Implementation of (un)supervised machine-learning models for the automatic classification of tumor aggressiveness

Medical Imaging & Big Data | Data Science
Università degli studi di Milano-Bicocca

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Phantom Setting

The anthropomorphic Alderson Thorax phantom (Radiology Support Devices, Inc.) was used to simulate man/woman thorax or breast body districts. Several synthetic lesions of irregular shape and both homogeneous and heterogeneous uptakes were realized and placed inside the thorax or the breasts of the anthropomorphic phantom within 18F-FDG radioactive background.

A strategy to produce realistic oncological lesions of irregular shape with a homogeneous or a heterogeneous uptake of 18F-FDG was adopted by using 3D-printed irregular shells filled with different concentrations of radioactive gels. To obtain realistic oncological lesions with irregular shape, we defined 3D shells by segmenting the lesion volumes of different oncological lesions on 18F-FDG PET/CT images of real patients. The segmented volumes were then processed in order to generate images of 3D surfaces of lesions, saved in digital files. These surfaces were then cut into two parts by image manipulation and 3D printed using a 3D printer (Renkforce RF1000 Single Extruder) equipped with plastic filaments of 3mm diameter (Renkforce PLA300 Plastic PLA 3 mm), thus manufacturing plastic moulds of patient-derived oncological lesions. The availability of the printed shells allowed obtaining the gold standard (GS) for the sphericity of the shells to be compared with geometrical characteristics of radiomic features as extracted from the PET images of the experimental studies performed with the phantom.

[REF] Gallivanone, F., Interlenghi, M., D'Ambrosio, D., Trifirò, G., & Castiglioni, I. (2018). Parameters Influencing PET Imaging Features: A Phantom Study with Irregular and Heterogeneous Synthetic Lesions. Contrast media & molecular imaging, 2018.

PET Acquisitions

For the PET experimental measurements, the shells were filled with a radioactive gel produced with a fast-setting, chromatic, dust-free alginate powder (phase plus, Zhermack Clinical SpA–Badia Polesine (RO), Italy) mixed with a water solution of 18F-FDG. Lesions with a uniform radioactive uptake were simulated using a gel preparation at a single radioactivity concentration, while gels obtained at different 18F-FDG concentrations were used for lesions simulating heterogeneous uptake.

18F-FDG PET-CT phantom measurements were performed on a Discovery 690 PET/CTsystem (General Electric Medical Systems). Each PET study had an acquisition time of 180 sec for each bed position (two bed positions for each PET acquisition).

Images were reconstructed with a standard protocol optimized for whole-body clinical oncological studies: ordered subset expectation maximization (OSEM) in 3D mode, including Point Spread Function (PSF) and Time of Flight modelling (TOF), 3 iterations and 18 subsets, 5mm filter cut-off and standard z axis filter, reconstructed matrix size 256 × 256, and transaxial field of view of 70 cm.

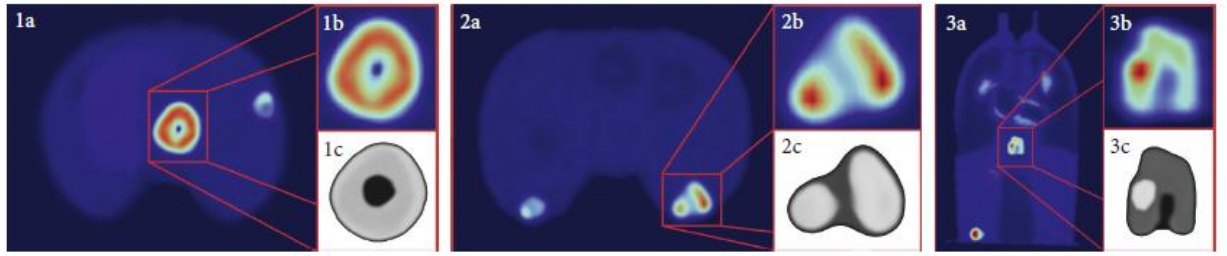


FIGURE 2: Examples of PET images of heterogeneous lesions (a-b, d-e, g-h), with 3D renders of lesions (c, f, i). (1) $V_{GS} = 32.3$ cc, $S_{GS} = 0.73$, $H_{GS} = 0.16$, $L/B_{GS} = 25$; (2) $V_{GS} = 10.5$ cc, $S_{GS} = 0.62$, $H_{GS} = 0.26$, $L/B_{GS} = 10$; (3) $V_{GS} = 8.6$ cc, $S_{GS} = 0.49$, $H_{GS} = 0.25$, $L/B_{GS} = 7$.

[REF] Gallivanone, F., Interlenghi, M., D'Ambrosio, D., Trifirò, G., & Castiglioni, I. (2018). Parameters Influencing PET Imaging Features: A Phantom Study with Irregular and Heterogeneous Synthetic Lesions. Contrast media & molecular imaging, 2018.

Image Segmentation

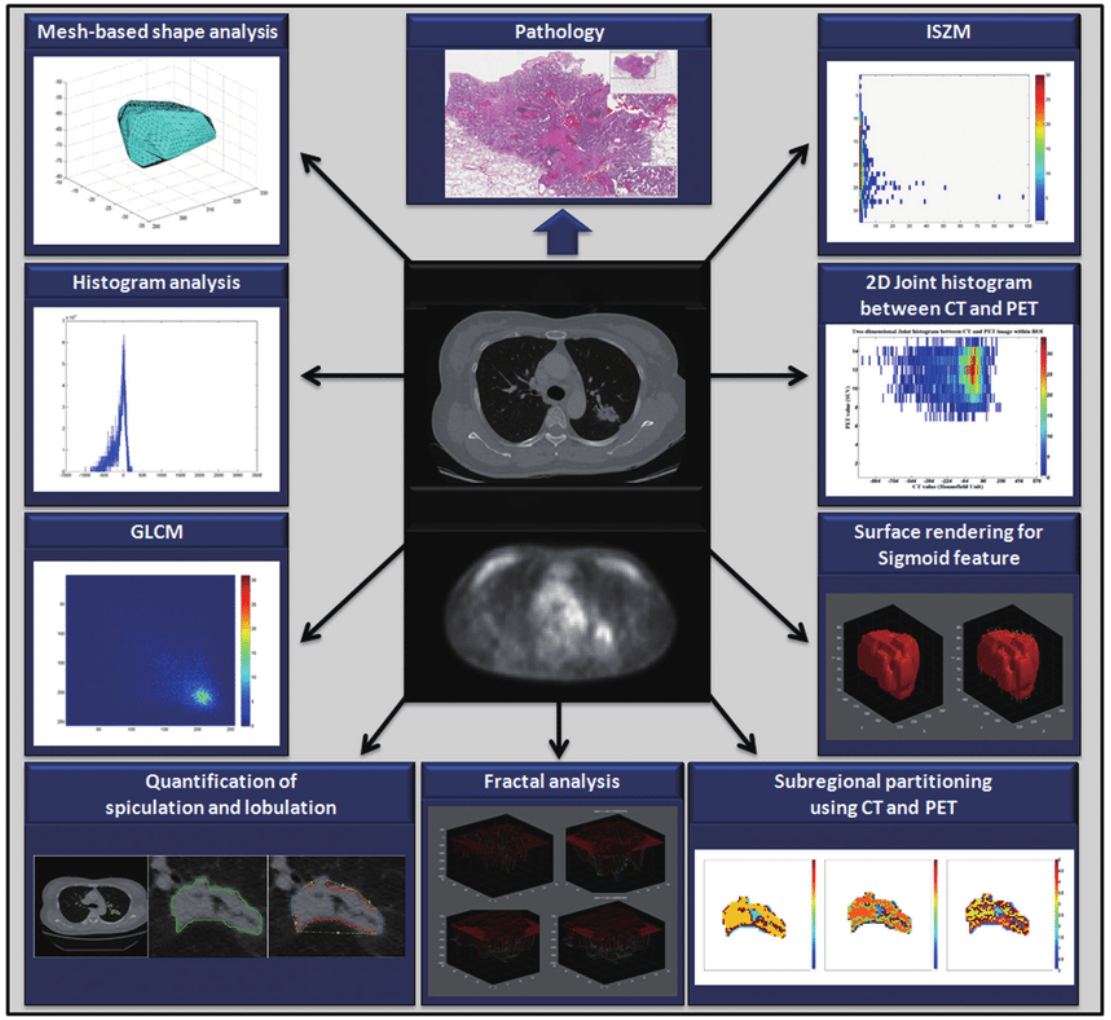
PET images of lesions were segmented in order to obtain the Metabolic Tumor Volume (MTV) from which we will extract the radiomic features. Segmentation methods used in this work included an adaptive threshold method and a fixed threshold method.

The adaptive method was (previously) calibrated and validated on a variety of synthetic lesions miming real oncological lesions (i.e., with spherical and non-spherical shape and with homogenous and non-homogenous 18F-FDG uptake), with an accuracy in the MTV measurement of 92%.

The fixed threshold method was implemented with a cut-off of 60% from the maximum lesion uptake value. This threshold is a good compromise between a good estimate of the lesion volume and a good estimate of the lesion uptake, minimizing the possibility to include radioactivity background in the estimate.

[REF] Gallivanone, F., Interlenghi, M., D'Ambrosio, D., Trifirò, G., & Castiglioni, I. (2018). Parameters Influencing PET Imaging Features: A Phantom Study with Irregular and Heterogeneous Synthetic Lesions. Contrast media & molecular imaging, 2018.

Feature Extraction | Radiomics

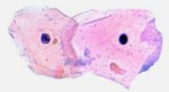
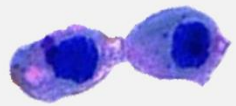
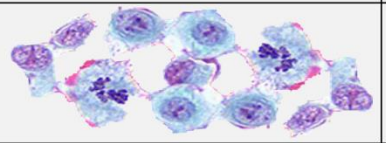
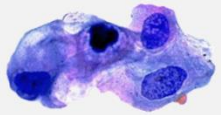
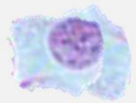
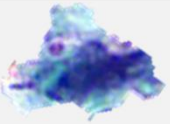


https://www.researchgate.net/figure/Various-radiomic-features-such-as-mesh-based-shape-histogram-gray-level-co-occurrence_fig3_315902486

Feature Extraction | Radiomics

Morphological features

1. Metabolic Target Volume (MTV)
2. Surface
3. Spherical disproportion
(ratio between measured surface of the lesion and surface of an equivalent-sphere in terms of volume)
4. Sphericity
5. Surface-to-volume ratio

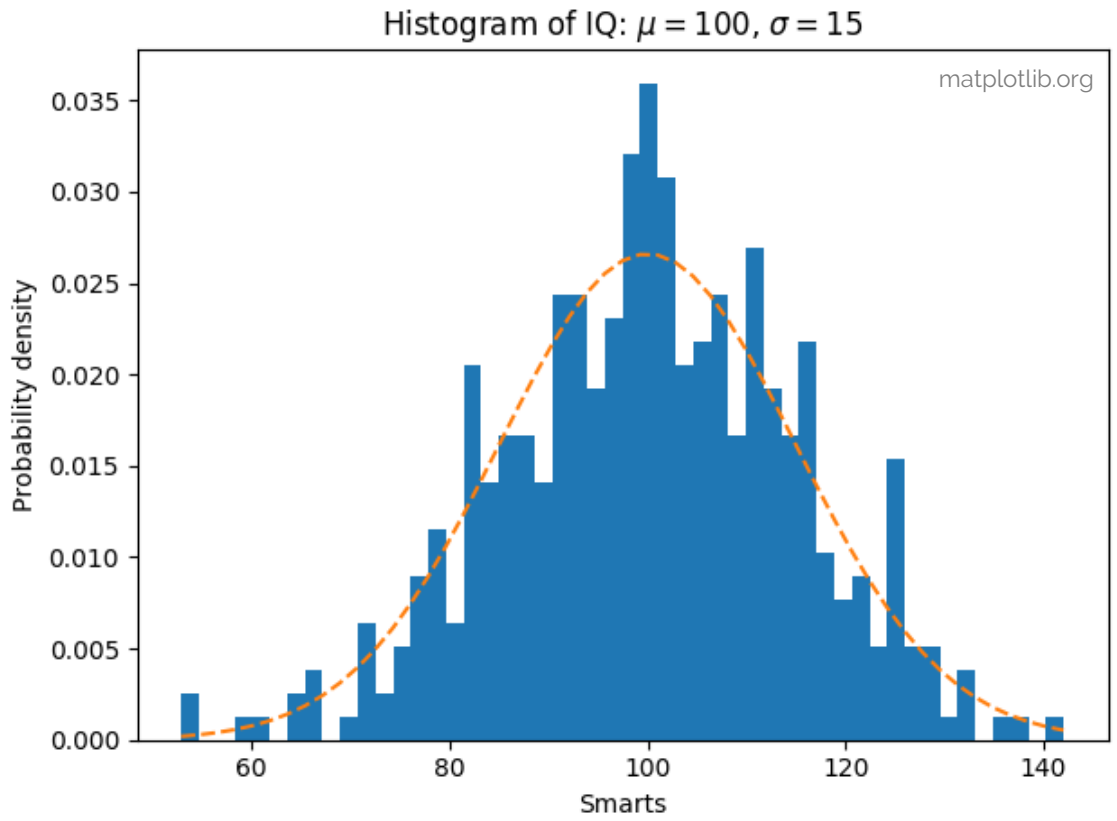
Normal	Cancer	
		Large, variably shaped nuclei
		Many dividing cells; Disorganized arrangement
		Variation in size and shape
		Loss of normal features

http://sphweb.bumc.bu.edu/otlt/MPH-Modules/PH/PH709_Cancer/PH709_Cancer7.html

Feature Extraction | Radiomics

Histogram-based features

1. Maximum
2. Minimum
3. Mean
4. Median
5. Mean Absolute Deviation (MAD)
6. Root Mean Square (RMS)
7. Energy
8. Entropy
9. Kurtosis
10. Skewness
11. Standard Deviation
12. Uniformity
13. Variance

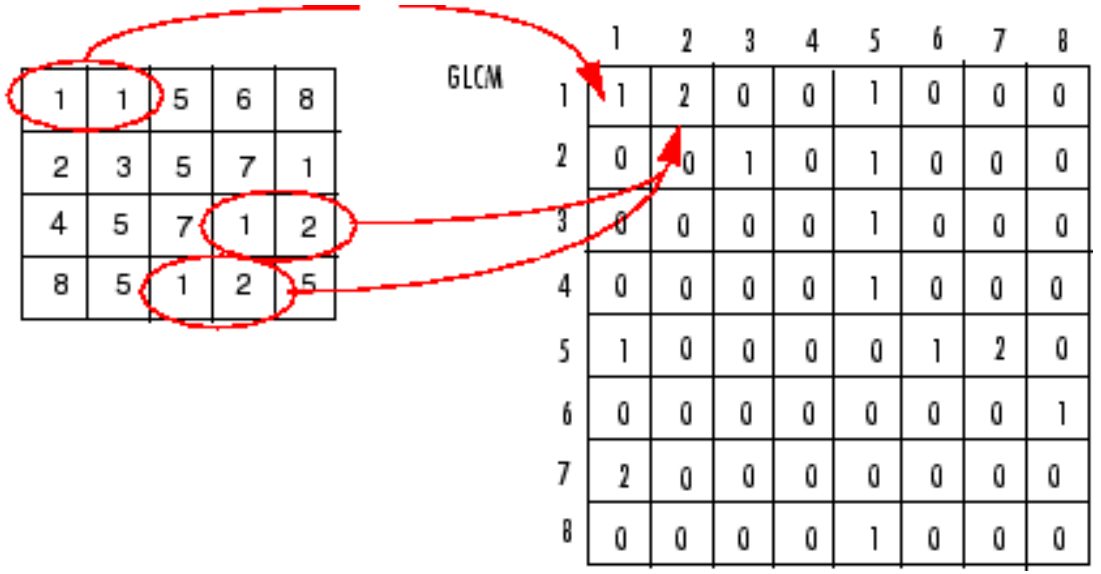


Feature Extraction | Radiomics

Texture descriptors
Gray-Level Co-occurrence Matrix (GLCM)*

1. Energy
2. Contrast
3. Entropy
4. Homogeneity
5. Correlation
6. Sum Average
7. Variance
8. Dissimilarity
9. Auto Correlation

* A Gray Level Co-occurrence Matrix (GLCM) quantifies the number of times the combination of levels X and Y occur in two pixels in the image that are separated by a distance of D pixels along angle A.



mathworks.com

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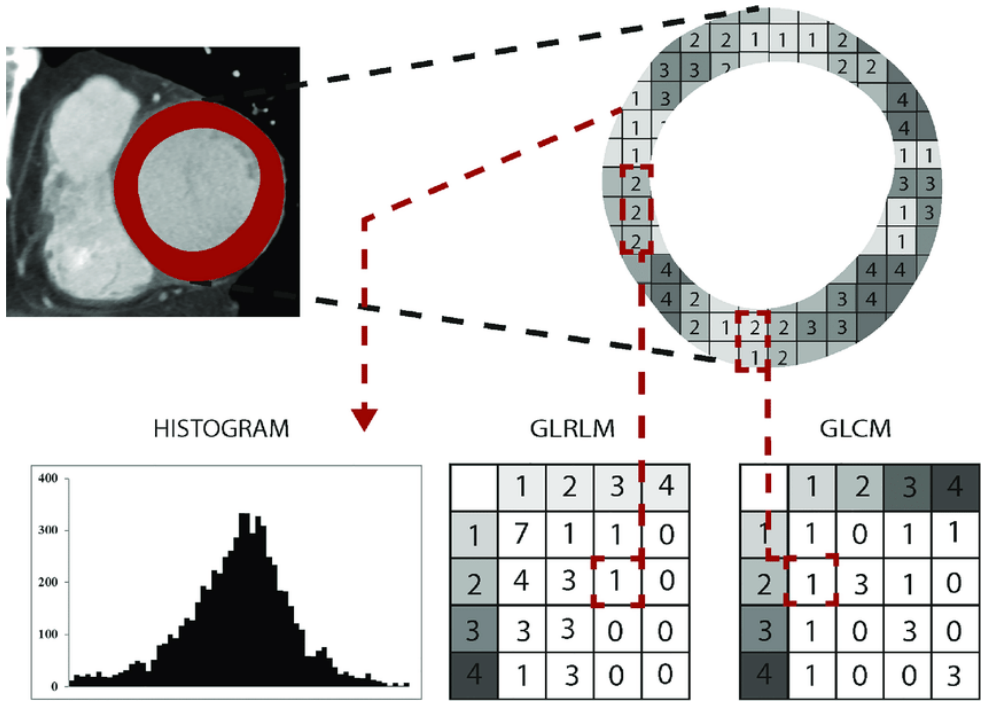
Texture descriptors

Gray-Level Run Length Matrix (GLRLM)*



	1	2	3	4
1	7	1	1	0
2	4	3	1	0
3	3	3	0	0
4	1	3	0	0

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

https://www.researchgate.net/figure/Principles-of-generating-texture-analysis-features-Principles-of-generating-the_fig2_320821651

*A Gray Level Run Length Matrix (GLRLM) quantifies gray level runs, which are defined as the length in number of pixels, of consecutive pixels that have the same gray level value.

It describes # runs with gray level G and length L that occur in the image along angle A.

Texture descriptors

Gray-Level Size Zone Matrix (GLSZM)

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

Level g	*Size zone*, s 1	2	3
1	2	1	0
2	1	0	1
3	0	0	1
4	2	0	1

http://thibault.biz/Research/ThibaultMatrices/GLSZM/GLSZM.html

* A gray level zone is defined as a the number of connected voxels that share the same gray level intensity.

Contrary to GLCM and GLRLM, the GLSZM is rotation independent, with only one matrix calculated for all directions in the ROI

Texture descriptors

Neighbouring Gray Tone Difference Matrix (NGTDM)*

$$\mathbf{I} = \begin{bmatrix} 1 & 2 & 5 & 2 \\ 3 & 5 & 1 & 3 \\ 1 & 3 & 5 & 5 \\ 3 & 1 & 1 & 1 \end{bmatrix}$$

i	n_i	p_i	s_i
1	6	0.375	13.35
2	2	0.125	2.00
3	4	0.25	2.63
4	0	0.00	0.00
5	4	0.25	10.075

https://pyradiomics.readthedocs.io/en/latest/features.html

* A Neighbouring Gray Tone Difference Matrix quantifies the difference between a gray value and the average gray value of its neighbours within distance D