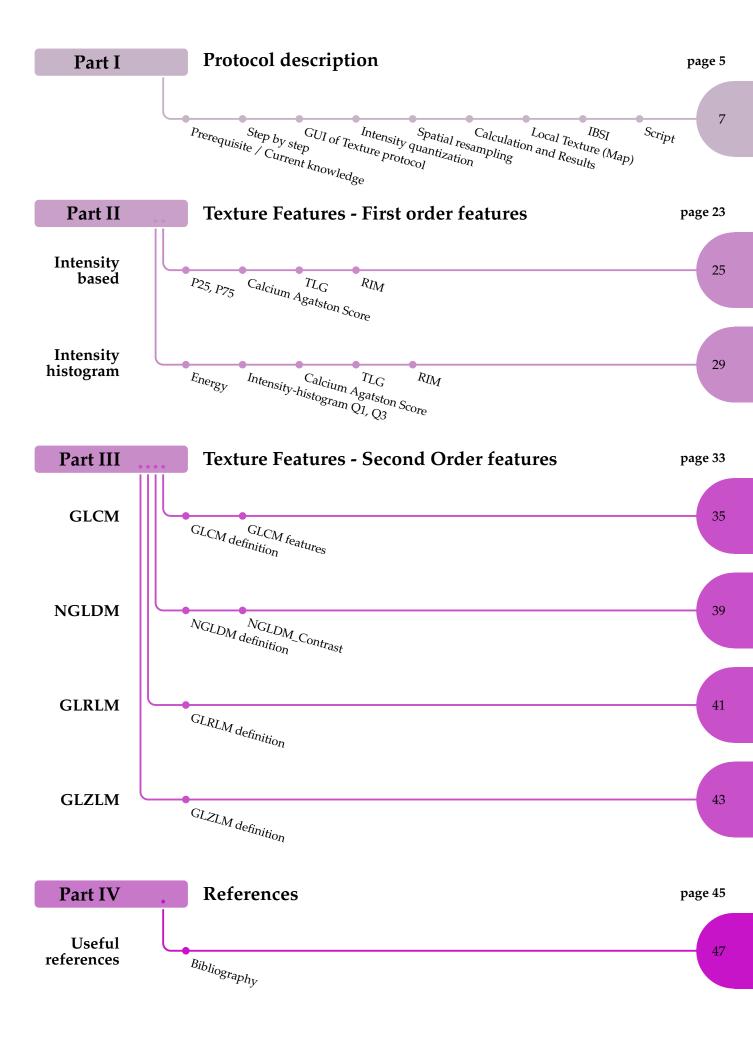
## Texture — User Guide

# Local Image Features Extraction — LIFEx —

C. Nioche, F. Orlhac, I. Buvat

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# Part I Protocol description

# Chapter 1

How to perform textural analysis and estimate conventional parameters?

- step by step -

### 1.1 Prerequisite / Current knowledge

### 1.1.1 Prerequisite

Textural analysis and measurement of conventional parameters from images are based on a number of rules related to the image series, ROI and pixel values, as described below:

### **Image series**

- Textural analysis is currently supported for PET, MR, CT, US and NM. Calculations for Computed radiography (CR), Digital Radiography (DX), Radio Fluoroscopy (RF), Slide Microscopy (SM) and Optical Images are available only if the images are in TIFF or JPG formats;
- Texture indices are calculated in a ROI for one or several layers (1 layer = 1 image series). To properly interpret the index values, it is important to know that the index are calculated for the selected image series (active layer) and, by default, for the voxel sampling of the selected image series.

### ROI:

- The ROI should include at least 64 voxels for 3D ROI and 16 voxels for 2D ROI;
- The ROI should be a single piece (contiguous voxels). It is possible to have a region
  including several clusters of voxels, in which case only the largest cluster is used
  for calculating textural indices;
- The ROI definition is an important step, as edges can largely affect textural index values as well as conventional index values (Orlhac et al 2017).
- In a script, you may add LIFEx.check = true. This line determines the ROI bounds
  to be used for intensity scaling when applying the Texture Protocol on a whole
  cohort.
- In a script, the line *LIFEx.cluster* = *true* look for ROI and check if they are numerous index for ROI in a file. That is to say if ROI are clustered.

### Input parameters:

- Number of grey levels: this is the number of grey levels (must be >0) used to resample the ROI content. Can typically be 16, 32, 64, 128. The initial pixel values will be resampled into that number of grey levels;
- Size of bin: the width of bin;
- Resampling: can be absolute (between fixed min and max values regardless of the ROI content) or relative (between the min and max values in the ROI); See Orlhac et al Plos One 2015 for the impact of resampling approach onto tissue classification;
- Min, max bound: to be set for absolute resampling only: min and max bounds define the range of resampled values.

### 1.1.2 Current knowledge

**In PET images.** By default, texture matrices are computed after a resampling step with 64 discrete values, between 0 and 20 SUV units, without spatial resampling [Orlhac 2015]. Six texture indices have been shown to be robust to segmentation and are relatively independent one from another:

- GLCM\_Homogeneity (from GLCM),
- GLCM\_Entropy (from GLCM),
- GLRLM\_Short-Run Emphasis (GLRLM\_SRE, from GLRLM),
- GLRLM\_Long-Run Emphasis (GLRLM\_LRE, from GLRLM),
- GLZLM\_Low Gray-level Zone Emphasis (GLZLM\_LGZE, from GLZLM),
- GLZLM\_High Gray-level Zone Emphasis (GLZLM\_HGZE, from GLZLM).

**Other indices.** A set of 30 texture indices, 35 histogram indices, 23 morphological indices and 7 conventional (or intensity-based) PET features are computed. For the resampling step, the user can choose the number of discrete values (default: 64) and the range (default: 0-20 SUV units) and the spatial resampling (default: dimension of voxel in the images).



Figure 1.1: Texture feature extract (Advanced settings of First Order features - Morphological - IntensityBased)



Figure 1.2: Texture feature extract (Advanced settings of First Order features - LocalIntensityBased - IntensityHistogram)



Figure 1.3: Texture feature extract (Advanced settings of First Order features - LocalIntensityHistrogram)



Figure 1.4: Texture feature extract (Advanced settings of Second Order features - IntensityBasedRIM)



Figure 1.5: Texture feature extract (Advanced settings of Second Order features - GLCM - GLRM)

### 1.2 Step by step

This section describes the steps needed to get textural and conventional index estimates.

- 1. Reading of the DICOM images for which index should be calculated (link);
- 2. Drawing or loading the ROI (link);
- 3. **Selection of an approach**: global(ROI) or local(Map). If you want to compute texture indices for your ROI, choose the global approach.



Figure 1.6: Texture feature extract (Advanced settings of Second Order features - NGTDM - GLSZM)

- 4. **Definition of the input parameters**: default values can be changed. Parameters without default values should be set;
- 5. **Definition of the output parameters of interest**: click on the *Settings* icon at the bottom left of the textural protocol menu. All indexes to be calculated should be selected;
- 6. **Running the process**: click on the *RUN* icon at the bottom right of the textural protocol menu;
- 7. The folder containing the *csv* file listing the results is open.

### 1.3 Graphic User Interface of Texture protocol

This section describes how to get textural and conventional index estimates.

The user interface (see figure 1.7 p.12) includes 3 sub-parts:

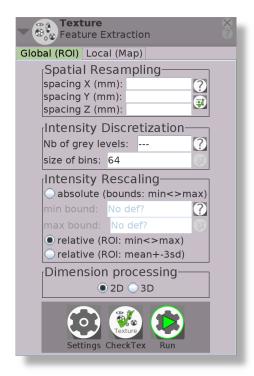
- 1. The "Spatial Resampling" and "Intensity Resampling" and "Intensity Discretization"
- 2. A panel to set advanced parameters (see figure ?? p.??)
- 3. The "Run" button to start the calculations

### 1.4 Intensity quantization and current limits

In PET, several studies have already investigated the impact of resampling settings. Default values for number of grey levels, bin width, resampling approach, and bounds, are set based on these studies.

In MR, CT, US, NM, CR, DX, RF, there is a lack of studies regarding the resampling settings. Studies are on-going to define robust parameter values. Meanwhile, users should interpret the results with caution.

Three types of intensity resampling are available:



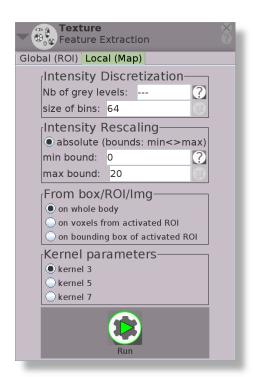


Figure 1.7: Display of textural GUI

**Absolute resampling bounds:** min←max ROI values are rescaled between the *min* and *max* values as set in the parameter box. These values should be set in the appropriate units depending on the image type (Hounsfield units, SUV, #). All voxels are accounted for in the texture index calculation.

**Relative resampling of ROI values:**  $min \iff max$  ROI values are automatically rescaled between the min and max values of the ROI content. All voxels are accounted for in the texture index calculation. Voxels with an initial value less than min are set to min. Voxels with an initial value greater than max are set to max.

**Relative resampling of ROI values: mean-3\*Sd**  $\Longrightarrow$  ROI values are automatically rescaled between mean-3\*Sd  $\Longrightarrow$  mean+3\*Sd of the ROI content, where mean and Sd are the mean and standard deviation of the voxels included in the ROI. All voxels are accounted for in the texture index calculation. Voxels with an initial value less than mean - 3 \* Sd are set to mean - 3 \* Sd. Voxels with an initial value greater than mean + 3 \* Sd are set to mean + 3 \* Sd.

### Summary regarding intensity resampling

- if relative min-max intensity resampling is selected:
  - boundMin = min value of ROI
  - boundMax = max value of ROI
  - binSize OR nbGreyLevels to be set
- if relative mean±3sd intensity resampling is selected:

- boundMin = mean value of ROI 3 sd of ROI
- boundMax = mean value of ROI + 3 sd of ROI
- binSize OR nbGreyLevels to be set
- if absolute intensity resampling is selected:
  - boundMin = get min text input
  - boundMax = get max text input
  - binSize OR/AND nbGreyLevels to be set

calculation of intensity resampling:

- if binSize set and nbGreyLevels not set: nbGreyLevels = ((boundMax - boundMin) / binSize) + 1
- if nbGreyLevels set and binSize not set: binSize = (boundMax - boundMin) / (nbGreyLevels - 1)
- discretizationValueOfVoxel = Floor ((nbGreyLevels \* (valueOfVoxel boundMin) / (boundMax boundMin)) + 1);

**Recommendation** In PET, we do not recommend to use the relative resampling. As shown in [Orlhac 2015], relative resampling results in a high correlation between many texture indices (TI) and the metabolic volume, that is mostly removed when using absolute resampling. Also, changes in TI can be counter-intuitive when using relative resampling instead of absolute resampling [Orlhac 2017]. In PET, resampling using 64 bins between 0 and 20 SUV units (e.g., size bin equal to 0.3) most often yields robust results (0-20 being a frequent range of SUV in oncology with FDG), although the maximum value may need to be changed in case of uptake actually higher than SUV=20.

### 1.5 Spatial resampling and current limits

Textural feature values can be significantly affected by the voxel size (Orlhac et al J Nucl Med 2016, Shafiq-Ul-Hassan et al Med Phys 2017). The voxel size to be used to calculate the textural feature values can be set in the "spacing X, Y, Z" fields in the textural feature dialog box. Unit is millimeter.

To avoid any memory (RAM) saturation, the values should be set in the range defined by 0.2\*Min (Xspacing, Yspacing, Zspacing) (lower limit) and 5\*Max (Xspacing, Yspacing, Zspacing) (upper limit). If this is not appropriate for you, please do not hesitate to contact us at **contact@lifexsoft.org**. In case of RAM saturation, an error message will be displayed: the voxel size in which the value should be performed should then be increased, or the RAM should be increased and the LIFEx application restarted.

A polynomial of degree 5 (Lagrangian polynomial) is used for interpolating the 3D voxel value within the ROI and performing the textural feature calculation at the requested voxel size. The original min and max values are restored after interpolation so that the interpolation does not change these extreme values.

### 1.5 Spatial resampling

Images acquired with an orientation matrix (image orientation patient (IOP)) different from the identity matrix are reoriented in the DICOM reference coordinate system. The voxel size (including the slice thickness) can vary according to the tilt of the images and no longer corresponds to the native voxel size.

### 1.6 Calculation and Results

**2D/3D processing:** It is possible to set how radiomic features are calculated: either in 2D on each 2D transaxial slice, or in 3D. Radiomic feature calculations in 2D can be performed when using 3D ROI. If the selection is 2D, the results will be identical to those executed if the region was divided into as many 2D ROI as there are axial sections. In the resulting file, there will be one row of results for each axial slice. A column is added in the result array named "z location (2D only)" and contains the position of the analyzed slice (in voxel unit).

A column is added in the result table named "z location (2D only)" and contains the position of the analyzed slice (in voxel unit). This feature is also available using scripts with the addition of the following lines:

```
# dimension calculation (3D is default) [ 2D || 3D ]
LIFEx.texture.DimensionProcessing=2D
```

**Calculation:** Calculation starts when the RUN button is clicked. All ROI selected on the reference image series are used for calculation.

**Error messages:** Error messages will be displayed if the prerequisites for calculation are not met. Once the prerequisites are met, calculations should run smoothly. If not, please contact@lifexsoft.org.

**Results ("patient" file):** Results of textural and conventional index are stored in an comma separated values (csv) filed named by default:

patientName\_patientID\_Texture\_time.csv; the time variable is an approximate estimate of date and time and is different for each created file (atomic variable).

**Open a CSV file in Excel:** Excel reads CSV files by default but in most cases when you open a CSV file in Excel, you see scrambled data that's impossible to read.

- open a new Excel document and navigate to the Data tab;
- click "From Text";
- navigate to the CSV file you wish to open and click "Import";
- from the newly-opened window, choose "Delimited". Then click "Next";
- check the box next to the type of delimiter comma. Then click "Next";
- Click "Finish"; That's it; you have just imported a CSV file to Excel!

The Result file is always created is the folder workdir/patientName/RoiValue.

**Results (session file):** A session file makes it possible to add columns in a result file for multi-patients study. It also makes it possible to close the application without loosing any result. For each new calculation, the application will update the session file if you check that option on the settings (advanced parameters) frame.

If the session file does not exist yet, it is automatically created in the workdir folder (see LIFEx\_UserGuide). The folder including the session file corresponds to the folders in which all patient folders are created. The directory workdir can be changed in the LIFEx preferences window (see Bottom toolbar p.27 in LIFEx UserGuide).

### 1.6 Calculation and Results

You can create several session files, by modifying the file name. Only the <code>Texture Session.csv</code> is created by the application if it does not exist. If the file already exists, new results are appended to this file.

Cautious: updating a previous csv file with additional index values is relevant only if the previously calculated index values are unchanged. For instance, file updating can be relevant for multi-patient studies, or multi-ROI studies, in which always the same indices are calculated.

### 1.7 Local Texture (Map) feature

Intensity discretization and intensity rescaling menus of the local texture map menus have the same meaning as in the global feature menu (see section 1.4 p.11; section 1.5, p.13).

Then, you have to decide whether you want to get a map of the textural feature in the whole image (which we do not recommend as it would be quite long to calculate) or only for the voxels included in a ROI:

- we recommend to calculate the textural feature map in a ROI only. For that, please select the ROI from which you want to get the parametric map.
- if you select « on voxels from activated ROI » in the menu, you will get the parametric texture map in the selected ROI.
- if you select on bounding box of activated ROI in the menu, you will get the parametric texture map in a rectangle including the ROI, which might be nicer for display purpose.

The kernel parameter is the size of the box the features are calculated from. If you select 3, in each and every voxel K, the features will be calculated from a 3 x 3 x 3 box centered on that voxel K and the feature parametric map corresponding to a given feature will display that feature value in voxel K. The box is moved by one voxel and the calculation is repeated. This is repeated on all voxels in your VOI to get a parametric map of the feature. Doing that, you can get a parametric map of Entropy, Homogeneity, aso.

When clicking the run button, all parametric maps available will be calculated. Then, on the right hand side of your image display window, you have buttons making it possible to display the parametric map of your choice, on top of the original image.

### 1.8 The image biomarker standardisation initiative (IBSI)

LIFEx participates in the image biomarker standardisation initiative. The primary aim of this initiative is to improve reproducibility of quantitative image analyses. LIFEx has been validated on the digital phantom provided by IBSI in nifti format for direct benchmarking of feature values, without image processing. This phantom has been designed specifically for the purpose of benchmarking software for radiomic feature calculation.

(see www.cancerdata.org/resource/doi:10.17195/candat.2016.08.1)

### 1.8.1 IBSI compliant features

Some of the morphological indices are IBSI compliant. Please refer to the

Find the IBSI id relevant to features of your interest on the figures of the previous section. Then look for that id inside the IBSI reference manual.



Figure 1.8: Texture feature extract - GLCM Map Results

### 1.8.2 IBSI non-compliant features

**compacity** The compacity feature reflects how compact the Volume of Interest is.

$$Compacity = \frac{A^{3/2}}{V} \tag{1.1}$$

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

**Volume** it the volume in mesh of ROI.

**VoxelsCounting** is not IBSI compliant. It is the number of voxels in the ROI.

**ApproximateVolume** is the number of voxels multiplied by the volume of a voxel.

**MaxValueCoordinates** is pretty self explanatory. It indicates the coordinates of the maximum value.

**CenterOfMass (COMCoor)** is the center of mass coordinates of the studied ROI in voxels.

**WeightedCenterOfMass (WCOMCoor)** is the weighted intensity center of mass coordinates of the studied ROI in voxels.

**HOCMax** is the distance in millimeter between the activity Hotspot with maxValue (private feature).

**HOC05mLPeak** is the distance in millimeter between the activity Hotspot with 0.5 mL peakValue (private feature).

**HOC1mLPeak** is the distance in millimeter between the activity Hotspot with 1 mL peakValue (private feature) [BOELLAARD 2015].

**NormalizedHOCradiusROI** is the distance in millimeter between the normalized ROI maximum radius of the activity hotspot with maxValue (private feature).

**NormalizedHOCradiusSphere** is the distance in millimeter between the normalized sphere radius of the activity hotspot with maxValue (private feature).

**NormalizedCenterOfMassShiftMaxRadiusROI** is the distance in millimeter between the normalized ROI maximum radius activity with weighted center of mass (private feature).

**NormalizedCenterOfMassShiftRadiusSphere** is the distance in millimeter between the normalized sphere radius of the activity hotspot with weighted center of mass (private feature).

**MaxValuePerimeter2DDistance** is the closest 2D distance between maxValue voxel to the segmented tumor border (private feature).

**MaxValuePerimeter3DDistance** is the closest 3D distance between maxValue voxel to the segmented tumor border (private feature).

**Peak05mLPerimeter2DDistance** is the closest 2D distance between Peak0.5mL voxel to the segmented tumor border (private feature).

**Peak05mLPerimeter3DDistance** is the closest 3D distance between Peak0.5mL voxel to the segmented tumor border (private feature).

**Peak1mLPerimeter2DDistance** is the closest 2D distance between Peak1mL voxel to the segmented tumor border (private feature).

**Peak1mLPerimeter3DDistance** is the closest 3D distance between Peak1mL voxel to the segmented tumor border (private feature).

**MaxValueNormalizedWithRadiusSpherePerimeter2DDistance** is the closest 2D distance between maxValue voxel to the segmented tumor border divided by the mean spherical radius (private feature).

**MaxValueNormalizedWithRadiusSpherePerimeter3DDistance** is the closest 3D distance between maxValue voxel to the segmented tumor border divided by the mean spherical radius (private feature).

**Peak05mLNormalizedWithRadiusSpherePerimeter2DDistance** is the closest 2D distance between Peak0.5mL voxel to the segmented tumor border divided by the mean spherical radius (private feature).

**Peak05mLNormalizedWithRadiusSpherePerimeter3DDistance** is the closest 3D distance between Peak0.5mL voxel to the segmented tumor border divided by the mean spherical radius (private feature).

**Peak1mLNormalizedWithRadiusSpherePerimeter2DDistance** is the closest 2D distance between Peak1mL voxel to the segmented tumor border divided by the mean spherical radius (private feature).

**Peak1mLNormalizedWithRadiusSpherePerimeter3DDistance** is the closest 3D distance between Peak1mL voxel to the segmented tumor border divided by the mean spherical radius (private feature).

**MaxValueNormalizedWithRadiusRoiPerimeter2DDistance** is the closest 2D distance between maxValue voxel to the segmented tumor border divided by the mean roi radius (private feature).

**MaxValueNormalizedWithRadiusRoiPerimeter3DDistance** is the closest 3D distance between maxValue voxel to the segmented tumor border divided by the mean roi radius (private feature).

**Peak05mLNormalizedWithRadiusRoiPerimeter2DDistance** is the closest 2D distance between Peak0.5mL voxel to the segmented tumor border divided by the mean roi radius (private feature).

**Peak05mLNormalizedWithRadiusRoiPerimeter3DDistance** is the closest 3D distance between Peak0.5mL voxel to the segmented tumor border divided by the mean roi radius (private feature).

**Peak1mLNormalizedWithRadiusRoiPerimeter2DDistance** is the closest 2D distance between Peak1mL voxel to the segmented tumor border divided by the mean roi radius (private feature).

**Peak1mLNormalizedWithRadiusRoiPerimeter3DDistance** is the closest 3D distance between Peak1mL voxel to the segmented tumor border divided by the mean roi radius (private feature).

**SphereDiameter** is the diameter of sphere equal to equivalent volume (in mm) (private feature).

**Standard Deviation** is the standard deviation of all voxels intensity.

IntensityPeakDiscretizedVolumeSought(0.5mL) See its equivalent of 1mL.

**GlobalIntensityPeak(0.5mL)** See its counterpart of 1mL.

**IntensityPeakDiscretizedVolumeSought(1mL)** is the peak intensity of volume 1mL, based on discretized values.

**GlobalIntensityPeak(1mL)** corresponds to IBSI\_0F91.

**LocalIntensityPeak** corresponds to IBSI\_VJGA.

### 1.9 Texture Script

**Related guide:** Scripting procedure for calculation without user interaction is available on LIFEx.

A special user guide is available under the name LIFEx-Script. You can consult it on the website in the documentation section. The texture protocol is fully automatic with scripts.

Part II

Texture Features -First order features

# Chapter 1 Intensity\_based Indices

**Context** The values (*Value*) relating to this part are extracted from the native values of the images.

### **1.1** *P*25, *P*75

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.

**Intensity\_based\_P25.** P25 corresponds more or less to the first quantile (Q1). It 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 percentile 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).

### 1.2 Calcium Agatston Score

**Intensity\_based\_P75.** The 75th percentile corresponds to the third quartile (Q3). It is the middle value between the median and the highest value of the data set. It is also known as the upper quartile and 75% of the data lies below this point.

**Intensity\_based\_TLG** is the Total Lesion Glycolysis defined as the product of *SUV mean* by *Volume* in mL [LARSON 1999]. It has no IBSI equivalent.

$$Intensity\_based\_Mean = V \cdot \frac{1}{N} \sum_{i} SUV_{i}$$
 (1.1)

Intensity based

### **1.2** Calcium Agatston Score

**CalciumAgatstonScore** reflects the *AgatstonScore* of the ROI. This feature is only available on CT images: see UserGuide of LIFEx "Calcium Quantitation - Agatston Score" for more information. It has no IBSI equivalent.

### **1.3** *Intensity\_based\_TLG(mL)*

is the Total Lesion Glycolysis defined as the product of *SUV mean* by *Volume* in mL. [LARSON 1999]

$$Intensity\_based\_Mean = V \cdot \frac{1}{N} \sum_{i} SUV_{i}$$
 (1.2)

### **1.4** Intensity — based\_RIM

is the Radial Intensity Mean "Intensity\_based\_RIM\_mean" of successive layers of voxels (envelope) from the outside of 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.

Other statistics are extracted from these envelopes, in particular:

- Intensity\_based\_RIM<sub>min</sub>: minimum value of voxel values from the envelopes
- *Intensity\_based\_RIM*<sub>mean</sub>: mean value of voxel values from the envelopes
- *Intensity\_based\_RIM*<sub>stdev</sub>: standard deviation value of voxel values from the envelopes
- *Intensity\_based\_RIM*<sub>max</sub>: maximum value of voxel values from the envelopes
- *Intensity\_based\_RIM*<sub>volume</sub>(*mL*): volume in milliliter unit of all voxels from the envelopes
- Intensity\_based\_RIM<sub>volume</sub>(vx): volume in voxel unit of all voxels from the envelopes
- Intensity\_based\_RIM<sub>sum</sub>: sum of voxel values from the envelopes

Example of results for 6 envelopes:

 $Intensity\_based\_RIM_{mean} = 1.2684131|1.2192162|1.2974288|1.3191646|1.271777|1.226076|$ 

The first value 1.2684131 is  $SUV_{mean}$  (if SUV is unit of voxel value), of the 1-voxel thick envelope of the ROI, 1.2192162 the mean of the envelope after an erosion of 1 voxel, ..., 1.226076 the mean of the smallest envelope (center of ROI).

All other features exist and are defined on the Image biomarker standardisation initiative (IBSI) document attached in the LIFEx package. Feel free to take the reference IDs of the features in order to make faster searches in this document.

Intensity based

# Chapter 2

# Intensity\_histogram calculation

To build a histogram *HISTO*, it is necessary to determine a bin width ("bin" parameter). The indices derived from the histogram will depend on this bin width parameter.

This dependence, similar to that found in texture index calculations, is often overlooked in publications.

In LIFEx, with the absolute model the histogram is built a number of bins equal to that entered by the user in the "number of grey level" and "size of bin" (or bin width or bw, see eq.2.1) fields of the resampling menu.

$$bw = \frac{max - min}{nbGreyLevel} \tag{2.1}$$

where *max* is maximum of intensity (in ROI), *min* is minimum of intensity (in ROI) and *nbGreyLevel* is the number of grey level.

In LIFEx, with the relative model the histogram is built only with "number of grey level" fields of the resampling menu that entered by the user and min and max are extracted values of each ROI.

### 2.1 Intensity\_histogram\_AUC\_CSH

reflects the cumulative intensity of histograms (p(i)) produce by a per cent volume of a ROI (derived from ROI semi-automatic ROI delineation methods) with an intensity above a certain threshold is plotted against that threshold value (j), which is varied from 1 to number of grey [Van Velden 2011].

Intensity histogram The area under of this new histogram (*Intensity\_histogram\_AUC\_CSH* feature) is a quantitative index of tracer uptake heterogeneity and/or heterogeneous response where lower values correspond with increased heterogeneity. In this case *Intensity\_histogram\_AUC\_CSH* is independent of value max (here, number of grey).

$$Intensity\_histogram\_AUC\_CSH = \sum_{j} \sum_{i \ge j} p(i) * bw$$
 (2.2)

where p(i) is the probability of occurrence of voxels with intensity i, j is the number of grey and bw the width of one bin (see eq.2.1).

All other features exist and are defined on the Image biomarker standardisation initiative (IBSI) document attached in the LIFEx package. Feel free to take the reference IDs of the features in order to make faster searches in this document.

**Context** The values (*Value*) relating to this part are extracted from the discretized values of the images.

### **2.2** Intensity\_histogram\_Q1, \_Q3

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.

Intensity\_histogram\_Q1: 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).

*Intensity\_histogram\_Q3*: 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

### **2.3** Intensity\_histogram\_CalciumAgatstonScore

reflects the *Intensity\_histogram\_CalciumAgatstonScore* of the ROI. This feature is only available on CT images: see UserGuide of LIFEx "Calcium Quantitation - Agatston Score" for more information.

### **2.4** *Intensity\_histogram\_TLG(mL)*

is the Total Lesion Glycolysis defined as the product of *SUV mean* by *Volume* in mL. [LARSON 1999]

$$Intensity\_histogram\_Mean = V \cdot \frac{1}{N} \sum_{i} SUV_{i}$$
 (2.3)

### **2.5** *Intensity\_histogram\_RIM*

is the Radial Intensity Mean "*Intensity\_histogram\_RIM\_mean*" of successive layers of voxels (envelope) from the outside of 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.

Other statistics are extracted from these envelopes, in particular:

- *Intensity\_histogram\_RIM*<sub>min</sub>: minimum value of voxel values from the envelopes
- *Intensity\_histogram\_RIM*<sub>stdev</sub>: standard deviation value of voxel values from the envelopes
- *Intensity\_histogram\_RIM*<sub>max</sub>: maximum value of voxel values from the envelopes
- *Intensity\_histogram\_RIM*<sub>volume</sub>(*mL*): volume in milliliter unit of all voxels from the envelopes
- $Intensity\_histogram\_RIM_{volume}(vx)$ : volume in voxel unit of all voxels from the envelopes
- *Intensity\_histogram\_RIM*<sub>sum</sub>: sum of voxel values from the envelopes

Example of results for 6 envelopes:  $Intensity\_histogram\_RIM_{mean} = 1.3|1.2|1.3|1.3|1.2|1.1|$ 

The first value 1.3 is  $SUV_{mean}$  (if SUV is unit of voxel value), of the 1-voxel thick envelope of the ROI, 1.2 the mean of the envelope after an erosion of 1 voxel, ..., 1.1 the mean of the smallest envelope (center of ROI).

All other features exist and are defined on the Image biomarker standardisation initiative (IBSI) document attached in the LIFEx package. Feel free to take the reference IDs of the features in order to make faster searches in this document.

Intensity histogram

**Part III** 

Texture Features -Second Order features

# Chapter 1 GLCM

### 1.1 GLCM definition

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  $\delta$ -voxel distance ( $\|\vec{d}\|$ ) 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:

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

$$(1.1)$$

where I(p,q) corresponds to voxel (p,q) in an image (I) of size N\*M. The vector

### 1.1 GLCM definition

 $\overrightarrow{d} = (\Delta x, \Delta y)$  covers the 4 directions (D1, D2, D3, D4, Figure 1.1) in 2D space or 13 directions (D1, D2, ..., D13, Figure 1.2) in 3D space and  $Pairs_{ROI}$  corresponds to the number of all voxel pairs belonging to the region of interest (ROI).

**Cost-effective creation of a transposed matrix.** To reduce runtime calculation of GLCM matrix involving 26 directions in 3D (8 directions in 2D) the transposed matrix accounting for 13 directions calculated in 3D (and 4 in 2D) is added to the original matrix.

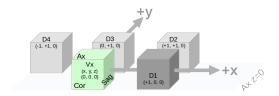


Figure 1.1: 2D Voxel (green) and associated 4 directions

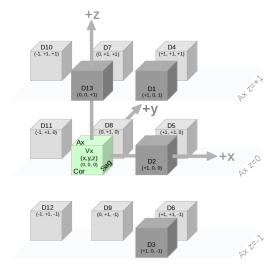


Figure 1.2: 3D Voxel (green) and associated 13 directions

The GLCM describes the distribution of co-occurring pixel values at a given offset. This offset ( $\delta$ ) set to 1 by default, meaning that only neighbour voxels are used to calculate GLCM. It is possible to change this default value from 1 to 10 in the "Distance with neighbours" box, which is in the "Settings" dialog box, GLCM subpart.

If you specify a distance of 5 voxels the matrix will be built not with the nearest neighbor (dist = 1) but with the neighbor with 5 voxels of distance and without taking into account the intermediate voxels of distance 2, 3, 4.

Be careful: if the distance is too large for small ROIs, some entries of the GLCM matrix will not have any meaning. This is detected and the corresponding results in the output csv file are noted NaN! or Num!

**GLCM** 

### **1.2** GLCM features

**IBSI compliance** In the following figure is a list of features available in the GLCM panel. They are followed by their IBSI id whenever the IBSI mentions them. Please look for the IBSI reference manual, 2018 for further details on the features. A quick search on that IBSI id will get you to the feature of your interest.

**GLCM** 

## Chapter 2 NGLDM

#### 2.1 NGLDM definition

The neighborhood grey-level difference matrix (NGLDM) [Amadasum1989] corresponds to the difference of grey-levels 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:

$$NGLDM(i,2) = \sum_{p} \sum_{q} \left\{ \begin{array}{l} |\overline{M}(p,q) - i| \text{ if } I(p,q) = i \\ 0 \text{ else} \end{array} \right.$$
 (2.1)

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

All other features exist and are defined on the Image biomarker standardisation initiative (IBSI) document attached in the LIFEx package. Feel free to take the reference IDs of the features in order to make faster searches in this document.

#### 2.2 Notes on NGLDM\_Contrast

**Divergence with pyRadiomic.** We must highlight that comparisons of results with other software supporting texture analysis should be performed with great care. The calculation of the texture indices resulting from the matrix NGLDM can differ between software. For instance, after the calculation of the matrix NGLDM, in LIFEx, the Contrast formula includes the number of voxels *E* in the region in the denominator as in Amadasum & King (link) formula (see below), while this number of voxels is squared in pyRadiomics, explaining the differences in resulting values.

NGLDM

$$NGLDM\_Contrast = \left[ \sum_{i} \sum_{j} NGLDM(i,1) \cdot NGLDM(j,1) \cdot (i-j)^{2} \right] \cdot \frac{\sum_{i} NGLDM(i,2)}{E \cdot G \cdot (G-1)}$$
 (2.2)

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

# Chapter 3 GLRLM

#### 3.1 GLRLM definition

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 in 2D) 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.

**Divergence with pyRadiomics.** We must highlight that comparisons of results with other software supporting texture analysis should be performed with great care. The calculation of the texture indices resulting from the matrix GLRLM can differ between software. For instance, in pyRadiomics (v1.1.1), after the calculation of the matrix GLRLM and before the extraction of the textural indices, the matrix is cropped (grey-level axis of GLRLMs cropped between minimum and maximum grey-levels and run-length axis of GLRLMs cropped to maximum run-length). This moves indexes (i,j) of the matrix and thus the values of the resulting textural indices.

In LIFEx, we do not shift the index so that it corresponds to grey level i, and j corresponds to the number of run j and we use the formulations defined below.

All other features exist and are defined on the Image biomarker standardisation initiative (IBSI) document attached in the LIFEx package. Feel free to take the reference IDs of the features in order to make faster searches in this document.

**GLRLM** 

# Chapter 4 GLZLM

### 4.1 GLZLM definition

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.

All other features exist and are defined on the Image biomarker standardisation initiative (IBSI) document attached in the LIFEx package. Feel free to take the reference IDs of the features in order to make faster searches in this document.

Part IV References

# Chapter 1 Useful references

### 1.1 Bibliography

Journal papers involving the use of LIFEx are listed in https://www.lifexsoft.org/index.php/resources/publications-journal-papers

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#### **1.1.6** 2012

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#### **1.1.7** 2011

Floris H. P. van Velden, Patsuree Cheebsumon, Maqsood Yaqub, Egbert F. Smit, Otto S. Hoekstra, Adriaan A. Lammertsma, Ronald Boellaard. Evaluation of a cumulative SUV-volume histogram method for parameterizing heterogeneous intratumoural FDG uptake in non-small cell lung cancer PET studies Eur J Nucl Med Mol Imaging (2011) 38:1636?1647. DOI 10.1007/s00259-011-1845-6 (link)

#### 1.1.8 2009

Thibault G, Fertil B, Navarro C, et al. Texture indexes and gray level size zone matrix. application to cell nuclei classification. Pattern Recognition Inf Process. 2009;140:145 (link)

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Wahl R, Jacene H, Kasamon Y and Lodge MA. From RECIST to PERCIST:evolving considerations for PET response criteria in solid tumors. J Nucl Med. 2009;50:122S-50S. (link)

#### 1.1.9 2004

Xu D-H, Kurani AS, Furst JD, Raicu DS. Run-length encoding for volumetric texture. Paper presented at: The 4th IASTED International Conference on Visualization, Imaging and Image Processing: VIP; September 6-8, 2004; Marbella, Spain (link)

#### **1.1.10** 1999

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