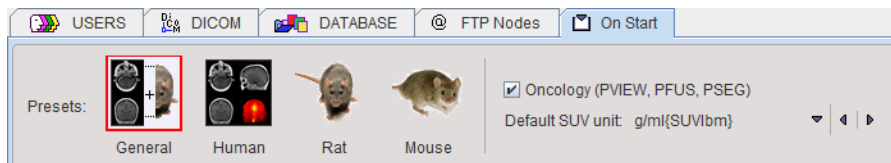


# PMOD Features dedicated to Oncology Research

While brain research using dynamic data has always been a main target of PMOD's developments, many scientists working with static oncology data have also found ways to leverage PMOD's unique functionality. However, their needs and workflows have not been specifically addressed by PMOD so far. This has changed in recent versions since PMOD3.9, with significantly improved functionality and usability for oncology research. This application note briefly illustrates 10 of the most salient new features. Please refer to the documentation for full coverage.

## 1. Global Oncology Configuration

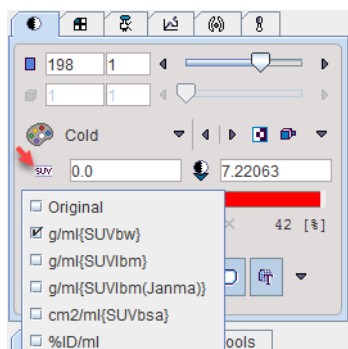
A new **Oncology** switch in the **On Start** section of the main configuration indicates to the program that high uptake lesion outlining, and assessment, will be the main application.



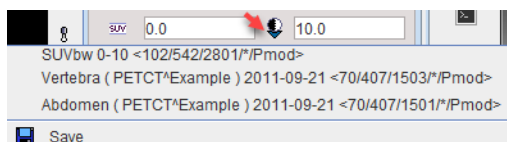
As a result, the preferred use of **SUV** units is preset for image viewing and statistics, with selection of the preferred SUV type. Outlined VOIs will be assumed to represent segmented lesions. Correspondingly, **MTV** (Metabolic Tumor Volume) and **TLG** (Total Lesion Glycolysis) will be output in the results of calculated statistics. For convenience and proper documentation, subject name and ID will by default appear in the image overlays.

## 2. SUV-based Image Viewing

The default **Oncology** display unit is the widely used SUV based on body mass. However, as illustrated below, additional SUV variants are available, including the Janmahasatian formula for obese patients, and can easily be selected from a drop-down list. The color table settings and regional statistics will be based on the selected display unit.



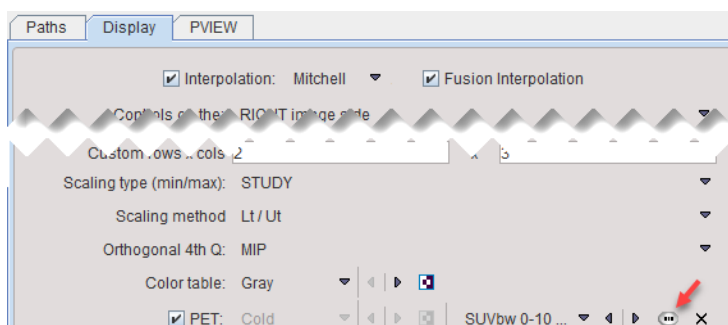
Color tables with a fixed SUV range for consistent image viewing can easily be configured. The first step is to configure or select the appropriate SUV type as described above and define the lower and upper thresholds (e.g. 0-10 [g/ml]). Next, the definition can be saved via the button between the upper and lower image thresholds.



Finally, the tool configuration utility is opened



and the color table set as default for PET data.

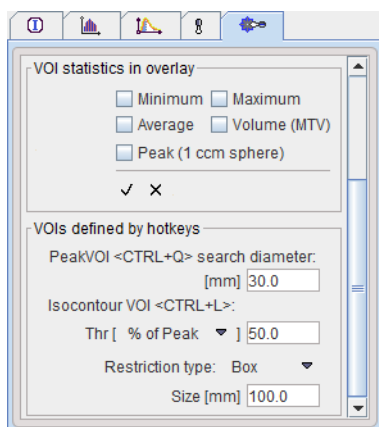


From then on, all DICOM PET images loaded will be displayed using the defined color table setting.

### 3. Lesion Segmentation and Statistics

Typically, oncologic lesions show up in PET images as bright areas of high uptake. Extensive literature exists on methods for delineating such lesions. In general, iso-contouring is applied in a box enclosing the lesion using either an absolute threshold, in SUV units, or a threshold relative to the  $SUV_{max}$  or  $SUV_{peak}$ . This can now easily be accomplished using hot-keys within the PMOD VOI functionality.

The required specifications are located in the **VOI Configuration** tab in the lower right section of the VOI definition interface.



The **VOI statistics in overlay** section allows a number of major VOI statistics to be enabled for automatic display in the image overlay. Once activated, the results for the currently selected VOI(s) are overlaid. This functionality is intended to facilitate the documentation of results using screen captures illustrating lesion segmentation and calculated statistics.

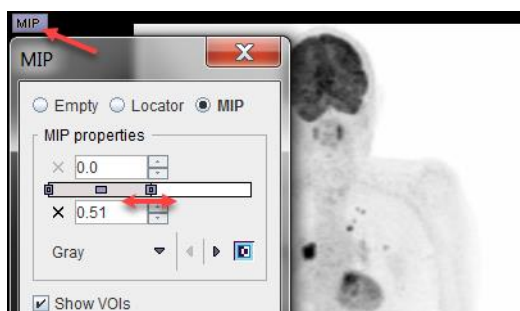
#### 4. Hot-key based Lesion Assessment


Three types of VOIs can be generated by pointing the cursor at a lesion and using a keyboard hot-key combination. Their configuration parameters are defined in the **VOI defined by hotkeys** section of the **VOI Configuration** tab illustrated above. Essentially, a default bounding space around the location pointed out by the user must be defined, combined with a threshold methodology for the iso-contouring. The options are:

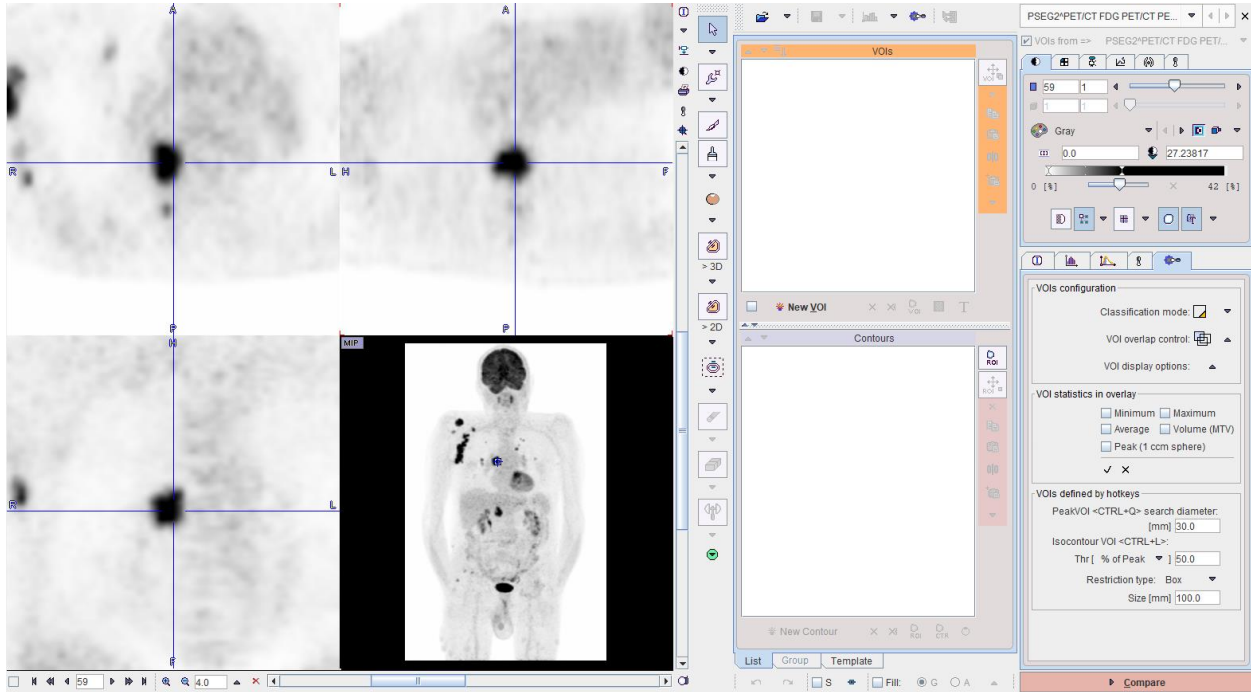
1. Spherical **Peak VOI (Ctrl+Q)**. Specification: Diameter of an enclosing sphere.
2. **Iso-contouring VOI** within a **bounding space** at a specified level (**Ctrl+L**). Specifications: Enclosing box or sphere dimension; contouring value defined as **Threshold in % of Max** or **% of Peak** in the enclosing space, or **absolute SUV**. Frequently used configurations are 50% of  $SUV_{peak}$  and 42% of  $SUV_{max}$ . In case an absolute SUV threshold is used, the corresponding SUV display unit should be selected for image viewing.
3. **Iso-contouring VOI** according to **PERCIST** recommendation at a threshold level obtained from a reference VOI in the liver (**Ctrl+Shift+U**, **Ctrl+U**, see below). A region-growing algorithm is applied from the seed point, connecting all pixels above the threshold.

When using hot-key lesion segmentation, working in the orthogonal planes mode is recommended, with sufficient zoom and a maximum intensity projection (MIP) image. This layout makes it easy to point out the lesions.

If the MIP image is not shown, it can be enabled and configured as illustrated below. Note the decreased upper threshold and the inverted gray color table.



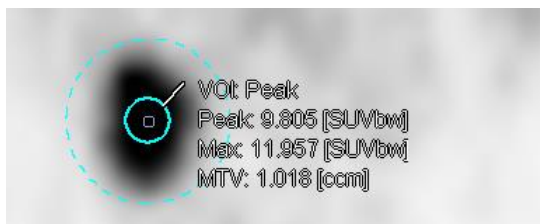
In order to apply hot-key iso-contouring once configured, the *VOI functionality must be active*. This means that the VOI definition tools need to be present. If they are not shown, the  button switches them on. The user interface should look something like this:



## 5. Spherical Peak VOI in Bounding Sphere (Ctrl+Q)

A lesion assessment introduced by the PERCIST methodology [1,2] is **Peak VOI** generation. In this method 1ml spheres are placed in the lesions such that their average is maximized. Naturally, this functionality is tailored for human data.

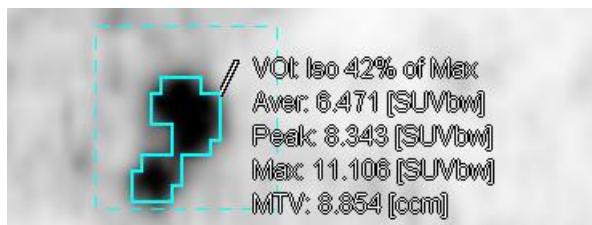
For the quick assessment of lesion peak SUV in PMOD, proceed as follows: Click on a lesion in the MIP so that the image display triangulates on the lesion. Then click in the image planes until the plane intersection indicated by the blue lines is approximately central to the lesion of interest. Finally apply the keyboard shortcut **Ctrl+Q**. A bounding sphere is set and then the location of the 1ml peak sphere is optimized for maximum average. The resulting peak sphere VOI is shown in the image, together with the bounding VOI in dashed strokes. If overlay statistics are enabled, they also appear in the display. For example:



This procedure can be repeated until all relevant lesions have been assessed.

## 6. Iso-Contouring VOI in Bounding Box (Ctrl+L)

For quick iso-contouring, triangulate the lesion center as described above, then activate the keyboard shortcut **Ctrl+L**. The defined bounding box is set and iso-contouring is performed within, using the configured methodology. The resulting contour is shown in the image, together with the bounding VOI. The example shown below used a bounding box and iso-contouring at 42% of the maximum value in the box.

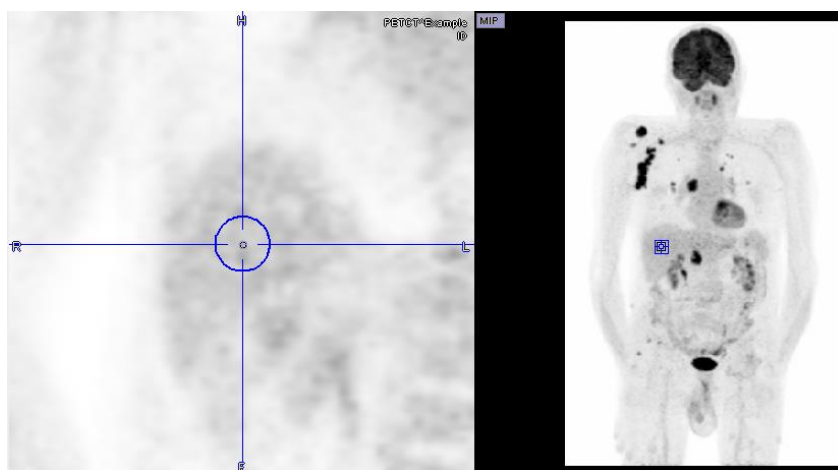


## 7. PERCIST-type Iso-contouring VOI based on Liver VOI (Ctrl+Shift+U, Ctrl+U)

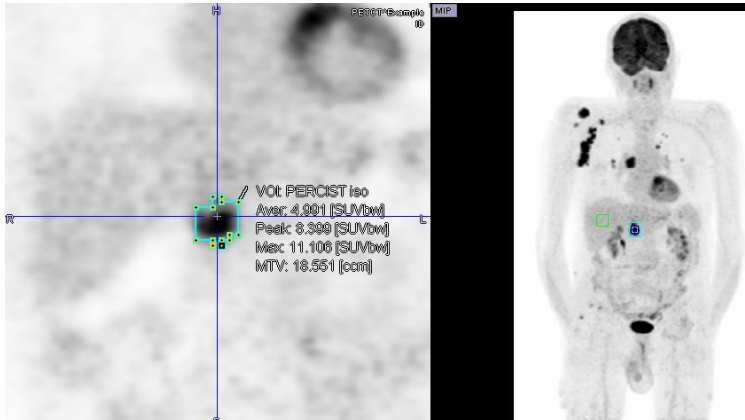
Instead of basing iso-contouring on the values in the lesion itself or an absolute SUV, the threshold can be obtained from the uptake in a reference tissue. PERCIST (PET Response Criteria in Solid Tumors) [1,2] obtains the background activity from a 3-cm diameter sphere placed in the right side of healthy liver, midway between the dome and inferior margin, excluding central ducts and vessels.

The procedure for a PERCIST-conformant assessment is as follows:

1. Triangulate the point in the liver as described above. Activate keyboard shortcut **Ctrl+Shift+U** to place the 3cm diameter reference sphere. The *minimal level of tumor uptake* is calculated as  $1.5 * Average_{liver} + 2 * StandardDeviation_{liver}$ . This value is used as iso-contouring threshold in the subsequent lesion assessment.



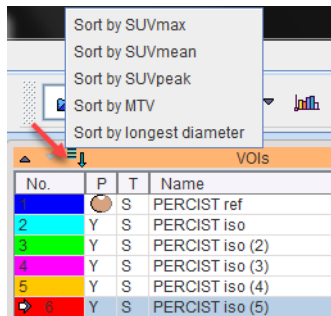
2. Triangulate the center of each lesion, then activate **Ctrl+U**. A region-growing algorithm is applied and the pixels above the threshold are outlined. The configured statistics are calculated and displayed. If uptake in the lesion remains below the minimal tumor level, no iso-contouring VOI is found and the lesion is not measurable with PERCIST.



Each lesion can be documented by screen capture as described below. Note the **Peak** value, which is the relevant outcome for PERCIST.

### 8. Sorting of Segmented Lesions

Once the lesions have been segmented, they can be ordered according to different criteria, such as size, MTV,  $SUV_{mean}$ ,  $SUV_{peak}$ ,  $SUV_{max}$ . In this way, the most relevant lesions are easily brought to the top of the list for further evaluation and documentation.

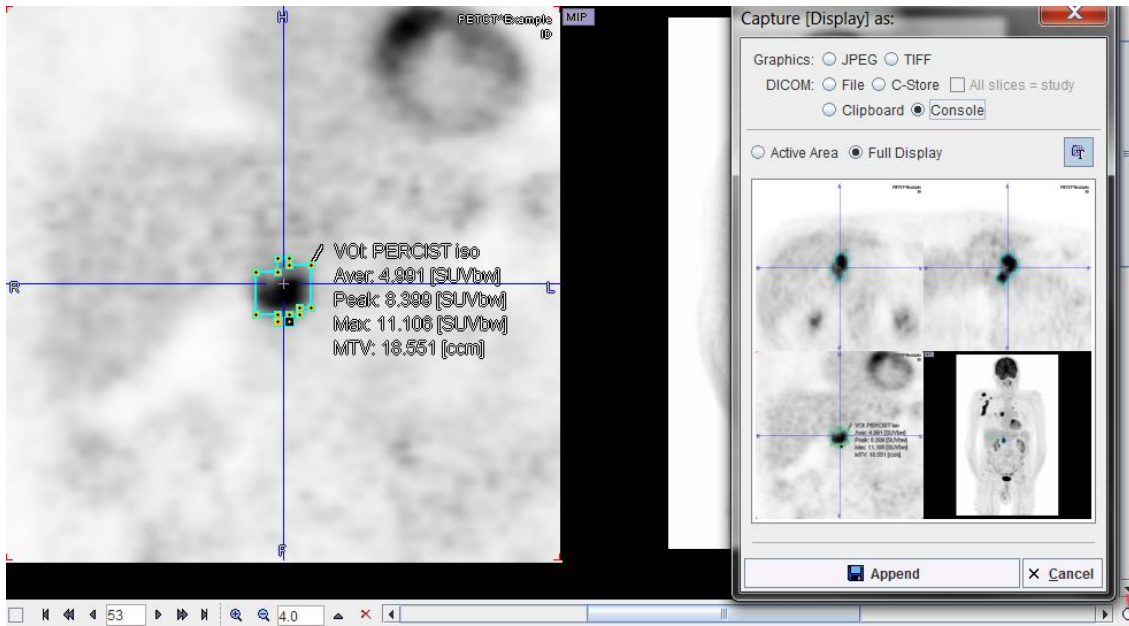


In contrast to RECIST, which employs the largest diameter in the measurement plane to quantify lesion size, PMOD supports the longest oblique diameter in three-dimensional space.

### 9. Documentation of Segmented Lesions

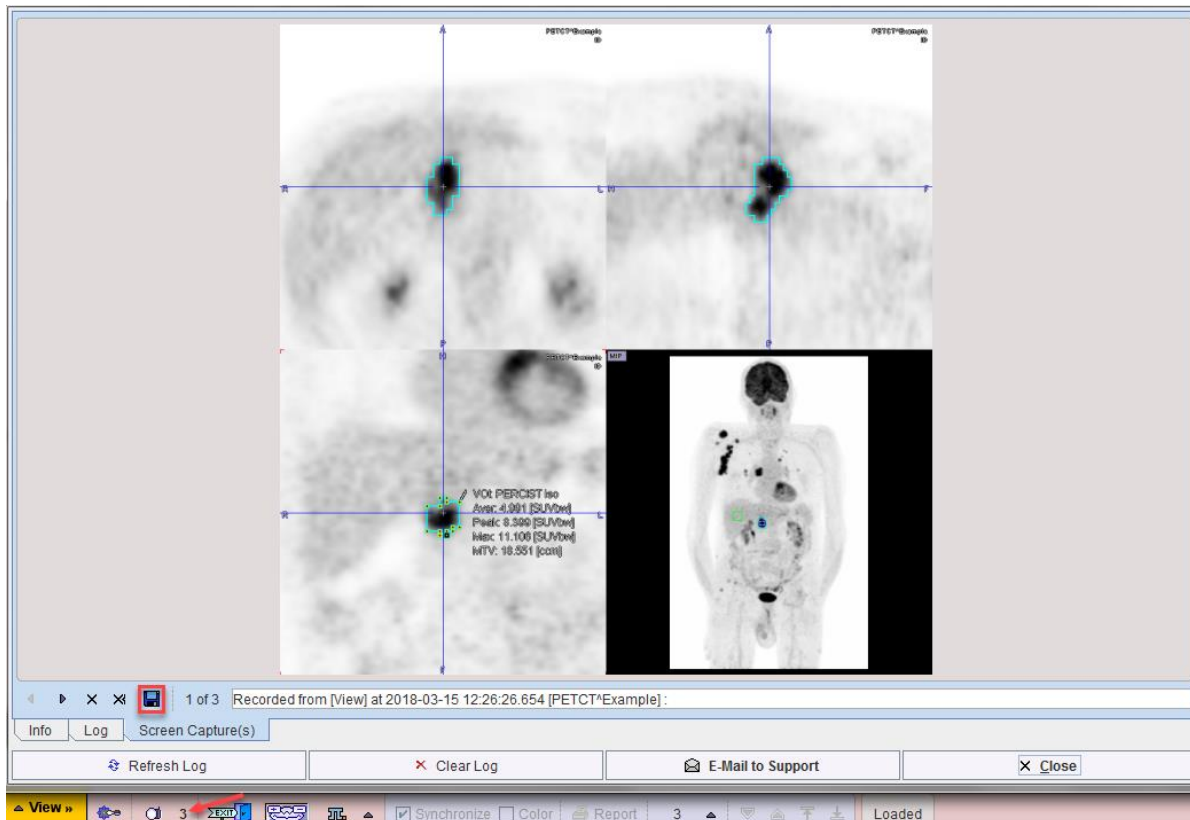
In order to document the segmentation and the resulting statistics, screen capturing has been improved. It can be called using the **Ctrl+E** keyboard shortcut or the corner button indicated below. The output is defined in the dialog window that appears.





**Active area** only captures the content of the selected quadrant, whereas **Full Display** captures the whole image area, including MIP. The output format is selected in the upper part: Either a DICOM secondary capture image can be saved or directly sent to a PACS system (**C-Store**), or a graphic image file format can be specified for saving.

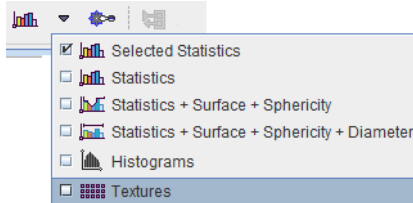
Note the new **Console** output, which sends the capture to an image buffer in the console. When opening the console later on, the captured images can be inspected and the relevant ones saved.



## 10. Texture Analysis

Texture analysis quantifies the variability of the pixel intensities within a structure such as a tumor. There is a plethora of texture metrics, any of which may facilitate in vivo lesion characterization and provide predictive information about the tumor malignancy.

PMOD provides a collection of 36 indexes that have been found to be most valuable in the context of PET imaging. Six are based on the pixel histogram within a VOI, 19 based on the gray level co-occurrence matrix (GLCM), and 11 based on the run length matrix (RLM). Once the lesions are segmented, texture analysis can simply be called from the statistics menu.



The resulting table lists the texture values for each defined lesion, and supports data export for further evaluation and research.

|                |   |             |
|----------------|---|-------------|
| Iso 42% of Max | Hist Mean                                       | 21.300801   |
|                | Hist Variance                                   | 38.248452   |
|                | Hist Skew                                       | -0.110998   |
|                | Hist Excess Kurtosis                            | -0.655459   |
|                | Hist Energy                                     | 0.006758    |
|                | Hist Entropy                                    | 5.113529    |
|                | GLCM Energy (Angular Second Moment, Uniformity) | 0.023226    |
|                | GLCM Contrast (Inertia, Variance)               | 5.622713    |
|                | GLCM Correlation                                | 0.988449    |
|                | GLCM Sum Of Squares Variance                    | 1088.590922 |
|                | GLCM Homogeneity (Inverse Different Moment)     | 0.580839    |
|                | GLCM Sum Average                                | 91.089088   |
|                | GLCM Sum Variance                               | 4329.765876 |
|                | GLCM Sum Entropy                                | 5.792591    |
|                | GLCM Entropy                                    | 9.266484    |
|                | GLCM Difference Variance                        | 25.309415   |
|                | GLCM Difference Entropy                         | 2.616597    |
|                | GLCM Information Correlation 1                  | 0.023762    |
|                | GLCM Information Correlation 2                  | 4.0         |

## 11. Lesion Segmentation in the PSEG Tool

The elements described above are available in the basic PMOD environment. To allow researchers assessing the tumor burden quickly and consistently they have also been combined into dedicated lesion segmentation workflows in the PSEG tool. As an additional benefit, the results can be documented in comprehensive reports, saved in a format which lends itself easily to group statistics.

## References

- [1] Wahl RL, Jacene H, Kasamon Y, Lodge MA: From RECIST to PERCIST: Evolving Considerations for PET response criteria in solid tumors. J Nucl Med 2009, 50 Suppl 1:122S-150S.
- [2] O JH, Lodge MA, Wahl RL: Practical PERCIST: A Simplified Guide to PET Response Criteria in Solid Tumors 1.0. Radiology 2016, 280(2):576-584.