Relationship Between Radiomics and Risk of Lymph Node Metastasis in Pancreatic Ductal Adenocarcinoma

SUPPLEMENTAL DIGITAL CONTENT

Contents

SUPPLEMENTAL DIGITAL CONTENT 1. RADIOMICS FEATURES

In this study we explored a feature-based approach to extract and quantify meaningful and reliable information from images. A total of 1029 quantitative imaging features were extracted. The methods of feature extraction used in this study included two categories: original feature classes and filter classes. Filter Classes included five categories: Wavelet, Square, Square Root, Logarithm, and Exponential. A total of 1029 2D and 3D features from primary tumors in each scan phase. The imaging traits were described in detail below.

1.1 Firstorder

Firstorder included 19 features.

1	Energy	$\text{energy} = \sum_{i=1}^{N} (X(i) + c)^2$ Here, *c* is optional value, defined by "voxelArrayShift", which shifts the intensities to prevent negative values in **X**. This ensures that voxels with the lowest gray values contribute the least to Energy, instead of voxels with gray level intensity closest to 0.
2	TotalEnergy	$\text{TotalEnergy} = V_{voxel} \sum_{i=1}^{N} (X(i) + c)^2$ Here, *c* is optional value, defined by "voxelArrayShift", which shifts the intensities to prevent negative values in **X**. This ensures that voxels with the lowest gray values contribute the least to Energy, instead of voxels with gray level intensity closest to 0.
3	Entropy	$\text{Entropy} = \sum_{i=1}^{N_i} p(i) log_2 (p(i)+\in)$ Here, $\in$ is an arbitrarily small positive number ($\approx$ 2:2 $\times 10^{-16}$)
4	Minimum	*minimum* = min(**X**)
5	10Percentile	$\text{energy} = \sum_{i=1}^{N} (X(i) + c)^2$

6	90Percentile	$\text{energy} = \sum_{i=1}^{N} (X(i) + c)^2$
7	Maximum	*maximum* = max(**X**)
8	Mean	$\text{mean} = \frac{1}{N}\sum_{i=1}^{N} X(i)$
9	Median	The median gray level intensity within the ROI.
10	InterquartileRange	$\text{InterquartileRange} = \boldsymbol{P}_{75} - \boldsymbol{P}_{25}$ Here **P**25 and **P**75 are the 25*th* and 75*th* percentile of the image array, respectively.
11	Range	*range* = max(**X**) - min(**X**)
12	MeanAbsoluteDeviation (MAD)	$\text{MAD} = \frac{1}{N}\sum_{i=1}^{N} \lvert X(i) - \bar{X} \rvert$ Mean Absolute Deviation is the mean distance of all intensity values from the Mean Value of the image array.
13	RobustMeanAbsoluteDeviation (rMAD)	$\text{rMAD} = \sum_{i=1}^{N} (X(i) + c)^2$
14	RootMeanSquared (RMS)	$\text{RMS} = \sqrt{\frac{1}{N}\sum_{i=1}^{N} (X(i) + c)^2}$ Here, *c* is optional value, defined by “voxelArrayShift”, which shifts the intensities to prevent negative values in **X**. This ensures that voxels with the lowest gray values contribute the least to RMS, instead of voxels with gray level intensity closest to 0.
15	StandardDeviation	$\text{StandardDeviation} = \sqrt{\frac{1}{N}\sum_{i=1}^{N} (X(i) + \bar{X})^2}$

16 Skewness

$$\text{Skewness} = \frac{\mu_3}{\sigma^3} = \frac{\frac{1}{N}\sum_{I=1}^{N}(X(i) - \bar{X})^3}{(\sqrt{\frac{1}{N}\sum_{I=1}^{N}(X(i) - \bar{X})^2})^3}$$

Where $\mu 3$ is the $3rd$ central moment.

17 Kurtosis

$$\text{Kurtosis} = \frac{\mu_4}{\sigma^4} = \frac{\frac{1}{N}\sum_{I=1}^{N}(X(i) - \bar{X})^4}{(\frac{1}{N}\sum_{I=1}^{N}(X(i) - \bar{X})^2)^2}$$

Where μ_4 is the 4^{th} central moment.

18 Variance

$$\text{Variance} = \frac{1}{N}\sum_{i=1}^{N}(X(i) - \bar{X})^2$$

19 Uniformity

$$\text{Uniformity} = \sum_{i=1}^{N_I} p(i)^2$$

Notations:

X is an image of *N* voxels included in the ROI.

Pi is the first order histogram with *Nl* discrete intensity levels, in which *Nl* is the number of non-zero bins.

pi is the normalized first order histogram and equal to $\frac{P_i}{\sum P_i}$(This definition is the same for the following sections).

10Percentile

The 10^{th} percentile of **X**.

90Percentile

The 90^{th} percentile of **X**

1.2 Shape Features

Shape features describe the morphological property of the tumor region and were features rated from only the image without filtration. They included 13 features.

1 Volume

The volume of the ROI is approximated by multiplying the number of voxels in the ROI by the volume of a single voxel

2 SurfaceArea

$$\text{SurfaceArea} = \sum_{i=1}^{N}\frac{1}{2}|a_i b_i \times a_i c_i|$$

N is the number of triangles forming the surface mesh of

		the volume (ROI) $a_i b_i$ and $a_i c_i$ are the edges of the ith triangle formed by points a_i, b_i and c_i Surface Area is an approximation of the surface of the ROI in mm2, calculated using a marching cubes algorithm.
3	SurfaceVolumeRatio	$\text{SurfaceVolumeRatio} = \frac{A}{V}$ Here, a lower value indicates a more compact (sphere-like) shape. This feature is not dimension less, and is therefore (partly) dependent on the volume of the ROI.
4	Sphericity	$\text{Sphericity} = \frac{\sqrt[3]{36\pi V^2}}{A}$ Sphericity is a measure of the roundness of the shape of the tumor region relative to a sphere. It is a dimensionless measure, independent of scale and orientation. The value range is $0 < \textit{sphericity} \leq 1$, where a value of 1 indicates a perfect sphere (a sphere has the smallest possible surface area for a given volume, compared to other solids).
5	Compactness1	$\text{Compactness1} = \frac{\mathrm{v}}{\sqrt{\pi A^3}}$
6	Compactness2	$\text{Compactness2} = 36\pi \frac{v^2}{A^3}$
7	SphericalDisproportion	$\text{SphericalDisproportion} = \frac{\mathrm{A}}{4\pi R^2} = \frac{\mathrm{v}}{\sqrt[3]{36\pi A V^2}}$
8	Maximum3DDiameter	Maximum 3D diameter is defined as the largest pairwise Euclidean distance between surface voxels in the ROI. Also known as Feret Diameter.
9	Maximum2DDiameterColumn	Maximum 2D diameter (Column) is defined as the largest pairwise Euclidean distance between tumor surface voxels in the row-slice (usually the coronal) plane.
10	Maximum2DDiameterRow	Maximum 2D diameter (Row) is defined as the largest pairwise Euclidean distance between tumor surface voxels in the column-slice (usually the sagittal) plane
11	MajorAxis	The line through the foci is called the major axis, and the
12	MinorAxis	line perpendicular to it through the center is called the
13	LeastAxis	minor axis. Least axis is seen as the sum of the axis

14	Elongation	$\text{Elongation} = \sqrt{\frac{\lambda_{minor}}{\lambda_{major}}}$ Here, λmajor and λminor are the lengths of the largest and second largest principal component axes. The values range between 1 (where the cross section through the first and second largest principal moments is circle-like (non-elongated)) and 0 (where the object is a single point or 1 dimensional line).
15	Flatness	$\text{Flatness} = \frac{\lambda_{least}}{\lambda_{major}}$ Here, λmajor and λleast are the lengths of the largest and smallest principal component axes. The values range between 1 (non-flat, sphere-like) and 0 (a flat object).

1.3 GLCM Features

GLCM features included 28 features

1	Autocorrelation	$Autocorrelation = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} ijp(i,j)$
2	AverageIntensity	$\mu_x = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j)\, i$
3	ClusterProminence (CP)	$CP = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g}(i + j - u_x(i) - u_y(j))^4\, p(i,j)$
4	ClusterShade	$ClusterShade = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g}(i + j - u_x(i) - u_y(j))^3\, p(i,j)$
5	ClusterTendency (CT)	$CT = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g}(i + j - u_x(i) - u_y(j))^2\, p(i,j)$
6	Contrast	$Contrast = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\lvert i - j\rvert^2 p(i,j)$
7	Correlation	$Correlation = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j)ij - \mu_x(i)u_y(j)}{\sigma_x(i)\sigma_y(j)}$

8	DifferenceAverage	$DifferenceAverage = \sum_{k=1}^{N_g-1} k\, p_{x-y}(k)$
9	DifferenceEntropy	$DifferenceEntropy = \sum_{k=1}^{N_g-1} p_{x-y}(k) log_2 (p_{x-y}(k) + \epsilon)$
10	DifferenceVariance	$DifferenceVariance = \sum_{k=1}^{N_g-1} k\, p_{x-y}(k)$
11	Dissimilarity	$Dissimilarity = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} \vert i-j \vert p(i,j)$
12	Energy	$Energy = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} [p(i,j)]^2$
13	Entropy	$Entropy = -\sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j)\, log_2[p(i,j)]$
14	Homofeaturesity1	$Homogeneity = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} \frac{p(i,j)}{1+\vert i-j \vert}$
15	Homofeaturesity2	$Homogeneity = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} \frac{p(i,j)}{1+\vert i-j \vert^2}$
16	Imc1	$Imc1 = \frac{HXY - HXY1}{max\{HX - HX\}}$
17	Imc2	$Imc2 = \sqrt{1 - e^{-2(HXY2-HXY)}}$
18	Idm	$Idm = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} \frac{p(i,j)}{1+\vert i-j \vert^2}, (i \neq j)$
19	Idmn	$Idmn = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} \frac{p(i,j)}{1+(\frac{\vert i-j \vert^2}{N_g})}$

20	Id	$Id = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\frac{p(i,j)}{1+\lvert i-j\rvert}$
21	Idn	$Idn = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\frac{p(i,j)}{1+(\frac{\lvert i-j\rvert}{N_g})}$
22	InverseVariance (IV)	$IV = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\frac{p(i,j)}{\lvert i-j\rvert^2}, (i \neq j)$
23	MaximumProbability	$MaximumProbability = \max(p(i,j))$
24	SumAverage	$Sum\ \ average = \sum_{i=2}^{2N_g}\left[ip_{x+y}(i)\right]$
25	SumEntropy	$Sum\ \ entropy = -\sum_{i=2}^{2N_g}Pp_{x+y}(i)\, log_2\left[p_{x+y}(i)\right]$
26	SumVariance	$Sum\ \ variance = \sum_{i=2}^{2N_g}(i-SE)^2 p_{x+y}(i)$
27	SumSquares	$Sum\ \ Squares = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g}(i-\mu_x)^2\, p(i,j)$

Notations:

P(*i; j*) is the co-occurence matrix for δ (distance) and α (angle)

$p(i; j)$ is the normalized co-occurence matrix

Ng is the number of discrete intensity levels in the image

$p_x(i) = \sum_{j=1}^{N_g} P(i,j)$ is the marginal row probabilities

$p_{xy}(j) = \sum_{j=1}^{N_g} P(i,j)$ is the marginal column probabilities

$u_x = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} P(i,j)i$ is the mean gray level intensity of p_x

$u_y = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} P(i,j)j$ is the mean gray level intensity of p_y

σx is the standard deviation of px

σy is the standard deviation of py

$p_{x+y}(k) = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} P(i,j)$, where $i + j = k$

$p_{x-y}(k) = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} P(i,j)$, where $|i - j| = k$

$\text{HX} = \sum_{i=1}^{N_j} p_x(i) log_2(p_x(i)+\in)$ is the entropy of p_x

$\text{HY} = \sum_{i=1}^{N_j} p_y(i) log_2(p_y(i)+\in)$ is the entropy of p_y

$\text{HXY} = -\sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j) log_2(p(i,j)+\in)$is the entropy of $p(i; j)$

$$\text{HXY1} = -\sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j) log_2(p(i,j)+\in)$$

$$\text{HXY2} = -\sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p_x(i)p_y(j) log_2\big(p_x(i)p_y(j)+\in\big)$$

1.4 GLSZM Features

GLSZM features included 16 features

1	SmallAreaEmphasis (SAE)	$SAE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\frac{\boldsymbol{P}(i,j)}{j^2}}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\boldsymbol{P}(i,j))}$
2	LargeAreaEmphasis (LAE)	$LAE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\boldsymbol{P}(i,j)j^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\boldsymbol{P}(i,j))}$
3	GrayLevelNonUniformity (GLN)	$GLN = \frac{\sum_{i=1}^{N_g}(\sum_{j=1}^{N_g}\boldsymbol{P}(i,j))^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\boldsymbol{P}(i,j)}$
4	GrayLevelNonUniformityNormalized (GLNN)	$GLNN = \frac{\sum_{i=1}^{N_g}(\sum_{j=1}^{N_g}\boldsymbol{P}(i,j))^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\boldsymbol{P}(i,j)^2}$
5	SizeZoneNonUniformity (SZN)	$SZN = \frac{\sum_{i=1}^{N_g}(\sum_{j=1}^{N_g}\boldsymbol{P}(i,j))^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\boldsymbol{P}(i,j)}$
6	SizeZoneNonUniformityNormalized (SZNN)	$SZNN = \frac{\sum_{i=1}^{N_g}(\sum_{j=1}^{N_g}\boldsymbol{P}(i,j))^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\boldsymbol{P}(i,j)^2}$

7	ZonePercentage (ZP)	$ZP = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\frac{\boldsymbol{P}(i,j)}{N_p}$
8	GrayLevelVariance (GLV)	$GLV = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g}(i-\mu)^2\, p(i,j)$ $\mu = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j)i$
9	ZoneVariance (ZV)	$ZV = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j)(j-\mu)^2$
10	ZoneEntropy (ZE)	$ZE = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j)log_2(p(i,j)+\in)$
11	LowGrayLevelZoneEmphasis (LGLZE)	$LGLZE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_s}\frac{\boldsymbol{P}(i,j)}{i^2}}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_s}P(i,j)}$
12	HighGrayLevelZoneEmphasis (HGLZE)	$HGLZE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_s}\boldsymbol{P}(i,j)\, i^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_s}P(i,j)}$
13	SmallAreaLowGrayLevelEmphasis (SALGLE)	$SALGLE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_s}\frac{\boldsymbol{P}(i,j)}{i^2j^2}}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_s}\boldsymbol{P}(i,j)}$
14	SmallAreaHighGrayLevelEmphasis (SAHGLE)	$SAHGLE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_S}\frac{\boldsymbol{P}(i,j)i^2}{j^2}}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_s}\boldsymbol{P}(i,j)}$
15	LargeAreaLowGrayLevelEmphasis (LALGLE)	$LALGLE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_s}\frac{\boldsymbol{P}(i,j)j^2}{i^2}}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_s}\boldsymbol{P}(i,j))}$
16	LargeAreaHighGrayLevelEmphasis (LAHGLE)	$LAHGLE == \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_S}\boldsymbol{P}(i,j)\, i^2j^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_s}\boldsymbol{P}(i,j)}$

Note:

P (*i; j*) is the size zone matrix

p (*i; j*) is the normalized size zone matrix

Ng is the number of discrete intensity values in the image

Ns is the number of discrete zone sizes in the image

Np is the number of voxels in the image

1.5 GLRLM Features

GLRLM features included 16 features

1	ShortRunEmphasis (SRE)	$SRE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\left[\frac{\boldsymbol{P}(i,j\|\theta)}{j^2}\right]}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$
2	LongRunEmphasis (LRE)	$LRE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} j^2\boldsymbol{P}(i,j\|\theta)}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$
3	GrayLevelNonUniformity (GLNNN)	$GLNN = \frac{\sum_{i=1}^{N_g}\left[\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)\right]^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$
4	GrayLevelNonUniformityNormalized (RLNN)	$RLNN = \frac{\sum_{i=1}^{N_r}(\sum_{j=1}^{N_g}\boldsymbol{P}(i,j\|\theta)^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$
5	RunLengthNonUniformity (RLN)	$RLN = \frac{\sum_{j=1}^{N_r}\sum_{i=1}^{N_g}(\boldsymbol{P}(i,j\|\theta))^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$
6	RunLengthNonUniformityNormalized (RLNN)	$RLNN = \frac{\sum_{j=1}^{N_r}(\sum_{i=1}^{N_g}\boldsymbol{P}(i,j\|\theta))^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$ RLNN measures the similarity of run lengths throughout the image, with a lower value indicating more homofeaturesity among run lengths in the image. This is the normalized version of the RLN formula
7	RunPercentage (RP)	$RP = \sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\frac{\boldsymbol{P}(i,j\|\theta)}{N_p}$

8	GrayLevelVariance (GLV)	$$GLV = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j\|\theta))(i-\mu)^2$$ Here, $\mu = \sum_{i=1}^{N_g}\sum_{j=1}^{N_r} p(i,j\|\theta))i$ GLV measures the variance in gray level intensity for the runs.
9	RunVariance (RV)	$$RV = \sum_{i=1}^{N_g}\sum_{j=1}^{N_r} p(i,j\|\theta))(j-\mu)^2$$ Here, $\mu = \sum_{i=1}^{N_g}\sum_{j=1}^{N_r} p(i,j\|\theta))j$ RV is a measure of the variance in runs for the run lengths.
10	RunEntropy (RE)	$$RE = \sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j\|\theta) log_2(p(i,j\|\theta)+\epsilon)$$ Here, ϵ is an arbitrarily small positive number (≈ 2:2 × 10^{-16}). RE measures the uncertainty/randomness in the distribution of run lengths and gray levels. A higher value indicates more heterofeaturesity in the texture patterns
11	LowGrayLevelRunEmphasis (LGLRE)	$$LGLRE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\frac{\boldsymbol{P}(i,j\|\theta)}{i^2}}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$$
12	HighGrayLevelRunEmphasis (HGLRE)	$$HGLRE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)i^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$$
13	ShortRunLowGrayLevelEmphasis (SRLGLE)	$$\text{SRLGLE} = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)i^2 j^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$$

14	ShortRunHighGrayLevelEmphasis (SRHGLE)	$SRHGLE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\frac{\boldsymbol{P}(i,j\|\theta)e^2}{j^2}}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$
15	LongRunLowGrayLevelEmphasis (LRLGLE)	$LRLGLE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\frac{\boldsymbol{P}(i,j\|\theta)}{i^2j^2}}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$
16	LongRunHighGrayLevelEmphasis (LRHGLE)	$LRHGLE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)i^2j^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\boldsymbol{P}(i,j\|\theta)}$

Notations:

$\boldsymbol{P}(i,j|\theta)$ is the run length matrix of direction θ

$p(i,j|\theta)$ is the normalized run length matrix

Ng is the number of discrete intensity values in the image

Nr is the number of discrete run lengths in the image

Np is the number of voxels in the image

TABLE 1. 1029 Radiomics Features

	Firstorder	Shape	GLCM	GLSZM	GLRLM
1	Energy	Volume	Autocorrelation	SmallAreaEmphasis	ShortRunEmphasis
2	TotalEnergy	SurfaceArea	AverageIntensity	LargeAreaEmphasis	LongRunEmphasis
3	Entropy	SurfaceVolumeRatio	ClusterProminence	GrayLevelNonUniformity	GrayLevelNonUniformity
4	Minimum	Sphericity	ClusterShade	GrayLevelNonUniformityNorm alized	GrayLevelNonUniformityNormalized
5	10Percentile	Compactness1	ClusterTendency	SizeZoneNonUniformity	RunLengthNonUniformity
6	90Percentile	Compactness2	Contrast	SizeZoneNonUniformityNorma lized	RunLengthNonUniformityNormalized
7	Maximum	SphericalDisproportion	Correlation	ZonePercentage	RunPercentage
8	Mean	Maximum3DDiameter	DifferenceAverage	GrayLevelVariance	GrayLevelVariance
9	Median	Maximum2DDiameterColumn	DifferenceEntropy	ZoneVariance	RunVariance
10	InterquartileRange	Maximum2DDiameterRow	DifferenceVariance	ZoneEntropy	RunEntropy
11	Range	MajorAxis	Dissimilarity	LowGrayLevelZoneEmphasis	LowGrayLevelRunEmphasis
12	MeanAbsoluteDeviation	MinorAxis	Energy	HighGrayLevelZoneEmphasis	HighGrayLevelRunEmphasis
13	RobustMeanAbsoluteDevi ation	LeastAxis	Entropy	SmallAreaLowGrayLevelEmph asis	ShortRunLowGrayLevelEmphasis
14	RootMeanSquared	Elongation	Homofeaturesity1	SmallAreaHighGrayLevelEmp hasis	ShortRunHighGrayLevelEmphasis
15	StandardDeviation	Flatness	Homofeaturesity2	LargeAreaLowGrayLevelEmph asis	LongRunLowGrayLevelEmphasis
16	Skewness		Imc1	LargeAreaHighGrayLevelEmp hasis	LongRunHighGrayLevelEmphasis
17	Kurtosis		Imc2		

(Continued on next page)

TABLE 1. *Continued*

	Firstorder	Shape	GLCM	GLSZM	GLRLM
18	Variance		Idm		
19	Uniformity		Idmn		
20			Id		
21			Idn		
22			InverseVariance		
23			MaximumProbability		
24			SumAverage		
25			SumEntropy		
26			SumVariance		
27			SumSquares		

Reference: van Griethuysen JJ, Fedorov A, Parmar C, et al. Computational radiomics system to decode the radiographic phenotype. *Cancer Res*. 2017;77:e104-e107.

SUPPLEMENTAL DIGITAL CONTENT 2. INTEROBSERVER AND INTRAOBSERVER REPRODUCIBILITY OF FEATURE EXTRACTION

Statistical Analysis

The interobserver and intraobserver agreement of feature extraction was evaluated by using the interclass correlation coefficient (ICC). An ICC of greater than 0.75 was considered to represent good agreement.

Results

To assess interobserver reliability, the region-of-interest segmentation was performed in a blinded fashion by two radiologists (reader 1, W.L., reader 2, F.X.) in a blinded fashion. To evaluate intraobserver reliability, reader 1 repeated the feature extraction twice in a 1-week period. Intra-class correlation coefficients (ICCs) were calculated. The interobserver ICCs were good, ranging from 0.80 to 0.92. The intraobserver ICCs also were good, ranging from 0.83 to 0.95.

SUPPLEMENTAL DIGITAL CONTENT 3. RADIOMICS FEATURES SELECTED BY LASSO REGULARIZATION

3.1 The Least Absolute Shrinkage and Selection Operator (LASSO) Algorithm

LASSO is a powerful algorithm for regression analysis with high dimensional predictors. In our study, the LASSO algorithm was combined with the logistic regression model for model development. We used the LASSO logistic regression model to select the most important predictive features and construct a radiomics signature in the training set. This algorithm minimizes a log partial likelihood subject to the sum of the absolute values of the parameters bounded by a constant:

$$\hat{\beta} = \arg\ \min\ \ell(\beta), \text{ subject to } \sum|\beta_j| \leq t$$

where $\hat{\beta}$ is the obtained parameters, $\ell(\beta)$ is the log partial likelihood of the logistic regression model, and $t > 0$ is a constant.

The LASSO algorithm shrinks some coefficients and reduces others to exactly 0 via the absolute constraint. Thus, LASSO is an outstanding method for feature selection by retaining the good features of both subset selection and ridge regression.

Reference: Tibshirani R. Regression shrinkage and selection via the lasso: a retrospective. *J R Statist Soc B.* 2011;73:273–282.

3.2 Radiomics Features Selected by LASSO Regularization

The LASSO logistic regression model was used with penalty parameter tuning that was conducted by a 10-fold cross-validation based on minimum criteria (Supplemental Fig. 1). Lasso penalty coefficient was o.42. The 12 radiomic signatures of the arterial phase were selected by the LASSO logistic regression model. Radiomics score was calculated by the following formula.

formula

Radiomics score (arterial phase) =-0.0387*exponential.glcm.Correlation

+0.1856*logarithm.glszm.GrayLevelNonUniformityNormalized

+0.0590*square.firstorder.Skewness

+0.0026*square.firstorder.Kurtosis

+0.0427*exponential.glrlm.RunLengthNonUniformity

+0.0181*exponential.glrlm.RunVariance

+0.0715*wavelet-LHL.firstorder.Mean

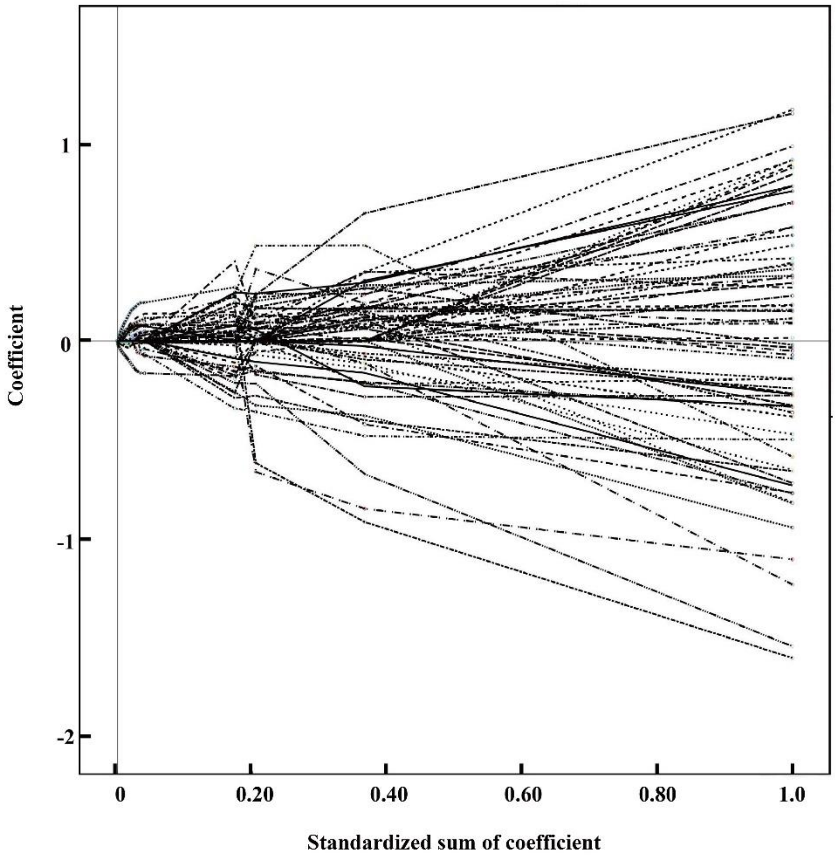
+0.0405*wavelet-LHL.glcm.ClusterShade

+0.0344*wavelet-LHL.glszm.LargeAreaHighGrayLevelEmphasis

+0.0018*wavelet-HLL.firstorder.Mean

+0.0091*wavelet-HLL.glszm.ZoneVariance

+0.0826*wavelet-HHH.glszm.LargeAreaHighGrayLevelEmphasis



SUPPLEMENTAL FIGURE 1. LASSO regression solution paths (LASSO, least absolute shrinkage and selection operator).