

RADIANCE

Radiotherapy Survival Rate Modeling Interface

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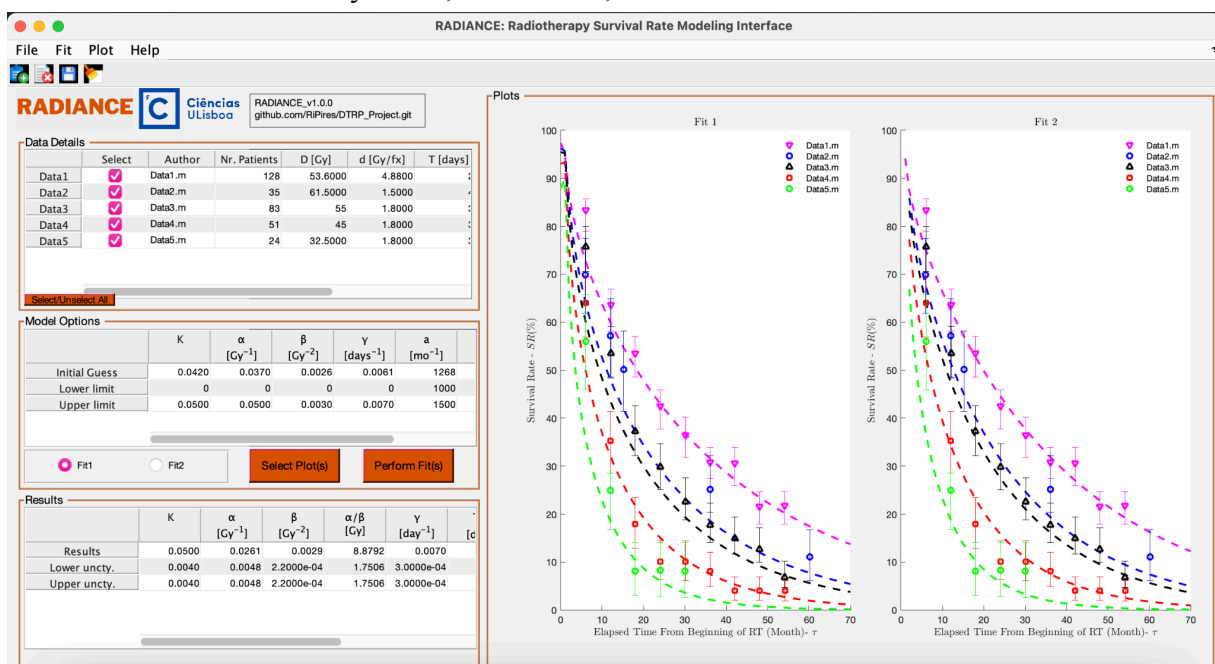
Source code available at: https://github.com/RiPires/DTRP_Project.git

This project was developed in the frame of the “Diagnosis and Therapy with Radiations and Protons” class of 2022/23, under the supervision of Prof. Brigida C. Ferreira, using the latest version of MATLAB - R2023a.

What is RADIANCE?

RADIANCE is a GUI (Graphical User Interface) to estimate radiobiological parameters by fitting different survival rate models to clinical data, with the aim of evaluating the radiobiological equivalence between different treatment regimes and designing new optimised dose fractionation schemes.

In the second release, two survival models, here called “Fit1” and “Fit2”, are available. These models are used by Tai A, Erickson B, et al., in their study to “Estimate radiobiologic parameters from clinical data for biologically based treatment planning for liver irradiation”. In our project, we automate the implementation of these formalisms in the form of the RADIANCE interface, that produce comparable results of the estimated parameters with the ones obtained by Tai A, Erickson B, et al.



Using the parameter values obtained after executing these fits, we can plot the values of the Survival Rate (SR) in function of the BED (Biologically Effective Dose), or the EQDX (Equivalent Dose in XGy fractions).

Thus, it is possible to obtain 6 different plots:

- FIT1: Fit curves of the first model applied to the data points (Survival Rate in percentage in function of time in months)
- FIT2: Fit curves of the second model applied to the data points (Survival Rate in percentage in function of time in months)
- BED1: Curves of the SR in function of the BED for some time values selected by the user, for the parameters obtained with the first fit.
- EQDX1: Curves of the SR in function of the EQDX for some time values selected by the user, for the parameters obtained with the first fit.
- BED2: Curves of the SR in function of the BED for some time values selected by the user, for the parameters obtained with the second fit.
- EQDX2: Curves of the SR in function of the EQDX for some time values selected by the user, for the parameters obtained with the second fit.

Plotted Functions

Fit 1:

$$SR(D, d, \tau) = e^{-K \exp(-p)}, \tau > T$$

$$p = \alpha \left(1 + \frac{d}{\alpha/\beta}\right) D - \gamma T - (a(\tau - T))^\delta$$

The survival rate, SR (%), depends on the elapsed time since the beginning of the treatment, τ (months), the total prescription dose, D (Gy), the dose per fraction, d (Gy/fx) and the total treatment time, T (day). $\gamma = \ln 2/Td$, α and β characterise the intrinsic radiosensitive of the cells. Td is the potential doubling time (day). K, a and δ are the remaining fit parameters.

Fit 2:

$$SR(D, d, \tau) = 1 - \frac{1}{\sqrt{2\pi}} \int_{-\infty}^t e^{-\frac{z^2}{2}} dz = \frac{1}{2} \left(1 - \operatorname{erf} \frac{t}{\sqrt{2}}\right)$$

$$t = \frac{e^{-p} - K_{50}/K_0}{\sigma_k/K_0}$$

$$p = \alpha \left(1 + \frac{d}{\alpha/\beta}\right) D - \gamma T - (\gamma(\tau - T))^\delta$$

On the second model, K50 is the critical number of tumour clonogens corresponding to death in 50 % patients. σ_k is the gaussian width for the distribution of critical clonogen numbers.

BED:

$$\text{BED} = \left(1 + \frac{d}{\alpha/\beta}\right) D - \frac{\gamma T}{\alpha}$$

The Biologically Effective Dose was calculated with the parameters obtained with Fit1 or Fit2 (α , β , and γ), a dose per fraction selected by the user, d , (default value: 2Gy/fx), and a treatment time, T , spanning from 1 to 100 . With the value of T it was calculated the number of fractions, n , and, then the dose values, D : $D = n \times d$

Below is an example of a BED calculation where the user selects d value of 2 Gy/fx. Note that on the weekends there is no dose.

Day (T)	Day of the week	D (Gy)	D (cumulative) (Gy)	BED
1	Monday	2	2	BED ₁
2	Tuesday	2	4	BED ₂
3	Wednesday	2	6	BED ₃
4	Thursday	2	8	BED ₄
5	Friday	2	10	BED ₅
6	Saturday	0	10	BED ₆
7	Sunday	0	10	BED ₇
8	Monday	2	12	BED ₈
9	Tuesday	2	14	BED ₉
10	Wednesday	2	16	BED ₁₀
11	Thursday	2	18	BED ₁₁
...

The Survival Rate in function of the BED is calculated with the following equations:

Fit 1:

$$SR(D, d, \tau) = e^{-K \exp(-p)}, \tau > T$$

$$p = \text{BED} \cdot \alpha - (a(\tau - T))^\delta$$

Fit2:

$$SR(D, d, \tau) = 1 - \frac{1}{\sqrt{2\pi}} \int_{-\infty}^t e^{-\frac{z^2}{2}} dz = \frac{1}{2} (1 - erf \frac{t}{\sqrt{2}})$$

$$t = \frac{e^{-p} - K_{50}/K_0}{\sigma_k / K_0}$$

$$p = BED.\alpha - (\gamma(\tau - T))^\delta$$

EQDX:

The Equivalent Dose in XGy fractions was calculated with the parameters obtained with Fit1 or Fit2 (α and β), a dose per fraction selected by the user, d, (default value: 2Gy/fx), and a treatment time, T, spanning from 1 to 100 . With the value of T it was calculated the number of fractions, n, and, then the dose values, **D**: $D = n \times d$

$$EQDX = D \frac{d + \frac{\alpha}{\beta}}{X + \frac{\alpha}{\beta}}$$

The Survival Rate in function of the EQDX is calculated with the following equations:

Fit 1:

$$SR(D, d, \tau) = e^{-Kexp(-p)}, \tau > T$$

$$p = EQDX.\alpha \left(1 + \frac{X}{\alpha/\beta} \right) - \gamma T - (\alpha(\tau - T))^\delta$$

Fit2:

$$SR(D, d, \tau) = 1 - \frac{1}{\sqrt{2\pi}} \int_{-\infty}^t e^{-\frac{z^2}{2}} dz = \frac{1}{2} (1 - erf \frac{t}{\sqrt{2}})$$

$$t = \frac{e^{-p} - K_{50}/K_0}{\sigma_k / K_0}$$

$$p = EQDX.\alpha \left(1 + \frac{X}{\alpha/\beta} \right) - \gamma T - (\gamma(\tau - T))^\delta$$

How to use RADIANCE?

The RADIANCE interface has a straightforward way of use. In this second release, the user starts by running the “**radiance.m**” script, with the latest version of MATLAB (remember that it was tested using version R2023a, we don’t guarantee that it will perfectly run with older or newer versions of MATLAB). In the same path of the “**radiance.m**” file should also be present the following files and folders:

- BED.m
- bedfunction.m
- calculate_n.m
- chi2_residuals.m
- Data folder
- drafts folder
- EQDX.m
- eqdxfunction.m
- fit1.m
- fit1bed.m
- fit1eqdx.m
- fit2.m
- fit2bed.m
- fit2eqdx.m
- Images folder
- perform_fit1.m
- perform_fit2.m
- sample.m
- secondfitting.m
- uncertainty_quocient.m

Inside the interface, the user will find 6 different areas to interact with:

- Menu and toolbars on the top left;
- “Data Details” panel with a table containing information about the clinical data;
- “Model Options” panel with a table containing input parameters to guarantee the convergence of the fits, a model selection radio-button feature that allows to choose the model to be applied, a “Select Plot(s)” button, and a “Perform Fit” button to run the fitting algorithm once the set-up is done;
- “Select Plot(s)” window where the user selects the plot(s) he wants to see
- “Results” panel with a table that will be filled with the fitted parameters;
- “Plots” panel with two axes, one for survival rate over time plot and the other for survival rate over BED plot.

Steps to use RADIANCE

Import study: the first step is to import the clinical data to be used. For that purpose, the user can click on the “AddFile” icon on the toolbar, or go to the menu “File/Add Files...”. Each file should correspond to a different study, with its own parameters N, D, d and T.

The files should have an appropriate name, with a “.m” extension (e.g. “Study1.m”), formatted in a four column way (**Tau SR up_error bot_error**), being Tau the elapsed time from the beginning of the treatment (in months), SR the survival rate (in %), up_error the upper error associated to the SR (%) and bot_error the bottom error associated to the SR (%). In the backend of the program, importing the files only keeps their names stored in the row

header of the “Data Details” table, that are then used to read the content of the files, when called by “Fit1.m”, “Fit2.m” or “BED” functions. In any case, if the input file doesn’t contain error bar values, these will be considered zero.

Study information: after importing the data files, the user should fill in the remaining information about the studies (N, D, d and T) in the corresponding fields of the “Data Details” table (warning and error messages are activated if the user prompts certain inputs such as characters in a numeric cell or negative numbers). **These parameters are mandatory to be filled before performing the fit! DON’T use COMMA separator.**

Delete study: at any time, the user can delete studies using either the “Delete unselected files” icon in the toolbar, or in the menu “File/Delete files”. All the information in the table related to the studies is deleted.

Save study information: one way to avoid adding files and filling in the table by hand every time the user closes and launches the interface is to save its current state on the menu “File/Save”. The information is saved in a “.mat” binary file, in the current path, with a name chosen by the user.

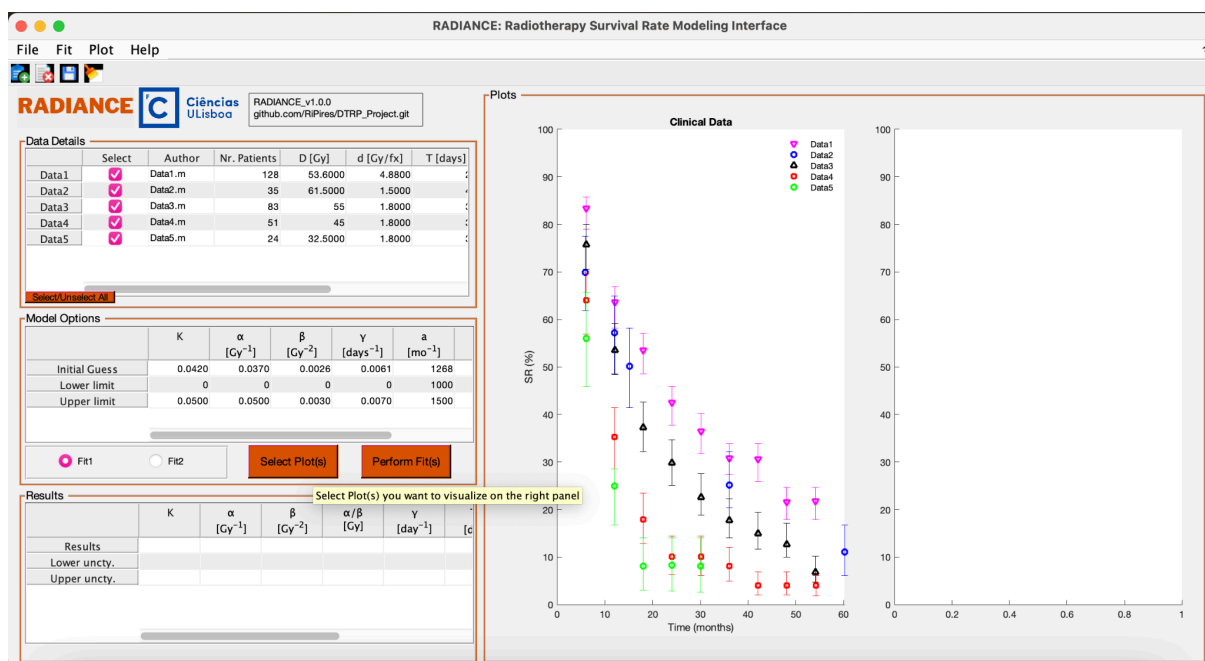
Open study information: afterwards, this information can be loaded via the menu “File/Open”.

Plot raw data: when the user selects a study, its data points appear on the first plot. If he wants to select or unselect all the imported studies, he can use the “Select/Unselect All” button.

Clear axes: at any time, the user can clear the axes using the “Clear Axes” icon on the toolbar, or the menu button “Plot/Clear axes”.

With all the details regarding the clinical data set up, the user may focus on the “Model Options” panel.

Selecting Plot(s): In order to perform the fits, the user has to first select the plot(s) he wants to see on the right panel. The minimum is 1 and the maximum is 2. By clicking on the “Select Plot(s)” button, a new window will appear where the user can make his choice. Note: to perform the fit(s) are needed at least 5 studies, therefore if the user doesn’t select at least 5 files from the Data Details table he won’t be able to continue.



Plot Selection

☒ Fit1: ☒ Fit2:

☐ Fit1 ☐ Fit2

☒ BED Select τ value(s). ☒ BED Select τ value(s).

☒ EQDX Select τ value(s). X ☒ EQDX Select τ value(s). X

d

Select Plot(s)

Once the window is opened, the user can select 1 or 2 plot(s). For the BED and EQDX plot(s), since there are curves dependent on the time in months, the user needs to select time values (tau value(s)). He can also select the X value for the EQDX, and the reference dose, d, for the BED. If he doesn't the variables assume default values of 2Gy per fraction.

Perform the fit: using the “Perform Fit” button on the “Model Options” panel or on the menu “Fit/Perform fit”.

Results: after performing the fit, the chosen curves are displayed in the “Plots” panel, together with the clinical data, and the results of the fitted parameters are displayed on the “Results” panel.

Choosing the model: to apply, either “Fit1” or “Fit2” as defined previously (apart from the “Model Options panel” this can also be done in the menu “Fit/Select model”). The headers on the corresponding table will change according to the selected model. A set of values is assumed by default taking into account the results shown by Tai A, Erickson B, et al.

A more realistic and accurate set of values for “Initial guess”, “Lower limit” and “Upper limit” should be inputted by the user, based on its clinical expertise (warning and error messages are activated if the user prompts certain inputs such as negative numbers).

Save plot: the axes can be saved in a separate file using the menu “Plot/Save”, where the user is prompted to choose which axes to save, the name and the extension of the file (.png, .pdf, .fig, .jpg, .jpeg, .svg).

Save results: the results table can be saved in a separate file using the menu “Fit/Save Results”, where the user is prompted to choose the name and extension of the file (either “.txt” or “.csv” work).

Functions

- radiance.m: the main file
 - AddFile_CB: makes the “Add File” button work
 - askTau: opens a box where the user can insert the tau values
 - BEDFit1Callback: handles the selection of BED1 in the plots selection
 - BEDFit2Callback: handles the selection of BED2 in the plots selection
 - check_match: to see if there is a match between the selected tau value(s) and the available one(s) (present on the data files)
 - ClearAxes: clears the plots axes
 - datauitable_Callback: validates the values on the “Data Details” table and calls the function that plots the data (PltData)
 - Del_CB: deletes selected data
 - Delete_count_row: function used by the delete table row button to delete individual rows, and also to count the number of rows selected by the user

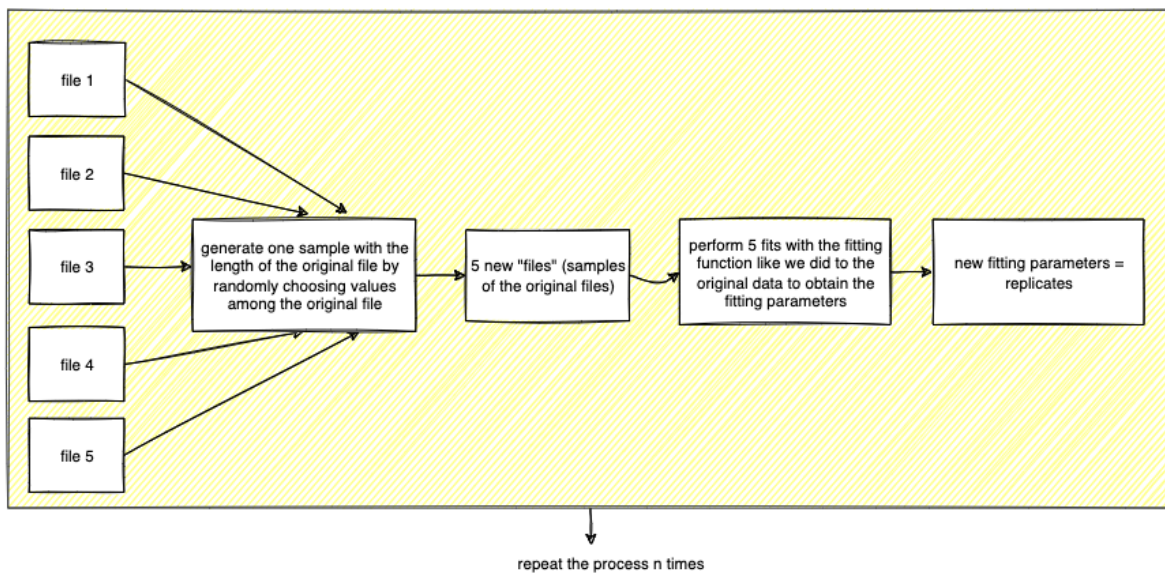
- dvalButtonCallback: opens a box where the user can put a reference value for d for the BED
 - EQDXFit1Callback: handles the selection of EQDX1 in the plots selection
 - EQDXFit2Callback: handles the selection of EQDX2 in the plots selection
 - Fit1Callback: handles the selection of FIT1 in the plots selection
 - Fit2Callback: handles the selection of FIT2 in the plots selection
 - fitoptionsuitable_Callback: validates the values on the "Model Options" tables
 - Help_Callback: opens this guide
 - PltData: plots the data files when these are selected on the "Data Details" table
 - pushbutton_Fit_Callback: makes the "Perform Fit(s)" button work, by performing the fit(s) and plotting the selected plot(s)
 - pushbutton_Plots_Callback: makes the "Select Plot(s)" button work (the one from the main figure), by opening a new window with the options
 - SavePlot: makes the "Save Plot" button work, by saving the selected plot(s)
 - SaveResults_Callback: makes the "Save Results" button work, by saving the parameter values of the selected Fit (on the bar: Fit>Save Results)
 - Saving_taus: stores the taus present on the data files
 - selectAllCallback: makes the "Select All/Unselect All" button work
 - SelectModel_Callback: controls which fit has its tables visible
 - SelectPlotsCallback: makes the "Select Plot(s)" button work (the one from the plot(s) selection window), by validating the user's choices and saving them on the handles structure
 - uimenu_fit1_callback: controls the state of the Fit1 radio button
 - uimenu_fit2_callback: controls the state of the Fit2 radio button
 - uimenu_open_callback: makes the "Open" button work (on the bar: File>Open)
 - uimenu_save_callback: makes the "Save Results" button work (on the bar: File>Save)
 - XvalButtonCallback: opens a box where the user can put a value for X for the EQDX
- BED.m: returns the plot(s) of the relation between the BED and the SR
 - bedfunction.m: returns the value of the bed function for given parameters
 - calculate_n.m: returns the number of fractions in function of the time in days
 - chi2_residuals.m: calculates the residuals of the points of the input datafile(s) to obtain the value of the chi-square function
 - Data folder: contains the data files
 - drafts folder: contains old functions (can be ignored and/or deleted)
 - EQDX.m: returns the plot(s) of the relation between the EQDX and the SR
 - eqdxfunction.m: returns the value of the eqdx function for given parameters
 - fit1.m: returns the results of the first fit - parameters, their uncertainties and plot(s)
 - fit1bed.m: returns the value of the survival rate for a given value of BED for the first fitting function
 - fileqdx.m: returns the value of the survival rate for a given value of EQDX for the first fitting function

- fit2.m: returns the results of the second fit - parameters, their uncertainties and plot(s)
- fit2bed.m: returns the value of the survival rate for a given value of BED for the second fitting function
- fit2eqdx.m: returns the value of the survival rate for a given value of EQDX for the second fitting function
- Images folder: contains the images present on the interface (logos, etc.)
- perform_fit1.m: performs the first fit and returns the fitting parameters and the value of the chi-square function
- perform_fit2.m: performs the second fit and returns the fitting parameters and the value of the chi-square function
- sample.m: generates a sample for a given datafile (Bootstrapping)
- secondfitting.m: fitting function for the 2nd fit. For the first fit we were able to define the fitting function as an Anonymous Functions. However, for the second fit this was not possible, since we had to account for complex values, that would affect the plot.
- uncertainty_quocient.m: returns the uncertainty of a quocient of two parameters (used for the uncertainties of Td and α/β)

Note - Uncertainties

The parameters uncertainties are obtained with the bootstrapping method. Currently, it is only working for 10 samples, to reduce the execution time.

Bootstrapping method:



Possible Future work

- ☐ Allow the user to choose the number of bootstrapping samples
- ☐ Create a warning when the user tries to add the same file more than once
- ☐ Allow the user to define two different d's for the BEDs (fit1 and fit2)

- ☐ Implement a progress bar to measure the amount of time the fit(s) take to be complete
- ☐ Put images on the plot selection window to help the user understand what plot(s) he is choosing
- ☐ Allow the user to change the author's name on the label
- ☐ Allow negatives values for alpha and beta
- ☐ Allow the user to change the fit parameters directly on the results table
- ☐ Allow the user to input the kick-off time (T_k). At the moment, it is 0

$$BED = D \left(1 + \frac{d}{\alpha/\beta} \right) - \frac{\ln 2}{\alpha T_d} (T - T_k)$$

References

- Tai A, Erickson B, Khater KA, Li XA. Estimate of radiobiologic parameters from clinical data for biologically based treatment planning for liver irradiation. Int J Radiat Oncol Biol Phys. 2008 Mar 1;70(3):900-7. doi: 10.1016/j.ijrobp.2007.10.037. PMID: 18262101