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

SUPPLEMENTAL DIGITAL CONTENT

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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

\[ \text{TotalEnergy} = V_{\text{voxel}} \sum_{i=1}^{N} (X(i) + c)^2 \]

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

\[ \text{Entropy} = \sum_{i=1}^{N_i} p(i) \log_2 (p(i)+\varepsilon) \]

Here, \( \varepsilon \) is an arbitrarily small positive number (\( \approx 2.2 \times 10^{-16} \))

4 Minimum

\( \text{minimum} = \min(X) \)

5 10Percentile

\[ \text{energy} = \sum_{i=1}^{N} (X(i) + c)^2 \]
|   | 90Percentile          | energy = \( \sum_{i=1}^{N} (X(i) + c)^2 \) |
|---|----------------------|-----------------------------------------------|
| 7 | Maximum              | maximum = \( \max(X) \)                      |
| 8 | Mean                 | mean = \( \frac{1}{N} \sum_{i=1}^{N} X(i) \) |
| 9 | Median               | The median gray level intensity within the ROI. |
| 10| InterquartileRange   | InterquartileRange = \( P_{75} - P_{25} \)   |
|   |                      | Here \( P_{25} \) and \( P_{75} \) are the 25th and 75th percentile of the image array, respectively. |
| 11| Range                | range = \( \max(X) - \min(X) \)              |
| 12| MeanAbsoluteDeviation| MAD = \( \frac{1}{N} \sum_{i=1}^{N} |X(i) - \bar{X}| \)                             |
|   | (MAD)                | Mean Absolute Deviation is the mean distance of all intensity values from the Mean Value of the image array. |
| 13| RobustMeanAbsoluteDeviation| rMAD = \( \sum_{i=1}^{N} (X(i) + c)^2 \)       |
| 14| RootMeanSquared (RMS)| 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    | StandardDeviation = \( \sqrt{\frac{1}{N} \sum_{i=1}^{N} (X(i) + \bar{X})^2} \) |
16 Skewness

Skewness = \frac{\mu_3}{\sigma^3} = \frac{\frac{1}{N} \sum_{i=1}^{N} (X(i) - \bar{X})^3}{\left(\frac{1}{N} \sum_{i=1}^{N} (X(i) - \bar{X})^2\right)^{\frac{3}{2}}}

Where \( \mu_3 \) is the 3rd central moment.

17 Kurtosis

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

Where \( \mu_4 \) is the 4th central moment.

18 Variance

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

19 Uniformity

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

Notations:

\( X \) is an image of \( N \) voxels included in the ROI.

\( P_i \) is the first order histogram with \( N_I \) discrete intensity levels, in which \( N_I \) is the number of non-zero bins.

\( p_i \) 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 10th percentile of \( X \).

90Percentile

The 90th 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

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) \( a_i b_i c_i \) are the edges of the \( i \)th
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 \( 0 < \text{sphericity} \leq 1 \), 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**

\[
\text{Compactness1} = \frac{v}{\sqrt{\pi A^3}}
\]

6 **Compactness2**

\[
\text{Compactness2} = 36\pi \frac{V^2}{A^3}
\]

7 **SphericalDisproportion**

\[
\text{SphericalDisproportion} = \frac{A}{4\pi R^2} = \frac{V}{\sqrt[3]{36\pi AV^2}}
\]

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

\[
\text{Elongation} = \sqrt{\frac{\lambda_{\text{minor}}}{\lambda_{\text{major}}}}
\]

Here, \(\lambda_{\text{major}}\) and \(\lambda_{\text{minor}}\) 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

\[
\text{Flatness} = \frac{\lambda_{\text{least}}}{\lambda_{\text{major}}}
\]

Here, \(\lambda_{\text{major}}\) and \(\lambda_{\text{least}}\) 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

\[
\text{Autocorrelation} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} ij p(i,j)
\]

2 AverageIntensity

\[
\mu_x = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i,j) i
\]

3 ClusterProminence (CP)

\[
\text{ClusterProminence} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} (i + j - u_x(i) - u_y(j))^4 p(i,j)
\]

4 ClusterShade

\[
\text{ClusterShade} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} (i + j - u_x(i) - u_y(j))^2 p(i,j)
\]

5 ClusterTendency (CT)

\[
\text{ClusterTendency} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} (i + j - u_x(i) - u_y(j))^2 p(i,j)
\]

6 Contrast

\[
\text{Contrast} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} |i - j|^2 p(i,j)
\]

7 Correlation

\[
\text{Correlation} = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i,j) ij - \mu_x(i) \mu_y(j)}{\sigma_x(i) \sigma_y(j)}
\]
8 Difference Average

\[ \text{Difference Average} = \sum_{k=1}^{N_g-1} k p_{x-y}(k) \]

9 Difference Entropy

\[ \text{Difference Entropy} = \sum_{k=1}^{N_g-1} p_{x-y}(k) \log_2(p_{x-y}(k) + \epsilon) \]

10 Difference Variance

\[ \text{Difference Variance} = \sum_{k=1}^{N_g-1} k p_{x-y}(k) \]

11 Dissimilarity

\[ \text{Dissimilarity} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} |i - j| p(i, j) \]

12 Energy

\[ \text{Energy} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} [p(i, j)]^2 \]

13 Entropy

\[ \text{Entropy} = -\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i, j) \log_2[p(i, j)] \]

14 Homofeature 1

\[ \text{Homogeneity} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{p(i, j)}{1 + |i - j|} \]

15 Homofeature 2

\[ \text{Homogeneity} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{p(i, j)}{1 + |i - j|^2} \]

16 Imc 1

\[ \text{Imc 1} = \frac{HXY - HXY1}{\max\{HX - HX\}} \]

17 Imc 2

\[ \text{Imc 2} = \sqrt{1 - e^{-2(HXY2 - HXY)}} \]

18 Idm

\[ \text{Idm} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{p(i, j)}{1 + |i - j|^2}, (i \neq j) \]

19 Idmn

\[ \text{Idmn} = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{p(i, j)}{1 + \left(\frac{|i - j|^2}{N_g}\right)} \]
\[ Id = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{p(i,j)}{1 + |i - j|} \]

\[ Idn = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{p(i,j)}{1 + \left( \frac{|i - j|}{N_g} \right)} \]

\[ IV = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{p(i,j)}{|i - j|^2} (i \neq j) \]

\[ Maximum Probability = \max(p(i,j)) \]

\[ Sum average = \sum_{i=2}^{2N_g} [i p_{x+y}(i)] \]

\[ Sum entropy = - \sum_{i=2}^{2N_g} P_{x+y}(i) \log_2 [p_{x+y}(i)] \]

\[ Sum variance = \sum_{i=2}^{2N_g} (i - \mu_x)^2 p_{x+y}(i) \]

\[ Sum Squares = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} (i - \mu_x)^2 p(i,j) \]

Notations:
- \( P(i,j) \) is the co-occurrence matrix for \( \delta \) (distance) and \( \alpha \) (angle)
- \( p(i,j) \) is the normalized co-occurrence matrix
- \( N_g \) 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
- \( p_{xy}(j) = \sum_{i=1}^{N_g} P(i,j) \) 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 \( p_y \)
- \( \sigma_x \) is the standard deviation of \( p_x \)
- \( \sigma_y \) is the standard deviation of \( p_y \)
\[ p_{x+y}(k) = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i, j), \text{ where } i + j = k \]

\[ p_{x-y}(k) = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i, j), \text{ where } |i - j| = k \]

\[ H_X = \sum_{i=1}^{N_g} p_x(i) \log_2 (p_x(i) + \varepsilon) \text{ is the entropy of } p_x \]

\[ H_Y = \sum_{i=1}^{N_g} p_y(i) \log_2 (p_y(i) + \varepsilon) \text{ is the entropy of } p_y \]

\[ H_{XY} = - \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i, j) \log_2 (p(i, j) + \varepsilon) \text{ is the entropy of } p(i; j) \]

\[ H_{XY1} = - \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i, j) \log_2 (p(i, j) + \varepsilon) \]

\[ H_{XY2} = - \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p_x(i)p_y(j) \log_2 (p_x(i)p_y(j) + \varepsilon) \]

1.4 GLSZM Features

GLSZM features included 16 features

1. **SmallAreaEmphasis (SAE)**

\[ SAE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{P(i, j)}{1^2}}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i, j)} \]

2. **LargeAreaEmphasis (LAE)**

\[ LAE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i, j)^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i, j)} \]

3. **GrayLevelNonUniformity (GLN)**

\[ GLN = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i, j)^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i, j)} \]

4. **GrayLevelNonUniformityNormalized (GLNN)**

\[ GLNN = \frac{\sum_{i=1}^{N_g} (\sum_{j=1}^{N_g} P(i, j))^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i, j)} \]

5. **SizeZoneNonUniformity (SZN)**

\[ SZN = \frac{\sum_{i=1}^{N_g} (\sum_{j=1}^{N_g} P(i, j))^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i, j)} \]

6. **SizeZoneNonUniformityNormalized (SZNN)**

\[ SZNN = \frac{\sum_{i=1}^{N_g} (\sum_{j=1}^{N_g} P(i, j))^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i, j)} \]
ZonePercentage (ZP)

\[ ZP = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{P(i,j)}{N_p} \]

GrayLevelVariance (GLV)

\[ GLV = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} (i - \mu)^2 p(i,j) \]

\[ \mu = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i,j)i \]

ZoneVariance (ZV)

\[ ZV = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i,j)(j - \mu)^2 \]

ZoneEntropy (ZE)

\[ ZE = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i,j)\log_2(p(i,j)+\epsilon) \]

LowGrayLevelZoneEmphasis (LGLZE)

\[ LGLZE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{P(i,j)}{i^2}}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i,j)} \]

HighGrayLevelZoneEmphasis (HGLZE)

\[ HGLZE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i,j) i^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i,j)} \]

SmallAreaLowGrayLevelEmphasis (SALGLE)

\[ SALGLE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{P(i,j)}{j^2}}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i,j)} \]

SmallAreaHighGrayLevelEmphasis (SAHGLE)

\[ SAHGLE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i,j)j^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i,j)} \]

LargeAreaLowGrayLevelEmphasis (LALGLE)

\[ LALGLE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} \frac{P(i,j)}{i^2}}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i,j)} \]

LargeAreaHighGrayLevelEmphasis (LAHGLE)

\[ LAHGLE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i,j)j^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_g} P(i,j)} \]
**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)**
   
   \[
   SRE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)}
   \]

2. **LongRunEmphasis (LRE)**
   
   \[
   LRE = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} j^2 P(i, j|\theta)}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)}
   \]

3. **GrayLevelNonUniformity (GLNN)**
   
   \[
   GLNN = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)}
   \]

4. **GrayLevelNonUniformityNormalized (RLNN)**
   
   \[
   RLNN = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)}
   \]

5. **RunLengthNonUniformity (RLN)**
   
   \[
   RLN = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} (P(i, j|\theta))^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)}
   \]

6. **RunLengthNonUniformityNormalized (RLNN)**
   
   \[
   RLNN = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)^2}{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)}
   \]

   RLNN measures the similarity of run lengths throughout the image, with a lower value indicating more homogeneity among run lengths in the image. This is the normalized version of the RLN formula

7. **RunPercentage (RP)**
   
   \[
   RP = \frac{\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} P(i, j|\theta)}{N_p}
   \]
8 GrayLevelVariance (GLV)

$$GLV = \sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i,j|\theta)(i - \mu)^2$$

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)

$$RE = \sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i,j|\theta) \log_2(p(i,j|\theta) + \epsilon)$$

Here, \( \epsilon \) is an arbitrarily small positive number (\( \approx 2.2 \times 10^{-16} \)).

RE measures the uncertainty/randomness in the distribution of run lengths and gray levels. A higher value indicates more heterogeneity in the texture patterns.

11 LowGrayLevelRunEmphasis (LGLRE)

$$LGLRE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i,j|\theta) i^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i,j|\theta)}$$

12 HighGrayLevelRunEmphasis (HGLRE)

$$HGLRE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i,j|\theta) i^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i,j|\theta)}$$

13 ShortRunLowGrayLevelEmphasis (SRLGLE)

$$SRLGLE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i,j|\theta) i^2 j^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i,j|\theta)}$$
ShortRunHighGrayLevelEmphasis (SRHGLE)

$SRHGLE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} P(i, j|\theta)e^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} P(i, j|\theta)}$

LongRunLowGrayLevelEmphasis (LRLGLE)

$LRLGLE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} P(i, j|\theta) \frac{i^2j^2}{i^2j^2}}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} P(i, j|\theta)}$

LongRunHighGrayLevelEmphasis (LRHGLE)

$LRHGLE = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} P(i, j|\theta) i^2j^2}{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} P(i, j|\theta)}$

Notations:

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

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

$N_g$ is the number of discrete intensity values in the image

$N_r$ is the number of discrete run lengths in the image

$N_p$ is the number of voxels in the image
| 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 | GrayLevelNonUniformityNormalized | GrayLevelNonUniformityNormalized |
| 5 10Percentile | Compactness1 | ClusterTendency | SizeZoneNonUniformity | RunLengthNonUniformity |
| 6 90Percentile | Compactness2 | Contrast | SizeZoneNonUniformityNormalized | 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 RobustMeanAbsoluteDeviation | LeastAxis | Entropy | SmallAreaLowGrayLevelEmphasis | ShortRunLowGrayLevelEmphasis |
| 14 RootMeanSquared | Elongation | Homofeaturesity1 | SmallAreaHighGrayLevelEmphasis | ShortRunHighGrayLevelEmphasis |
| 15 StandardDeviation | Flatness | Homofeaturesity2 | LargeAreaLowGrayLevelEmphasis | LongRunLowGrayLevelEmphasis |
| 16 Skewness | Imc1 | LargeAreaHighGrayLevelEmphasis | LongRunHighGrayLevelEmphasis |
| 17 Kurtosis | Imc2 |

(Continued on next page)
| 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 0.42. 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.glc.m.Corr + 0.1856*logarithm.glsz.m.GrayLevelNonUnif.Normalized + 0.0590*square.firstorder.Skewness + 0.0026*square.firstorder.Kurts + 0.0427*exponential.glrl.m.RunLengthNonUnif + 0.0181*exponential.glrl.m.RunVar + 0.0715*wavelet-LHL.firstorder.Mean + 0.0405*wavelet-LHL.glc.m.CluShade + 0.0344*wavelet-LHL.glsz.m.LargeAreaHighGrayLevelEmphasis + 0.0018*wavelet-HLL.firstorder.Mean + 0.0091*wavelet-HLL.glsz.m.ZoneV + 0.0826*wavelet-HHH.glsz.m.LargeAreaHighGrayLevelEmphasis
SUPPLEMENTAL FIGURE 1. LASSO regression solution paths (LASSO, least absolute shrinkage and selection operator).