**Supplementary data**

**S-text-1**

**Radiomics features:**

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| --- | --- | --- |
| **Summary of radiomic features used in this study** | | |
| **Feature classes** | **No. of features** | **3 representative features** |
| First order intensity | 19 | Energy, Entropy, Mean, …. |
| Shape | 13 | Mesh Volume, Surface Area, Compactness |
| GLSZM | 16 | Small Area Emphasis, Large Area Emphasis, Gray Level Non-Uniformity, …. |
| GLRLM | 16 | Short Run Emphasis, Long Run Emphasis, Non-Uniformity Normalized, …. |
| NGTDM | 5 | Coarseness, Contrast, Busyness, …. |
| GLDM | 14 | Uniformity, Variance, Emphasis, …. |
| GLCM | 23 | Autocorrelation, Joint Average, Cluster Prominence, …. |
| Log-sigma | 368 | Log-sigma 2-mm, 3-mm, 4-mm, 5-mm-related features, …. |
| Wavelet | 736 | Wavelet-HHH-related features, …. |
| Total | 1210 |  |
| GLSZM = gray level size zone matrix，GLRLM = gray level run-length matrix; NGTDM = neighborhood gray-tone difference matrix, GLDM = gray level difference matrix, GLCM = grey level co-occurrence matrix | | |

1) First-order statistics describe the histogram of voxel intensity values within the ROI through commonly used and basic metrics.

Let:

be a set of voxels included in the ROI,

be the first order histogram with discrete intensity levels, where is the number of non-zero bins, equally spaced from 0 with a width defined in the binWidth parameter,

be the normalized first order histogram and equal to.

1. Energy:

2. Total Energy

3. Entropy:

Here, is an arbitrarily small positive number (≈2·2×10−16)

4. Minimum:

5. 10th Percentile

The 10th percentile of, a robust alternative to the minimum gray-value.

6. 90th Percentile

The 90th percentile of, a robust alternative to the maximum gray-value.

7. Maximum:  
The maximum gray level intensity within the ROI.

8. Mean:

The average gray level intensity within the ROI.

9. Median:  
The median gray level intensity within the ROI.

10. Interquartile Range:

Here and are the 25th and 75th percentile of the image array, respectively.

11. Range:  
The range of gray values in the ROI.

12. Mean Absolute Deviation (MAD):

MAD is the mean distance of all intensity values from the Mean Value of the image array.

Where is the mean of

13. Robust Mean Absolute Deviation (rMAD):

rMAD is the mean distance of all intensity values from the Mean Value calculated on the subset of image array with gray levels in between, or equal to the 10th and 90th percentile.

14. Root Mean Square (RMS):

Here, is optional value, defined by voxelArrayShift, which shifts the intensities to prevent negative values in . 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. Standard Deviation:

Where is the mean of .

16. Skewness:

Skewness measures the asymmetry of the distribution of values about the Mean value.  
where is the mean of .

17. Kurtosis:

Where is the mean of .

18. Variance:

19. Uniformity:

2) Shape features describe the three-dimensional size and shape of the ROI. These features are independent from the gray level intensity distribution in the ROI and are therefore only calculated on the non-derived image and mask.

Let:

the volume of the ROI in mm3,

the surface area of the ROI in mm2.

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. Surface Area:  
Where: is the number of triangles forming the surface mesh of the ROI and are the edges of the ithith triangle formed by points , and .

3. Surface to Volume Ratio:

4. Sphericity:

Sphericity is a measure of how much the volume resembles a sphere.

5. Compactness 1:

Compactness is a measure of how much the volume resembles a sphere [1].

6. Compactness 2:

7. Spherical Disproportion:

Spherical disproportion is a measure of how much the volume resembles a sphere.

Where is the surface area and is the radius of a sphere with the same volume as the tumor.

8. Maximum 3D diameter:

Maximum 3D diameter is defined as the largest pairwise Euclidean distance between surface voxels in the ROI.

9. Maximum 2D diameter (Slice):

Maximum 2D diameter (Slice) is defined as the largest pairwise Euclidean distance between tumor surface voxels in the row-column (generally the axial) plane.

10. Maximum 2D diameter (Row):

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. Maximum2D diameter (Column):

Maximum 2D diameter (Column) is defined as the largest pairwise Euclidean distance between tumor surface voxels in the row-slice (usually the coronal) plane.

12. Major Axis:

13. Minor Axis:

14. Least Axis:

15. Elongation:

Here, and are the lengths of the largest and second largest principal component axes.

16. Flatness

Here, and are the lengths of the largest and smallest principal component axes.

3) Statistics-based textural features describe patterns or the spatial distribution of voxel intensities, which were calculated from respectively gray-level co-occurrence matrix (GLCM), gray-level run length matrix (GLRLM), and gray-level size zone matrix (GLSZM) features.

Gray Level Co-occurrence Matrix (GLCM) Features

A normalized GLCM is defined as , a matrix with size describing the second-order joint probability function of an image, where the element represents the number of times the combination of intensity levels and occur in two pixels in the image, that are separated by a distance of pixels in direction . The distance δ from the center voxel is defined as the distance according to the infinity norm. For δ=1, this results in 2 neighbors for each of 13 angles in 3D (26-connectivity).

Let:

be an arbitrarily small positive number (≈2·2×10−16)

be the co-occurence matrix for an arbitrary and , ,

be the normalized co-occurence matrix and equal to,

be the number of discrete intensity levels in the image,

be the marginal row probabilities,

be the marginal column probabilities,

be the mean gray level intensity of ,

be the mean gray level intensity of ,

be the standard deviation of ,

be the standard deviation of ,

, where , and ,

, where , and ,

be the entropy of ,

be the entropy of ,

be the entropy of ,

,

1. Autocorrelation

2. Joint Average

3. Cluster Prominence:

4. Cluster Shade:

5. Cluster Tendency:

6. Contrast:

7. Correlation:

8. Difference Average:

9. Difference Entropy:

10. Difference Variance:

11. Dissimilarity:

12. Joint Energy:

13. Joint Entropy:

14. Homogeneity 1:

15. Homogeneity 2:

16. Informal Measure of Correlation (IMC) 1:

17. Informal Measure of Correlation (IMC) 2:

18. Inverse Difference Moment (IDM)

19. Inverse Difference Moment Normalized (IDMN):

20. Inverse Difference (ID):

21. Inverse Difference Normalized (IDN):

22. Inverse Variance:

23. Maximum Probability:

24. Sum Average:

25. Sum Entropy:

26. Sum of Squares:

Gray Level Run Length Matrix (GLRLM) Features

A GLRLM quantifies gray level runs, which are defined as the length in number of pixels, of consecutive pixels that have the same gray level value. In a gray level run length matrix , the element describes the number of runs with gray level and length occur in the image along angle .

Let:

be the number of discreet intensity values in the image,

be the number of discreet run lengths in the image,

be the number of voxels in the image,

be the number of runs in the image along angle , which is equal to , and ,

be the run length matrix for an arbitrary direction,

be the normalized run length matrix, defined as,

1. Short Run Emphasis (SRE):

2. Long Run Emphasis (LRE):

3. Gray Level Non-Uniformity (GLN):

4. Gray Level Non-Uniformity Normalized (GLNN):

5. Run Length Non-Uniformity (RLN):

6. Run Length Non-Uniformity Normalized (RLNN):

7. Run Percentage (RP):

8. Gray Level Variance (GLV):

Here,

9. Run Variance (RV):

Here,

10. Run Entropy (RE):

Here, is an arbitrarily small positive number (≈2.2×10−16)

11. Low Gray Level Run Emphasis (LGLRE):

12. High Gray Level Run Emphasis (HGLRE):

13. Short Run Low Gray Level Emphasis (SRLGLE):

14. Short Run High Gray Level Emphasis (SRHGLE):

15. Long Run Low Gray Level Emphasis (LRLGLE):

16. Long Run High Gray Level Emphasis (LRHGLE):

Gray Level Size Zone Matrix (GLSZM) Features

A GLSZM describes the amount of homogeneous connected areas within the volume, of a certain size and intensity, thereby describing tumor heterogeneity at a regional scale [2]. A voxel is considered connected if the distance is 1 according to the infinity norm (26-connected region in 3D). In a GLSZM , the element equals the number of zones with gray level and size appear in image. Contrary to GLCM and GLRLM, the GLSZM is rotation independent, with only one matrix calculated for all directions in the ROI. The mathematical formulas that define the GLSZM features correspond to the definitions of features extracted from the GLRLM.

Let:

be the number of discreet intensity values in the image,

be the number of discreet zone sizes in the image,

be the number of voxels in the image,

be the number of zones in the ROI, which is equal to , and

be the size zone matrix,

be the normalized size zone matrix, defined as .

1. Small Area Emphasis (SAE):

2. Large Area Emphasis (LAE):

3. Gray Level Non-Uniformity (GLN):

4. Gray Level Non-Uniformity Normalized (GLNN):

5. Size-Zone Non-Uniformity (SZN):

6. Size-Zone Non-Uniformity Normalized (SZNN):

7. Zone Percentage (ZP):

8. Gray Level Variance (GLV):

Here,

9. Zone Variance (ZV):

Here,

10. Zone Entropy (ZE):

ZE measures the uncertainty/randomness in the distribution of zone sizes and gray levels. A higher value indicates more heterogeneneity in the texture patterns.

Here, is an arbitrarily small positive number (≈2·2×10−16)

11. Low Gray Level Zone Emphasis (LGLZE):

12. High Gray Level Zone Emphasis (HGLZE):

13. Small Area Low Gray Level Emphasis (SALGLE):

14. Small Area High Gray Level Emphasis (SAHGLE):

15. Large Area Low Gray Level Emphasis (LALGLE):

16. Large Area High Gray Level Emphasis (LAHGLE):