

Supplementary Material

Table S1. The 94 radiomic features of ¹⁸F-FDG PET-CT extracted from LIFEx software.



Supplementary Material

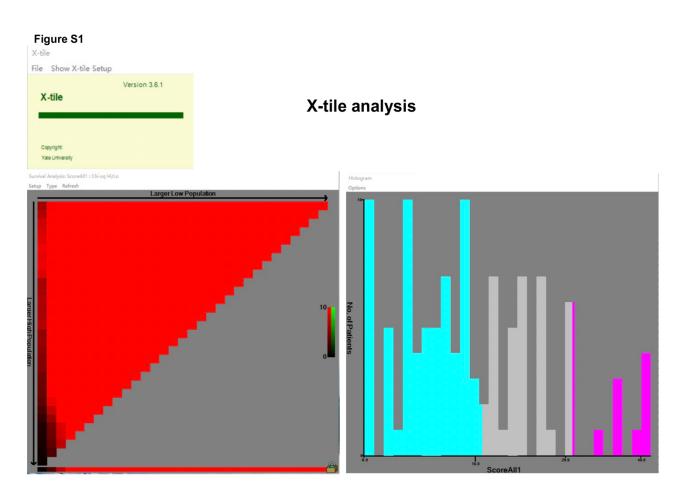


Figure S1. Novel validated recurrence stratification system was divided into low-, intermediate-, and high-risk groups according to cutoff values determined by X-tile plots.



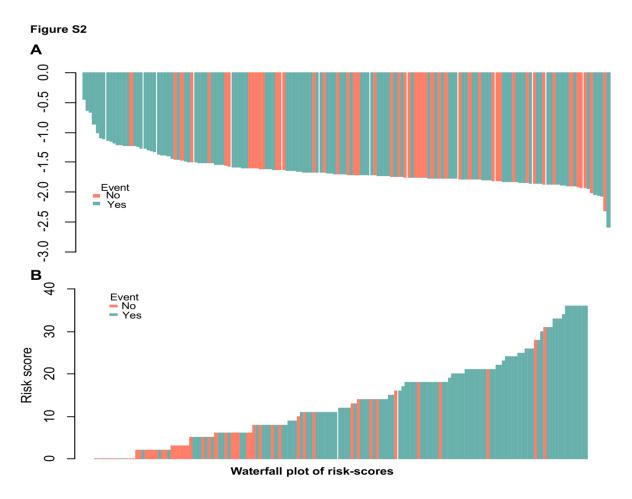
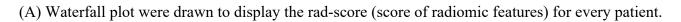


Figure S2.



(B) Waterfall plot according to the risk score for every RPC patient.



Definition of texture features

First order features:

1. Conventional Indices

1.1 CONV 01,02,03

A quartile is a type of quantile which divides the number of data points into four more or less equal parts, or quarters. Due to the fact that the data needs to be ordered from smallest to largest in order to compute quartiles, quartiles are a form of Order statistic.

CONVENTIONALQ1: The first quartile (Q1) is defined as the middle number between the smallest number and the median of the data set. It is also known as the lower quartile or the 25th empirical quartile and it marks where 25% of the data is below or to the left of it (if data is ordered on a timeline from smallest to largest).

CONVENTIONALQ2: The second quartile (Q2) is the median of a data set and 50% of the data lies below this point. CONVENTIONALQ3: The third quartile (Q3) is the middle value between the median and the highest value of the data set. It is also known as the upper quartile or the 75th empirical quartile and 75% of the data lies below this point.

1.2 CONVmin, CONVmean, CONVmax, CONVpeak

CONVmin: reflects the minimum of value (in choosen unit) in the Volume of Interest.

CONVmean: reflects the average value (in choosen unit) in the Volume of Interest.

CONVmax: reflects the maximum value (in choosen unit) in the Volume of Interest.

CONVpeak: reflects the CONVmean in a sphere with a volume of ~1 mL and located so that the average value in the VOI is maximum.

1.3 CONV TLG(mL), CONV RIM

CONV TLG(mL) is the Total Lesion Glycolysis defined as the product of SUVmean by Volume in mL.

is the envelope Intensity Mean "CONV RIM mean" of successive layers of voxels from the outside of CONV RIM is the region to the inside. Each layer is 1 voxel thick. These envelopes are getting smaller and smaller (3D erosion of 1 voxel) up to the center of the ROI.

2. Indices from Histogram

2.1 HISTO Skewness

is the asymmetry of the grey-level distribution in the histogram. *HISTO_Skewness*= $\frac{\frac{1}{E}\sum_{i}(HISTO(i)-\overline{HISTO})^{3}}{(\sqrt{\frac{1}{E}\sum_{i}(HISTO(i)-\overline{HISTO})^{2}})^{3}}$

Where HISTO(i) corresponds to the number of voxels with intensity *i*, *E* the total number of voxels in the Volume of Interest and HISTO the average of grey-levels in the histogram.

2.2 HISTO Kurtosis

reflects the shape of the grey-level distribution (peaked or flat) relative to a normal distribution.

 $HISTO_Kurtosis = \frac{\frac{1}{E} \sum_{i} (HISTO(i) - \overline{HISTO})^{4}}{(\sqrt{\frac{1}{E} \sum_{i} (HISTO(i) - \overline{HISTO})^{2}})^{2}}$

Where HISTO(i) corresponds to the number of voxels with intensity *i*, *E* the total number of voxels in the Volume of Interest and HISTOthe average of grey-levels in the histogram.

2.3 HISTO Entropy log10, HISTO Entropy log 2 reflects the randomness of the distribution. *HISTO_Entropylog*10 =- $\sum_{i} p(i) \cdot \log_{10}(p(i) + \varepsilon)$ *HISTO_Entropylog*10 =- $\sum_{i} p(i) \cdot \log_2(p(i) + \epsilon)$ Where p(i) is the probability of occurrence of voxels with intensity *i* and $\varepsilon = 2e-16$.



2.4 HISTO_Energy reflects the uniformity of the distribution. $HISTO_Energy=\sum_i p(i)^2$

3. Indices from shape

3.1 SHAPE_Sphericity is how spherical a Volume of Interest is. Sphericity is equal to 1 for a perfect sphere.

SHAPE_Sphericity= $\frac{\pi^{1/3} \cdot (6V)^{2/3}}{A}$

Where V and A correspond to the volume and the surface of the Volume Of Interest based on the Delaunay triangulation.

3.2 SHAPE_Volume (mL and voxels) is the Volume of Interest in mL and in voxels. $SHAPE_Volume=\sum_i V_i$ Where *Vi* corresponds to the volume of voxel *i* of the Volume Of Interest.

3.3 SHAPE_Compacity reflects how compact the Volume of Interest is.

 $SHAPE_Compacity=\frac{A^{3/2}}{V}$

Where V and A correspond to the volume and the surface of the Volume Of Interest based on the Delaunay triangulation.

Second order features:

1. GLZLM

The grey-level zone length matrix (GLZLM) [Thibault] provides information on the size of homogeneous zones for each grey-level in 3 dimensions (or 2D). It is also named Grey Level Size Zone Matrix (GLSZM). From this matrix, 11 texture indices are computed. Element (i, j) of GLZLM corresponds to the number of homogeneous zones of j voxels with the intensity i in an image and is called GLZLM(i, j) thereafter.

1.1 GLZLM_SZE, GLZLM_LZE

Short-Zone Emphasis or Long-Zone Emphasis is the distribution of the short or the long homogeneous zones in an image.

 $GLZLM_SZE = \frac{1}{H} \sum_{i} \sum_{j} \frac{GLZLM(i,j)}{j^{2}}$ $GLZLM_LZE = \frac{1}{H} \sum_{i} \sum_{j} GLZLM(i,j) \cdot j^{2}$

Where H corresponds to the number of homogeneous zones in the Volume of Interest.

1.2 GLZLM LGZE, GLZLM HGZE

Low Gray-level Zone Emphasis or High Gray-level Zone Emphasis is the distribution of the low or high grey-level zones

$$\begin{split} & \textit{GLZLM_LGZE} {=} \frac{1}{H} \sum_{i} \sum_{j} \frac{\textit{GLZLM}(i,j)}{i^{2}} \\ & \textit{GLZLM_HGZE} {=} \frac{1}{H} \sum_{i} \sum_{j} \textit{GLZLM}(i,j) \cdot i^{2} \end{split}$$

1.3 GLZLM_SZLGE, GLZLM_SZHGE

Short-Zone Low Gray-level Emphasis or Short-Zone High Gray-level Emphasis is the distribution of the short homogeneous zones with low or high grey-levels.

$$GLZLM_SZLGE = \frac{1}{H}\sum_{i}\sum_{j}\frac{GLZLM(i,j)}{i^{2}\cdot j^{2}}$$
$$GLZLM_SZHGE = \frac{1}{H}\sum_{i}\sum_{j}\frac{GLZLM(i,j)\cdot i^{2}}{j^{2}}$$



1.4 GLZLM_LZLGE, GLZLM_LZHGE

Long-Zone Low Gray-level Emphasis or Long-Zone High Gray-level Emphasis is the distribution of the long homogeneous zones with low or high grey-levels.

 $GLZLM_LZLGE = GLZLM_SZHGE = \frac{1}{H}\sum_{i}\sum_{j}\frac{GLZLM(i,j)\cdot j^{2}}{i^{2}}$ $GLZLM_LZHGE = \frac{1}{H}\sum_{i}\sum_{j}GLZLM(i,j)\cdot i^{2}\cdot j^{2}$

1.5 GLZLM_GLNUz, GLZLM_ZLNU

Gray-Level Non-Uniformity for zone or Zone Length Non-Uniformity is the nonuniformity of the grey-levels or the length of the homogeneous zones.

$$GLZLM_GLNUz = \left(\frac{1}{H}\sum_{i} \left(\sum_{j} GLZLM(i, j)\right)^{2}\right)$$
$$GLZLM_ZLNU = \left(\frac{1}{H}\sum_{j} \left(\sum_{i} GLZLM(i, j)\right)^{2}\right)$$

1.6 GLZLM_ZP

Zone Percentage measures the homogeneity of the homogeneous zones.

$$GLZLM_ZP = \frac{H}{\sum_{i} \sum_{j} (j \cdot GLZLM(i,j))}$$

2. GLRLM

The grey-level run length matrix (GLRLM) [Xu] gives the size of homogeneous runs for each grey level. This matrix is computed for the 13 different directions in 3D (4 in2D) and for each of the 11 texture indices derived from this matrix, the 3D value is the average over the 13 directions in 3D (4 in 2D). The element (i, j) of GLRLM corresponds to the number of homogeneous runs of j voxels with intensity i in an image and is called GLRLM(i, j) thereafter.

2.1 GLRLM_SRE, GLRLM_LRE

Short-Run Emphasis or Long-Run Emphasis is the distribution of the short or the long homogeneous runs in an image. $GLRLM_SRE = Average \ over \ 13 \ (or \ 4) \ directions \left(\frac{1}{H}\sum_{i}\sum_{j}\frac{GLRLM(i,j)}{j^2}\right)$

 $GLRLM_LRE = Average \ over \ 13 \ (or \ 4) \ directions \left(\frac{1}{H}\sum_{i}\sum_{j}GLRLM(i, j) \cdot j^{2}\right)$

Where H corresponds to the number of homogeneous runs in the Volume of Interest

2.2 GLRLM LGRE, GLRLM HGRE

Low Gray-level Run Emphasis or High Gray-level Run Emphasis is the distribution of the low or high grey-level runs.

 $GLRLM_LGRE = Average \text{ over } 13 \text{ (or 4) } directions\left(\frac{1}{H}\sum_{i}\sum_{j}\frac{GLRLM(i,j)}{i^{2}}\right)$ $GLRLM_HGRE = Average \text{ over } 13 \text{ (or 4) } directions\left(\frac{1}{H}\sum_{i}\sum_{j}GLRLM(i,j)\cdot i^{2}\right)$

2.3 GLRLM_SRLGE, GLRLM_SRHGE

Short-Run Low Gray-level Emphasis or Short-Run High Gray-level Emphasis is the distribution of the short homogeneous runs with low or high grey-levels.

 $GLRLM_SRLGE = Average \text{ over } 13 \text{ (or 4) } directions\left(\frac{1}{H}\sum_{i}\sum_{j}\frac{GLRLM(i,j)}{i^{2}\cdot j^{2}}\right)$ $GLRLM_SRHGE = Average \text{ over } 13 \text{ (or 4) } directions\left(\frac{1}{H}\sum_{i}\sum_{j}\frac{GLRLM(i,j)\cdot i^{2}}{j^{2}}\right)$

2.4 GLRLM LRLGE, GLRLM LRHGE

Long-Run Low Gray-level Emphasis or Long-Run High Gray-level Emphasis is the distribution of the long homogeneous runs with low or high grey-levels.



 $GLRLM_LRLGE = Average \text{ over } 13 \text{ (or 4) } directions\left(\frac{1}{H}\sum_{i}\sum_{j}\frac{GLRLM(i,j)\cdot j^{2}}{i^{2}}\right)$ $GLRLM_LRHGE = Average \text{ over } 13 \text{ (or 4) } directions\left(\frac{1}{H}\sum_{i}\sum_{j}GLRLM(i,j)\cdot i^{2}\cdot j^{2}\right)$

2.5 GLRLM_GLNUr, GLRLM_RLNU

Gray-Level Non-Uniformity for run or Run Length Non-Uniformity is the nonuniformity of the grey-levels or the length of the homogeneous runs.

 $GLRLM_GLNUr= Average \text{ over } 13 \text{ (or 4) } directions\left(\frac{1}{H}\sum_{i}\left(\sum_{j} \text{GLRLM}(i, j)\right)^{2}\right)$ $GLRLM_RLNU= Average \text{ over } 13 \text{ (or 4) } directions\left(\frac{1}{H}\sum_{j}\left(\sum_{i} \text{GLRLM}(i, j)\right)^{2}\right)$

2.6 GLRLM_RP Run Percentage measures the homogeneity of the homogeneous runs. $GLRLM_RP = Average \ over \ 13 \ (or \ 4) \ directions \frac{H}{\sum_i \sum_j (j \cdot GLRLM(i,j))}$

3. NGLDM

The neighborhood grey-level different matrix (NGLDM) [Amadasum1989] corresponds to the difference of greylevels between one voxel and its 26 neighbours in 3 dimensions (8 in 2D). Three texture indices can be computed from this matrix. An element (i, 1) of NGLDM corresponds to the probability of occurrence of level i and an element (i, 2) is equal to:

 $NGLDM(i, 2) = \sum_{p} \sum_{q} \begin{cases} |\overline{M}(p, q) - i| \text{ if } I(p, q) = i \\ 0 \text{ else} \end{cases}$

where $\overline{M}(p, q)$ is the average of intensities over the 26 neighbour voxels of voxel(p, q).

3.1 NGLDM_Coarseness is the level of spatial rate of change in intensity $NGLDM_Coarseness = \frac{1}{\sum_{i} NGLDM(i,1) \cdot NGLDM(i,2)}$

3.2 NGLDM_Contrast is the intensity difference between neighbouring regions. $NGLDM_Contrast=\left[\sum_{i}\sum_{j} NGLDM(i, 1) \cdot NGLDM(j, 1) \cdot (i - j)^{2}\right] \cdot \frac{\sum_{i} NGLDM(i, 2)}{E \cdot G \cdot (G - 1)}$

where E corresponds to the number of voxels in the Volume of Interest and G the number of grey-levels.

3.3 NGLDM_Busyness is the spatial frequency of changes in intensity. $NGLDM_Busyness = \frac{\sum_{i} NGLDM(i,1) \cdot NGLDM(i,2)}{\sum_{i} \sum_{j} |(i \cdot NGLDM(i,1) - j \cdot NGLDM(j,1))|}$ with NGLDM(i, 1) $\neq 0$, NGLDM(j, 1) $\neq 0$

4. GLCM

The grey level co-occurrence matrix (GLCM) [Haralick] takes into account the arrangements of pairs of voxels to calculate textural indices. The GLCM is calculated from 13 different directions in 3D with a d-voxel distance ($|| \rightarrow ||$) relationship between neighboured voxels. The index value is the average of the index over the 13 directions in space (X, Y, Z). Seven textural indices are computed from this matrix. An entry (i, j) of GLCM for one direction is equal to: $1 \text{ if } (I(p,q) = i, I(p + \Delta x, q + \Delta y) = j)$

$$GLCM_{\Delta x,\Delta y}(i,j) = \frac{1}{Pairs_{ROI}} \sum_{p=1}^{N-\Delta x} \sum_{q=1}^{M-\Delta y} \begin{cases} I \ I \ ((p,q) = 1, \ (p+\Delta x, q+\Delta y) = j, \\ and \ I(p,q), I \ (p+\Delta x, q+\Delta y) \in ROI \\ 0 \ otherwise \end{cases}$$

where I(p, q) corresponds to voxel (p, q) in an image (I) of size N × M. The vector $\rightarrow = (\Delta x, \Delta y)$ covers the 4 directions



(D1, D2, D3, D4) in 2D space or 13 directions (D1, D2, ..., D13) in 3D space and Pairs_{ROI} corresponds to the number of all voxel pairs belonging to the region of interest (ROI). The GLCM describes the distribution of co-occurring pixel values at a given offset.

4.1 GLCM_Homogeneity

is the homogeneity of grey-level voxel pairs.

GLCM_Homogeneity= Average over 13 (or 4) *directions* $\left(\sum_{i} \sum_{j} \frac{\text{GLCM}(i,j)}{1+|i-j|}\right)$

4.2 GLCM_Energy also called Uniformity or Second Angular Moment, is the uniformity of grey-level voxel pairs. $GLCM_Energy=Average \ over \ 13 \ (or \ 4) \ directions(\sum_i \sum_j GLCM(i, j)^2)$

4.3 GLCM_Correlation is the linear dependency of grey-levels in GLCM.

 $GLCM_Correlation=Average over 13 (or 4) directions\left(\sum_{i} \sum_{j} \frac{(i-\mu_{i}) \cdot (j-\mu_{j}) \cdot GLCM(i,j)}{\sigma_{i} \cdot \sigma_{j}}\right)$

where μ_i or μ_j corresponds to the average on row *i* or column *j* and σ_i and σ_j correspond to the variance on row *i* or column *j*

4.4 GLCM_Entropy_log10 is the randomness of grey-level voxel pairs. $GLCM_Entropy_log10 = Average \ over \ 13 \ (or \ 4) \ directions(-\sum_i \sum_j GLCM(i, j) \cdot \log 10(GLCM(i, j) + \epsilon)).$ Where $\epsilon = 2e^{-16}$ $GLCM_Entropy_log2$ is the randomness of grey-level voxel pairs. $GLCM_Entropy_log2 = Average \ over \ 13 \ (or \ 4) \ directions(-\sum_i \sum_j GLCM(i, j) \cdot \log 2(GLCM(i, j) + \epsilon)).$ Where $\epsilon = 2e^{-16}$

4.5 GLCM_Contrast also called Variance or Inertia, is the local variations in the GLCM $GLCM_Contrast=$ Average over 13 (or 4) directions $(\sum_i \sum_j (i - j)^2 \cdot GLCM(i, j))$

4.6 GLCM_Dissimilarity is the variation of grey-level voxel pairs. $GLCM_Dissimilarity = Average \ over \ 13 \ (or \ 4) \ directions(\sum_i \sum_j |i, j| \cdot GLCM(i, j))$