

Quantitative Radiomics System Decoding the Tumor Phenotype

John Quackenbush and Hugo Aerts



DANA-FARBER/BRIGHAM AND WOMEN'S



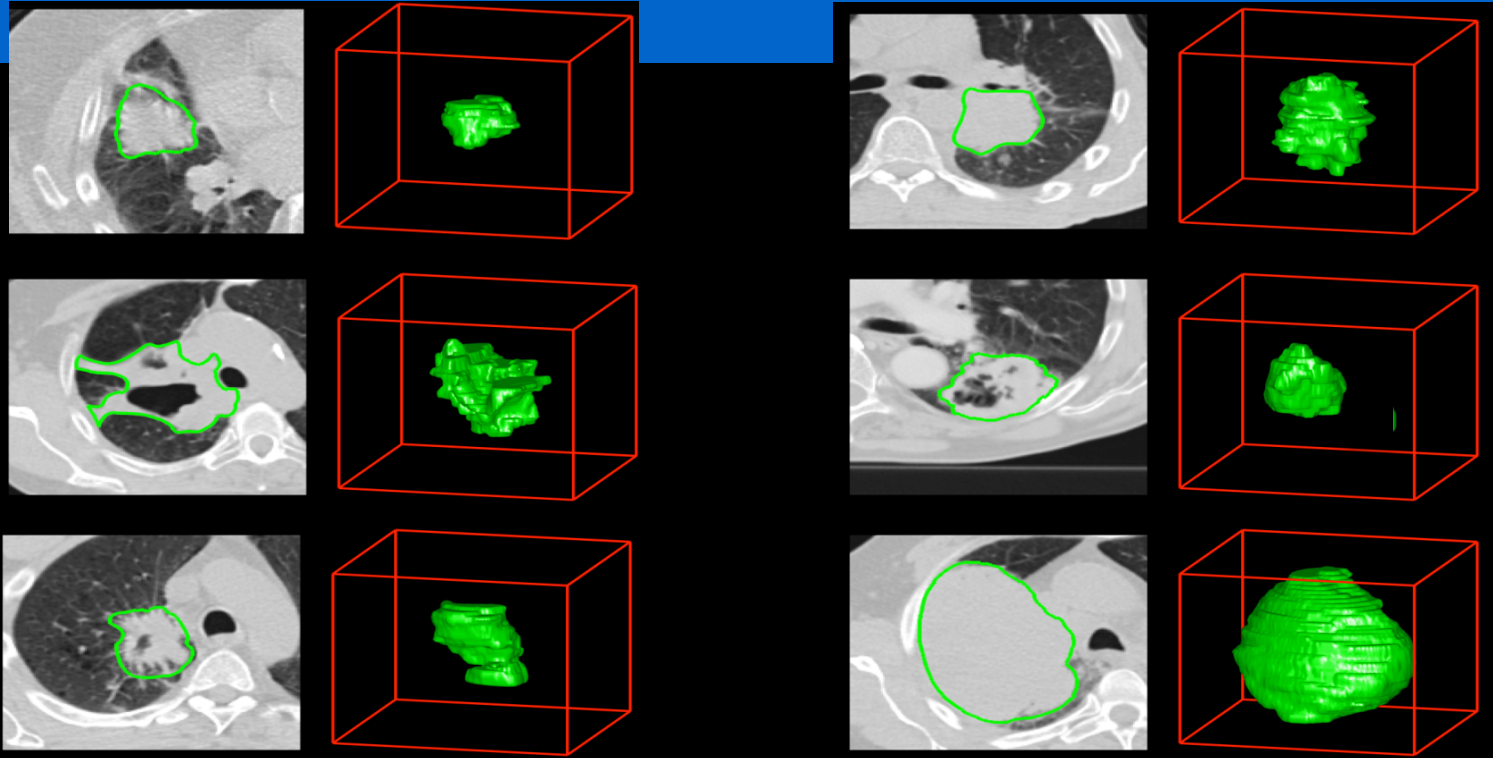
CANCER CENTER



The Radiomics Hypothesis

- **The tumor's structural phenotype reflects its molecular and clinical properties.**
- This is an extension of the clinical use of radiology in which features like volume and density are used to make predictions.
- In Radiomics, we extend this clinical use by extracting and using quantitative image features.
- We extend the use to making predictions of clinical and molecular features.

Representative CT images of lung cancer



Tumors are different

Medical imaging can capture these phenotypic differences

Advantages and Disadvantages

Advantages of Imaging:

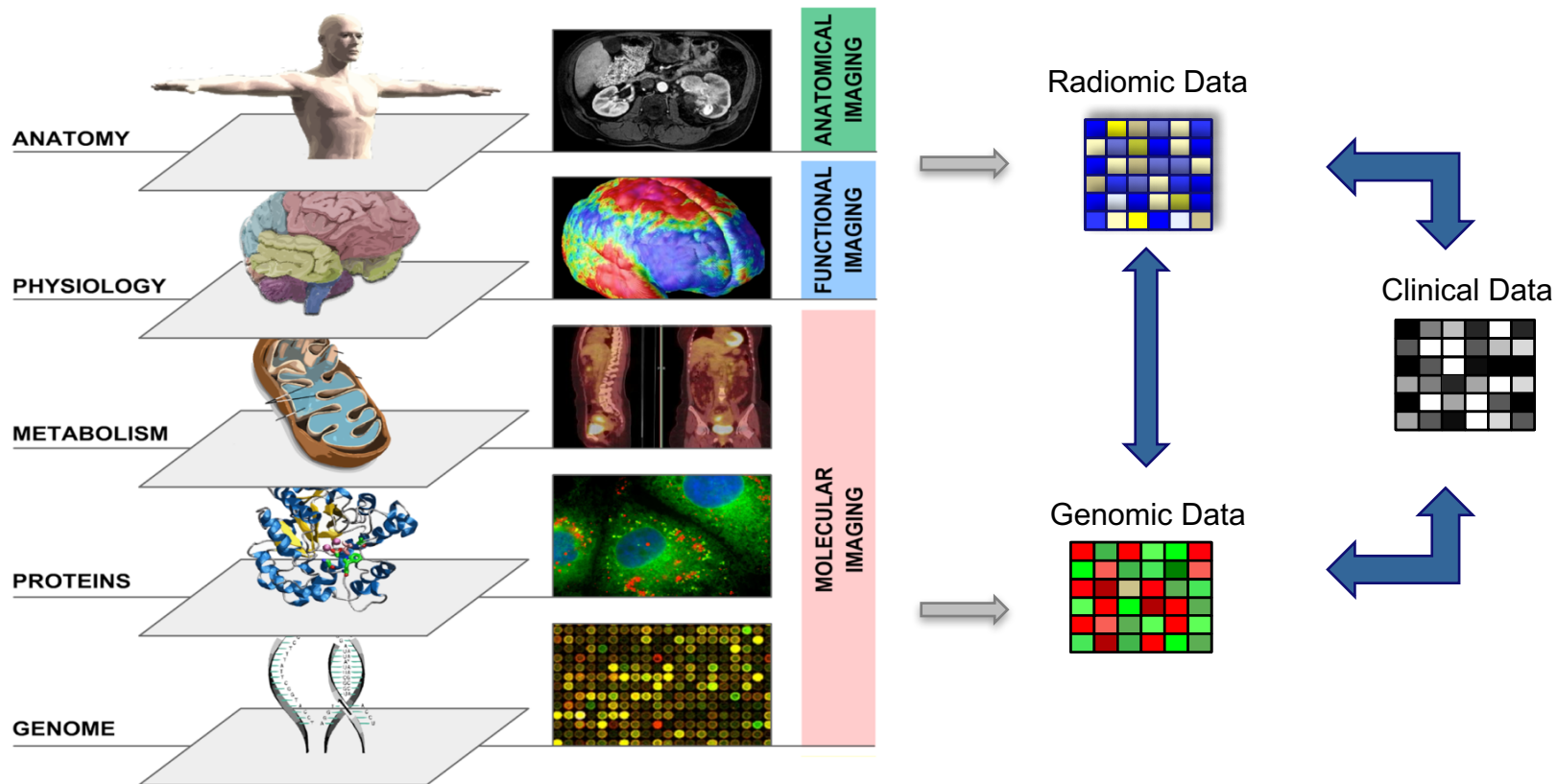
- Performed non-invasively
- Provides 3D picture of the entire cancer
- Already performed in clinical practice
- Multiple times during treatment for diagnosis, staging, radiation oncology planning, response assessment
- Captures a cancer's appearance over time and space

Advantages and Disadvantages

Disadvantages of Imaging:

- Probes the cancer at the macroscopic level
- Often qualitative not quantitative
- Very heterogeneous acquisition protocols:
 - comparisons between patients difficult
 - comparisons same patient in time difficult
- Storage of only reconstructed images (not the raw data)

Multi-level patient data



RADIOMIC TECHNOLOGIES



ENGINEERED FEATURES

Engineered features are those extracted from physician-annotated images of ROI's. They measure quantities including intensity, shape, texture and wavelet. They are then tested for stability across cohorts. Pyradiomics allows for the extracting of such features.

The Present



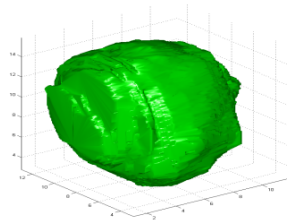
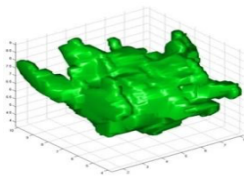
DEEP LEARNING

Deep learning features refers to feature vectors in neural nets' hidden layers. Deep radiomics involves utilizing convolutional neural nets - or convnets - in extracting these features and building prognostic models for supervised and unsupervised learning.

The Future

Radiomic Engineered Feature Set (current release ~1600 features)

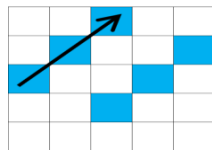
Shape



Texture

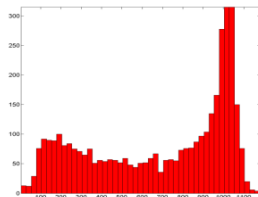


GLCM



GLRL

Stats



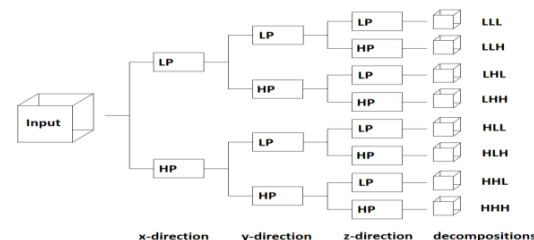
Kurtosis:
$$Kur = \frac{1}{XY} \sum_{x=1}^X \sum_{y=1}^Y \left\{ \left[\frac{I(x, y) - \mu}{\sigma} \right]^4 \right\} - 3$$

Entropy:
$$H = - \sum_{i=1}^{XY} P(i) \cdot \log_2 P(i)$$

LoG



Wavelet



Radiomic features to capture tumor phenotypic details

Imaging-Genomics across cancer types



*Aerts *et al.* Nature Comm. 2014

- Radiomics analysis on CT imaging of >1000 patients with Lung or H&N cancer
- Developed and validated a prognostic radiomics signature that can be applied across cancer types
- Imaging-Genomics analysis showed strong correlations between radiomics and genomics data

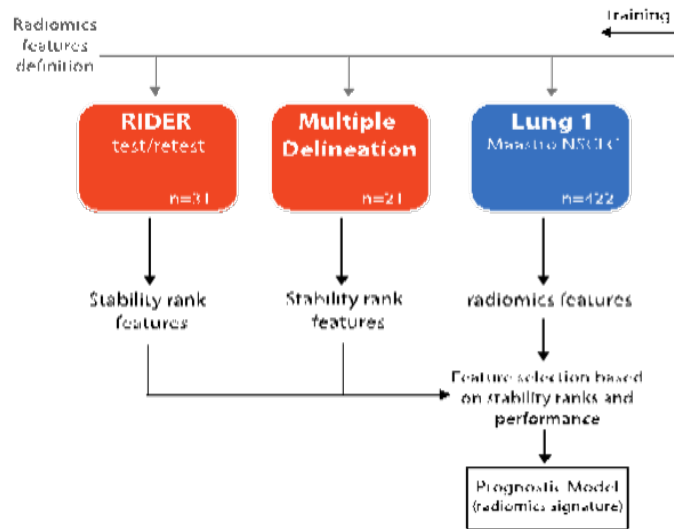
*Aerts *et al.* Nature Comm. 2014



This image cannot currently be displayed.

Lung1 Dataset
422 NSCLC Patients MAASTRO Clinic

Radiomics CT Workflow

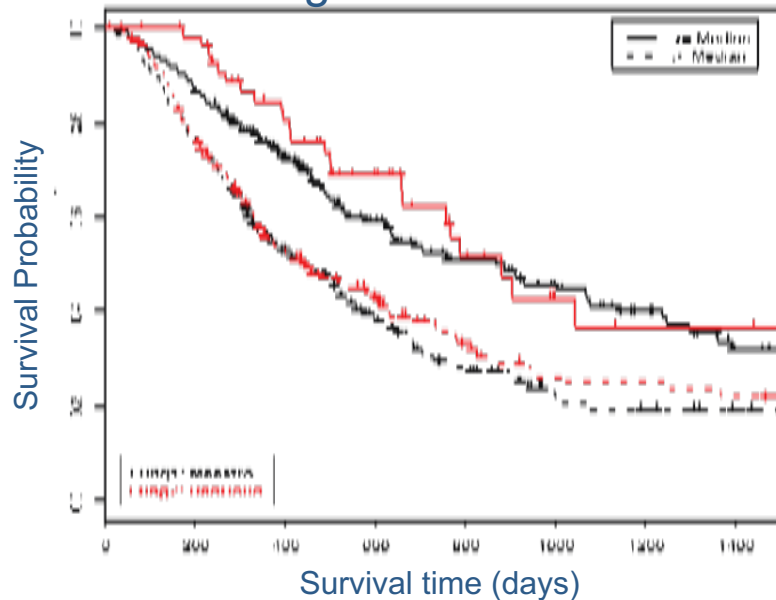


Radiomics Signature:

- 1 "Statistics Energy"
- 2 "ShapeCompactness"
- 3 "Gray Level Nonuniformity"
- 4 Wavelet "Gray Level Nonuniformity HLH"

Radiomics CT Signature Performance

Lung cancer cohorts



Performance Model:

- CI = 0.65 on the Lung2 Validation Dataset (n=225)

Somatic Mutations & Imaging Phenotypes in Lung Adenocarcinoma

Somatic Mutations & Imaging Phenotypes in Lung Adenocarcinoma

PROFILE

(n = 213)

EGFR+ (38/17.8%)

KRAS+ (89/41.7%)

TIANJIN

(n = 257)

EGFR+ (115/45%)

KRAS+ (20/8.1%)

HARVARD - RT

(n = 162)

EGFR+ (19/11.7%)

KRAS+ (59/36.4%)

MOFFITT

(n = 131)

EGFR+ (11/8%)

KRAS+ (47/35.8%)

Mixed histologies

Mixed treatments

Diagnostic CT's

OncoMap panel

Adenocarcinomas

Tx. Surgery

Diagnostic CT's

EGFR and KRAS

Mixed histologies

Tx. Radiotherapy

RT - planning CT's

EGFR and KRAS

Mixed histologies

Tx. Surgery

Diagnostic CT's

EGFR, KRAS, P53 and
STK11

Integrative analysis in 764 patients with lung adenocarcinoma

Question: Can imaging features predict KRAS/EGFR mutational status?

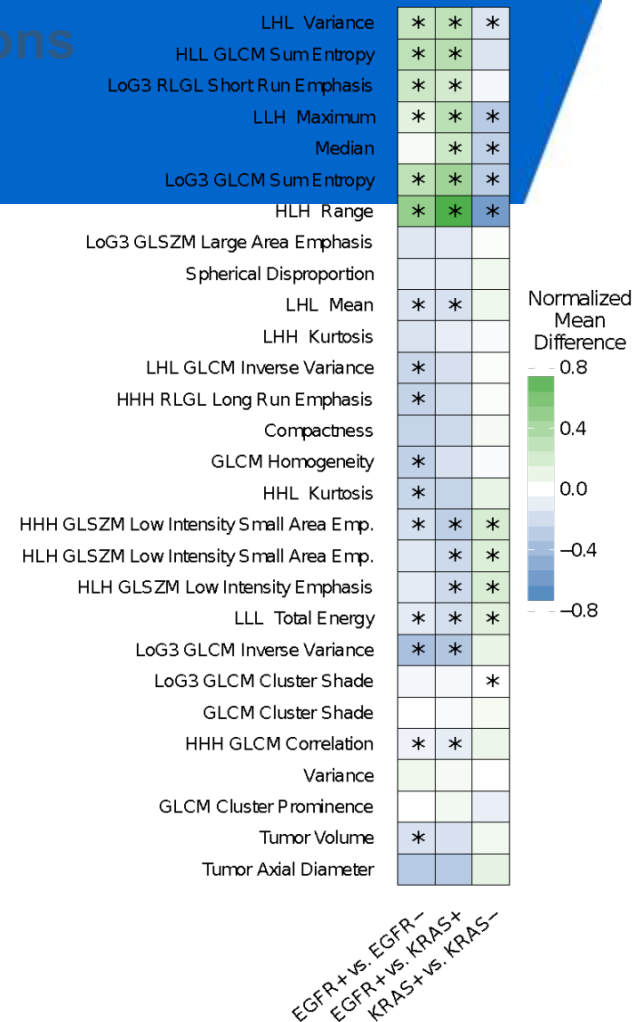
Somatic genotype - imaging phenotype associations

Approach:

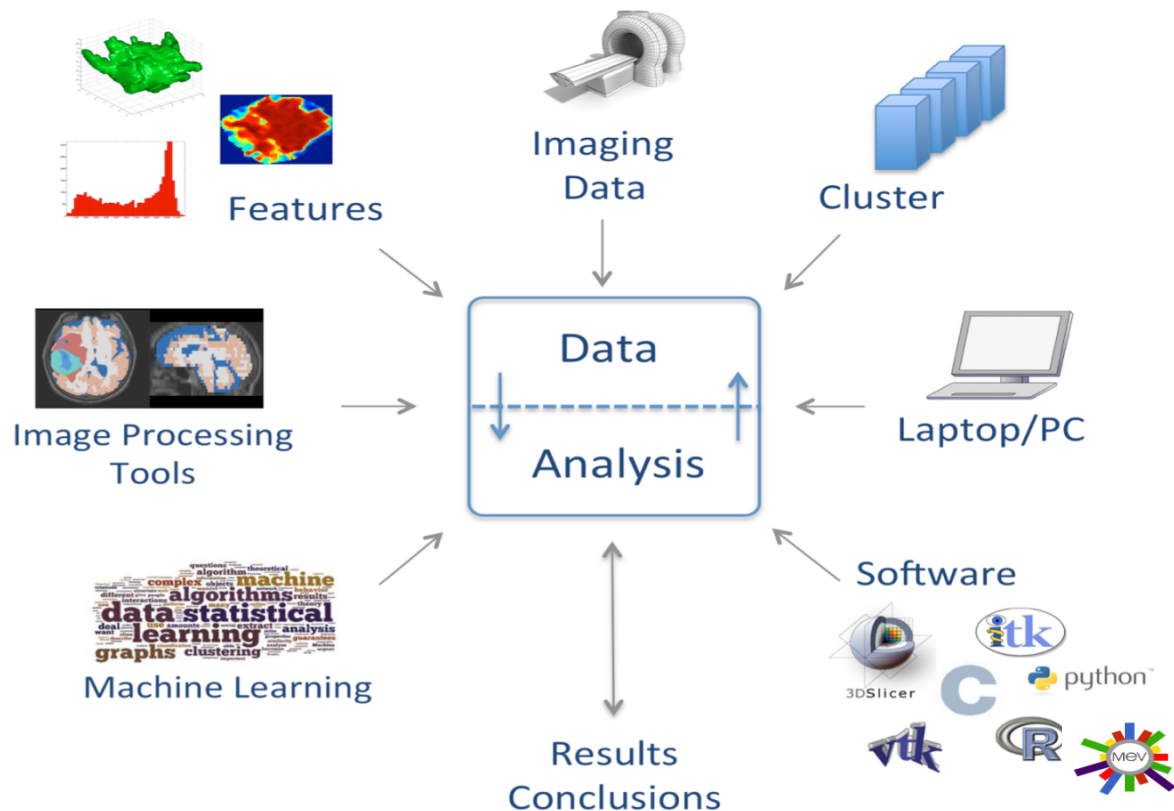
- Use complete integrated dataset to incorporate diversity of genotypic and phenotypic variations across the datasets.
- *A priori*, 26 features were selected based on robustness (test-retest) and independence
- These features were evaluated for differences between mutational subtypes (FDR of 5%).

Results:

- We found 16 radiomic features to be significantly associated with EGFR mutations, and 10 features associated with KRAS mutations.
- EGFR mutated tumors has a higher radiographic heterogeneity, a smaller volume, and presenting overall lower density.
- KRAS mutated tumors were more likely to be homogeneous, with a similar size compared to non-KRAS mutated tumors.



Radiomics Informatics Platform



[www.radiomics](http://www.radiomics.com)



RADIOMICS

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[CODE](#)

[DATA](#)

[TEAM](#)

Quantitative Radiographic Phenotyping

CODE

Radiomic feature extraction and analysis tools

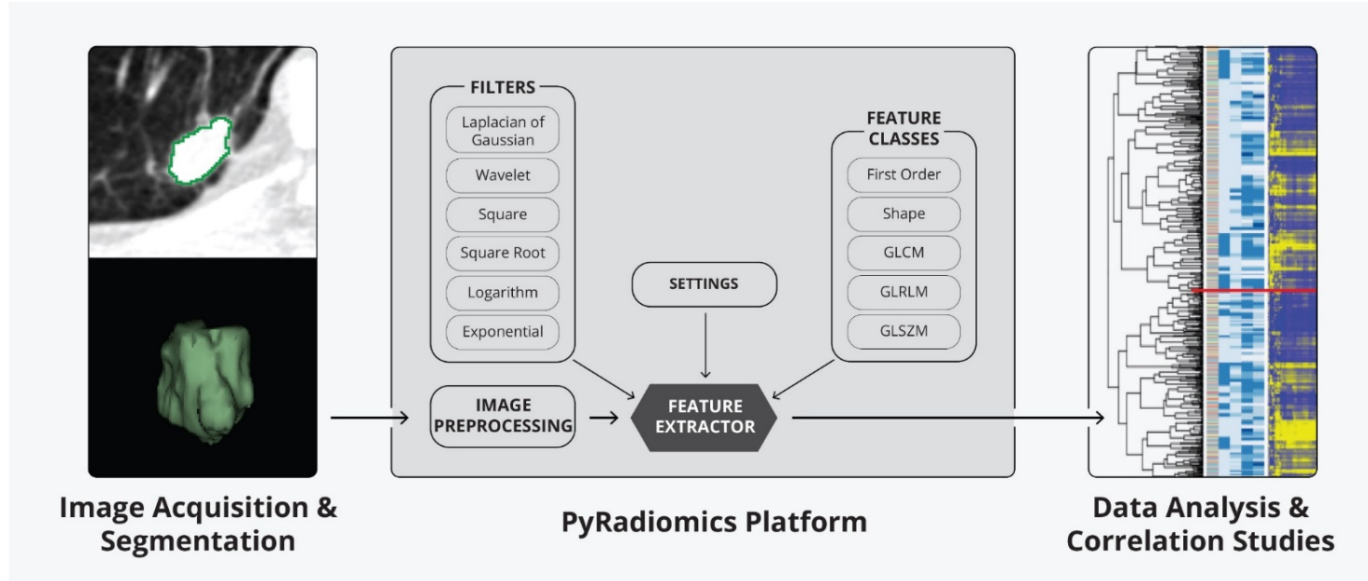
[ALL](#)[ENGINEERED FEATURES](#)[DEEP LEARNING](#)

 python
+
∞ RADIOMICS

 3DSlicer
+
∞ RADIOMICS



PyRadiomics



Open source python package for Radiomic Feature extraction

- Aims to establish a reference standard
- increase awareness of radiomics capabilities
- Supports extraction in 2D and 3D

Extracting engineered features in python

- Easy to use
 - Does not require extensive programming expertise
- Readable source code
 - Supporting users and developers
- Modular design
 - Easy addition of feature classes / filters
 - Pipeline defined in one module for easy usage
- Extracts ~2000 engineered features per image
- Continuous Testing to ensure correct calculation

Easy customization

- All settings combined in 1 parameter file
 - Yaml structured text

```
20 setting:
21   binWidth: 25
22   label: 1
23   interpolator: 'sitkBSpline' # This is an enumerated value, here None is not allowed
24   resampledPixelSpacing: # This disables resampling, as it is interpreted as None, to enable it, specify spacing in x, y, z as [x, y, z]
25   verbose: True
26   weightingNorm: # If no value is specified, it is interpreted as None
27
28 # Input images to use: original for unfiltered image and/or any other filters, see documentation of featureextractor.py
29 # for possible values
30 inputImage:
31   Original: {} # for dictionaries / mappings, None values are not allowed, '{}' is interpreted as an empty dictionary
32
33 # Featureclasses, from which features must be calculated. If a featureclass is not mentioned, no features are calculated
34 # for that class. Otherwise, the specified features are calculated, or, if none are specified, all are calculated.
35 featureClass:
36   shape: # for lists none values are allowed, in this case, all features are enabled
37   firstorder: [] # specifying an empty list has the same effect as specifying nothing.
38   glcm:
39   glrlm:
40   glszm:
41
```

Hosted on GitHub

The screenshot shows the GitHub repository page for **Radiomics / pyradiomics**. The repository is described as an "Open-source python package for the extraction of Radiomics features from 2D and 3D images and binary masks." with a link to <http://pyradiomics.readthedocs.io/>. The repository has 661 commits, 10 branches, 4 releases, and 10 contributors. A table of recent commits is displayed, showing the commit message and the time since the commit.

Commit Message	Time Ago
ENH: Add mask correction and customizable tolerance	9 days ago
DOCS: Restructure documentation on customization	9 days ago
MATH: Remove SumVariance, rename SumVariance2	a month ago
DOCS: Update requirements in documentation	30 minutes ago
BUG: Fix incorrect name for settings in feature extractor	2 days ago
Tests by building against the base Docker	2 months ago
BUG: notebook in python 3 failing	8 days ago
ENH: Define return values for 0-division errors	8 days ago
ENH: Add mask correction and customizable tolerance	9 days ago
ci: Do not test for Docker 17.05.0: images no longer are available	7 months ago

Extensive documentation

pyradiomics

latest

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Radiomic Features

Developers

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Release Notes



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Read the Docs

v: latest

Docs • Welcome to pyradiomics documentation!

Edit on GitHub

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If you publish any work which uses this package, please cite the following publication: *Joost JM van Griethuysen, Andriy Fedorov, Chintan Parmar, Ahmed Hosny, Nicole Aucoin, Vivek Narayan, Regina GH Beets-Tan, Jean-Christophe Fillion-Robin, Steve Pleper, Hugo JWL Aerts, "Computational Radiomics System to Decode the Radiographic Phenotype"; Submitted 2017*

Note

This work was supported in part by the US National Cancer Institute grant 5U24CA194354, QUANTITATIVE RADIOIMCS SYSTEM DECODING THE TUMOR PHENOTYPE.

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values implies more asymmetry about the mean while a lower value indicates a peak near the mean value and less variation about the mean.

```
getClusterShadeFeatureValue()
```

4. Cluster Shade

$$cluster\ shade = \sum_{i=1}^{N_x} \sum_{j=1}^{N_y} (i+j - \mu_x(i) - \mu_y(j))^3 p(i,j)$$

Cluster Shade is a measure of the skewness and uniformity of the GLCM. A higher cluster shade implies greater asymmetry about the mean.

```
getClusterTendencyFeatureValue()
```

5. Cluster Tendency

$$cluster\ tendency = \sum_{i=1}^{N_x} \sum_{j=1}^{N_y} (i+j - \mu_x(i) - \mu_y(j))^2 p(i,j)$$

Cluster Tendency is a measure of groupings of voxels with similar gray-level values.

```
getContrastFeatureValue()
```

6. Contrast

$$contrast = \sum_{i=1}^{N_x} \sum_{j=1}^{N_y} (i-j)^2 p(i,j)$$

Contrast is a measure of the local intensity variation, favoring values away from the diagonal ($i=j$). A larger value correlates with a greater disparity in intensity values among neighboring voxels.

```
getCorrelationFeatureValue()
```

7. Correlation

$$correlation = \frac{\sum_{i=1}^{N_x} \sum_{j=1}^{N_y} p(i,j)ij - \mu_x(i)\mu_y(j)}{\sigma_x(i)\sigma_y(j)}$$

Correlation is a value between 0 (uncorrelated) and 1 (perfectly correlated) showing the linear dependency of gray level values to their respective voxels in the GLCM.

Note

When there is only 1 discrete gray value in the ROI (flat region), σ_x and σ_y will be 0. In this case, an arbitrary value of 1 is returned instead. This is assessed on a per-angle basis.

```
getDifferenceAverageFeatureValue()
```

Slicer Extension

3D Slicer 4.7.0-2017-01-06

File Edit View Help

Modules: Radiomics

3DSlicer

Help & Acknowledgement

Parameters

Input Image Volume: brain1_image

Input LabelMap: brain1_label

Input Segmentation: None

Features: ☒ firstorder ☒ glcm ☒ shape ☒ glrlm ☒ glszm

Toggle Features: All Features No Features

Options

Output

Output table: Table

Apply

Data Probe

☐ Show Zoomed Slice

L
F
B

Python Interactor

```
>>> starting storescp process
(u'Starting E:/Builds/Slicer2013R/Slicer-build/./DCMTK-build/bin/Release/storescp.exe with ', ['5778', '--accept-all', '--output-directory', 'u:C:/Users/Jjoost\\Documents/SlicerDICOMDatabase/incoming', '--exec-sync', '--exec-on-reception', 'u:E:/Builds/Slicer2013R/Slicer-build/./DCMTK-build/bin/Release/dcmdump.exe --load-short --print-short --print-filename --search PatientName "C:/Users/Jjoost\\Documents/SlicerDICOMDatabase/incoming/#?"]')
process E:/Builds/Slicer2013R/Slicer-build/./DCMTK-build/bin/Release/storescp.exe now in state Starting
-----E:/Builds/Slicer2013R/Slicer-build/./DCMTK-build/bin/Release/storescp.exe-----
```

3D View: brain1_label (100%) B: brain1_image

2D View: brain1_label (100%) B: brain1_image

2D View: brain1_label (100%) B: brain1_image

	A	B	C	D	
1	Label	Input image type	Feature Class	Feature Name	Value
2	brain1_label_label_1	general	info	BoundingBox	(162, 84, 11, 47, 70, 7)
3	brain1_label_label_1	general	info	GeneralSettings	('distances': [1], 'additionalInfo': True, 'enableExtensions': True, 'force2D': False, 'interpolator': 'sitkBSpline', 'resampledPixelSpacing': None, 'label': 1, 'norm
4	brain1_label_label_1	general	info	ImageHash	5c9ce3ca174f0f8324ae4d277e0fe82dc5ac566
5	brain1_label_label_1	general	info	ImageCaption	/E:/Builds/Slicer2013R/Slicer-build/./DCMTK-build/bin/Release/storescp.exe

Thank you for your attention

Visit us at

www.radiomics.io

Look at our code at

github.com/radiomics

Watch the movie at

www.youtube.com/watch?v=oN-qZx8VjQc