User Manual IDAC-Alpha

Version: 1.01

By Martin Andersson

Short overview

- IDAC-Alpha is a user-friendly software [1] with a graphical interface, developed to perform realistic alpha dosimetry calculations for normal organs and tissues in molecular radiotherapy based on biokinetic models.
- Optimal dosimetry for alpha emitting radionuclides should use patient-specific data for each radiopharmaceutical. However, in most cases this not possible and generic data can help improve the absorbed dose calculations.
- IDAC-ALPHA assumes that after the first decay, the daughter is released from the radiopharmaceutical molecule and can be biokinetically treated according to the properties of its own element, meaning:
    - Individual biokinetic models created for all daughter elements.
    - Activity is uniformly distributed and the daughter nuclides are transferred through the blood.
    - There will be a continuous biological transfer of the nuclides within the models to e.g. faeces and urine.
- The software includes separate transfer of daughter nuclides. Including the biokinetics of the progenies provides improved absorbed dose estimates and an improved prediction of the normal tissue radiotoxicity.
- Depending on the purchased license, IDAC-Alpha can perform dosimetry for the molecular radiotherapy nuclides ^{225}Ac, ^{211}At, ^{212}Bi, ^{213}Bi, ^{212}Pb, ^{223}Ra, ^{224}Ra, ^{149}Tb and ^{227}Th, and including the behaviour and biokinetic transfer of daughter products.
- The absorbed and effective dose calculation is performed on all organs and all nuclides in the decay chain.
- The dosimetry follows the ICRP computational framework, including reference phantoms and effective dose given in ICRP Publication 103 [2].

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User Manual IDAC-Alpha

Intended Use

IDAC-Alpha is a user-friendly software with a graphical interface, developed to perform realistic alpha dosimetry calculations for normal organs and tissues in molecular radiotherapy based on biokinetic models.

This version of IDAC-Alpha is not certified as a medical device. All calculations provided by IDAC-Alpha are intended only for scientific research. Any other use is entirely at the discretion and risk of the user.

Intended User

This user manual is for personal who has a background in dosimetry calculations for normal organs and tissues and molecular radiotherapy.

Technical Description

The software includes separate transfer of the various progenies. To include the biokinetics of the progenies provides improved absorbed dose estimates and an improved prediction of the normal tissue radiotoxicity. Depending on the purchased license, IDAC-Alpha performs dosimetry for the molecular radiotherapy nuclides ^{225}Ac, ^{211}At ^{212}Bi, ^{213}Bi, ^{212}Pb, ^{223}Ra, ^{224}Ra, ^{149}Tb and ^{227}Th, and including the behaviour and biokinetic transfer of their daughter products. All elements in the decay chain for all included radionuclides have their own biokinetic models including excretion and transfer rates between organs and blood and as the time integrated activities are calculated using a numeric differential equation, once the radionuclide has decayed, the calculations immediately follow the models for the daughter radionuclides. The calculations follow the computational framework of internal dosimetry given in ICRP Publication 130 [3].

References

1. M Andersson, A Kluge, T Meyer, E Koumarianou, S Mattsson, IDAC-ALPHA: AN ALPHA DOSIMETRY SOFTWARE FOR NORMAL ORGANS AND TISSUES, *Radiation Protection Dosimetry*, Volume 195, Issue 3-4, October 2021, Pages 327–333, https://doi.org/10.1093/rpd/ncab046

2. ICRP, 2007. The 2007 Recommendations of the International Commission on Radiological Protection. ICRP Publication 103. Ann. ICRP 37 (2-4).

3. ICRP, 2015. Occupational Intakes of Radionuclides: Part 1. ICRP Publication 130. Ann. ICRP 44(2).

System Requirements

- Operating System: Windows 7 (Service Pack 1), Windows 10 (Version 1803 or higher)
- Processor: minimum Intel or AMD x86-64
- Disk: minimum 5 GB
- RAM: minimum 4GB
- Graphics: no specific graphics card required

Workflow for alpha dosimetry

1. *Select licensed radionuclide.*

Select one of the molecular radiotherapy radionuclides ^{225}Ac, ^{211}At, ^{212}Bi, ^{213}Bi, ^{212}Pb, ^{223}Ra, ^{224}Ra, ^{149}Tb and ^{227}Th, see figure 12. If the menu "1) Select radionuclide" shows "Get License", either you don't have a valid license (expired or the license file is not placed in the same folder as the IDAC-Alpha.exe folder). The Software checks for license file during software start up.

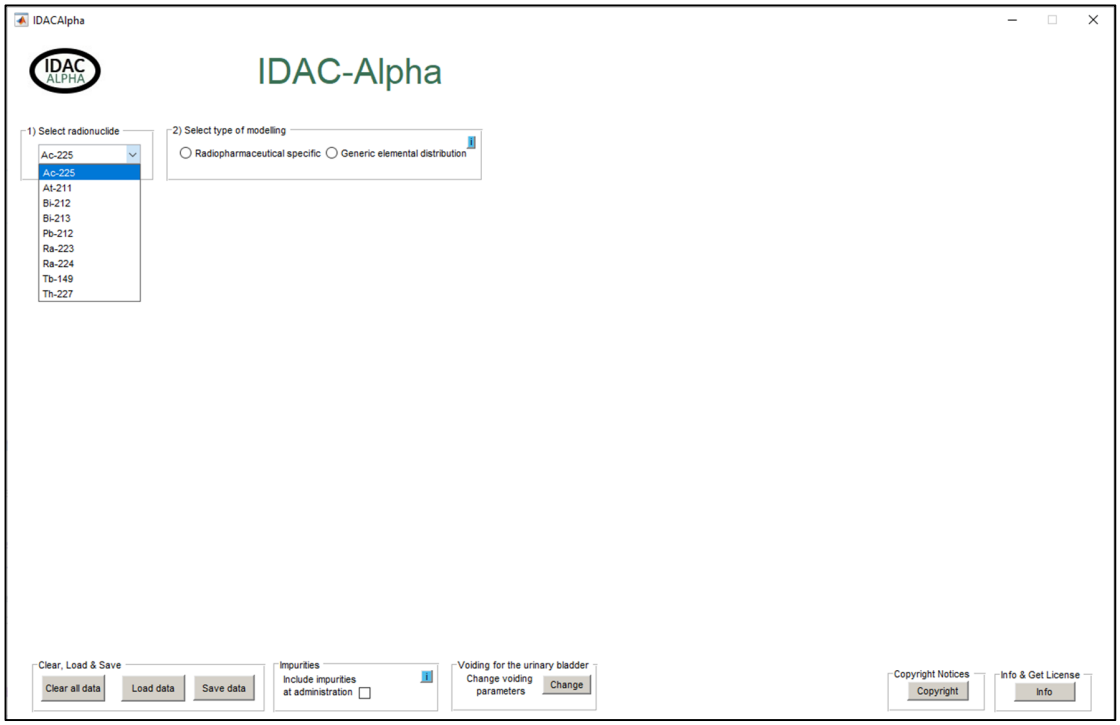


Figure 12. The graphical interface of IDAC-Alpha.

2. *Select type of modelling*

The purpose of IDAC-Alpha is to add generic reference data to the radiopharmaceutical specific data and fill in the biokinetic information missing to enable realistic biokinetic behaviour of daughter nuclides. This set of including generic data to the radiopharmaceutical specific data in the software is called "Radiopharmaceutical specific". After selecting parent radionuclide, the user can select "Radiopharmaceutical specific" and has to follow the steps from *i* to *vii* in section 2a. For the "Generic elemental distribution" follow the steps in section 2b. The selection menu is shown in Figure 13.

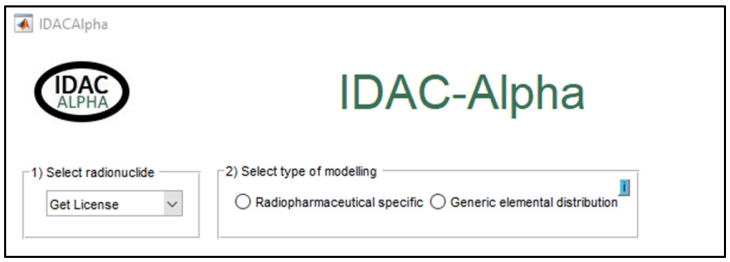


Figure 13. The Select type of modelling.

a) Radiopharmaceutical specific

IDAC-alpha is a software where users insert activity data form a specific alpha emitting radionuclide, see Figure 14. The energy released from the first alpha decay is high enough to break the chemical bonds of the molecule. So, the daughter nuclides will follow the chemical properties of this their own element instead of that of the injected radiopharmaceutical. This means that daughter-specific generic biokinetic models can be used, to include the biokinetic transfer between organs. For radiopharmaceutical-specific modelling, the user inserts the time-specific activity points after administration for the injected parent radionuclides for all relevant organs. The software makes a compartmental representation for each organ, a compartmental model which defines the activity in each organ at all-time points. Based on the selected organs, a unique biokinetic model is created based on the inserted data and including specific biokinetic models for each daughter nuclide. The created biokinetic problem is solved with a numerical solver and stepwise (8 sec steps) follows the biokinetic transfer within the body, simulated during one year (365 days) after administration. Once all decays for the whole decay chain have been calculated, IDAC-Alpha calculates the organ-specific absorbed dose and effective dose using the computational framework from the International Commission on Radiological Protection (ICRP), given in ICRP Publication 130.

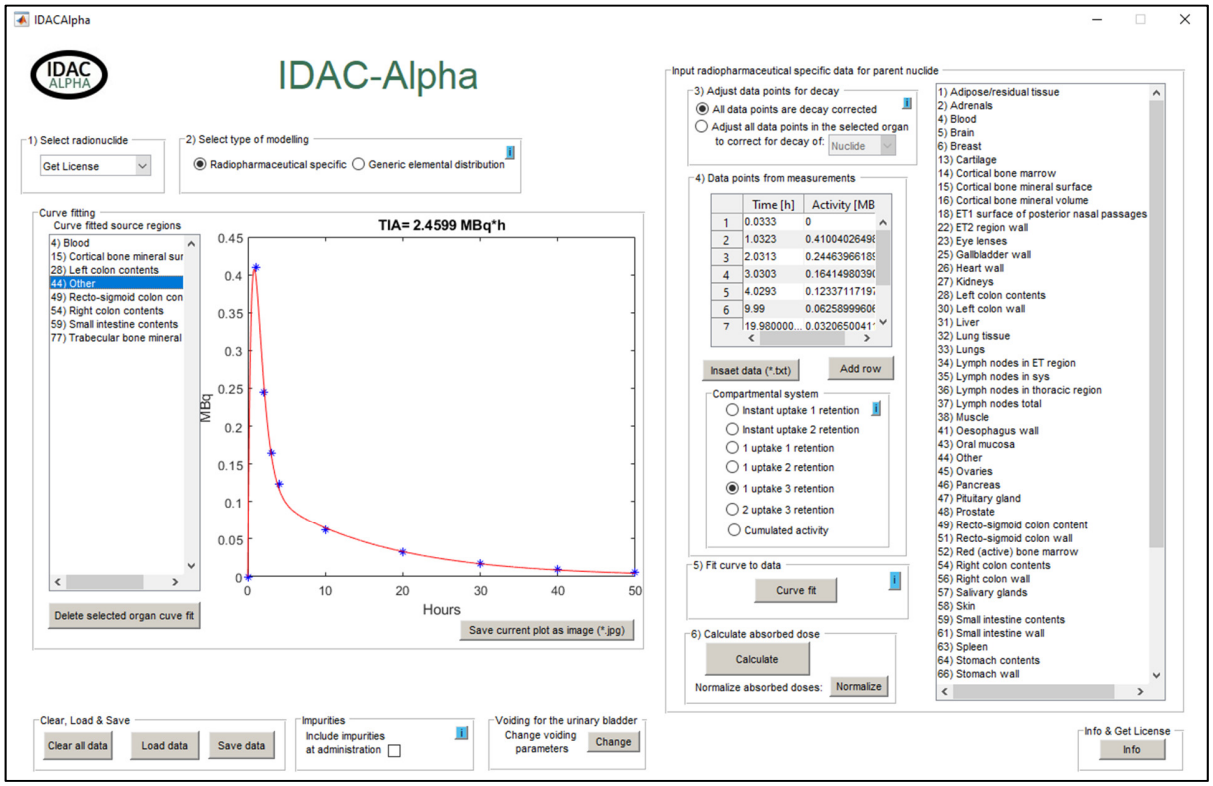


Figure 14. The graphical interface of radiopharmaceutical-specific modelling in IDAC-Alpha.

i. Adjust data points for decay

The software uses decay-corrected data points to create the biokinetic transfer. The user can either insert the data points decay-corrected directly into the table or insert non-decay-corrected data points, and the software will decay-correct the inserted activity data points. As seen in Figure 15 the decay correction can be from different radionuclides, e.g. using a diagnostic imaging agent (^{18}F, ^{68}Ga, ^{99m}Tc, ^{111}In, ^{124}I, ^{131}I) instead of the therapeutic radionuclide.

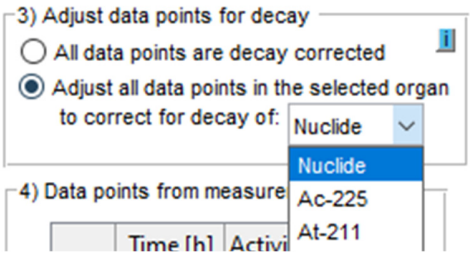


Figure 15. The option of including non-decay-corrected data the software will decay-correct the data points.

ii. Data points from measurements

Activity Data points should be included in MBq and hours after administration. The data can either be inserted manually or from a specific text template, see Figure 16. Data are inserted separately for each organ.

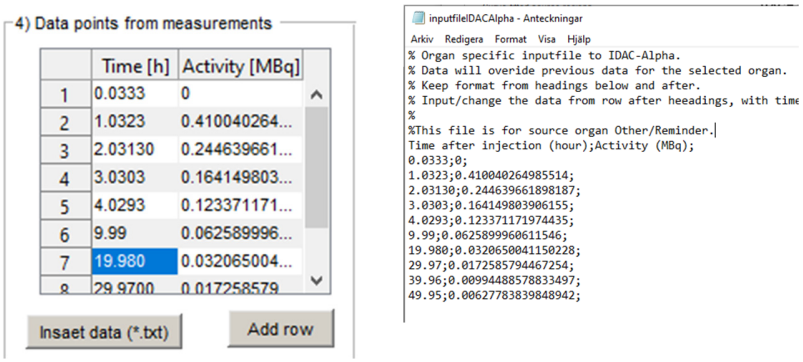


Figure 16. Left insert activity data manually in MBq and time since administration in hours. Right insert organ data by a template text file.

iii. Compartmental system

Once all data from one organ has been included, the software makes a compartmental fitting to the data points. The configuration of compartment modelling represents different biological processes, uptakes and retentions of the radiopharmaceutical in the organ. The user needs to determine which compartment configuration fits best the inserted data, see Figure 17. For instance, and configuration of 1 uptake and 2 retention means that the organ has 0 activity initially and has one uptake phase and 2 retentions e.g. one fast process and one slower. Instant uptake means that the organ-specific activity does not start with zero activity, instead the uptake can be assumed to be immediate. For example, this always applies to blood when administered intravenously.

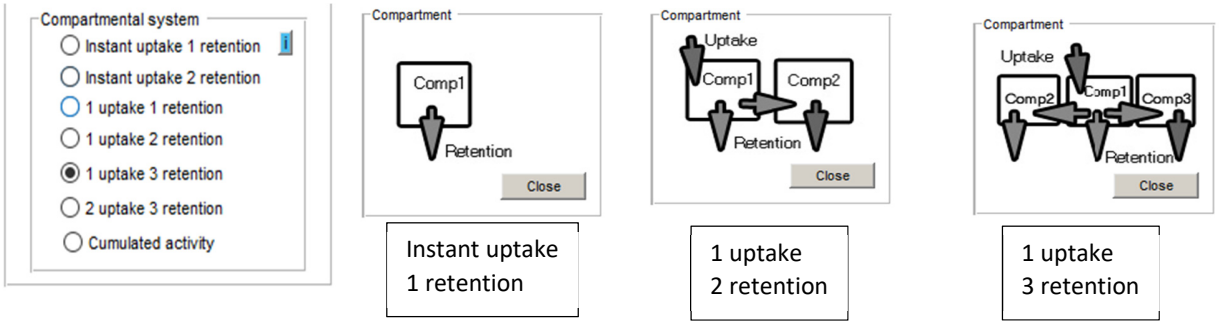


Figure 17. The different possible compartmental configurations to use in the curve fit.

iv. Fit curve to data

Once the configuration has been selected, the software will use a nonlinear optimization with a gradient-based method to find the optimal parameter curve fit to the inserted data points. Each time the users presses “Curve fit” the software makes 25 independent optimizations with randomly selected input values and storing the best fit. This means that if a local optimization is found, repressing the “Curve fit” button could lead to a better fit. Otherwise just change the compartmental configuration and press “Curve fit” again. Once the fit is completed, the organ is also shown in the left menu bar.

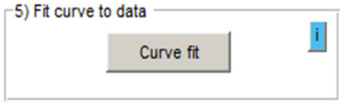


Figure 18. The Curve fitting button.

v. Curve fitting tool

After the “Curve fit” button has been pressed, the model prediction of inserted data points is displayed graphically in a figure, see Figure 19. The estimated organ-specific time-integrated activity for the parent nuclide is presented above of the graph in MBq*h. The selected source organ is also included in the “Curve fitted source regions” menu to let the user know which organ is included in the biokinetic calculation. Once a good model prediction has been made, the user can select the next source organ to include in the biokinetic model, restart from a new source organ. In Figure 19, the best configuration and model prediction for the source region “Other” (previously called remainder) was 1 uptake and 3 retentions. In the left menu are all performed curved fitted organs. The user can select and delete previously completed organs.

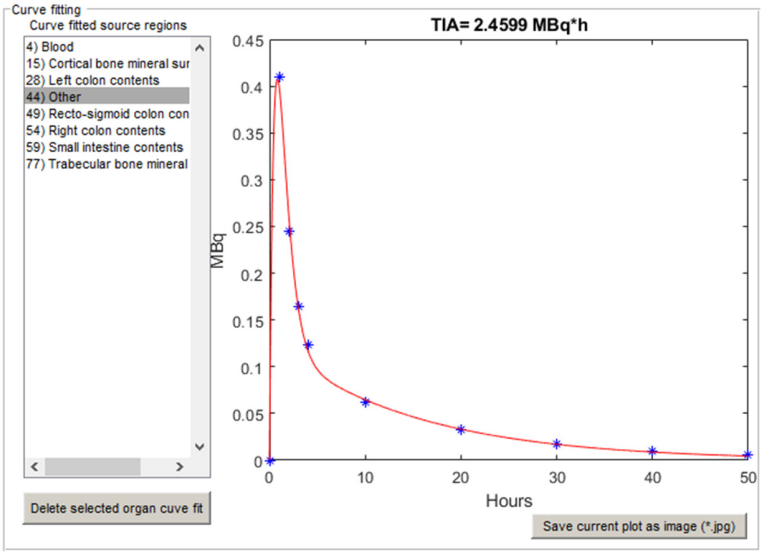


Figure 19. The figure shows a fitted curve for the source region “Other”, based on ten data points. The left menu shows the organ which has a curve fit and will be included in the calculations.

vi. Calculate absorbed dose

All generated curve fitted organs in the left menu of Figure 19 will be included in the biokinetic modelling and included in the absorbed dose calculations. If users want to normalize the input data before pressing “Calculate” and changing the time integrated activities (TIA) to time integrated activities coefficients (TIAC), the user can include the administered activity by clicking on button “Normalize”. All input data will be divided by the administered activity. Once the user klicks the “Calculate” button, the biokinetic and dosimetric calculations will start, based on the data given in the left menu in Figure 19.

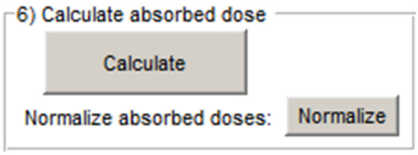


Figure 20. The button to perform the biokinetic and absorbed dose calculations. The button “Normalize” is to allow users to change the calculations from TIA to TIAC.

vii. Clear, Load and Save data

There is a possibility to store all data generated in the input menu, by pressing the button “Save data”. The software will create a data file (*.mat). The saved data can be accessed in the software by pressing the button “Load data”. This provides the possibility to save the data in different steps. By pressing the button “Clear all data”, all data are cleared and set to initial default values. All three buttons are given in Figure 21.

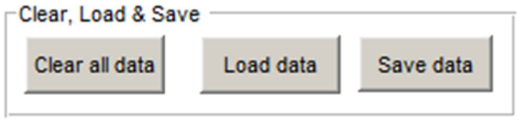


Figure 21 The save, load and clear data buttons.

b) Generic elemental distribution

The generic elemental distribution is an option where the parent nuclide also is assumed to follow the elemental behaviour of its own element. Radium dichloride could be one of these cases. Another possibility with this generic distribution is that if the parent radionuclide releases from the molecule, it will follow the biokinetic of its own element instead of the biokinetic of the radiopharmaceutical during the time from release to decay.

Just insert the injected activity in the blue box and the fraction (values between 0 and 1) of inserted activity in the organ boxes, where 0 represents 0% and 1 represents 100%. For a 25 MBq intravenously administration this would correspond to 25 MBq in the blue box and 1 in the box for “Blood” as shown in Figure 22.

Figure 22. The graphical interface of generic modelling of parent nuclide in IDAC-Alpha.

c) Additional data included in the biokinetic modelling

The additional data can be included in the calculations if the user thinks this is needed.

To account for decays of the radiopharmaceuticals in the sample before injection, use “Impurities”. If the time between the true sample of the radiopharmaceutical and the injection is long, the radiopharmaceutical will decay within the sample and the daughter nuclides will also be injected. This sub-module shown in Figure 23 accounts for this, and including also decayed daughter nuclides in the sample into the calculation of biokinetic transfer.

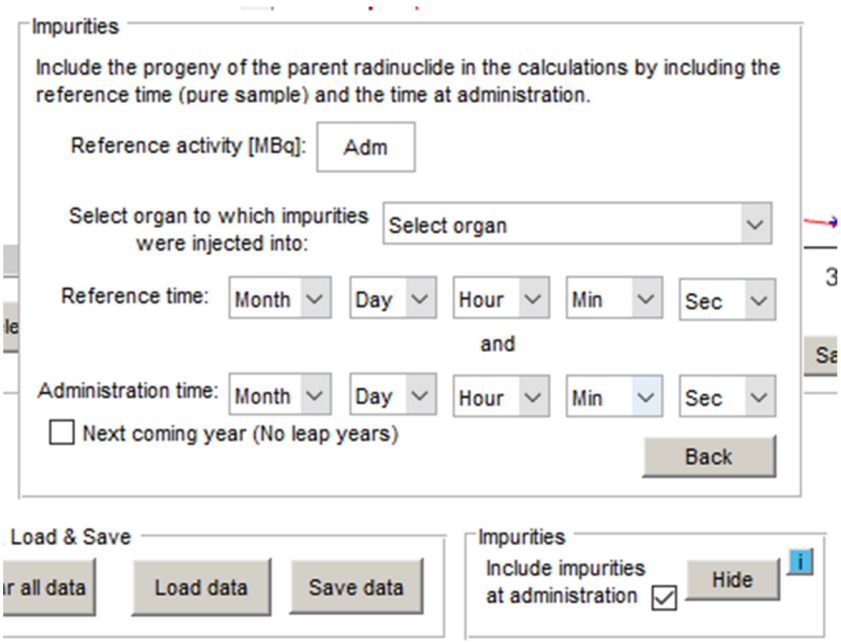


Figure 23. The input view for including decays of parent radionuclide in the sample, between pure sample and injection.

i. Urinary bladder voiding

IDAC-Alpha assumes that the urinary bladder is voided each 3.5 hours with a fraction of 1 (complete voiding). These parameters can be changed if needed, see Figure 24. If the parent radiopharmaceutical is inserted with urinary bladder data, these should be inserted with no voiding. The software will perform the voiding on the parent nuclide with the same interval and fraction as for all daughter nuclides.

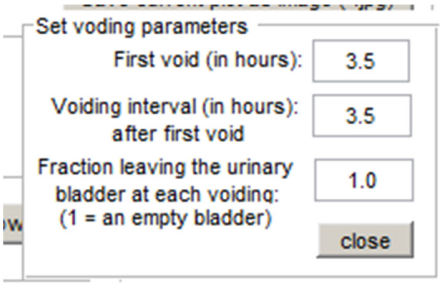


Figure 24. The voiding and filling parameters for the urinary bladder.

3. *Absorbed dose calculations*

Once all data have been inserted and selected organs have been curve fitted and the user has pressed the "Calculate button", the software solves the created biokinetic model and calculates the absorbed dose and effective dose. In the results view, shown in Figure 25, it is possible to select the different absorbed dose for the different radiation types (photon, electron or alpha) or look at the different dose from the different nuclides in the decay chain. For the effective dose calculation, it is also possible to change the default ICRP radiation weighting factors. The results can also be stored as a dose report (*.pdf) or as a text (*.csv) file.

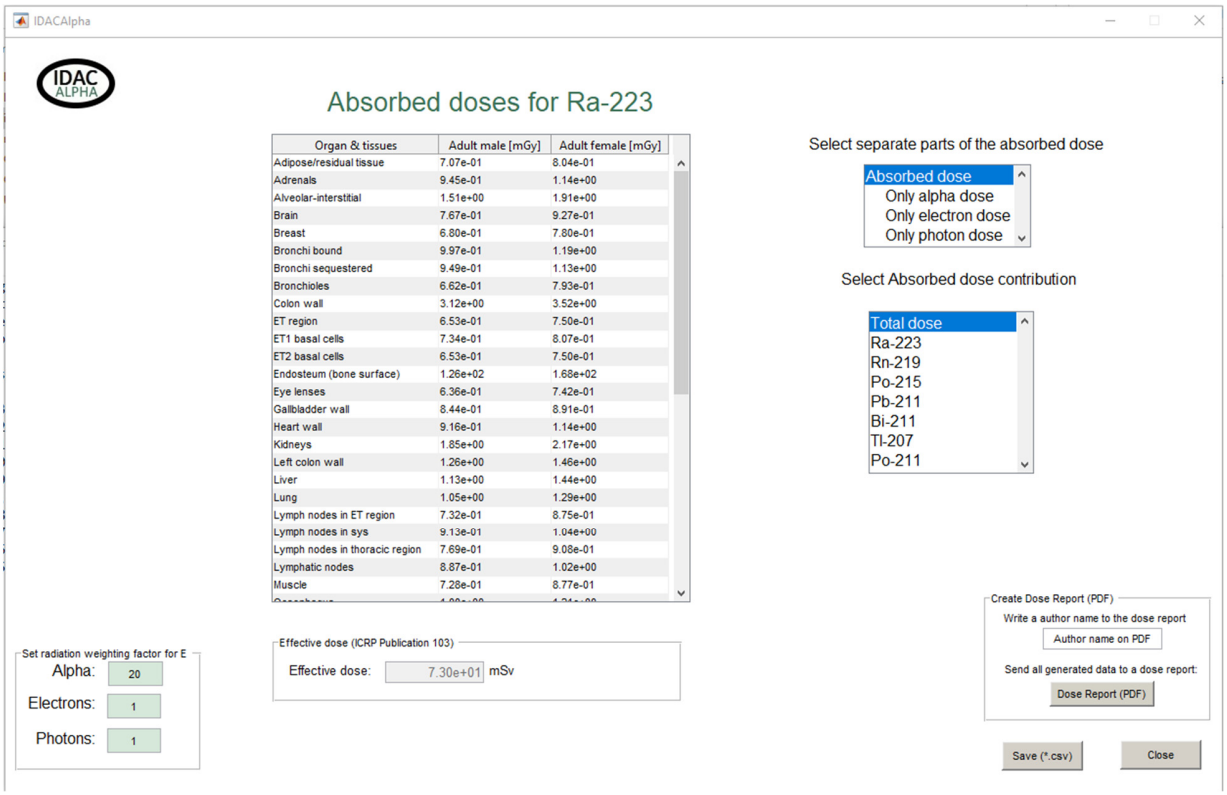


Figure 25. The graphical interface of the results view of IDAC-Alpha.

a) Radiation weighting factors for effective dose

In the effective dose calculations IDAC-Alpha uses the ICRP radiation weighting factors given in ICRP Publication 103 [2]. The user has the possibility to change the radiation weighting factors for the effective dose calculations, see Figure 26.

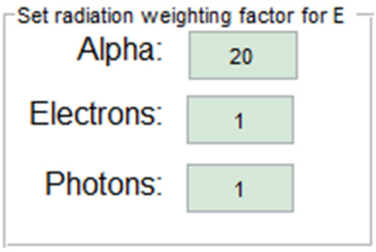


Figure 26. The radiation weighting factor used in the effective dose calculations.

b) Select absorbed dose from different radionuclides and radiation types

In the results view, shown in Figure 27, it is possible to select the different absorbed dose for the different radiation types (photon, electron or alpha) or look at the different dose from the different nuclides in the decay chain. “Total dose” includes the total absorbed dose from all included radionuclides. “Absorbed dose” shows the absorbed dose from all radiation types.

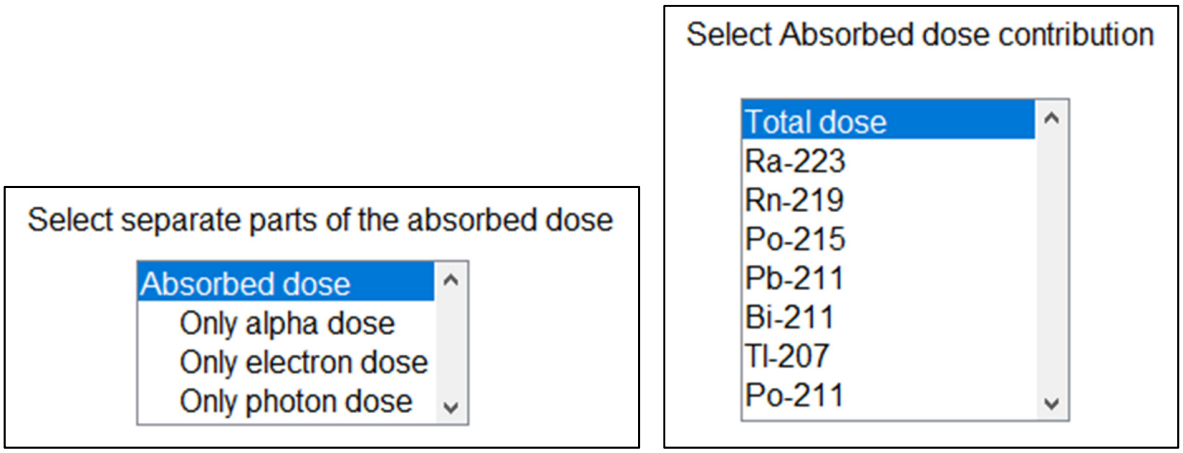


Figure 27. Shows the different choices for a ^{223}Ra calculation

c) Store the data in a text file or a dose report

Once the absorbed dose calculations are completed, there are two ways to store the generated data. IDAC-Alpha can generate a text file (*.csv) including all calculated dose values, see Figure 28. The second option is to collect all data and graphs in a dose report, there the software creates a *.pdf document including all data, see Figure 29. By pressing the “Close” button the user can go back to the main window and change the input parameters, before the software preforms a re-calculation of the biokinetic and dosimetric problem.

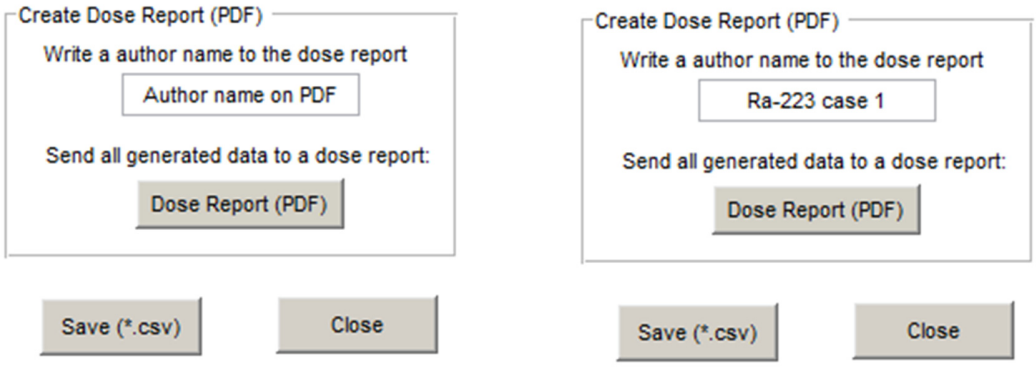
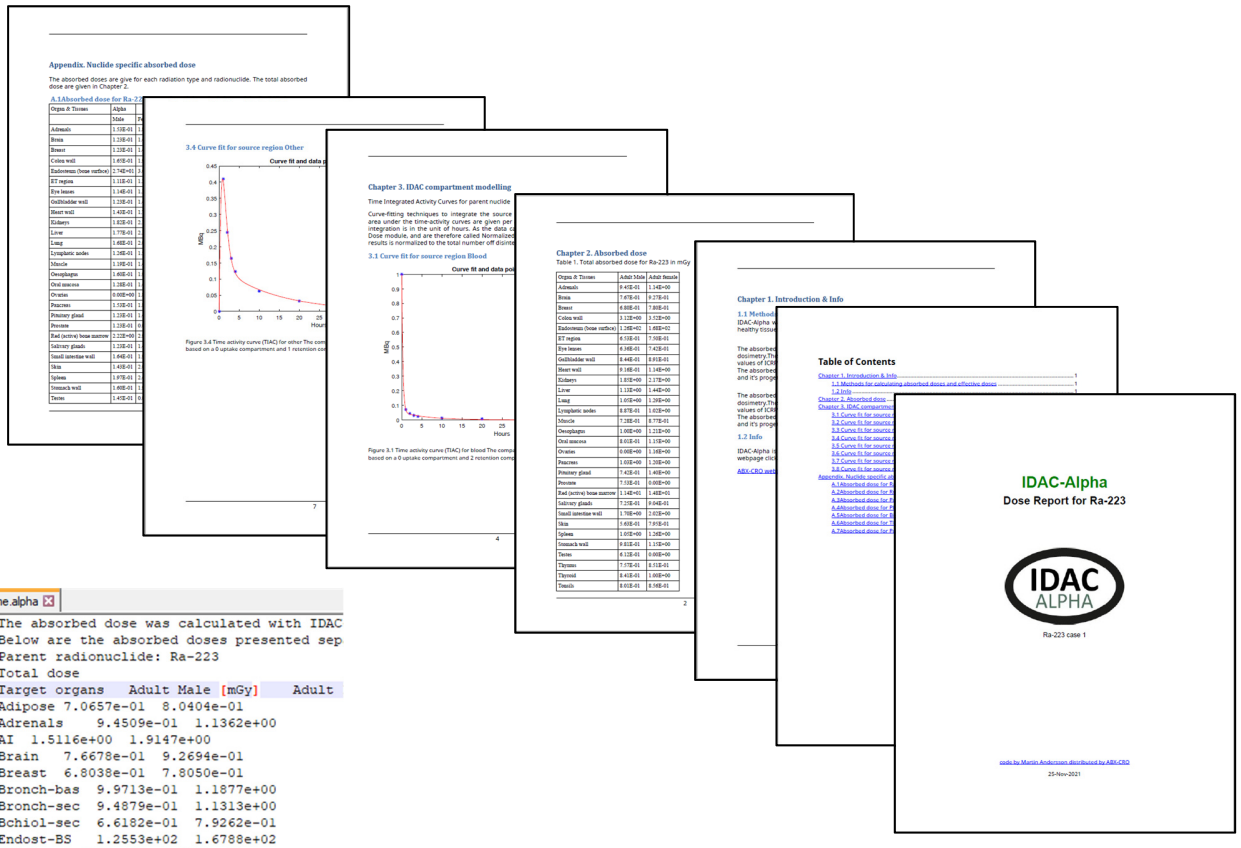


Figure 28. The save buttons to store a text file or pdf. For the dose report an author name can be included on the front page of the report.



Filename.alpha

```
The absorbed dose was calculated with IDAC
Below are the absorbed doses presented sep
Parent radionuclide: Ra-223
Total dose
Target organs   Adult Male [mGy]    Adult
Adipose 7.0657e-01  8.0404e-01
Adrenals    9.4509e-01  1.1362e+00
AI  1.5116e+00  1.9147e+00
Brain   7.6678e-01  9.2694e-01
Breast  6.8038e-01  7.8050e-01
Bronch-bas  9.9713e-01  1.1877e+00
Bronch-sec  9.4879e-01  1.1313e+00
Bchiol-sec  6.6182e-01  7.9262e-01
Endost-BS   1.2553e+02  1.6788e+02
ET1-bas 7.3355e-01  8.0691e-01
ET2-bas 6.5306e-01  7.5020e-01
Eye-lens    6.3594e-01  7.4237e-01
GB-wall 8.4393e-01  8.9053e-01
Ht-wall 9.1581e-01  1.1418e+00
Kidneys 1.8455e+00  2.1747e+00
LC-stem 1.2644e+00  1.4592e+00
Liver   1.1285e+00  1.4352e+00
LN-ET   7.3218e-01  8.7509e-01
LN-Sys  9.1274e-01  1.0445e+00
LN-Th   7.6943e-01  9.0849e-01
Muscle  7.2834e-01  8.7656e-01
```

Figure 29. This figure shows a condensed view of the Dose Report and also the saved text file.