


Radiomics Features

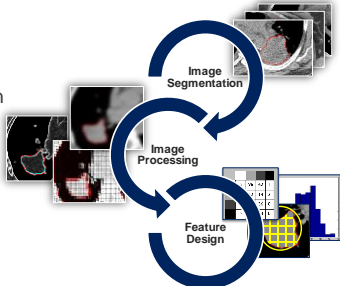
Xenia Favè, PhD
August 1, 2018

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RETHINKING MEDICAL PHYSICS



Outline for this talk

- o Common Features
- o Image Segmentation
- o Image Processing
- o Image Modality



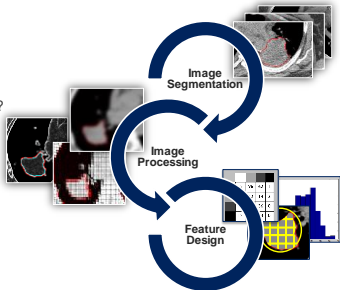
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RETHINKING MEDICAL PHYSICS

X. Favè, Radiomics Features

Outline for this talk

- o How are radiomic features defined?
- o Where did they come from?
- o What should you consider when calculating them?
- o How can you improve their reproducibility?
- o How do imaging modality/parameters affect feature reproducibility?



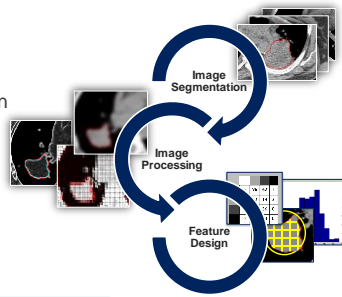
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Main Feature Categories

- 1st Order Statistics
 - Histogram-based
 - Uses all or part of the intensity distribution in ROI
 - Spatial distribution is not evaluated
- 2nd Order (Textural)
 - Characterize spatial relationships between pixel intensities
- Higher Order
 - Filters are applied to image to extract repetitive or non-repetitive data
 - Examples include wavelets, Laplacian of Gaussian
 - 1st and/or 2nd order features are calculated post-filtering
- Shape
 - Ignores pixel intensity entirely

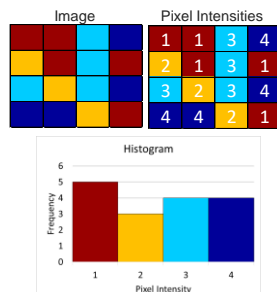
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Histogram

- Typical Features
 - Maximum
 - Minimum
 - Mean
 - Standard Deviation
 - Entropy
 - Skewness
 - Kurtosis

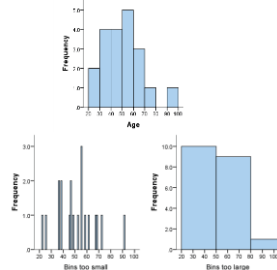


Figures adapted from https://github.com/petcarlson/petcarlson.github.io/blob/master/_posts/2015-7-10-radionics-package.md

Histogram

- Parameters: Bin width
 - Want to pick a width that fairly represents the distribution of your data
 - Can reduce data noise

Bin	Frequency	Scores Included in Bin
20-30	2	22,23
30-40	4	36,38,36,38
40-50	4	46,42,48,46
50-60	5	55,52,52,58,55
60-70	3	68,67,61
70-80	1	72
80-90	0	-
90-100	1	91

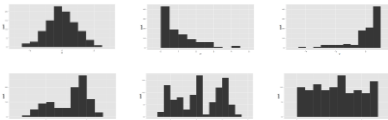


<https://statistics.laerd.com/statistical-guides/understanding-histograms.php>
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Histogram Shapes

- Histograms for your feature calculation can be any shape
- Ideally there will be a difference in the shapes of the histograms for tumors with/without the characteristic you are looking for



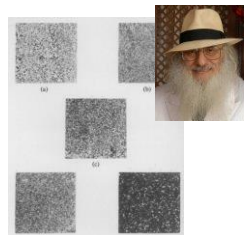
Images from: <https://en.wikipedia.org/wiki/Histogram>

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RETHINKING MEDICAL PHYSICS

Gray Level Co-occurrence Matrix (GLCM/COM) features

- The COM features were defined by Robert Haralick in 2 papers in 1973 and 1979.
- Were tested on
 - Photomicrographs of 5 kinds of sandstone (89% accurate)
 - Aerial photographs of 8 land-use categories (82% accurate)
 - Satellite images of 7 land-use categories (83% accurate)



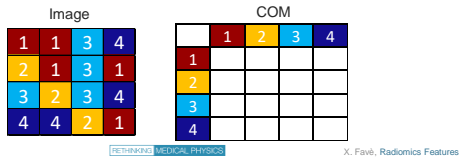
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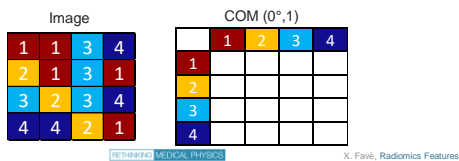
Gray-Level Co-occurrence Matrix (GLCM/COM)

- The COM is a frequency plot of spatial relationships



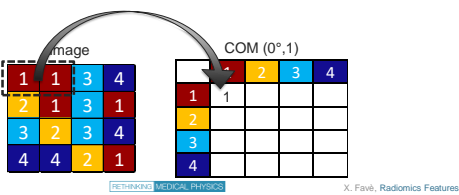
Gray-Level Co-occurrence Matrix (GLCM/COM)

- The COM is a frequency plot of spatial relationships
- Is directional and step size dependent



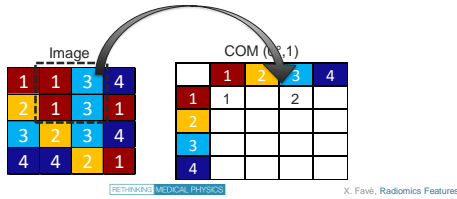
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Gray-Level Co-occurrence Matrix (GLCM/COM)

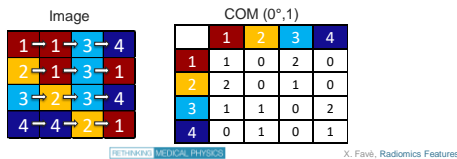
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Gray-Level Co-occurrence Matrix (GLCM/COM)

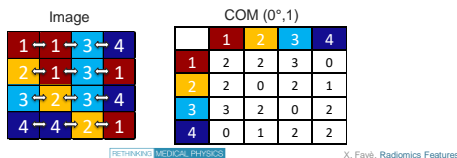
- The COM is a frequency plot of spatial relationships
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Gray-Level Co-occurrence Matrix (GLCM/COM)

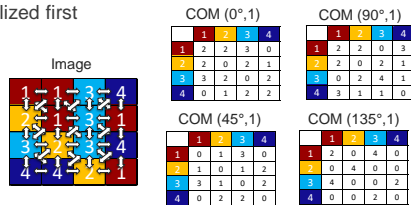
- The COM is a frequency plot of spatial relationships
- Is directional and step dependent
- For radiomics, the matrices are typically symmetric



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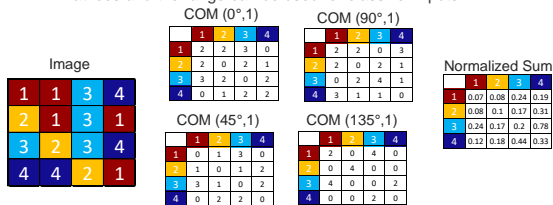
Gray-Level Co-occurrence Matrix (GLCM/COM)

- Features can be calculated from matrices for each direction individually, though the matrices would be normalized first



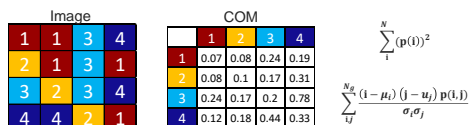
Gray-Level Co-occurrence Matrix (GLCM/COM)

- Features are typically calculated from a normalized sum of the directional matrices or
- The average of the feature values measured from the 4 directional matrices and the range can be used for classifier inputs



Gray-Level Co-occurrence Matrix (GLCM/COM)

- Haralick defined 14 features that can be measured from his matrix
- Features assume texture information is contained in average spatial relationship between gray tones (and thus calculable from the matrices)
- "Even though these features contain information about the textural characteristics of the image, it is hard to identify which specific textural characteristic is represented by each"



COM Features

Parameters:

- Bin size
- Step size
- Directions(4 for 2D and 13 for 3D)
- Symmetric/Asymmetric

	1	2	3	4
1	0.07	0.08	0.24	0.19
2	0.08	0.1	0.17	0.31
3	0.24	0.17	0.2	0.78
4	0.12	0.18	0.44	0.33

- Auto-correlation
- Cluster prominence
- Cluster shade
- Cluster tendency
- Contrast
- Correlation
- Difference entropy
- Dissimilarity
- Energy
- Entropy
- Homogeneity
- Homogeneity 2
- Information measure correlation 1
- Information measure correlation 2
- Inverse difference moment norm
- Inverse difference norm
- Inverse variance
- Max probability
- Sum average
- Sum entropy
- Sum variance
- Variance

Gray-level run-length matrix (GLRLM/RLM)

- Defined by Galloway in 1975
- Used to classify same terrain samples as in Haralick's study
- Had 83% accuracy so similar results to the COM



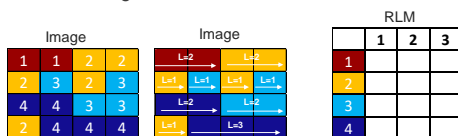
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Gray-level run-length matrix (GLRLM/RLM)

- Matrix of run lengths
- Number of columns defined by max run length in the image



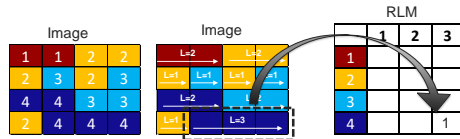
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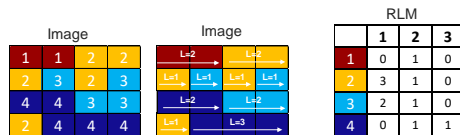
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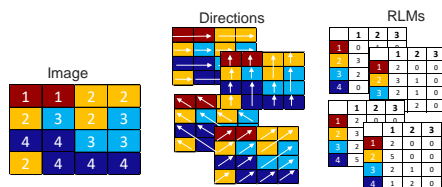
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Gray-level run-length matrix (GLRLM/RLM)

- Calculated for multiple directions and can be summed like the COM



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RLM Features

- Features emphasize different areas in the matrix to highlight noise (short runs) or signal (long runs)
- 11 Features
 - Short runs emphasis
 - Long runs emphasis
 - Gray level non-uniformity
 - Run length non-uniformity
 - Run percentage
 - Short run low gray level emphasis
 - Short run high gray level emphasis
 - Long run low gray level emphasis
 - Long run high gray level emphasis
 - Low gray level run emphasis
 - High gray level run emphasis
- Parameters
 - Pixel intensity binning
 - Directions (2D or 3D)



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Gray-level size zone matrix

- Defined by Thibault *et al* in 2013 to classify cell nuclei to diagnose patients with Progeria disease
- "A homogenous texture is composed of large areas of the same intensity and not of small groups of pixels or segments in a given direction"

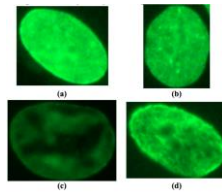
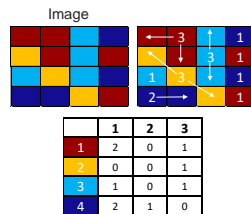


Fig.1 – Examples of nuclei highlighted with FITC : above two homogeneously textured nuclei (a and b) and below two nuclei with an inhomogeneous texture.

Image from Thibault et al. Shape and texture indexes application to cell nuclei classification. *Int. J. Path. Recongn. Artif. Intell.* 27, 1357002 (2013). <https://doi.org/10.1142/S02618901415070024>

Gray-level size zone matrix (GLSZM)

- Designed to quantify regions of contiguous pixels in the image
- Set up in the same way as the GLRLM but with zone sizes instead of run lengths as the columns
- Does not have to be calculated for multiple directions



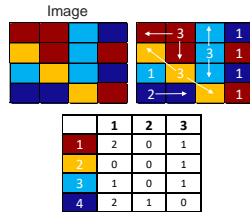
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Gray-level size zone matrix (GLSZM) Features

- Same 11 features as the RLM
 - Short runs emphasis
 - Long runs emphasis
 - Gray level non-uniformity
 - Run length non-uniformity
 - Run percentage
 - Short run low gray level emphasis
 - Short run high gray level emphasis
 - Long run low gray level emphasis
 - Long run high gray level emphasis
 - Low gray level run emphasis
 - High gray level run emphasis
- Parameters:
 - Pixel intensity binning
 - 2D vs 3D



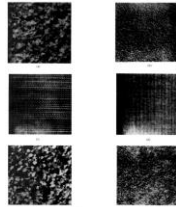
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Neighborhood Grey-Tone Difference Matrix (NGTDM/NDM)

- Defined by Amadasun in 1989
- Specifically designed to correlate to human visual perception (busyness, coarseness, etc)
- Used to rank natural textures: cork, straw matting, beach pebbles



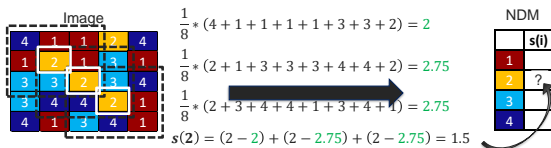
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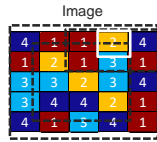
Neighborhood Grey-Tone Difference Matrix (NGTDM/NDM)

- NDM is a 1 column matrix with a value for each intensity
- Value is the difference between the intensity and the average value of the neighborhood around that intensity
- Specific to a chosen neighborhood size (e.g. 3)



Neighborhood Grey-Tone Difference Matrix (NGTDM/NDM)

- Features
 - Busyness
 - Coarseness
 - Contrast
 - Complexity
 - Texture Strength
- Parameters
 - Pixel intensity binning
 - Neighborhood size and 2D/3D
 - Will pixels on the border contribute?



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Locally Calculated Features

- Studies so far have focused on globally calculated features:
 - Calculate it once for the segmented tumor
- Could calculate it locally from multiple neighborhoods of predetermined size covering the tumor
- Then used the standard deviation of that feature or its max to evaluate whether any portion of the tumor has a high heterogeneity region

Globally Calculated

- Feature Value = 12



Locally Calculated

- Feature value varies across neighborhoods in tumor



Laplacian of Gaussian

- Laplacian of Gaussian Filter highlights edges in an image.

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

- Increasing σ will change the filter scale from fine to coarse.
- Features are computed from the filtered image's histogram.
- Parameters
 - Filter scale, sigma
 - Histogram bin size

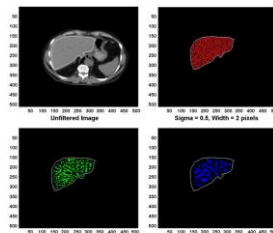
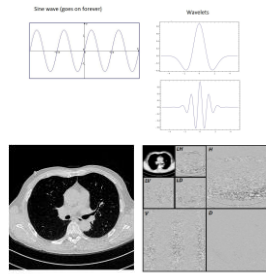


Fig. 1. Unfiltered and filtered images at different sigma values in the non-contrast enhanced image.

Garcia et al. Texture analysis in non-contrast enhanced CT: impact of malignancy on texture in apparently disease-free area of the liver. European J. of Radiology 75(1), 101-110 (2008).

Wavelets

- Wavelets are 'mini-waves', versus sine or cosine that go on forever and used in Fourier transforms
- Coefflet wavelet transformation is popular
- Result is wavelet transformed image in different directions (ex: vertical, horizontal, diagonal)
- For decomposition images can then compute histogram or textural features



Zhou et al. Reproducibility of radiomics for deciphering tumor phenotype with imaging (Bioinformatics Journal, Scientific Reports 6, 2438 (2016)).

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Fractals

- Fractal dimension: measures self similarity of a structure at multiple scales
- Often used to characterize non-Euclidean structures in biology
- Describes a structures complexity and homogeneity
- Box counting method:
 - How many (N) squares include the image border for different square sizes (d)
 - Slope of a log-log fit to the data is the fractal dimension

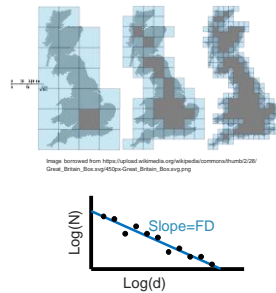


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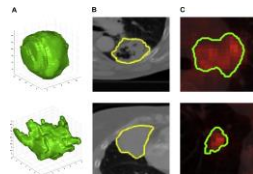
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Shape Features

- Innately connected to reproducibility and repeatability of segmentation
- Less spherical tumors are commonly believed to correlate with higher probability of metastasis and poorer outcome
- Unaffected by pixel intensity
- Features

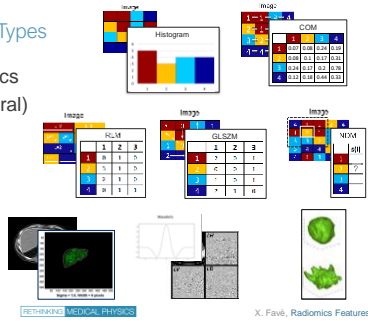
- Volume
- Surface area
- Surface area density
- Compactness1
- Compactness2
- Convex
- Convex hull volume
- Convex hull volume 3D
- Mass
- Maximum 3D diameter
- Mean breadth
- Number of objects
- Orientation
- Roundness
- Spherical disproportion
- Sphericity



Lambin et al. Radiomics: Extracting more information from medical images using advanced feature analysis. European Journal of Cancer 2012; 48: 441-448DOI: (10.1016/j.ejca.2011.11.036). Copyright © 2011 Elsevier Ltd. Terms and Conditions

Summary: Feature Types

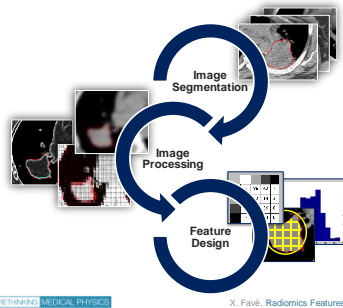
- 1st Order Statistics
- 2nd Order (Textural)
- Higher Order
- Shape



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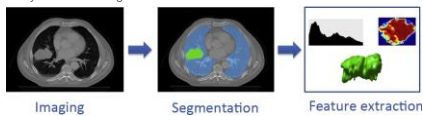
- Common Features
- **Image Segmentation**
- Image Processing
- Image Modality



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Image Segmentation

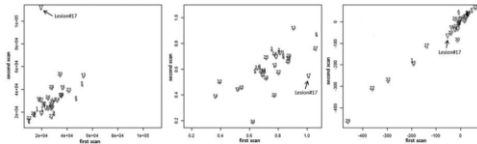
- Segmentation is performed to define the region of interest from which features will be measured
- Techniques:
 - Manual delineation by an expert
 - Semi-automated segmentation
 - Fully automated segmentation



Lambin et al. Radiomics: Extracting more information from medical images using advanced feature analysis. *European Journal of Cancer* 2012 48, 441-446 DOI: (10.1016/j.ejca.2011.11.036). Copyright © 2011 Elsevier Ltd.

Segmentation can affect features

- In a study by Zhao *et al.*, a tumor that was inconsistently contoured on repeat imaging resulted in large changes for certain features, and thus large changes in calculated CCC

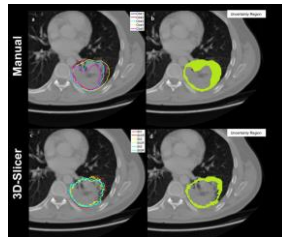


Zhao *et al.* Reproducibility of radiomics for deciphering tumor phenotype with imaging. *Scientific Reports*, 6, 23428 (2016). doi:10.1038/srep23428.

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Auto-segmentation can improve feature variability

- Study by Velazquez *et al* compared
 - Semiautomatic CT-based segmentation method using region-growing in 3D-Slicer
 - Manual physician-drawn contours
 - Macroscopic diameter of tumor in pathology (gold standard)
- Overlap fractions from 3D-Slicer were >0.9
- Both methods were strongly correlated to pathology ($r=0.89$ for auto-segmentation, and $r=0.92$ for manual)

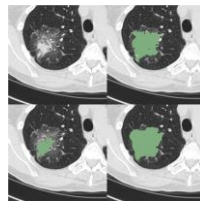


Velazquez *et al.* Volumetric CT-based segmentation of NSCLC using 3D-Slicer. *Scientific Reports*, 3, 3529 (2013). doi:10.1038/srep03529.

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Choice of auto-segmentation tool can affect features

- Kalpathy-Cramer *et al* used patient images from 5 collections in The Cancer Imaging Archive (TCIA)
- 3 institutions with independent auto-segmentation algorithms submitted results for 3 repeat runs for each tumor
- Compared spatial overlaps of submitted volumes and found algorithms differed significantly in their measurements
- Recommendation: The same algorithm should be used for all images in a study



Kalpathy-Cramer *et al.* A comparison of lung nodule segmentation algorithms: methods and results from a multi-institutional study. *J Digit Imaging*, 29(4), 2016. doi:10.1007/s10278-016-9859-z.

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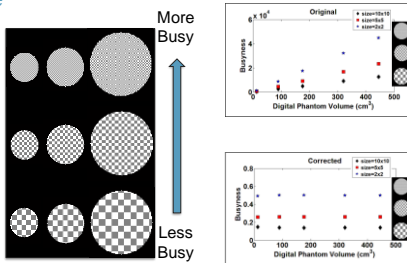
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RETRONIX MEDICAL PHYSICS

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Impact of Volume

- Study by Fave et al used digital phantoms with known textures to evaluate dependence on volume
- Identified four features that were innately volume dependent and proposed corrective factors

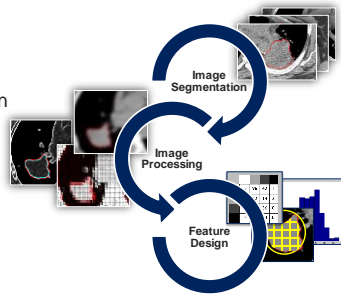


Figures selected from Fave, X. (2017). Detecting and evaluating therapy induced changes in radiomics features measured from non-small cell lung cancer to predict patient outcomes (Doctoral Dissertation). Retrieved from digitallibrary.utoronto.ca

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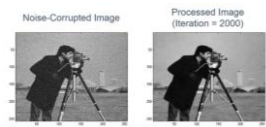
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Common types of image processing

- Image smoothing
- Image enhancement
- Image deblurring
- Thresholding
- Discretization



Images borrowed from <https://chingweishang.weebly.com/image-analysis.html>

Goals are to reduce noise, improve feature usefulness and increase reproducibility while maintaining a feature's dynamic range.

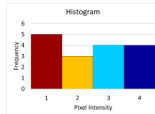
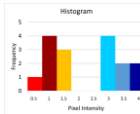
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Discretization versus bin width

- Discretization is the resampling of image intensity values
- AKA binning, downsampling
- Instead of selecting the bin width on the histogram and texture matrices individually, you can downsample your original image set
- Feature value results will be the same

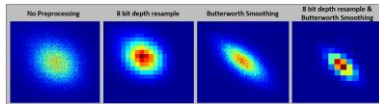


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Image processing affects resulting texture matrices and thus feature values



- Visualization of the impact of different image processing methods on a co-occurrence matrix from the same image

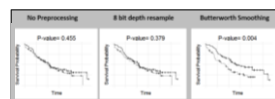
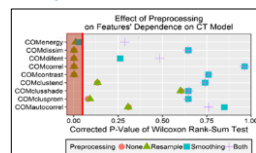
RETHINKING MEDICAL PHYSICS

X. Fave, Radiomics Features

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Image preprocessing can significantly impact usefulness of features

- Study by Fave *et al* evaluated the impact of four preprocessing methods on features'
 - Independence from CT scanner
 - Ability to predict patient outcome
- Results:
 - Differences in features due to CT scanner can be removed with appropriate image processing
 - Image processing directly impacts prognostic ability of a feature

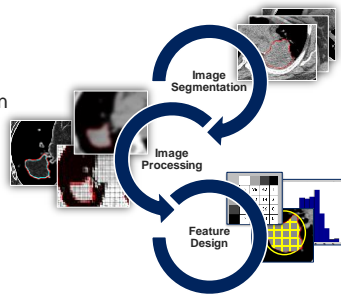


Figures adapted from Fave, X. (2017). Detecting and evaluating therapy-induced changes in radiomics features measured from non-small cell lung cancer by positron emission tomography. Doctoral Dissertation. Retrieved from <https://search.proquest.com/docview/234444444>

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Outline for this talk

- Common Features
- Image Segmentation
- Image Processing
- Image Modality**



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X. Favé, Radiomics Features

Design Goal: Features that are reproducible and repeatable

- Repeatability:** Variability in features extracted from images under the same conditions

- Same subject, imaging system, and acquisition parameters



- Reproducibility:** Variability in features extracted from images acquired under different conditions

- Same subject but with different scanner, imaging parameters, etc



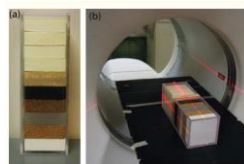
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X. Favé, Radiomics Features

Radiomics features from CT vary with manufacturer and imaging parameters

- 3 studies by Mackin et al used a CT radiomics phantom to assess impact of different scanners and imaging parameters on features
- Results:**

- Variations due to differences in scanners were similar in range to the variations between NSCLC patient features on the same scanner
- Variations in features due to differences in pixel size could be corrected by resampling and using low-pass Butterworth filtering



Mackin et al. Measuring CT scanner variability of radiomics features. *Invest. Radiol.* 50(11): 757-766 (2015). doi: 10.1097/RLI.0000000000000180

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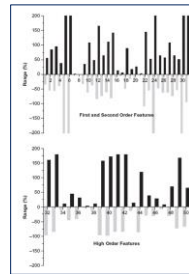
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Variability of PET Features

- Galavis et al evaluated impact of PET acquisition modes and reconstruction parameters on features
- 20 patients imaged
- 50 features were calculated using 5 different reconstruction parameters
- Results: 40/50 features demonstrated large variations >30% and up to 200%

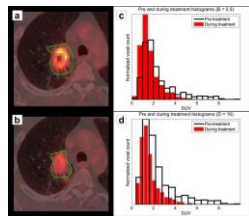


Galavis et al. Variability of textural features in FDG-PET images due to different acquisition modes and reconstruction parameters. *Acta Oncologica*, 49(7):1012-1016. doi.org/10.3109/0284186X.2010.498437

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PET Discretization

- Leijenaar et al studied effect of SUV discretization on radiomics features
- Compared dividing SUV range into equally spaced bins (to maintain a constant intensity resolution) versus maintaining the same number of bins between patients
- Results: Patient ranks changed depending on discretization method



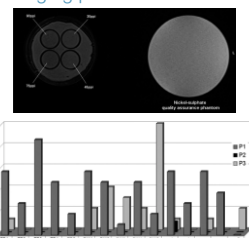
Leijenaar et al. The effect of SUV discretization in quantitative FDG-PET radiomics: the need for standardized methodology in tumor texture analysis. *Scientific Reports*, 5:11075, (2015). doi.org/10.1038/srep11075

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X. Favè, Radiomics Features

Impact of field strength and MR imaging protocol on MR-based features

- Waugh et al measured features from 4 foam phantoms
- Imaged with fast gradient echo sequences and 2 breast RF coils with 3 protocols
- Repetition time, bandwidth echo time and flip angle were altered for each protocol
- Results: Wavelet and COM features correctly differentiated the four phantoms regardless of imaging parameters

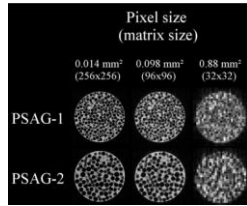


Waugh et al. The influence of field strength and different clinical breast MRI protocols on the outcome of texture analysis using foam phantoms. *Med. Phys.*, 38: 5058-5066, (2011). doi:10.1118/1.3622605

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Impact of MR imaging parameters on features

- Study by Mayerhoefer *et al* investigated sensitivity of features to variations in number of acquisitions, repetition time, echo time, and sampling bandwidth at different spatial resolutions
- Used 2 polystyrene spheres and agar gel phantoms
- Results:
 - Increases in spatial resolution increased the features' sensitivity to acquisition parameters
 - COM features were able to discriminate different patterns despite changes in acquisition parameters

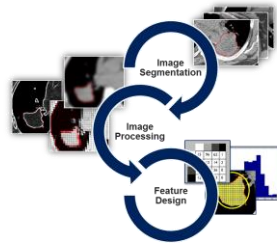


Mayerhoefer et al Effects of MRI acquisition parameter variations and protocol heterogeneity on the results of texture analysis and pattern discrimination: An application-oriented study. *Med. Phys.*, 36: 1236-1243, (2009). doi:10.1118/1.3081408

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Summary

- Take your time designing a feature set
- Image segmentation and acquisition parameters will impact feature values and reproducibility
- Image processing can be used to minimize differences due to acquisition techniques
- Final features should be highly reproducible with a large dynamic range
- Evaluate feature reproducibility and repeatability prior to clinical outcome testing
- Describe selected parameters and image processing as specifically as possible when publishing



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X. Favè, Radiomics Features

Thank you!

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