Metabolic Tumor Volume (MTV) — User Guide

Local Image Features Extraction
— LIFEx —

C. Nioche, A.S. Cottereau, I. Buvat

Part I
Protocol description

Chapter 1

How to perform MTV analysis?
– step by step –

MTV analysis

1.1 Introduction

The Metabolic Tumor Volume (MTV) protocol computes semi-automatically the MTV. User must thus choose thresholds to define tumor bounds. MTV is then processed by the protocol. Additionally, user may refine the process both automatically and manually. The former requires threshold adjustments and ends by running the protocol again, the latter entails modifications of the Volume of Interest (VOI), once they are generated by the protocol.

Many values describing the MTV are given following the protocol processing. Among them, user may find a two-value summary in the MTV head menu, highlighting the total MTV, D_{max} and D_{maxVox}. All MTV-related values can be saved in a *.csv* file for further analyses.

1.2 Current knowledge

MTV protocol returns two key values: the MTV and D_{max}. D_{max} has been discussed by Cottereau *et al.* (2020).

In this paper, D_{max} is said to represent the tumor burden dissemination. The team concludes D_{max} further improves patient risk stratification in different stages when combine with other parameters such as MTV.

Please note that proof of concept was established on diffuse large B-cell lymphoma patients with the help of the LIFEx MTV protocol.

1.3 Prerequisite

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

Image series

- MTV analysis is currently supported for PET and NM;

- If needed, CT images may be loaded **after** loading PET images.

1.4 Step by step

This section describes the 3 steps needed to get an estimation of the metabolic tumor volume.

1. **Step 1: Construction of the greyscale fill tree.**

    th0: Starting threshold value: 2.4 in absolute SUV
    step : SUVmaxValue / 20. if step less than 1 then step is setting to 1.

The volume is thresholded with a value th0. Only values greater than this threshold are kept and form a binary mask. This binary mask is then labelled with a labeling algorithm to label connected components (kernel of neighbors search in 3D and 2D). In each label mask, a thresholding is performed again with an additional grey level step

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double absoluteStepThresholdValue = maxValue / 20d; // SUV if (absoluteStepThresholdValue < 1) absoluteStepThresholdValue = 1;

2. **Step 2: Threshold refinement.**

3. **Step 4: Computation.** The last insert of the MTV protocol panel corresponds to saving and running the process.

   Please note that the liver ROI will disappear once you start running the protocol. Remember to save the ROI if needed.

   Running the protocol. Each time, the user changes the filter options, the protocol must be processed in its entirety. Click on the Run icon in order to do so. Please note that the MTV protocol erases any existing ROI before its processing starts.

4. **Saving the results.** Once the results are satisfying enough, a click on the *Save Results* icon sends the results in a *.csv* file. A pop-up window shows where the results have been sent to.

   Results quick overview. Once the protocol has run, a quick overview is displayed at the end of the panel. Five values are given.

   - **TLG** is the Total Lesion Glycolysis. Its unit is SUV*mL;

   - **sTLG**, the Standardized Total Lesion Glycolysis, corresponds to $TLG/PatientWeight$. It is measured in SUV*mL/kg;

   - **MTV** is the protocol main value, the total Metabolic Tumor Volume. Its unit is mL (or cm^3);

   - **sMTV** is Standardized Metabolic Tumor Volume. More specifically, it is measured as $MTV/PatientWeight$ and is in mL/kg;

   - $\mathbf{D_{max}}$ is the distance between the two lesions that are the furthest apart (with ROIs center of mass as origin). It is one way to measure tumor dissemination;

   - $\mathbf{wD_{max}}$ is the distance between the two lesions that are the furthest apart calculated from a weigthed center of mass;

   - $\mathbf{D_{maxVox}}$ is the distance between the two lesions that are the furthest apart (with the outermost voxel).

   D_{maxVox} and the total MTV are featured in the MTV protocol head menu.

   Please note that all values are updated in real-time whenever changes are brought upon the ROI by the user.

MTV analysis

ROI statistics. Each ROI statistics are displayed in their bar menu. Their respective MTV and TLG are showcased in the bar under their name. Further statistics are displayed when dropping-down their own menu: click on the plain dark grey arrow on the left of a ROI menu, then select the appropriate series.

The **size** corresponds to the MTV in cm^3. User may also find the ROI center of mass coordinates and those of its weighted counterpart.

Part II
Graphic User Interface / Script

Chapter 1
GUI

1.1 Graphic User Interface (tunable method)

This section describes how to get MTV estimates and how to navigate through the MTV panel and features.

The user interface (see figure 1.1 p.14) includes 4 sub-parts:

1. **Init thresholds**. Step 1 is the sole mandatory step within the MTV protocol;

2. **Setting thresholds**. Step 2 consists in a two sub-step process. Firstly, user chooses segmentation methods and secondly, they define the minimum requirements to merge the segmentation results;

3. **Volume Refinement**. Step 3 is a final pruning to further refine the ROIs of the MTV.

4. **Run / Results**. This conclusive insert groups up the protocol controller and some statistics.

GUI

Figure 1.1: Display of the MTV protocol GUI

Default settings. At any point in time, the user may decide to stick with the default settings. The software keep in memory the last values imparted. As such, enabling and disabling the options will not reset their values. Click on the dedicated icon (see figure 1.2) to set back default parameters.

Figure 1.2: Default Setting Icon

Step 1. Step 1 of the MTV protocol is shown in figure 1.3 where the defaults parameters are showcased. To modify the values, user may click on the icon of either the **Absolute SUV threshold** or **Pruning volume** options. Pop-up windows will then guide the user to input new range values.
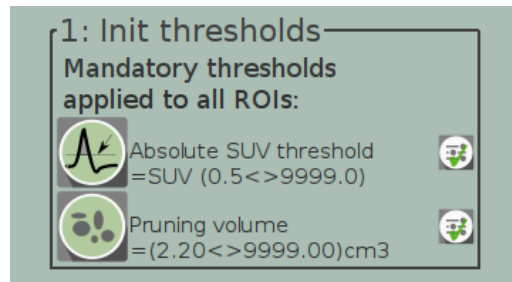
Figure 1.3: MTV protocol Step 1 Menu - Initialization thresholds

The absolute SUV range panel (see figure 1.4) lets the user choose the minimum and maximum values. If not known, the maximum value should be left at 9999SUV.
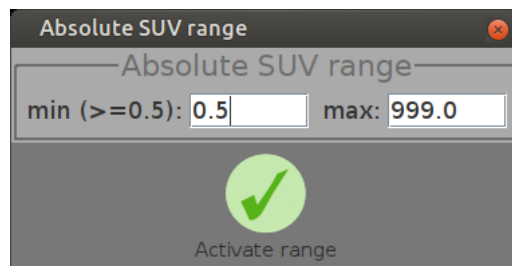
Figure 1.4: MTV protocol Step 1 - Absolute SUV Range

The pruning pop-up window (see figure 1.5 p.16) is identical to the aforementioned panel, except for its units which are cm^3.

Step 2. User may enable up to five segmentation methods by specifying a threshold. Once the choice is made, user must choose the degree of cooperation (N) between methods. As the user specifies options, the icons dedicated to the cooperative approach will

1.1 GUI-tunable method
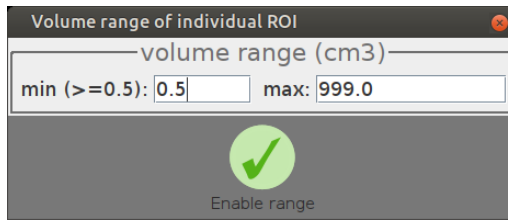
Figure 1.5: MTV protocol Step 1 - Pruning volume

where three methods have been selected.
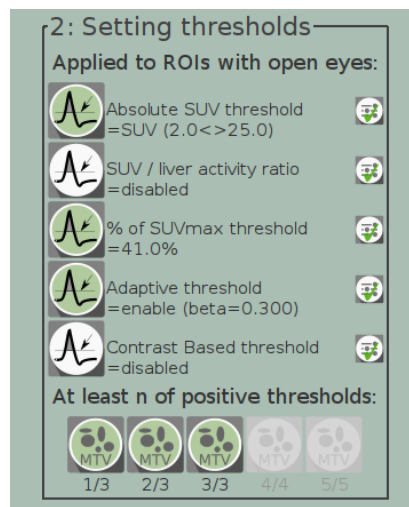
Figure 1.6: MTV protocol Step 2 Menu - Setting thresholds

The software first computes the segmentation on the ROI (generated in Step 1) method by method. Afterwards, the degree of cooperation is used to process each voxel. If the voxel is characterized as tumor in at least N segmentation methods, the voxel is retained; if not, the voxel is dismissed from its ROI.

Pop-up windows help the user navigates through the segmentation methods. First on the list is a second absolute SUV threshold (see figure 1.7). Please note that ROI volume is only affected if the given range is more restrictive than the one specified earlier on Step 1.

The second segmentation method suggested is based on a ROI the user defines. It must correspond to the liver and be named as thus. The software then acknowledges the existence of the liver ROI. User can choose to base the segmentation method either on the SUV_{mean} or SUV_{max} of the liver area. As shown on the figure 1.8, user may click twice on one of the hand icon for the software to process the value automatically.

If either is known, user may input directly the liver SUV_{mean} or SUV_{max}. In this particular case, there is no need to set up the ROI named liver.
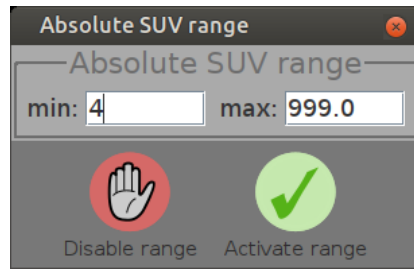
Figure 1.7: MTV protocol Step 2 - Absolute SUV range

By default a comparison coefficient of 1.5 is implemented. User can modify its value in the panel last input tag. With this segmentation method, ROI voxels with SUV 1.5 superior to either the SUV_{mean} or SUV_{max} of the liver will be retained.

In figure 1.8, it is the SUV_{max} that is used as a baseline. The comparison coefficient has been changed to 2.
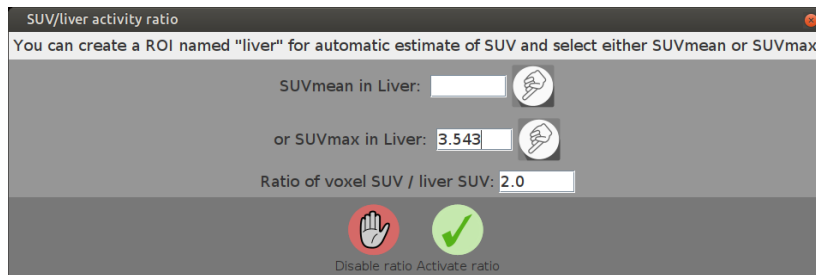
Figure 1.8: MTV protocol Step 2 - Segmentation based on the liver

The third segmentation method also needs the user to input a threshold. As seen in figure 1.9, by default, the voxel SUV threshold is 41% of the SUV_{max}. As ROI are treated individually, the SUV_{max} varies depending on the ROI under scrutinization. Hence the relativity of this threshold.
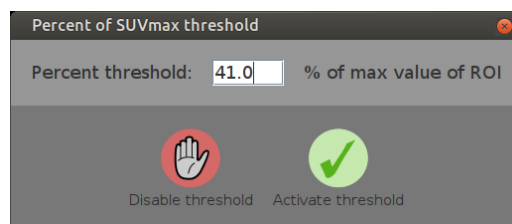
Figure 1.9: MTV protocol Step 2 - SUVmax segmentation

As for the Nestle segmentation, the pop-up window requires a single value: the β parameter (see figure 1.10 p.18). This value is specific to the device used for acquisition. If needed, please ask a technologist or a physicist about it for that value is mandatory to compute the Nestle threshold.

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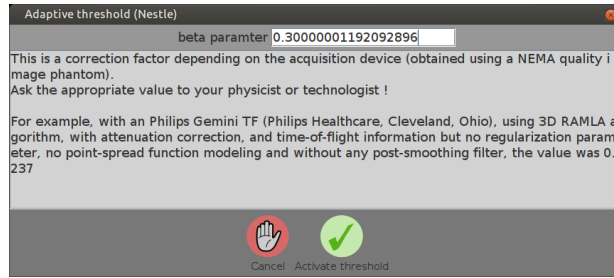
Figure 1.10: MTV protocol Step 2 - Nestle threshold

The last segmentation method is a contrast-based filter. The user can only switch it on or off. As the method is enabled its white icon switch to a green one.

Cooperative Approach. Once the user has chosen the segmentation methods he wants to apply, he needs to settle the cooperative approach stringency. As an example, in figure 1.6 p.16, the stringency level is at its lowest: of the three segmentation methods to be computed, all voxels retained in at least one of them is to be kept in the MTV. Another example is given in figure 1.11, just below. It shows how to heighten the stringency by one level. Thus voxels must be retained in at least two of the three chosen methods.
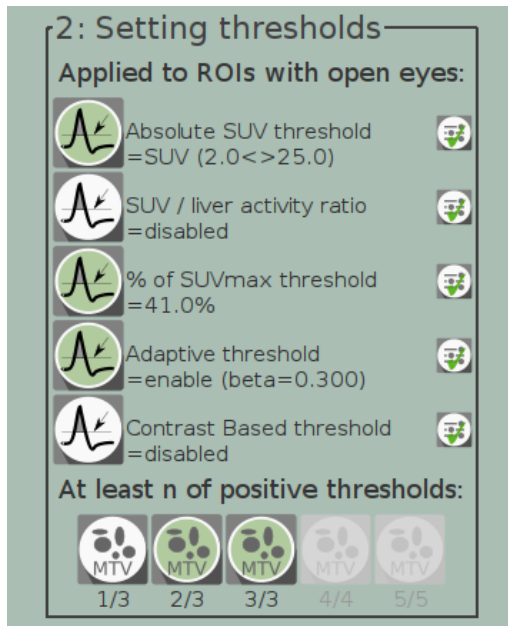
Figure 1.11: MTV protocol Step 2 - An example of cooperative approach

Step 3. Step 3 of the MTV protocol consists in pruning each ROI. More specifically, the voxels retained by the cooperative approach of step 2 are refined. Depending on the range imputed in the pop-up window (see figure 1.12 p.19), pruning may reduce the volume of the ROI compared to the earlier step 1 pruning.
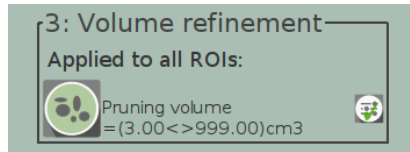
Figure 1.12: MTV protocol Step 3 Menu - Volume Refinement

To specify another range than the default, click on the pruning icon and follow the pop-up window instructions. These are identical to the earlier pruning in Step 1.

GUI

Saving results. In the last panel insert of the MTV protocol, one can both run and save their results. The two icons (**Run** and **Save results**) are displayed in figure 1.13 p.19. Below these is a summary of key values computed by the MTV protocol. They are updated whenever modification is brought upon ROI or when the whole MTV protocol is reprocessed.
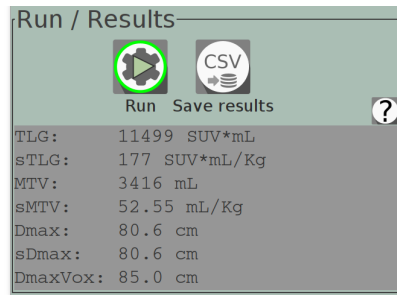
Figure 1.13: MTV protocol Menu Closure - Run / Results

Please note that the saving format and results are further discussed in *Part III Calculation and Results*.

1.2 Graphic User Interface (Automated method)

Segmentation can be fully automated with the "Automated method".

The sequence of steps is described below:

- absolute threshold with 2.7 SUV value;

- clustering with labeling;

- determination of SUVmax for each cluster;

- absolute threshold with (SUVmax * 0.1)

- clustering with labeling;

- ROI creation for each result cluster

- pruning volume with 0.2 mL for each ROI

GUI
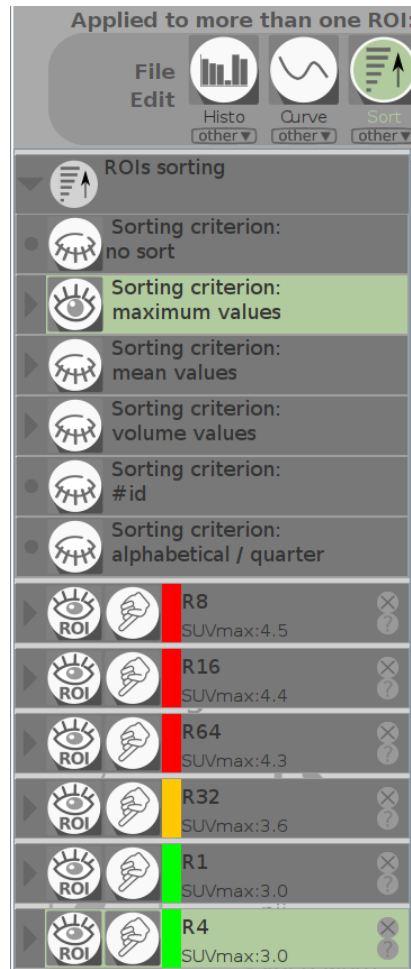
Figure 1.14: MTV protocol Sorting Tools - Panel Details

1.3 Sorting MTV ROI

MTV protocol resulting ROI.   Once the protocol has finished processing, new ROI are displayed in the right side panel. Those ROI compose the MTV.

User may modify the results produced by the protocol. Any change is automatically reflected in the MTV results. For example, one may adjust 3D volume of a ROI by adding or removing some volume. User can dispose of a ROI in case it is wrongly identified as a tumor. Lastly, user may mark lesion on their own by creating new ROI. All those changes are automatically reflected in MTV results accordingly.

ROI visualization.   Sorting tools have been designed to better visualize the prospective tumors. These tools consist in sorting models for ROI. They differ by the parameter they take for scaling: SUV_{max}, SUV_{mean}, ROI volume, ROI identification number (namely #id, *e.g.* R42) and alphabetical order or quarter division.
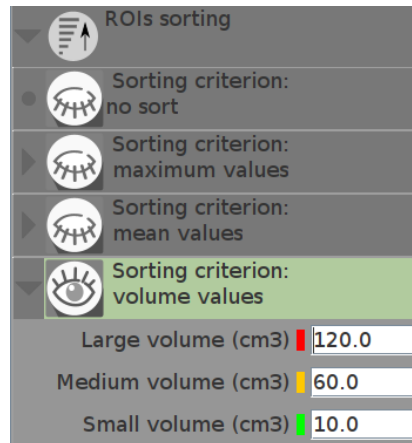
Figure 1.15: MTV protocol Sorting Tools - Scaling options

GUI

To sort ROI, look for the *Sort* icon in the right panel, in the *File Edit* menu, **applied to more than one ROI**. The option *Sort* may already been displayed in one of the three showcased icons (see figure 1.14 p.20, where the *Sort* icon is already highlighted in green for it is activated).

Each ROI are then reorganised in the specified fashion. In figure 1.14, ROI are sorted by maximal SUV. Any scaling may be modified. As it is shown in the detailed figure 1.15 p.21, one may change any of the lower bound. On that same figure, ROI coloring is as follow:

- green if the ROI SUV_{max} is between 10 and 60

- orange if the ROI SUV_{max} is between 60 and 120

- red if the ROI SUV_{max} is greater than 120

There is a particular *Sort* filter that is not based on a scale. It is the *Quarter* sorting method (see Quarter icon in figure 1.16). It divides the patient body in four regions: top and bottom, either left or right. Each region is differently colored. Axes are shown on the coronal image viewer. User may move the origin of the axes and modify the orientation of the axes to fit the patient position.

Figure 1.16: MTV protocol Sorting Tools - Quarter Icon
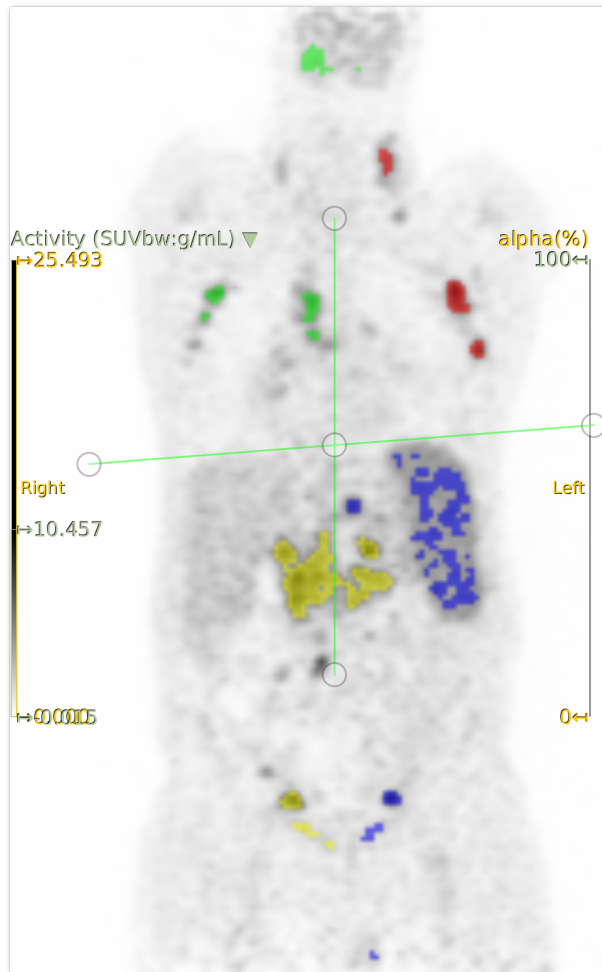
Figure 1.17: MTV protocol Sorting Tools - Quarter Sorting Tools

Chapter 2
Script

2.1 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 MTV protocol is fully automatic with scripts.

Part III
Calculation, Results

Chapter 1
Calculation and Results

1.1 Calculation

This section deals with all segmentation methods and filters. It explains calculation and computation strategies.

Absolute SUV range.   This segmentation method uses voxel SUV as its baseline unit. Here, voxels are filtered in a binary manner: outside the range they are dismissed, they are retained otherwise (see formula (1.1)).

$$SUV_{min} \leq SUV_{voxel} \leq SUV_{max} \tag{1.1}$$

If next to each other, a unique ROI is created. When discontinuous, different ROI are generated.

Pruning volume.   Pruning affects the global volume of the MTV. If the ROI volume is outside the specified volume range, the ROI is dismissed.

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1.1 Calculation

$$Volume_{min} \leq Volume_{ROI} \leq Volume_{max} \qquad (1.2)$$

Whenever formula (1.2) is true, ROIs are passed onto the following processing step.

Liver-based segmentation. This threshold is based on liver statistics. Two computation methods may be implemented: either with the liver SUV_{max} or the liver SUV_{mean}. Depending on the type of SUV chosen, a ratio is build. By default, the MTV protocol will use a comparison coefficient (C) of 1.5.

$$\frac{SUV_{voxel}}{SUV_{liver}} \geq C \qquad (1.3)$$

Whenever formula (1.3) is true, voxels are kept within the MTV of the liver-based segmentation.

SUVmax segmentation. This segmentation method is relative to the ROI it is working on. The software identifies the ROI SUV_{max}. Hence the maximal value is varying throughout the segmentation process. Once the SUV_{max} is found, the percentage value (P) imparted by the user is made use of. Thus this method filters voxels based on their SUV and the SUV_{max}.

$$\frac{SUV_{voxel}}{SUV_{max}} \geq P\% \qquad (1.4)$$

By default P is set to 41%. Whenever formula (1.4) is true, voxels pass the SUVmax segmentation.

Nestle Threshold. The Nestle threshold (or adaptive method) has been implemented as mentioned in the paper by Nestle *et al.* (2005). It requires a β parameter, namely a correction factor, specific to the device used.

The threshold is computed by the method as described:

$$threshold_{Nestle} = (\beta * SUV_{mean70}) + SUV_{Background} \qquad (1.5)$$

Here, in formula (1.5), two values are computed to shape the Nestle threshold.

1. **SUV$_{mean70}$** is obtained by identifying the ROI SUV_{max}. Once known, all the lesion voxels of SUV greater or equal to 70% the newly found SUV_{max} are added up. Their average SUV forms the SUV_{mean70}.

2. **SUV$_{Background}$** is defined as an average of voxel SUV. Background voxels are those neighboring the putative tumor.

Putative tumor voxel SUV is then compared to the Nestle threshold. If greater or equal, voxels are retained. They are dismissed otherwise.

Constrat-based segmentation. The contrast-based method is a similar approach to the Nestle threshold. Here the factor is arbitrarily set at 0.5. Moreover, the SUV_{mean70} and $SUV_{Background}$ are first rounded up (see formula (1.6)). The contrast-based method stringency is thus roughly lessened compared to the Nestle threshold.

$$threshold_{CBM} = 0.5 * (SUV_{mean70} + SUV_{Background}) \qquad (1.6)$$

1.2 Results

This section deals with the results both as they are saved in the *.csv* file and as displayed in the different panels.

Key Value Summary. The head menu of the MTV protocol highlights two values. These are the **MTV** and **D$_{\text{maxVox}}$**.

- **MORPHOLOGICAL_MTV** is the Metabolic Tumor Volume computed by the MTV protocol. It is measured in mL (or cm^3), and regroups all ROI.

- **MORPHOLOGICAL_D$_{\text{maxVox}}$** corresponds to the distance between the two lesions that are the furthest apart (with the outermost voxel).

In-panel overview. By the end of the MTV protocol drop-down menu is a sum-up of different statistics. User can find several results computed by the MTV protocol.

- **MORPHOLOGICAL_COM**: Center of Mass of ROI with:

    - COM_x: the center of mass in x axis;
    - COM_y: the center of mass in y axis;
    - COM_z: the center of mass in z axis;
    - *vx_count*: the number of voxels included in the ROI;
    - $vx\_coor_x(k)$: the x coordinate of voxel k;
    - $vx\_coor_y(k)$: the y coordinate of voxel k;
    - $vx\_coor_z(k)$: the z coordinate of voxel k.

<div style="float:right">**Calculation and Results**</div>

$$COM_x = \frac{1}{vx\_count} \sum_{k=1}^{vx\_count} vx\_coor_x(k) \tag{1.7}$$

$$COM_y = \frac{1}{vx\_count} \sum_{k=1}^{vx\_count} vx\_coor_y(k) \tag{1.8}$$

$$COM_z = \frac{1}{vx\_count} \sum_{k=1}^{vx\_count} vx\_coor_z(k) \tag{1.9}$$

- **MORPHOLOGICAL_WCOM**: weigthed Center of Mass of ROI with:

    - $wCOM_x$: the center of mass in x axis;
    - $wCOM_y$: the center of mass in y axis;
    - $wCOM_z$: the center of mass in z axis;
    - *vx_count*: the number of voxels included in the ROI;
    - $vx\_coor_x(k)$: the x coordinate of voxel k;
    - $vx\_coor_y(k)$: the y coordinate of voxel k;
    - $vx\_coor_z(k)$: the z coordinate of voxel k;
    - *sum_vx_value*: the sum of all *vx_value* in the ROI;

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$$wCOM_x = \frac{1}{sum\_vx\_value} \sum_{k=1}^{vx\_count} vx\_coor_x(k) * vx\_value(k) \qquad (1.10)$$

$$wCOM_y = \frac{1}{sum\_vx\_value} \sum_{k=1}^{vx\_count} vx\_coor_y(k) * vx\_value(k) \qquad (1.11)$$

$$wCOM_z = \frac{1}{sum\_vx\_value} \sum_{k=1}^{vx\_count} vx\_coor_z(k) * vx\_value(k) \qquad (1.12)$$

- **MORPHOLOGICAL_D$_{max}$** corresponds to the distance between the center of mass of the two most distant tumors. As introduced by Cottereau *et al.* (2020), it is one way to represent the tumor dissemination and refine tumor staging. It's defined as the distance (in cm) between the two lesions (or ROI) the furthest apart. It uses the ROI center of mass as a baseline.

- **MORPHOLOGICAL_WD$_{max}$** is defined as the distance (in cm) between the furthest apart ROI. It uses the ROI *weigthed* center of mass (*wCOM*) as a baseline.

- **MORPHOLOGICAL_MTV** is the Metabolic Tumor Volume (of a ROI).

- **MORPHOLOGICAL_TMTV** or Total Metabolic Tumor Volume (in mL) is defined as:

$$TMTV = \sum_{k=1}^{nROI} MTV_{ROI_k} \qquad (1.13)$$

Beware for it is sometimes referred to as **MTV** in lieu of **TMTV**.

- **MORPHOLOGICAL_STMTV** or Standardized Total Metabolic Tumor Volume (in mL/kg) is defined as:

$$STMTV = \frac{TMTV}{PatientWeight} \qquad (1.14)$$

- **MORPHOLOGICAL_TLG** or Total Lesion Glycolysis (in SUV*mL) is defined as:

$$TLG = MTV * \sum_{k=1}^{nROI} SUV_{ROI_k mean} \qquad (1.15)$$

- **MORPHOLOGICAL_STLG** or Standardized Total Lesion Glycolysis (in SUV*mL/kg) is defined as:

$$STLG = \frac{TLG}{PatientWeight} \qquad (1.16)$$

- **MORPHOLOGICAL_SUMmeanWB** or SUVmean of whole body (in SUV) is defined as:

$$SUVmean_{wb} = \frac{TLG}{TMTV} \qquad (1.17)$$

ROI specific statistics. In the right control panel, user can find the ROI-related tools. All ROI have their own statistical summary. User may view the statistics by dropping down the menu and choose the appropriate series. The drop-down command is shown as a dark gray arrow on the left of each ROI bar menu.

Calculation and Results

Within the summary, user can find standard statistics such as minimum, maximum, mean and sum of the ROI voxels in the currently displayed unit, although usually SUV. There are others statistics such as the number of voxel (nbVx), the coordinates of the maximal value (coorMax), the position of the center of mass (COM) and its weighted counterpart (wCOM). Lastly, user may find the distance between the two centers of mass (distCOM).

Results file. The result file saves the results on user demand. It consists in various metadata and statistics. After the header, each line describes a ROI computed by the MTV protocol.

» Firstly, metadata about the patient, study and acquisition parameters are marked down. If unknown, data are left blank.

- **INFO_PatientName**. Name of the patient.

- **INFO_PatientWeight**. Weight of the patient (in kg).

- **INFO_PatientID**. Patient identification code. Same as patient's name if anonymized.

- **INFO_SeriesDescription**. May be the year or any other descriptor provided by the image header.

- **INFO_Modality**. Type of image used as a baseline for MTV computation, *e.g.*: PET scan

- **INFO_ZYXspacing**. Voxel spacing from images in Z, Y and X dimensions.

- **INFO_ActualFrameDuration**. Imaging acquisition duration.

» Secondly, characteristics describing the ROI and the MTV are written down.

- **INFO_NumberOfROI**. The total count of ROI composing the MTV and found by the protocol.

- **INFO_NameOfROI**. Name of the ROI described in the line. If untouched, likely to be: R1 ... R42, *etc*.

» Thirdly, is a summary of the ROI center of mass statistics. These distance statistics are measured in centimeters. The columns of measures are paired with another column on their right. In these columns, minimum and maximum are highlighted by the following mentions: **<-min** or **<-max**.

Please note that the *current ROI* corresponds to the ROI described in the line the user is reading in the *.csv* file. Hereafter, the *Center of mass* is abbreviated as **COM**.

- **MORPHOLOGICAL_COM (Center of mass) of ROI**. Current ROI COM coordinates in Z, Y and X dimensions.

- **MORPHOLOGICAL_sumBindCOM**. Sum of 3D distances between the current ROI COM and all other ROIs COM.

- **MORPHOLOGICAL_avBindCOM**. Average of sumBindCOM: $\frac{sumBindCOM}{NumberOfROI}$.

Calculation and Results

- **MORPHOLOGICAL_stdBindCOM**. Standard deviation of 3D distances between the current ROI COM and all the other ROIs COM.

- **MORPHOLOGICAL_minBindCOM**. Minimum of 3D distance between the current ROI COM and all the other ROIs COM.

- **MORPHOLOGICAL_maxBindCOM**. Maximum of 3D distance between the current ROI COM and all the other ROIs COM. Among them is D_{max}.

- **MORPHOLOGICAL_avTotBindCOM**. Mean of 3D distances between ROIs COM. This value is shared by all ROIs. It is computed as seen in the equation below:

$$avTotBindCOM = \sum_{k=1}^{NumberOfRoi} sumBindCOM_k * \frac{1}{n(n-1)/2} \qquad (1.18)$$

» Fourthly, is a summary of the weighted center of mass statistics. The distances described below are measured in centimeters. Minimum and maximum are also highlighted in another column.

Hereafter, the *weighted center of mass* is abbreviated as **wCOM**.

- **MORPHOLOGICAL_WCOM (Weighted Center of mass) of ROI**. Current ROI wCOM coordinates in Z Y and X dimensions.

- **MORPHOLOGICAL_sumBindWeightedCOM**. Sum of 3D distances between the current ROI wCOM and all other ROIs wCOM.

- **MORPHOLOGICAL_avBindWeightedCOM**. Average of sumBindWeightedCOM: $\frac{sumBindWeightedCOM}{NumberOfROI}$.

- **MORPHOLOGICAL_stdBindWeightedCOM**. Standard deviation of the 3D distances between the current ROI wCOM and all other ROIs wCOM.

- **MORPHOLOGICAL_minBindWeightedCOM**. Minimum of 3D distance between the current ROI wCOM and all other ROIs wCOM.

- **MORPHOLOGICAL_maxBindWeightedCOM**. Maximum of 3D distance between the current ROI wCOM and all other ROIs wCOM. Among them is sD_{max}.

- **MORPHOLOGICAL_avTotBindWeightedCOM**. Mean of 3D distances between ROIs wCOM. This value is shared by all ROIs. It is computed as seen in the equation below:

$$avTotBindWeightedCOM = \sum_{k=1}^{NumberOfRoi} sumBindWeightedCOM_k * \frac{1}{n(n-1)/2}$$
$$(1.19)$$

Results long overview.

- **MORPHOLOGICAL_Bulk** The largest lesion

- **MORPHOLOGICAL_TLG** is the Total Lesion Glycolysis. Its unit is SUV*mL;

- **MORPHOLOGICAL_sTLG**, the Standardized Total Lesion Glycolysis, corresponds to $TLG/PatientWeight$. It is measured in SUV*mL/kg;

- **MORPHOLOGICAL_MTV** is the protocol main value, the total Metabolic Tumor Volume. Its unit is mL (or cm^3);

- **MORPHOLOGICAL_sMTV** is Standardized Metabolic Tumor Volume. More specifically, it is measured as $MTV/PatientWeight$ and is in mL/kg;

- **MORPHOLOGICAL_D$_{max}$** is the distance between the two lesions that are the furthest apart (with ROIs center of mass as origin). It is one way to measure tumor dissemination;

- **MORPHOLOGICAL_wD$_{max}$** is the distance between the two lesions that are the furthest apart calculated from a weigthed center of mass;

- **MORPHOLOGICAL_D$_{maxVox}$** is the distance between the two lesions that are the furthest apart (with the outermost voxel).

- **MORPHOLOGICAL_VolSpread** is the sum of the differences in volume between all lesions

- **MORPHOLOGICAL_VolSpreadBulk** is the sum of the differences in volume between the largest lesion and all other lesions

- **MORPHOLOGICAL_DiffSUVmax** is the difference in SUVmax between the lesion with the highest SUVmax and the lesion with the lowest SUVmax

- **MORPHOLOGICAL_DiffSUVmaxSum** is the sum of the differences in SUVMax of all lesions

- **MORPHOLOGICAL_DiffSUVmaxBulk** is the difference in SUVmax between the largest lesion and the minimum of all SUVmax of other lesions

- **MORPHOLOGICAL_DiffSUVmaxSumBulk** is the sum of the differences in SUVmax between the largest lesion and all other lesions

- **MORPHOLOGICAL_DiffSUVmaxSumHot** is the sum of the differences in SUVmax between the lesion with the highest SUVmax and all SUVmax of other lesions

- **MORPHOLOGICAL_DiffSUVpeak** is the difference in SUVpeak between the lesion with the highest SUVpeak and the lesion with the lowest SUVpeak

- **MORPHOLOGICAL_DiffSUVpeakSum** is the sum of the differences in SUVpeak of all lesions

- **MORPHOLOGICAL_DiffSUVpeakBulk** is the differences between the SUVpeak of the largest lesion and the SUVpeak of the lowest SUVpeak of all other lesions

- **MORPHOLOGICAL_DiffSUVpeakSumBulk** is the sum of the differences in SUVpeak between the largest lesion and all other lesions

- **MORPHOLOGICAL_DiffSUVpeakSumHot** is the sum of the differences between the lesion with the highest SUVpeak and SUVpeak of all other lesions

- **MORPHOLOGICAL_sumBindCOM** is the sum of 3D distances between the current ROI COM and all other ROIs COM

- **MORPHOLOGICAL_meanBindCOM** is the mean of sumBindCOM = sumBindCOM / NumberOfROI

Calculation and Results

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- **MORPHOLOGICAL_stdBindCOM** is the standard deviation of 3D distances between the current ROI COM and all the other ROIs COM

- **MORPHOLOGICAL_minBindCOM** is the minimum of 3D distance between the current ROI COM and all the other ROIs COM

- **MORPHOLOGICAL_maxBindCOM** is the maximum of 3D distance between the current ROI COM and all the other ROIs COM. Among them is Dmax

- **MORPHOLOGICAL_avTotBindCOM** is the mean of 3D distances between ROIs COM. This value is shared by all ROIs. It is computed as seen in the equation below

- **MORPHOLOGICAL_sumBindWCOM** is the sum of 3D distances between the current ROI wCOM and all other ROIs wCOM

- **MORPHOLOGICAL_meanBindWCOM** is the mean of BindWeightedCOM = sumBindWeightedCOM / NumberOfROI

- **MORPHOLOGICAL_stdBindWCOM** is the standard deviation of 3D distances between the current ROI wCOM and all the other ROIs wCOM

- **MORPHOLOGICAL_minBindWCOM** is the minimum of 3D distance between the current ROI wCOM and all the other ROIs wCOM

- **MORPHOLOGICAL_maxBindWCOM** is the maximum of 3D distance between the current ROI wCOM and all the other ROIs wCOM

- **MORPHOLOGICAL_meanTotBindWCOM** is the mean of 3D distances between ROIs wCOM. This value is shared by all ROIs. see formula in documentation

- **MORPHOLOGICAL_SUM_MTV** is the metabolic Tumor Volume of whole patient

- **MORPHOLOGICAL_SUM_sMTV** is the standardized Metabolic Tumor Volume of whole patient
= SUM_MTV / PatientWeight

- **MORPHOLOGICAL_SUM_TLG** is the total Lesion Glycolysis of whole patient

- **MORPHOLOGICAL_SUM_STLG** is the standardized Total Lesion Glycolysis of whole patient
= SUM_TLG / PatientWeight

- **MORPHOLOGICAL_MAX_sumBindCOM** is the maximum value of sumBindCOM

- **MORPHOLOGICAL_MAX_meanBindCOM** is the maximum value of meanBindCOM

- **MORPHOLOGICAL_MAX_stdBindCOM** is the maximum value of stdBindCOM

- **MORPHOLOGICAL_MAX_minBindCOM** is the maximum value of minBindCOM

- **MORPHOLOGICAL_MIN_minBindCOM** is the minimum value of minBindCOM

- **MORPHOLOGICAL_MAX_maxBindCOM** is the maximum value of maxBind-COM

- **MORPHOLOGICAL_MAX_meanTotBindCOM** is the maximum value of mean-TotBindCOM

» In a fifth part, are conventional indices describing the ROI MTV. Minimum and maximum are also highlighted in another column.

- **MORPHOLOGICAL_SUVmin**. Minimal SUV within the ROI.

- **MORPHOLOGICAL_SUVmean**. Average SUV within the ROI.

- **MORPHOLOGICAL_SUVstd**. Standard deviation of SUV within the ROI.

- **MORPHOLOGICAL_SUVmax**. Maximal SUV within the ROI.

- **MORPHOLOGICAL_MTV (# vx)**. Total voxels within the ROI.

- **MORPHOLOGICAL_MTV (mL)**. ROI total volume.

- **MORPHOLOGICAL_sMTV**. Standardized Metabolic Tumor Volume. Its unit is mL/kg.

- **MORPHOLOGICAL_TLG**. Total Lesion Glycolysis, measured in SUV*mL

- **MORPHOLOGICAL_STLG**. Standardized Total Lesion Glycolysis. Its unit is SUV*mL/kg.

Calculation and Results

» Lastly, the values imparted to the protocol are described as a reminder. Thus, all ROI lines have identical values.

- **Absolute SUV threshold: min**. Minimal SUV used by the protocol in Step 2.

- **Absolute SUV threshold: max**. Maximal SUV used by the protocol in Step 2.

- **% of SUVMax threshold**. Percentage of SUV_{max} above which the voxels are kept in the relative threshold segmentation.

- **Adaptive threshold (Nestle): beta**. β parameter (namely correction factor), imparted to the Nestle segmentation method.

- **MTV% (%)**. Percentage of (total) MTV from Step 1 passing onto Step 3.

- **Pruning volume: min**. Lower limit of volume pruning in Step 3.

- **Pruning volume: max**. Upper limit of volume pruning in Step 3.

Part IV
References

Chapter 1
Useful references

1.1 Contact

If you were to still have questions on the MTV protocol after reading this manual, please do contact the LIFEx support team and send us an email at **contact@lifexsoft.org**.

We will happily welcome any suggestion users may have to improve this user guide!

Please note that a quick *MTV protocol* **Step-To-Step** slideshow is also available here.

1.2 Bibliography

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

1.2 Bibliography

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Useful references