QDOSE Dosimetry Software

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Version 1.2.12

User Manual

User Manual Version 1.2.12 Including Instructions for Use and Technical Description

Effective date: 15 May 2025

CE 0123

Used Symbols:

Date of manufacture
Year of manufacturing of the present software version

Manufacturer
Name and address of the manufacturer of the software

Operating Instructions
Every user is obliged to thoroughly read the user manual and to familiarize with the operation before using the software.

Medical Device
Indicates the item is a medical device

Unique Device Identifier
Indicates the unique device identifier information

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1 Introduction

1.1 Short Overview

QDOSE is a software solution focused on targeted internal radiation therapy for treatment of oncological patients. It is used to process medical image data acquired during nuclear medicine imaging procedures such as planar scintigraphy, Single Photon Emission Computed Tomography (SPECT), Positron Emission Tomography (PET) as well as anatomical imaging methods such as X-ray Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). It includes tools for two-dimensional (2D) and three-dimensional (3D) coregistration of multimodal data sets, drawing regions of interest, segmentation of organs, calculation of time-activity-curves, dose analysis and report generation. It is intended to be used by medical physicists and physicians in clinical routine and scientific investigations.

1.2 Contact Details

KeV Medical Imaging

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11147, Galatsi, Greece

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Telephone: +30 2111154521

Website: https://www.qdose.net

1.3 Intended Purpose

The medical device is intended to estimate the absorbed dose to organs and tissues based on intracorporal administration of radiopharmaceuticals and radio-labelled micro-spheres in oncology (cancer diseases). The medical device is not intended to be used for therapy planning.

1.4 Intended Use

The medical device QDOSE is intended to estimate the absorbed dose to organs based on intracorporal administration of radiopharmaceuticals in patients with cancer. At a whole organ level, this is done using a deterministic phantom-based model; in single organs, a spherical model or the Voxel S model are applied. The input for QDOSE is image data representing the biodistribution of an administered radionuclide or time activity curves or cumulated activities for organs.

The results of QDOSE evaluations should not be used as stand-alone assessment of radiation exposure or assessment of internal radiation therapy. In the clinical environment different sources are available that should be included in every clinical process.

Other non-QDOSE based methods of monitoring organ function and patient status should be available; QDOSE should not be the only tool for making clinical decisions.

QDOSE allows the user to display multimodal medical image data limited to Computed Tomography (CT) data sets in axial slices, Magnetic Resonance Imaging (MRI) data sets in axial slices, Positron Emission Tomography (PET), Single-Photon Emission Computed Tomography (SPECT) and planar nuclear medicine images.

QDOSE enables the user to perform measurements based on the data sets. Tools are available allowing coregistration of data sets, defining regions or volumes of interest (ROI/VOI) in data sets, performing fits of time-activity-curves and calculating cumulated activity. Cumulated activity values will be used to calculate absorbed dose based on deterministic models on whole organ level, or for single organs.

The life span of QDOSE is 5 years starting from the signature date of the license agreement.

1.5 Indication

The indication for QDOSE is oncology (cancer diseases).

1.6 Clinical Applications

The application area of QDOSE is oncology (radiopharmaceutical cancer imaging and treatment). With QDOSE, the user can perform personalized dosimetry. Two clinical issues can be addressed with QDOSE: safety dosimetry and efficacy dosimetry.

Safety dosimetry	***Efficacy dosimetry***
Dosimetry performed to determine organ absorbed doses and whole body effective dose to evaluate the overall treatment related risk for a patient.	Dosimetry performed to determine the dose received by a tumour to evaluate the treatment efficacy.
The clinical question is:	The clinical question is:
"Is there too much dose to healthy organs?"	*"Is there enough dose to the tumour?"*

With QDOSE, the trade-off between safety and efficacy can be analysed for the following applications.

1.6.1 Application 1: Dosimetry of Systemic Internal Radiation Therapy

QDOSE can be used to perform post-treatment dosimetry of systemic internal radiation therapy. Nuclear medicine image data (planar scintigraphy images and/or SPECT or PET) at multiple time points (minimum 2 time points) after administration of a radiopharmaceutical to a patient have to be available. Image data sets can be coregistered and ROIs/VOIs can be drawn and segmentations can be performed. For each segmentation over multiple time points different curve fit models can be used to

calculate the cumulated activity. Based on the cumulated activities for the segmentations the absorbed doses as well as effective doses can be calculated.

1.6.2 Application 2: Dosimetry of Diagnostic Radiopharmaceuticals

QDOSE can be used to perform dosimetry of diagnostic radiopharmaceuticals. Nuclear medicine image data (planar scintigraphy images and/or SPECT or PET) at multiple time points (minimum 2 time points) after administration of the diagnostic radiopharmaceutical to a patient have to be available. Image data sets can be coregistered and ROIs/VOIs can be drawn, and segmentations can be performed. For each segmentation over multiple time points different curve fit models can be used to calculate the cumulated activity. Based on the cumulated activities for the segmentations the absorbed doses as well as effective doses can be calculated. The doses can be extrapolated to other nuclides and activities.

1.6.3 Application 3: Dosimetry of Selective Internal Radiation Therapy

QDOSE can be used to perform dosimetry of selective internal radiation therapy (treatment of liver metastases). Nuclear medicine image data (SPECT or PET) have to be available. A pre-therapeutic image (e.g. ^{99m}Tc-MAA scans) as well as a post-therapeutic ^{90}Y PET image can be used. It is possible to only evaluate pre-therapeutic images or post-therapeutic images or both. Image data sets can be coregistered and ROIs/VOIs can be drawn and segmentations can be performed. The absorbed doses for the segmented regions can be calculated for the pre-therapeutic data set and the post-therapeutic data set. Extrapolation to other values of administered activity is possible.

1.7 Intended User

QDOSE is intended to be used by trained medical professionals including radiologists, nuclear medicine physicians, and medical physicists. The user must have experience in using medical imaging software and needs an understanding in the concept of dosimetry. The user requires training by qualified personnel in order to use QDOSE.

1.8 Information about Product Safety and Residual Risks

The medical device poses the risk, that wrong dose values lead to clinical decisions that can harm the patient. The professional duty to the patient in providing healthcare services lies solely with the healthcare professional providing patient care services. The user takes full responsibility for the use of information provided by QDOSE in patient care. The use of the product in no way is intended to replace or substitute for professional judgement.
The following information must be followed by the user for a safe clinical use of QDOSE.

1.8.1 Safety Information

The safety information for QDOSE is indicated in the following way:

⚠ CAUTION
Caution description. A CAUTION indicates a hazardous situation which, if not avoided, leads to a software output that could result in minor or moderate injury.

Please read the following safety information carefully before using the software.

⚠ CAUTION
The Activity Prediction tool is not intended to be used clinically. According to the intended use of QDOSE, the Activity Prediction tool for SIRT mode must not be used for treatment planning. The Activity Prediction tool is only for research purposes. Depending on the calculation method and the input values, there may be wide differences between the activities calculated by the different methods. The planning of treatment should not be performed based on the displayed values. Instead, the instructions of the manufacturer of the spheres should be used.

⚠ CAUTION
Incorrect input image data causes incorrectly calculated dose values. All calculated values depend on the quality of the input data. It is the user's responsibility to check for completeness and correctness of the image data. The image data must be suitable to perform dose calculation. The user should always check available image data for completeness and correctness before performing analysis steps.

⚠ CAUTION
Voxel S dosimetry of lung, bone or bone lesions results in incorrect values. Voxel S kernels are only valid for soft tissue. Voxel S dose calculations for other tissues such as bone or lung are not valid. Voxel S methodology should not be used for lung, bone, bone metastases or other lesions in the bone. Furthermore, the user has to decide how meaningful Voxel S dose calculations are for their specific image data, as the activity distribution used as base for calculation may be incorrect due to partial volume effect.

⚠ CAUTION
Dose calculation of alpha emitters underestimates the dose. Dose calculations for radiopharmaceuticals with alpha emitters are only performed for the parent nuclides. Daughter nuclides in a decay chain are not accounted for. The user should be aware that dose estimation for radiopharmaceuticals with alpha emitters may be too low.

⚠ CAUTION
QDOSE should be used in a secure network. IT security is in the responsibility of the user.

⚠ CAUTION
Unauthorised persons can access sensitive data. Unauthorised access is prevented by user authentication (login) and authorization (roles and rights) measures. In addition, since QDOSE version 1.2.4 the databases are encrypted to prevent unauthorised access to the data by third parties. Users should upgrade old databases for encryption when proposed by the program. Still, the software should be used in an environment where user access is regulated by user accounts at the level of the operating system. No responsibility is taken for the access to sensitive data by unauthorised persons deliberately bypassing the security measures. It is in the user's responsibility to guarantee data protection strategies.

⚠ CAUTION
QDOSE is not intended to store data permanently. It is the user's responsibility to perform backups of data and to assure data integrity. The user has to make sure all relevant data that needs to be archived for a defined period of time is saved in appropriate location.

⚠ CAUTION
Conversion of organ names after upgrade may result in different dose calculations. New names will be used for some organs in version 1.1.4 of QDOSE and following versions. If a case created in a previous version of QDOSE is opened, the organ names in that case may have changed in version 1.1.4 or higher. If a case from an older version of QDOSE is loaded with ODOSE version 1.1.4 or higher, the user should check the available organs and the corresponding segmentations. The user can create new organs if necessary or change the segmentation of the organs.

⚠ CAUTION
User defined organ names may not be included in dose calculation. If the user creates organs by defining own names, the cumulated activity of those names may not be considered for model-based dose calculation (IDAC-Dose). It is recommended to use only organ names that are in the predefined organ list.

⚠ CAUTION
Incorrect coregistration can lead to false segmentation. The coregistration results depend on the quality of the image data. The user must check the coregistration result for each time point. The user can adjust the display of the data sets as well as the overlay of the reference and 2:nd data set in order to compare the alignment between the data sets. The results from copying ROIs or VOIs to other time points depend on the quality of the registration between the data sets. After copy and paste of ROIs/VOIs, the ROIs/VOIs may not contain the organ or region at all time points due to local misalignment between the time points. The position of the ROI/VOI must be checked by the user for each organ and time point prior to performing further

processing steps. If the positions of the ROIs/VOIs are insufficient, the user can draw ROIs/VOIs on each time point separately or edit ROIs/VOIs manually after copying to the time points.

⚠ **CAUTION**

Incorrect organ segmentation results in incorrect dose values.

The dose calculation is based on the activity in the segmented regions. Phantom-based dose calculation is based on the assumption that the activity arises from the whole organ. If only a part of the organ is segmented or the segmentation also includes other organs, the calculated doses may be incorrect. The user should only include the organ corresponding to the selected organ name in the segmentation.

⚠ **CAUTION**

Incomplete or incorrect images result in incorrect dose values.

All calculated values depend on the quality of the input data. The input image data must be suitable to perform dose calculation. The user must check the image quality prior to any analysis. The user should always check available image data for completeness and correctness before performing analysis steps.

⚠ **CAUTION**

Incorrect quantified SPECT and PET image data result in incorrect dose values.

SPECT and PET images are assumed to be quantified in units of Bq/ml. Quantitatively reconstructed SPECT and PET images can be directly imported. In case SPECT or PET images are not reconstructed quantitatively, a scaling factor must be provided by the user and entered for each data set. Scaling factors for quantitative data may be stored in private tags of the DICOM image header depending on the manufacturer. It is the user's responsibility to check for the scaling factor. Please ask the manufacturer of your imaging system for further information.

⚠ **CAUTION**

Incorrect acquisition time result in incorrect dose values.

For data sets with multiple files the acquisition time of the first (earliest) slice is used as acquisition time. Acquisition time can be adapted in **Edit Case**.

⚠ CAUTION
Changing nuclide will reset added organs with precalculated Ã. Additional organs with precalculated Ã can be added in Dose Analysis window. The cumulated activity of those organs will be reset after changing the nuclide in Edit Case or in Dose Analysis. Always check the input to IDAC-Dose calculation by clicking the button **Input data**.

⚠ CAUTION
Simultaneous changes to the users' database might be lost The users' database should only be accessed by one admin at a time. Simultaneous changes to the user management might lead to data loss on the user management that was opened as second instance. Save changes immediately and do not leave the user management open for a longer period of time.

1.8.2 Important Advice

Important advice for QDOSE is structured as described here:

NOTICE
Notice description. A NOTICE is used to address practices not related to physical injury.

Please read the following important advice carefully before using the software.

NOTICE
Always check data for plausibility. User actions affect the results of the software. All displayed information including images, segmentation results, registration results, time-activity-curves and dose values should be checked for plausibility by the user.

NOTICE
Source organ naming influences the dose calculation. IDAC-Dose 1.0 and IDAC-Dose 2.1 use defined organs as input. It is highly recommended to use the predefined organ names from the organ list when creating a new organ. For IDAC-Dose 1.0 and IDAC-Dose 2.1 dose calculation, the user should check the input data by clicking on the button **Input data** in the tab **ICRP – IDAC-Dose** in the dose analysis step.

NOTICE
QDOSE dose values before version 1.1.4 will be reset. The user should be aware, that dose calculations of cases, which were created with a QDOSE version prior to 1.1.4, will be reset. In order to document the dose calculation performed with an older QDOSE version (prior to version 1.1.4), please export a report and/or CSV (comma-separated values) file of the case prior to updating to the new QDOSE version.

NOTICE

The default organ list differs between cases.

The user can select the organs that are displayed in the default organ list when creating new organs. Changes in the default organ list, which can be edited in the window **QSettings** using the button **Edit Organs …** to open the window **PreDefinedOrgans**, will only affect new cases. If the user opens other cases, the default organ list may differ from the current setting.

NOTICE

Source organs of OLINDA EXM 1.0, IDAC-Dose 1.0 and IDAC-Dose 2.1 have different definitions.

In some cases, OLINDA EXM 1.0 and IDAC-Dose 1.0 and IDAC-Dose 2.1 use different definitions of organs.

- The organs "Right colon contents (RC)", "Left colon contents (LC)" and "Rectosigmoid colon contents (RSC)" are used by IDAC-Dose 2.1 and are the default organs in QDOSE. If any or all of these source organs exist, the OLINDA source organs "ULI contents" and "LLI contents" will be created and Ã will be calculated according to:
  - ULI = RC + 0.478873 · LC
  - LLI = RSC + 0.521127 · LC
- If organs "Uterus/cervix" and "Uterus" both exist, the OLINDA export will use "Uterus" and will ignore "Uterus/cervix".
- If organ “LLI” exists, but also “RC” and/or “RSC”, OLINDA export will use the organ “LLI” and will not calculate Ã based on “RC” and “RSC”.
- If organ “ULI” exists, but also “RC” and/or “LC”, OLINDA export will use the organ “ULI” and will not calculate Ã based on “RC” and “LC”.

The user should check which organs were used for model-based dose calculation by clicking the button **Input data** in the window **Dose Analysis**.

NOTICE

Display of image data influences image processing.

The user has the responsibility to ensure the quality of the monitor and ambient light conditions.

NOTICE
Computer hardware influences performance. The performance of specific functions may vary for different hardware. No responsibility is taken for the execution time of specific functions.

2 Getting Started

Description of system requirements, installation process and how to set up QDOSE for first use.

2.1 System Requirements

- Windows 10 (64 bit), Windows 11 (64 bit)
- Memory of 8 GB; at least 12 GB are recommended for 3D coregistration
- Hard drive with at least 5 GB free space for the application. Database space depends on the number of cases and image data.
- Intel Core i-5 processor or higher
- Screen resolution minimum 1600x900 pixel
- Dedicated graphics card with OpenCL support (e.g. NVIDIA from generation GT200 or ATI from generation HD 4730, 5830, 6930, 7730, R7 240) for improved performance for 3D registration.
- PDF viewer (for viewing Report and User Manual)

2.2 Requirements IT Infrastructure

⚠ **CAUTION**
QDOSE should be used in a secure network. The IT security of the environment where QDOSE is operated is in the responsibility of the user.

⚠ **CAUTION**
Unauthorised persons can access sensitive data. Unauthorised access is prevented by user authentication (login) and authorization (roles and rights) measures. In addition, since QDOSE version 1.2.4 the databases are encrypted to prevent unauthorised access to the data by third parties. Users should upgrade old databases for encryption when proposed by the program. Still, the software should be used in an environment where user access is regulated by user accounts at the level of the operating system. No responsibility is taken for the access to sensitive data by unauthorised persons deliberately bypassing the security measures. It is in the user's responsibility to guarantee data protection strategies.

QDOSE is a standalone software that is not intended to be used with other devices or in an IT network. However, the user must provide a system that is secure. The following requirements must be provided by the user:

- Microsoft Windows operating system (Windows 10 or 11) with current safety update status
- Established firewall and established anti-virus application.

If a case was corrupted due to a failure to maintain security, the case might not be loadable anymore.

2.3 Installation

The installation of QDOSE is intended to be made by the user or an IT administrator. For installation of QDOSE please follow these instructions:

1. Run the provided QDOSE installer and follow the installation instructions.

   Note: During the first installation and if not already present, the MATLAB Runtime Compiler will be automatically installed on your system. Therefore, administration privileges are required.

2. Start the application QDOSE.exe via the program menu or using the QDOSE icon.

In case, the system (hardware or software) is changed, QDOSE needs to be installed again on the system, following the instructions above.

2.4 License Activation

If QDOSE does not find a valid license, it will prompt the user to import a valid license. In order to activate QDOSE with a valid license, follow these steps:

1. Please export the fingerprint file using the button **Export Key.**
2. Save the file on your file system and send it to QDOSE Support: qdose@kevimaging.gr
3. QDOSE Support will generate a valid license and send it back to you.
4. QDOSE Support will send the one-time token in a separate mail.
5. Start QDOSE and click on **Import License**.
6. Select the license file from your file system. After import and accepting the End User License Agreement and Data Processing Agreement, a **Login** window will appear.
7. Enter the super admin credentials with the one-time token and confirm:
   - User name: SuperAdmin
   - Password: <*token from QDOSE Support*>
8. The window **QSettings** will open. There, select an archive path as described in chapter 2.7.
9. Save the settings. Next, the **Patient Browser** will open.
10. Create and manage users and administrators as described in chapter 14.

In case a license has expired or a new license is required, QDOSE will prompt the user to import a new valid license. Follow the steps 1 to 9 again to activate a new license. A new one-time token will be necessary again.

In case the one-time token was consumed, and no QDOSE user or QDOSE administrator can access the program anymore, a new license with a new one-time token must be requested by the user. Please follow again steps 1 to 9.

2.5 Instructions for Use

The User Manual contains the instructions for use and technical description of the medical device QDOSE. They are supplied in electronic form instead of in paper form. The User Manual is available for download in different languages via QDOSE website (www.qdose.net) (using the country password provided upon product commissioning) and upon request from our support centre.
Please contact qdose@kevimaging.gr to get the current version in your local language.
A printed hardcopy (paper format) of the QDOSE User Manual can be requested for free by contacting the manufacturer, see contact information in chapter 1.2.
It will be delivered within 7 calendar days after receiving the request.

2.6 Start-up and Shutdown

To start the application, double click on the QDOSE icon or start it from your program menu.

To safely shut down the application, save your current work if necessary and close the software via **File > Quit** or via closing the window.

2.7 Archive path

⚠ **CAUTION**
QDOSE is not intended to store data permanently. It is the user's responsibility to perform backups of data and to assure database availability. The user has to make sure, all relevant data that needs to be archived for a defined period of time is stored at an appropriate location.

⚠ **CAUTION**
QDOSE database is not intended to be used by several users in parallel.

The database must only be accessed by one QDOSE instance at the time. If several users access the same database in parallel, data might be lost.

⚠ **CAUTION**

Encryption of database recommended.

Since QDOSE version 1.2.4 there is the possibility to encrypt the archive to protect the patient health data from unauthorised access outside of QDOSE. New archives are automatically encrypted. Archives created with versions prior to version 1.2.4 were encoded in a proprietary format and will be checked and the user can decide to encrypt them. This procedure is recommended to protect sensitive data.

The archive path defines the location of the database where the QDOSE cases are stored. Please choose the desired database location by following these instructions:

1. In the window **Patient Browser** click on the button **File** in file menu bar.
2. Select **Settings** to open the window **QSettings**
3. Browse through the file system to select an archive path by clicking on the button **Browse** or enter an existing archive path manually.
4. Click on the button **Save** to save the settings.

The user can create several databases (folders on the filesystem), but only one database can be selected in the software. A backup of the database can be created by copying the folder on the file system. By selecting this copy as archive path, the backup can be accessed.

2.8 Software Updates

Software updates and upgrades are issued by the manufacturer as new installation files. Please follow these steps to update the software program:

1. Download the new installation file as explained by QDOSE support.
2. Perform the installation as explained in chapter 2.3.
3. A new version of QDOSE requires a new license key. The user has to activate a new license key as described in chapter 2.4.
4. The successful installation as well as the license are validated. The user can check the installed version with the help of the version number displayed under **Help > About**.

2.9 Decommissioning

⚠ CAUTION
QDOSE databases must be carefully disposed by the user. The database(s) created and used by the user for QDOSE are not deleted. It is the user's responsibility to safely decommission or dispose the data or databases, which might contain sensitive data Since QDOSE version 1.2.4 all database are encrypted to protect patient health data. Old databases were encoded in a proprietary format and should always be upgraded for encryption, see **Notice** in section 2.7.

In order to decommission the application safely after it is no longer used, the software shall be deinstalled from the system. The deinstallation can be done using the program manager or by right-click on the application icon.

3 QDOSE Concept

This section describes the concept behind QDOSE and how it can be utilized for the calculation of internal radiation doses.

3.1 What is QDOSE?

QDOSE is a stand-alone software solution for calculating internal radiation dose distribution. QDOSE provides the following systemic workflows (Figure 1):

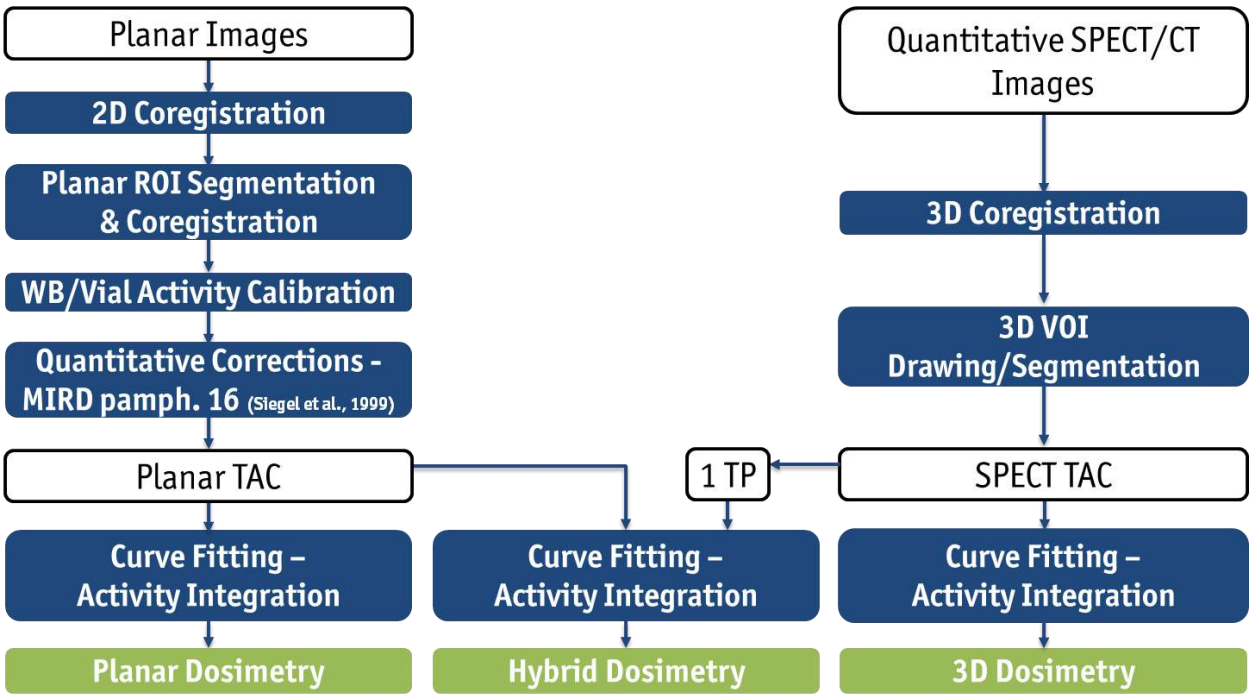


Figure 1: Systemic workflows: Planar, Hybrid, 3D.

3.1.1 Planar Workflow

In planar mode, multiple time points (TP) of planar scans (using conjugate plane view) are the base of dose calculations using the quantitative methodology according to MIRD pamphlet No. 16 (Siegel et al. 1999).

3.1.2 Hybrid Workflow

In hybrid mode, QDOSE performs dose calculations using multiple time points of conjugate view imaging (as in planar) for calculation of the kinetics, while one quantitative SPECT/CT is used to calibrate the time-activity-curve (TAC) according to MIRD pamphlet No. 16, Section IV.B SPECT (Siegel et al. 1999) and MIRD pamphlet No. 23, Section Hybrid Planar/SPECT Methods (Dewaraja et al. 2012)

The activity distribution within an organ is provided by Voxel S dose calculation. The volumetric scan can also be used for calculation of the organ volume and subsequently for the organ mass for more patient-specific dose calculation.

3.1.3 Volumetric (3D) Workflow

QDOSE volumetric mode uses multiple time points of volumetric images (at least two) for calculation of organ kinetics as well as organ volume/mass and activity distribution. All calculations are hence performed using the 3D data.

3.1.4 SIRT/MAA Workflow

This mode is used for Selective Internal Radiation Therapy (SIRT) for:

- Post-treatment dosimetry using a single time point ^{90}Y PET/CT or Bremsstrahlung SPECT/CT
- Pre-treatment dosimetry using ^{99m}Tc-MAA SPECT/CT

3.2 Basic workflow

QDOSE provides a workflow which guides the user through the steps required to perform the chosen calculation method as described above. Even though QDOSE promotes a certain workflow, the workflow is dynamic. The user can go back and forth anytime and redo previous steps.

The generally required steps are displayed in the flowchart and outlined below (see Figure 2).

Figure 2: Internal dosimetry steps.

- *Case creation*: A case is the data container keeping all data for one radionuclide therapy or diagnostic dosimetry evaluation together, e.g. it contains all data for one dose cycle of radionuclide for one patient.

- *Upload of images*: Depending on the selected workflow, images can be selected either one-by-one through the menu **Data Import** or bundled using the menu option **Multiload** for fast data loading.
- *Planar (2D) coregistration*: Registration of planar images (planar and hybrid workflow only) to accelerate ROI drawing (next step).
- *Region of interest (ROI) drawing*: To define boundaries of different organs. There is no need to exactly delineate the organ, as organ segmentation will be done in the next step. The following two organs are handled separately:
    - Total body: Definition of the organ **Total Body** for calculation of the organ **Remaining Body**. QDOSE requires an organ **Total Body** to exist in order to provide access to the next step, in which the whole body (WB) is used for activity calibration of the planar images.
    - Vial: An organ called **Vial** can be defined for a vessel containing a portion of the same radionuclide as the injected one. The reference vial can be coregistered separately to the transmission image. This is necessary for proper attenuation correction, if the reference vial is chosen for the activity calibration.
- *ROI segmentation*: Each organ is segmented based on a reference time point, within the boundary defined in the ROI drawing step. The segmented area (organ) is further used for a second organ-based coregistration to compensate for organ movements.
- *Volume of interest (VOI) segmentation*: If volumetric data are uploaded, the CT and NM data (SPECT or PET) can be fused for visualization purpose. 3D boundaries can be defined and volume and activity within each boundary can be calculated. QDOSE provides two separate VOIs for calculating the anatomical volume on the one hand side and the activity volume on the other hand side. This is based on the assumption that the VOI containing the activity should be larger than the VOI of the anatomical volume. The reason is the inferior resolution of the NK image, which results in partial volume effect.
- *3D coregistration*: Since multiple volumetric time points can be loaded simultaneously, QDOSE also provides a volumetric coregistration tool. The coregistration tool enables coregistration of different time points (based on the CT images) or within each time point (CT-NM).
- *Dose calculation*: For this step, QDOSE provides tools for:
    - Mono-, bi- or tri-exponential curve fitting for TACs
    - Calculation of cumulated activity
    - Safety dosimetry using phantom-based dose calculation (IDAC-Dose 1.0 or IDAC-Dose 2.1 software (Andersson et al., 2017), export case file to OLINDA/EXM 1.1 (Stabin et al., 2005)), spherical model or Voxel S

- Efficacy dosimetry using Voxel S or spherical model
- Dose prediction (activity extrapolation and/or nuclide replacement)
- Dose calculation for SIRT for post-treatment dosimetry (^{90}Y) or pre-treatment dosimetry (^{99m}Tc-MAA)

- *Report generation*: Reports can be generated in PDF format using QDOSE report generator.

4 Settings

The window **QSettings** allows editing general settings for the use of QDOSE.

The window **QSettings** can be opened by using the file menu bar in the window **Patient Browser** by clicking on **File** > **Settings**. The following settings can be accessed and edited (see Figure 3):

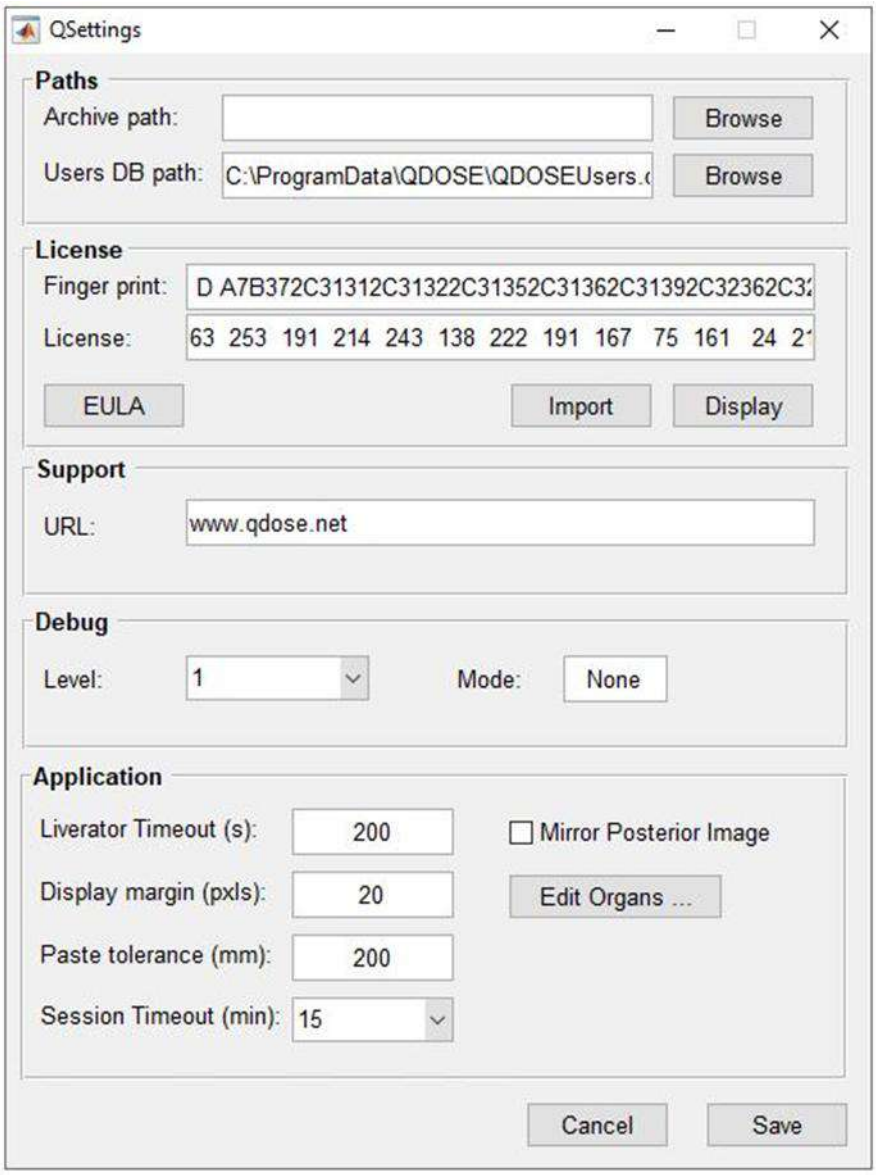


Figure 3: Window QSettings.

- **Paths**:
    - **Archive path***:* In the archive path the case database is stored. This path can be changed in order to create another QDOSE case database.

  - **Users DB path***:* In the users DB (database) path the database for the user management is stored. By default, the users' database is created under '*C:\ProgramData\QDOSE*'. This path can be changed to another database file (*.db7) in case of multiple QDOSE installations. See chapter 14.2.5 for more details how to setup the user management for multiple QDOSE installations

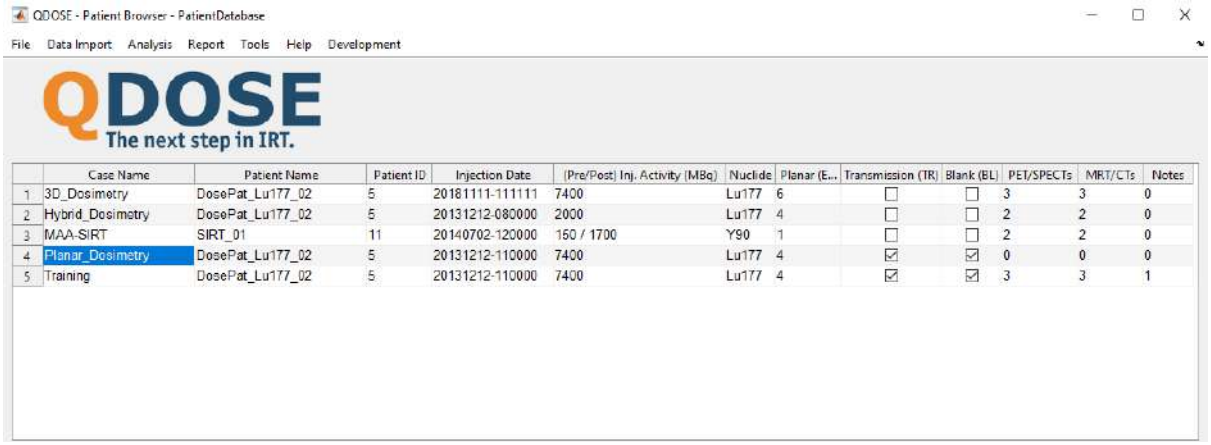
- **License**: The fingerprint of the system and the current license is displayed.
  - Clicking on the button **Display** shows detailed license information.
  - Clicking on the button **Import** enables selecting and importing a license file.
- **Support**: The web address of the QDOSE support homepage is displayed and can be edited.
- **Debug**: Defines the level of debug information that is printed in the log file.
- **Application**: Parameters for different processing steps are defined here.
  - **Liverator timeout (s)***:* The timeout in seconds for which the automatic AIT-Liverator segmentation algorithm cancels the processing.
  - **Display margin (pxls)***:* The margin in pixels that is additionally shown around the drawn boundary in the window **ROI Segmentation**.
  - **Paste tolerance (mm)***:* The acceptable tolerance in mm for copy and paste of VOIs between different time points.
  - **Session Timeout (min):** The period of a session after which the current user is automatically logged out. After timeout, the access to the program is declined. The user has to authenticate again to grant access to the software again.
  - **Mirror Posterior Image***:* Select if the posterior planar image should be displayed mirrored.
  - **Edit organs**: Dialog window for defining the organs that are displayed by default in the window **Create Organ**

5 Patient Browser

The window **Patient Browser** offers the possibility to overview all cases in the database, manage cases (create, delete, edit), handle image data (load and edit) and start the analysis steps

5.1 Jump Start

The window **Patient Browser** is the QDOSE main screen to manage cases, launch different tools or import the required image data for dosimetry evaluation. All tools can be accessed via the file menu bar. An overview of the cases is displayed in the table in the window center (see **Figure 4**).



	Case Name	Patient Name	Patient ID	Injection Date	(Pre/Post) Inj. Activity (MBq)	Nuclide	Planar (E...	Transmission (TR)	Blank (BL)	PET/SPECTs	MRT/CTs	Notes
1	3D_Dosimetry	DosePat_Lu177_02	5	20181111-111111	7400	Lu177	6	☐	☐	3	3	0
2	Hybrid_Dosimetry	DosePat_Lu177_02	5	20131212-080000	2000	Lu177	4	☐	☐	2	2	0
3	MAA-SIRT	SIRT_01	11	20140702-120000	150 / 1700	Y90	1	☐	☐	2	2	0
4	Planar_Dosimetry	DosePat_Lu177_02	5	20131212-110000	7400	Lu177	4	☑	☑	0	0	0
5	Training	DosePat_Lu177_02	5	20131212-110000	7400	Lu177	4	☑	☑	3	3	1

Figure 4: Window and main screen Patient Browser.

1. Create a case with information about nuclide, injected activity, injection date and time as well as the desired dosimetry workflow (Default, SIRT/MAA) by clicking on **File** > **New Case**. An empty case will be created and displayed in the window **Patient Browser**.
2. Select the case and import image data by either right-clicking on the case in the table or using the file menu option by clicking on **File** > **Data Import**.

   Note:

   - The option **Multiload** will scan through the user-selected root directory and display an overview of all DICOM images found in that specific folder and its subfolders.
   - If using the option **Multiload**, once scanning is completed, press **CTRL** and click on the desired series to select/unselect the images (planar, blank, transmission, SPECT/PET, CT, MR) that need to be loaded into your case.

- Once all required series are imported, the window **Multiload** will prompt the loading result for each series, either successful or failed with a description. This window can then be closed.
- Alternatively, images can be loaded via a modality-specific loading dialog by clicking on **File** > **Data Import**. Options are: **Planar Joined ANT-POST** or **Planar Separate ANT-POST**, **SPECT**, **PET**, **CT**. E.g. the option **SPECT** allows selecting a specific SPECT series in the file system for upload.

3. To check/edit loaded image data for that specific case, click on **File** > **Edit Case**.

   Note:

   - For planar data, the energy window for analysis and the nuclide used in the transmission and blank scan (for attenuation correction) can be selected. The type of image can also be changed in column **Type** from the default **Emission (EM)** to **Transmission (TR)** or **Blank (BL)**. This step is required, as all planar images are initially uploaded as emission images in the window **Multiload**.
   - For SPECT data, the scaling factors to convert pixel values to Bq/ml can also be defined in the columns **Image Unit** and **Scale F.**

4. For a selected case, the different analysis steps can be started from the **Patient Browser** using the file menu by clicking on **Analysis** > **Dose Analysis** or right-clicking on the selected case and selecting **Dose Analysis**.

   Note: The case data is not saved until manual saving by clicking on **File** and select **Save Case** in the file menu or by pressing the shortcut **CTRL + S**.

Shortcuts

- **CTRL + S*:*** Save case (image data and evaluation steps and results)
- **Right-click*:*** opens the context menu of the selected case to load data or access the specific evaluation steps.
- **CTRL + Click:** Add/remove item to/from the current selection in the window **Multiload**.

5.2 Menu Bar Items

The following options are available in the file menu bar in the window **Patient Browser**:

5.2.1 File

- **New Case**: Creates a new case.
- **Edit Case**: Opens a window to view and handle case related image data and case information (see 5.4)

- **Save Case**: Saves current status of the case including regions and evaluations performed.
- **Save Case As**: Saves a copy of the current case with different case name.
- **Delete Case**: Removes the selected case.
- **Import Case**: Imports a QDOSE case from the file system.
- **Export Case**: Exports the selected case with all information to the file system.
- **Settings**: Opens the QDOSE Settings.
- **Quit**: Quits QDOSE.

5.2.2 Data Import

⚠ CAUTION
Store input image data in a secure place. DICOM images that are intended to be used as input for QDOSE should always be stored in secure place that prevents unauthorised access to sensitive data (patient health data). Storage mediums should either be encrypted or stored in a Picture Archiving and Communication System (PACS) and access to these data should be controlled. After import of image data, QDOSE will store an encrypted copy of the input images in its database in its proprietary format (not DICOM). DICOM image data that is no longer used, should be deleted from the storage medium.

⚠ CAUTION
Preview and report images are not for clinical review. Preview images and images in the report are only for data set identification purpose. They must not be used for diagnostic purposes of any kind.

⚠ CAUTION
Incomplete or incorrect image data results in incorrect dose values. The option **Multiload** can identify associated planar scintigraphy images, whose anterior and posterior views are stored in separate files. In that case, the separated files are loaded jointly as one image time point. The user should check in the window **Edit Case**, whether the anterior and posterior views are correctly associated to ANT and POST, respectively. If not, the anterior and posterior images can be swapped.

NOTICE
Invalid image data results in incorrect dose values. QDOSE only supports anterior and posterior planar scintigraphy images, SPECT, PET, CT in axial slices and MRI in axial slices (only morphological, T1, T2 weighting). Unsupported modalities or image data may result in incorrect function of the software. Unsupported data sets may be rejected during loading. The user should always check the available image data for completeness and correctness before performing analysis steps.

- **Multiload**: Dialog box to scan through folders and subfolders for DICOM series. It only allows loading of relevant DICOM data types (planar scintigraphy images, SPECT, PET, CT (axial slices), MRI (axial slices)).
- **Planar Joint ANT/POST**: Dedicated dialog for loading planar data where ANT and POST views are stored within one file.
- **Planar Separate ANT/POST**: Dedicated dialog for loading planar data where ANT and POST views are stored in separate files.
- **SPECT**: Dedicated dialog for loading SPECT data.
- **PET**: Dedicated dialog for loading PET data.
- **CT**: Dedicated dialog for loading CT data.

5.2.3 Analysis

- **2D Coregistration**: Opens a window for coregistration of planar data.
- **ROI Drawing**: Opens a window to define (draw) boundaries on planar data.
- **ROI Segmentation**: Opens a window to segment and coregister organs on planar data in the predefined boundaries.
- **3D Coregistration**: Opens a window for volumetric coregistration between time points and within each time point.
- **VOI Segmentation**: Opens a window to define 3D organ boundaries and segment within the boundaries.
- **Dose Analysis**: Opens a window for curve fitting and dose calculation.

5.2.4 Report

- **Generate Report**: Generates a report for the selected case.
- **Notes**: Opens the notes dialog to view or add case related notes.

5.2.5 Tools

- **Activity Prediction:** Activity calculation tool for SIRT.
- **Change password:** Dialog to change the current user's password.
- **Change user:** Dialog to change the current user by re-authentication.
- **User Management:** Opens a window to manage users and roles.

5.2.6 Help

- **QDOSE Help**: Opens the QDOSE user manual.
- **About**: Opens the about dialog with version, unique device identifier (UDI) and support contact information.
- **License**: Displays the modules and nuclides available in the current license.
- **End User License Agreement**: Displays the terms and conditions for using the QDOSE license.
- **Data Processing Agreement**: Displays the terms and conditions of Data Processing.
- **Copyright**: Opens the copyrights statement window.
- **Export log file**: Creates a log file at a specified file path.
- **Support**: Opens the support website to raise support requests.
- **User Manual**: Opens the QDOSE user manual.

5.3 Create Case

NOTICE
The calibration method for planar images influences the dose calculation. For the activity/sensitivity calibration of planar images, the user can define whether to use a whole body (WB) calibration or Vial calibration.

A case is the data container keeping all data for one radionuclide therapy or diagnostic dosimetry evaluation together, e.g. it contains all data for one dose cycle of radionuclide for one patient.

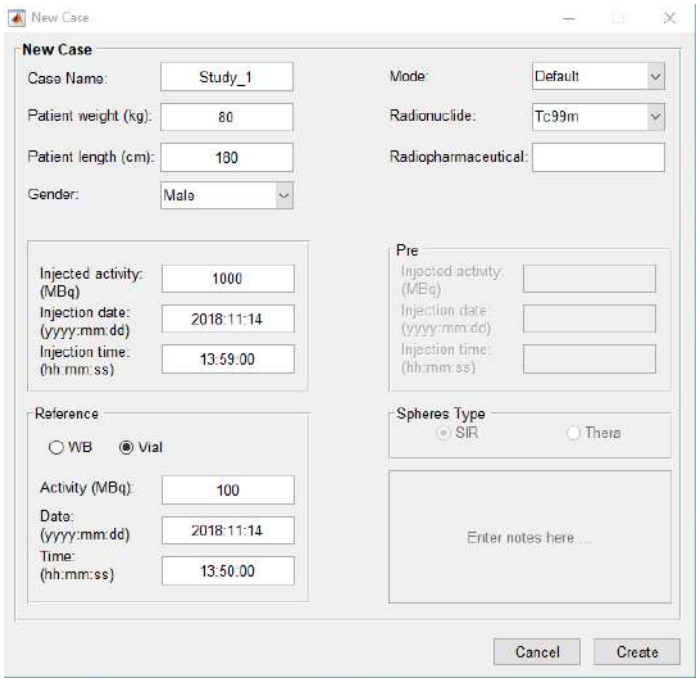


Figure 5: Window New Case.

1. In the window **Patient Browser** click on the button **File** in the file menu bar.
2. Select **New Case** to open the window **New Case** (see Figure 5).
3. Enter all required information. The case name is saved case-insensitive. Therefore, two cases with the same names are not allowed.

   The date format is year:month:day (yyyy:mm:dd), e.g. 2018:11:14 and the time format hour:minute:second (hh:mm:ss), e.g. 13:59:00.

   Note: The required information depends on the chosen **Mode: Default | MAA/SIRT.**
4. Click on the button **Create** to save the case.

5.4 Edit Case

⚠ CAUTION
Incorrectly quantified SPECT and PET image data result in incorrect dose values. SPECT and PET images are assumed to be quantified in units of Bq/ml. Quantitatively reconstructed SPECT and PET images can be directly imported. In case SPECT or PET images are not reconstructed quantitatively, a scaling factor must be provided by the user and entered for each data set. Scaling factors for quantitative data may be stored in DICOM tags (including private tags) of the DICOM image header depending on the manufacturer, e.g. Real World Value Mapping Sequence, Rescale Slope. It is the user's responsibility to check for the scaling factor. Please ask the manufacturer of your imaging system for further information.

⚠ CAUTION
Changing nuclide will reset added organs with precalculated Ã. Additional organs with precalculated Ã can be added in Dose Analysis window. The cumulated activity of those organs will be reset after changing the nuclide in Edit Case. Always check the input to IDAC-Dose calculation by clicking the button **Input data**.

NOTICE
Different scans lengths between planar time points may influence time activity curve. All planar images are normalized to the total scan duration given in the DICOM header to correct for different scan speeds for different time points. It is assumed that the images have the same scan length.

NOTICE
PET data that are decay corrected to time of administration cannot be analysed. QDOSE evaluates the DICOM tag 'Decay Correction', Only image data with values 'NONE' and 'START' can be evaluated with QDOSE. For PET, the acquisition time of the temporally first (earliest) slice is regarded as acquisition time for the entire PET image. Acquisition times can be manually adapted in the corresponding image tables in **Edit Case**. Images that are decay corrected to the time point of administration of the radiopharmaceutical (value 'ADMIN'), cannot be imported into QDOSE.

NOTICE
Changes to the data sets and the times are applied instantly. In Edit Case different information about the case and the imported data sets can be edited. Changes to the data sets entered in the data set tables (e.g. acquisition times, scaling factors), changes to the time of injection and the selected nuclide will instantly change the case information even without clicking the Apply button. Also, the deletion of data sets cannot be undone.

The window **Edit Case** offers the possibility to view and handle case related image data and case information.

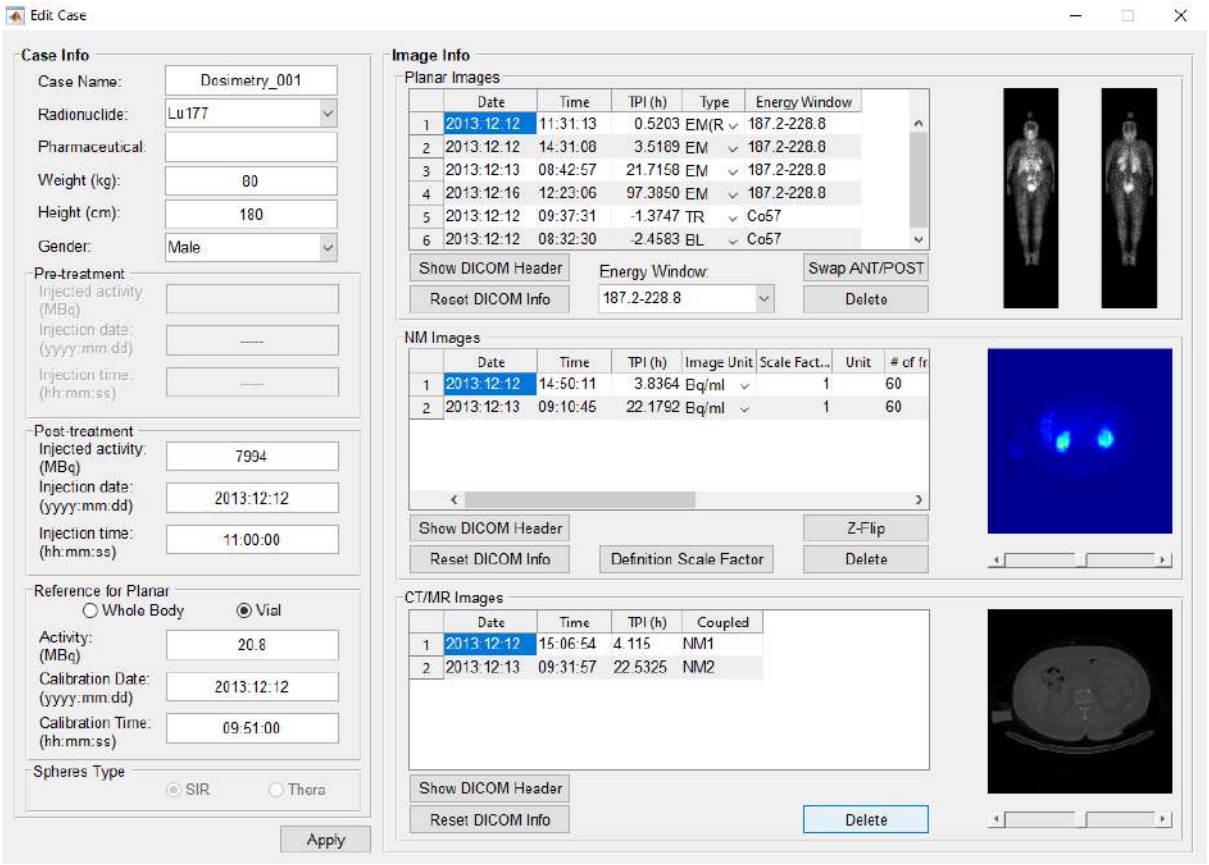


Figure 6: Window Edit Case.

1. In the window **Patient Browser** click on the button **File** in the file menu bar. Select **Edit Case** to open the window **Edit Case** (see Figure 6).
2. Edit the required information of the case. The information is structured in the following panels and tables:
    - **Case info**: For editing all case related input values

- **Image info**:
    - **Planar Images**: Table containing loaded planar image data for all time points.
    - **NM Images**: Table containing loaded nuclear medicine (NM) image data for all time points.
    - **CT/MR Images**: Table containing loaded CT/MRI image data for all time points.

3. In the **Planar Images** table define the type of the image (EM: emission scan, BL: blank scan, TR: transmission scan) in the column **Type**. Select the energy window for analysis in the column **Energy Window**. For transmission and blank scan, you can select the nuclide (Co57 or Tc99m).

   Note: An asterisk ***** behind the image type indicates which image is already coregistered.

   Note: **(R)** indicates which image is chosen as reference image for coregistration.

4. Define the image units and scale factors for the nuclear medicine data sets in the table **NM Images** in the columns **Image Unit** and **Scale Factor**. More details can be found in section 5.4.1.

   Note: The DICOM field Real World Value Mapping Sequence will not be taken into account. Please enter the value of the Real World Value Slope as **Scale Factor**.

5. For single NM images, select the associated morphological images (CT or MR) in the table **NM Images** in the column **AssociatedCT**.

   Note: If NM and CT images were acquired simultaneously, the CT images are automatically coupled to the corresponding NM image, see column **Coupled** in table **CT/MR Images**. In case, single NM images are acquired and no corresponding CT/MR series is available, they can be associated manually as described above.

6. For **SIRT/MAA** mode, select whether the NM image is to be used as pre-treatment data set (option **PRE**) or as post-treatment data set (option **POST**) by selecting the corresponding option in the table **NM Images** in the column **AnalysisGroup**.

Note: An asterisk ***** behind the coupled NM image indicates which image is chosen as reference for coregistration. The following additional actions can be performed:

- Deletion of selected data sets (separately for planar images, NM images, CT/MR images).
- Modification of the time information of the selected data set.
- Display of DICOM header information of the selected data set.
- Reset of the selected data set to the original DICOM information.

5.4.1 System Calibration Factor

There are two ways to determine a system calibration factor for image units “Counts” for a particular radionuclide: by scanning a point source/vial or a uniformity phantom. Depending on the quality of the scatter correction of the reconstruction algorithm, the user has to decide which method is more appropriate. If scatter correction is not adequate (likely case) a calibration based on a uniformity phantom close in size and hence scatter properties to a patient is recommended.

5.4.1.1 Point Source

1. Prepare a point source with a known total activity (activity should be below dead time effects)
2. Perform a SPECT/CT scan of the source with scanning parameters similar to the patient protocol
3. Reconstruct the data including scatter and attenuation correction using the same reconstruction algorithm as for the patient data
4. Draw a VOI around the point source to measure all counts belonging to the source
5. Divide the measured counts by the total number of projection for 360° multiplied with the time per projection
6. Divide the known total activity in the point source by the calculated counts per scan time which will give you the calibration factor to be entered into QDOSE.

$$\mathrm{SF}\left[\frac{\mathrm{Bq}}{\mathrm{cps}}\right] = \frac{\text{Activity in Vial [Bq]}}{\dfrac{\text{Total Counts}}{(\text{Number of Projections for } 360° \cdot \text{ Time per Projection [s]})}}$$

5.4.1.2 Uniformity Phantom

1. Prepare a uniformity phantom with a known activity concentration e.g. using a cylinder phantom
2. Perform a SPECT/CT scan of the phantom with scanning parameters similar to the patient protocol
3. Reconstruct the data including scatter and attenuation correction using the same reconstruction algorithm as for the patient data
4. Draw a VOI inside a homogenous region of the phantom to measure the total counts inside the VOI
5. Divide the measured counts by the total number of projections for 360° multiplied with the time per projection multiplied with the volume of the drawn VOI in ml
6. Divide the known activity concentration in the phantom by the calculated counts per scan time which will give you the calibration factor to be entered into QDOSE.

$$\mathrm{SF}\left[\frac{\mathrm{Bq}/\mathrm{ml}}{\mathrm{cps}/\mathrm{ml}}\right] = \frac{\text{Activity Concentration in Phantom } \left[\mathrm{Bq}/\mathrm{ml}\right]}{\dfrac{\text{Total Counts in VOI}}{(\text{Number of Projections for } 360° \cdot \text{ Time per Projection [s]}) \cdot \text{VOI Volume [ml]}}}$$

6 2D Coregistration

2D Coregistration allows fused view as well as automatic and manual coregistration of whole-body planar image between different time points.

⚠ **CAUTION**
Incorrect coregistration can lead to incorrect segmentation. The coregistration results depend on the quality of the image data. The user must check the coregistration result for each time point. The user can adjust the display of the data sets as well as the overlay of the reference and 2:nd data set in order to compare the alignment between the data sets.

The window **2D Coregistration** provides functionality to view and coregister the planar images from different time points including the transmission image. The tool also enables the user to choose the active view for the blank- and transmission images that are consequently used for attenuation correction throughout the planar calculations (see Figure 7).

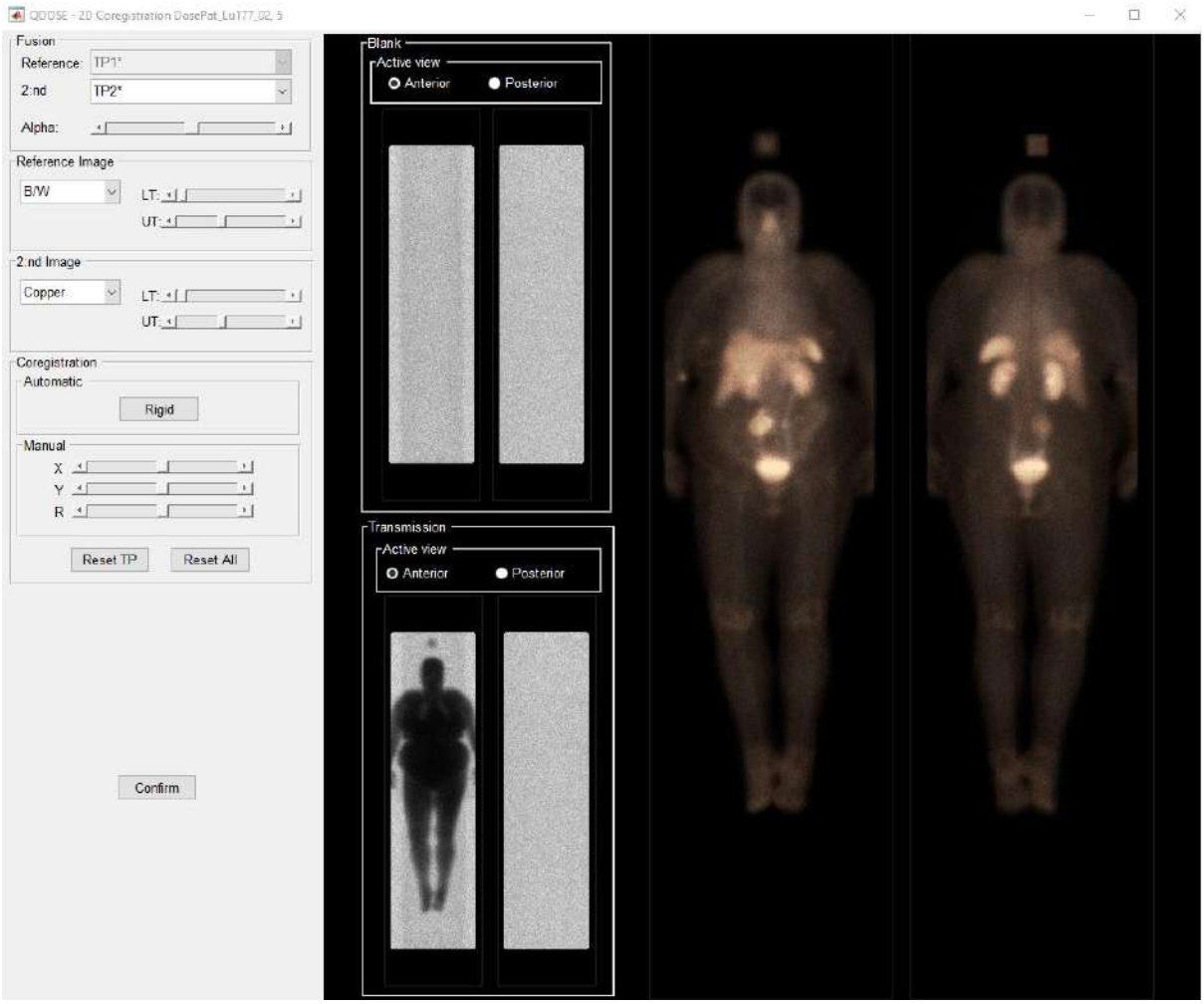


Figure 7: Window 2D Coregistration.

1. The panel **Fusion** contains two dropdown menus to select the images to be coregistered. Select an appropriate reference image from the menu **Reference** and the intended image from menu **2:nd** for fused view with an alpha blending defined by the slider **Alpha**.
2. Select the color maps and windowing for both images in the panels **Reference** and **2:nd**.
    - The color map can be chosen from the dropdown menu.
    - The windowing can be adjusted using the sliders for **UT** (Upper Threshold) and **LT** (Lower Threshold).
3. Perform coregistration between the reference and the chosen image in the panel **Coregistration** using the following options:
    - **Automatic**: Perform automatic rigid coregistration by clicking on the button **Rigid**.
    - **Manual**: Alternatively, or additionally, manual coregistration (translation and rotation) between the displayed image data can be performed by clicking on the sliders:

- **X**: for translation in X-direction
- **Y**: for translation in Y-direction
- **R**: for rotation around the image center.

Note: After the first coregistration the reference image is fixed.

Note: Coregistered images are indicated by an asterisk ***** in the dropdown menu in panel **Fusion.**

4. Select the next image to be registered from the dropdown menu **2:nd** and perform coregistration (automatic and/or manual).

   Note: The coregistered image is resized to the reference image. Moving the chosen image outside the boundary of the active view can lead to a truncation of image sections. To revert to the original view, the coregistration can be reset.

   Note: The coregistration can be reset for single time points by clicking on the button **Reset TP** or for all time points by clicking on **Reset All** to undo all changes and revert to the originally uploaded coordinates.

5. Select the active view for the blank and transmission images in the panel **Blank** and **Transmission**.

6. After all time points are coregistered, press the button **Confirm** to save the analysis steps and to close the window.

7 ROI Drawing

ROI Drawing allows for defining organ boundaries and background region for each organ on planar data for later segmentation.

As described in the QDOSE concept, organ segmentation is performed in two different steps. In the first step, organ boundaries are defined (drawn) and in a second step, organ segmentation based on the boundaries is performed. Organ drawing can be performed on anterior or posterior view, zoomed view, also on any time point, and organ boundaries can be copied and pasted to other time points (see Figure 8).

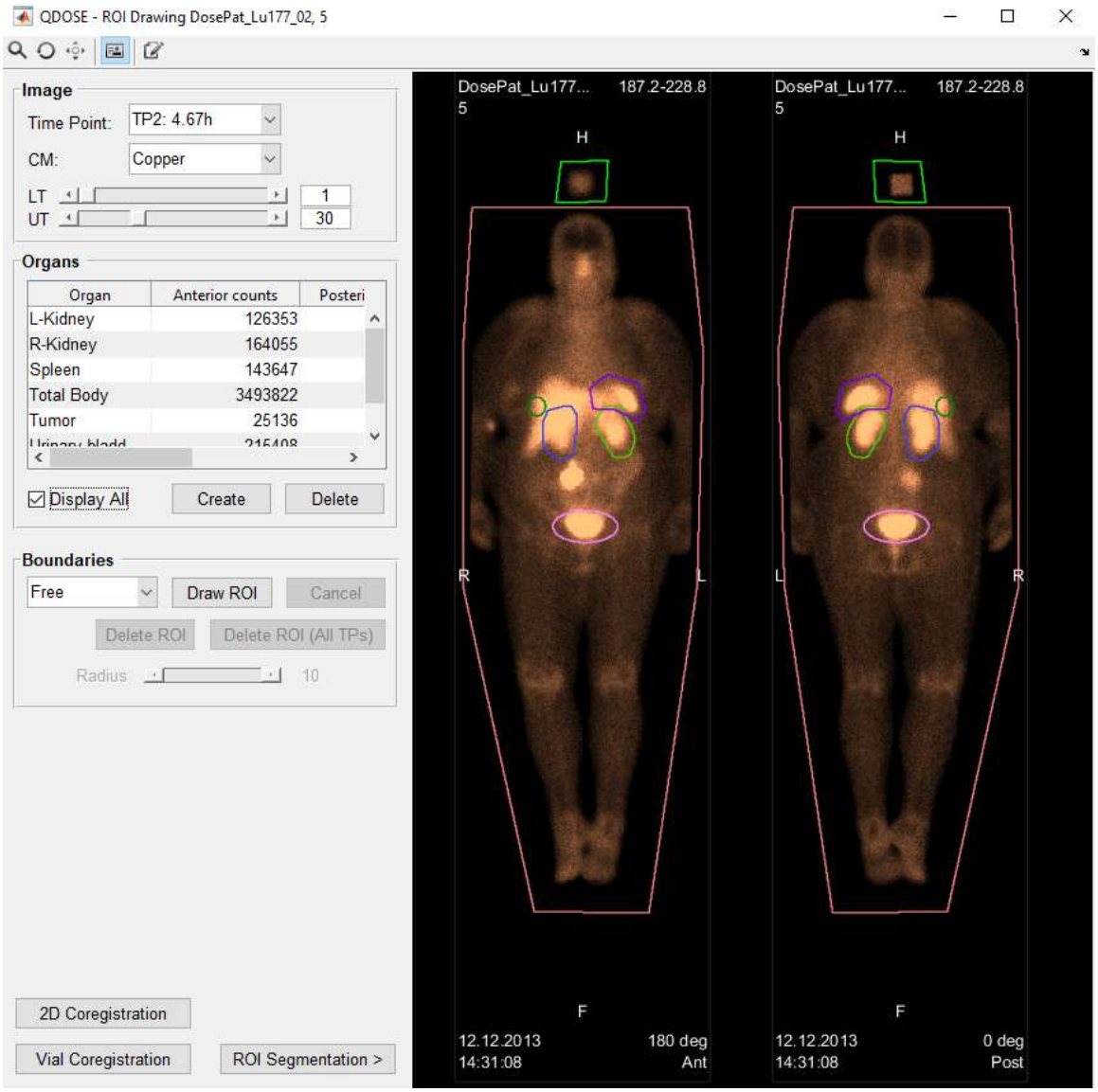


Figure 8: Window ROI Drawing.

7.1 Define an Organ

⚠ CAUTION
Incorrect organ segmentation results in incorrect dose values. The user should check the correct position of the boundary for organ delineation. The user can adjust the display of the image in order to improve visibility of the image data relative to the drawn boundary.

⚠ CAUTION
Vial calibration should be used with blank and transmission scans. If **Vial** is set as activity reference, it is highly recommended to use transmission and blank scans for correct attenuation correction. For this purpose, the organ **Vial** in the emission scans can be separately coregistered to the transmission scan in the window **Vial Coregistration** (see section 7.6).

NOTICE
Whole body calibration needs a segmentation of organ Total Body. If the **Whole Body** is set as activity reference, an organ **Total Body** will be mandatory to proceed with the evaluations.

NOTICE
Vial calibration needs a segmentation of a Vial. If a **Vial** is set as activity reference, an organ **Vial** will be mandatory to proceed with evaluation.

An organ is the central element for the dosimetry. In QDOSE the source organs of the radioactivity need to be defined to calculate the dose for all other body organs. Organs need to be created and then boundaries and segmentations for ROIs in 2D and VOIs in 3D can be assigned to them.

1. Select the intended image in panel **Image** from the dropdown menu **Time Point**.
2. Select the color maps and windowing in the panel **Image**:
    - The color map can be chosen from the dropdown menu **CM**.

- The windowing can be adjusted using the sliders for **UT** (Upper Threshold) and **LT** (Lower Threshold) or the field right next to it.

3. Create an organ by clicking the button **Create** in the panel **Organs**. Select from the predefined organ list in the dropdown menu or select the option **New…** and enter a name (e.g. for tumour). Confirm by clicking on **Create** (see Figure 9).

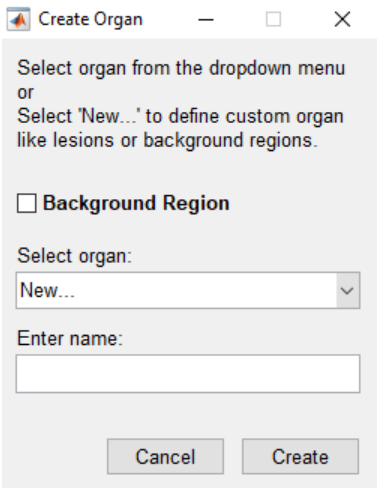


Figure 9: Window Create Organ.

4. Select a drawing mode from the dropdown menu in the panel **Boundaries**. Drawing options are:
    - **Free**: Draw a boundary by keeping the left mouse button pressed and painting with the mouse like with a pencil.
    - **Polygon**: Draw a boundary by clicking position-by-position around the region in the image. The positions are combined automatically to a polygon.
    - **Ellipse**: Draw a boundary by spanning the ellipse with the left mouse button pressed to the desired size.
5. Click on the button **Draw ROI** in the panel **Boundaries**.
6. Activate the anterior or posterior view by clicking into the image. A white box highlights the activated view.
7. Zoom and pan over an organ if needed using the toolbar elements (see section 16).
8. Draw the boundary to delineate the organ roughly as described for the drawing options. Further editing can be done following the steps in section 7.3.
9. Click on the button **Save ROI** in the panel **Boundaries** to save the drawn boundary.
10. Information on the organ is automatically updated in the table **Organs**.

7.2 Define Background ROI

⚠ CAUTION
Background correction is only applied when background ROI and Patient/Organ thickness is defined. Background correction for 2D planar images can only be performed, if a background ROI is connected to an organ and the patient and the organ thickness is defined for that organ. Otherwise, no background correction is performed. Background ROIs can be created and connected to an organ in the window **ROI Drawing**. Patient and organ thickness can be measured in the window **VOI Segmentation** or can be entered in window **Organ Properties** via the window **Dose Analysis**.

Detailed information about the correction mechanisms including background correction and the necessary steps can be found in section 11.2.

1. Select the intended image in panel **Image** from the dropdown menu **Time Point**.
2. Select the color maps and windowing in the panel **Image**:
    - The color map can be chosen from the dropdown menu **CM**.
    - The windowing can be adjusted using the sliders for **UT** (Upper Threshold) and **LT** (Lower Threshold) or the field right next to it.
3. Create an organ by clicking the button **Create** in the panel **Organs**. Select from the predefined organ list in the dropdown menu or select the option **New…** and enter a name for the background ROI (e.g. Background).
4. Tick the checkbox Background (see Figure 10).
5. Confirm by clicking on **Create**. The background ROI is displayed in the organ table with an appended **(bkg)**.
6. Draw a ROI the same way as described in section 7.1, steps 4 - 10.
7. Link the background ROI to an organ by right-clicking on the intended organ in the table Organs and selecting the background ROI as shown in Figure 11.

Note: It is possible to use one background ROI for different organs.

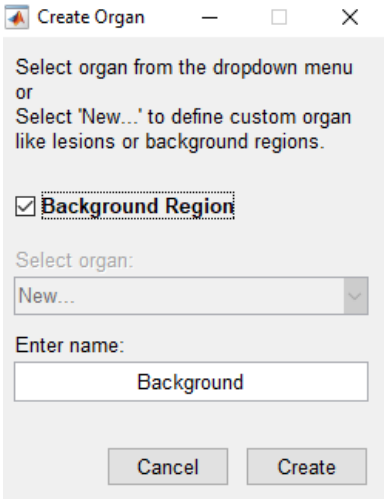


Figure 10: Option Background in window Create Organ.

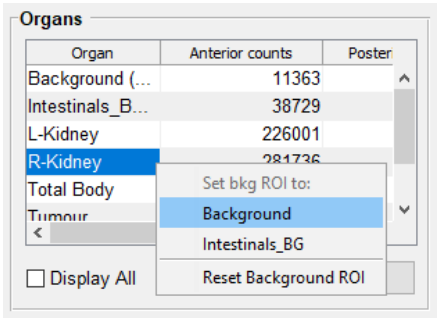


Figure 11: Option to link Background ROI to Organ in table Organs.

7.3 Edit Organ

1. Select the organ to be edited from the table **Organs**, if not already selected.
2. Click on the drawn boundary in the image. The boundary will turn to white color.
3. You have two options to edit the ROI:
    - *Moving*: to move the entire region, press **Shift** and move the whole object to the new location via drag and drop.

      Note: Do not click to closely to the white boundary when moving via drag and drop.
    - *Painting*: to paint the boundary brush-like, keep the left mouse button pressed until a white circle is displayed (see Figure 12). Edit the boundary from the region outside or inside, by moving the circle like a brush. The left mouse button needs stay pressed. The radius of the circle can be changed using the slider **Radius** in the panel **Boundaries**.

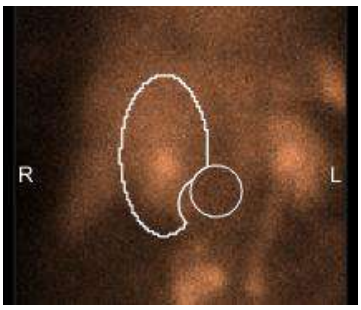


Figure 12: Brush Tool.

4. Click on the button **Save ROI** in the panel **Boundaries** to save the edited boundary or click on the button **Cancel** in the panel **Boundaries** to discard any changes to the boundary.
5. Information for the organ is automatically updated in the table **Organs**.

7.4 Copy/Paste Organ

⚠ **CAUTION**
Incorrect organ segmentation results in incorrect dose values. After copy and paste of ROIs, the ROIs may not contain the organ or region at all time points due to local misalignment between the time points. The user must check the position of the ROI for each organ at each time point. This can be done by selecting the organs in the table **Organs** and scrolling through all time points while checking the position in the window **ROI Segmentation**. If the positions of the ROIs are not sufficient, the user can edit the organ boundary for each time point in the window **ROI Drawing**.

The source organs must be defined in the images for all time points in order to include them in the time-activity-curve calculation. The ROIs for the organs can be copied and pasted from one time point to another.

1. Select the intended image in panel **Image** from the dropdown menu **Time Point**.
2. Select the organ to be copied from the table **Organs**, if not already selected.
3. Right-click on the image will open an options list. Select **Copy ROI**.
4. Select the next intended time point in panel **Image** from the dropdown menu **Time Point**.
5. Right-click on the image will open an options list (see Figure 13). Here you have the following options:
    - **Paste ROI**: Pastes the copied ROI to this time point only.
    - **Paste ROI to All**: Pastes the copied ROI to all time points in this case, including the transmission scan.
6. Alternatively, the option **Propagate** (see Figure 13) can be used to copy and paste all organs from the chosen time point to all time points.

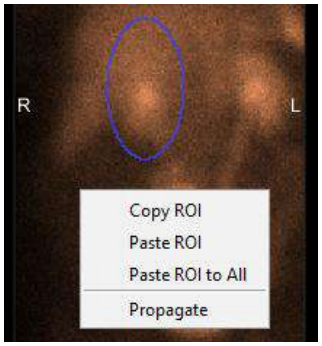


Figure 13: Options list for copy and paste of regions.

Shortcuts

- **Right-click:** on the image to open the context menu for copy/paste

7.5 2D Coregistration

⚠ **CAUTION**
Changes in 2D Coregistration might influence Vial Coregistration. Additionally, to the 2D Coregistration, a vial coregistration can be performed (see section 7.6). Changing the 2D Coregistration might affect the vial coregistration. If a vial coregistration was already performed, the user should check if the vial coregistration is still valid and if necessary, perform a new vial coregistration.

QDOSE provides rigid 2D coregistration between different time points. As the copy/paste process between different time points accelerates the boundary definition process, we strongly recommend users to undergo the coregistration process. QDOSE will prompt the user if images have not been coregistered. More details on 2D coregistration can be found in section 6 of this manual.

The user can go back to the window **2D Coregistration** by clicking on the corresponding button in the lower left corner.

7.6 Vial Coregistration

Since a **Vial** can be used for sensitivity calibration, the accuracy of the estimated vial counts is very important. Therefore, QDOSE provides a dedicated tool that coregisters the ROI of the vial at each time point with the transmission image for improved attenuation correction. Click on the button **Vial Coregistration** to perform this step. The button **Vial Coregistration** is only highlighted if an organ **Vial** has been drawn on all time points.

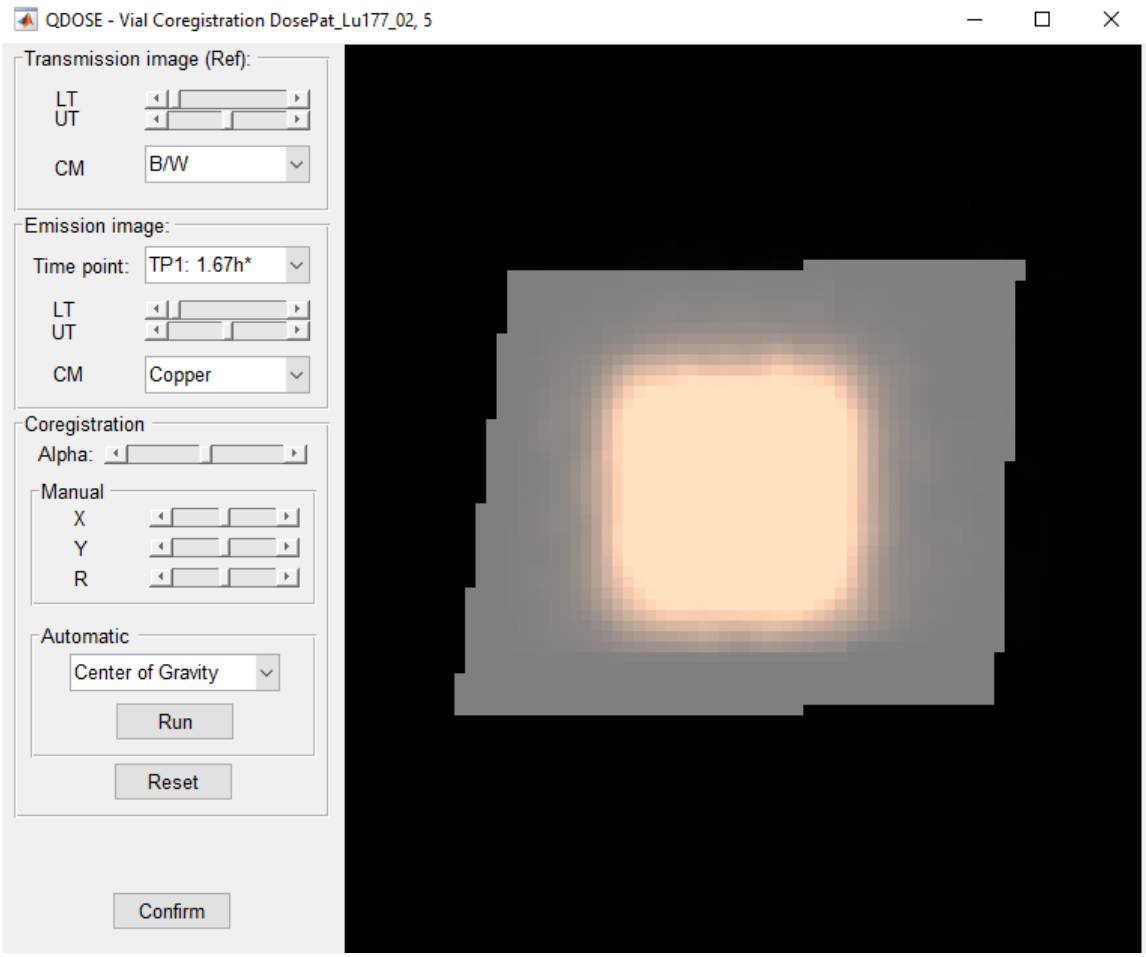


Figure 14: Window Vial Coregistration.

1. The view is already fused, while the reference image is the transmission scan. The alpha blending can be adjusted in the panel **Coregistration** with the slider **Alpha**.
2. Select the color maps and windowing for both images in the panels **Transmission image (Ref)** and **Emission image**.
    - The color map can be chosen from the dropdown menu **CM**.
    - The windowing can be adjusted using the sliders for **UT** (Upper Threshold) and **LT** (Lower Threshold).
3. Perform coregistration between the reference and the chosen image in the panel **Coregistration** using the following options:

- **Manual**: Manual coregistration (translation and rotation) between the displayed image data can be performed by clicking on the sliders:
    - **X**: for translation in X-direction
    - **Y**: for translation in Y-direction

- **Rotate**: for rotation around the image center.

- **Automatic**: Perform automatic rigid coregistration by selecting an algorithm from the dropdown menu and clicking on the button **Run**. Available algorithms are:
  - **Mutual information**: coregistration based on the entropic correlation between the information of the two images
  - **Center of Gravity:** coregistration based on the geometrical centroid of the image intensity

  Note: By clicking on **Run**, the coregistration is automatically applied to all time points, as indicated by an asterisk ***** in the dropdown menu. The results can be checked by selecting each time point.

  Note: The coregistration can be reset for all time points by clicking on the button **Reset**.

4. After all time points are coregistered, press the button **Confirm** to save the analysis steps and to close the window.

8 ROI Segmentation

ROI Segmentation allows organ based coregistration and segmentation within the boundaries defined on the planar data for determination of time-activity-curves for each organ.

The organ coregistration enables the correction of relative organ movements within the time points, where the coregistration is based on the segmented region. The threshold-based segmentation, within the boundary definition, makes organ definition faster, more reproducible and less operator dependent.

Each organ with boundaries defined at all time points is set as completed and is ready to be further coregistered and segmented. The quality of the coregistration is further illustrated by the alignment curves in the lower section below the images. The alignment curves illustrate the agreement of the reference image (gray line) and each time point using sum profiles in X- and Y-direction (blue line).

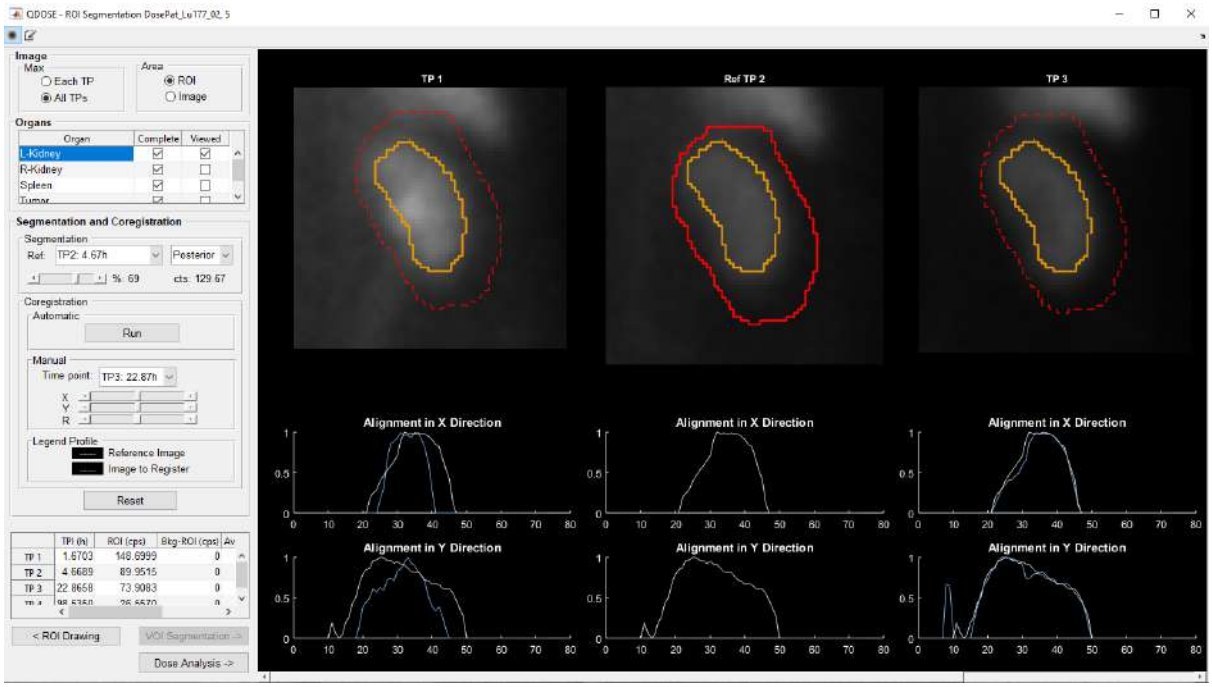


Figure 15: Window ROI Segmentation.

1. Adjust the display of the images by image normalization in the panel **Image**. Options are:
   - **Max**: For image normalization, the maximum value is taken from each time point separately (option **Each TP**) or from all time points (option **All TPs**).
   - **Area***:* For image normalization, the maximum value is taken from the selected view for segmentation (see step 5) only within the defined ROI (option **ROI**) or the entire image (option **Image**).

Note: The table **Organs** indicates in the checkboxes whether an organ has already been viewed (column **Viewed**) and if all boundaries have been drawn in previous stage (column **Complete**).

2. Select the organ to be segmented in the table **Organs**.
3. The ROI of the selected organ is displayed in the image view for all time points, with the following boundaries:
    - **Red**: indicates the drawn boundary from the previous step of ROI drawing.
    - **Orange**: indicates the segmentation result.
    - **Solid | dashed**: the solid line indicates which time point is currently chosen as reference time point. The images of the other time points need to be registered and therefore outlined with a dashed line.

    Note: In the beginning, a segmented ROI is shown based on a default threshold segmentation (50% of maximum value within the boundary). If the organ has already been segmented, the threshold will be the same as previously set.
4. Select the reference time point for segmentation from the dropdown menu **Ref.** in the panel **Segmentation**, typically the one which best displays the organ activity.

    The selected reference time point is also reflected in the alignment curves as gray line.
5. Select the view for segmentation from the dropdown menu: **Posterior** or **Anterior**.
6. Define threshold for segmentation using the slider in panel **Segmentation**. For planar images, only a grayscale-based, manual threshold segmentation is available. The threshold is expressed as percentage value of the drawn boundary. The segmentation result from the reference time point (solid orange line) is put on all other time points (dashed orange lines).
7. After the segmentation on the reference image is sufficient, perform a coregistration of the ROIs to account for organ movements which may not have been covered by 2D coregistration. The alignment curves are updated automatically. Options in panel **Coregistration** are:
    - **Automatic**: Perform automatic organ coregistration for all time points by clicking on Run.
    - **Manual**: Perform manual organ coregistration for the chosen time point in the dropdown menu **Time Point**, by using the sliders:
        - **X**: for translation in X-direction
        - **Y**: for translation in Y-direction
        - **R**: for rotation around the image center.

Note: For manual segmentation, each time point has to be coregistered separately, while the automatic coregistration is applied to all time points.

Note: Counts per second (counts normalized to total scan duration) values for all time points are updated in the table in the lower left corner.

Depending on the mode and uploaded images, various options are available as next steps which can be performed by clicking on the buttons:

- **VOI Segmentation**: if volumetric data are available (see section 10). This is required if volumetric or hybrid dose calculations are to be performed.
- **Dose Analysis**: if no volumetric image is available or hybrid or volumetric calculations are not required (see section 11).

9 3D Coregistration

3D Coregistation allows volumetric coregistration of all time points using CTs as reference, or for each time point between CT and NM images.

⚠ CAUTION
Incorrect coregistration can lead to incorrect segmentation. The coregistration results depend on the quality of the image data. The user must check the coregistration result for each time point. The user can adjust the display of the data sets as well as the overlay of the reference and 2nd data set in order to compare the alignment between the data sets.

NOTICE
Volumetric coregistration is time consuming. Volumetric coregistration with large CTs can be time and memory consuming. Furthermore, to accelerate the manual coregistration process, it is recommended to first perform the translations (in X- and Y-direction) before rotation is applied.

⚠ CAUTION
Insufficient image overlap can lead to incorrect deformable coregistration. The coregistration results depend on the quality of the image data. The user must check if the image content of the image to be coregistered is overlapping with the reference image before performing a deformable (elastic) coregistration. The user can adjust the display of the data sets as well as the overlay of the reference and 2nd data set in order to compare the alignment between the data sets. If the overlap is insufficient, the user must perform a manual or automatic rigid coregistration before applying the deformable coregistration.

3D coregistration can be done:

- to either coregister image pairs (CT and NM images) between different time points, or
- to coregister a CT with its corresponding NM image for each time point

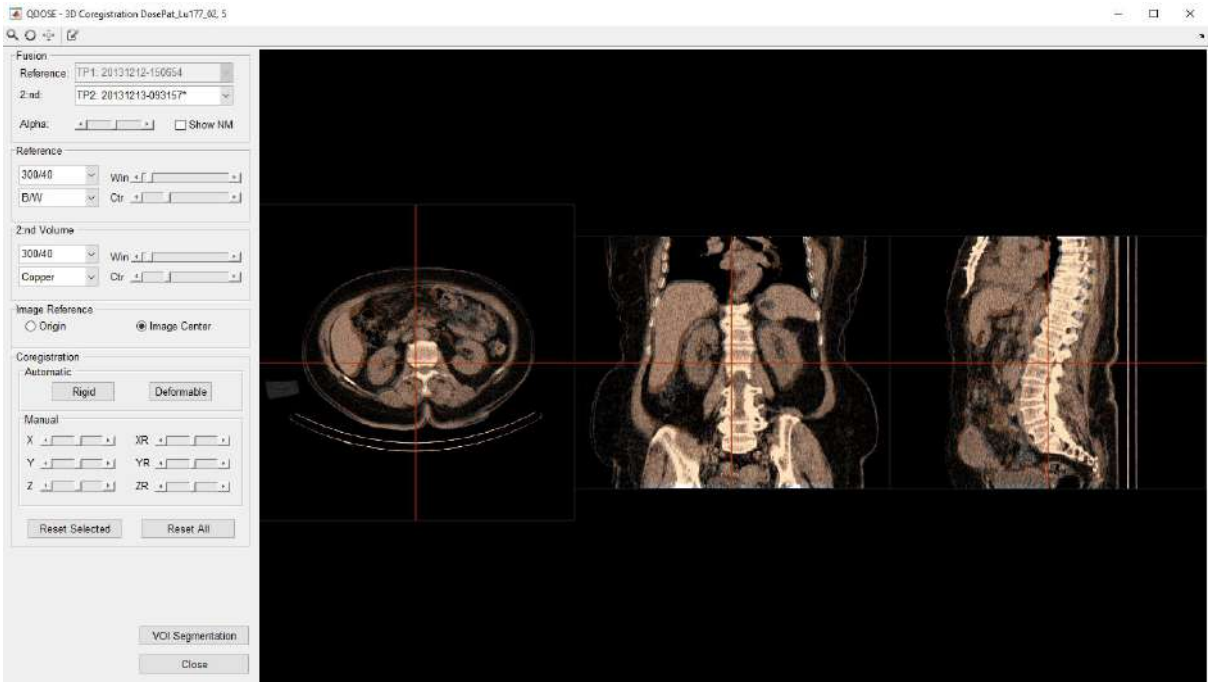


Figure 16: Window 3D Coregistration.

1. The panel **Fusion** contains two dropdown menus to select the images to be coregistered. Select an appropriate reference image from the menu **Reference** and the intended image from menu **2nd** for fused view.

2. The alpha blending can be adjusted using the slider **Alpha**. The checkbox **Show NM** enables choosing, if you want to coregister only CT images or if you want to coregister between CT and NM image. A marked checkbox **Show NM** indicates the coregistration between CT and NM image. In this case the panel **Reference** and **2nd Volume** (see Figure 17) are changed into **CT** and **NM** (see Figure 18).

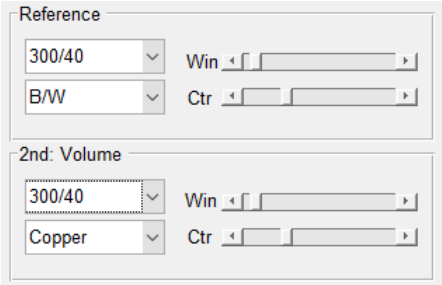


Figure 17: Panels for coregistration of only CT images.

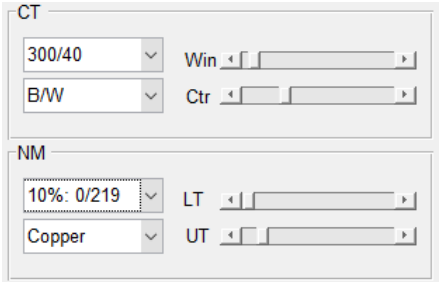


Figure 18: Panels for coregistration of CT and NM images.

3. Select the windowing for CT images in the panels **Reference**, **2:nd Volume** or **CT** (see Figure 17):
    - **Window**: In the upper dropdown menu, a window can be chosen from a list of predefined windows. The syntax is defined as window width/window center in Hounsfield Units (HU) (e. g. **300/40** means a window with a width of 300 HU around a center of 40 HU.
    - **Win**: slider for fine adjustment of window width
    - **Ctr**: slider for fine adjustment of window center
4. Select the windowing for NM images in the panels **NM** (see Figure 18):
    - **Window**: In the upper dropdown menu, a window can be chosen from a list of predefined windows. The syntax is defined as lower threshold/upper threshold in counts (e. g. **10%: 0/219** means a window from 0 to 219 counts, representing up to 10% of the maximum counts).
    - The windowing can be adjusted using the sliders for **UT** (Upper Threshold) and **LT** (Lower Threshold).
5. Select the colour maps for both images in the panels **Reference** and **2:nd Volume** or **CT** and **NM** respectively. The colour map can be chosen from the lower dropdown menu.
6. Set the reference for image alignment in panel **Image Reference**. Options are:
    - **Origin**: uses the DICOM information for origin of coordinate system
    - **Image Center***:* recalculates the coordinates based on the image center. For NM images (**Show NM** activated), the image center corresponds to the image center of the coupled or associated CT image.
7. Perform coregistration between the reference and the chosen image in the panel **Coregistration** using the following options:
    - **Automatic**: Perform automatic coregistration by clicking the button **Rigid** for rigid or the button **Deformable** for elastic coregistration.
    - **Manual**: Alternatively or additionally, manual coregistration (translation and rotation) between the displayed image data can be performed by clicking on the sliders:
        - **X**: for translation in X-direction
        - **Y**: for translation in Y-direction
        - **Z**: for translation in Y-direction
        - **XR**: for rotation around the X-axis
        - **YR**: for rotation around the Y-axis
        - **ZR**: for rotation around the Z-axis

Note: The button **Deformable** for elastic automatic coregistration is only enabled for coregistration of CT images.

Note: For optimal results, perform manual or automatic rigid coregistration to align the images before performing deformable automatic coregistration. This should be done both for the coregistration between CTs as well as the coregistration between CTs and NMs (**Show NM** activated).

Note: Coregistered images are indicated by an asterisk ***** in the dropdown menu in panel **Fusion.** In **3D Coregistration**, the reference image is not marked with an asterisk *****, even if it is coregistered.

Note: The coregistration between CT images is also applied to the coupled NM images. However, they are not marked with an asterisk ***** automatically. The asterisk ***** is only set, if the NM was coregistered to a CT explicitly.

8. Select the next image to be registered from the dropdown menu **2:nd Volume** and perform coregistration (automatic and/or manual).

   Note: The coregistration can be reset for single time points by clicking on the button **Reset Selected** or for all time points by clicking on **Reset All** to undo all changes and revert to the originally uploaded coordinates.

9. After all time points are coregistered, press the button **Confirm** to save the analysis steps and to close the window.

10 VOI Segmentation

VOI Segmentation allows for viewing, drawing boundaries and segmenting within the boundaries to determine time-activity-curves for each organ.

The image display can display the single modality (NM or CT/MR) as well as fused images. The VOIs consist of 3 parts:

- *Boundary* (outlined in orange): delineated region to separate it from its surroundings. This area is then used for further segmentation.
- *Segmented volume* (outlined in red): **Volume VOI** used for calculation of organ volume.
- *Segmented activity* (outlined in yellow): **Activity VOI** used for calculation of organ activity to be used in the dose calculation step.

The tool **VOI Segmentation** also provides a set of tools for segmentation of an organ within a boundary in either NM, CT, or fused mode. Organ and patient limits (thickness) for background correction of planar data (when using Hybrid mode) can also be defined here.

The functionalities provided are:

- Image display including color and LUT manipulation.
- Organ creation including suborgans.
- Drawing and editing of organ boundaries.
- Segmentation of volume and activity VOIs.
- Definition of patient and organ limits (thickness).

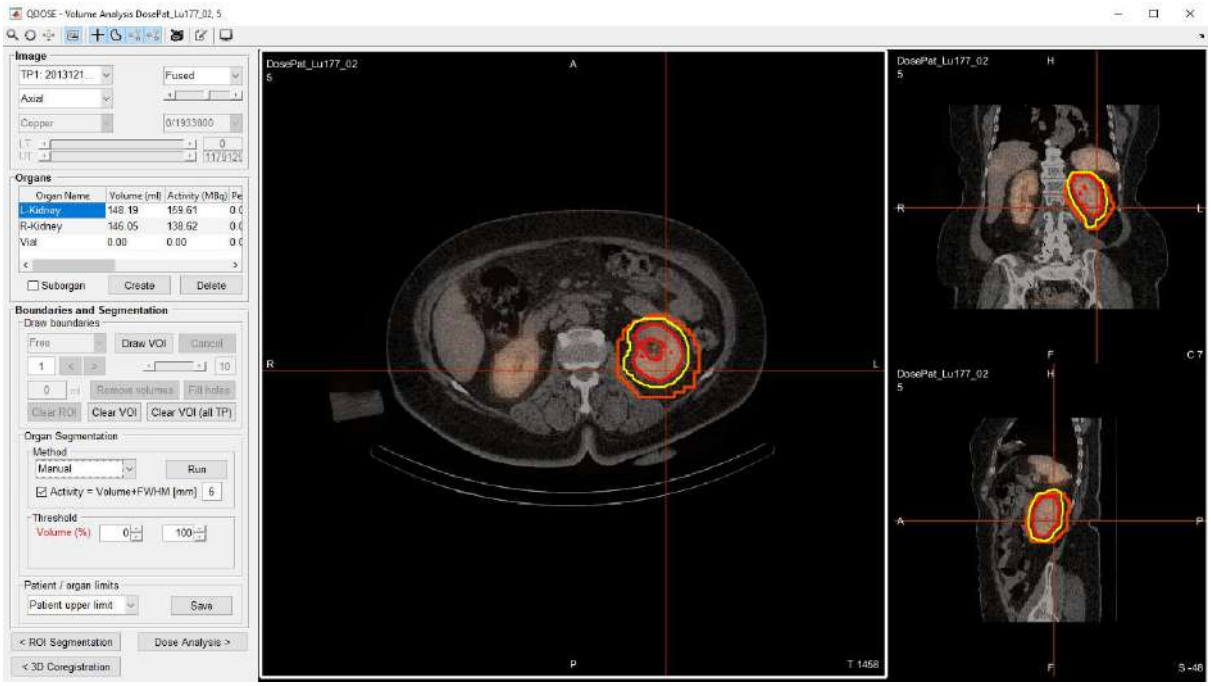


Figure 19: Window VOI Segmentation. The boundary of the organ displayed as orange line, the Activity VOI as yellow line and the Volume VOI as red line.

Shortcuts

- **Arrow Keys Up/Down:** to move one slice in the active view
- **Arrow Keys Left/Right:** to move 10 slices in the active view
- **Shift + Left-click:** when in edit mode enables moving the volume
- **Left-click:** click in the active view changes all views to the selected point (Shift + Left-click when in boundary drawing mode)
- **Right-click:** in the images opens the context menu for copy-/pasting organs between time points

10.1 Image View

1. Select the intended image time point in the panel **Image** from the dropdown menu **Time Point**. The time points are ordered based on the date and time of the image.
2. Select the main image slicing plane from the dropdown menu: **Axial**, **Coronal** or **Sagittal**. The main plane is displayed large in the window center while the other two planes are displayed smaller on the right side.
3. Select the image modality from the dropdown menu in the right upper corner of the panel **Image**: **PET/SPECT**, **CT/MR** or **Fused**.

4. Select the windowing for image view. Depending on the image modality, different windowing options are available:

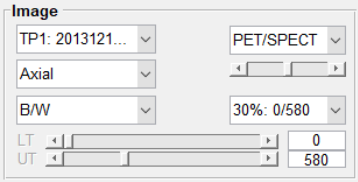


Figure 20: Windowing options for modality PET/SPECT.

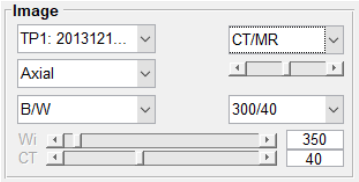


Figure 21: Windowing options for modality CT/MRT.

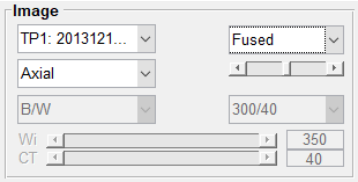


Figure 22: Windowing options for modality Fused.

Select the windowing for PET/SPECT images in the panel **Image** (see Figure 20):

- **Window**: In the upper dropdown menu, a window can be chosen from a list of predefined windows. The syntax is defined as lower threshold/upper threshold in counts (e. g. **10%: 0/219** means a window from 0 to 219 counts, representing up to 10% of the maximum counts).
- The windowing can be adjusted using the sliders for **UT** (Upper Threshold) and **LT** (Lower Threshold).

Select the windowing for CT/MR images in the panel **Image** (see Figure 21):

- **Window**: In the upper dropdown menu, a window can be chosen from a list of predefined windows. The syntax is defined as window width/window center in Hounsfield Units (HU) (e. g. **300/40** means a window with a width of 300 HU around a center of 40 HU.
- **Wi**: slider for fine adjustment of window width
- **CT**: slider for fine adjustment of window center

For mode **Fused**, the windowing options are disabled as the settings from the single modalities are used. The alpha blending between the two images can be adjusted using the slider under the dropdown menu for the image modality.

Note: The Window/Center and UT/LT are preset from the DICOM header. For CT images, a window optimized for soft- and lung tissue is provided.

Note: When changing the image time point, relative scaling of the previous image is used to display the selected time point.

5. Select the color map for the selected modality from the lower dropdown menu in panel **Image**.

10.2 Organ Handling

1. Create an organ by clicking the button **Create** in the panel **Organs**. Select from the predefined organ list in the dropdown menu or select the option **New…** and enter a name (e.g. for tumour). Confirm by clicking on **Create** (see Figure 9).
2. To create a suborgan to a currently available organ, select the parent organ from the table **Organs** and tick the checkbox **Suborgan** Then click the button **Create**. Select from the predefined organ list. If the organ is not available (e.g. Tumour), select **New...** from the list and enter a name.
3. Delete an organ by selecting the organ from the table **Organs** and clicking on the button **Delete**.

10.3 Define Organ

⚠ **CAUTION**
Incorrect organ segmentation results in incorrect dose values. The user should check the correct position of the boundary for organ delineation. The user can adjust the display of the image in order to improve the visibility of the image data relative to the drawn boundary.

NOTICE
Segmentation on image data with different resolutions influences the segmentation results. The resolution of the drawn boundary is depending on the underlying image resolution (voxel size). Hence, if a boundary is drawn on the NM image, it will have a much lower resolution than on the CT image. The VOI is accessible in the other corresponding images for calculation independent of its origin (the image where it has been drawn).

- Set the time point, modality (NM, CT, Fused), main view (axial, coronal, sagittal), colour maps and windowing as described in section 10.1.
- Select an existing organ or create an organ following step 1 in section 10.2.
- Start drawing a boundary to roughly delineate the organ and save as described in the following section 10.3.1. Boundary drawing can be performed in the active view.
- Segment **Volume** and **Activity** VOI within the boundary to define anatomical region and region from which the activities are collected, as described in the following section 10.3.2. It is possible to define activity and volume regions independently on CT/MR and/or NM.

Note: Organ statistics are displayed in the table **Organs** providing specific information about each organ.

10.3.1 3D Boundary Drawing

A 3D boundary or VOI consist of a stack of 2D ROIs, which can either be propagated from one slice to the neighbouring slices or be redrawn separately on each slice. All tools are collected in the panel **Draw Boundaries** in the panel **Boundaries and Segmentation**.

Shortcuts

- **Shift + Left-click*:*** For setting the cross position in drawing mode.

10.3.1.1 Draw Regions

1. Click on the button **Draw ROI** in the panel **Draw Boundaries**.
2. Select a display to become active by clicking into the image. A white box highlights the activated view.
3. Select a drawing mode from the dropdown menu in the panel **Draw Boundaries**. Start drawing by using the following drawing options:
    - **Free**: Draw a boundary by keeping the left mouse button pressed and painting with the mouse like with a pencil.
    - **Polygon**: Draw a boundary by clicking position-by-position around the region in the image. The positions are combined automatically to a polygon.
    - **Ellipse**: Draw a boundary by spanning the ellipse with the left mouse button pressed to the desired size.
4. Click on the button **Save ROI** in the panel **Draw Boundaries** to save the drawn boundary.
5. Edit the ROI, if necessary, by moving or painting it. First click again the button **Draw VOI** to go to editing mode, then:
    - *Moving*: to move the entire region, press **Shift** and move the whole object via drag and drop to the new location.

      Note: Do not click to closely to the white boundary when moving via drag and drop.
    - *Painting*: to paint the boundary brush-like, keep the left mouse button pressed until a white circle is displayed (see Figure 12). Edit the boundary from the region outside or inside, by moving the circle like a brush. The left mouse button needs to stay pressed. The radius of the circle can be changed using the slider **Radius** in the panel **Boundaries.**

6. Click on the button **Save ROI** in the panel **Draw Boundaries** to save the drawn boundary.
7. Information for the organ is automatically updated in the table **Organs.**

10.3.1.2 Propagate Region

Propagating serves to quickly copy and paste drawn ROIs from one slice to another slice.

1. The visible region on the current slice can be propagated to the next or previous slice(s) by using the buttons **<** and **>** in the panel **Draw Boundaries**. The button **<** will propagate the ROI to next slice the active view (e.g. For axial view, the next axial slice in cranial direction, as displayed in Figure 23). The button **>** will propagate the ROI in the opposite direction.

   Note: The number of slices the region will be propagated to can be defined simultaneously in the field on the left side of the button **<** (see Figure 23).

Regions can be edited / redrawn at any time while in draw mode.

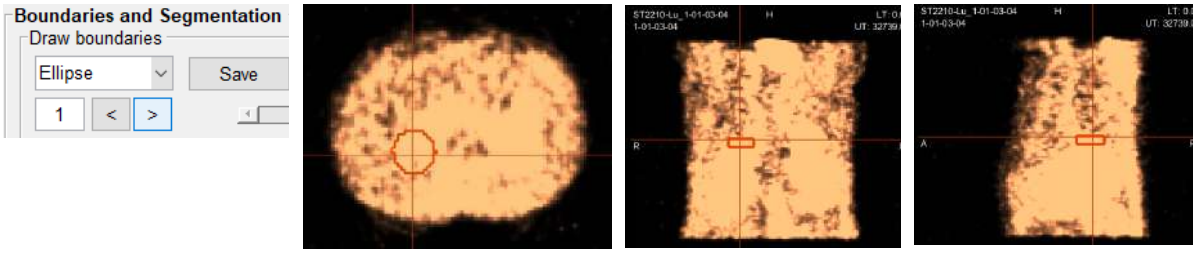


Figure 23: Propagation of ROIs over neighbouring slices using the buttons < and >.

10.3.1.3 Interpolate between ROIs

Interpolation serves to only draw ROIs in some slices and interpolate the missing ROIs in-between.

1. Draw separate ROIs only in some slices to roughly define an organ as described in section 10.3.1.1.
2. When clicking the button **Save**, a dialog window will pop up asking if the missing ROIs are to be interpolated. Confirm the interpolation. The calculation may take a few seconds to minutes.

10.3.1.4 Delete ROIs

If necessary, ROIs/VOIs can be deleted using the following buttons in the panel **Draw Boundaries**:

- **Clear ROI:** removes the ROI from the selected slice.
- **Clear VOI:** removes all ROIs from all the slices, i.e. the entire volume.
- **Clear VOI (all TP)**: removes the VOIs of the selected organ from all the time points.

10.3.2 3D Segmentation

⚠ CAUTION
Incorrect organ segmentation results in incorrect dose values. The segmentation depends on the quality of the image data sets. The user should check the result of the segmentations by viewing all slices and checking if the outline of the segmentation is correct and the results can be used for further analysis.

As previously described in the QDOSE concept, QDOSE is using two distinct regions for the calculation of organ volume and activity. While the volume calculation is based on the modality the segmentation was performed on, activity segmentation is always calculated from the NM data.

Volume and activity regions can be segmented independently from SPECT and/or CT/MR images. Alternatively, they can be calculated from the same image, while the activity is based on the volume obtained from CT or MR convolved with a Gaussian function (representing the point spread function (PSF) of the NM imaging system) to compensate the spill-out from the inferior resolution of NM images. In general, the visualized image is the base for segmentation. All tools are collected in the panel **Organ Segmentation** in the panel **Boundaries and Segmentation**.

10.3.2.1 Manual Segmentation

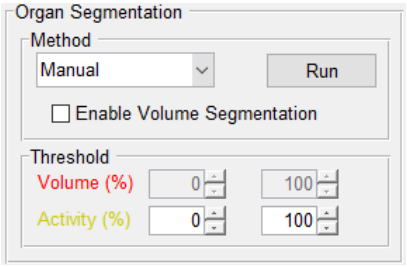


Figure 24: Panels for manual segmentation of NM images.

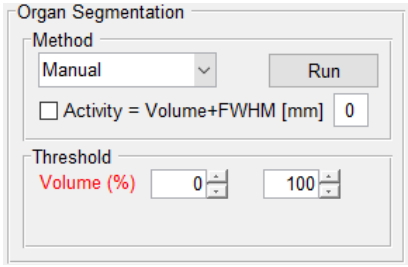


Figure 25: Panels for manual segmentation of CT/MR images.

When a NM image is displayed:

1. In the panel **Organ Segmentation** select the option **Manual** from the dropdown menu **Method**.
2. In the panel **Threshold** below, the threshold for activity segmentation to obtain the VOI corresponding to activity can be defined. For NM images, only the activity VOI can be segmented. Set the values for the lower and upper threshold using the fields and arrow buttons

indicated by **Activity (%)** (see Figure 24). The threshold values are expressed as percentage of the maximum value within the drawn boundary.

3. Click on the button **Run**. The segmentation result is displayed as a yellow boundary in the image.
4. Adjust the thresholds if necessary.
5. Tick the checkbox **Enable Volume Segmentation** to segment the anatomical volume based on a separately defined threshold.
6. Set the lower and upper threshold for the anatomical VOI in the field indicated by **Volume (%)** (see Figure 25).
7. Click on the button **Run**. The segmentation result is displayed as a red boundary in the image.

When a CT or MR image is displayed:

1. In the panel **Organ Segmentation,** select the option **Manual** from the dropdown menu **Method**.
2. In the panel **Threshold** below, the threshold for volume segmentation to obtain the VOI corresponding to anatomical volume can be defined. For CT/MR images, only the volume VOI can be segmented. Set the values for the lower and upper threshold using the fields and arrow buttons indicated by **Volume (%)** (see Figure 25). The threshold values are expressed as percentage of the maximum value within the drawn boundary.
3. Click on the button **Run**. The segmentation result is displayed as a red boundary in the image.
4. Adjust the thresholds if necessary.
5. Tick the checkbox **Activity = Volume+FWHM [mm]** to segment the activity volume obtained from CT or MR convolved with a PSF with the specified full width half maximum (FWHM).
6. Set the value for the full width half maximum (FWHM) in the field right next to it (see Figure 25).
7. Click on the button **Run**. The segmentation result is displayed as a red boundary in the image.

10.3.2.2 Auto SBR Segmentation

⚠ CAUTION
Incorrect organ segmentation results in incorrect dose values. The calibration data for the Auto SBR Segmentation algorithm was generated using a specific SPECT scanner. Hence, the segmented VOIs based on automatic thresholds from this calibration may not be equally appropriate for other SPECT scanners. Check the segmentation result by scrolling through all slices for the segmentation.

NOTICE
Auto SBR is only available for NM images. This option is only available when NM images are displayed and for selected nuclides where calibration data is available. The display of CT/MR images can be activated by selection of the option CT/MR from the dropdown in the panel **Image**.

NOTICE
Segmentation results with Auto SBR are depending on the volume size. The results of volume and activity segmentation with Auto SBR are depending on the signal-to-background ratio within the VOI. For small volumes, this is not sufficient due to partial volume effect. The optimal threshold is depending on the signal-to-background ratio and the volume size. This may have an impact on the segmentation results with Auto SBR in a way that the activity is overestimated for small volumes (e.g. tumour lesions) and underestimated for large volumes. Check the segmentation result by scrolling through all slices for the segmentation.

The algorithm Auto SBR automatically determines the volume and activity threshold based on a calibration curve. Activity segmentation as well as Volume segmentation is performed on the NM image. It is only available for NM images.

1. This option can be applied by selecting **Auto SBR** from the dropdown menu **Method.**
2. Click on the button **Run**. The segmentation result is displayed in the image (Volume segmentation outlined in red and Activity segmentation outlined in yellow).

10.3.2.3 Fuzzy C Means Cluster Segmentation

⚠ CAUTION
Incorrect organ segmentation results in incorrect dose values. The option **Fuzzy C Means** segmentation automatically segments the organs/structures on CT/MR or SPECT/PET images. Depending on the quality of the images, the result of this segmentation may vary. Check the segmentation result by scrolling through all slices for the segmentation.

The algorithm of **Fuzzy C Means** cluster segmentation defines clusters based on the counts histogram in the defined boundary. Segmentation will then be performed on data clusters to be included or excluded as defined by the user.

1. This option can be applied by selecting **Fuzzy C Means** from the dropdown menu **Method.**
2. If a CT/MR image is displayed, tick the checkbox **Enable Activity Segmentation** to enable activity segmentation or vice versa tick **Enable Volume Segmentation** on SPECT/PET.
3. Click on **Run**. The window **Cluster Segmentation Configuration** will open (see Figure 26).
4. Set values for the following parameters:
    - **Number of clusters** defines the number of clusters in which the greyscale histogram is divided. The histogram is display above. Change this parameter using the slider or the entry field. Set the total number of clusters to correspond to the expected number of data clusters: e.g. background, scatter, spill-over and uptake.
    - **Weight exponent:** defines the crispiness/fuzziness of clusters. Change this parameter using the slider or the entry field.
    - **Included regions volume:** For CT/MR images, it defines the lower and upper cluster of all clusters that are included in the segmentation. Change the values using the dropdown menus.
    - **Included regions activity:** For NM images, it defines the lower and upper cluster of all clusters that are included in the segmentation. Change the values using the dropdown menus.
    - **Only One Region:** This checkbox defines that the segmentation result will only be one VOI.

    Note: Good first results can be achieved with the following settings:

    Number of clusters = 10

    Weight exponent = 1.1

Included regions volume/ activity = 2 - 10

5. To start the segmentation with the selected parameters click **Run** in window **Cluster Segmentation Configuration**. The segmentation result is displayed as a red boundary for the volume VOI and a yellow boundary for the activity VOI in the image.

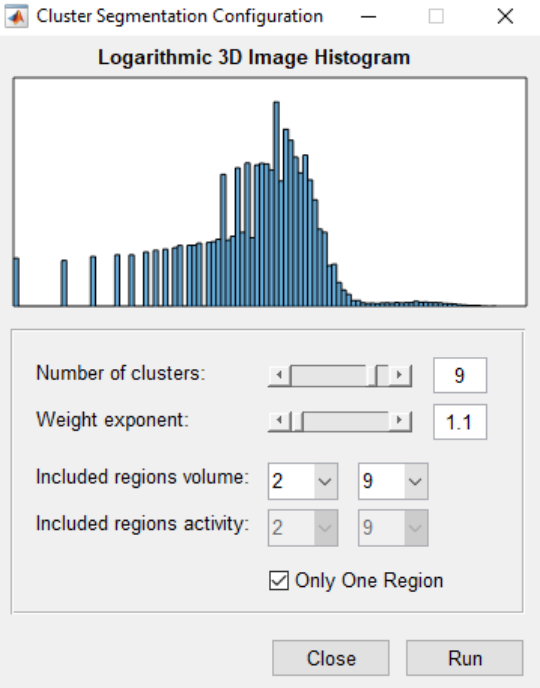


Figure 26: Window Cluster Segmentation Configuration.

10.3.2.4 Convolution

The algorithm **Convolution** automatically determines the activity VOI based on the volume segmentation obtained from CT or MR convolved with a PSF with the specified full width half maximum (FWHM). This means a volume VOI needs to be defined beforehand.

1. This option can be applied by selecting **Convolution** from the dropdown menu **Method.**
2. Tick the checkbox **Activity = Volume+FWHM [mm]**.
3. Set the value for the full width half maximum (FWHM) in the field right next to it (see Figure 25).
4. Click on the button **Run**. The segmentation result is displayed as a yellow boundary for the activity VOI in the image.

10.3.2.5 AIT-Liverator

⚠ CAUTION
False organ segmentation results in false dose values. The algorithm **AIT-Liverator** automatically segments the liver on CT images. Depending on the quality of the images the result of this segmentation may vary. Low-resolution CT images (e.g. CT images acquired for attenuation correction) are not suitable. Check the segmentation result by scrolling through all slices for the segmentation.

NOTICE
AIT-Liverator is only available for CT images. The algorithm **AIT-Liverator** is only available if CT image data is available and selected. The display of CT images can be activated by selection of the option **CT/MR** from the dropdown menu in the panel **Image**.

The **AIT-Liverator** automatically segments the liver, the kidneys and the spleen on CT images.

1. Draw a boundary around the liver, following the steps in section 10.3.1.
2. Select the option **AIT-Liverator** from the dropdown menu **Method**.
3. If the activity volume needs to be segmented too, tick the checkbox **Activity = Volume+FWHM [mm]** to segment the activity volume.
4. Set the value for the full width half maximum (FWHM) in the field right next to it (see Figure 25).
5. Click on the button **Run**. The segmentation result is displayed as a red boundary for the volume VOI and as a yellow boundary for the activity VOI in the image.

Note: If the segmentation process was terminated with the message “Failed to run liverator – timeout”, the parameter for the **Liverator Timeout** can be increased under **File > Settings**.

10.4 Define Background VOI

For volumetric dosimetry, correction of background activity can be performed. Detailed information about the correction mechanisms including background correction and the necessary steps can be found in section 11.2. The steps are the same as for 2D, as previously described in section 7.2. The only difference is that a background VOI is drawn, instead of a background ROI.

1. Select the intended image in panel **Image** from the dropdown menu **Time Point**.
2. Select the color maps and windowing in the panel **Image**:

- The color map can be chosen from the dropdown menu **CM**.
- The windowing can be adjusted using the sliders for **UT** (Upper Threshold) and **LT** (Lower Threshold) or the field right next to it.

3. Create an organ by clicking the button **Create** in the panel **Organs**. Select from the predefined organ list in the dropdown menu or select the option **New…** and enter a name for the background ROI (e.g. Background).
4. Tick the checkbox **Background** (see Figure 10).
5. Confirm by clicking on **Create**. The background ROI is displayed in the organ table with an appended **(bkg)**.
6. Draw a background VOI near the source organ the same way as described in section 10.3.1.1.
7. Link the background VOI to an organ by right-clicking on the intended organ in the table Organs and selecting the background VOI as shown in Figure 11.

Note: It is possible to use one background ROI for different organs.

10.5 Edit Organ VOIs

1. Select the active display by clicking into the image. A white box highlights the activated view.
2. Select the VOI to be edited (volume, activity, boundary) by left-clicking on the region.
3. There are two options to edit the VOI:
   - *Moving*: to move the entire region, press **Shift** and move the whole object to the new location via drag and drop.

     Note: Do not click too closely to the white boundary when moving via drag and drop.
   - *Painting*: to paint the boundary brush-like, keep the left mouse button pressed until a white circle is displayed (see Figure 12). Edit the boundary from the region outside or inside, by moving the circle like a brush. The left mouse button needs to stay pressed. The radius of the circle can be changed using the slider **Radius** in the panel **Draw Boundaries**.
4. Click on the button **Save VOI** in the panel **Draw Boundaries** to save the edited boundary or click the button **Cancel** in the panel **Draw Boundaries** to discard changes to the boundaries.
5. Information for the organ is automatically updated in the table **Organs**.

10.6 Copy/Paste Organ

⚠ CAUTION
Incorrect organ segmentation results in incorrect dose values. After copying and pasting of VOIs, the VOIs may not contain the organ or region at all time points due to local misalignment between time points. The user must check the position of the VOI for each organ at each time point. This can be done by selecting the organs in the table **Organs** at each time point and scrolling through all slices of the data set. If the positions of the VOIs are not sufficient, the user can edit the organ boundary for each time point or redraw the whole boundary and perform a new segmentation.

1. Select the intended image in panel **Image** from the dropdown menu **Time Point**, if not already selected.
2. Select organ from the table **Organs**, if not already selected, by clicking on it.
3. Right-click on the image, select **Copy** and one of the options from the list (see Figure 27):
    - **All***:* copies boundary, activity segmentation and volume segmentation
    - **Boundary***:* copies only the boundary of the organ (orange line)
4. Select the next intended time point in panel **Image** from the dropdown menu **Time Point.**
5. Right-click on the image will open an options list (see Figure 28). Here you have the following options:
    - **Paste**: pastes the copied VOI(s) to this time point only.
    - **Force Paste**: this way the copied VOI can be pasted to another organ.

      Note: The target organ must be selected from the table **Organs** before clicking **Force Paste.**
6. Alternatively, the option **Propagate** (see Figure 28) can be used to copy and paste all organs from the chosen time point to all time points. Here you have the following options:
    - **All regions**: pastes all VOI(s), including boundary, activity and volume segmentation, of all organs to all time points.
    - **New only**: pastes VOI(s) to time points that do not have a drawn VOI, including boundary, activity and volume segmentation, of all organs to all time points.
7. If needed, VOIs can be edited separately at each time point, as required (see section 10.5).

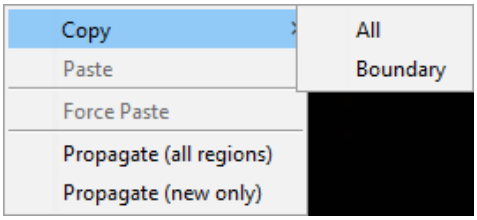


Figure 27: Options for copying regions.

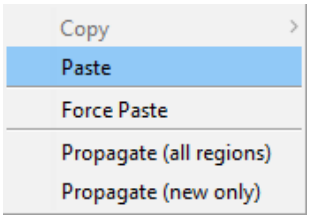


Figure 28: Options for pasting and propagating regions.

10.7 Define Organ Thickness

⚠ **CAUTION**
Patient and Organ Thickness influence the dose calculation. If the patient and/or organ thickness is edited in the window **Organ Properties**, the edited values will be used for background correction of planar data for the further dose calculations in planar or hybrid mode automatically. No further confirmation of applying the background correction is necessary.

The organ and patient thickness for each organ can be defined for planar background correction. There are two possible ways of defining the thickness values: entering them manually or measuring them on 3D images. For further information about the correction mechanisms and the necessary input values, please refer to section 11.2.

The first method is explained in section 11.5.

The second method is explained here, as follows:

1. Set the cross-hair point to the position of the patient/organ limit in the image.
2. Select the corresponding limit type from the dropdown menu in the panel **Patient / organ limits**.
3. Click on the button **Save** right next to it.
4. Repeat this for all four limit types of the dropdown menu.

   Note: Thicknesses will be displayed in the table **Organs** after both upper and lower limit is set for organ or patient.

11 Dose Analysis

Dose Analysis allows curve fitting, activity integration, dose calculation using IDAC-Dose, spherical model or Voxel S and report generation/value export to Olinda.

Dose Analysis allows curve fitting and dose calculation for different dosimetry modes – i.e. planar, hybrid, volumetric. For each mode, the curve fitting, and dose calculation can be performed separately based on the regions defined in previous steps, to compare the different dosimetry approaches.

Dose Analysis further provides dose calculation using:

- IDAC-Dose 1.0
- IDAC-Dose 2.1
- Spherical model
- Voxel S
- Export of obtained cumulated activities and residence times as a case file readable by Olinda/EXM 1.1.

Shortcuts

- **Right-click** *on a selected organ:* to open context menu for curve fitting, organ properties.

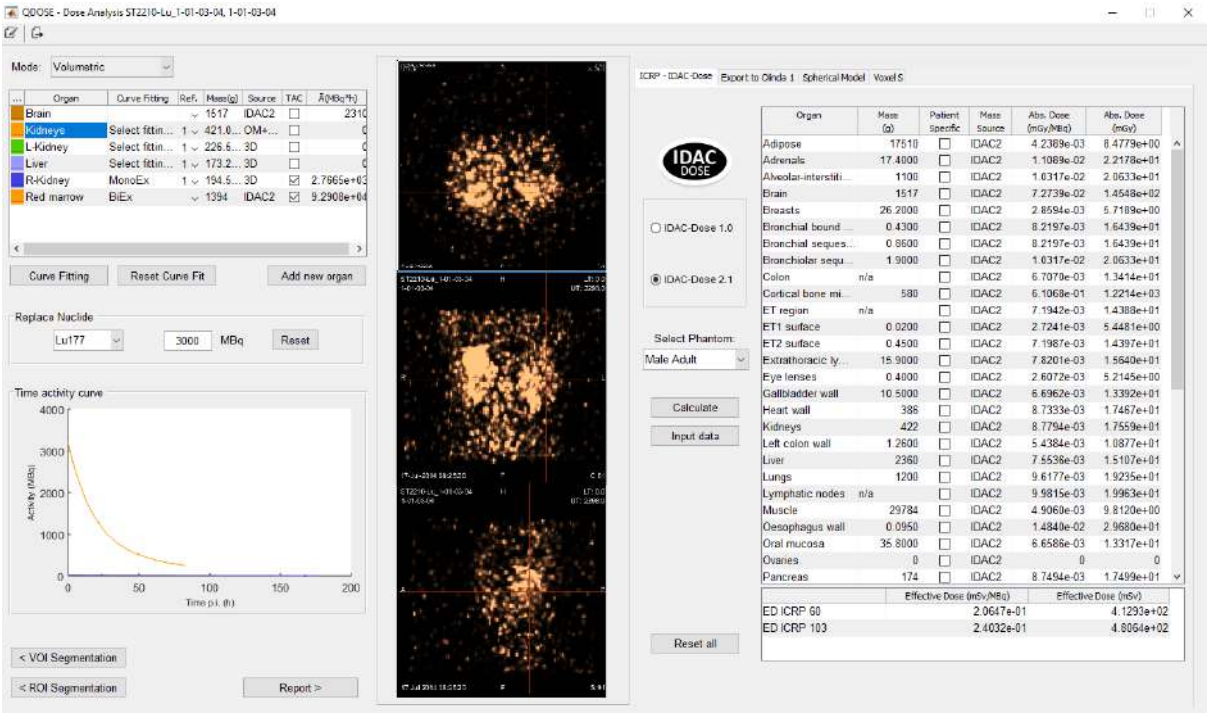


Figure 29: Window Dose Analysis.

11.1 Mode

As explained in the QDOSE concept, QDOSE can calculate doses using either planar, hybrid or volumetric methodology. Based on the data used for analysis, different modes will be available. The calculations done in each mode are independent from other modes.

1. Select the mode for the intended dose calculation from the dropdown menu **Mode**: **Planar, Hybrid, Volumetric.**

11.2 Correction Mechanisms

The correction mechanisms are specific for the image modality (2D or 3D). The applied corrections are independent of each other. E. g. for a case with 2D and 3D data, the corrections for the 2D data are independent of the corrections applied to the 3D data.

11.2.1 2D Corrections for Planar and Hybrid Mode

The activity A for each ROI is calculated using the formula below applying the corrections according to MIRD pamphlet 16 (Siegel et al., 1999):

$$A = \sqrt{\frac{I_A \cdot I_p}{e^{\mu t}}} \cdot f \cdot F \cdot C$$

where:

- I_A and I_P are the anterior and posterior measured counts
- $e^{\mu t}$ is the attenuation map for attenuation correction with μ being the linear attenuation coefficient and t the patient thickness,
- f is the self-attenuation correction factor
- F is the background correction factor
- C is the calibration factor (based on whole body or vial)

Correction of	What is it?	What needs to be done by the user?	How is it applied to the data?
Attenuation	The patient body absorbs partially the radioactivity from the source(s) before it can be recorded with a gamma camera. To obtain the attenuation effect of the body parts, transmission scans are typically used. A planar source or a scanning line source is positioned inside the conjugate view to homogeneously emit a low dose radiation. A transmission measurement (TR or I) with the patient present and a corresponding measurement without the patient present (blank – BL or I_0) are acquired. Pixel-by-pixel division of the two images leads to a 2D attenuation map that can be applied to the emission data according to equation 3 of the MIRD Pamphlet No. 16 (Siegel et al. 1999): $$T = \frac{I}{I_0} = e^{-\mu_e t}$$	• Load transmission and blank image of the patient • Coregister the transmission image to the emission images of all time points	Automatically, if transmission and blank images are available
Background activity	Over- and underlying activity from neighbouring tissue will contribute to the counts in the ROI. A correction for this background is usually needed, in combination with attenuation correction, for an accurate quantification of activity without overestimation. To compensate this, a background ROI is typically used, where the geometry and uptake should be as close to the source ROI as possible. The fraction of counts originating from the source can then be calculated according to equation 6 of the MIRD Pamphlet No. 16 (Siegel et al. 1999): $$F = \{[1-(I_{ADJ}/I_A)(1-t_j/t)]\cdot [1-(I_{ADJ}/I_P)(1-t_j/t)]\}^{1/2}$$ This correction is applied on the ROI level using total activities and average organ and patient thickness.	• Draw a background ROI near the source organ • Apply the background ROI to the intended source organ(s) • Add a patient/organ thickness by either: ○ Entering the thickness manually. ○ Deriving the thickness from a measurement in a 3D image.	Automatically, if background ROI is applied to source organ(s) and a patient/organ thickness is available
Source self-attenuation	This is a correction for the source region attenuation coefficient and source thickness. It is applicable for extended sources as opposed to a point source. It is implemented according to equation 2 in MIRD pamphlet 16. The implementation in QDOSE assumes as an approximation that the activity is distributed, i.e. the source is extended over the whole patient thickness. $$f = \frac{\mu t}{\sinh(\mu t)}$$ $$\mu t = \ln\left(\frac{BL}{TR}\right)$$ It is applied on the pixel level.	• Load transmission and blank image of the patient • Coregister the transmission image to the emission images of all time points	Automatically, if transmission and blank images are available

11.2.2 3D Corrections for Volumetric mode

Correction of	What is it?	What needs to be done by the user?	How is it applied to the data?
Background	This is a recovery coefficient type of correction to account for the spill out from a source region due to partial volume effect. At the same time, it aims to subtract the background activity underlying the spilled-out activity: $A_{corr} = A_{organ} - (V_{ActSeg} - V_{VolSeg}) \cdot AC_{bkg}$ $AC_{bkg} = \frac{A_{bkg}}{V_{bkg}}$ A_{organ} activity of organ **Activity** VOI V_{ActSeg} volume of organ **Activity** VOI V_{VolSeg} volume of organ **Volume** VOI A_{bkg} activity of background **Activity** VOI V_{bkg} volume of background **Activity** VOI	• Draw a large boundary around the source organ • Segment a large **Activity** VOI for the source organ, e.g. tumour • Segment a proper **Volume** VOI of the source organ • Draw a boundary for the background near the source organ • Segment **Activity** VOI for the background (to calculate AC_{bkg}) • Link background to the intended source organ(s)	Automatically, if • background VOI segmented (Activity VOI) and • background VOI is linked to source organ(s)

11.3 Organ Table

The table **Organs** displays the organs available for each mode. The organs available are depending on the images loaded to the system as well as the available ROIs/VOIs. The table gives an overview of the performed curve fitting, selected reference time point (if multiple available), if the time-activity-curve (TAC) is to be drawn and the cumulated activity Ã.

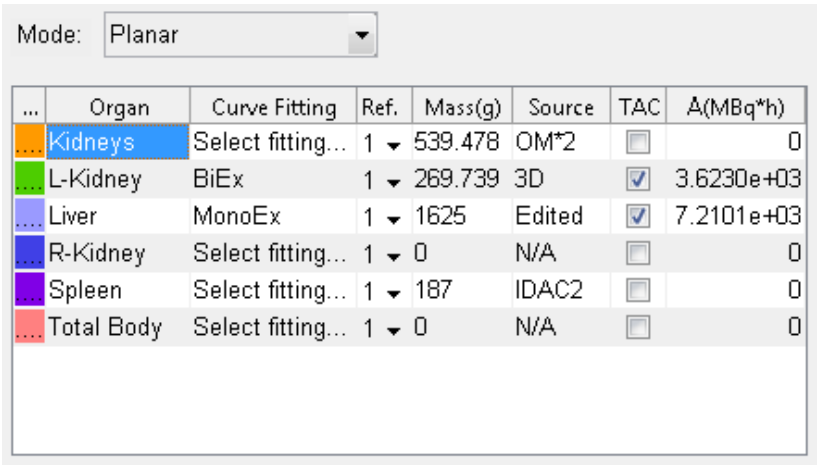


Figure 30: Table Organs with example organs.

- Column **Organ**: Displays the organ name
- Column **Curve Fitting**: Displays the curve fit type selected in the Curve Fitting Step (see 11.6)
- Column **Ref**: Displays the selected 3D reference time point used for TAC calibration in Hybrid mode, to get the patient-specific mass of the organ which was defined during 3D segmentation and to obtain the activity distribution for Voxel S.
- Column **Mass**: Displays the mass of the organ.
- Column **Source**: Displays the source of the mass for the organ. Available options are:
    - **N/A**: no source available
    - **IDAC2**: default mass from the IDAC-Dose 2.1 dose calculator
    - **3D**: mass taken from the 3D volume segmentation
    - **Edited**: mass was edited using in the window **Organ Properties**
    - **OM+OM**: organ mass was calculated from the sum of the left and right counterpart organs (e.g. L-Kidney + R-Kidney)
    - **OM*2**: organ mass was calculated by doubling the mass of one of the counterpart organs

  Note: For paired organs the mass is calculated depending on the available organ masses of the left and right counterpart organs in the respective dosimetry mode, see Appendix 19.4 for detailed information.

- Column **TAC**: The user can select whether the TAC for the organ should be displayed in the TAC overview.
- Column **Ã(MBq*h)**: Displays the cumulated activity (in exponential notation, 4 decimal places) of the organ that was calculated during the Activity Integration step (see 11.6).

  Note: For paired organs the cumulated activity is calculated depending on the available activities of the left and right counterpart organs in the respective dosimetry mode, see Appendix 19.5 for detailed information.

11.4 Add New Organ

QDOSE makes it possible to add organs with corresponding data manually without the need of imaging data. This option can be used if the organ data has been acquired by other means e.g. blood sampling.

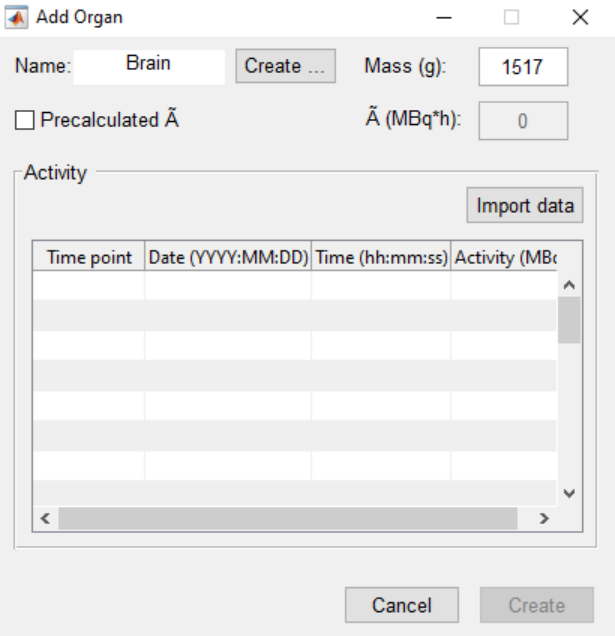


Figure 31: Window Add Organ.

1. Click on the button **Add new organ** below the table **Organs**. The window **Add Organ** opens.
2. Click on the button **Create …** in the upper center of the window **Add Organ**.
3. Select a predefined organ name from the dropdown list or select **New…** and enter an organ name.
4. To confirm, click the button **Create**.
5. Enter or edit the organ mass (OM); Organ masses used by the phantoms from IDAC-Dose 2.1 (ICRP 110) are displayed by default in the table **IDAC DOSE** in column **Mass (g)**. Organ masses differ between female and male and are automatically set according to the sex specification in the case.
6. There are 3 ways to enter information about additional organs in the window **Add Organ**.
    - **Precalculated Ã**: Allows you to enter a cumulated activity Ã (MBq*h), if the value was calculated elsewhere. Tick the checkbox **Precalculated Ã** to use this option and enter the value in the field **Ã (MBq*h)**. If this option is selected, curve fitting will not be possible for this organ.

      Note: The precalculated cumulated activity Ã is the same for all **Modes** (Planar, Hybrid, Volumetric). The cumulated activity will not be reset after changing case information like

e.g. calibration method or adding/deleting of image data. Only changing nuclide information (case nuclide or replacement nuclide) will reset the cumulated activity of added organs (see section 5.4 and 11.8).

- **Time-Activity Values**:
  - In the table, enter the time point, date, time and activity manually by clicking into the table.
  - It is also possible to import a TAC from a CSV file, where each time point is saved in a separate line as: yyyymmdd,hhmm,activity

  Note: It is not possible to enter Time-Activity values for left or right organs. Externally added left/right organs can only be added by entering **Precalculated Ã.**

7. Click the button **Create** to create the new organ.

11.5 Organ Properties

⚠ **CAUTION**
Editing organ properties may influence the dose calculation. Changing organ properties affecting the previously calculated TACs or Ã, will reset the curve fitting.

⚠ **CAUTION**
Patient and Organ Thickness influence the dose calculation. If the patient and/or organ thickness were edited in the window **Organ Properties**, the edited values will be used for background correction of planar data for further dose calculations in planar or hybrid mode.

NOTICE
Organ masses influence the dose calculation. Organ masses (OM) will be used with the following priority: 1. OM edited by user (via window **Organ Properties**) 2. OM from VOI segmentation step 3. Default organ mass from IDAC-Dose 2.1. The organ masses are converted to volumes by using the density values as described in Appendix 19.6.

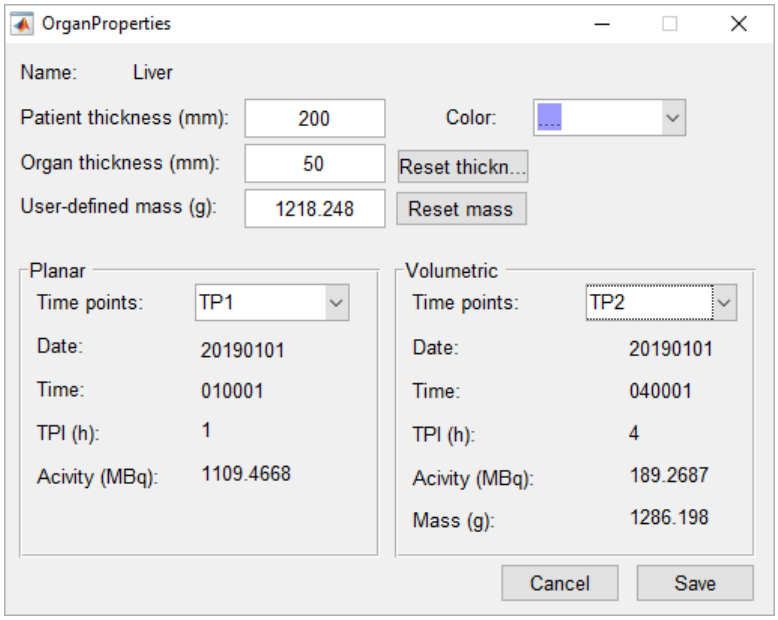


Figure 32: Window Organ Properties.

1. Select an organ from the table **Organs**.
2. Right-click on the selected organ and select the option **Organ Properties** from the options list.
3. Edit the following properties:
    - **Color**: Choose an organ color from the dropdown menu.
    - **Patient / Organ Thickness (mm)**: Define the patient / organ thickness in millimeters using the entry field. The entered values will override the values from the measurement in the window **VOI Segmentation** if available. The changes can be undone by clicking the button **Reset thickn...**.
    - **User defined mass (g)**: Define the organ mass. The entered values will override the default organ mass or measured organ mass from the window **VOI Segmentation** if available. The changes can be undone by clicking the button **Reset mass**.
    - **Planar**: Select a time point for a planar image from the dropdown menu to display information about the organ at this time point.
    - **Volumetric**: Select a time point for a NM image from the dropdown menu to display information about the organ at this time point.
4. Confirm the changes by clicking on the button **Save**.

11.6 Curve Fitting and Activity Integration

⚠ CAUTION
Incorrect units can result in incorrect dose calculation. For hybrid mode, the activity values in the table **Organ** in the window **Curve Fitting** are in arbitrary units.

Curve Fitting allows fitting an analytic function to the measured data points to create a time-activity-curve (TAC). Activity Integration allows calculation of the cumulated activity by integrating the area under the curve (AUC).

The window **Curve Fitting** provides following functionality:

- Different curve fitting models (monoexponential, biexponential, triexponential)
- Defining start parameters for the curve fit
- Exclusion of data points for curve fitting and activity integration.
- Activity integration using different means.

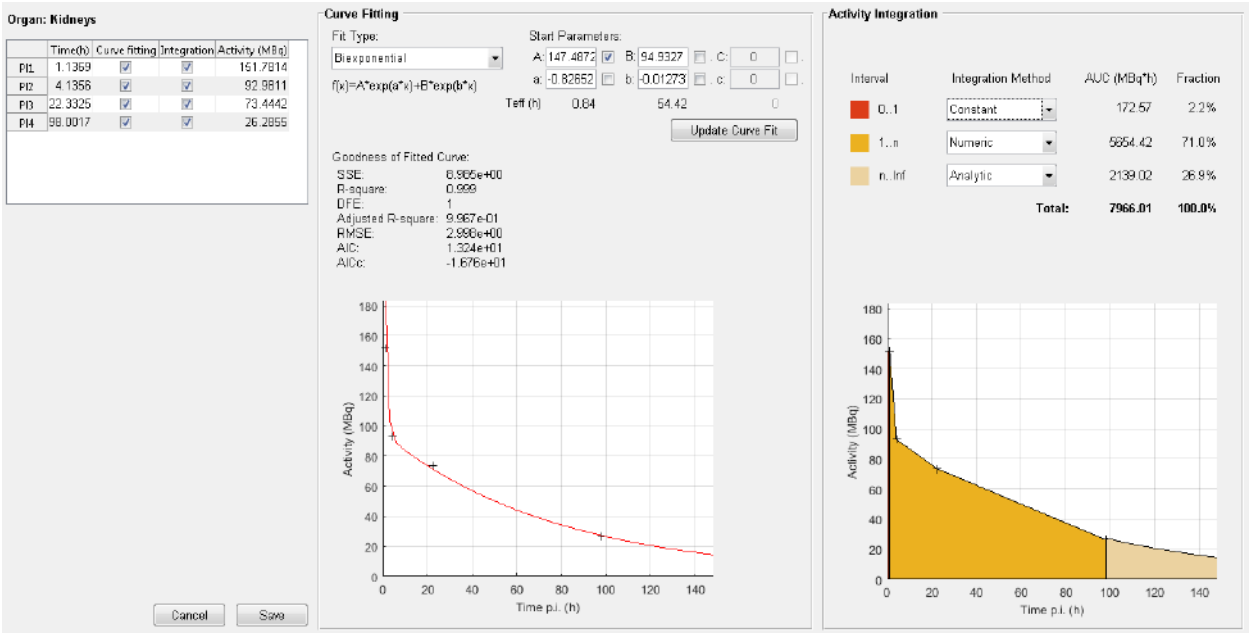


Figure 33: Window Curve Fitting.

1. Select an organ from table **Organs** in the window **Dose Analysis**.
2. If necessary, select a reference time point using the dropdown menu in the column **Ref**. in the table **Organs.**

- For Planar, Hybrid and Volumetric mode: the reference defines the time point in 3D to be used as source for the organ mass. The segmented volume of this time point is converted into an organ mass.
- Special for Hybrid mode: the reference also defines the time point to be used for calibration of the TAC. The time point is indicated by a circle in the TAC, see Figure 34.

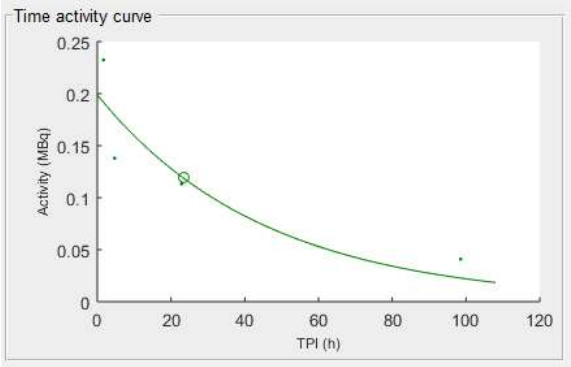


Figure 34: TAC in Hybrid mode calibrated to the second time point, which is indicated by the circle.

3. Click on the button **Curve Fitting** or right-click on the selected organ and select **Curve Fitting** from the options list. A separate window **Curve Fitting** is opened.
4. If necessary, exclude single time points from curve fitting and/or activity integration separately by clicking the corresponding checkboxes in the columns **Curve Fitting** and **Integration** in the table **Organ**.
5. Select the curve fit type from the dropdown menu **Fit Type** in the panel **Curve Fitting**. Available curve fit types are:
   - **Monoexponential:** consists of one exponential function
   - **Biexponential:** consists of two exponential functions
   - **Triexponential:** consists of three exponential functions
6. If necessary, edit the start parameters for the curve fit (***A, B, C, a, b, c***) by using the corresponding fields. By ticking the checkbox behind the parameter, the displayed value will be fixed and not be further optimized during the curve fitting. Only unchecked parameters will be optimized during the curve fitting.
7. Click on the button **Update Curve Fit** to apply the changes.

   The curve fit result together with the data points are displayed in the graphic below.

   Parameters for the **Goodness of Fitted Curve** are displayed below and indicate the following characteristics:

- **SSE:** Sum of squares due to error. This measures the total deviation of the response values from the fit of the response values.
- **R square:** Square of correlation between response values and predicted response values and is therefore a measure of how good the fit explains the variation of the data.
- **DFE:** Degree(s) of freedom in the error.
- **Adjusted R square:** R square adjusted by the residual degrees of freedom
- **RMSE:** Root mean square error
- **AIC:** Akaike information criterion. This is a means for model selection used in the curve fit.
- **AICc:** AIC with correction for small sample sizes.

8. Select the calculation method for the calculation of the cumulated activity in the panel **Activity Integration**. The integration is divided up in 3-time intervals with different available integration methods:

   - **0 … 1**: Interval from time point of injection to the first measurement time point
     - **Linear**: uses linear increasing activity from 0 to the first measurement time point.
     - **Constant**: uses a constant activity between 0 and first measurement time point that is equal to the activity of the first data point.
     - **Analytic**: uses the analytic curve fit result.
     - **Exclude**: excludes this interval from activity integration.
   - **1 … n**: Interval from first measurement time point to last measurement time point
     - **Numeric**: uses numeric integration of measurement data.
     - **Analytic**: uses the analytic curve fit result.
     - **Exclude**: excludes this interval from activity integration.
   - **n … Inf**: Interval from last measurement time point to infinity
     - **Analytic**: uses the analytic curve fit result.
     - **Decay only**: uses specific physical half-life of the nuclide.
     - **Exclude**: excludes this interval from activity integration.

   Note: For each interval, the area under the curve (AUC in MBq*h) and the fraction of each interval are displayed in the table **Activity Integration,** in the columns **AUC (MBq*h)** and **Fraction**.

9. Confirm the TAC and AUC calculations by clicking on the button **Save**.

11.7 Dose calculation

11.7.1 IDAC Dose Calculation

⚠ CAUTION
Dose calculation differs between IDAC-Dose 1.0 and IDAC-Dose 2.1. IDAC-Dose 1.0 and IDAC-Dose 2.1 use different source and target organs. Please refer to section 19.1 for detailed information about source organ conversion between IDAC-Dose 2.1 and IDAC-Dose 1.0. User defined organs may not be included as source organs into the dose calculation. Always check the input to IDAC-Dose calculation by clicking the button **Input data**.

NOTICE
Specific organ mass only considered for self-dose The patient specific mass (measured mass from Volume segmentation, edited mass) of a source organ can also be used for dose calculation with IDAC-Dose. The patient specific mass is only considered for calculation of the self-absorbed dose of the source organ. In case the source organ has no cumulated activity and therefore is not considered for dose calculation (check via button **Input data**), the patient specific mass has no effect on the dose.

NOTICE
Salivary glands not calculated automatically Different salivary glands can be segmented in the image data (L-Parotid gland, R-Parotid gland, L-Submaxillary gland, R-Submaxillary gland, L-Sublingual gland, R-Sublingual gland). The single salivary glands are not automatically considered for IDAC dose calculation. If salivary glands should be considered as input for IDAC dose calculation, the organ Salivary glands has to be added manually (**Add new Organ**). The cumulative activity for salivary glands can be entered using the information from the single salivary glands. Always check the input to IDAC-Dose calculation by clicking the button **Input data**.

NOTICE
User-defined organs and tissues are not considered for remainder body calculation The activity for 'Remainder' is calculated by subtracting the organ activities from the 'Total Body' activity. Only the activities of organs defined within the phantom (e.g. IDAC 2.1) are considered for the calculation of the 'Remainder' activity, but not the activities of additional user-defined structures, such as tumour lesions. To check which cumulated activities of organs and remainder body are used for the IDAC Dose calculation, use the button **Input Data**.

IDAC dose calculations can be performed using either IDAC-Dose 1.0 or IDAC-Dose 2.1 (Andersson et al., 2017).

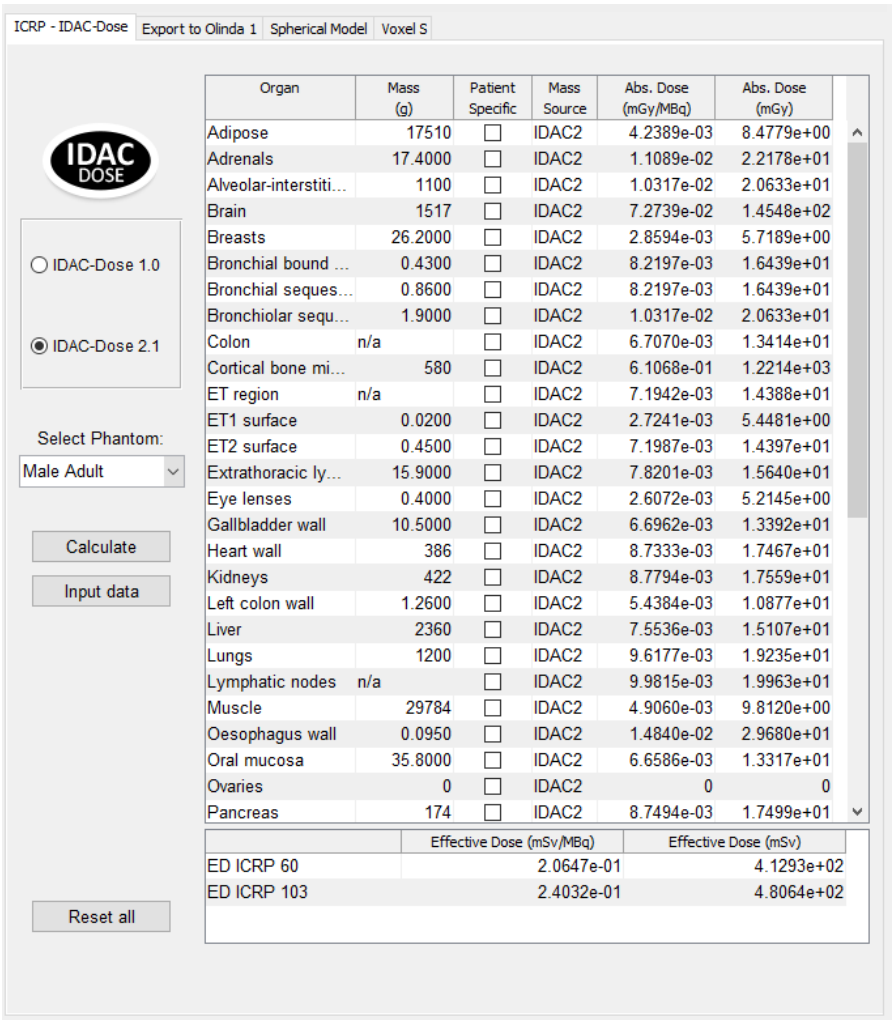


Figure 35: Tab ICRP - IDAC-Dose in the window Dose Analysis.

1. Select the tab **ICRP – IDAC-Dose**.
2. Select the intended version of IDAC-Dose from the options panel: **IDAC-Dose 1.0** or **IDAC-Dose 2.1**
3. Select a phantom from the dropdown menu **Select Phantom**.

   If you want to patient-specific organ masses for source organs, please tick the checkbox in column **Patient Specific** in the table **Doses** for those organs.
4. Click on the button **Calculate** to calculate the absorbed doses and effective doses which are displayed in the lower table. The calculation uses only valid source organs as input. The dose values are in exponential notation (4 decimal places).
5. Click on the button **Input data** to check which organs from the table **Organs** are used for dose calculation.

11.7.2 Voxel S

⚠ **CAUTION**
Voxel S dosimetry of lung, bone or bone lesions results in incorrect values. Voxel S kernels are only valid for soft tissue. Voxel S dose calculations for other tissues such as bone or lung are not valid. Furthermore, the user must decide how meaningful Voxel S dose calculations are for their specific image data as the activity distribution used as base for calculation may be incorrect due to partial volume effect.

NOTICE
Voxel S is only available in Hybrid and Volumetric mode. Segmentation of organs has to be performed on 3D data sets (PET or SPECT images).

Voxel S calculation computes the self-absorbed dose for an organ based on the activity distribution in the volume segmentation of the selected reference time point. The dose values are in exponential notation (4 decimal places).

The range of supported voxel sizes is attached in Appendix 19.3.

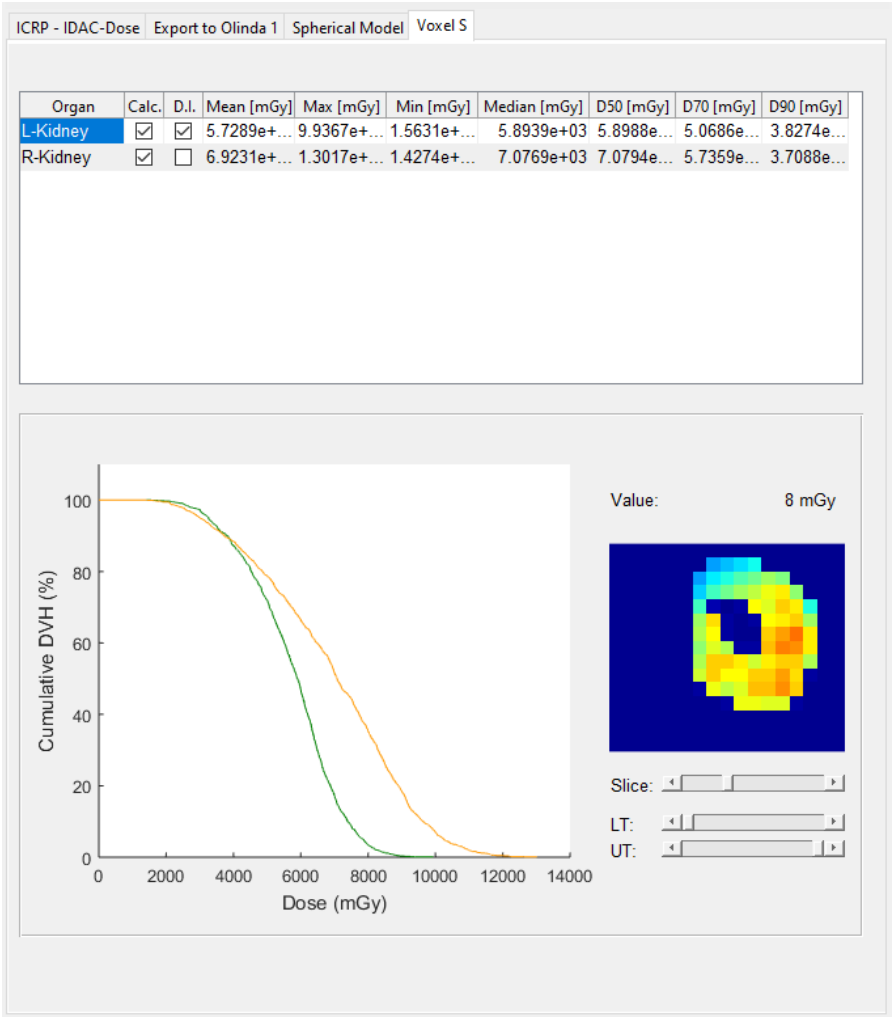


Figure 36: Tab Voxel S in window Dose Analysis.

1. Select the tab **Voxel S**.
2. Tick the checkbox in column **Calc.** in the table to run the Voxel S calculation for the selected organ.

   The region statistics for each organ are displayed in the dose table, and the cumulative dose volume histogram (DVH) is displayed.
3. Tick the checkbox in column **D.I.** in the table to display the dose image as slices.
4. Hover over the dose image on the right side to display the dose value of the corresponding pixel. The slice can be changed using the slider **Slice** and the lower and upper threshold can be adjusted using the sliders **LT** and **UT**.

11.7.3 Spherical Model

⚠ CAUTION
Using the spherical model for non-spherical organs may result in incorrect doses. It is the responsibility of the user to judge whether it is correct to assume a spherical shape for an organ or a structure for dose calculation.

Absorbed doses are calculated for the defined organs based on a spherical model approach (Stabin and Konijnenberg, 2000), which calculates the absorbed doses for a number of predefined sphere masses. For the specific organ masses, the dose is calculated in QDOSE by interpolation of the volume/mass by a power function.

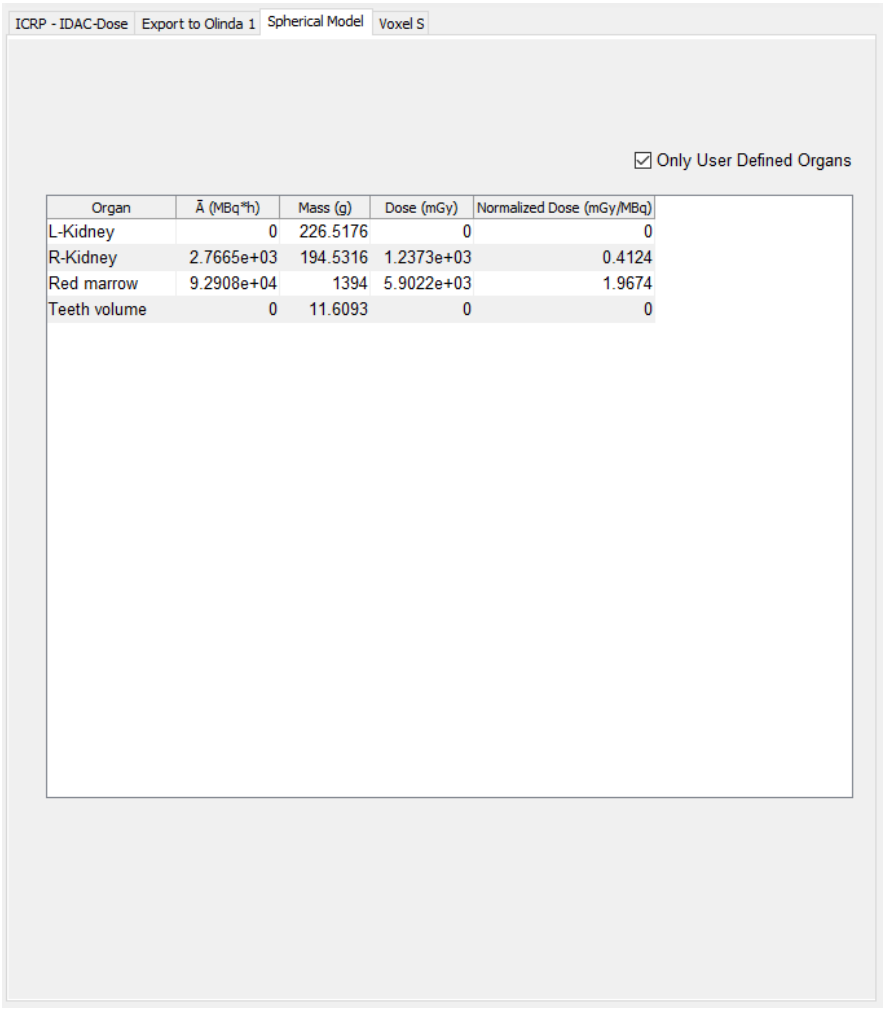


Figure 37: Tab Spherical Model in window Dose Analysis.

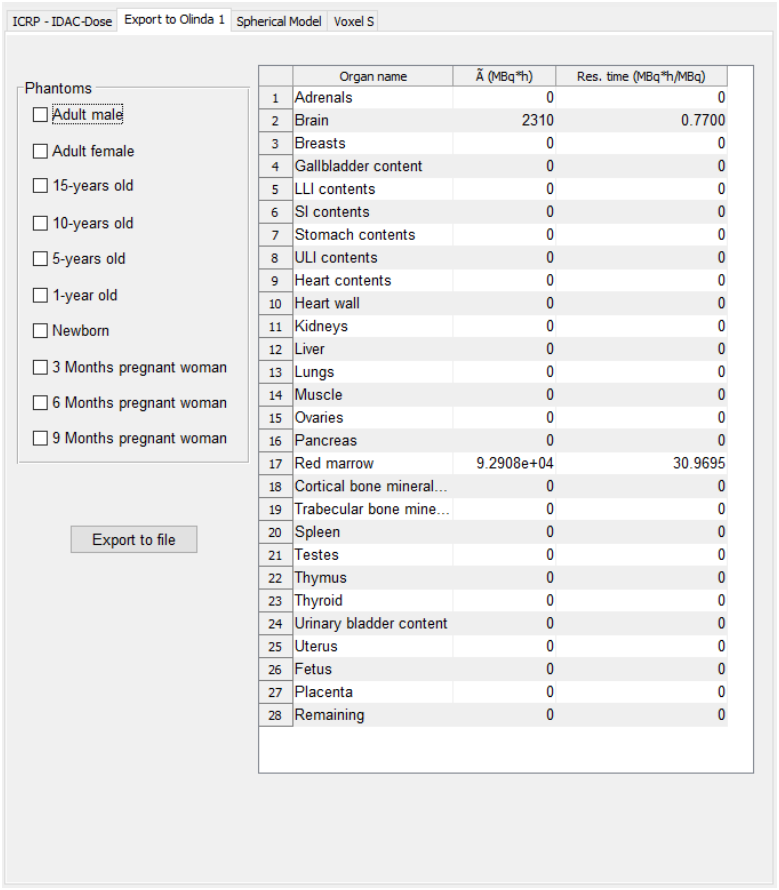
1. Select the tab **Spherical Model**.
2. Select if only the user-defined organs, such as a tumour, should be shown, by ticking the checkbox **Only User Defined Organs**.
3. The dose calculation results are shown in the resulting table. The dose values are in exponential notation with 4 decimal places.

11.7.4 Export to OLINDA/EXM 1.1

NOTICE

Source organs of OLINDA EXM 1.0, IDAC-Dose 1.0 and IDAC-Dose 2.1 are defined differently.
 	
In some cases, OLINDA EXM 1.0 and IDAC-Dose 1.0 and IDAC-Dose 2.1 use different definitions of organs.
 	
• The organs "Right colon contents (RC)", "Left colon contents (LC)" and "Rectosigmoid colon contents (RSC)" are used by IDAC-Dose 2.1 and are the default organs in QDOSE. If any or all of these source organs exist, the OLINDA source organs "ULI contents" and "LLI contents" are created and Ã will be calculated according to:
  ○ ULI = RC + 0.478873 · LC
  ○ LLI = RSC + 0.521127 · LC
• If the organs "Uterus/cervix" and "Uterus" both exist, the OLINDA export will use "Uterus" and ignores "Uterus/cervix".
• If the organ "LLI" exists, but also "RC" and/or "RSC", OLINDA export will use the organ "LLI" and does not calculate the Ã based on "RC" and "RSC".
• If the organ "ULI" exists, but also "RC" and/or "LC", OLINDA export will use the organ "ULI" and does not calculate the Ã based on "RC" and "LC".
 	
The user should check which organs were used for model-based dose calculations by clicking the button **Input data** in the window **Dose Analysis**.

Calculated residence times can be exported into an OLINDA 1.1 case file to be used for dose calculation within OLINDA. The values to be exported to OLINDA/EXM 1.1 (Stabin et al. 2005) are displayed in the table.



	Organ name	Ã (MBq*h)	Res. time (MBq*h/MBq)
1	Adrenals	0	0
2	Brain	2310	0.7700
3	Breasts	0	0
4	Gallbladder content	0	0
5	LLI contents	0	0
6	SI contents	0	0
7	Stomach contents	0	0
8	ULI contents	0	0
9	Heart contents	0	0
10	Heart wall	0	0
11	Kidneys	0	0
12	Liver	0	0
13	Lungs	0	0
14	Muscle	0	0
15	Ovaries	0	0
16	Pancreas	0	0
17	Red marrow	9.2908e+04	30.9695
18	Cortical bone mineral...	0	0
19	Trabecular bone mine...	0	0
20	Spleen	0	0
21	Testes	0	0
22	Thymus	0	0
23	Thyroid	0	0
24	Urinary bladder content	0	0
25	Uterus	0	0
26	Fetus	0	0
27	Placenta	0	0
28	Remaining	0	0

Figure 38: Tab Export to Olinda 1 in window Dose Analysis.

1. Select the tab **Export to Olinda 1**.
2. Select the phantoms to be exported by ticking the corresponding checkbox in panel **Phantoms**.
3. Click on the button **Export to file** and select a target file in the dialog window.

11.8 Replacement Nuclide / Dose Extrapolation

⚠ CAUTION
Nuclide replacement is only valid for identical biological behaviour. The methodology applied for nuclide replacement assumes that the biological behaviour of a radiopharmaceutical is identical for the original nuclide/isotope and its replacement. Differences in calculated biological half-lives originate from uncertainties of the curve fitting. Activities and cumulated activities are scaled linear with the extrapolated activity.

⚠ CAUTION
Image data with original nuclide must be suitable for nuclide replacement. Image data with the original nuclide must ensure to capture the complete biological behaviour of the radiopharmaceutical for the organs/tissues of interest, otherwise the results with the replacement nuclide might not be reliable. Negative biological half-lives after nuclide replacement need to be investigated and might be a hint that further imaging is required to completely retrieve the biological behaviour of the radiopharmaceutical for a specific organ/tissue.

⚠ CAUTION
Nuclide replacement may enhance the effect of inaccuracies in fitted pharmacokinetic parameters. Replacing a nuclide for another one with a significantly different half-life (e.g. much longer half-life) may result in over- or under-estimation of the absorbed doses for organs/tissues for which the actual pharmacokinetics of the organ/tissue cannot be completely and accurately determined from the available image data.

⚠ CAUTION
Dosimetry of replacement nuclide must always be verified. Dosimetry using a replacement nuclide does not replace performing the dosimetry with the replacement nuclide directly or verifying the results with a different method. The results should only be used as a rough estimate of the doses and should not be used to determine patient safety.

⚠ CAUTION
Changing nuclide will reset added organs with precalculated Ã. Additional organs with precalculated Ã can be added in **Dose Analysis** window. The cumulated activity of those organs will be reset after changing the nuclide. Always check the input to IDAC-Dose calculation by clicking the button **Input data**.

It is possible to perform a nuclide substitution using QDOSE. The TACs of the organs are automatically corrected for physical decay of the original nuclide to the time of injection, leaving only the biological clearance. In a second step, the physical decay of the replacement nuclide is applied to the TACs.

Curve fitting and dose calculation can then be performed for the replacement nuclide. In addition, or alternatively, the user can enter an extrapolated activity for dose extrapolation.

1. Select a replacement nuclide from the dropdown menu in the panel **Replace Nuclide** (see Figure 29).
2. Enter a value for the extrapolated Activity in MBq in entry field.
3. Perform curve fitting and activity integration again for this nuclide.
4. Click the button **Reset** in order to reset the calculations to the original values.

12 Dose Analysis SIRT/MAA

Dose Analysis SIRT/MAA allows dose calculation using Voxel S, injected activity prediction and report generation/value export.

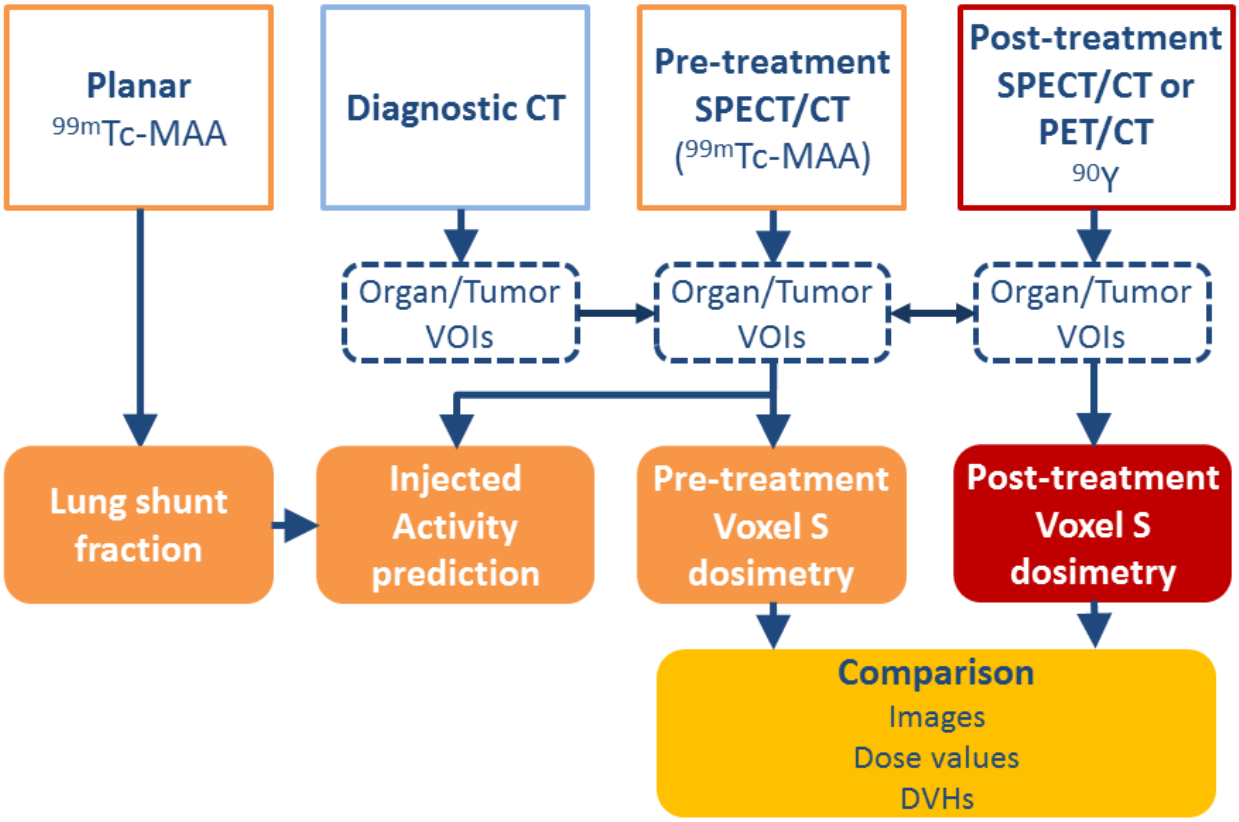


Figure 39: SIRT/MAA Flowchart.

12.1 Setting up the Case

NOTICE
Only one pre- and one post-treatment data set can be evaluated per case. It is only possible to assign one NM image data set to analysis group PRE and one NM image data set to analysis group POST in the scope of one case.

1. Create a case as described in section 5.3. In the window **New Case** select the option **MAA/SIRT** in the dropdown menu **Mode**.
2. Load the image data to the case as described in section 5.1 step 2.
3. After loading the image data to the case, open the window **Edit Case**.
4. For NM data sets, define the analysis group in the table **NM Images** from the dropdown menu in column **Analysis Group**. Available options are:
    - **PRE**: Pre-treatment SPECT image data.
    - **POST**: Post-treatment PET image data
    - **CT/MR**: Only additional morphological image for improved organ segmentation.
    - **N/A**: not applicable.

12.2 Coregistration and Volume Segmentation

The steps of 2D ROI Drawing, 3D Coregistration and VOI Segmentation are the same as for the other workflows. Please refer to the corresponding sections 7, 9 and 10 on how to proceed.

12.3 Dose Calculation

⚠ CAUTION
Incorrect organ segmentation results in incorrect dose values. Only the segmented volume (see Volume Segmentation, section 10.3) is to be used for dose analysis.

NOTICE
Pre-treatment dosimetry based on ^{90}Y Voxel S kernel It is possible to perform pre-treatment dosimetry (^{99m}Tc-MAA-Scan). Pre-treatment dosimetry is based on the ^{90}Y Voxel S kernel.

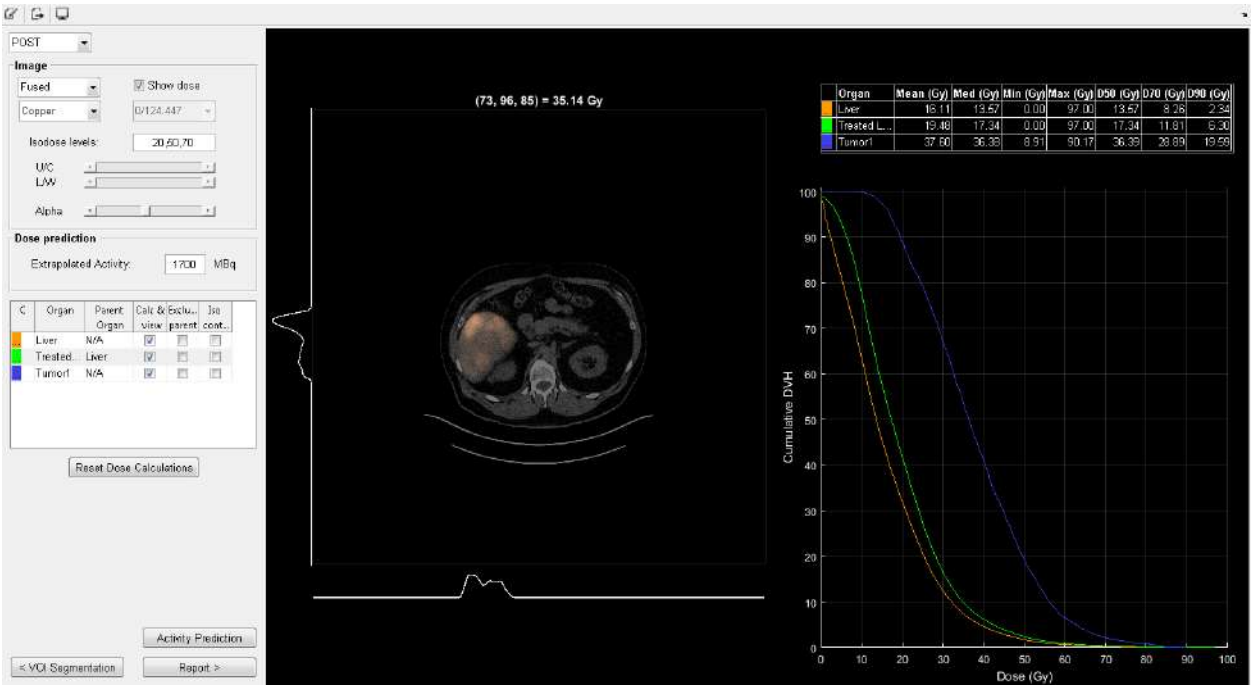


Figure 40: Window Y90 Voxel S for SIRT dose analysis.

1. Select the analysis group in the dropdown menu on the upper left corner of the window **Y90 Voxel S**: **PRE, POST** or **PRE vs POST**.
2. Select the image modality from the drop-down menu in the left upper corner of the panel **Image**: **NM**, **CT** or **Fused**.
3. Select the colour map for the selected modality from the lower dropdown menu in panel **Image**.
4. Select the windowing for image view. Depending on the image modality different windowing options are available:

   Select the windowing for CT/MR images in the panel **Image** (see Figure 40):

   - **Window**: In the upper drop-down menu, a window can be chosen from a list of predefined windows. The syntax is defined as window width/window center in Hounsfield Units (HU) (e. g. **300/40** means a window with a width of 300 HU around a center of 40 HU.
   - **U/C**: slider for fine adjustment of window center **C**

- **L/W**: slider for fine adjustment of window width **W**

Select the windowing for NM images in the panel **Image** (see Figure 40):

- The windowing can be adjusted using the sliders for **U/C** (Upper Threshold **U**) and **L/W** (Lower Threshold **L**).

For mode **Fused**, the windowing options are disabled as the settings from the single modalities are used. The alpha blending between the two images can be adjusted using the slider **Alpha**.

5. Select the intended organ from the table **Organs** for which dose calculation is to be performed.
6. Start the calculation by ticking the checkbox in column **Calc & view** in the table **Organs**.
7. Tumours can be excluded from the parent (treated liver) organ to determine the absorbed dose to the healthy treated liver tissue. In addition, the treated liver tissue can be excluded from its parent liver to calculate the dose to the untreated part of the liver. In order to do so, tick the checkbox in column **Exclude from parent** in the table **Organs**.
8. The cumulated dose volume histogram (**Cumulative DVH**), dose image and dose statistics table for the organs are calculated and displayed.
9. Tick the checkbox of the intended organ in column **Isocontour** in the table **Organs** to display the isocontours in the dose image. The Isodose levels can be adjusted in the entry field **Isodose levels** in panel **Image**.

12.4 Dose Prediction

The tool Dose Prediction allows predicting the dose to each organ based on the user-defined extrapolated activity.

1. Enter the extrapolated activity for the treatment in MBq in the panel **Dose prediction** in the field **Extrapolated Activity**, in the window **Dose Analysis**.
2. The absorbed dose values are recalculated and updated in the dose statistics table, dose image and graphics for the cumulative DVH.

12.5 Injected Activity Prediction

⚠ CAUTION
Activity Prediction tool is not intended to be used clinically. The Activity Prediction tool is not intended to be used to make decisions for clinical use (e.g. treatment planning). It is for research purposes only. Different calculation methods can result in different calculated activities. Treatment should not be planned based on the displayed values. Instead, the instructions of the manufacturer of the spheres should be used.

NOTICE
Incorrect naming of organs influences calculations. The segmented tumour volume and activity must contain the word ‘tumour’ or ‘tumor’ in order to be taken into account for activity prediction.

NOTICE
Definition of analysis groups influence initial values for activity prediction. If no PRE or POST analysis group is defined values for volumes and activities are taken from the first data set.

The tool **Injected Activity Prediction** allows predicting the activity that needs to be injected in order to get the intended activity to the liver. The calculation can be performed using different calculation methods and limiting factors such as dose values for specified organs.

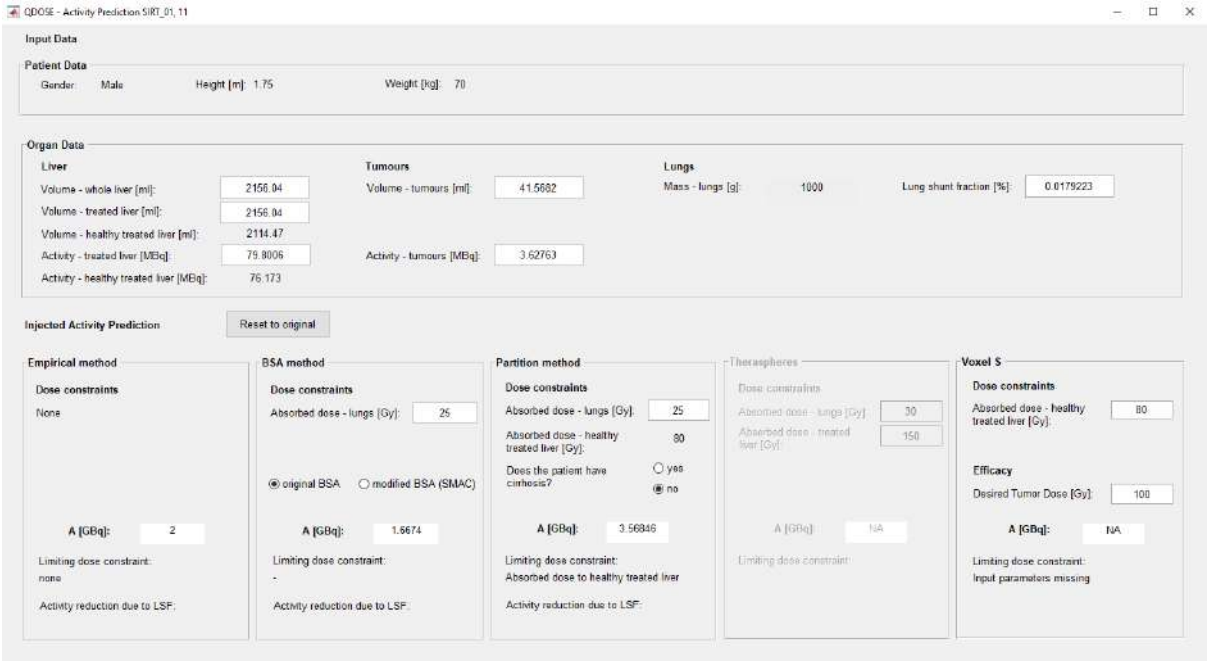


Figure 41: Window Activity Prediction.

1. Click on the button **Activity Prediction** in lower left corner of the window **Dose Analysis**. The window **Activity Prediction** opens (see Figure 41).

2. In the panel **Organ Data**, the volumes and activity values for the Liver and Tumours are displayed, which were obtained from the VOI segmentation. The lung shunt fraction is calculated in the field **Lungs shunt fraction [%]**. These values can be edited using the corresponding field and pressing **Enter**.

   Note: If you want to undo any editing, click on the button **Reset to original**.

3. After entering all input values, the calculation method can be chosen. The injected activity can be predicted for SIR-spheres (Sirtex Medical Limited, Australia) or Theraspheres (BTG International Limited, United Kingdom). For SIR-spheres the following methods are available:

   - **Empirical method**
   - **BSA method**: Body Surface Area (BSA) and modified BSA (SMAC) method
   - **Partition method**

   A separate calculation method is available for Theraspheres in panel **Theraspheres**.

   In addition, activity prediction using Voxel S is available for both sphere types in panel **Voxel S**. The user can define calculation constraints based on the dose for organs in the fields: Absorbed dose – lungs [Gy], Absorbed dose – healthy treated liver [Gy] and Desired Tumor Dose [Gy]. Confirm by pressing **Enter**.

4. The resulting values for the predicted activity for injection are displayed in the field **A [GBq]** in each panel in the field **Activity Prediction**.

   Note: For the method **Voxel S**, the injected activity will be calculated using the Voxel S dosimetry results. The displayed injected activity corresponds to the more restricting absorbed dose value (healthy treated liver or tumours). This method requires prior Voxel S dose calculation including the healthy treated liver (with the tumour excluded from the parent treated liver).

13 Reporting

The automatically generated report combines the results of all evaluation steps in an overview document. It is also possible to export a variety of results tables in CSV format for further processing.

13.1 Report Generation

The generated report is based on KeV Medical Imaging's generic template. To be able to generate a report, the curve fitting step must have been performed, first.

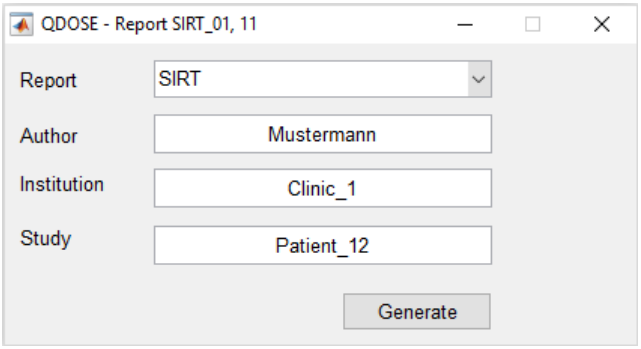


Figure 42: Window Report.

1. In the window **Patient Browser**, click on **Report** in the file menu and select **Generate Report**. The window **Report** opens.
2. Select the dosimetry workflow to generate report for from the dropdown menu **Report** depending on the available data: **Planar, Hybrid, Volumetric, SIRT.**
3. Enter the author name, organization (optional), and study in the fields **Author**, **Institution** and **Study**.
4. Click on the button **Generate** and select the target file from to save as a PDF file. The precision in the report is 2 decimal places for **IDAC Dose** (1.0 & 2.1) and **Spherical Model**, and 3 decimal places for **Voxel S**.

13.2 CSV Export

⚠ CAUTION
Processing of exported values can lead to different results. The format of the exported values using the *CSV Export* tool may differ from the PDF report. Further processing of the exported values with other software may lead to different results than those displayed in QDOSE. The user must check the correctness of the exported values especially when using the exported values for further post-processing.

1. Click on the icon **Save CSV File**  in the toolbar of the window **Dose Analysis** The window **Report** opens.
2. Select the data to be exported as a CSV file from the upper dropdown menu.
3. Click on the button **Export** and select the target file from to save as a CSV file

Note: If the full table is selected, the listed individual tables are combined to contain all the information in one table.

13.3 Notes

Notes by the user can be added to the case which will be printed along with the report.

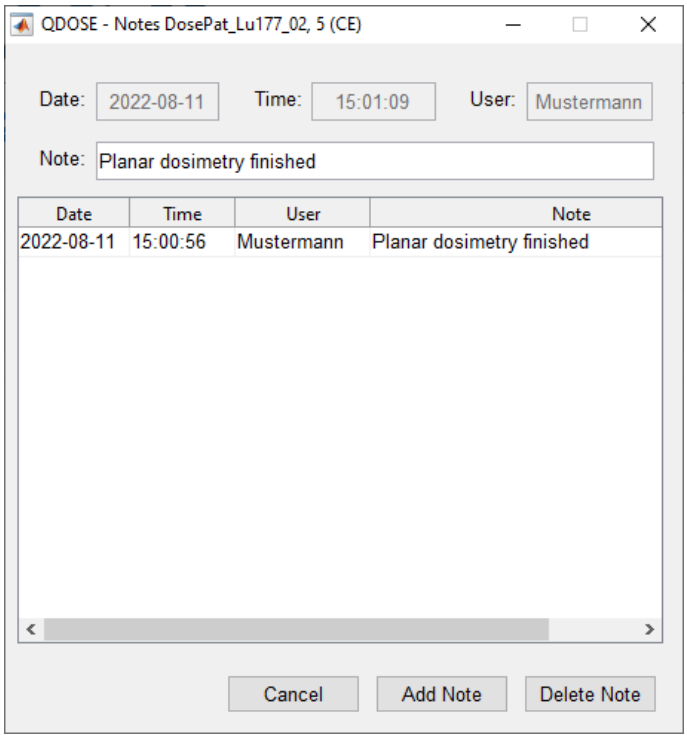


Figure 43: Notes Window.

13.3.1 Add Notes

1. Click on the icon **Add Notes** in the toolbar of any window or use the file menu in the **Patient Browser** by clicking on **Report** > **Notes**.
2. Type the note in the corresponding text field. The date, time and current username are automatically entered.
3. Click on the button **Add Note**. The note is saved and displayed in the list.

Note: Entered notes are available even when case is not saved.

13.3.2 Delete Notes

1. Select a note in the **Notes** window.
2. Click on the button **Delete Note**.
3. Confirm deletion of the note. The note is deleted and is removed from the list.

Note: Deleted notes are no longer available even when case is not saved.

14 User Management

The user management tool allows to create and manage users with different roles (user and admin) to authorise functionalities and to authenticate users before accessing the program. The username of the current active user is also saved as author when creating notes to a case.

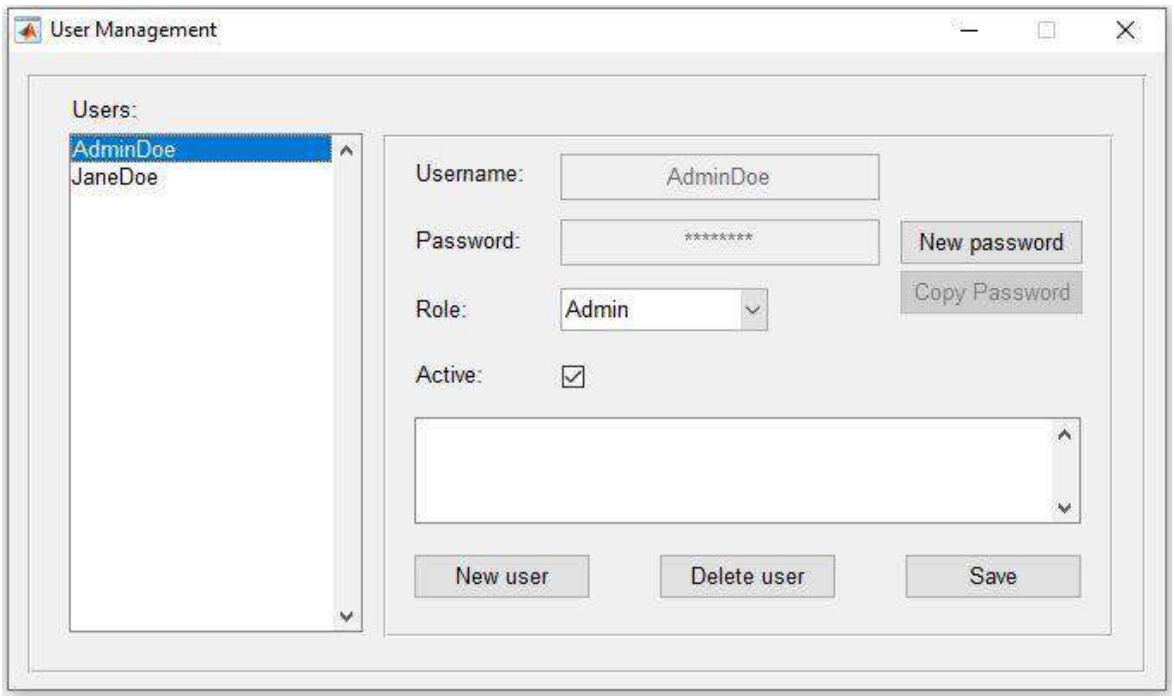


Figure 44: Window User Management.

14.1 Creation of users

14.1.1 User roles

In QDOSE, two different kinds of user roles are available: user and admin (abbreviation of administrator user). These roles can be discriminated by the actions they are authorised to perform, see Table 1.

Table 1: Authorised actions for user roles

Role	User	Admin
Perform dosimetry	✓	✓
Reset own password	✓	✓
Set/reset other users' and admins' password		✓
Create, delete, manage users and admins		✓
Manage/change users database		✓

14.1.2 Login credential requirements

Usernames must be compliant to the following requirements:

- at least one character, maximum 50 characters,
- usernames must consist of following characters only: A-Z; a-z; 0-1, - (minus) and _ (underscore); no special characters are allowed.

Passwords must be compliant to the following requirements:

- at least 8 characters, maximum 50 characters,
- at least one digit,
- at least one uppercase character,
- at least one lowercase character,
- following characters are allowed: A-Z; a-z; 0-1, - (minus) and _ (underscore); no special characters are allowed.

14.1.3 Create admins

NOTICE
One-time super admin token is only valid once. The super admin token is a one-time token. It is consumed by first creation of an admin. Then the 'SuperAdmin' account is deactivated. In case all admin accounts were deactivated, they can only be reactivated by a super admin. A new license with a new one-time token needs to be generated by QDOSE support. The new license needs to be imported into QDOSE. Then one-time access by the super admin account is possible. After reset of admin passwords, the super admin is deactivated again.

NOTICE
Create an admin account for backup. In case an admin has forgotten his/her password, the account can only be reactivated, and the password can only be reset by another admin role. It is recommended to create at least two admin accounts and save the credentials of one admin account as a backup. Store the backup admin account credentials in a save and restricted location, e.g. a password safe. Accounts will not become invalid after time.

For the first set-up of users, the authenticated 'SuperAdmin' has to create at least one admin. Further administrators or users can then be created by 'SuperAdmin' or any other admin.

Once an admin was created by the ‘SuperAdmin’, the 'SuperAdmin' account is deactivated. The ‘SuperAdmin’ can continue the session but cannot login again.

Only admins and the ‘SuperAdmin’ are authorised to create users.

In order to create an admin, follow these steps:

1. Click on **Tools > User Management**. The window **User Management** opens (see Figure 44) without any contents.
2. Click on the button **New User**, if necessary.
3. Enter a **Username** compliant to the requirements in chapter 14.1.2.
4. Enter a **Password** compliant to the requirements in chapter 14.1.2.
5. Select the role “**Admin**” from the dropdown menu **Role**.
6. Set account to active in checkbox **Activity**, if necessary.
7. Enter a comment (optional).
8. Click on button **Save**.
9. The user is created and displayed in the list of **Users** on the left side of the window.

14.1.4 Create users

In order to create users, follow the same steps 1 to 9 as described in section 14.1.3, except for selecting the role “**User**” in step 5.

14.2 Maintaining and authorization of users

14.2.1 Reset passwords

Only admins are authorised to reset passwords for other users and admins.
In order to reset a password, follow this instruction:

1. Click on **Tools > User Management**. The window **User Management** opens (see Figure 44).
2. Select the name of the account from the list **Users** which needs to be reset.
3. Click on the button **New Password**.
4. Enter a new **password** compliant to the requirements in chapter 14.1.2.
5. Confirm by clicking **OK**.
6. Click on button **Save**.

14.2.2 Activate/Deactivate users

An activated user has access to the software tool after successful authentication (login), while a deactivated user does not. After three failed login attempts a user account is deactivated automatically. Only admins are authorised to activate and deactivate other users and admins.

In order to activate/deactivate, follow this instruction:

1. Click on **Tools > User Management**. The window **User Management** opens (see Figure 44).
2. Select the name of the account from the list **Users** which needs to be activated/deactivated.
3. Click inside the checkbox **Activity** to activate (enabled checkbox) or deactivate (disabled checkbox) the account.
4. Click on button **Save**.

14.2.3 Delete users

Only admins are authorised to delete users and admins.
In order to delete an account, follow this instruction:

1. Click on **Tools > User Management**. The window **User Management** opens (see Figure 44).
2. Select the name of the account from the list **Users** which needs to be deleted.
3. Click on the button **Delete user**.
4. Click on button **Save**.

14.2.4 Changing Users Database Path

Changing of users database can only be performed by admin. In order to change the location of the users database, the user has to copy and paste an existing database to the new intended location. By default the users database is created under:
'C:\ProgramData\QDOSE\QDOSEUsers.db7'.

To change the path, please follow these steps:

1. Copy the file '*QDOSEUsers.db7*' from the folder '*C:\ProgramData\QDOSE\'.*
2. Paste it to the new location.
3. In window **QSettings** select the new location under **Users DB Path** by clicking on the button **Browse** and select the corresponding file on the file system.

14.2.5 Maintaining users for multiple installations

⚠ CAUTION
Simultaneous changes to the database might be lost The user database should only be accessed by one admin at a time. Simultaneous changes to the user management might lead to data loss on the user management that was opened as second instance. Save changes immediately and do not leave the user management open for a longer period of time.

NOTICE
Import of a new license will reset only the super admin token of the master license. When importing a new license, only the one-time super admin token of the master license will be reset. One-time super admin tokens of sublicenses that use the same users' database will not be reset.

For the use case that multiple QDOSE installations with separate licenses want to use the same users' database, an admin can set-up a common shared users database.
One license will act as the master of that database while the other licenses are sublicenses of that database.
In order to set-up a common shared database for multiple QDOSE installations, follow these instructions carefully:

1. Identify the system on which the master license is activated by clicking on **Help > License** in the **Patient Browser**.
2. The license details will be displayed. In the tag **User DB Master** either '0' or '1' is displayed:
    - '0' indicates that this license is a sublicense.
    - '1' indicates that this license is a master license.
3. Once you have identified the master license system as in step 2, you can set-up the users and admins in window **User Management** on this system. If you have already set-up all accounts, continue with step 4.
4. In window **QSettings**, check the location of the users database in the field **Users DB Path**. The default location is: '*C:\ProgramData\QDOSE\QDOSEUsers.db7'.*
5. Copy the file '*QDOSEUsers.db7*' from the folder '*C:\ProgramData\QDOSE'.*
6. Paste it to the new location where all intended systems with their users have access. Please check access rights (reading and writing rights) on the file system beforehand and adapt if necessary.
7. In window **QSettings** select the new location under **Users DB Path** by clicking on the button **Browse** and select the corresponding file on the file system.
8. Identify the system on which the sublicense is activated as described in step 2.

9. On this system, again select the new location in window **QSettings** under **Users DB Path** by clicking on the button **Browse** and select the corresponding file on the file system.
10. Repeat steps 8 and 9 for all systems on which sublicenses are activated.

14.3 Best practices

1. **Set strong passwords to protect sensible patient health data from unauthorised access.**
   Password recommendations [German Federal Office for Information Security, BSI]:
   - Rule 1: ***The longer the better!***
   - Rule 2: ***Easy to remember!***
   - Use all available characters and symbols.
   - Tip: Take a sentence and use the first character of each word for your password. One can also replace number words by digit characters.
   - Do not use popular weak passwords like ‘123456’ or ‘qwert’.
   - Do not us names of family members, pets, best friends, popular stars, birth dates and so on, because they can easily be guessed.
   - Use a password manager or password safe to manage different passwords securely.

2. **Create a backup admin account.**
   In case an admin has forgotten his/her password, the account can only be reactivated and the password can only be reset by another admin role. It is recommended to create at least two admin accounts and save the credentials of one admin account as a backup. Store the backup admin account credentials in a save and restricted location, e.g. a password safe. Accounts will not become invalid after time.
3. **Ask users and admins to change their password after first set-up.**
   Always request users and admins to change their password after it was created by an admin to prevent breach of privileges.

15 User Authentication

15.1 Login

NOTICE
Account will be deactivated after to many failed login attempts. If a user enters a wrong password three times in a row, the account is automatically deactivated and needs to be activated again by an admin, see chapter 14.2.2.

After start of the application, a login window appears, see Figure 45.
In order to authenticate:

1. Enter the **Username** and **Password** provided by the QDOSE admin.
2. Click **OK**.

Figure 45: Window Login.

15.2 Change password

If you want to change or are required to change your own password, e.g. after first login, follow these steps:

1. Click on **Tools > Change password**. The window **Old password** opens (see Figure 46).
2. Enter your current (old) password that you would like to change.
3. Click **OK**. The window **New password** opens (see Figure 47).
4. Enter your new password compliant to password requirements in chapter 14.1.2 and confirm the password. Take into consideration our password recommendations in chapter 14.3.
5. Click **OK**. A dialogue window will confirm the successful change of the password.

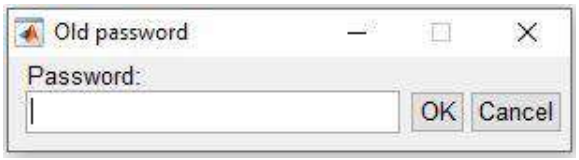


Figure 46: Window Old password.

Figure 47: Window New password.

15.3 Change user

In order to change to another account, you need to authenticate again. The intended account must already exist. Please follow these steps:

1. Save your current case, if necessary.
2. Go to **Tools > Change user**. A login screen similar to Figure 45 will appear.
3. Enter the **Username** and **Password** provided of the account you want to change to.
4. Click **OK**. A dialogue window will confirm the successful login as the new user.

15.4 Session timeout

NOTICE
Check to save the current case before changing users and after session time-out. The work on the current case is not automatically saved, not even at auto-logoff or change of users, but must be actively saved by the current user. Note, if the user is changed after the auto-logoff, it must be checked if the current case needs to be saved.

For security reasons, QDOSE will automatically log-out users after a defined time of inactivity. The access to the program is blocked and the information in the **Patient Browser** are hidden. Users have to re-authenticate to be granted access to the program again, see Figure 48.

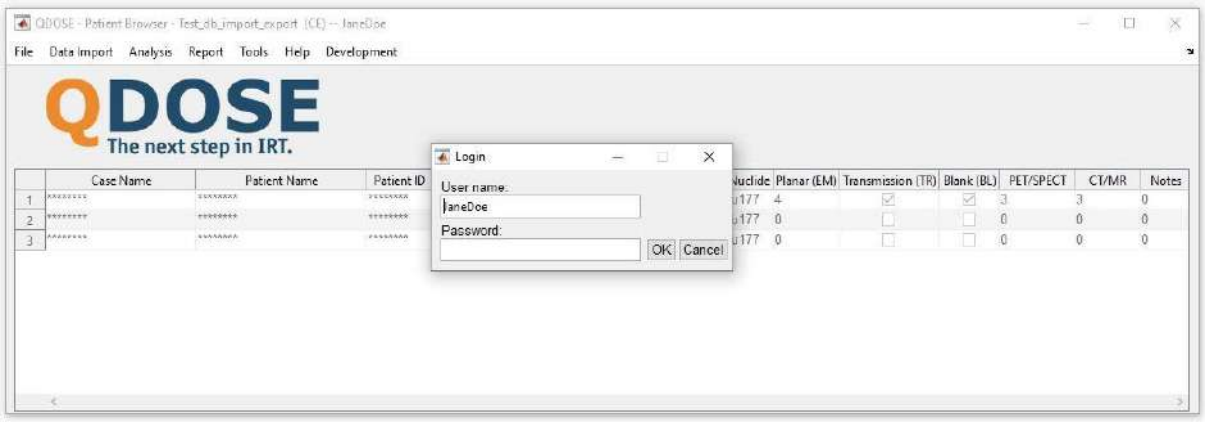


Figure 48: Window login after auto-log-out and hidden information in window Patient Browser.

The period of the session timeout is set to 15 minutes by default and can be adapted in the window **QSettings** under **Application > Session Timeout (min)**, see chapter 4.

16 Toolbar Elements

Save CSV File	Export dosimetry data as CSV file
Add Notes	Add notes in software which are printed to the report (PDF)
Zoom In	Click on the image to zoom in step-wise Draw a rectangle to zoom into this section Right-click on the image to zoom out step-wise
Reset Zoom	Reset zoom to full view
Pan	Pan over the image by dragging the image
Enable/Disable Image Information	Enable/disable the display of image information
Display Cross	Enable/disable the display of the cross hair
Display Boundaries	Enable/disable the display of the boundaries (orange line)
Display Activity Segmentation	Enable/disable the display of the activity segmentation (yellow line)
Display Volume Segmentation	Enable/disable the display of the volume segmentation (red line)
Display MIP (Maximum Intensity Projection)	Enable/disable the display of the Maximum Intensity Projection
Screenshot of Main View	Make a screenshot of the figure in the main view to be included in the report (PDF)
Enable/Disable Filter for Image Data	Enable/disable the display of the filtered image

17 Abbreviations

Abbreviation		Explanation
2nd	:	Second (image)
2D	:	Two Dimensional
3D	:	Three Dimensional
Ã	:	Cumulated Activity
ANT	:	Anterior
AUC	:	Area Under the Curve
BL	:	Blank
BSA		Body Surface Area
CSV	:	Comma Separated Value
CT	:	Computed Tomography
DICOM	:	Digital Imaging and Communications in Medicine
DVH	:	Dose Volume Histogram
ED	:	Effective Dose
EM	:	Emission
FWHM		Full Width at Half Maximum
ICRP	:	International Commission on Radiological Protection
IDAC	:	Internal Dose Assessment by Computer
LT	:	Lower Threshold
LUT	:	Look Up Table
MAA	:	Microaggregated Albumin
MRI	:	Magnetic Resonance Imaging
NM	:	Nuclear Medicine
OM	:	Organ Mass
PDF	:	Portable Document Format
PET	:	Positron Emission Tomography
POST	:	Posterior
POST	:	Post-treatment
PRE	:	Pre-treatment
PSF	:	Point Spread Function
ROI	:	Region Of Interest
SBR	:	Signal to Background Ratio

SIRT	:	Selective Internal Radiation Therapy
SPECT	:	Single Photon Emission Computed Tomography
TAC	:	Time Activity Curve
TP	:	Time Point
TPI	:	Time Post Injection
TR	:	Transmission
UDI	:	Unique Device Identifier
UT	:	Upper Threshold
VOI	:	Volume Of Interest
WB	:	Whole Body

18 Reporting of Events

KeV Medical Imaging distributes QDOSE and has the responsibility of ensuring that it is working properly. QDOSE is fully tested and validated. There may be problems, nevertheless.

The users must communicate issues, so that KeV Medical Imaging can perform corrective measures and make improvements, and, if necessary, inform other users. Please report malfunctions or changes in performance that may affect safety to the manufacturer or distributor. Every issue will be evaluated on an individual basis. In case of a serious incident, please report immediately to the manufacturer or distributor, and the competent authority in your country.

Please use the following template when reporting an event or problem:

Who is reporting?

Name of Institution:
Street:
ZIP code/city:
State:
Country:
Contact person:
Telephone:
Fax:
E-mail:
Date:
Signature:

Device Information:

Software version or UDI:

Description of Event

Send notifications to

KeV Medical Imaging
Sokratous 3, 11147, Galatsi, Greece
E-mail: qdose@kevimaging.gr
Web: https:// www.qdose.net
Telephone: +0030 2111154521

KeV Medical Imaging will not accept hardware for safety reasons.

19 Specifications and Performance Characteristics

19.1 IDAC-Dose 1.0 and IDAC-Dose 2.1

19.1.1 Radionuclides

The dose calculation with IDAC-Dose 1.0 and IDAC-Dose 2.1 can be performed using the following nuclides (depending on the software license):

^{225}Ac, ^{211}At, ^{213}Bi, ^{11}C, ^{64}Cu, ^{67}Cu, ^{18}F, ^{68}Ga, ^{166}Ho, ^{124}I, ^{131}I, ^{111}In, ^{177}Lu, ^{15}O, ^{212}Pb, ^{223}Ra, ^{224}Ra, ^{186}Re, ^{188}Re, ^{44}Sc, ^{153}Sm, ^{89}Sr, ^{99m}Tc, ^{227}Th, ^{86}Y, ^{90}Y, ^{89}Zr

19.1.2 Conversion of Source Organs (Cumulated Activities / Residence Times) between IDAC-Dose 2.1 and IDAC-Dose 1.0

IDAC-Dose 2.1	IDAC-Dose 1.0
Adrenals	Adrenals
Urinary bladder content + Urinary bladder wall	Bladder cont.
Brain	Brain
Stomach contents	Stomach cont.
SI contents	SI contents
RC cont+0.478873*LC cont	ULI contents
0.521127*LC cont+RSC cont	LLI contents
Kidneys	Kidneys
Liver	Liver
Lungs + Lung tissue + Alveolar-interstitial + Bronchi + Bronchi bound + Bronchi seq + Bronchioles + Bronchioles bound + Bronchioles seq	Lungs
Muscle	Other tissue
Ovaries	Ovaries
Pancreas	Pancreas
Red (active) bone marrow	Red marrow
Cortical bone mineral surface[*1)] + Cortical bone mineral volume[*1)] + Cortical bone marrow + 0.5*Cartilage + 0.5*Yellow (inactive) bone marrow	Bone (cort.)[*1)]
Trabecular bone mineral surface[*1)] + Trabecular bone mineral volume[*1)] + Trabecular bone marrow + 0.5*Cartilage + 0.5*Yellow (inactive) bone marrow	Bone (trab.)[*1)]
Spleen	Spleen

IDAC-Dose 2.1	IDAC-Dose 1.0
Testes	Testes
Thyroid	Thyroid
Heart wall	Heart wall
Gallbladder content + Gallbladder wall	Gall bl. cont.
Stomach wall + Stomach mucosa	Stomach wall
SI wall + SI mucosa + SI villi	SI wall
RC wall + 0.478873*LC wall + RC mucosa + 0.478873*LC mucosa;	ULI wall
0.521127*LC wall + RSC wall + 0.521127*LC mucosa + RSC mucosa	LLI wall
Blood	Blood
Other + Teeth surface activity + Teeth volume activity + LN in ET region + LN in sys + LN in thoracic region + LN total + ET1 Surface of anterior nasal passages + ET1 Surface of posterior nasal passages wall + ET2 region Bound+ ET2 region Sequestered + ET2 + Ureters + Uterus/cervix + Breast + Adipose/residual tissue + Oral cavity + Oral mucosa + Pituitary gland + Prostate + Respiratory tract air + Skin + Thymus + Tongue + Tonsilsregion Surface + ET2 region wall + Eye lenses + Oesophagus fast + Oesophagus slow + Oesophagus wall + Salivary glands	Remainder

*1) Bone activity is typically assigned to the bone surface for nuclides/isotopes with physical half-lives < 15 day, while it is assigned to the bone volume for half-lives > 15 days. Therefore, a mixture of bone surface and volume activity should generally not occur.

19.1.3 Conversion of Source Organs (Cumulated Activities / Residence Times) between IDAC-Dose 2.1 and Export to OLINDA 1.1

IDAC-Dose 2.1	OLINDA 1.1
Adrenals	Adrenals
Urinary bladder content + Urinary bladder wall	Bladder cont.
Brain	Brain
Breasts	Breasts
Stomach contents + Stomach wall + Stomach mucosa	Stomach
SI contents + SI wall + SI mucosa + SI villi	SI contents
RC cont + 0.478873*LC cont	ULI contents
0.521127*LC cont + RSC cont	LLI contents
Kidneys	Kidneys
Liver	Liver
Lungs + Lung tissue + Alveolar-interstitial + Bronchi + Bronchi bound + Bronchi seq + Bronchioles + Bronchioles bound + Bronchioles seq	Lungs

IDAC-Dose 2.1	OLINDA 1.1
Muscle	Muscle
Ovaries	Ovaries
Pancreas	Pancreas
Red (active) bone marrow	Red marrow
Cortical bone mineral surface*1) + Cortical bone mineral volume*1) + Cortical bone marrow + 0.5*Cartilage + 0.5*Yellow (inactive) bone marrow	Bone (cort.)*1)
Trabecular bone mineral surface*1) + Trabecular bone mineral volume*1) + Trabecular bone marrow + 0.5*Cartilage + 0.5*Yellow (inactive) bone marrow	Bone (trab.)*1)
Spleen	Spleen
Testes	Testes
Thyroid	Thyroid
Heart wall	Heart wall
Gallbladder content + Gallbladder wall	Gall bl. cont.
Uterus/cervix	Uterus
RC wall + 0.478873*LC wall + RC mucosa + 0.478873*LC mucosa;	ULI wal
0.521127*LC wall + RSC wall + 0.521127*LC mucosa + RSC mucosa	LLI wal
Thymus	Thymus
Other + Teeth surface activity + Teeth volume activity + LN in ET region + LN in sys + LN in thoracic region + LN total + ET1 Surface of anterior nasal passages + ET1 Surface of posterior nasal passages wall + ET2 region Bound + ET2 region Sequestered + ET2 + Ureters + Uterus/cervix + Breast + Adipose/residual tissue + Oral cavity + Oral mucosa + Pituitary gland + Prostate + Respiratory tract air + Skin + Tongue + Tonsilsregion Surface + ET2 region wall + Eye lenses + Oesophagus fast + Oesophagus slow + Oesophagus wall + Salivary glands	Remainder

*1) Bone activity is typically assigned to the bone surface for nuclides/isotopes with physical half-lives < 15 day, while it is assigned to the bone volume for half-lives > 15 days. Therefore, a mixture of bone surface and volume activity should generally not occur. In OLINDA/EXM the user can specify whether to assign the cumulated activity/residence time of cortical and trabecular bone to the surface or the volume of the bone.

19.2 Spherical Model

Spherical model calculation is available for following nuclides (depending on the software license):

^{225}Ac, ^{213}Bi, ^{64}Cu, ^{67}Cu, ^{18}F, ^{68}Ga, ^{124}I, ^{131}I, ^{177}Lu, ^{212}Pb, ^{223}Ra, ^{224}Ra, ^{188}Re, ^{99m}Tc, ^{90}Y, ^{89}Zr

The spherical model can only be calculated in certain mass ranges depending on the selected nuclide. Following table gives an overview over ranges:

Nuclide	Mass range (in g)	
	Minimum	Maximum
^{225}Ac	0.01	6000
^{213}Bi	0.1	6000
^{64}Cu	0.01	6000
^{67}Cu	0.01	6000
^{18}F	0.1	1000
^{68}Ga	0.5	6000
^{124}I	1	6000
^{131}I	0.1	2000
^{177}Lu	0.01	6000
^{212}Pb	0.01	6000
^{223}Ra	0.01	6000
^{224}Ra	0.01	6000
^{188}Re	1	6000
^{99m}Tc	2	1000
^{90}Y	1	6000
^{89}Zr	1	1000

19.3 Voxel S

Voxel S dose kernels are available for following nuclides (depending on the software license):

^{131}I, ^{177}Lu, ^{186}Re, ^{188}Re, ^{153}Sm, ^{89}Sr, ^{99m}Tc ^{90}Y

The dose kernels are based on the published kernels from Lanconelli et al (Lanconelli et al. 2012). Voxel S assumes a tissue density of 1.0 g/cm³. The range of voxel sizes for Voxel S calculations is as follows:

Nuclide	Voxel size (in mm)	
	Minimum	Maximum
^{131}I, ^{177}Lu, ^{186}Re, ^{188}Re, ^{153}Sm, ^{89}Sr, ^{90}Y	2.21	9.28
^{99m}Tc	4.4181	

19.4 Calculation of Paired Organ Masses

Organ mass of paired organ		**Planar Mode**	**Hybrid mode**	**Volumetric mode**
Only L organ defined	in 2D and 3D	$OM_L * 2$	$OM_L * 2$	$OM_L * 2$
Only R organ defined	in 2D and 3D	$OM_R * 2$	$OM_R * 2$	$OM_R * 2$
L & R organ defined*	in either 2D or 3D	$OM_L + OM_R$	$OM_L + OM_R$	$OM_L + OM_R$

'Defined' means that a region was drawn and activity and volume was segmented in all time points.

** This applies even if the L & R organs are defined in only planar or volumetric mode. Once defined, mass will be used in all modes.

19.5 Calculation of Paired Organ Activity

Cumulated activity Ã of paired organ		**Planar Mode**	**Hybrid mode**	**Volumetric mode**
Only L organ defined	in 2D and 3D	$\tilde{A}_L * 2$	$\tilde{A}_L * 2$	$\tilde{A}_L * 2$
	in 2D	$\tilde{A}_L * 2$	-	-
	in 3D	-	-	$\tilde{A}_L * 2$
Only R organ defined	in 2D and 3D	$\tilde{A}_R * 2$	$\tilde{A}_R * 2$	$\tilde{A}_R * 2$
	in 2D	$\tilde{A}_R * 2$	-	-
	in 3D	-	-	$\tilde{A}_R * 2$
L & R organ defined*	in 2D and 3D	$\tilde{A}_L + \tilde{A}_R$	$\tilde{A}_L + \tilde{A}_R$	$\tilde{A}_L + \tilde{A}_R$
	in 2D	$\tilde{A}_L + \tilde{A}_R$	-	-
	in 3D	-	-	$\tilde{A}_L + \tilde{A}_R$
L & R organ defined & R (or L) organ defined	in 2D in 3D	$\tilde{A}_L + \tilde{A}_R$	$\tilde{A}_R * 2$	$\tilde{A}_R * 2$
L & R organ defined & R (or L) organ defined	in 3D in 2D	$\tilde{A}_R * 2$	$\tilde{A}_R * SPECTFactor_{L+R}$	$\tilde{A}_L + \tilde{A}_R$

'Defined' means that a region was drawn and an activity was segmented in all time points.

19.6 Density values for mass-to-volume conversion

Organ	**Density (g/cm³)**
Blood	1.06
Brain	1.04
Breast	1.02

Cortical bone marrow, Cortical bone mineral surface, Cortical bone mineral volume	1.92
Eye lens	1.07
Muscle	1.20
Lungs	1.05
Ovaries	1.05
Testes	1.04
All other	1.06

19.7 Performance Validation & Accuracy

QDOSE has undergone extensive verification and validation to confirm its accuracy in estimating absorbed dose values. The software was tested against established dosimetry benchmarks, including **IDAC-Dose 2.1** and **Olinda/EXM 1.1**, which are widely accepted in the field of nuclear medicine dosimetry.

- **Accuracy:** The absorbed dose estimates produced by QDOSE showed deviations of **4% for critical organs** and **up to 15% for specific organ dose calculations**, which fall within clinically acceptable limits.
- **Validation Results:** Performance tests using **phantom studies** and Monte Carlo simulations confirm that QDOSE's volumetric dose calculations have an error margin of **<5%** in controlled test environments.
- **Planar vs. Hybrid vs. Volumetric Workflows:** The accuracy across different workflows was assessed:
    - **Planar workflow:** deviation of **1.3%**
    - **Hybrid workflow:** deviation of **0.3%**
    - **Volumetric workflow:** deviation of **0.04%**
- **Comparison to Industry Standards:** The results were benchmarked against similar dosimetry solutions, demonstrating comparable or superior performance in specific dosimetric calculations.

19.8 Reproducibility and Repeatability

QDOSE ensures consistent results across multiple test scenarios, with validation focusing on inter-operator and intra-operator variability.

- **Inter-operator variability:** Results differ by **≤3%** when different users analyze the same dataset.

- **Intra-operator consistency:** Repeated dose calculations by the same user yield variations of **≤2%**.
- **Clinical validation:** Studies confirm that deviations in dosimetry calculations between different implementations remain within the expected **6% for organs** and **10% for tumors**, confirming repeatability in real-world scenarios.
- **Regression testing:** QDOSE has undergone software regression testing to ensure consistent performance across updates.

19.9 Limitations and Considerations

While QDOSE provides highly accurate dose estimations, certain limitations should be considered:

- **Data Quality Dependency:** The accuracy of dose calculations is directly affected by the quality of input images, scanner calibration, and patient motion artifacts. Users should verify the integrity of image data before performing analysis.
- **Voxel S Model Constraints:** The Voxel S method is optimized for soft tissues and is **not validated for bone or lung tissues**, where density variations may introduce calculation errors.
- **Alpha Emitter Dosimetry Limitations:** The software currently models only the parent nuclide in alpha-emitter dosimetry. **Daughter nuclides in decay chains are not accounted for**, leading to possible underestimation of absorbed dose.

19.10 Software Validation

QDOSE has undergone extensive verification and validation testing to ensure compliance with regulatory and industry standards.

- **Phantom Model Validation:** The software was tested using **Monte Carlo simulation models** to verify absorbed dose estimations under controlled conditions.
- **Clinical Dosimetry Comparisons:** QDOSE results were benchmarked against patient-specific dosimetry data and compared with leading dosimetry tools, confirming accuracy within acceptable clinical thresholds.
- **Regulatory Compliance:** The software validation process complies with **ISO 62304 (Medical Device Software – Software Life Cycle Processes)** and is aligned with requirements under **MDR (EU) 2017/745**.

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