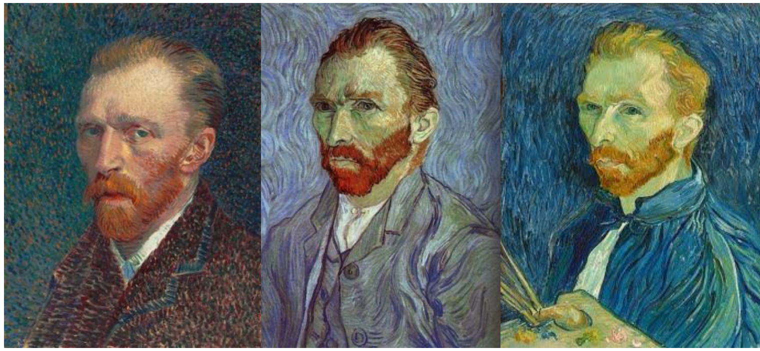
Textural features are more reproducible with respect to maximum and mean SUV.
63% of features stable (Intraclass correlation coefficient > 0.9)

Translational Oncology (2014) 7, 72–87

van Velden, et al., Mol. Img. and Bio., 18(5), 2016

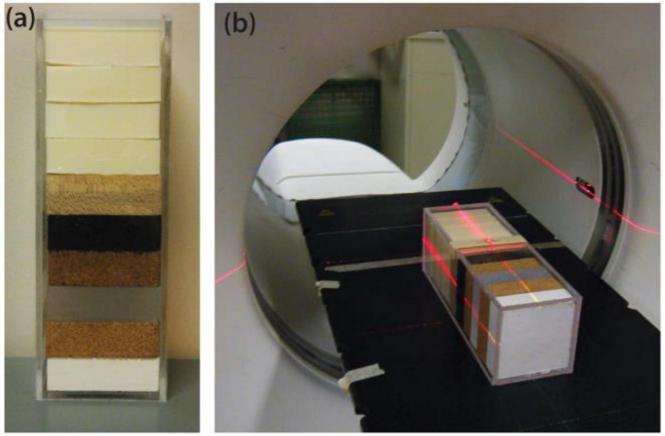
Robustness: CT

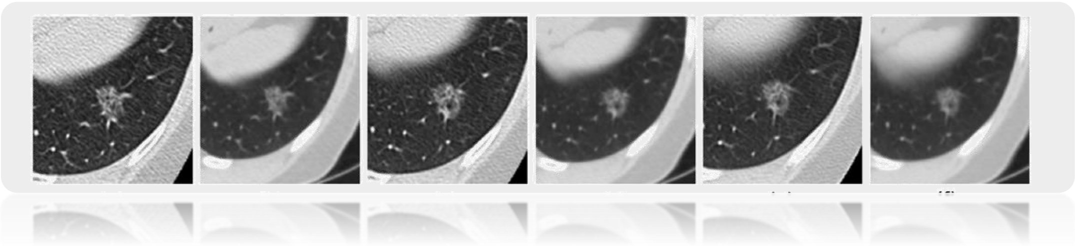
- Robustness is variability with changing conditions (e.g. reconstruction parameters, scanner, patient position)



Radiomic features from CT are sensitive to:

- Scanner
- Slice thickness
- reconstruction algorithms
- Segmentation





Traverso Int J Radiation Oncol Biol Phys, Vol. 102, No. 4, pp. 1143-1158, 2018

Robustness: PET

- Image reconstruction algorithm (OSEM, TOF, PSF, PSFTOF)
- The method of quantization or discretization, where voxel intensities are grouped into equally spaced bins, also affects reproducibility
- Scan duration (≈ noise)
- Segmentation

PET 3D phantom

Tumor 1 **Tumor 2** **Tumor 3**

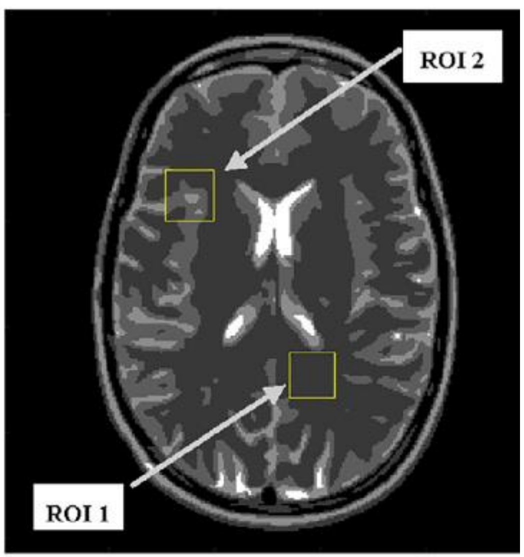
Pfaehler, Medical Physics, 46 (2), February 2019

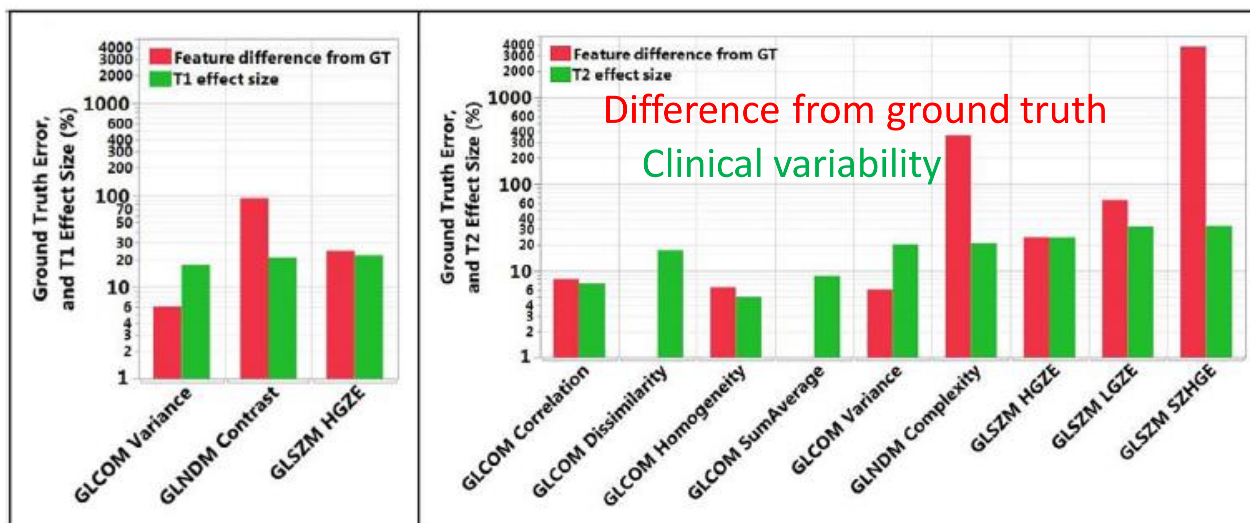
Robustness: MRI

- Radiomic features extracted from MRI scans depend on the pulse sequence, field of view, field strength, and slice thickness
- Effect of recostruction (iterative vs non iterative) algorithm is small

Digital ground truth phantom used as input to a MRI simulator in Matlab.

a)





Yang, Physica Medica 50 (2018) 26–36

Which are the most stable features?

	FIRST ORDER	SHAPE METRICS	TEXTURE ANALYSIS	COMMENTS
ROI SEGMENTATION				
MANUAL DELINEATION	♦	♦♦♦	♦♦♦	Mainly PET studies and one multi-center CT study.Shape metrics from PET may be less subject to inter-observer differences. Semi-automated methods generally improve reproducibility.
SEMI-AUTO / AUTO	♦	♦♦	♦♦	
IMAGE RECONSTRUCTION				
RECONSTRUCTION FILTER	♦	♦♦	♦♦♦	Consistent in a few CT and PET studies of NSCLC.
VOXEL SAMPLING	♦♦	♦♦	♦♦♦	
IMAGE ACQUISITION SETTINGS				
RESPIRATORY MOTION	♦♦	♦♦	♦♦	Consistent over single-institution PET and CBCT studies of NSCLC.
SCATTERED RADIATION	♦♦	?	♦♦	In one CBCT study of NSCLC, but did not evaluate shape metrics.
CT SCANNER	♦♦	♦♦	♦♦	In one multi-institutional CT study in NSCLC , effects were similar in magnitude to inter-patient differences.
DIGITAL IMAGE PRE-PROCESSING				
NOISE AND SMOOTHING	♦♦	?	♦♦	Single-center CBCT and planning CT study in H&N; smoothing and noise have less effect than high-pass and logarithmic filters.
INTENSITY DISCRETIZATION	♦♦	♦♦	♦♦	Consistent in H&N studies of perfusion CT and PET, bin size may have less impact in PET.
CONSENSUS ABOUT MOST STABLE OR LEAST STABLE RADIOMIC FEATURES	Entropy was consistently among the most repeatable/reproducible first-order features. There were inconsistent findings for skewness and kurtosis.	Certain shape metrics may be reproducible in PET, and slightly less reproducible in CT, though it is unclear which individual features prove to be stable.	No emergent pattern or consensus for highly reproducible textural features. Coarseness and contrast were among the least reproducible.	

♦ less likely ♦♦ probable ♦♦♦ highly likely influenced by parameters

Good repeatability is a necessary, but not sufficient condition for high predictive power of a feature,

If a feature has a low repeatability, its predictive power must be low, too

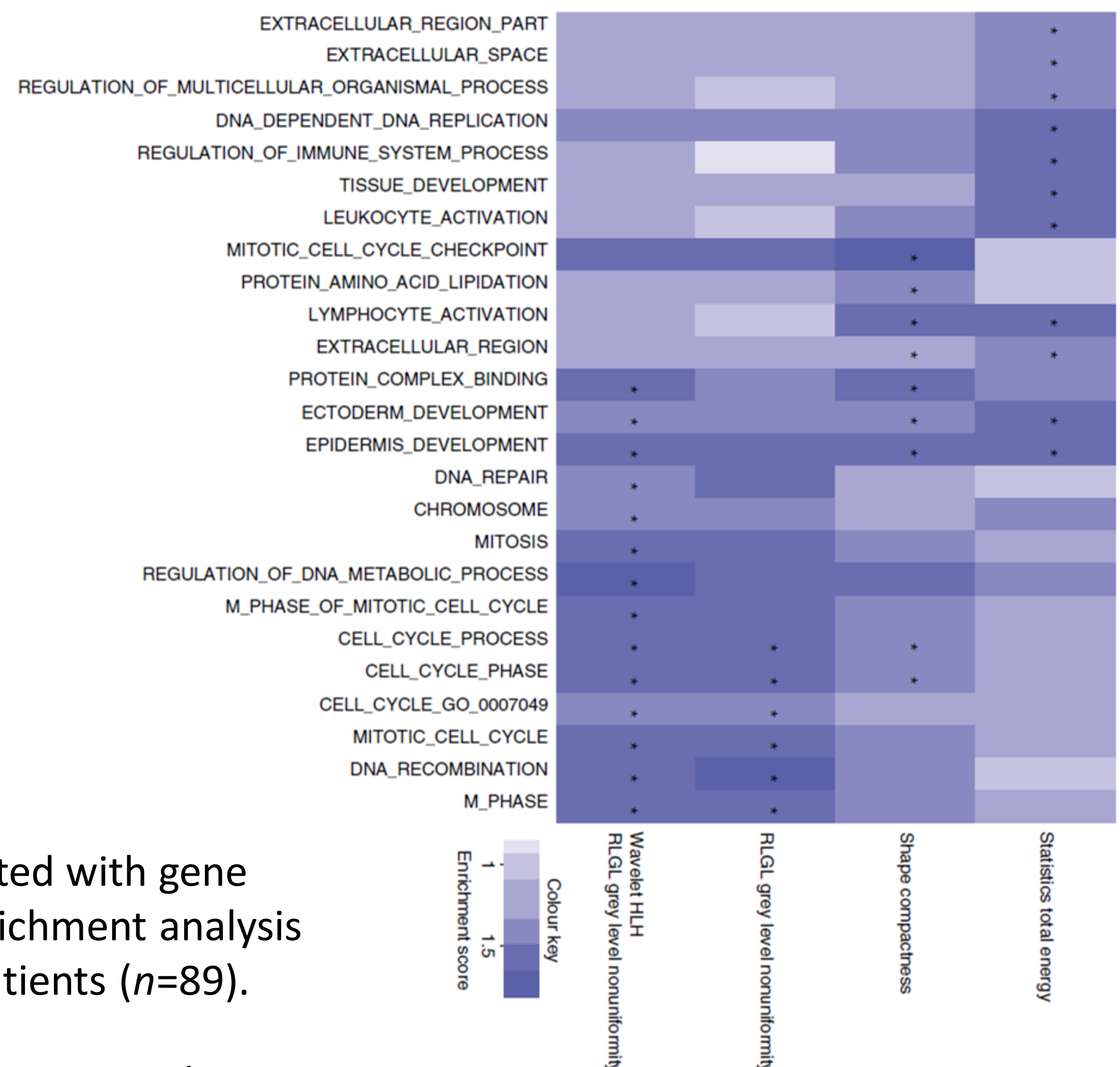
If a feature has a good repeatability, we cannot conclude anything about its predictive power

Traverso Int J Radiation Oncol Biol Phys, Vol. 102, No. 4, pp. 1143-1158, 2018

Radiomics and biology

- Radiomic features provide a description of the appearance of the tumor in the medical image
- Medical images are not the tumor, but a representation, but…
- …in biopsy-based assays, the extracted sample does not always represent the entire population of tumor cells, and…
- radiomic features assess the comprehensive three-dimensional tumor bulk by means of imaging information

Radiomics and biology



Radiomic features are associated with gene expression using gene-set enrichment analysis (GSEA) in a data set of lung patients (n=89).

Aerts et. al Nat. Comm. 5:4006 10.1038/ncomms5006

Radiomics and biology

- Tumor histology (squamous cell carcinoma, large cell carcinoma, adenocarcinoma and “not otherwise specified”)

Patil, Tomography 2 (4) DECEMBER 2016

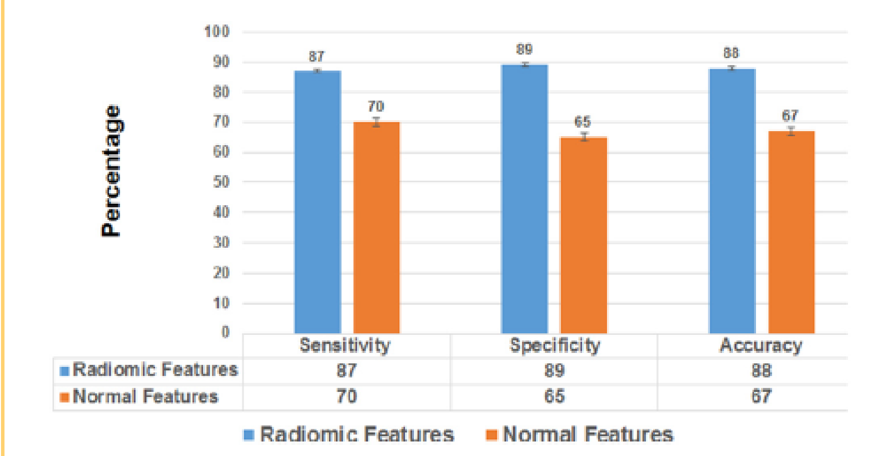


Figure 2. Classification metrics using radiomic and normal features.

- *ALK/ROS1/RET* fusion-positive tumor

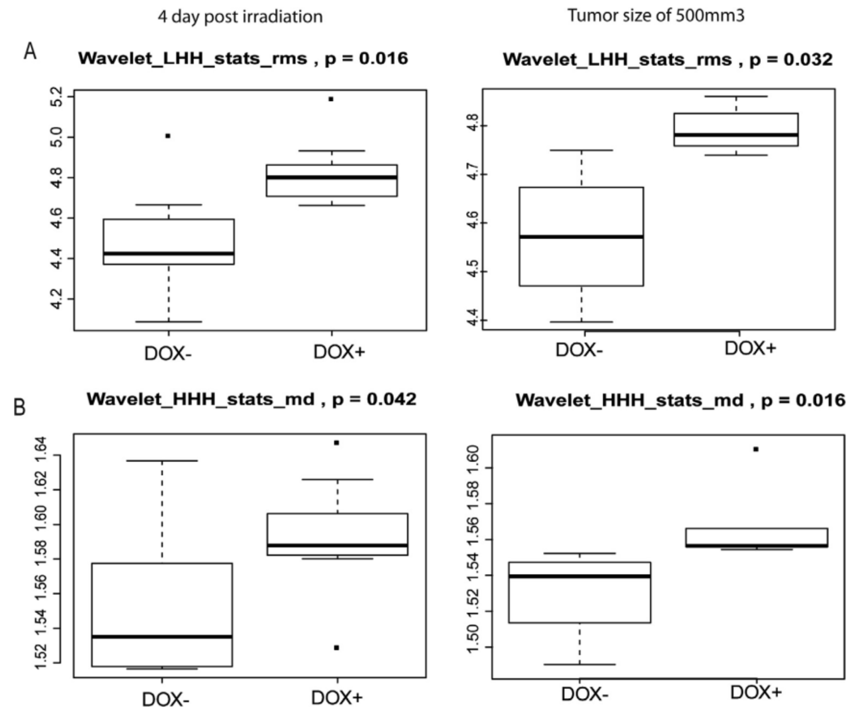
- younger age, advanced tumor stage, solid tumor on CT, SUV_{max} tumor mass, kurtosis and variance

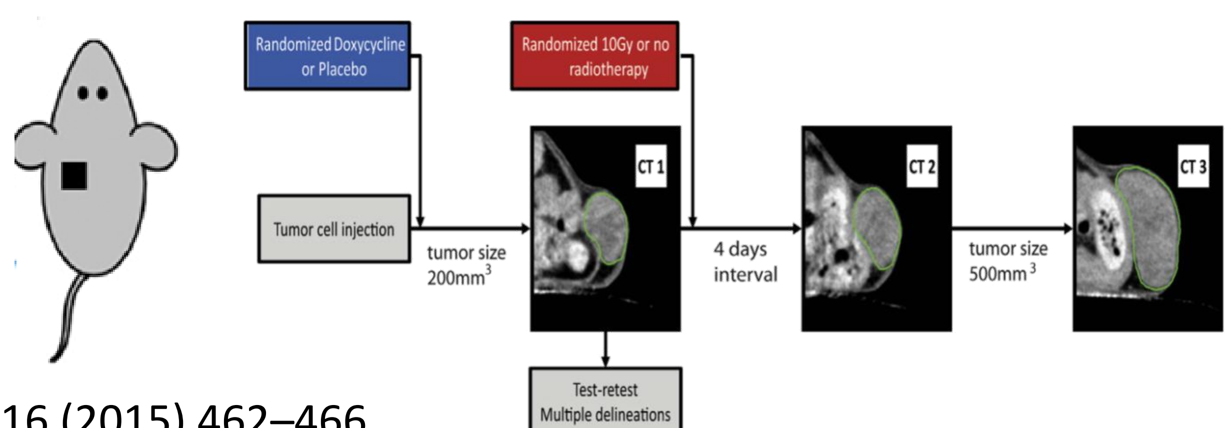
- sensitivity and specificity, 0.73 and 0.70, respectively.

Medicine Volume 94, Number 41, October 2015

Biology and radiomics: causal effect?

- Tumor cells of colon cancer(HCT116, GADD34 inducibili) injected in the flank of nude mices
- Some mices had placebo other received a drug which induces overexpression of gene GADD34 in the rumor
- CT scan was acquired and radiomic features extracted in both cohorts





Panth et al. Radiother and Oncol 116 (2015) 462–466

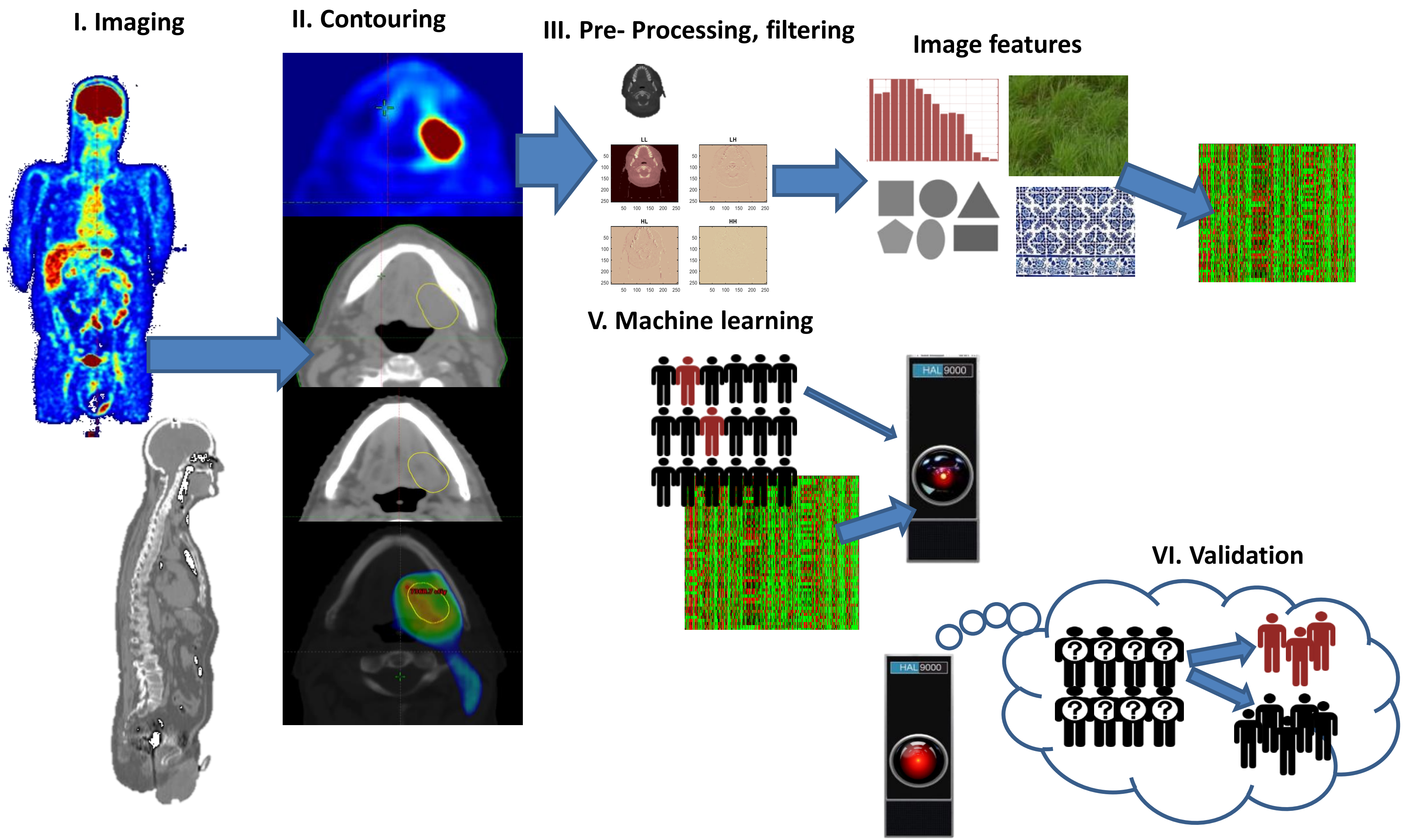
Definition of radiomics

- The term radiomics originates from the words "radio" which refers to radiology, i.e. medical images in the broad sense (CT, PET, MRI, US, mammography etc.), and "omics", first used in the term genomics to indicate the mapping of human genome, indicating large scale analysis
- The goal of radiomics is prediction of biological or clinical endpoints by:

- quantitative analysis of tumor/organ at risk through extraction of a large amount of radiomic features
- use of machine learning for building predicting models

Avanzo et al. Phys Med 38 (2017) 122-139

Radiomics: workflow



Pre-processing

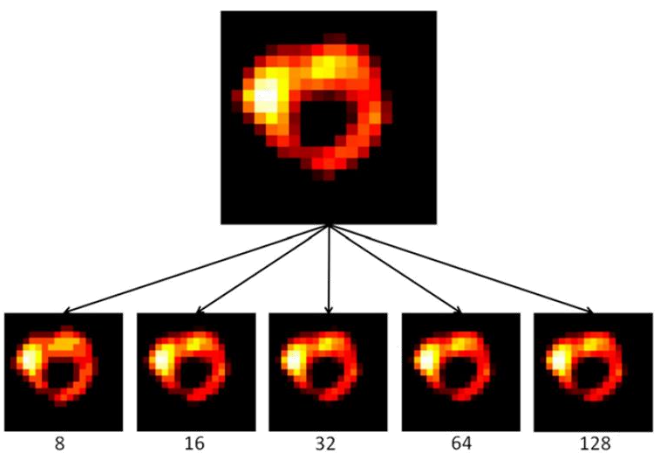
Preprocessing aims at reduce noise and calculation time and to harmonize images of different patients:

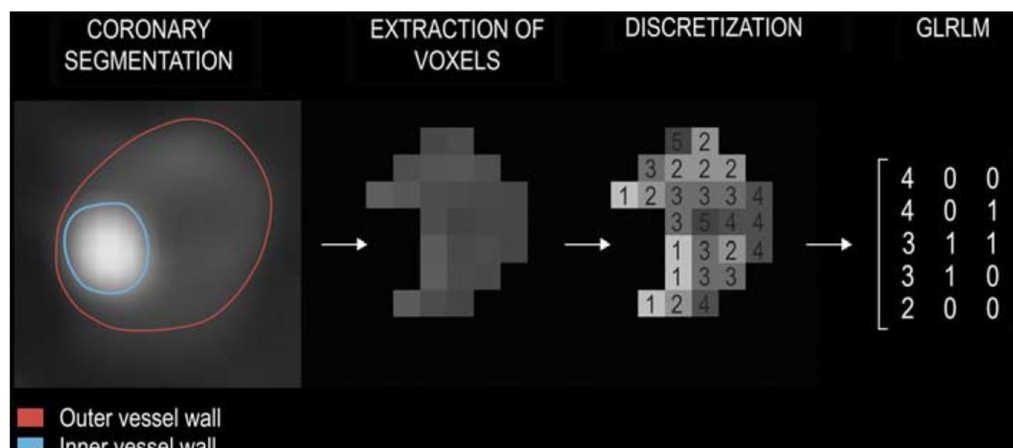
1) Discretization of the intensity levels. 2 methods are used: :

- “fixed bin size”, where intensity levels are grouped into bins of fixed size, such as 25 Hounsfield Units nella CT
- “fixed bin number”, where the number of levels are fixed, e.g. 32 or 64

2) Resampling of image into voxels with size e.g. 3x3x3 mm^3.

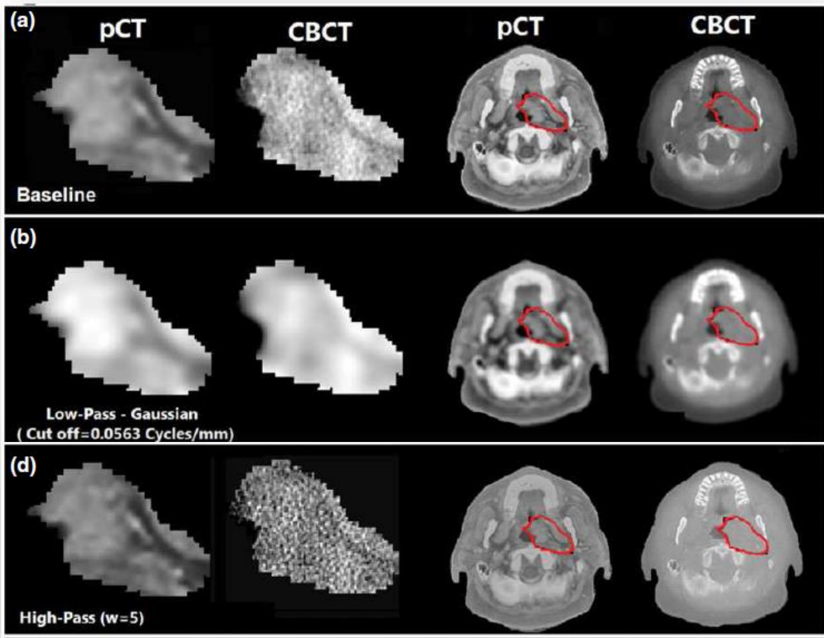
Interpolation algorithms used: nearest neighbour, trilinear, tricubic convolution, tricubic spline interpolation





Filtration

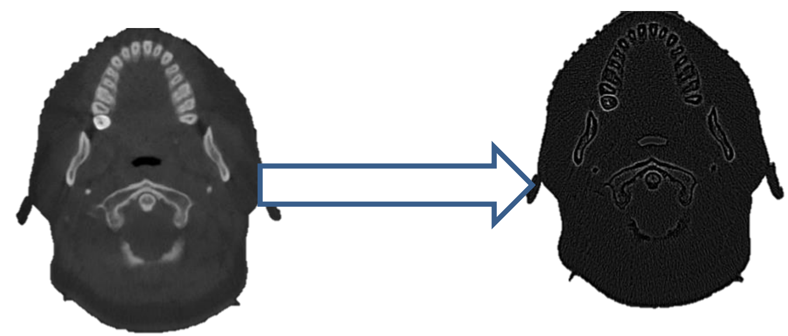
Low-pass and high pass filters:



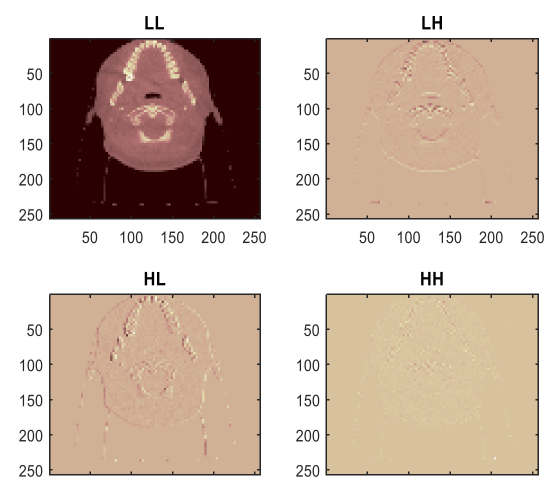
Filter Laplacian of Gaussian (LOG):

$$Log(x,y) = -\frac{1}{\pi\sigma^4}\left[1 - \frac{x^2+y^2}{2\sigma^2}\right]e^{-\frac{x^2+y^2}{2\sigma^2}}$$

σ = radius of gaussian



Wavelet Transform 2D:



Bagher-Ebadian et al. Med. Phys. 44 (5), May 2017, 1755

Definitions of radiomic features

- Some papers report comprehensive formulas of radiomic features:

Kickengereder et al, Radiology 2016;:160845.

Aerts et. Al, NATURE COMMUNICATIONS | 5:4006 | DOI: 10.1038/ncomms5006

- Some inconsistencies in definitions:

Paper 1

$$compactness\ 2 = 36\pi\frac{V^2}{A^3}$$

Paper 2

$$compactness\ 2 = 36\pi\frac{A^2}{V^3}$$

Cornell University

arXiv.org > cs > arXiv:1612.07003

Computer Science > Computer Vision and Pattern Recognition

Image biomarker standardisation initiative

Alex Zwanenburg, Stefan Leger, Martin Vallières, Steffen Löck, for the Image Biomarker Standardisation Initiative

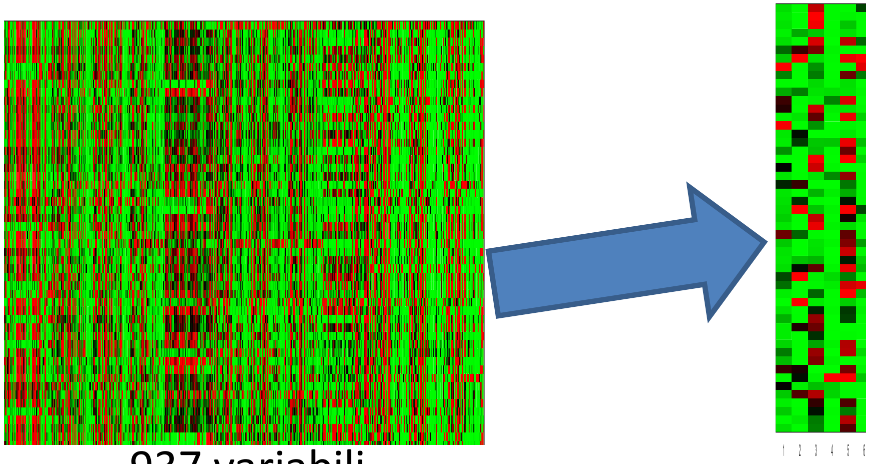
(Submitted on 21 Dec 2016 (v1), last revised 17 Sep 2018 (this version, v7))

Open-source softwares

- 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 selection

- The building of a radiomic models has two phases.
- In the first, feature selection, the variables are reduced by eliminating those that are:
- Redundant, because they are inter-correlated
- Not predictive (not associated with the outcome)



937 variabili

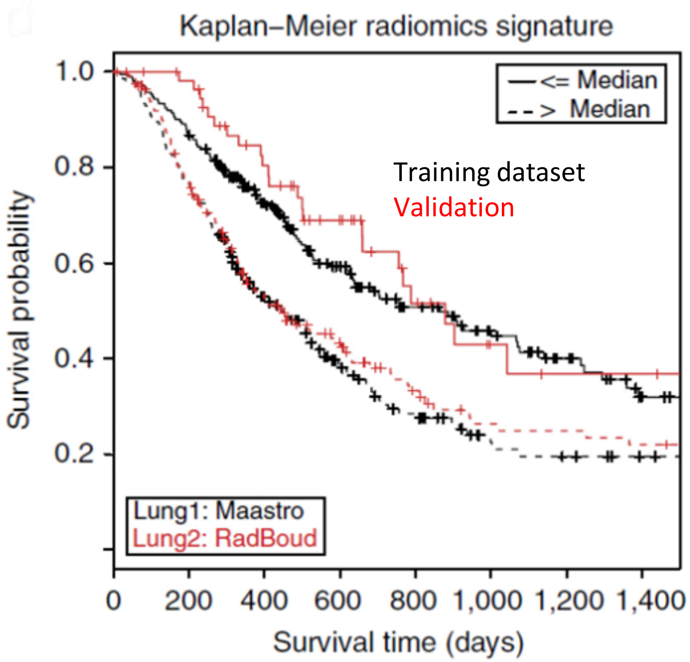
6 - 9 variabili

Feature selection methods

- *minimum redundancy maximum relevance (mRMR)* calculates mutual information (MI) between a set of features and the outcome. The set of features with maximum MI is selected.
- *RELIEF (RELevance In Estimating Features)*, ranks the features according to hw well they separate patients with different outcomes but similar values of features:
- Better score to features with different values in patients with different outcome
- Penalizes features which have different values in patients with the same outcome
- *Stepwise selection* is an iterative process which adds or removes features to a model at each step. Then the variables are included in the model according to a statistical test whith null hypothesis that the variable has zero coefficient in the model-

Machine learning

- Radiomic signature: combination of variables with high predictive power
- Classificator: model to classify the patient e.g. responder, non responder to therapy



Aerts et. Al, NATURE COMMUNICATIONS | 5:4006

TABLE 6. Summary of Classification Results Obtained by 10-Fold CV

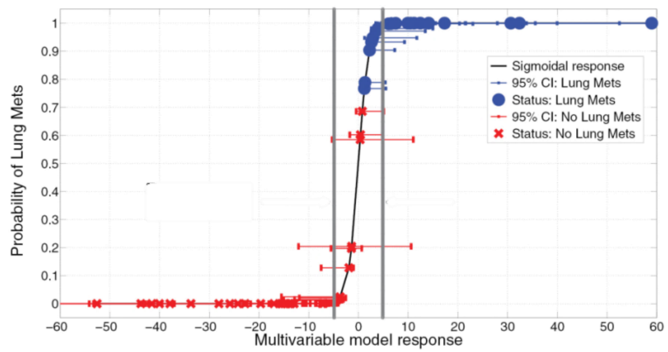
Parameter set	Algorithm	TP rate	FP rate	Specificity	Precision
T1	ANN	0.968	0.091	0.909	0.968
	k-NN	0.935	0.091	0.909	0.967
T2	ANN	0.968	0.273	0.727	0.909
	k-NN	0.935	0.182	0.818	0.935
DWI	ANN	0.903	0.182	0.818	0.933
	k-NN	0.968	0.182	0.818	0.938

FP, false-positive; TP, true-positive.

J. MAGN. RESON. IMAGING 2016;44:445–455.

Machine learning

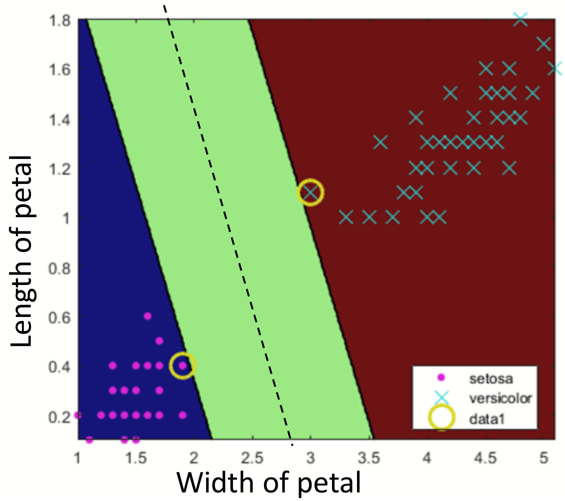
- Logistic Regression



- Support Vector Machine

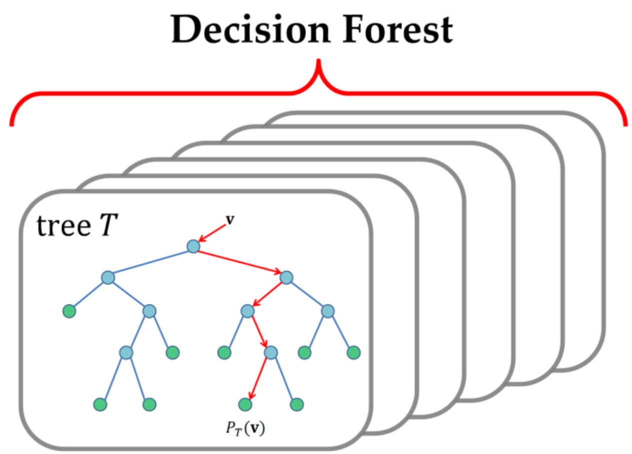
https://www.mathworks.com/help/stats/support-vector-machines-for-binary-classification.html

Classificazione automatica dell'iris

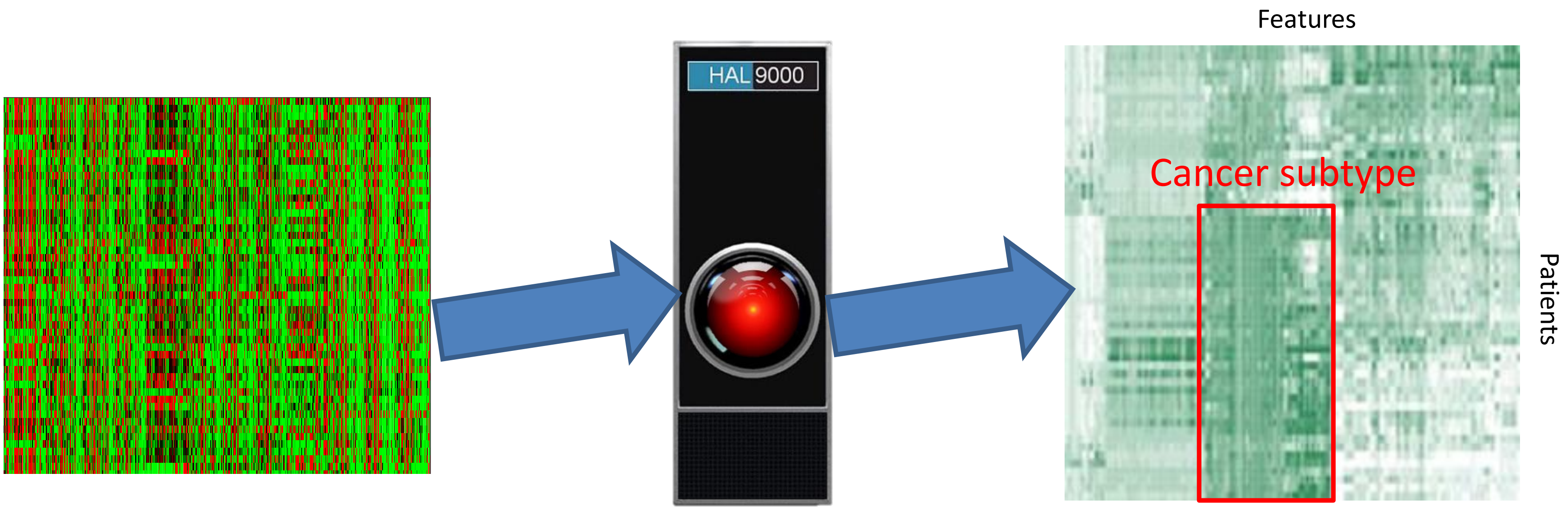


Machine learning

- Random forest

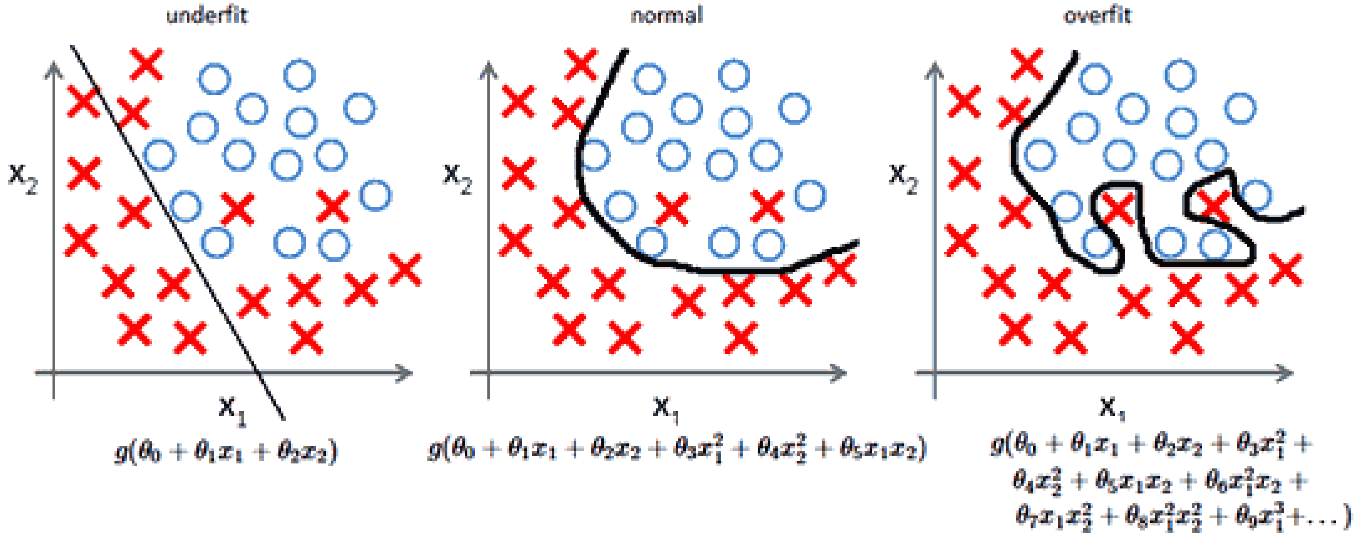


- Unsupervised methods



Overfitting

- Too many variables --> risk of overfitting



- The overfitted model fails when used on a dataset different from the training dataset (poor generalizability)
- Overfitting can be avoided with careful feature selection and validation

http://mlwiki.org/index.php/Overfitting

Validation

According to TRIPOD (Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis) criteria, there are the following validation methods:

1) Developing and validating on the same data, which gives apparent performance. This evaluation is usually optimistic estimation of the true performance

2) Developing the models using all the data, then using resampling techniques to evaluate the performance

3) Randomly split the data into 2 groups for development and validation separately

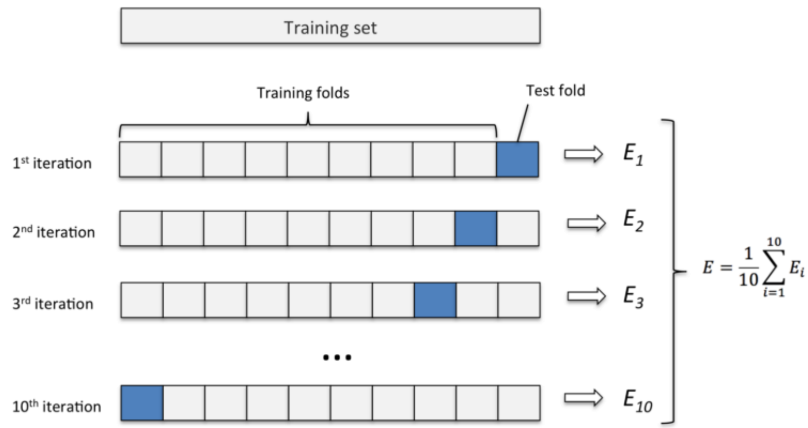
4) Split the data non-randomly (e.g. by location or time), which is stronger than 3)

5) Develop the model using one data set and validate on separate data. Stronger than performing posterior splitting of data

Ann Intern Med. 2015;162(1):W1-W73

Resampling techniques

- Cross validation



- Bootstrap

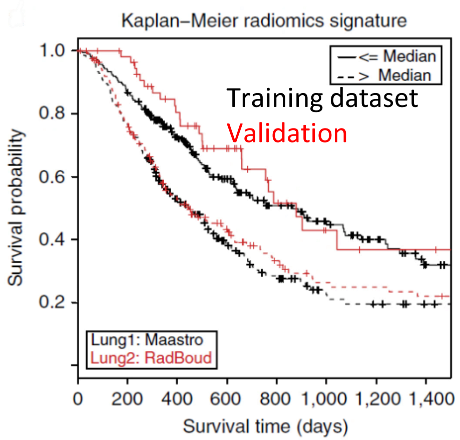
~~1~~ 2 ~~3~~ 4 ~~5~~ 6 7 8 9 10 1 ~~2~~ 3 ~~4~~ ~~5~~ 6 7 ~~8~~ 9 10

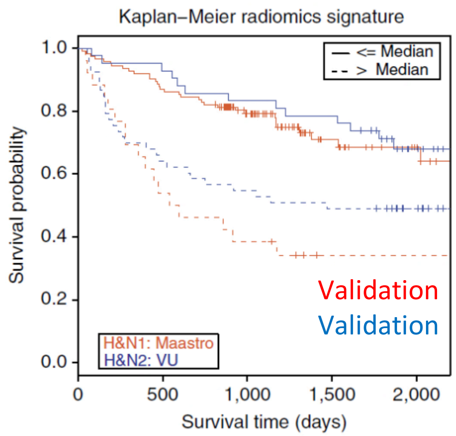
Bootstrap sample 1 Bootstrap sample 2 ....

1 4 3 5 5 3 7 8 9 10 1 2 3 1 5 8 5 8 9 1

- Other techniques: “jackknife” or leave-one-out (LOOCV), where a patient is removed from analysis at each itaration

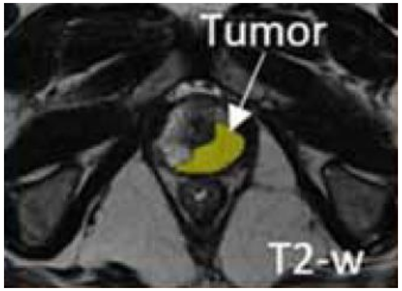
Examples of predictive models

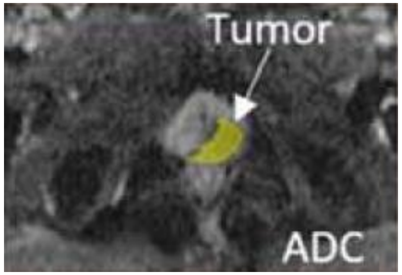




- Survival for lung and H&N squamous cell carcinoma

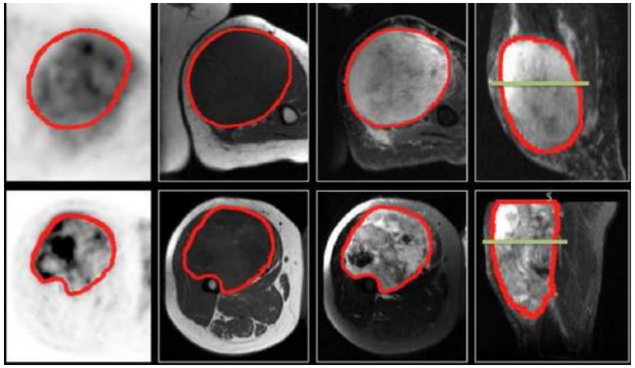
Aerts et. al NATURE COMMUNICATIONS | 5:4006 | DOI: 10.1038/ncomms5006





Gleason score and biovhemical relapse in prostate tumor

Gnep, J. MAGN. RESON. IMAGING 2016

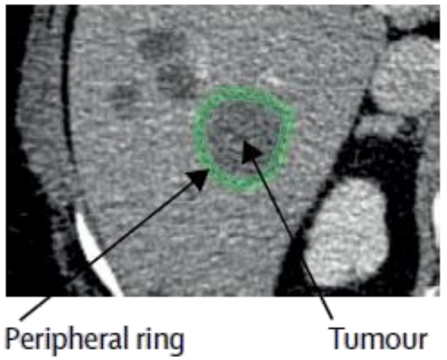


Distant metastases from sarcoma of extremities

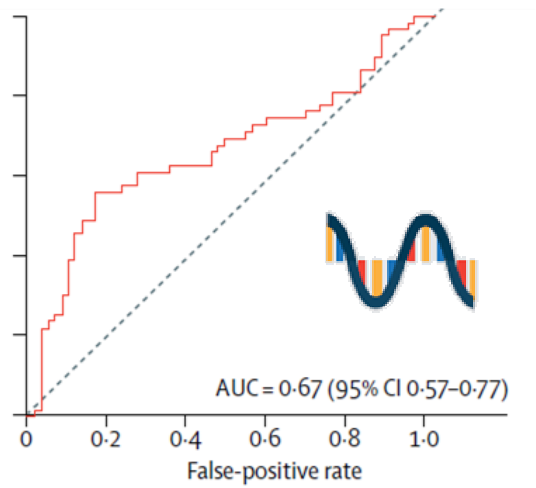
Vallieres, Phys. Med. Biol. **60** (2015) 5471

Immunotherapy

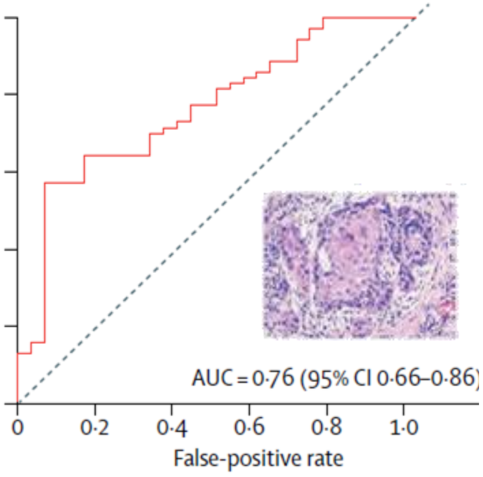
- Model for immunotherapy
- Training set of 135 patients with different tumors
- Radiomic signature for presence of CD8 antigens estimated from RNA sequencing



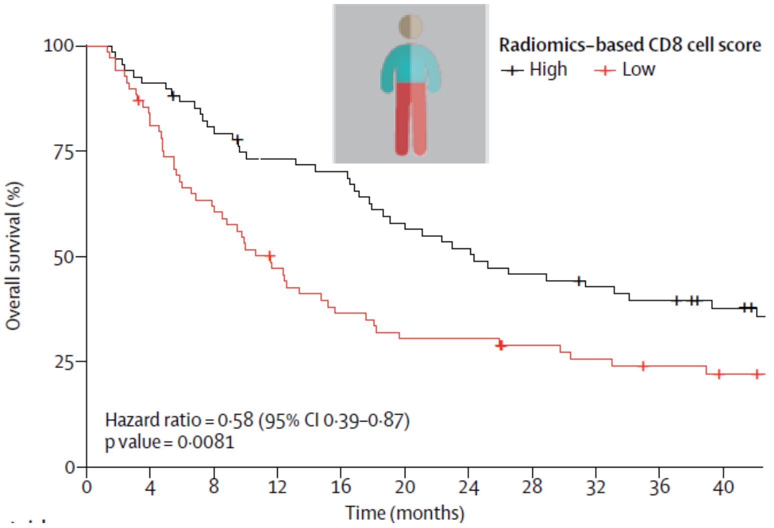
Gene expression of CD8 cells (119 pts)



Phenotype of tumor desert-immune (few CD8 cells) vs inflamed (many cells CD8), 100 pts



Survival of patients treated with immunotherapy (137 pts)



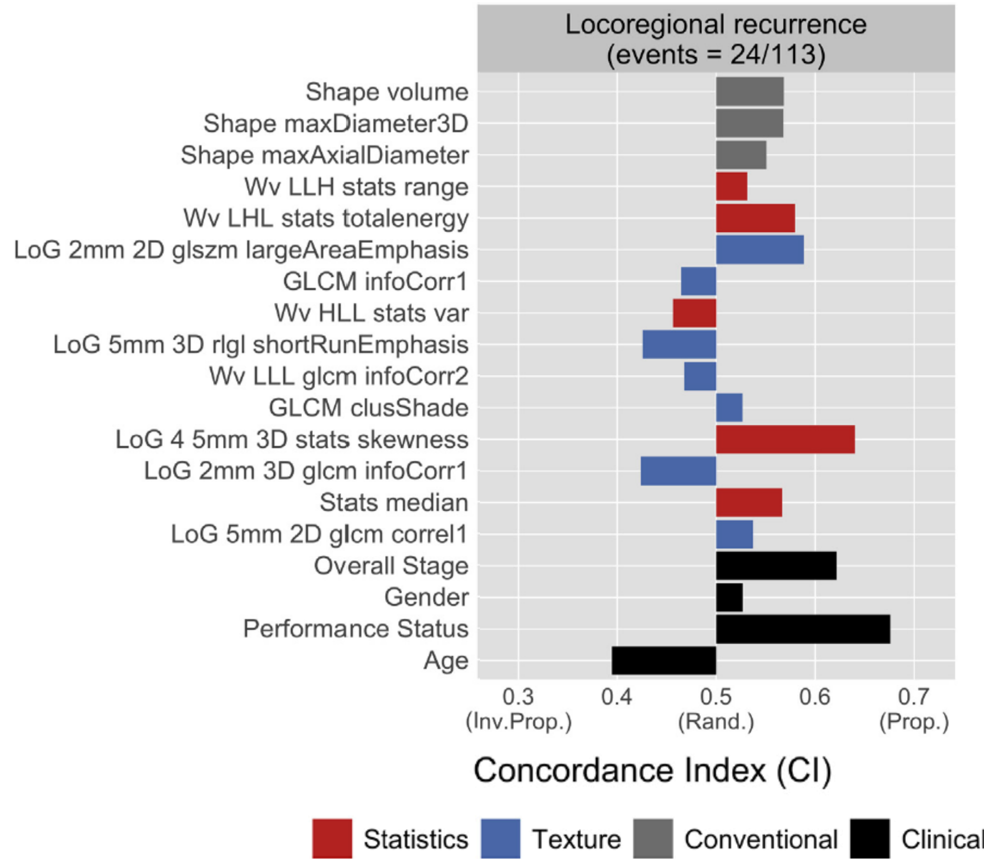
Sun et al. Lancet Oncol 2018; 19: 1180–91

Prediction for local recurrence in SBRT

113 patients

close to the chest wall:
10–12 Gy * 5 fractions,
12–14 Gy * 4 fractions
Other: 18 Gy * 3

Free breathing CT



No feature had significant correlation with recurrence!

Huynh, Radiotherapy and Oncology 120 (2016) 258–266

Prediction for local recurrence in SBRT from PET

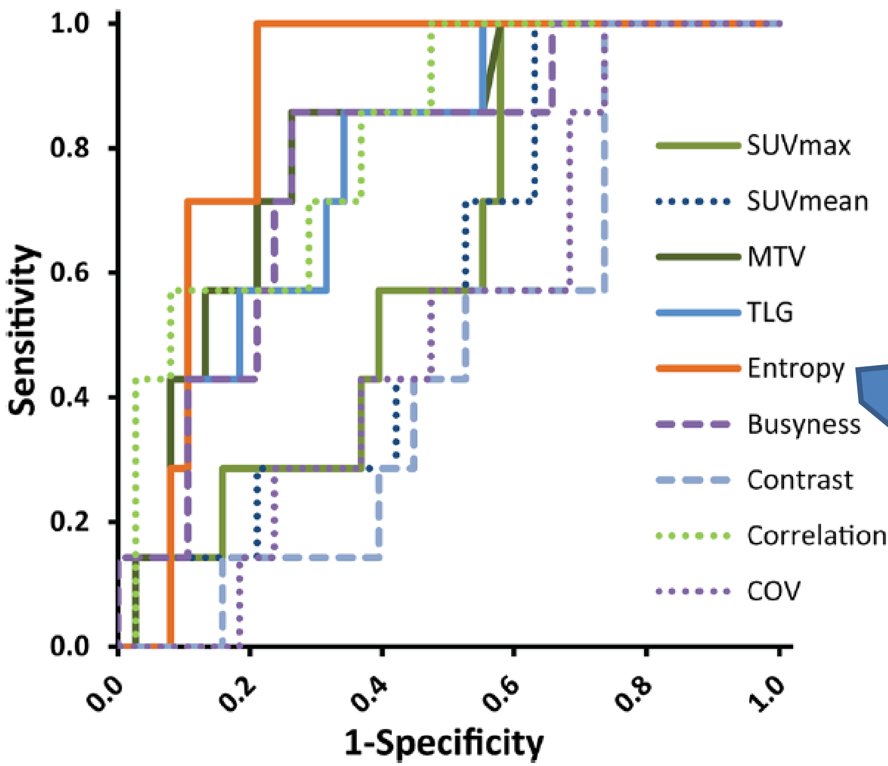


Figure 1 Value of textural and standard PET parameters for prediction of local recurrence. ROC curves for prediction of local recurrence through different PET parameters. Coarseness is the same curve as busyness.

45 patients

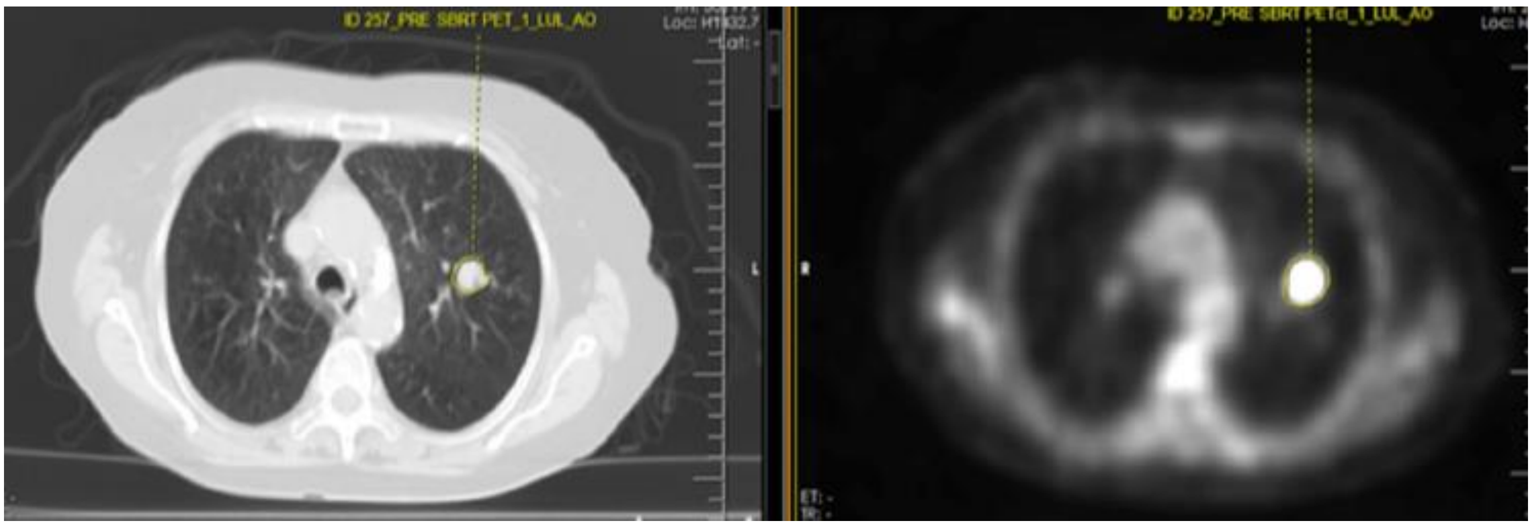
24–45 Gy delivered in 3–5 fractions. Dose prescribed to the 60% isodose which had to cover 100% PTV

Significant correlation of several textural parameters with local recurrence.
AUC value for entropy of 0.872

Pyka et al. Radiation Oncology (2015) 10:100 DOI 10.1186/s13014-015-0407-7

Regional control after SBRT:PET/CT

- Radiomics on PET/CT for prediction of control and survival in SBRT-treated lung cancer patients.

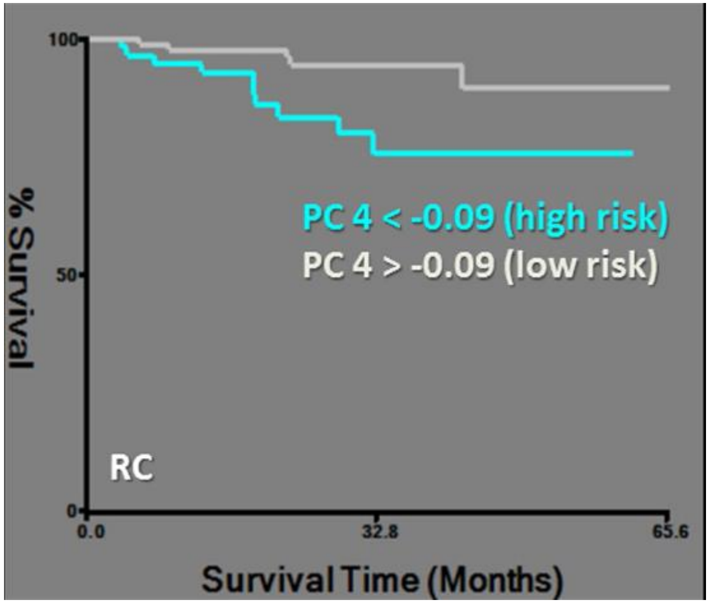


150 patients, 172 cancers
48-56 Gy SBRT Fractionation not included

Oikomonou SCIenTIfIC REPOrTS | *(2018) 8:4003* | DOI:10.1038/s41598-018-22357-y

Regional control after SBRT:PET/CT

- Radiomics on PET/CT for prediction of control



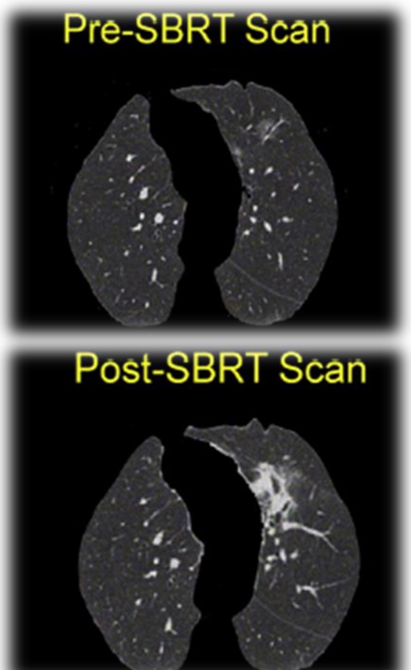
Subgroups of low and high recurrence free survival were determined by a cut-off value of 0.09 for radiomic signature PC4

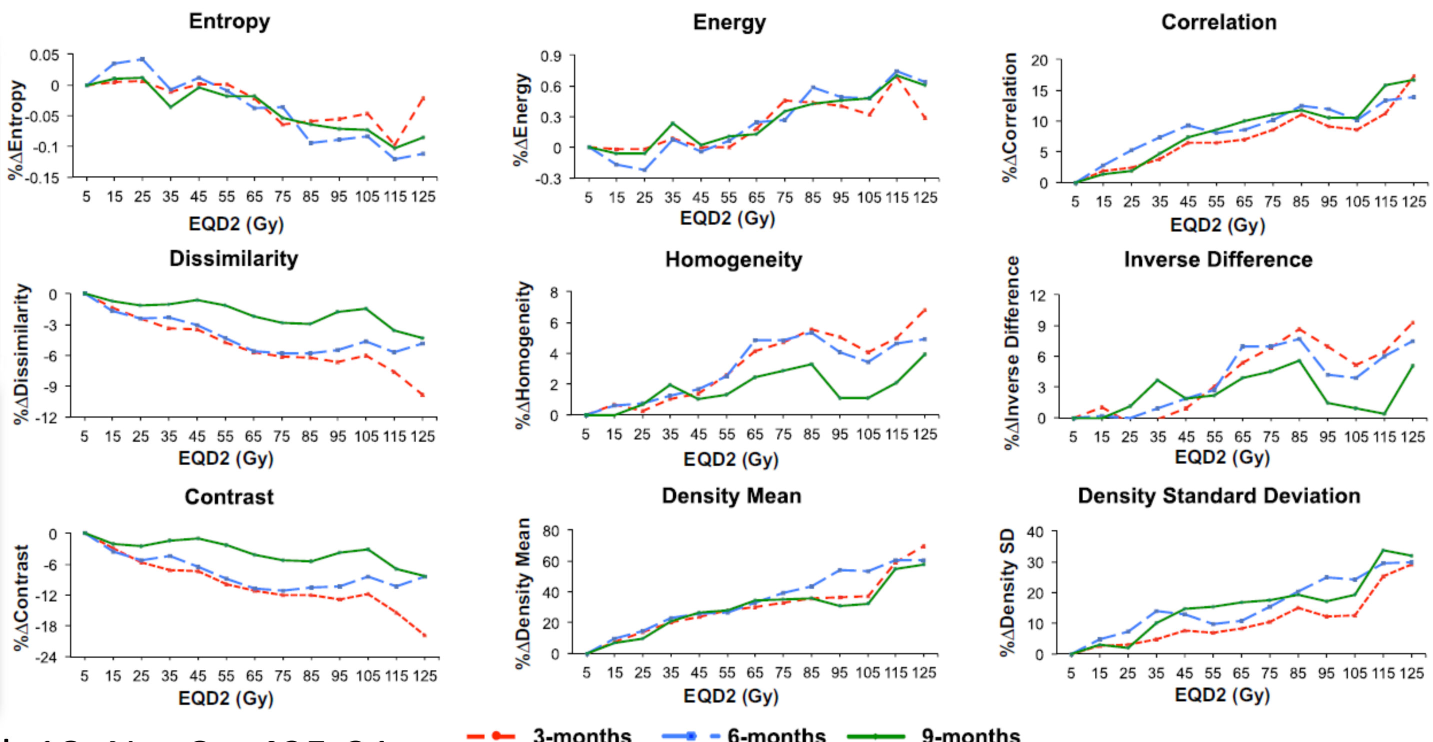
Radiomic signature "PC4"	
1st order	Kurtosis (*PET*)
	Skewness* (*PET*)
Textural	Homogeneity (*PET*)
	Normalized Entropy (*PET*)
Shape	Area regularity (*PET*)
	Area regularity (CT)
	Perimeter regularity (2) (*PET*)

Oikomonou SCIenTIfIC REPOrTS | *(2018) 8:4003* | DOI:10.1038/s41598-018-22357-y

Lung injury

- Radiomic features significantly correlates with lung-injury scored by oncologist post-SBRT (18 Gy*3, 12.5 Gy*4, 12 Gy*5)
- GLCM features outperformed histogram features

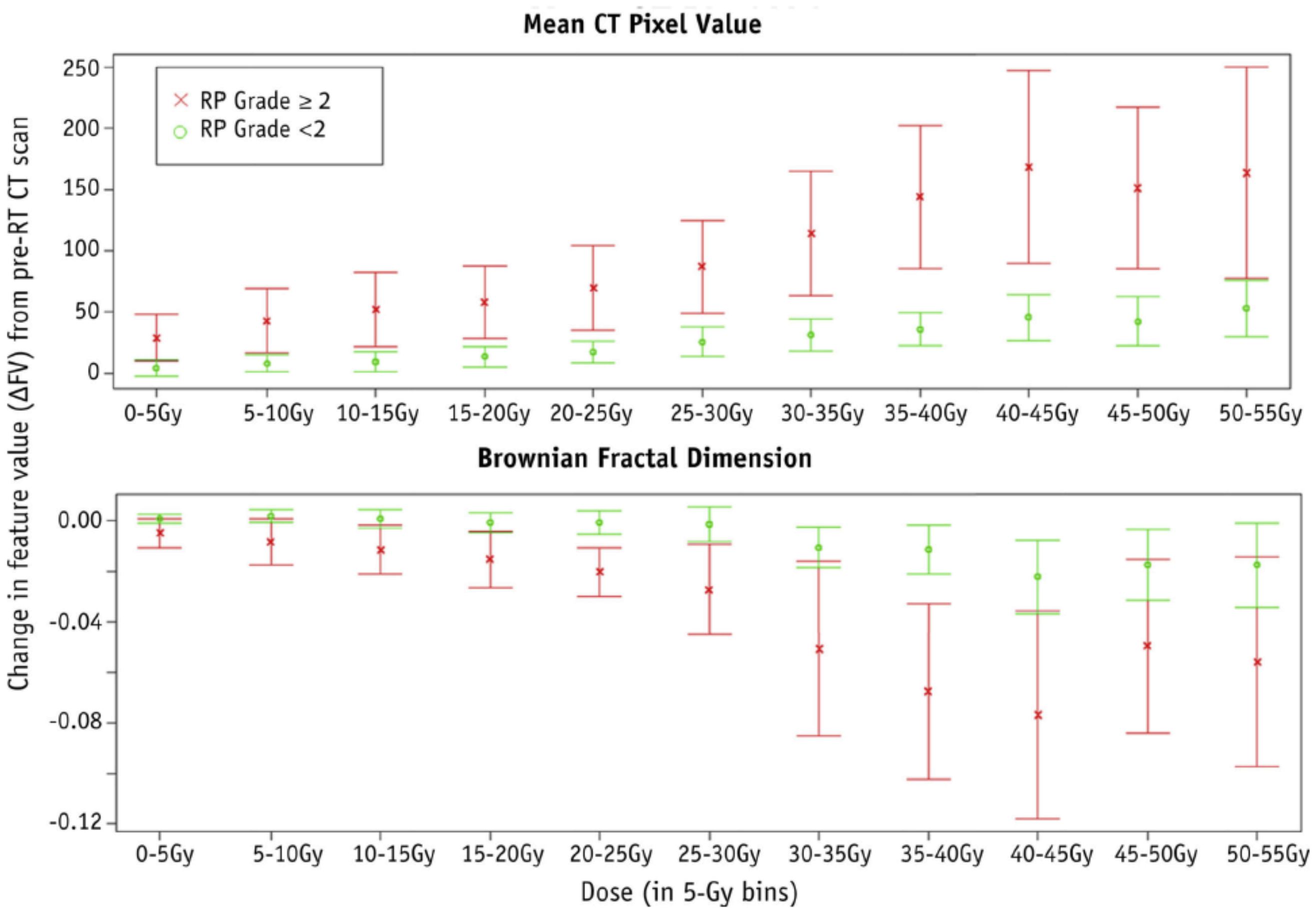




Clinical Lung Cancer, Vol. 18, No. 6, e425-31

Prediction of radiation pneumonitis

- 50.4 Gy, non-SBRT, esophageal cancer

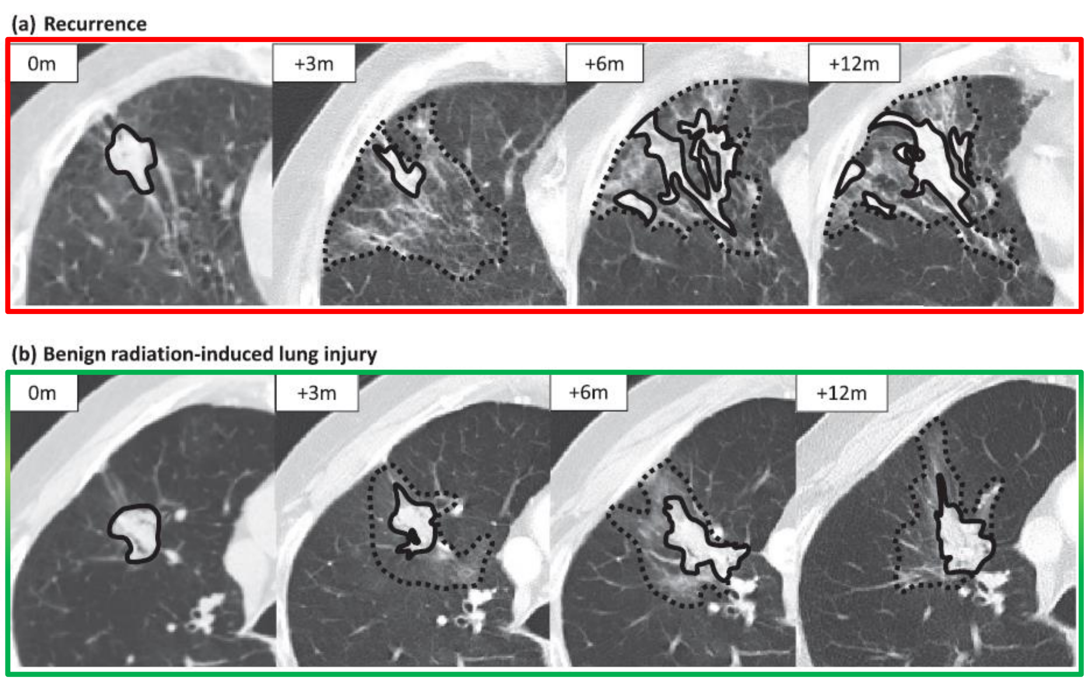


Int J Radiat Oncol Biol Phys. 2015 April 1; 91(5): 1048–1056

Differentiation of recurrence

- On two-fold CV, first-order features yielded 73% accuracy, second order 76%–77%
- longest axial diameter and 3D volume, gave 60% and 57%

Recurrence



Benign changes

FIG. 2. Manual delineations of post-SABR consolidative and ground-glass opacity findings throughout follow-up for a patient with recurrence (a) and radiation-induced lung injury (b). The zero-month (0m) time point indicates the pretreatment lesion. The solid lines enclose consolidative regions and the dashed lines enclose ground-glass opacity regions.

Mattonen et al. Med. Phys. 41 (3), March 2014

Radiomics of oropharyngeal tumor

- Observational, retrospective, monoinstitutional study at the CRO - Aviano
- Collaboration among Medical Physics, Radiotherapy, Nuclear Medicine, Radiology
- Has the objective of building a predictive model for:
- HPV status, and
- response (complete/not complett) at 3 months from the end of radiotherapy

From radiomic analysis of pretreatment images of the patient and dose distribution

Radiomics and HPV status

- The tumors in HPV-positive patients appear more homogeneous and small in CT

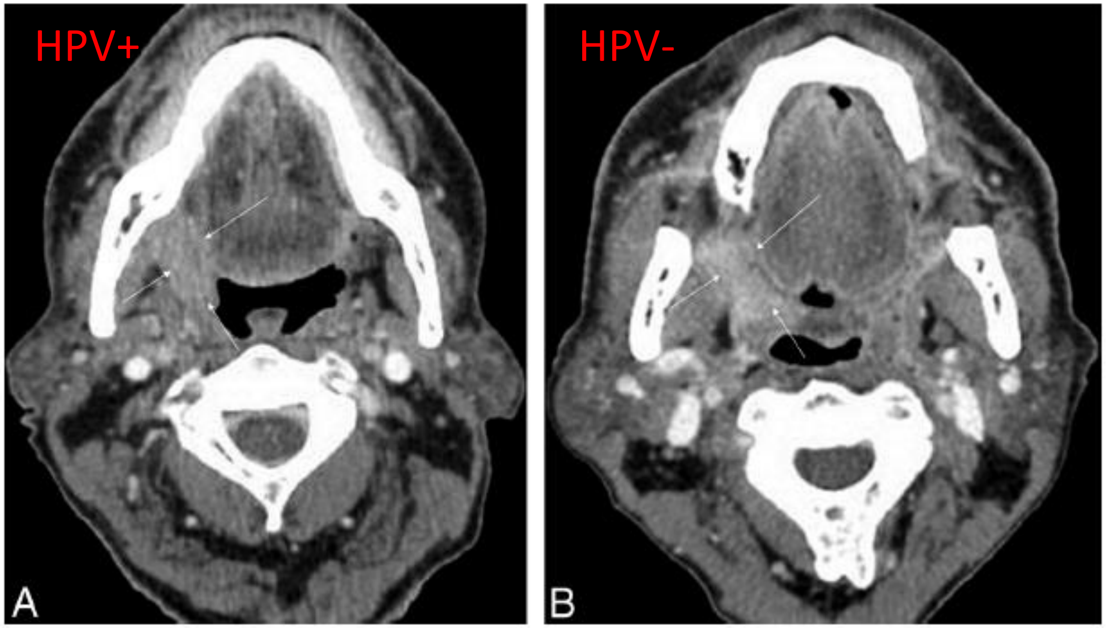
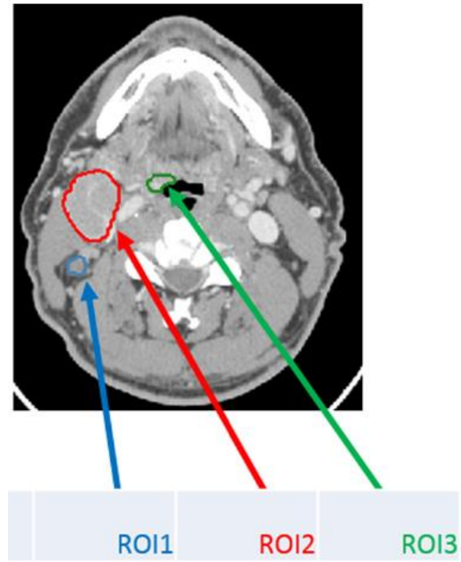


FIG 3. Representative examples of patients with HPV-positive and HPV-negative SCC. *A*, HPV-negative right tonsillar squamous cell carcinoma (*arrows*) in a 65-year-old man. *B*, HPV-positive right tonsillar squamous cell carcinoma (*arrows*) in a 65-year-old man.

AJNR Am J Neuroradiol 36:1343–48 Jul 2015

Radiomics and HPV status

- Model based on contrast-enhanced CT, 315 patients oropharingeal
- 150 patients for training, 165 validation
- Model had AUC of 0.915 in validation



Yu K, Clinical and Translational Radiation Oncology 7 (2017) 49–54

- Model for prediction of HPV determined from p16
- CT, no contrast
- Multicentric database of 778 patient, randomly split into training dataset (80%) and validation (*N* = 150).
- The model scored AUC=0.764 in validation

Leijenaar, Br J Radiol 2018; **91**: 2017049811075

Oropharyngeal: local control

- 465 pazienti
- Local control proven pathologically (biopsy and/or resection) or radiologically
- Analysis on contrast enhanced CT
- Radiomic signature based on:

- Intensity Direct Local Range Max: average of range (max-min) for every voxel with respect to surrounding region
- Neighbor Intensity Difference Complexity: measures the perceived complexity in the image

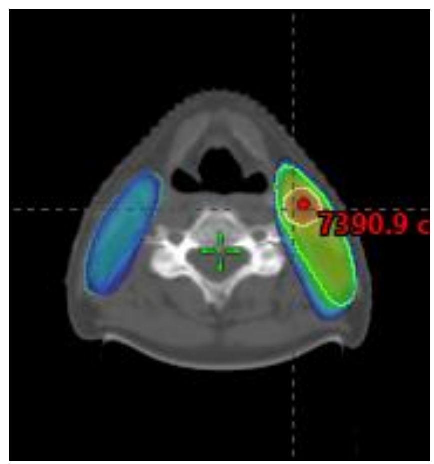
The radiomic signature had higher predictiove capability than variables HPV status and administered therapy

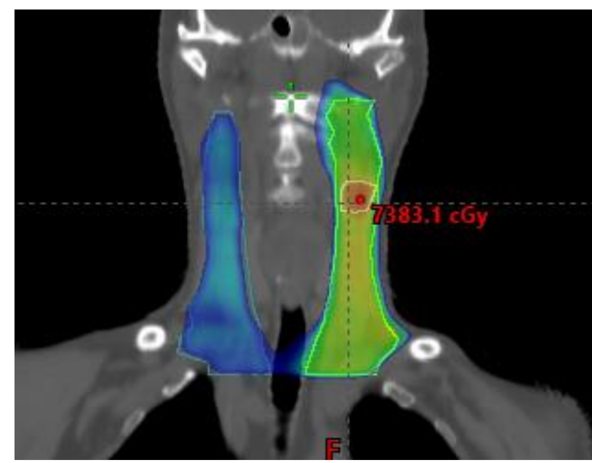
SCIENTIFIC **ReportS** | *(2018) 8:1524* | DOI:10.1038/s41598-017-14687-0

Methods

- 51 Pazients treated with IMRT
- 70.95 Gy to microscopic disease
- 62,70 Gy to high risk lymph-nodes
- 59,10 Gy “ low risk “ “

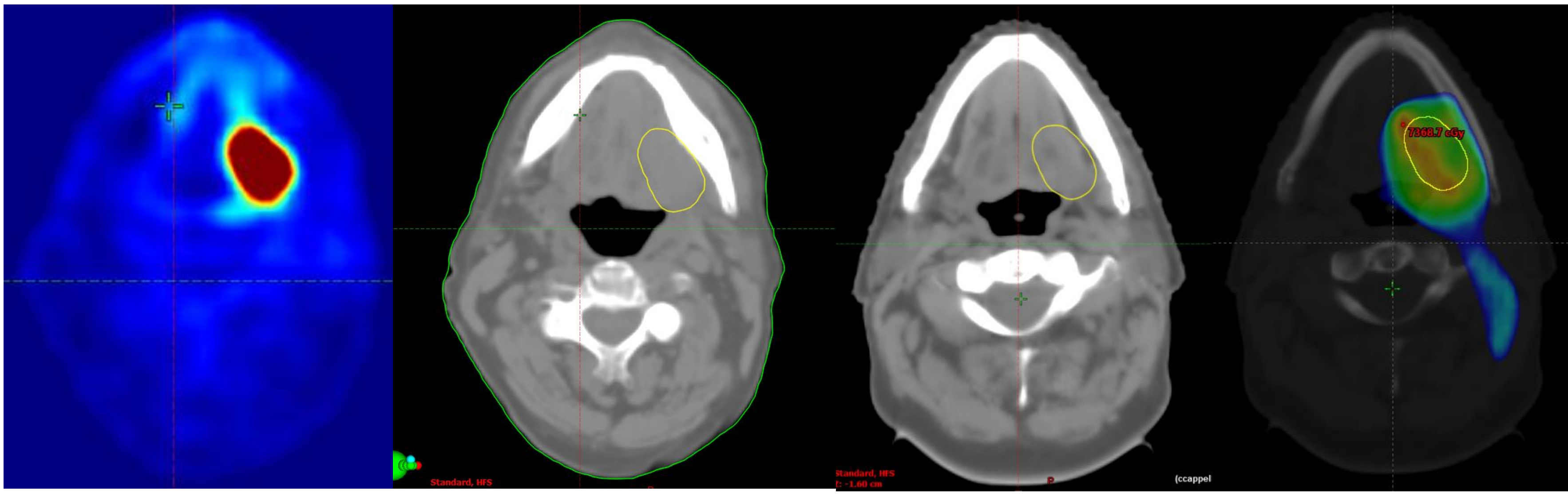
Characteristics of patients	
Patients	51
Male/female	41/10
Chemotherapy (no, Concomitant, neoadjuvant, neoad.+conc.)	1/12/36/2
Stage TNM 8°: 1, 2, 3, 4A, 4B	14/8/4/21/4
HPV Status (+,-)	28/23





Methods

PET | CT-PET | CT-SIM | Dose



- Tumor was contoured by one clinician using PET
- Contour reported on CT-PET and simulation CT using image registration
- Variables extracted also from dose distribution

Protocols of acquisition

PET Philips Gemini TF 16

Average injected activity of ^{18}F-FDG was 280 MBq

Algorithm of reconstruction PET “Blob-OS-TF”,

a 3D ordered subset iterative TOF reconstruction technique

Matrici 144 × 144 con voxel 4 × 4 × 4 mm^3

CT-PET Philips Gemini TF 16

- 120 kV, 108 mA average, pitch 0.83, acquisition time 0.5 s
- Slice thickness 5 mm, kernel: ‘B’ body

CT-SIM Toshiba Aquilion/LB

- 120 kV, average tube current 300 mA , rotation time 0.75 s
- Slice thickness 2 mm, kernel: ‘C13’

Methods

- Software written “in-house” in Matlab, benchmarking with Ibex

IBEX is Intended for Research Use Only.

IBEX V1.0β

Imaging Biomarker Explorer Software

- 21 shape variables
- 47 textural (+ filters gaussian, LOG, median)
- 5 higher order (“ “ “)
- In total: 937 features per patient

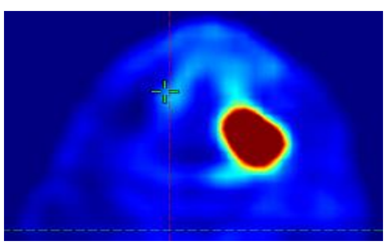
- Stepwise feature selection, support vector machine
- Cross-validation

Preliminary results (1)

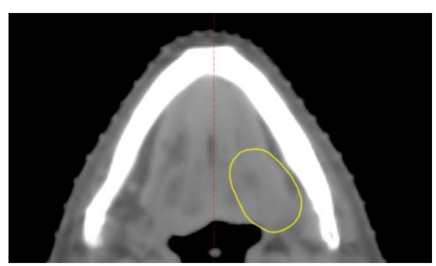
- Model for HPV status:
- 1 shape (solidity), 2 simulation CT, 1 PET, 2 dose variables were selected
- In the cross-validation:

- Sensitivity (positive on patient with HPV+): 85,2%%
- Specificity (negative on patient HPV-): 83,3%

		Real	
		HPV+	**HPV-**
Predicted	**HPV+**	23	4
	HPV-	4	20



Inv.Diff.Norm PET
Measures local inhomogeneity

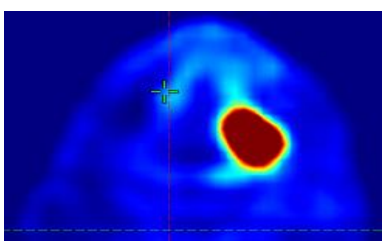


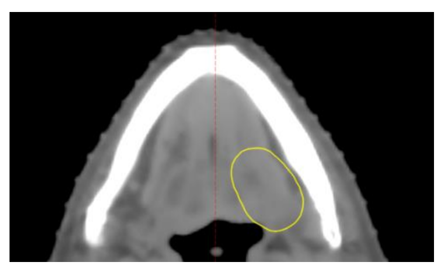
GLCM Cluster Prominence
Measures variability of values

Preliminary results (2)

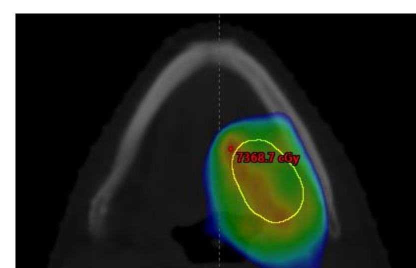
- Model for complete response 3 months from therapy:
- 1 shape (roundness), 3 simulation CT, 4 PET features were selected
- In the cross-validation:
- Sensitivity (positive on patient with HPV+): 100,%
- Specificity (negative on patiente HPV-): 95,1%

Matrice di confusione		Real	
		RC+	RC-
Predicted	RC+	39	2
	RC-	0	10


SRLGE PET
Describes presence of stripes of low value voxels


Long run emphasis CT-SIM
Presece of stripes of voxels with same value

Dose Range
Related to inhomogeneity of dose



Conclusions

- Radiomics is entering its mature phase:
  - The number of radiomic papers is increasing exponentially
  - More and more radiomic studies have solid validation
  - more attention than in the past to feature reproducibility
- If you want to approach radiomics:
  - Read some of the many excellent reviews on the subject
  - Read the Imaging Biomarker Standardisation Initiative
  - Download and use open source software

School on Medical Physics for Radiation Therapy: Dosimetry and Treatment Planning for Basic and Advanced Applications

ICTP

25 March – 5 April 2019
Trieste, Italy

Further information:
Activity URL: http://indico.ictp.it/event/8651/
smr3278@ictp.it

Thank you for your attention!

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