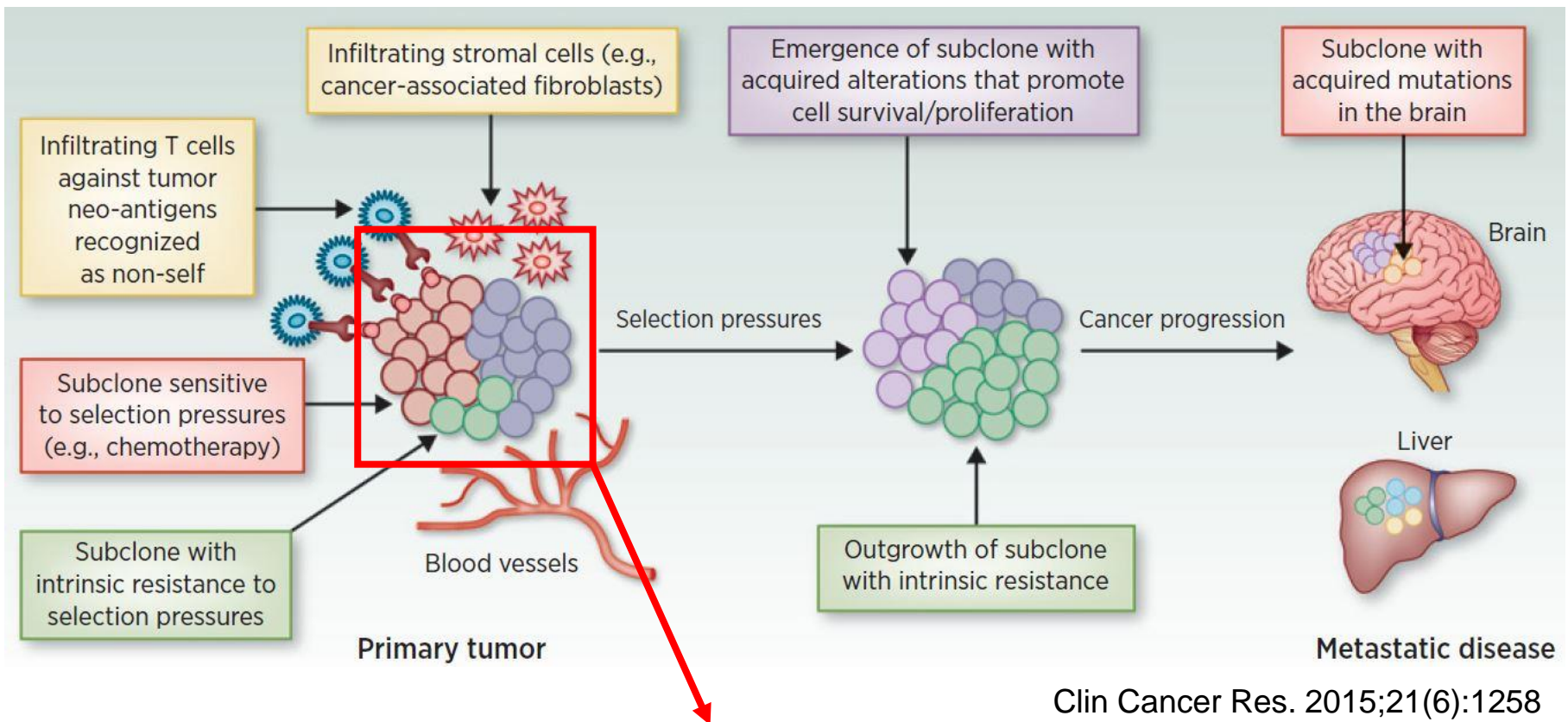


# **Texture features of PET images in cancer research**

鄭乃銘

Nuclear Medicine  
Keelung Chang Gung Memorial Hospital



**Texture analysis → tumor heterogeneity**

## Article types

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[FDG PET/CT radiomics for predicting the outcome of locally advanced rectal cancer.](#)

1. Lovinfosse P, Polus M, Van Daele D, Martinive P, Daenen F, Hatt M, Visvikis D, Koopmansch B, Lambert F, Coimbra C, Seidel L, Albert A, Delvenne P, Hustinx R. Eur J Nucl Med Mol Imaging. 2017 Oct 18. doi: 10.1007/s00259-017-3855-5. [Epub ahead of print] PMID: 29046927

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[Radiomics in paediatric neuro-oncology: A multicentre study on MRI texture analysis.](#)

1. Fetit AE, Novak J, Rodriguez D, Auer DP, Clark CA, Grundy RG, Peet AC, Arvanitis TN. NMR Biomed. 2017 Oct 26. doi: 10.1002/nbm.3781. [Epub ahead of print] PMID: 29073725  
[Similar articles](#)

# Outline

1. Techniques overview
2. Application
3. Variations & Limitations

# Texture work flow

Original images

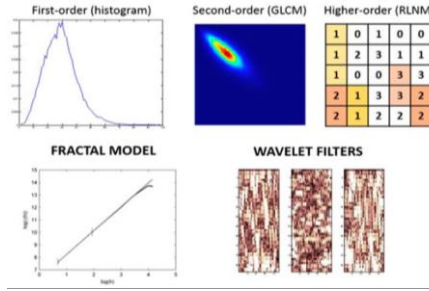


Segmentation

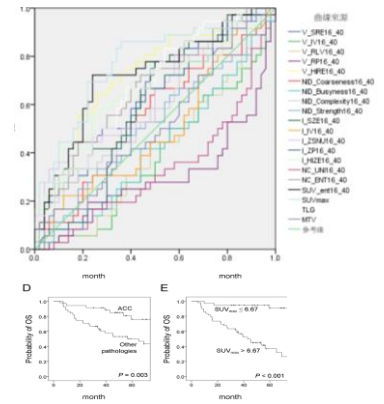


Processing

$$\hat{\gamma}(x) = \left[ \gamma_{\lambda} \times \frac{|\mathcal{W}\mathcal{F}\mathcal{X}(\hat{\gamma}(x)) - \mathcal{W}\mathcal{F}\mathcal{X}(\gamma(x)) + 1|}{|\hat{\gamma}(x) - \mathcal{W}\mathcal{F}\mathcal{X}(\hat{\gamma}(x))|} \right]$$



Analysis



# Techniques

## **A. Statistical methods:**

- 1) Histogram
- 2) Normalized gray-level co-occurrence matrix (NGLCM)
- 3) Neighborhood grey-tone difference matrix (NGTDM)
- 4) Gray level run length matrix (GLRLM)
- 5) Gray level size zone matrix (GLSZM)
- 6) Shape analysis

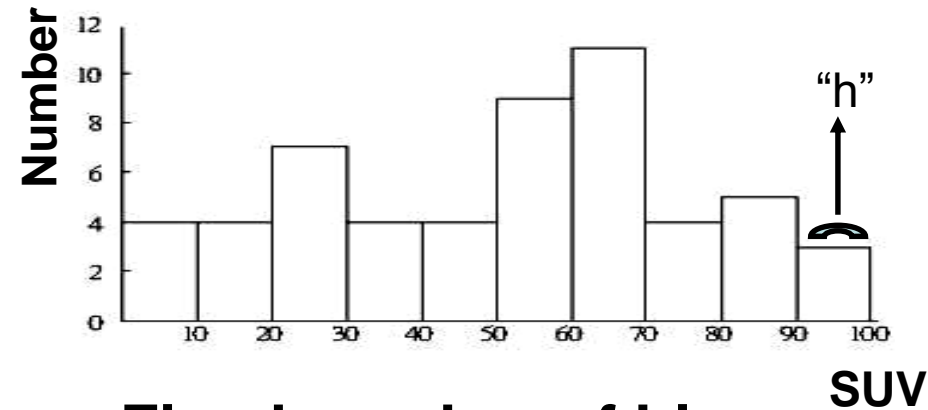
## **B. Fractal analysis**

- 1) Box counting
- 2) Fractional Brownian motion method
- 3) Power spectral method

## **C. Transform-based methods**

- 1) Wavelet transform
- 2) Laplacian of Gaussian (LoG)

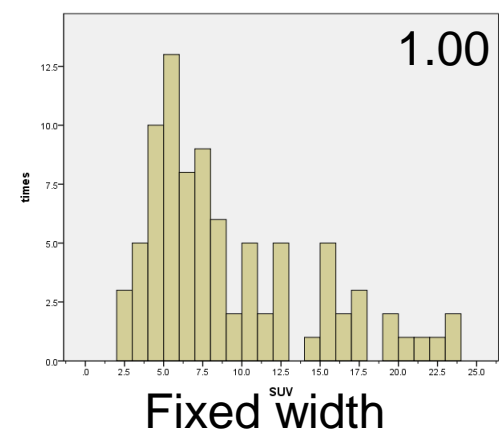
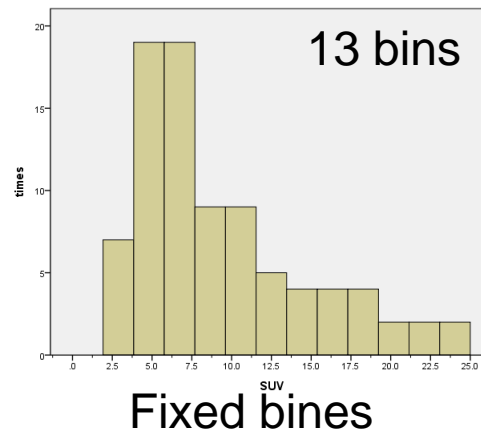
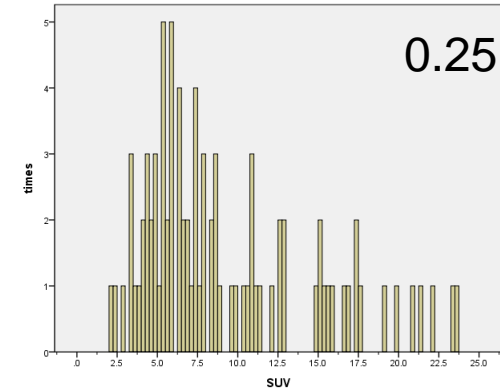
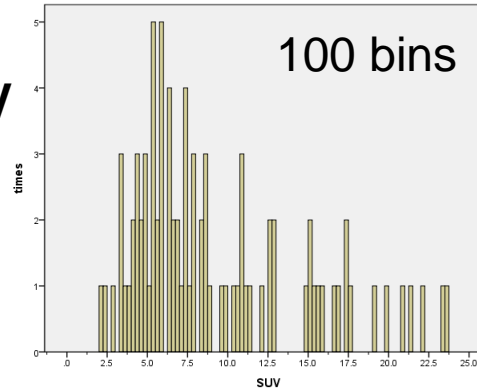
# 1) Histogram



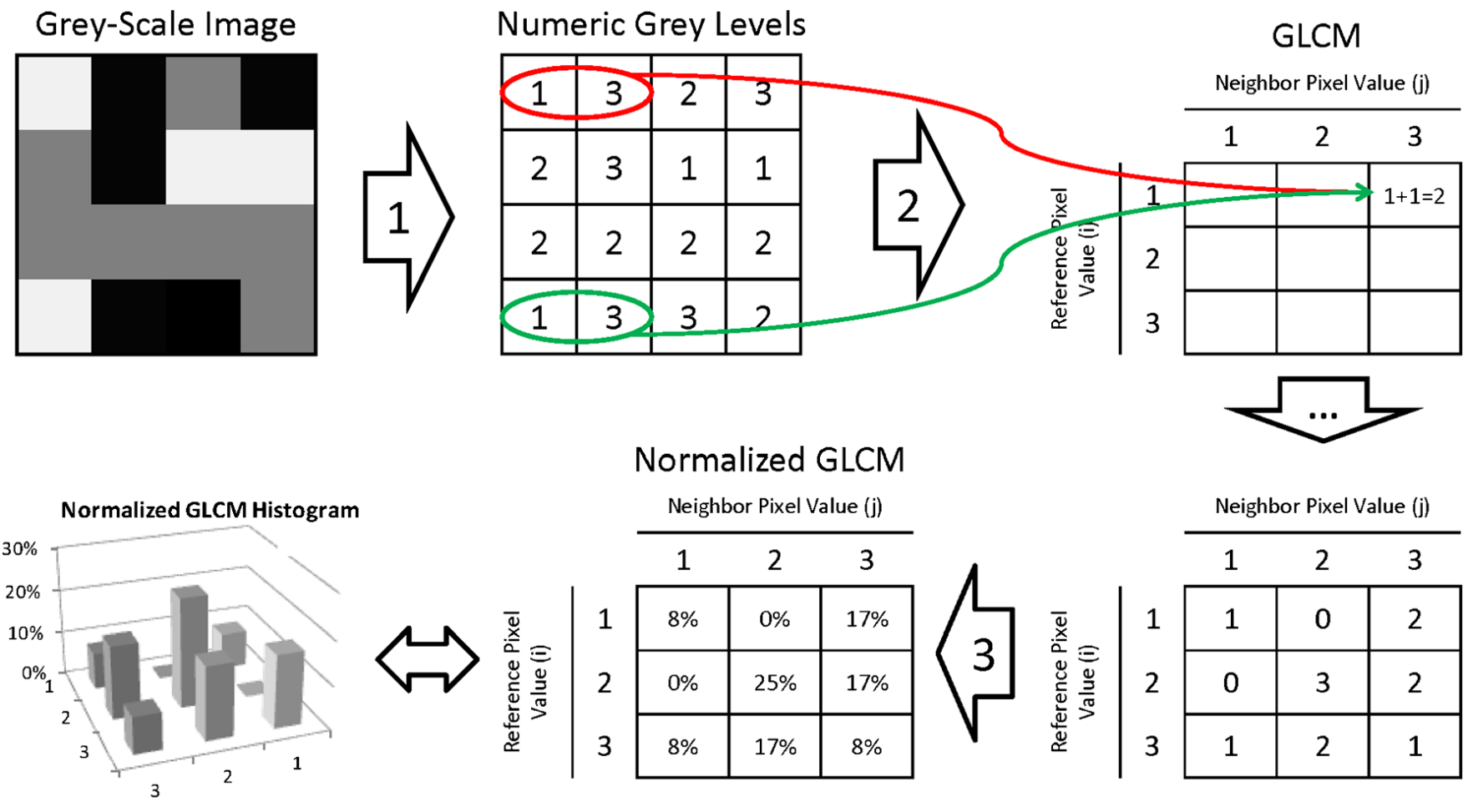
- **Fixed number of bins**
  - Bins (K) = [max – min] / h
- **Fixed width**
- **Parameters**

- SUV<sub>max</sub>
- SUV mean
- MTV
- TLG
- Entropy<sub>hist</sub>
- Skewness
- Kurtosis

$$-\sum_{I=1}^k [P(I)] \log_2 [P(I)]$$



# 2) Normalized gray level co-occurrence matrix (NGLCM)





- Parameters:**

Uniformity (UNI)

$$\sum C_{ij}^2$$

Entropy (ENT)

$$-\sum C_{ij} \log C_{ij}$$

Dissimilarity (DIS)

$$\sum C_{ij} |i - j|$$

Contrast (CON)

$$\sum C_{ij} (i - j)^2$$

Inverse difference (INV)

$$\sum \frac{C_{ij}}{1 + |i - j|}$$

Inverse difference moment (IDM)

$$\sum \frac{C_{ij}}{1 + (i - j)^2}$$

Correlation (COR)

$$\sum \frac{(i - \mu_x)(j - \mu_y)C_{ij}}{\sigma_x \sigma_y}$$

### 3). Neighborhood grey-tone difference matrix (NGTDM)

- Matrix formed by summing the value of the pixel minus the average of the pixels in neighborhood

- Ex: 5x5 image, specify  $d = 1$

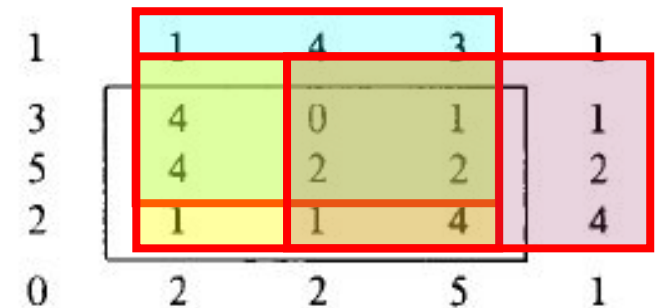
- Neighborhood:  $w = 3 \times 3$

- $s(0) = |0 - (21/8)| = 2.625$

- $s(2) = |2 - (17/8)| + |2 - (15/8)| = 0.250$

- .....

	$s(i)$
0	2.625
1	4.125
2	0.250
3	0.000
4	4.875



# Parameters

Coarseness  $\left[ \epsilon + \sum_{i=0}^{G_h} p_i s(i) \right]^{-1}$

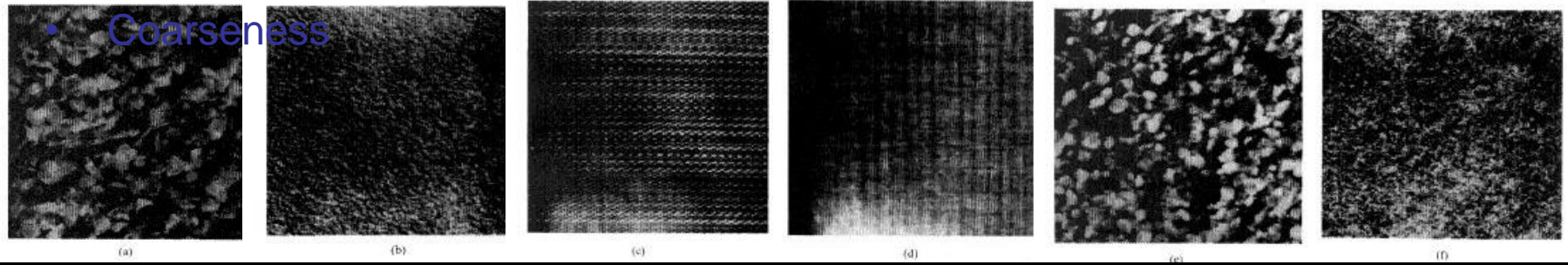
Contrast  $\left[ \frac{1}{N_g(N_g - 1)} \sum_{i=0}^{G_h} \sum_{j=0}^{G_h} p_i p_j (i - j)^2 \right] \left[ \frac{1}{n^2} \sum_{i=0}^{G_h} s(i) \right]$

Busyness  $\left[ \sum_{i=0}^{G_h} p_i s(i) \right] / \left[ \sum_{i=0}^{G_h} \sum_{j=0}^{G_h} i p_i - j p_j \right]$

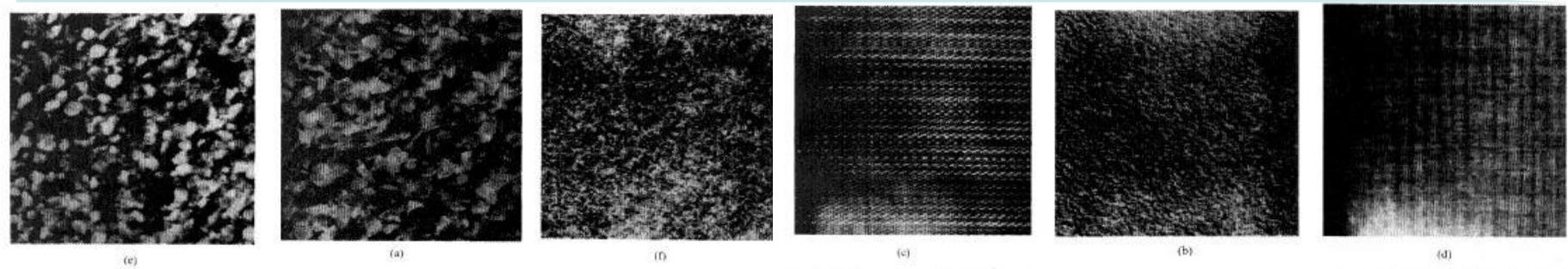
Complexity  $\sum_{i=0}^{G_h} \sum_{j=0}^{G_h} \left\{ (|i - j|) / (n^2 (p_i + p_j)) \right\} \{ p_i s(i) + p_j s(j) \}$

Strength  $\left[ \sum_{i=0}^{G_h} \sum_{j=0}^{G_h} (p_i + p_j) (i - j)^2 \right] / \left[ \epsilon + \sum_{i=0}^{G_h} s(i) \right]$

## Original images



## Coarseness



## 4) Gray level run length matrix (GLRLM)

- Counting the number of pixel segments having the same intensity in a given direction, then representing the results in a matrix

	Image	=>	<table style="border-collapse: collapse; width: 100%; text-align: center;"> <tr> <td style="border: 1px solid black; padding: 5px;">Gray Level (i)</td> <td colspan="4" style="border: 1px solid black; padding: 5px;">Run Length (j)</td> </tr> <tr> <td style="border: 1px solid black; padding: 5px;"></td> <td style="border: 1px solid black; padding: 5px;">1</td> <td style="border: 1px solid black; padding: 5px;">2</td> <td style="border: 1px solid black; padding: 5px;">3</td> <td style="border: 1px solid black; padding: 5px;">4</td> </tr> <tr> <td style="border: 1px solid black; padding: 5px;">1</td> <td style="border: 1px solid black; padding: 5px;">4</td> <td style="border: 1px solid black; padding: 5px;">0</td> <td style="border: 1px solid black; padding: 5px;">0</td> <td style="border: 1px solid black; padding: 5px;">0</td> </tr> <tr> <td style="border: 1px solid black; padding: 5px;">2</td> <td style="border: 1px solid black; padding: 5px;">1</td> <td style="border: 1px solid black; padding: 5px;">0</td> <td style="border: 1px solid black; padding: 5px; background-color: #e0f2f1;">1</td> <td style="border: 1px solid black; padding: 5px;">0</td> </tr> <tr> <td style="border: 1px solid black; padding: 5px;">3</td> <td style="border: 1px solid black; padding: 5px;">3</td> <td style="border: 1px solid black; padding: 5px;">0</td> <td style="border: 1px solid black; padding: 5px;">0</td> <td style="border: 1px solid black; padding: 5px;">0</td> </tr> <tr> <td style="border: 1px solid black; padding: 5px;">4</td> <td style="border: 1px solid black; padding: 5px;">3</td> <td style="border: 1px solid black; padding: 5px;">1</td> <td style="border: 1px solid black; padding: 5px;">0</td> <td style="border: 1px solid black; padding: 5px;">0</td> </tr> </table>	Gray Level (i)	Run Length (j)					1	2	3	4	1	4	0	0	0	2	1	0	1	0	3	3	0	0	0	4	3	1	0	0
Gray Level (i)	Run Length (j)																																
	1	2	3	4																													
1	4	0	0	0																													
2	1	0	1	0																													
3	3	0	0	0																													
4	3	1	0	0																													
	<table style="border-collapse: collapse; text-align: center;"> <tr> <td style="padding: 0 10px;">1</td> <td style="padding: 0 10px;">2</td> <td style="padding: 0 10px;">3</td> <td style="padding: 0 10px;">4</td> </tr> <tr> <td style="padding: 0 10px;">1</td> <td style="padding: 0 10px;">3</td> <td style="padding: 0 10px;">4</td> <td style="padding: 0 10px;">4</td> </tr> <tr> <td style="padding: 0 10px;">3</td> <td style="padding: 0 10px; background-color: #e0f2f1;">2</td> <td style="padding: 0 10px; background-color: #e0f2f1;">2</td> <td style="padding: 0 10px; background-color: #e0f2f1;">2</td> </tr> <tr> <td style="padding: 0 10px;">4</td> <td style="padding: 0 10px;">1</td> <td style="padding: 0 10px;">4</td> <td style="padding: 0 10px;">1</td> </tr> </table>	1	2	3	4	1	3	4	4	3	2	2	2	4	1	4	1																
1	2	3	4																														
1	3	4	4																														
3	2	2	2																														
4	1	4	1																														

Set direction to be  $0^\circ$

Intensity = 1 & length = 1  $\rightarrow$  4

Intensity = 2 & length = 1  $\rightarrow$  1

## 5) Gray level size zone matrix (GLSZM)

- Counting the number of pixel areas having the same intensity, then representing the results in a matrix
- No direction needed

Image									
1	2	3	4	=>	Gray Level (i)	Size Zone (j)			
1	3	4	4		1	2	3	4	
3	2	2	2		2	0	0	1	0
4	1	4	1		3	0	0	1	0
					4	2	0	1	0

## • Parameters

– Short zone emphasis

$$\frac{1}{n_r} \sum_{i=1}^M \sum_{j=1}^N \frac{p(i, j)}{j^2} = \frac{1}{n_r} \sum_{j=1}^N \frac{p_r(j)}{j^2}$$

– Long zone emphasis

$$\frac{1}{n_r} \sum_{i=1}^M \sum_{j=1}^N p(i, j) \cdot j^2 = \frac{1}{n_r} \sum_{j=1}^N p_r(j) \cdot j^2$$

– Grey level variability

$$\frac{1}{n_r} \sum_{i=1}^M \left( \sum_{j=1}^N p(i, j) \right)^2 = \frac{1}{n_r} \sum_{i=1}^M p_g(i)^2$$

– Size zone variability

$$\frac{1}{n_r} \sum_{j=1}^N \left( \sum_{i=1}^M p(i, j) \right)^2 = \frac{1}{n_r} \sum_{j=1}^N p_r(i)^2$$

( $p$ : point number)

– Zone percentage

$$\frac{n_r}{n_p} \quad n_r: \text{total runs}; n_p: \text{total pixels}$$

- Low-intensity zone emphasis  $\frac{1}{n_r} \sum_{i=1}^M \sum_{j=1}^N \frac{p(i, j)}{i^2} = \frac{1}{n_r} \sum_{i=1}^M \frac{p_g(i)}{i^2}$
- High-intensity zone emphasis  $\frac{1}{n_r} \sum_{i=1}^M \sum_{j=1}^N p(i, j) \cdot i^2 = \frac{1}{n_r} \sum_{i=1}^M p_g(i) \cdot i^2$
- Low-intensity short-zone emphasis  $\frac{1}{n_r} \sum_{i=1}^M \sum_{i=1}^N \frac{p(i, j)}{i^2 \cdot j^2}$
- High-intensity short-zone emphasis  $\frac{1}{n_r} \sum_{i=1}^M \sum_{i=1}^N \frac{p(i, j) \cdot i^2}{j^2}$
- Low-intensity long-zone emphasis  $\frac{1}{n_r} \sum_{i=1}^M \sum_{j=1}^N \frac{p(i, j) \cdot j^2}{i^2}$
- High-intensity long-zone emphasis  $\frac{1}{n_r} \sum_{i=1}^M \sum_{j=1}^N p(i, j) \cdot i^2 \cdot j^2$



2	2	2	1
2	2	2	1
2	2	1	1
1	1	1	1

(A)

2	2	1	1
2	2	1	1
1	1	2	2
1	1	2	2

(B)

2	2	1	2
1	2	1	1
1	1	2	1
2	1	2	2

(C)

**Histogram analysis:**

Maximal; mean; MTV; TLG; entropy:

→ A = B = C

**NGLCM: (R't)**

Uniformity:

→ A = 0.347, B = C = 0.278

A > B = C

**NGTDM:**

Coarseness:

→ A = 1.33, B = 1.00, C = 0.89

A > B > C

**GLRLM: (R't)**

Run-length variability

→ A = 1.57, B = 4.0, C = 3.33;

B > C > A

**GLSZM:**

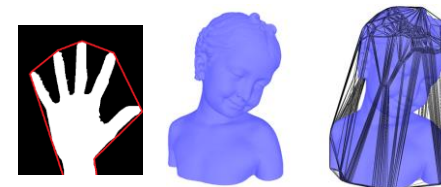
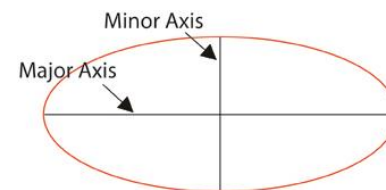
Size zone variability

→ A = 1.0, B = 2.0, C = 1.33;

B > C > A

## 6) Shape analysis

- Eccentricity:  $EC = 1 - \sqrt{\frac{b^2}{a^2}}$ 
  - Minor axis (b) to the major axis (a) of the best-fitted ellipsoid to the region of interest
- Euler number:  $E = C - H$ 
  - The number of connected objects (C) minus the number of holes (H);  $E = C - H = 1 - 3$
- Convexity:
  - The ratio of perimeters of the convex hull over that of the original contour
    - Convex hull: the smallest convex polygon that can contain the region
- Solidity:  $S = A_s / H$ 
  - $A_s$ : surface area of the object;  $H$ : convex hull area
    - The solidity of a convex shape is 1
    - A measurement of convexity
- Extent:  $Ex = A_s / B_b$ 
  - $A_s$ : surface area of the object;  $B_b$ : bounding box
    - Bounding box: the smallest rectangle containing the region
- Asphericity (ASP):
  - For a sphere,  $H=1$ ,  $ASP=0$



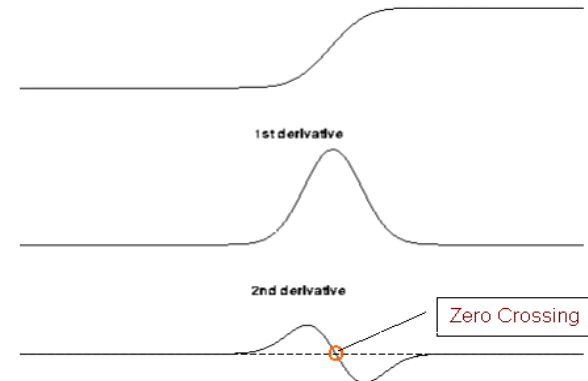
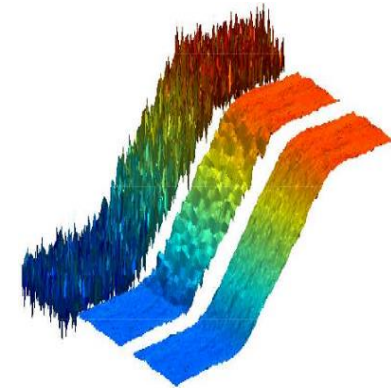
$$ASP = 100 * \left( \sqrt[3]{H} - 1 \right) \text{ with } H = \frac{1}{36\pi} \frac{S^3}{V^2}$$

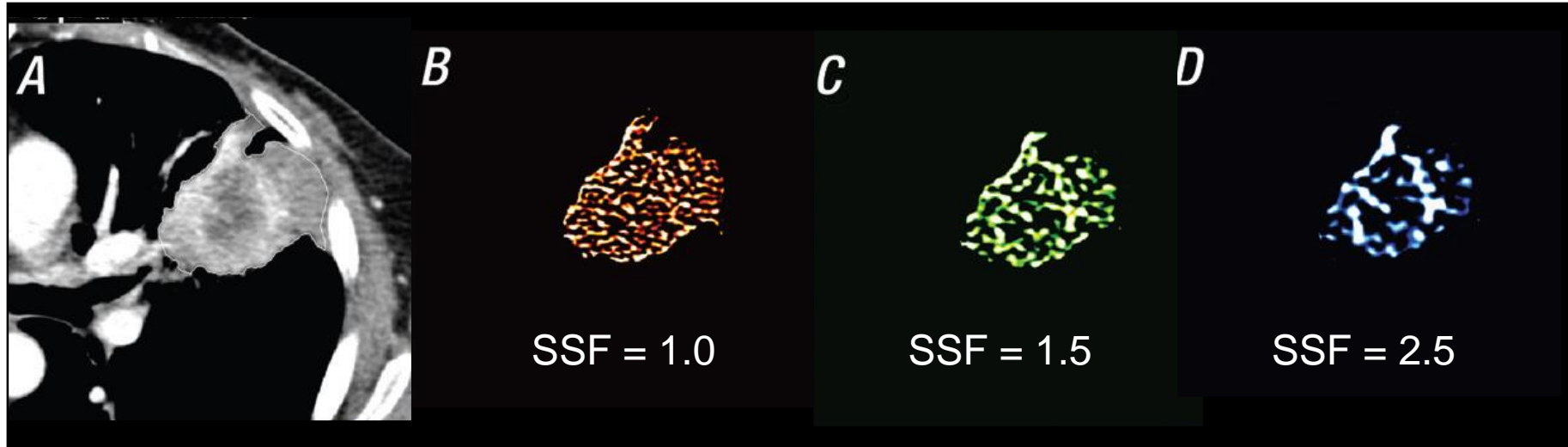
# 7) Laplacian of Gaussian (LoG)

$$\nabla^2 = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2}$$

$$G(x, y) = e^{-\frac{x^2+y^2}{2\sigma^2}}$$

$$\begin{aligned} \nabla^2 G(x, y) &= \frac{\partial^2 G(x, y)}{\partial x^2} + \frac{\partial^2 G(x, y)}{\partial y^2} \\ &= \frac{\partial}{\partial x} \left[ \frac{-x}{\sigma^2} e^{-\frac{x^2+y^2}{2\sigma^2}} \right] + \frac{\partial}{\partial y} \left[ \frac{-y}{\sigma^2} e^{-\frac{x^2+y^2}{2\sigma^2}} \right] \\ &= \left[ \frac{x^2}{\sigma^4} - \frac{1}{\sigma^2} \right] e^{-\frac{x^2+y^2}{2\sigma^2}} + \left[ \frac{y^2}{\sigma^4} - \frac{1}{\sigma^2} \right] e^{-\frac{x^2+y^2}{2\sigma^2}} \end{aligned}$$

ROI1<sub>original</sub>ROI1<sub>SSFa</sub>ROI1<sub>SSFb</sub>ROI2<sub>original</sub>ROI2<sub>SSFa</sub>ROI2<sub>SSFb</sub>



$$SD = \left\{ \frac{1}{(n-1)} \sum_{(x,y) \in R} [a(x,y) - \bar{a}]^2 \right\}^{\frac{1}{2}},$$

$$MPP = \frac{1}{n_+} \sum_{(x,y) \in R} [a_+(x,y)],$$

$$UPP = \sum_{l=1}^k [p(l)]^2,$$

SSF: spatial scale filter

MPP: mean of positive pixels

UPP: uniformity of positive pixels

Radiology;2013,266(1):326



# Applications

# PET

Pattern Recognit. 2009 Jun 1;42(6):1162-1171.

## Exploring feature-based approaches in PET images for predicting cancer treatment outcomes.

El Naqa I<sup>1</sup>, Grigsby P, Apte A, Kidd E, Donnelly E, Khullar D, Chaudhari S, Yang D, Schmitt M, Laforest R, Thorstad W, Deasy JO.

Segmentation	Texture matrix	Results
40% SUV <sub>max</sub>	8/16/32 bins; Histogram; NGLCM	Shape; Homogeneity <sub>NGLCM</sub> → HNC OS. Energy → Cx ca Tx failure

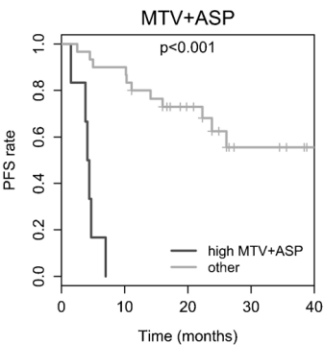
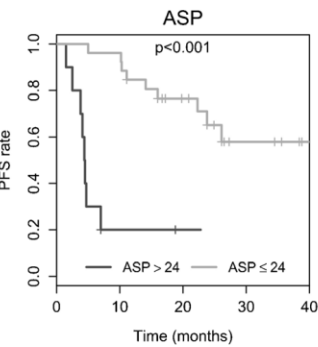
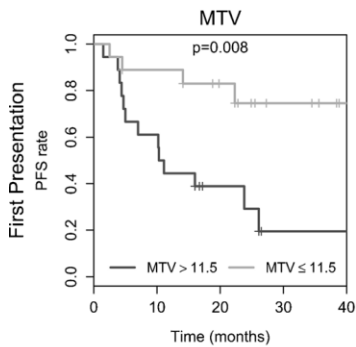
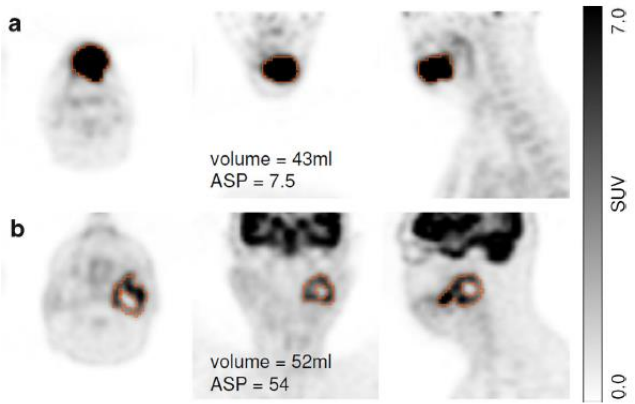
	Cx ca	HNC
Texture-based features		
Energy	0.7245	0.5000
Contrast	0.6020	0.8000
Local homogeneity	0.6224	0.8250
Entropy	0.6531	0.5250
Shape-based features		
Eccentricity	0.6429	0.6500
Euler number	0.6327	0.8500
Solidity	0.7245	0.8500
Extent	0.5612	0.8500

*Eur Radiol.* 2014 Sep;24(9):2077-87

**Asphericity of pretherapeutic tumour FDG uptake provides independent prognostic value in head-and-neck cancer.**

Apostolova I<sup>1</sup>, Steffen IG, Wedel F, Lougovski A, Marnitz S, Derlin T, Amthauer H, Buchert R, Hofheinz F, Brenner W.

Segmentation	Texture matrix	Results
Adaptive threshold	Histogram; Shape	MTV; ASP → PFS.



Eur J Nucl Med Mol Imaging. 2016 Jul;43(8):1461-8.

## Intratumoral heterogeneity of (18)F-FDG uptake predicts survival in patients with pancreatic ductal adenocarcinoma.

Hyun SH<sup>1</sup>, Kim HS<sup>1</sup>, Choi SH<sup>2</sup>, Choi DW<sup>2</sup>, Lee JK<sup>3</sup>, Lee KH<sup>3</sup>, Park JO<sup>3</sup>, Lee KH<sup>1</sup>, Kim BT<sup>1</sup>, Choi JY<sup>4</sup>.

Segmentation	Texture matrix	Results
Gradient-based	64 bins; Histogram; NGTDM; GLRLM; GLSZM	Entropy <sub>hist</sub> → OS.

Variable	Univariable analysis			Multivariable analysis		
	HR	95 % CI	<i>P</i> value	HR	95 % CI	<i>P</i> value
Age (1-year increase)	1.01	0.987 – 1.023	0.609	0.99	0.977 – 1.017	0.747
Sex, men vs. women	1.28	0.878 – 1.889	0.195	1.32	0.893 – 1.970	0.162
Clinical stage						
IIB vs. IIA	1.88	1.04 – 3.40	0.036	1.79	0.98 – 3.26	0.054
III-IV vs. IIA	5.17	2.84 – 9.41	< 0.001	3.66	1.95 – 6.87	< 0.001
Tumour size (cm) <sup>a</sup>	1.28	1.13 – 1.44	< 0.001	1.17	0.99 – 1.37	0.053
Serum CA19-9 (U/ml, log <sub>2</sub> scale) <sup>a</sup>	1.13	1.07 – 1.19	< 0.001	1.09	1.03 – 1.15	0.002
Entropy <sup>a</sup>	12.74	3.42 – 47.42	< 0.001	5.59	1.20 – 25.86	0.028
TLG (log <sub>2</sub> scale) <sup>a</sup>	1.28	1.14 – 1.44	< 0.001	0.98	0.81 – 1.19	0.875



J Nucl Med. 2013 Oct;54(10):1703-9.

## Textural features of pretreatment 18F-FDG PET/CT images: prognostic significance in patients with advanced T-stage oropharyngeal squamous cell carcinoma.

Cheng NM<sup>1</sup>, Fang YH, Chang JT, Huang CG, Tsan DL, Ng SH, Wang HM, Lin CY, Liao CT, Yen TC.

Segmentation	Texture matrix	Results
SUV 2.5	4/16/32/64 bins; Histogram; NGLCM; NGTDM	TLG, Uniformity <sub>NGLCM</sub> → PFS., DSS., OS.

### Multivariate Analysis of PFS, DSS, and OS Rates

Variable	PFS		DSS		OS	
	HR	<i>P</i>	HR	<i>P</i>	HR	<i>P</i>
HPV-positive	0.35 (0.11–1.11)	0.075	0.31 (0.09–1.05)	0.059	0.31 (0.11–0.89)	0.029
≥52 y (median age)	0.37 (0.18–0.75)	0.006	0.43 (0.21–0.88)	0.020	0.58 (0.31–1.08)	0.088
Female vs. male	0.98 (0.09–10.68)	0.985	0.88 (0.08–10.02)	0.917	2.37 (0.46–12.29)	0.304
Tobacco use	1.79 (0.48–6.61)	0.385	1.29 (0.32–5.12)	0.722	1.80 (0.55–5.89)	0.329
T stage						
T4 vs. T3	0.89 (0.38–2.08)	0.782	1.45 (0.57–3.73)	0.436	1.16 (0.52–2.62)	0.713
N stage						
N0-N2a vs. N2b-N3	0.94 (0.38–2.36)	0.901	0.81 (0.32–2.03)	0.646	0.87 (0.38–1.99)	0.747
AJCC stage						
Stage III vs. IVa vs. IVb	1.03 (0.48–2.19)	0.948	1.34 (0.61–2.96)	0.467	0.86 (0.43–1.76)	0.687
PET/CT parameters						
SUV <sub>max</sub> *	0.99 (0.24–4.01)	0.983	0.60 (0.14–2.64)	0.498	0.56 (0.16–1.97)	0.363
Tumor TLG <sup>†</sup>	7.15 (1.36–37.7)	0.020	7.28 (1.27–41.81)	0.026	5.85 (1.49–22.92)	0.011
Uniformity <sup>‡</sup>	0.32 (0.16–0.64)	0.001	0.28 (0.13–0.57)	0.001	0.46 (0.24–0.87)	0.017

Laryngoscope. 2017 Jan;127(1):E22-E28.

**Tumor heterogeneity measured on F-18 fluorodeoxyglucose positron emission tomography/computed tomography combined with plasma Epstein-Barr Virus load predicts prognosis in patients with primary nasopharyngeal carcinoma.**

Chan SC<sup>1,2</sup>, Chang KP<sup>3</sup>, Fang YD<sup>4</sup>, Tsang NM<sup>5</sup>, Ng SH<sup>6</sup>, Hsu CL<sup>7</sup>, Liao CT<sup>3</sup>, Yen TC<sup>2,8</sup>.

Segmentation	Texture parameters	Results
SUV 2.5	32/64 bins; Histogram; NGLCM; NGTDM	Skewness <sub>hist</sub> → RFS. Uniformity <sub>NGLCM</sub> → OS.

Multivariate Analysis of Risk Factors in Relation to Overall Survival and Recurrence-Free Survival.

Risk Factor	OS		RFS	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Age	2.668 (1.345-5.291)	.005	—	N/A
T classification	—	NS	—	NS
Tumor stage	—	NS	—	NS
EBV DNA load	6.284 (2.404-16.421)	.0002	—	N/A
TLG	—	NS	—	NS
Skewness	—	NS	0.394 (0.199-0.781)	.008
Uniformity	0.314 (0.162-0.609)	.001	—	N/A

J Nucl Med. 2013 Jan;54(1):19-26.

## Are pretreatment 18F-FDG PET tumor textural features in non-small cell lung cancer associated with response and survival after chemoradiotherapy?

Cook GJ<sup>1</sup>, Yip C, Siddique M, Goh V, Chicklore S, Roy A, Marsden P, Ahmad S, Landau D.

Segmentation	Texture parameters	Results
45% SUV <sub>max</sub>	16/32/64/128 bins; Histogram; NGTDM	Coarseness <sub>NGTDM</sub> → DSS.

Characteristic	OS		Multivariable		PFS		Multivariable	
	Univariable HR	P	HR	P	Univariable HR	P	HR	P
Age*	1.26 (0.86–1.83)	0.23	1.43 (0.95–2.17)	0.09	1.03 (0.74–1.44)	0.85		
Male sex	1.13 (0.56–2.28)	0.73			1.29 (0.68–2.46)	0.44		
Stage 1 or 2	1	0.42			1	0.81		
Stage 3a	0.90 (0.32–2.56)				1.38 (0.51–3.72)			
Stage 3b	1.47 (0.52–4.16)				1.28 (0.47–3.49)			
Squamous cell carcinoma histology	1.04 (0.48–2.26)	0.91			0.86 (0.44–1.69)	0.67		
SUVpeak <sup>†</sup>	0.87 (0.63–1.18)	0.36			0.87 (0.65–1.16)	0.34		
TLG <sup>‡</sup>	0.93 (0.72–1.21)	0.59			0.82 (0.64–1.05)	0.11	1.06 (0.74–1.51)	0.76
High coarseness	3.48 (1.41–8.63)	0.007	4.86 (1.32–17.9)	0.02	3.18 (1.48–6.85)	0.003	2.41 (0.82–7.09)	0.11
High contrast	0.47 (0.20–1.10)	0.08	1.11 (0.41–2.99)	0.84	0.40 (0.19–0.85)	0.02	0.60 (0.24–1.48)	0.27
High busyness	0.51 (0.25–1.04)	0.06	1.12 (0.44–2.92)	0.80	0.46 (0.24–0.88)	0.02	0.97 (0.37–2.53)	0.95
High complexity	0.59 (0.28–1.25)	0.17	1.11 (0.43–2.87)	0.82	0.61 (0.32–1.18)	0.17	0.87 (0.40–1.92)	0.73

Eur J Nucl Med Mol Imaging. 2017 Oct 18. doi: 10.1007/s00259-017-3855-5. [Epub ahead of print]

## FDG PET/CT radiomics for predicting the outcome of locally advanced rectal cancer.

Lovinfosse P<sup>1</sup>, Polus M<sup>2</sup>, Van Daele D<sup>2</sup>, Martinive P<sup>3</sup>, Daenen F<sup>4</sup>, Hatt M<sup>5</sup>, Visvikis D<sup>5</sup>, Koopmansch B<sup>6</sup>, Lambert F<sup>6</sup>, Coimbra C<sup>7</sup>, Seidel L<sup>8</sup>, Albert A<sup>8</sup>, Delvenne P<sup>9</sup>, Hustinx R<sup>10</sup>.

Segmentation	Texture parameters	Results
FLAB	64 bins; Histogram; NGLCM; NGTDM; GLSZM	Coarseness <sub>NGTDM</sub> → DSS.

Parameter	Univariate			Multivariate		
	P-value	HR	95% CI	P-value	HR	95% CI
Weight loss	0.0048	19.7	2.48-156	0.020	13.9	1.52-128
CA 19-9 > 37 U/ml	0.011	7.17	1.56-33			
Differentiation	0.0067	5.17	1.58-16.9			
cT	0.0003	12	3.07-46.7			
Surgery	0.0098	0.17	0.04-0.65	0.0022	0.07	0.01-0.38
TLG	0.0073	6.44	1.65-25.1			
ASM	0.011	0.18	0.05-0.68			
Contrast <sub>GLCM</sub>	0.027	0.10	0.01-0.77			
Entropy	0.0024	7.93	2.08-30.2			
Correlation	0.015	13.2	1.64-106			
Dissimilarity	0.033	0.11	0.01-0.84			
Coarseness	0.0037	10.2	2.13-49.2	0.024	7.06	1.29-38.7
Contrast <sub>NGTDM</sub>	0.024	0.09	0.01-0.72			
Busyness	0.031	5.57	1.17-26.4			
Intensity variability	0.015	14.1	1.69-117			
Size zone variability	0.036	0.24	0.07-0.92			

FLAB (fuzzy locally adaptive Bayesian)

Eur J Nucl Med Mol Imaging. 2015 Mar;42(3):419-28.

## Zone-size nonuniformity of 18F-FDG PET regional textural features predicts survival in patients with oropharyngeal cancer.

Cheng NM<sup>1</sup>, Fang YH, Lee LY, Chang JT, Tsan DL, Ng SH, Wang HM, Liao CT, Yang LY, Hsu CH, Yen TC.

Segmentation	Texture parameters	Results
SUV 2.5; 42% SUV <sub>max</sub> ; Adaptive threshold	64 bins; Histogram; GLRLM; GLSZM	Size-zone variability <sub>GLSZM</sub> → PFS., DSS. Uniformity <sub>NGLCM</sub> → PFS., DSS

**Table 2** Multivariate Cox regression analysis of progression-free survival rate

Characteristic	Dichotomized variables		Continuous variables	
	Hazard ratio (95 % confidence interval)	<i>P</i> value	Hazard ratio (95 % confidence interval)	<i>P</i> value
Textural parameters				
Uniformity	0.27 (0.14 – 0.53)	< 0.001	0.05 (0.01 – 0.26) <sup>a</sup>	< 0.001
Zone-size nonuniformity (16 bins)	4.38 (1.69 – 11.34)	0.002	1.64 (1.24 – 2.17) <sup>b</sup>	0.001
HPV positivity	0.65 (0.24 – 1.78)	0.400	0.80 (0.30 – 2.13)	0.654
Age >50 years	0.58 (0.28 – 1.22)	0.152	0.48 (0.23 – 1.00)	0.050
Tobacco use	2.96 (0.64 – 13.69)	0.164	2.36 (0.53 – 10.54)	0.262
Alcohol use	1.57 (0.60 – 4.10)	0.362	2.11 (0.78 – 5.74)	0.143
T stage				
T4 vs. T3	1.50 (0.66 – 3.39)	0.332	1.11 (0.48 – 2.58)	0.808
N stage				
N0-N2a vs. N2b-N3	1.82 (0.62 – 5.32)	0.275	2.15 (0.73 – 6.38)	0.167
AJCC stage				
Stage III vs. IVa vs. IVb	0.84 (0.43 – 1.62)	0.596	0.71 (0.35 – 1.42)	0.332

*Eur J Nucl Med Mol Imaging*. 2017 Aug 3. doi: 10.1007/s00259-017-3787-0. [Epub ahead of print]

## A pilot study for texture analysis of $^{18}\text{F}$ -FDG and $^{18}\text{F}$ -FLT-PET/CT to predict tumor recurrence of patients with colorectal cancer who received surgery.

Nakajo M<sup>1</sup>, Kajiya Y<sup>2</sup>, Tani A<sup>3</sup>, Jinguji M<sup>3</sup>, Nakajo M<sup>2</sup>, Kitazono M<sup>4</sup>, Yoshiura T<sup>3</sup>.

Segmentation	Texture parameters	Results
SUV 2.5	64 bins; Histogram; NGLCM; GLSZM	FDG size-zone variability <sub>GLSZM</sub> → PFS. FDG Intensity variability <sub>GLSZM</sub> → PFS.

### $^{18}\text{F}$ -FDG-PET/CT

SUVmax	0.89	0.74–1.07	0.21
SUVmean	0.78	0.55–1.11	0.17
MTV	1.94	0.46–8.11	0.37
TLG	1.14	0.28–4.54	0.86
COV	0.89	0.71–1.12	0.33
Entropy	7.92	0.87–72.09	0.066
Homogeneity	2.91	0.06–146.14	0.59
Dissimilarity	1.08	0.88–1.32	0.45
IV	1.13	1.06–1.21	<0.001
SZV	1.006	1.002–1.010	0.002
ZP	0.10	0.01–41.86	0.45

### $^{18}\text{F}$ -FLT-PET/CT

SUVmax	1.10	0.84–1.44	0.47
SUVmean	1.06	0.53–2.11	0.87
MTV	1.04	0.98–1.10	0.18
TLP	1.01	0.99–1.03	0.26
COV	0.92	0.52–1.63	0.78
Entropy	13.66	1.05–177.77	0.046
Homogeneity	1.94	0.46–8.11	0.37
Dissimilarity	0.99	0.79–1.25	0.95
IV	1.07	0.91–1.27	0.41
SZV	1.003	0.996–1.010	0.38
ZP	0.03	0.01–74.11	0.37

# MR

Radiology. 2017 Mar;282(3):665-675.

## Breast Cancer Heterogeneity: MR Imaging Texture Analysis and Survival Outcomes.

Kim JH<sup>1</sup>, Ko ES<sup>1</sup>, Lim Y<sup>1</sup>, Lee KS<sup>1</sup>, Han BK<sup>1</sup>, Ko EY<sup>1</sup>, Hahn SY<sup>1</sup>, Nam SJ<sup>1</sup>.

Segmentation	Texture parameters	Results
Manual T2W; DCE T1	256 bins; Histogram	T1, T2 entropy <sub>hist</sub> → RFS.

### Multivariate Cox Proportional Hazard Analysis of Survival Outcomes

Variable	RFS	
	Hazard Ratio	P Value
<b>N stage</b>		
0	Reference category	
1	3.32 (0.92, 11.99)	.068
2	11.63 (2.34, 57.85)	.003
3	11.15 (2.40, 51.85)	.002
<b>Breast parenchymal enhancement level</b>		
1	Reference category	
2	2.75 (0.88, 8.64)	.083
3	1.11 (0.22, 5.66)	.904
4	0 (0, 0)	.994
<b>Mass shape</b>		
Round or oval	Reference category	
Irregular	2.35 (0.78, 7.12)	.131
<b>Mass margin</b>		
Circumscribed	Reference category	
Not circumscribed	3.37 (0.59, 19.21)	.172

<b>Internal enhancement</b>		
Homogeneous	Reference category	
Heterogeneous	1.839193 (0, 0)	.992
Rim enhancement	8.83456 (0, 0)	.992
<b>Molecular subtype</b>		
Luminal A	Reference category	
Luminal B	1.65 (0.46, 6.00)	.445
HER2 enriched	0.77 (0.08, 7.27)	.821
Triple negative	16.91 (3.58, 79.82)	<.001
<b>Adjuvant chemotherapy</b>		
No	2.61 (0.73, 9.43)	.142
Yes	Reference category	
<b>T1 entropy</b>		
Low risk	Reference category	
High risk	4.55 (1.29, 16.13)	.018
<b>T2 entropy</b>		
High risk	9.84 (2.60, 37.26)	.001
Low risk	Reference category	

Radiology. 2017 Sep;284(3):748-757.

**Endometrial Carcinoma: MR Imaging-based Texture Model for Preoperative Risk Stratification-A Preliminary Analysis.**

Ueno Y<sup>1</sup>, Forghani B<sup>1</sup>, Forghani R<sup>1</sup>, Dohan A<sup>1</sup>, Zeng XZ<sup>1</sup>, Chamming's F<sup>1</sup>, Arseneau J<sup>1</sup>, Fu L<sup>1</sup>, Gilbert L<sup>1</sup>, Gallix B<sup>1</sup>, Reinhold C<sup>1</sup>.

Segmentation	Texture parameters	Results
Manual T2W; DCE; DWI	LoG	Deep myometrial invasion (DMI); Lymphovascular space invasion (LVSI)

Outcome and Type of Image	Feature	SSF	Feature Importance
LVSI			
T2 weighted	Kurtosis	2	0.031
DCE (delayed)	Kurtosis	5	0.024
T2 weighted	Mean	5	0.022
ADC map	Entropy	6	0.018
DCE	Mean of positive pixels	6	0.013
ADC map	Entropy	4	0.013
T2 weighted	Mean	4	0.012
ADC map	Mean of positive pixels	4	0.012
T2 weighted	Mean	2	0.009
ADC map	Standard deviation	2	0.008
ADC map	Entropy	5	0.007
DCE (second)	Mean	0	0.006



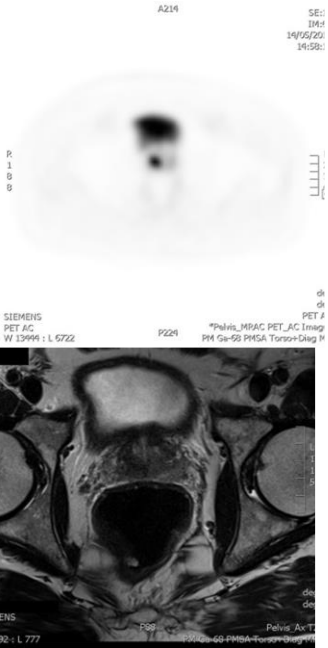
# PET/MRI

Eur Radiol. 2017 Jun 12. doi: 10.1007/s00330-017-4877-x. [Epub ahead of print]

## Prostate-specific membrane antigen PET/MRI validation of MR textural analysis for detection of transition zone prostate cancer.

Bates A<sup>1,2</sup>, Miles K<sup>3,4</sup>.

Segmentation	Texture parameters	Results
Manual T2W	LoG	Lower MPP, SD in PSMA (+) slices



	PSMA-negative median value and (range)	PSMA-positive median value and (range)	p-value	AUC
MPP	279 (84.4 to 496)	211 (76.0 to 454)	<0.0001	0.726
	289 (81.3 to 748)	217 (57.6 to 538)	<0.0001	0.736
	287 (71.8 to 807)	210 (63.1 to 693)	<0.0001	0.756
	282 (44.7 to 775)	202 (64.1 to 760)	<0.0001	0.736
	276 (45.5 to 621)	195 (53.6 to 855)	<0.0001	0.755
SD	352 (162 to 513)	284 (133 to 591)	<0.000	0.686
	371 (179 to 627)	297 (145 to 753)	<0.000	0.706
	374 (218 to 669)	306 (139 to 870)	<0.000	0.706
	367 (211 to 691)	306 (132 to 921)	<0.000	0.7
	355 (185 to 703)	310 (139 to 913)	0.000	0.755

# Variations & Limitations

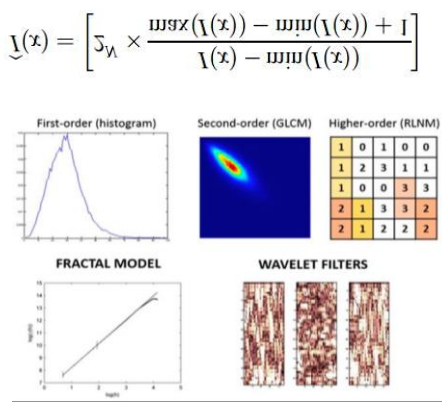
Original images



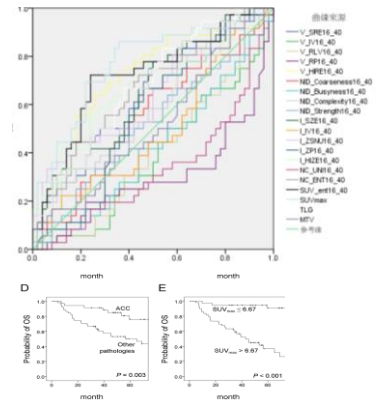
Segmentation



Processing



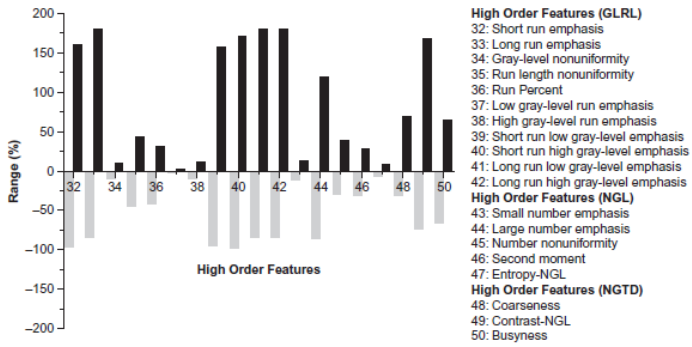
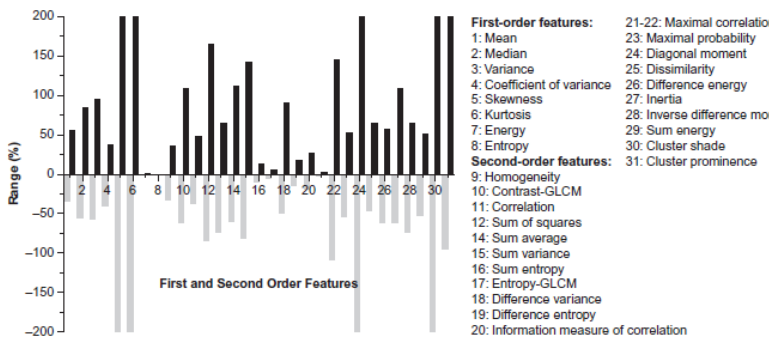
Analysis



Original images



• PET reconstruction parameters



$$\%Diff = \frac{100 \times (X - X_{mean})}{X_{mean}}$$

- Low variability features:**
- Histogram analysis:**
- entropy
- NGLCM:**
- entropy,
  - energy,
  - correlation
- GLRLM:**
- LGRE
  - HGRE
- GLSZM:**
- GLNUz

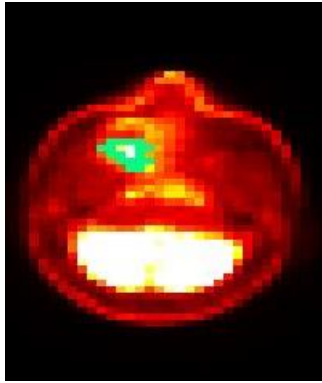
Reconstruction algorithm	Variation over the default reconstruction settings	Impact of iteration number on image features (FWHM: 2.5 mm; grid size: 256 × 256)	Impact of FWHM on image features (iteration: 2; grid size: 256 × 256)	Impact of grid size on image features (iteration: 2; FWHM: 2.5 mm)
OSEM	Iteration: 2; FWHM: 2.5 mm; grid size: 256 × 256	Iteration: 1, 2, 3	FWHM: 2.5, 3.5, 4.5, 5.5 mm	Grid size: 256 × 256; 128 × 128
OSEM + PSF	Iteration: 2; FWHM: 2.5 mm; grid size: 256 × 256	Iteration: 1, 2, 3	FWHM: 2.5, 3.5, 4.5, 5.5 mm	Grid size: 256 × 256; 128 × 128
OSEM + TOF	Iteration: 2; FWHM: 2.5 mm; grid size: 256 × 256	Iteration: 1, 2, 3	FWHM: 2.5, 3.5, 4.5, 5.5 mm	Grid size: 256 × 256; 128 × 128
OSEM + PSF + TOF	Iteration: 2; FWHM: 2.5 mm; grid size: 256 × 256	Iteration: 1, 2, 3	FWHM: 2.5, 3.5, 4.5, 5.5 mm	Grid size: 256 × 256; 128 × 128

$$\text{COV} = \text{SD}/\text{mean} \times 100(\%)$$

### Impact of FWHM on Image Features

Feature	COV ≤ 5%	5% < COV ≤ 10%	10% < COV ≤ 20%	COV > 20%
SUV		SUV <sub>mean</sub> , SUV <sub>peak</sub>	SUV <sub>max</sub>	
FOS	<u>Entropy</u>	COV, kurtosis, energy		Variance, skewness
GLCM	<u>Energy</u> , <u>entropy</u> , ID, SE, DE, IMC, IDN, IDMN, DM	Dissimilarity, homogeneity, MP, SA, SDN	Autocorrelation, contrast, correlation, SOS, SV, DV	CS
GLRLM	GLNr, RP, <u>LGRE</u> , <u>HGRE</u>	RLN	SRE, LRE, SRLGE, SRHGE, LRLGE, LRHGE	
GLSZM	LGZE	<u>GLNz</u> , ZLN, HGZE	LZE, SZHGE, LZLGE, WVGLZ_N, WVGLZ_S	SZE, ZP, SZLGE, LZHGE
NGLDM	Entropy	SNE, NN, SM	LNE	
NGTDM		<u>TS</u>	<u>Coarseness</u> , contrast, busyness	Complexity

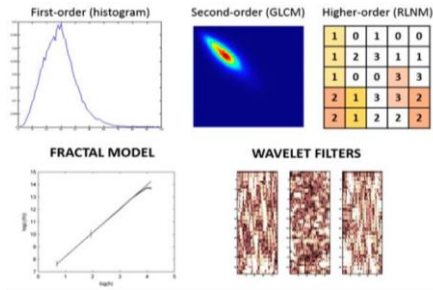
## Segmentation



- Fixed value:
  - SUV 2.5
- Fixed %:
  - T30, T40, T42, T45, T50, T60
- Adaptive threshold
  - Background varied
- Automatic:
  - FLAB, regional growing
- Which threshold best for prediction survival?
  - SUV: 5.5-7.0 or 40%-68% of  $SUV_{max}$  → **NO** major impact on the predictive value of MTV in OPSCC

## Processing

$$\underline{y}(x) = \left[ \bar{y}_x \times \frac{w_1 g(x(\underline{y}(x))) - w_2 w(\underline{y}(x)) + 1}{x(x) - w_1 w(\underline{y}(x))} \right]$$



- Fixed bins vs. fixed width

- Fixed bins:

- Highly correlated with tumor volume

PLoS One. 2015;10(12):e0145063

- Double baselines studies

- Fixed bins:

- More reliable in PET

- Fixed width

- More reliable in CT of PET/CT

		Bland-Altman analysis		ICC
		Mean (%)	S.D. (%)	
SUVmax		3.5	19.3	0.964
SUV mean		3.0	17.0	0.970
MTV		-1.4	11.1	0.997
Aspericity		0.3	10.0	0.946
Entropy <sub>fos</sub>		0.1	4.0	0.991
Entropy <sub>NGLCM</sub>	64 bins	-0.1	2.6	0.984
	Fixed 0.5 SUV	5.7	22.6	0.969
Uniformity	64 bins	-0.5	18.6	0.949
	Fixed 0.5 SUV	-11.3	41.8	0.904
ZSNU	64 bins	-1.1	13.7	0.995
	Fixed 0.5 SUV	2.1	2.3	0.988

Radiology. 2017 Aug;284(2):552-561. d

## Primary Rectal Cancer: Repeatability of Global and Local-Regional MR Imaging Texture Features.

Gourtsoyianni S<sup>1</sup>, Doumou G<sup>1</sup>, Prezzi D<sup>1</sup>, Taylor B<sup>1</sup>, Stirling JJ<sup>1</sup>, Taylor NJ<sup>1</sup>, Siddique M<sup>1</sup>, Cook GJR<sup>1</sup>, Glynne-Jones R<sup>1</sup>, Goh V<sup>1</sup>.

- Double baseline T2W
  - Coefficient of variation (COV), repeatability coefficient (r)
- Better repeatability for histogram parameters

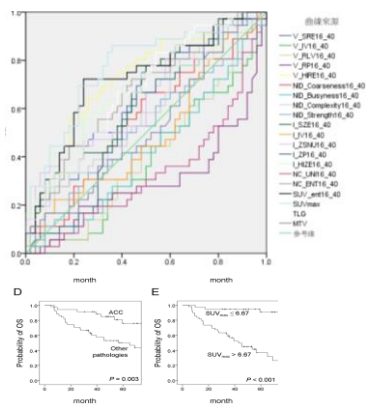
Parameter and Reader	wCV (%)	Repeatability Coefficient
<b>Mean</b>		
Reader 1	8.85	47.28
Reader 2	9.05	49.36
<b>Median</b>		
Reader 1	8.69	45.22
Reader 2	9.12	48.21
<b>Skewness</b>		
Reader 1	25.23	0.64
Reader 2	27.67	0.87
<b>Kurtosis</b>		
Reader 1	17.73	2.79
Reader 2	26.50	5.25
<b>Entropy</b>		
Reader 1	2.97	0.41
Reader 2	2.40	0.34

Parameter and Reader	wCV (%)	Repeatability Coefficient
<b>Entropy</b>		
Reader 1	5.73	0.64
Reader 2	5.40	0.58
<b>Homogeneity</b>		
Reader 1	5.87	0.094
Reader 2	3.38	0.058
<b>Energy</b>		
Reader 1	27.63	0.028
Reader 2	21.18	0.030
<b>Contrast</b>		
Reader 1	21.00	3.39
Reader 2	24.35	3.24

Parameter and Reader	wCV (%)	Repeatability Coefficient
<b>Coarseness</b>		
Reader 1	19.43	44.76
Reader 2	9.08	14.34
<b>Contrast</b>		
Reader 1	34.70	0.0099
Reader 2	45.25	0.008
<b>Busyness</b>		
Reader 1	48.42	2.05
Reader 2	26.71	1.18
<b>Complexity</b>		
Reader 1	85.10	0.02
Reader 2	19.81	0.004
<b>Texture strength</b>		
Reader 1	32.3	1.43
Reader 2	38.3	0.61



## Analysis



- Nomenclature
  - Histogram features = global features = FOS
  - NGLCM = 2<sup>nd</sup> order texture features = local features = Haralick features
    - Uniformity = energy = 2<sup>nd</sup> angular moment
    - Contrast = inertia
  - GLRLM, GLSZM = regional features
- Software
  - Black-box
- Texture features highly inter-correlated
  - Over-fitting
- Retrospectively studies
  - External validation
  - Training-validation
  - Leave-one-out cross validations
- Biological interpretation

J Nucl Med. 2016 Nov;57(11):1823-1828.

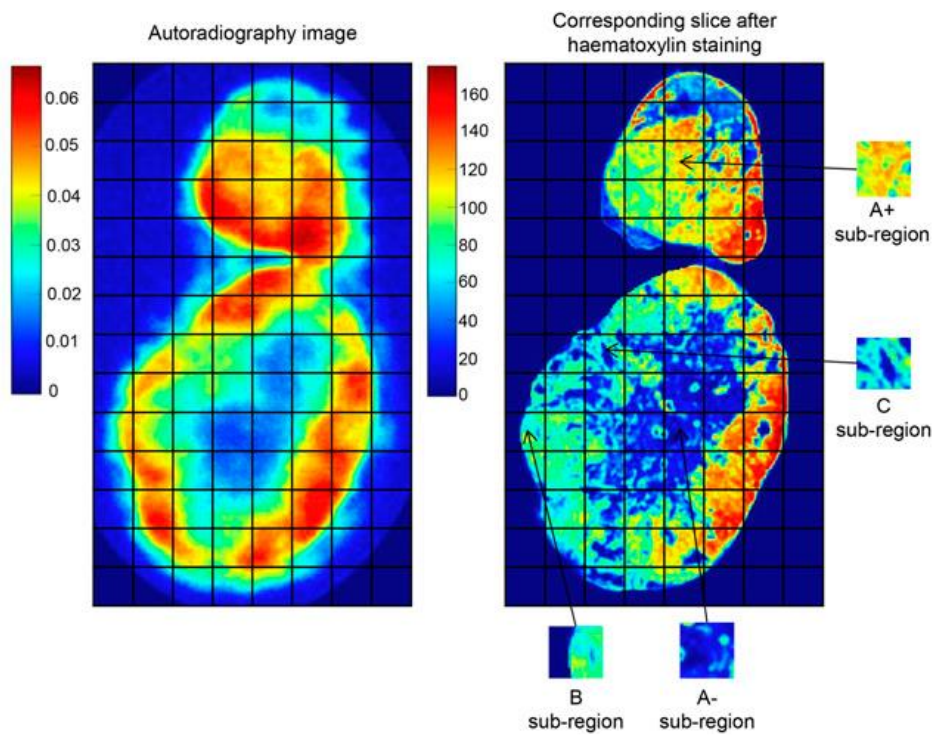
### Multiscale Texture Analysis: From 18F-FDG PET Images to Histologic Images.

Orlhac F<sup>1</sup>, Thézé B<sup>2</sup>, Soussan M<sup>2,3</sup>, Boisgard R<sup>2</sup>, Buvat I<sup>2</sup>.

Texture index	VOI-PET vs. VOI-AR	VOI-H vs. VOI-AR	VOI-H vs. VOI-PET
Homogeneity	0.66*	-0.18	-0.23
Entropy	0.57*	0.31	0.13
SRE	0.67*	-0.25	-0.13
LRE	0.70*	-0.41*	-0.54*
LGZE	0.83*	-0.23	-0.06
HGZE	0.85*	0.32	0.29
Maximum intensity	0.75*	0.20	0.09

\*P < 0.05.

AR: autoradiography  
H: histology

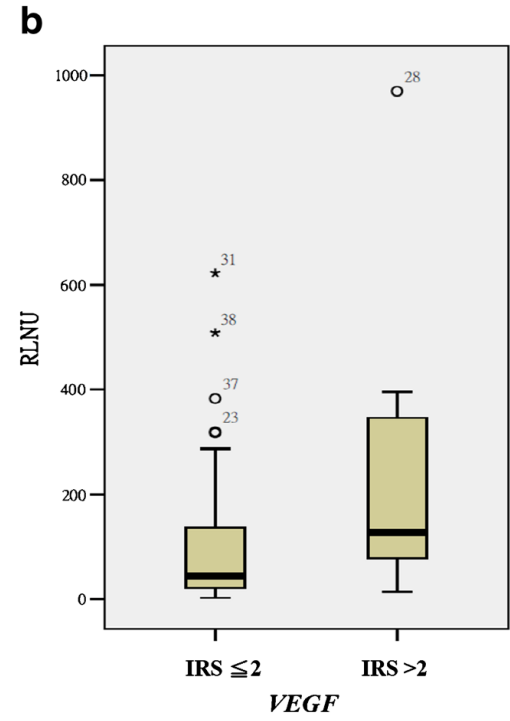
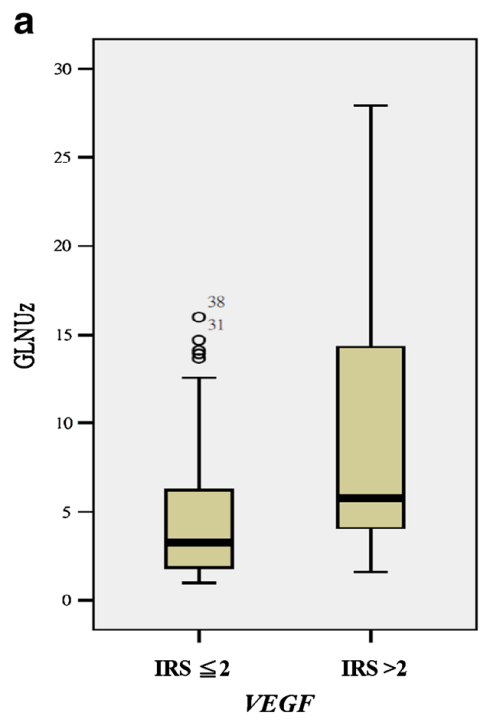


Eur J Nucl Med Mol Imaging. 2017 Apr;44(4):567-580.

**Correlation of pretreatment 18F-FDG PET tumor textural features with gene expression in pharyngeal cancer and implications for radiotherapy-based treatment outcomes.**

Chen SW<sup>1,2,3,4</sup>, Shen WC<sup>5,6</sup>, Lin YC<sup>1,7</sup>, Chen RY<sup>8</sup>, Hsieh TC<sup>9,10</sup>, Yen KY<sup>9,10</sup>, Kao CH<sup>11,12,13</sup>.

Classification of matrix	Index
CT-based volume	GTV
Classical PET-related parameter	SUVmax
	MTV2.5
	TLG40%
Gray-level co-occurrence matrix (GLCM)	Homogeneity
	Energy
	Correlation
	Contrast
	Entropy
Gray-level run length matrix (GLRLM)	Dissimilarity
	SRE
	LRE
	LGRE
	HGRE
	SRLGE
	SRHGE
	LRLGE
	LRHGE
	GLNUr
	RLNU
RP	
Neighborhood gray-level different matrix (NGLDM)	Coarseness
	Contrast
	Busyness
Gray-level zone length matrix (GLSZM)	SZE
	LZE
	LGZE
	HGZE
	SZLGE
	SZHGE
	LZLGE
	LZHGE
	GLNUz
	ZLNU
	ZP

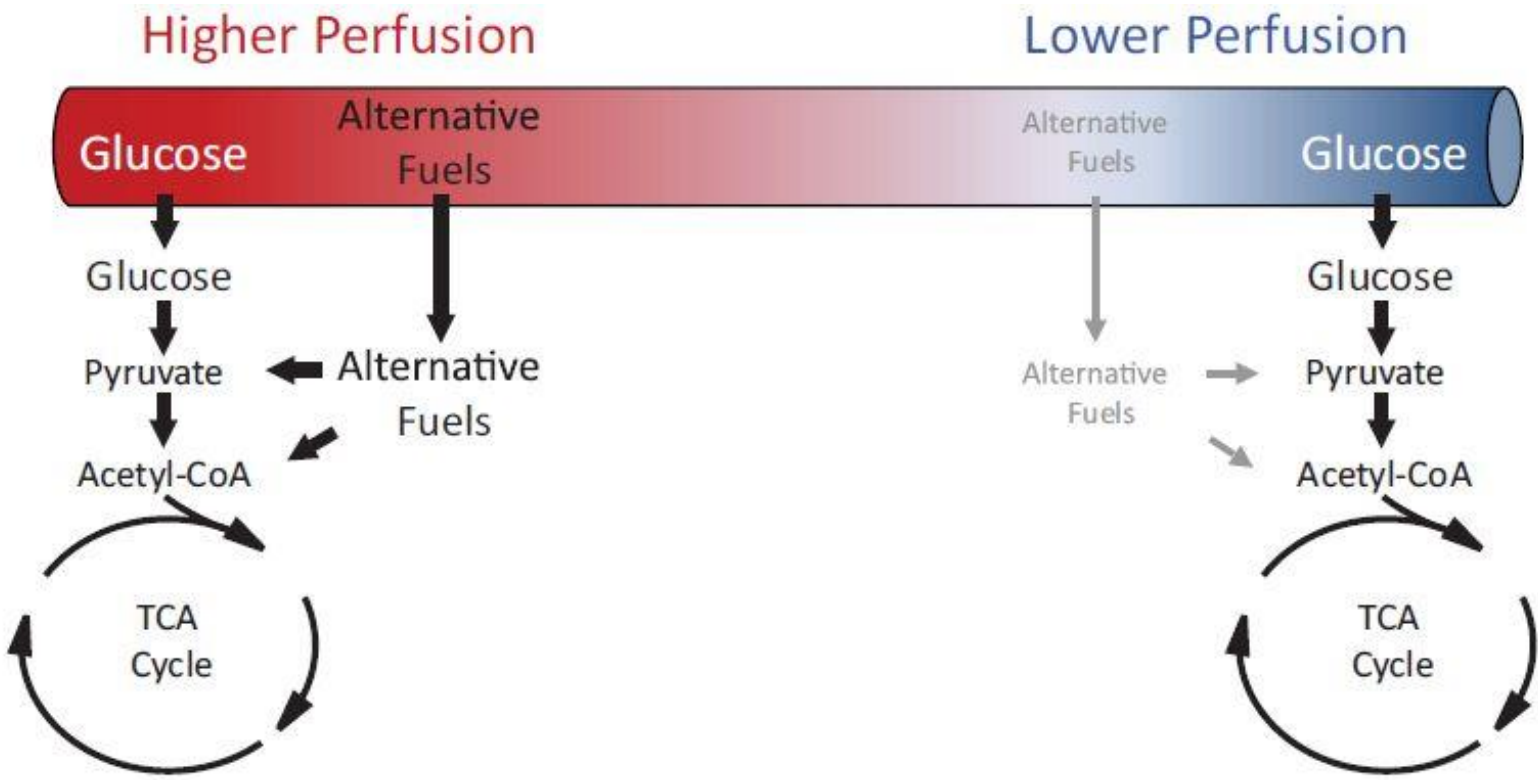


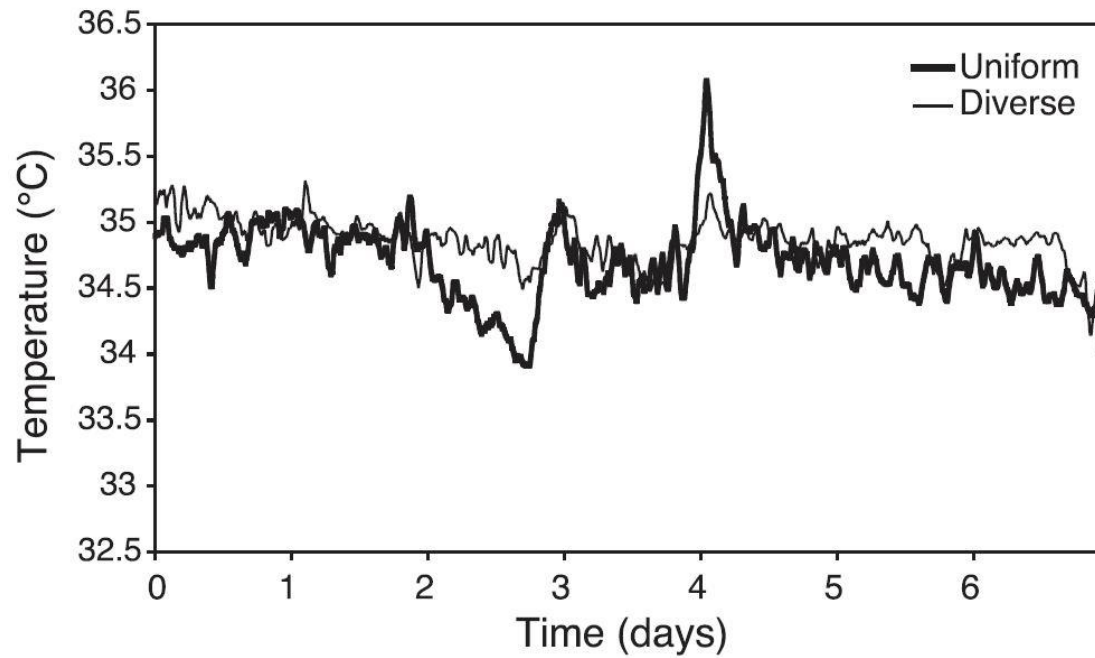
VEGF immunoreactive score (IRS) associated with GLNUz, RLNU

Cell. 2016 Feb 11;164(4):681-94.

### Metabolic Heterogeneity in Human Lung Tumors.

Hensley CT<sup>1</sup>, Faubert B<sup>1</sup>, Yuan Q<sup>2</sup>, Lev-Cohain N<sup>3</sup>, Jin E<sup>4</sup>, Kim J<sup>1</sup>, Jiang L<sup>1</sup>, Ko B<sup>1</sup>, Skelton R<sup>5</sup>, Loudat L<sup>5</sup>, Wozzak M<sup>6</sup>, Klimko C<sup>1</sup>, McMillan E<sup>7</sup>, Butt Y<sup>8</sup>, Ni M<sup>1</sup>, Oliver D<sup>8</sup>, Torrealba J<sup>8</sup>, Malloy CR<sup>9</sup>, Kernstine K<sup>10</sup>, Lenkinski RE<sup>11</sup>, DeBerardinis RJ<sup>12</sup>.





# Software

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Chang-Gung Image Texture Analysis toolbox

Wiki

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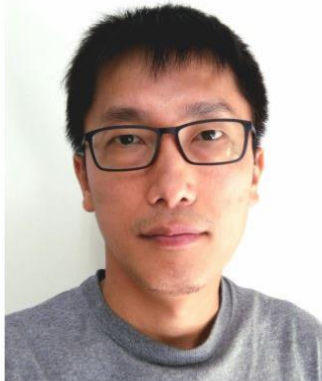
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# Conclusions

- Texture analysis
  - Promising
  - Deal with caution
  - Validation



**THANK YOU**