

QAV-PET: A Free Software for Quantitative Analysis and Visualization of PET Images

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1 Getting Started

1.1 What is QAV-PET used for?

Quantitative Analysis and Visualization of PET Images (QAV-PET) is an open-source software implemented in the popular MATLAB coding environment that allows easy, intuitive, and efficient visualization and quantification of multi-modal medical images. In particular, the software is well suited for PET-CT as well as MRI-PET images. It allows multi-modal images to be viewed simultaneously which allows the research to incorporate information that is not available on a single modality image for improved quantification and analysis. Additionally, the software includes a framework for quantification and analysis which can be easily manipulated and tuned to fit any medical imaging application. In the following sections we outline the framework and how to use this software.

1.2 Downloading and Installation Instructions

The software is freely available on the MATLAB file exchange. Once the .zip file is downloaded, un-zip the folder and open up MATLAB. Once MATLAB has launched, set the current folder to the un-zipped folder. Launch the GUI by right clicking on the *FusedSUV.m* file and left click on run.

2 Visualization

2.1 Opening the Images

After the GUI is run, a pop-up menu will appear asking the user to first select the functional image file (PET) in the analyze (.hdr and .img) or DICOM format. After the file is selected, press the OK button. After several seconds (may be up to about 20 seconds if the image file is very large) another pop-up menu will appear asking for the anatomical image (CT or MRI) file in either analyze or DICOM format.

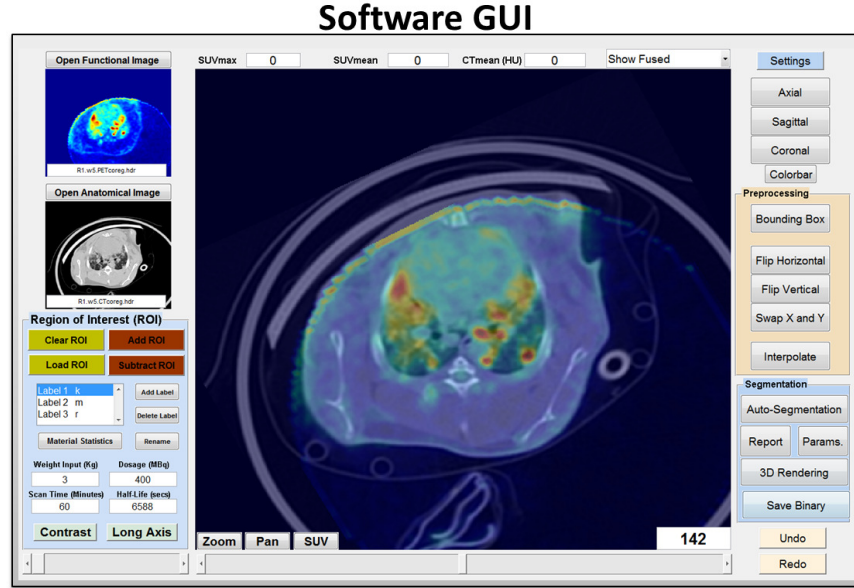


Fig. 1: The QAV-PET GUI with a PET-CT of a rabbit infected with tuberculosis shown.

Once the GUI is launched, you will see something very similar to Figure 1. The default display shows a fusion between the anatomical and functional images. There is a drop-down menu at the top right which shows the current image being viewed. Currently it is 'Show Fused'.

2.2 Adjusting Contrast and Brightness

2.2.1 Anatomical or Functional

The contrast and brightness can be easily and intuitively adjusted by only using the mouse buttons and cursor motion. First, the brightness is controlled by holding down the left mouse button and moving the mouse cursor *vertically*. Secondly, the contrast is adjusted by holding down the left mouse button and dragging the cursor *horizontally*, see Figure 2. If at any time the user wishes to return back to the default contrast and brightness there is a button titled 'Contrast' in the bottom left of the gui.

2.2.2 Fused Image

Adjusting the econtrast and brightness is slightly different for the image fusion case. The reason for this is to allow the user to quickly and easily change the opacity between the functional and anatomical images by using the mouse. In this case, holding the left mouse button and moving it *vertically* adjusts the

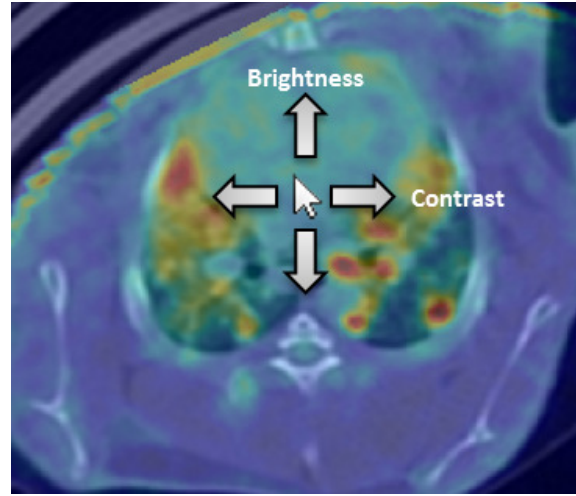


Fig. 2: Adjusting the contrast and brightness for the functional and anatomical view cases.

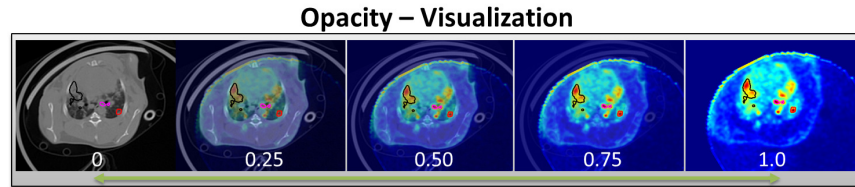


Fig. 3: Example of varying the opacity between PET and CT on the segmentations from Fig. 4. The opacity ranges from 0, fully anatomical (CT) information, to 1, fully functional (PET) information.

opacity between the anatomical and functional images. Holding the left mouse button and moving the cursor *horizontally* adjusts the threshold that is applied to the functional image, essentially adjusting the contrast and brightness of the PET image. This threshold is applied to the PET image in order to remove the background areas for improved visibility of the underlying anatomical image. Additionally, the opacity can be adjusted by the slider in the bottom left of the gui. You will notice that the slider moves in relation to the opacity change made by the mouse movement. See Figure 3 for an example of the effects on the fusion view on a fused PET-CT image.

2.3 Zoom and Panning

Now that the contrast, brightness, and opacity can be adjusted for optimal viewing, the zoom and pan features allows the user to focus on only the most

important sections of the image. Both the zoom and panning can be activated in two different ways. First, there is a mouse button plus cursor motion mode. For panning, the button is the right mouse button and for the zooming the button is the middle mouse button. Holding these buttons while moving the mouse cursor will adjust the pan and zoom. Secondly, there are two buttons in the bottom middle of the GUI named PAN and ZOOM which, after clicking, activates the default zoom and pan features within MATLAB. They follow the standard behavior that one would expect in MATLAB.

Tip:

Please note that if the user uses either the zoom or pan buttons within the GUI, the user must click on the respective button again to turn the zoom or pan feature of MATLAB off before the contrast, brightness and other features that utilize the cursor movement can be used.

Table of the buttons and their result:

Keys	Result
Q	Cycle between Functional, Anatomical, and Fused
Space Bar	Add ROI to the current image label
Control	Subtract from the current image label
Left Mouse	Drag vertically to change brightness
	Drag horizontally to change contrast
Middle Mouse	Drag to zoom in and out
Right Mouse	Drag to pan up, down, left, and right
Mouse Wheel	Scroll to change the current slice shown

2.4 Changing Current Slice

The current slice can be changed by use the mouse wheel or by clicking and dragging on the GUI slider in the bottom middle of the GUI.

2.5 Changing Image Shown—Functional, Anatomical, Fused

As stated previously, the default view is a fusion of the anatomical and functional images. There is a drop-down menu at the top right which shows the current image being shown. There are three ways of changing the current image view in QAV-PET. First, the drop-down menu can be used to select the image to be shown. Secondly, the user can press the ‘Q’ key which automatically cycles between the three image views—functional, anatomical, and fused. This allows the user to quickly cycle through the imaging views while segmenting the region of interest in the images. This key can be easily changed in the ‘Settings’ button in the top right of the GUI. Lastly, the user can left mouse click on the images on the top left which shows the anatomical and functional image of the currently selected slice. This opens up the respective imaging view that was chosen.

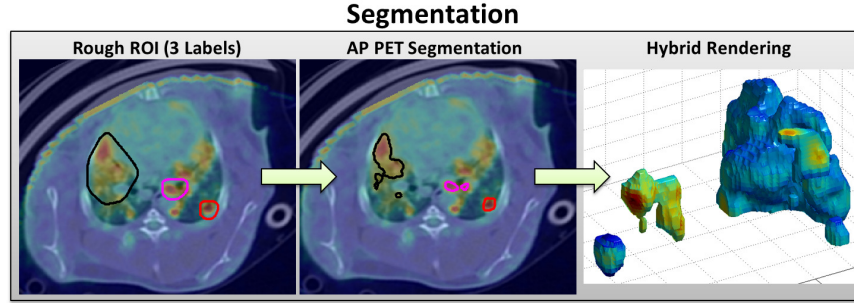


Fig. 4: Example of a segmentation involving 3 labels. **Left:** A rough ROI is created by the user. **Middle:** The AP PET segmentation is applied to the rough ROI for refinement of the boundary. **Right:** A hybrid rendering of the segmentations, with functional information overlaid, is provided. The redder areas correspond to higher radiotracer uptake areas while bluer areas have less uptake.

3 Segmentation

3.1 Rough ROI Definition

A rough region of interest (ROI) can be easily added to the images. First, the user selects an image label in the listbox on the left. The first label created is named 'Label 1 k'. Adding a new label, deleting a label, and changing a label's color will be outlined in the following subsections. In order to add an ROI to the currently selected label, the user can click on the red 'Add ROI' button. Then, left mouse click in the main image view and, while holding the left mouse button down, drag the cursor around the region of interest. Once completed, release the left mouse button and the ROI will be changed to the color of the currently selected label. To subtract from the current label, the user can click on the red 'Subtract ROI' button and follow the same procedure as before.

Additionally, in order to speed up the process of adding and subtracting ROIs we added another way instead of clicking on the red buttons each time. If the user clicks the 'Space Bar', this is essentially the same as clicking the 'Add ROI' button while the 'Control' key is the same as the red 'Subtract ROI' button. These default keys can be changed to other keyboards keys by using the 'Settings' button in the top right of the GUI. These buttons allow for very efficient adding and subtracting to the ROIs.

3.2 Interpolation

Interpolation can be done between two ROIs on the same image label on two different slices. Then, the user should click on the 'Interpolate' button in the right of the GUI and the software will interpolate between the two slices. Inter-

polation between slices of the ROI allows for quick and efficient ROI definition by the user.

3.3 ROI Refinement

3.3.1 Affinity Propagation (AP) Image Segmentation

Once the rough ROI is created, the segmentation can be automatic refined using a segmentation algorithm named Affinity Propagation (AP) PET image segmentation [1, 2]. The automatic segmentation algorithm allows the user to refine the rough manual segmentations to the exact boundary of the high uptake region which increases accuracy and lowers variability while also decreasing total segmentation time. It was shown in [1] that the AP segmentation algorithm is more accurate than the current state-of-the-art PET image segmentation methods for diffuse, multi-focal uptake regions commonly seen in pulmonary infections such as tuberculosis.

Very briefly, the segmentation method estimates and smoothes the histogram of the region of interest via kernel density estimation [3] to estimate and remove the points along the histogram that are most likely to be noise. Then, a novel similarity (affinity) function is applied to the histogram to estimate the similarity of the points along the histogram with the assumption that points that are most similar are more likely to belong to the same classification, i.e. image label. Lastly, the Affinity Propagation clustering algorithm [4] is applied to these similarities to automatically calculate the number and membership of the classes within the image.

All parameters of the AP image segmentation algorithm can be easily adjusted, if needed, within the software. The rough ROI definition followed by a fully automated segmentation algorithm dramatically decreases the total segmentation time and inter- and intra-observer variability while also increasing overall accuracy.

3.4 Image labels

ROI labels can be easily added to have multiple ROI definitions giving the researcher the ability to separate and study pathological high uptake regions individually. This is done by clicking on the ‘Add Label’ button on the left side of the GUI. The letter that is after the label name is the color of the label. If the user wishes to change the color of a particular label, this can be easily accomplished by using the ‘Rename’ button and changing the letter to the first letter of the desired color. For a list of all possible colors, please check the MATLAB documentation; however, a number of basic colors are allowed.

4 Quantification

Region of Interests (ROIs) must be defined before any type of quantification or analysis can take place. Essentially, the ROI tells the computer “where” the

object of interest is on the image so the image properties of this region, such as the highest Standardized Uptake Value (SUV_{max}), can be computed. The software allows rough ROIs to be generated by the user followed by automatic refinement (segmentation), as described in the following subsection. For this initial rough ROI, the user first selects the label to assign the object of interest to such as Label 1, 2, 3, etc. Then, the software tracks the position of the mouse cursor while the user manually draws the boundary of the object of interest.

Once an ROI is created, the statistics of the defined region can be computed and displayed as a table or exported as a .CSV file. These statistics include the *volume*, SUV_{max} , and SUV_{mean} of all the slices for the given label which have been shown to be of particular importance for quantifying the pathologies in infectious lung diseases in longitudinal small animal models [5].

4.1 Getting Label Statistics

A table of the imaging statistics of the current image can be obtained by clicking on the ‘Material Statistics’ button underneath the label listbox. A pop-up menu will appear asking if the user wants these values in a MATLAB generated table (for easy copying and pasting or processing within MATLAB) or does the user wish to save the table as a .CSV file (for opening in Excel or similar software).

The SUV_{max} , SUV_{mean} , and mean hounsfield units (CT_{mean} (HU)) is displayed at the top of the GUI for the particular slice selected. In addition, the SUV at a particular point can be investigated by clicking on the SUV button on the bottom left of the main imaging viewer. This allows the researcher to get the SUV at a particular point on the image regardless of whether the PET image is currently show or not. This can be potentially very useful when determining the radiotracer uptake on a particular anatomical abnormality.

4.2 Auto-reporting and Renderings

This software has a novel auto-reporting feature which, in an automated fashion, produces a report which includes the most important information needed for quantifying the disease and high uptake regions. It is meant to complement, not replace, the exported quantification as a .CSV file. After hitting the report button in the software, the user selects whether to create a report for each label individually or to create a single report for all the labels, essentially considering all the labels as one single label.

The report includes both quantitative and qualitative data. The quantitative data includes the SUV_{max} , SUV_{mean} , and the *volume* of the current label, and, additionally, it provides the location of the SUV_{max} on the axial, sagittal, and coronal view of the PET image, the CT image, and the PET-CT fused image for a total of 9 images on the first page of the report. All of this information allows the user to get a quick view of the highest uptake lesion, which is important for disease severity quantification. For an even better visualization, the boundary of the current uptake region is colored as the same color as the label the user used

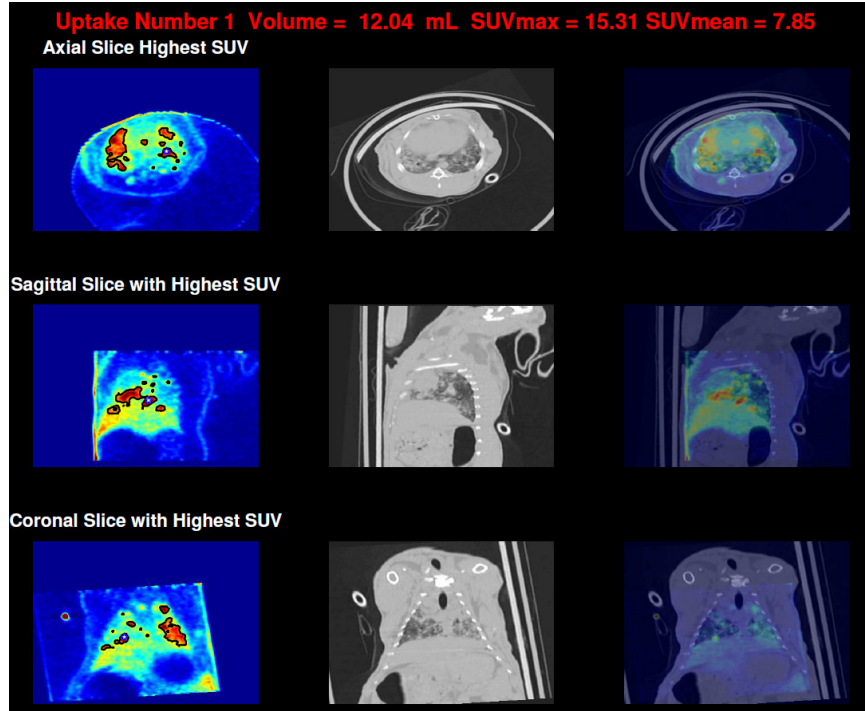


Fig. 5: Example page from the auto-generated report. On top, the title includes the lesion number along with the Volume, SUV_{max} , and SUV_{mean} for easy comparison between the various high uptake regions. The first row shows the location of the SUV_{max} with a star on the axial image while the second and third rows show the sagittal and coronal slices respectively. The PET image (first column), CT image (second column), and registered PET-CT image (third column) are provided in the first, second, and third column respectively.

to create the segmentation for continuity between the segmentation creation and report generation. See Figure 5 for an example of the first page of the report.

In addition to these views, the software provides a three dimensional representation of the segmented high radiotracer uptake region by generating a rendering of the segmented lesions. First, it creates a rendering using the boundary and shape information from the labels. Then, the renderings are overlaid with the functional information from the PET image to give the distribution of the radiotracer uptake along the surface of the uptake region in order to visualize the information in a way that is simply not possible by only looking at 2D images. We refer to this type of rendering as a “hybrid rendering” since it contains information from different imaging modalities fused together, functional and anatomical. An example of this rendering from three different labels is shown in Figure 4. The redder areas correspond to higher uptake areas (more severe disease) while bluer areas have less uptake. Notice how easily the distribution of the radiotracer uptake is visualized. Lastly, the report generates a rendering of all the various labels and colored using the same coloration and 3D coordinates as when the user was segmenting the regions. This allows the user to get a good sense of the spatial distribution of the various labels within the images.

5 Concluding Remarks

There are many potential applications for the QAV-PET open source software, and only a few will be highlighted here. Perhaps the most direct application is for the quantification and visualization of abnormalities on PET-CT images of small animal infectious disease studies. The segmentation algorithm that is implemented has been shown to be particularly well-suited for the segmentation of diffuse, multi-focal PET radiotracer uptakes that are commonly seen with infectious diseases, and the intuitive and efficient work flow of the software will aid researchers in analysing these types of images since there is currently no software which allows for easy segmentation of abnormalities on PET-CT images. Another potential application for this software is for visualization of the pathologies in three dimensions with the PET functional information overlaid for determining the optimal histology slice localization. When taking histology slices from a diseased organ, this three dimensional view of the distribution of the disease will aid researchers in determining the best location to take the histology slices from for the best characterization. Lastly, the open source nature of the software will allow researchers to quickly add features or modify existing features for novel applications. For instance, if the user needs to segment abnormalities based upon the fused PET and CT information a novel segmentation algorithm such as [6] can be easily added to the image analysis and quantification framework presented here.

The software and code is freely available on the Matlab File Exchange, a popular and free-to-downloaded site for MATLAB software. This software allows researchers to easily and intuitively visualize, segment, render, and automatically generate a report that can be used in the analysis of medical im-

ages. If you should have any questions or comments please feel free to contact the authors.

Contact Us

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