**Appendix E1**

**The Acquisition Parameters and Retrieving Procedure**

MRI (magnetic resonance imaging) was performed using a 1.5-TAchieva scanner (Philips Medical Systems, Best, Netherlands) with a dedicated bilateral phased array breast coil. The patient was instructed to lie in a prone position and images of both breasts were acquired. The MRI examination consisted of turbo spin-echo T1- and T2-weighted sequences and a 3-dimensional dynamic contrast-enhanced (DCE) sequence. The imaging parameters for the T2-weighted images were as follows: repetition time/echo time (TR/TE), 3800/120; slice thickness, 1.5 mm; matrix size, 376 × 358; field of view, 30 cm; and acquisition time, 5 min. The DCE-MRI scans were acquired using the following parameters: TR/TE=6.5/2.5; slice thickness=1.5 mm; flip angle=10°; matrix size=376 × 374; and field of view=32 cm × 32 cm. DCE-MRI was performed using axial imaging with one pre-contrast and six post-contrast dynamic series. Contrast-enhanced images were acquired at 30, 90, 150, 210, 270, and 330 s after contrast injection. The length of each dynamic series was 1.05 min. Image subtraction was performed after the dynamic series. A 0.1-mmol/kg bolus of gadobutrol (Gadovist; Bayer Healthcare Pharmaceutical, Berlin, Germany) was injected, and subsequently, a 20-mL saline flush was injected.

**Appendix E2**

 **MR Imaging Preparation for Radiomic Analysis**

A region of interest (ROI) was drawn around the entire visible tumor on the contrast-enhanced T1-weighted subtraction images by a radiologist with 10 years of experience in breast MRI (E.S.K.) who was blinded to the clinical and pathological findings but was aware of the diagnosis of invasive ductal carcinoma (IDC). The defined ROI was co-registered onto three other MR imaging series with a nine-parameter affine transform using mutual information as the similarity measure (1). The co-registration process allows the researcher to define the ROI once and apply it to other imaging series of the same patient in a consistent manner. The ROI was drawn to be as large as possible, but did not include edge voxels to avoid a partial volume effect. In the case of multifocal or multicentric disease, the largest tumor was selected as the index cancer for the analysis.

**Appendix E3**

 **MR Imaging Interpretation**

The radiologists assessed the shape (oval, round, irregular), margin (circumscribed, irregular, spiculated), and internal enhancement characteristics (homogeneous, heterogeneous, rim, dark internal septation) of each mass.

The DCE-MRI were transferred to a computer-aided diagnosis system (CADstream, version 4.1.3; Merge Healthcare, Chicago, IL, USA) that analyzed the signal intensities within each voxel of the FOV obtained during the dynamic sequences. Using CADstream, a color overlay showing the changes in signal intensity over time was automatically made for all slices using a predefined minimum threshold. We set the minimum threshold as a 50% or greater increase in a pixel-by-pixel comparison between the precontrast and second post-contrast images. When the relative enhancement increase was more than 100% of the precontrast image, we defined it as “rapid uptake,” and when it was 50–100%, we defined it as “medium uptake.” When the signal intensity continued to show an increase of more than 10% in the sixth postcontrast-enhanced images when compared with the second postcontrast-enhanced images, we defined it as “persistent.” When the signal intensity showed a decrease of more than 10%, it was defined as a “washout,” and when the signal intensity remained within a 10% range, it was defined as a “plateau.” Volumetric assessment of the kinetic components refers to the assessment of the percentage volume of each kinetic component found within the tumors during early and delayed phases of enhancement.

**Appendix E4**

**Computer code used to compute the Radiomics Features**

Our study employed a combination of open source code and in-house generated computer code implemented in MATLAB to compute radiomics features. For most features (7 out of 156), we used the open source software PyRadiomics so that the results could be easily reproduced. For the seven features not available in PyRadiomics, we used our in-house MATLAB code which is provided as a supplement material. The locally implemented features were four histogram based features (percentile features at 2.5%, 25%, 75%, and 97.5% level), two GLSZM features (size-zone variability and intensity variability), and one morphological feature (convexity).

**Appendix E5**

 **Categorical Concepts of Radiomic Features and the Mathematical Definition of Adopted Feature Algorithms**

The morphological features (eight features) quantify shape-related properties, such as roundness, of the tumor and it is only dependent on the ROI, not the underlying imaging series. The histogram-based features (19 features) quantify tumor intensity characteristics, such as mean intensity, using first-order statistics calculated from the histogram of the ROI. The histogram-based features were computed for each series separately resulting in 76 features. The higher-order texture features (18 features) quantify intra-tumoral heterogeneity using a gray level co-occurrence matrix (GLCM) or gray level size zone matrix (GLSZM). The GLCM-related features (16 features) consider intensity values of a neighborhood instead of one voxel, thus quantifying how similar voxel intensities are within a neighborhood. The intensity values were discretized using 256 bins for the GLCM matrix. GLCMs were computed for 13 directions and the average of 13 matrices was used for feature computation. The GLSZM features (two features) assume that an ROI could be further divided into sub-regions with uniform intensity with variable size and thus GLSZM could quantify how many sub-regions and how often certain sub-regions occur within the tumor (2). Image intensities were discretized to 32 levels for robust computation of the GLSZM. The higher-order texture features were computed for each series separately resulting in 72 features.

**Appendix E6**

 **Radiomics Score (Rad-score) Calculation Formula**

The radiomic features with a nonzero coefficient in the LASSO Cox regression model were as follows: SVR\_SHAPE, Cluster tendency\_GLCM\_T2, Variance\_GLCM\_T2, and Sum\_variance\_GLCM\_T2. The radiomic signature was constructed with a Rad-score calculated using the following formula:

Rad-score= -0.0125 × std\_SVR\_SHAPE + (-0.0084) × std\_Cluster tendency\_GLCM\_T2 + (-0.0415) × std\_Variance\_GLCM\_T2 + (-0.0082) × std\_Sum\_variance\_GLCM\_T2

The optimal log lambda value was -2.159. The optimal log alpha which is a mixing parameter of elastic net was -0.916. The detail description about the regularization parameters can be found (3, 4).

**Appendix Table 1**.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Classes of texture features** | **Based methods** | **Parameter** | **Formula** | **Description** |
| **Statistical based** | **1st order features** (Histogram based features) | Maximum | Where denote the 3d image matrix | Measures maximum intensity value of a histogram |
| Minimum | Where denote the 3d image matrix | Measures minimum intensity value of a histogram |
| Median | Where denote the 3d image matrix | Measures median intensity value of a histogram |
| Mean | Where denote the 3d image matrix with voxel. | Measures mean intensity value of a histogram |
| Variance |  | Measures squared distances of each value of a histogram from the mean  |
| *Energy* | Where denote the 3d image matrix with voxel. | Measures squared magnitude value of a histogram |
| Standard deviation | Where denote the 3d image matrix with voxel. | Measures amount of variation of a histogram. |
| Skewness | Where is the mean of , is the standard deviation of , is the expectation operator. | Measures asymmetry of a histogram. |
| Kurtosis | Where is the mean of, is the standard deviation of , is the expectation operator. | Measures “peakedeness” of a histogram (flatness of histogram) |
| Root mean square (RMS) | Where denote the 3d image matrix with voxel. | Measures the square-root of the mean of the squares of the values of the histogram. This feature is another measure of the magnitude of a histogram |
| Inter quartile range | Where denote the 3rd quartile of histogram, denote the 1st quartile of histogram | Measures of variability, based on dividing a histogram into quartiles |
| Range |  | Measures difference between the highest and lowest voxel values of a histogram |
| Entropy | Where denote the first order histogram with discrete intensity levels. | Measures irregularity of a histogram. |
| Uniformity | Where denote the first order histogram with discrete intensity levels. | Measures uniformity of a histogram. |
| Percentile |  | Measures intensity value at the 2.5th , 25th ,50th ,75th , and 97.5th percentile on histogram |
| **Higher order features**(GLCM based features) | Autocorrelation |  | Measures of the magnitude of the fineness and coarseness of texture |
| Cluster tendency |  | Measures of the homogeneity of GLCM |
| Maximum probability |  | Measures maximum value of GLCM matrix |
| Contrast |  | Measures of the local intensity variation of GLCM |
| Difference entropy |  | Measures entropy of processed GLCM matrix Px-y |
| Dissimilarity |  | Measures differences of entries in GLCM  |
| Energy |  | Measures of the homogeneity of GLCM |
| Entropy |  | Measures irregularity of GLCM |
| Homogeneity1 |  | Measures closeness of GLCM |
| Informational measure of correlation 1 (IMC1) |  | Secondary measure of Homogeneity1 |
| Variance |  | Measures dispersion of the parameter values around the mean of the combinations of reference and neighborhood pixels |
| Sum average (SA) |  |  |
| Sum entropy |  |  |
| Sum variance |  |  |
| Inverse variance |  |  |
| Inverse Difference Moment Normalized (IDMN) |  |  |
| Where is the gray level co-occurrence matrix for (,is the number of discrete intensity value in the image, is the number of voxels in the ROI, is the marginal row probabilities, is the marginal column probabilities, is the expected value of marginal row probability, is the expected value of marginal column probability, is the standard deviation of , is the standard deviation of ,,, is the entropy of , is the entropy of ,is the entropy of . |
| **Higher order features**(GLSZM based features) | Size-zone variability |  | Variability in the size |
| Intensity variability |  | Variability in the intensity |
| Where is the intensity size zone matrix  represents the number of homogeneous areas in tumor, is the number of distinct intensity values, is the size of homogeneous area in the matrix  |
| **Morphological features** | **Shape and Size based features** | Compactness | Where denote the volume and denote the surface area of the volume of interest (VOI) | Quantifies how close an object to the smoothest shape, the circle |
| Surface area | Where is the total number triangle (coved surface area) and are edge vectors | The surface area of the ROI  |
| Convexity | Where denote tumor volume and denote convex hull volume | Measures ratio of the ROI volume contained within the tumor to the calculated convex hull volume |
| Sphericity | Where denote area and denote tumor volume | Measures of the roundness of the ROI |
| Maximum 3D diameter | See description in the next column | Measures of the maximum 3D ROI diameter. It is measured as the largest pairwise Euclidean distance, between surface voxels of the ROI |
| Spherical disproportion | Where is the radius of a sphere with the same volume as the ROI | The ratio of the surface area of the ROI to the surface area of a sphere with the same volume as the ROI |
| Surface to volume ratio (SVR) | Where is area and is volume | Surface to volume ratio  |
| **Physical based features** | Volume | Where denote the 3d image resolution | Volume of tumor (ROI) |

**Appendix References**

1. Meyer CR, Boes JL, Kim B, et al. Demonstration of accuracy and clinical versatility of mutual information for automatic multimodality image fusion using affine and thin-plate spline warped geometric deformations. Med Image Anal.1997; 1:195–206.
2. Tixier F, Le Rest CC, Hatt M, et al. Intratumor heterogeneity characterized by textural features on baseline 18F-FDG PET images predicts response to concomitant radiochemotherapy in esophageal cancer. J Nucl Med*.* 2011; 52:369–378.
3. Friedman J, Hastie T, Tibshirani R. Regularization Paths for Generalized Linear Models via Coordinate Descent. J Stat Soft 2010;33(1):1-22
4. Zou H, Hastie T. Regularization and Variable Selection via the Elastic Net. J R Stat Soc Series B Stat Methodol. 2005;67(2):301-320