

**Software ModeSAL for Quality Control
of Radiation Processing**

User Manual

Introduction

The computer technology for simulation of practical tasks in radiation sterilization process in accordance with Method 1, Standard ISO 11137 and IAEA Code of Practice was developed. The technology was realized on the base of the RT-Office modules for modeling by Monte Carlo method of an absorbed dose in an irradiated heterogeneous targets with electron beam (EB), X-ray and gamma-ray and specialized software ModeSAL.

The software ModeSAL is intended for simulation and comparative analysis of a sterility assurance level (SAL) and a sterilizing dose for bioburden to achieve a required SAL in an irradiated product.

The mathematical approach of the technology is based on the detailed and precise consideration of a self-consistent physical and geometrical models of calculation an EB, X-ray and gamma-ray dose maps in an irradiated product, a SAL, a sterilizing dose and the spatial and time uncertainties for dose provided to an irradiated product.

1. Motivation

Radiation sterilization process of health care products is well established technology and becomes one of the continuously growing branches of radiation processing. Quality Assurance and Quality Control (QA&QC) for all procedures of radiation sterilization is regulated by standards ISO 11137, ISO 13485 [1,2]. For determination of the sterilization dose for required sterility assurance level (SAL) of microbial population on/in an irradiated product, the mathematical model and methods simulation 1 and 2 were developed and experimentally verified [1,3,4,5]. The methods are based on a probability model for the inactivation of microbial population.

The features of mathematical model which is used in the Method 1 are following [4,5]:

- the probability of microbial survival within the population diminishes exponentially with increasing radiation treatment of product by EB, X-ray or gamma-ray;
- the inactivation of any one type of microorganism contributing to the bioburden of the product units can be described by its own unique D_{10} value, where D_{10} is characterize the radiation resistance of microbes. D_{10} is the radiation dose that will reduce a microbial population by 90%;
- the probability of survival of population from N microbes (bioburden) at irradiation is determined by binomial law;
- the number of microbes on/in product unit is defined by Poisson distribution.

In this model, it is suggested that dose value in all product volume during time of irradiation is constant. The constant is chosen as minimum value of an absorbed dose (D_{min}) in the dose map of an irradiated product. D_{min} is called as a sterilization dose. The value of sterilization dose (D_{min}) required to achieve a given SAL for average bioburden of microbial population with standard distribution of resistances (SDR) are presented in the Tables form in the ISO 11137 and IAEA Code [1,3].

The mathematical model for calculation a sterilization dose do not take into consideration the spatial non-uniformity of absorbed dose in an irradiated materials and the uncertainties of irradiation process on results sterilization. It is well known, that under irradiation with EB, X-ray or gamma-ray of heterogeneous targets near the boundaries of contacting materials with different density and/or atomic number an appearance of anomalies in a dose map is observed [6,7]. Under products sterilization, the characteristics of radiation facility can be fluctuated and changed during time irradiation. These effects can be essential influence on the probability of microbial survival and on a sterilizing dose value. Authors developed the computer methodology for simulation of practical tasks in radiation sterilization process based on the detailed and precise consideration of a self-consistent physical and geometrical models for simulation EB, X-ray and gamma-ray dose maps in irradiated product, the uncertainties of irradiation process, a SAL and a sterilizing dose [8].

The objective of this study was the detailed computer analysis of influence of the space non-uniformity of EB absorbed dose distribution in irradiated products and the uncertainties of irradiation process on characteristics of EB sterilization process.

Computation Approach to Decision of Practical Tasks in Radiation Sterilization Process

Authors have developed the information system for analysis and optimization of problem tasks of the radiation sterilization process on the base of specialized simulation modules of Radiation Technological Office (RT-Office) [6].

The system includes the RT-Office modules for simulation of an absorbed dose in irradiated targets with electron beam (EB), X-ray and gamma-ray and specialized software ModeSAL [8]. The software ModeSAL is intended for simulation and comparative analysis of a SAL and a sterilizing dose for bioburden in an irradiated product. The ModeSAL code is a scientific tool which is accessible for broad audience of users, such as microbiologists, dosimetrists, physicists, and other specialists working with radiation sterilization tasks.

Some practical tasks which can be decided with help of the ModeSAL code are as follows:

1. Software ModeSAL allows calculate the sterilized dose required to achieve a given SAL for an arbitrary values of average bioburden having SDR on the base of D_{\min} accordingly Method 1 ISO 11137 and IAEA Code.

It means that:

- for all values average bioburden from the Tables of ISO 11137 and IAEA Code having SDR, the data calculated by ModeSAL and the Tables data are in an absolute agreement;
- for an arbitrary values of average bioburden having SDR and which are absent in the Table, the Software ModeSAL calculates exactly the value of sterilized dose required to achieve a given SAL. I.e. in this case, user can use these data without interpolation of the Table 5 data.

2. Software ModeSAL allows calculate the sterilized dose required to achieve a given SAL for an arbitrary values of average bioburden having any distribution of resistances on the base of D_{\min} accordingly Method 1 ISO 11137 and IAEA Code.

It is useful in case, when user works with known dangerous viruses or known microbial populations which are differed from SDR, for example, in case of bioterrorism (anthrax, bird's influenza, etc.). User can take the value of microbial resistances for dangerous viruses, for example from "Database on Microbial Resistance to Radiation", and enter as input data to the Software ModeSAL [10]. With help of the Software ModeSAL user can made PC experiment to estimate the necessary absorbed dose and radiation facility parameters to eliminate the known dangerous viruses or known microbial populations.

3. Software ModeSAL allows calculate the sterilized dose required to achieve a given SAL for an arbitrary values of average bioburden having any distribution of resistances on the base of D_{\min} accordingly Method 1 ISO 11137 and IAEA Code with due regard for:

- an uncertainty effect of absorbed dose and of parameters of process irradiation;
- an uncertainty effect in a composition and in radiation resistances of microbial population.

4. Software ModeSAL allows calculate the sterilized dose required to achieve a given SAL for above points 1, 2, and 3 with regard to the dose distribution in an irradiated product. Comparison of calculation results on the base of D_{\min} accordingly Method 1 ISO 11137 and IAEA Code with regard to the dose distribution in an irradiated product allows to estimate the "safety factors" for mathematical models which are used in the Standard ISO 11137 and in the Software ModeSAL.

Analysis and solution of problem tasks in radiation sterilization technology were performed as follows:

- The RT-Office modules for specific EB, X-ray and gamma-ray radiation facility and irradiated products optimize a thickness of irradiated products, a configuration of package for the product, the method of irradiation as one- or two-sided types, the choice of irradiation regimes.
- The RT-Office modules simulate a profile of an absorbed dose map in an irradiated product for optimal irradiation regimes.
 - Simulation prediction for the dose map should be periodically verified in special dosimetric experiments.
- The output results for EB, X-ray and gamma-ray processing simulated with the RT-Office modules for an absorbed dose in forms of probability distribution and space distribution (dose map) are used directly as input data for the software ModeSAL;
- The software ModeSAL determines the sterilization dose and scale factor for parameters of radiation facility to achieve a required SAL for microbial population on/in an irradiated product in accordance with Method 1 ISO 11137 or IAEA Code. The software ModeSAL decides as well known and established tasks, so the specific practical tasks in radiation sterilization technology.
- The RT-Office modules optimize the operational parameters of radiation facility on the base of scale factor data.

Such execution sequence of work provides a computer technology for sterilization process in accordance with Method 1 ISO 11137 and IAEA Code with regard to the spatial and time uncertainties for dose delivery to irradiated product.

The Features of Sterilization Process Under Spatially Non-Uniform Dose Distribution

The results of EB absorbed dose in an irradiated target simulated with the software ModeStEB are used as input data for the software ModeSAL.

The features of mathematical model of the software ModeSAL are the following:

- The generalized stochastic model of radiation sterilization process is developed.
- The basic stochastic parameters proper in the modern radiation technologies are taken into account.
- To such stochastic parameters refer to: the bioburden in a product and in its separate parts; a spatial distribution of microbes in a product; a spatial dose distribution in an irradiated product; uncertainties because of nonstability of radiation facility parameters in time of irradiation; operational characteristics of radiation facility required to achieve a given SAL.

The feature of the theoretical approach at development of the generalized stochastic model of radiation sterilization process is introduction of the **scale factor (SF)**. SF is the basic characteristic of change of an irradiation process for the analysis of uncertainties effect. It is well-known, that the dose map depends on major number of parameters of an irradiation process. For example, beam current, energy of ionizing particles, width of scanning, conveyer speed, as well as the characteristics of irradiated product are related to the basic operational parameters which are influenced on the dose map.

However, if we are interested the uncertainties related only with irradiation system, it is logical to assume, that profile of an absorbed dose distribution will change much less than a dose value in separate points. I.e. small changes of irradiation facility parameters basically results in proportional (scale) change of a dose value in all points of the dose map. This fact is obvious for basic operational irradiation parameters, such as a beam current and a conveyor speed. Less obviously, however, with good precision it refers to both to scanning width and to distance from exit window of accelerator to irradiated object. Concerning changes of a dose map at change of energy of ionizing particles, this supposition generally is not valid.

Thus the radiation interaction with a product in the stochastic model is described by some dose map, for which all changes are considered as proportional to a SF value. Consequently, stochastic uncertainty is easily reduced to uncertainty of SF value. The statistical distribution of a SF is supposed as a normal distribution. Therefore, a value of one standard deviation of SF is selected as characteristic of statistical uncertainty for specific radiation processing.

The computer technology represents a simulation results in a graphical and tabular forms. That provides cognitive and comparative analysis of influence of uncertainty values of radiation processing and bioburden characteristics on a SAL of irradiated product.

EB Dose Mapping in Heterogeneous Target

As example, for decision of some practical tasks in sterilization technology, the EB sterilized process was analyzed with the use software ModeStEB for simulation of EB absorbed dose in heterogeneous targets [9, 11]. The software ModeStEB was specially designed for simulation by a Monte Carlo method in 3D model of the absorbed dose and charge distributions within multilayer packages irradiated with scanned EB on industrial radiation facility that is based on the pulsed or continuous type of electron accelerators in the electron energy range from 0.1 to 25 MeV.

The self-consistent physical and geometrical models of the program ModeStEB include in detail the features of electron beam transport and dose field formation in the multi-layer targets. The feature of the software ModeStEB is unique high running speed of calculation schemes. It is reached due to use of specially developed algorithm on the basis of a method of translation of an electron trajectory and an optimum choice of free parameters of modeling.

Multi-layer target consists of some identical packages with flat sheets of materials with various density and atomic number. The number of packages are in the range from 1 to 10. The number of layers in the each package with various geometrical sizes are in the range from 1 to 6. Multi-layer target with/without packing box can be located on the conveyer platform horizontal, vertical or under arbitrary angle relatively incident EB axis.

The software ModeStEB use as input data a detailed characteristics of radiation facility and irradiated target including:

Parameters of electron beam - average beam current, or pulse duration and repetition rate in pulsed accelerators, electron energy spectrum, beam diameter and spatial distribution of the beam intensity.

Parameters of scanned system - modes of operation - the triangular or non-diverging irradiation treatment field in target material; height of scan horn and width of scanning; distance scan - conveyer; form of current in magnet of scanned system; repetition frequency of scanning.

Parameters of conveyer line - speed and geometrical characteristics.

Parameters of irradiated product - geometrical characteristics of the irradiated product; elemental composition of the target; material and size of the covering for irradiated product.

The software ModeStEB provides users with data set in the graphic and tabular form for dose map and charge deposition within each layer of the multi-layer target irradiated with a scanned EB. The output results for EB absorbed dose in an irradiated target are represented in forms of probability distribution and space distribution (dose map). The results for EB absorbed dose in multi-layer target were directly used as input data for the software ModeSAL for further analysis of radiation sterilization process.

Some simulation results

Fig.1 represent the form of the software ModeSAL with loaded input data of EB absorbed dose for calculation of SAL and sterilized dose. The absorbed dose in an EB irradiated target was simulated by software ModeStEB. The absorbed dose is represented in form of probability distribution (graphs and Table) and space distribution (see Fig.1, left side).

There is a possibility to calculate, analyze and compare results for microbial population with SDR taken from ISO 11137-2, 2006 and IAEA Code, for distributions of resistances MD1-MD20 taken from the paper, as well as on the base of any microbial population for which a distribution of resistances can be enter as input data by manually (see **Fig.1**, Table, right side) [5].

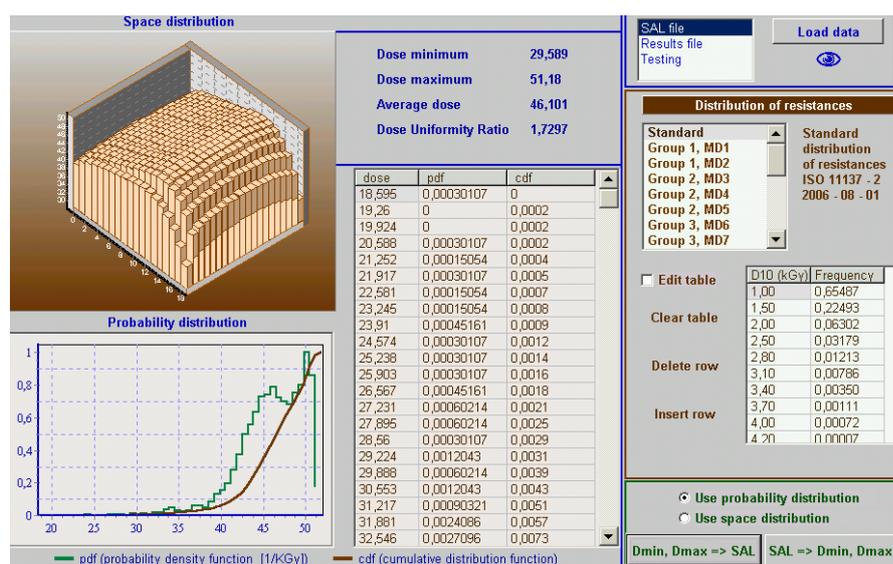


Fig.1. The forms with input data on absorbed dose in PE block under one-sided irradiation with scanned 10 MeV electron beam on moving conveyer. 3D view - dose map, 2D view and Table data – probability distribution of absorbed dose.

The results of SF, D_{\max} and D_{\min} calculation as function of average bioburden ($Av.B$) for microbial population with distributions of resistances MD15 are presented in Fig.2. Microbial population is located on/in PE block under two-sided irradiation with 10MeV electron beam. Calculations were made on the base of EB dose map presented in Fig.1. for $Av.B = 1000$, $SAL=10^{-6}$ and uncertainties $\pm 5\%$ the $SF = 0.4956$. It is necessary to change the operational parameters of EB radiation facility (EB current, conveyer speed,...) on $SF = 0.4956$ value to achieve a required $SAL=10^{-6}$.

The calculations results for comparative analysis of a SAL and a sterilizing dose for microbial population with distributions of resistances both as SDR and MD15 types for $Av.B = 1000$ in two-sided irradiated product with 10MeV EB are presented in Fig.3. Calculations were made for non-uniform dose distribution of EB presented in Fig.1. As it is seen from Fig.3, for microbial population MD15 at calculated $SF = 0.4956$ and uncertainties $\pm 5\%$, the $SAL=10^{-6}$ for $Av.B = 1000$.

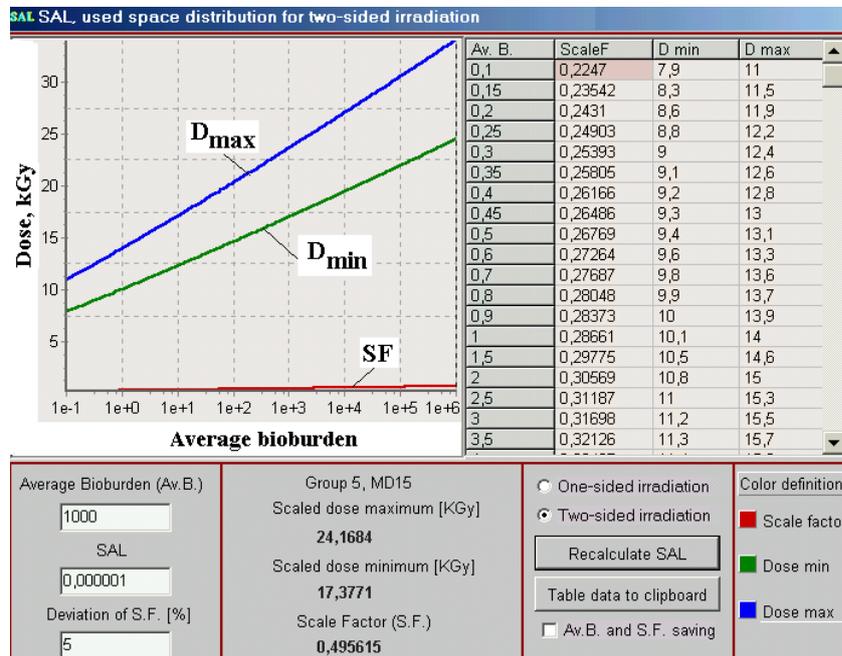


Fig.2. The values of D_{max} , D_{min} and SF as function of average bioburden for microbial population MD15 in graphical and tubular forms. PE block is two-sided irradiated with 10 MeV electron beam.

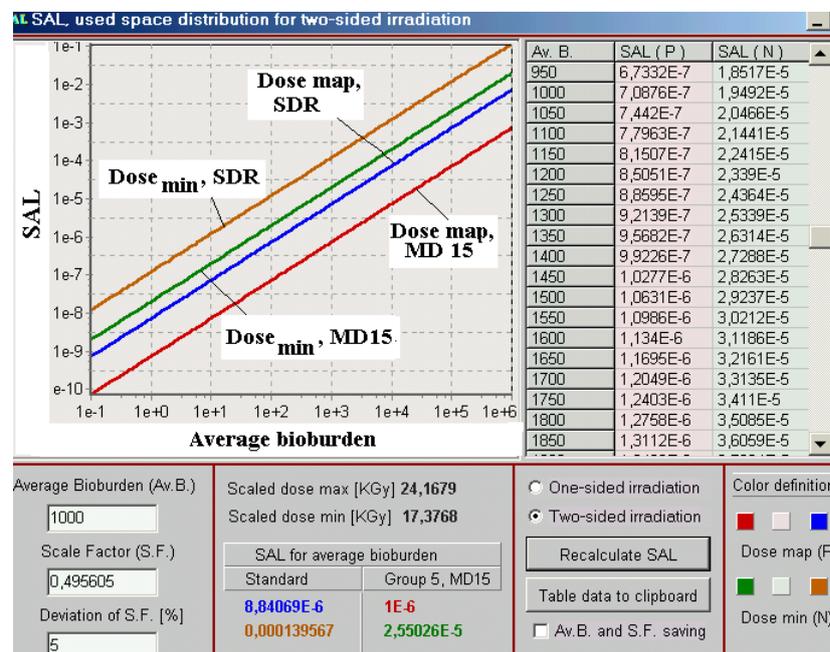


Fig.3. The values of SAL as function of average bioburden for microbial populations SDR in graphical form and MD15 in graphical and tubular forms. PE block is two-sided irradiated with 10 MeV EB, Av.B = 1000, SF = 0.4956, and uncertainties $\pm 5\%$.

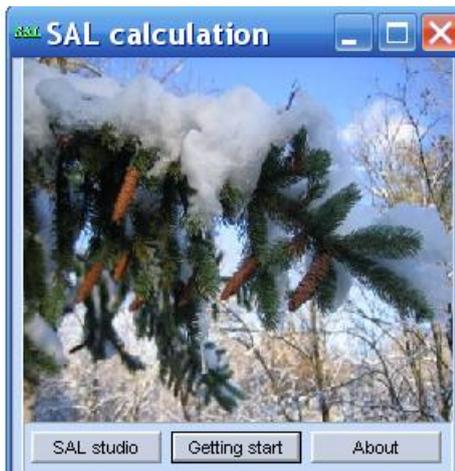
The results of comparative analysis of values of SF and EB sterilized dose for microbial populations with distributions of resistances both as SDR and MD15 types calculated on the base of D_{min} and dose map PE block under two-sided irradiation with 10MeV with 10MeV EB are presented in the Table.

Table. The results of comparative analysis of values of SF and EB sterilized dose for microbial populations SDR and MD15 calculated on the base of D_{\min} and dose map.

Microbial population	Unc, %	Dose map (P), kGy			Dose min (N), kGy		
		SF	SD_{\min}	SD_{\max}	SF	SD_{\min}	SD_{\max}
SDR	0	0,5715	20,04	27,87	0,709	24,86	34,57
	10	0,6218	21,8	30,32	0,775	27,18	37,8
MD15	0	0,4852	17,01	23,66	0,5968	20,9	29,1
	10	0,5332	18,7	26,0	0,6601	23,14	32,19

The analysis of results represented in Fig.3 and the Table data shows, that for microbial populations of SDR and MD15 types in all range of average bioburden the SAL value calculated on the base of suggestion, that D_{\min} is constant in all irradiated product volume, is greater than the SAL calculated on the base of a spatial EB dose distribution in the irradiated product. It follows from these results that value of EB sterilizing dose in case of calculation on the base of D_{\min} is greater in comparison with calculation of sterilizing dose on the base of dose map in an irradiated product. Taking into account the uncertainties due to fluctuation of irradiation parameters leads to increasing of sterilizing dose value. Irradiation regime on the base of D_{\min} concept leads to overdosing of the sterilized product. And as result, it can reduce the throughput and worsen quality of the products.

Software ModeSAL. How to get results



Entering of input data

- Click the "SAL studio" button in the Main Form of Software ModeSAL. (see Fig.1).
The Form for entering of input data will be opened (see Fig.2).

Fig.1. Main Form of Software ModeSAL.

- Select the directory "SAL file", "Results file", or "Testing", with working files of input data in the window "Load data".
- Click the button "Load data". The selected directory will be opened.
- Then Select and load any file from these directories. (see Fig.3).
- The Form with input data from the loaded file will be opened for calculation (see Fig.3, example from the loaded file "ModePEB.sal").

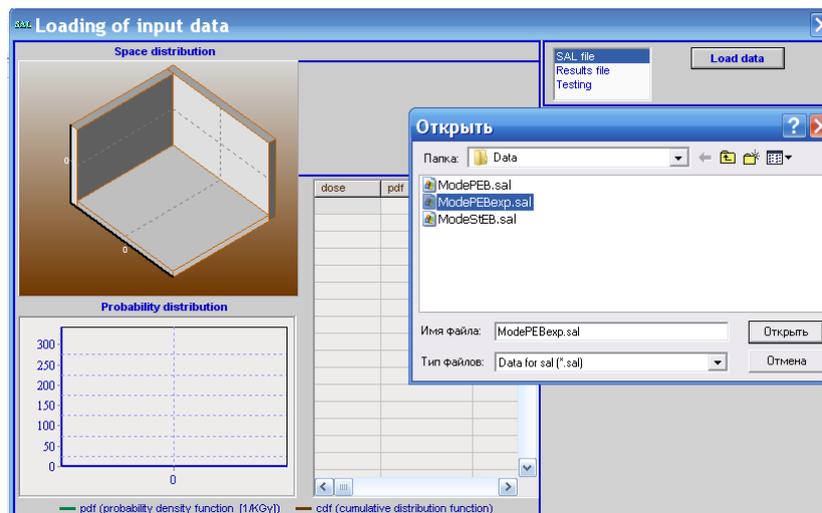


Fig.2. The Form of the Software ModeSAL for entering of input data.

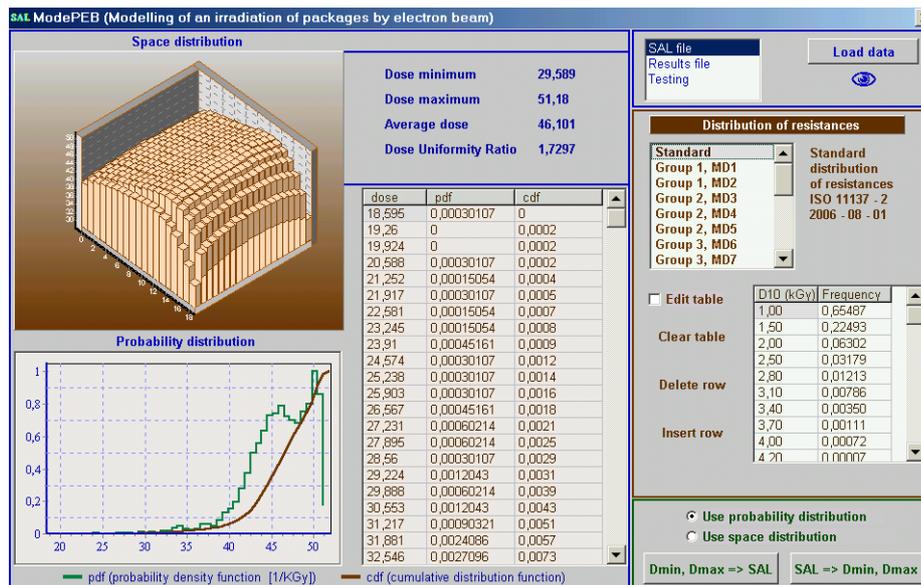


Fig.3. The Form with **input data** from the loaded file “ModePEB.sal”. Input data on absorbed dose in PE block under one-sided irradiation with scanned 10 MeV electron beam on moving conveyer.

- The frame “**Space distribution**” (see Fig.3 – left side) present the results of characteristics of EB dose map in irradiated target, including **Dose minimum**, **Dose maximum**, **Average dose**, **Dose Uniformity Ratio**.

3D view - dose map, 2D view and Table data – probability distribution of absorbed dose.

- After loading the files from the directories “**SAL file**” and “**Testing**” the button with sign “**Eye**” will appear near the button “**Load data**” (see Fig.3)).
- **Click** the button “**Eye**”.

The Table with **all input data** which were used for **EB dose map simulation** will be open (see Fig.4)).

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SAL Input data for SAL calculation
ModePEB (Modelling of an irradiation of packages by electron beam)
Source: Pulsed regime = No; Average current = 1,000
Spectrum: MonoEnergy = Yes; Spectrum = No; Energy = 10,000
Angular spread: MonoDirect = No; Angular spread = Yes; ((A;I);(0,000;1,000);(12,000;0,000);)
Space spread: Point beam = No; Distribute beam = Yes; Beam diameter = 4,000; Full width on half maximum = 1,000
Scanning system: Speed = 1,000; Frequency = 1,000; Width = 120,000; Height = 80,000
Scan-conv. distance = 20,000; Scanning width = 40,000; Y angle of target = 0,000; X angle of target = 0,000
Non-diverging beam = No; Triangular scanning = Yes; Default mode = Yes; Custom mode = No
Irradiated volume: Packages = 1; Layers in each package = 1; Width of packages = 39,010; Horizontal orientation = Yes
((Layer;Thickness;Width;Density);(1;5,90;39,00;0,65))
((Layer;Z;W);(1;1,000;2,000);(1;6,000;12,000))
The following package and layer were registered in gotten results:Package = 1; Layer = 1

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Fig.4. Table with **input data** which were used for **EB dose map simulation**.

Note.

The files “*.sal” type are stored in the **directory "SAL file"**.

The files “*.mon” type are stored in the **directory " Results file"**.

The files “*.sal” and “*.mon” types present the results of MC simulation of Dose Map in targets irradiated with scanned electron, X-ray or Gamma ray beams on moving conveyer.

These files were prepared with specialized simulation modules of **RT-Office: ModeRTL, ModePEB, ModeXR, ModeSXR, ModeGR,....**

The software ModeSAL and ModeRTL, ModePEB, ModeXR, ModeSXR, ModeGR,.... are the simulation modulus of the **RTOffice**. Input and output data for all simulation modulus of the **RTOffice** are self-consistent between themselves.

The files **“*.tst”** type are stored in the **directory "Testing”**. These files with special form of the Dose Map in an irradiated target were prepared manually.

Selection of the distribution resistances for calculation and analysis.

Frame **“Distribution of resistances”** (see Fig.3 – right side).

You can calculate, make analysis and compare results for:

- **standard distributions of resistances (SDR)** taken from ISO 11137-2, 2006,
- **distributions of resistances MD1-MD20** taken from the paper - A.Tallentire, Rad.Phys.&Chem, 98, 83-94,
- **as well as on the base of any distributions of resistances** which can be enter as input data manually.

For do it, **Select** the window **“Edit Table”** with a tick and **Create Table manually** (see Fig.3)).

Selection of the calculation regimes.

The **Form for selection of calculation regimes** is located in the down right corner of the **Form with input data** (See Figs. 3 and 5).

The image shows a software interface for selecting calculation regimes. It features two radio buttons at the top: 'Use probability distribution' (which is selected) and 'Use space distribution'. Below these are two buttons: 'Dmin, Dmax => SAL' and 'SAL => Dmin, Dmax'.

Fig.5. The Form for selection of calculation regimes.

You can decide and calculate the **direct task**:

Calculation of SAL on the base of **probability distribution for EB absorbed dose** in an irradiated target and on the base of **spatial distribution (dose Map) for EB absorbed dose** in an irradiated target.

- **Select “Use probability distribution”** or **“Use space distribution”** with a tick.
- **Click** the button **“ $D_{min}, D_{max} \rightarrow SAL$ ”**

You can decide and calculate the **inverse task**:

Calculation of the Scale Factor (S.F.) on the base of **probability distribution for EB absorbed dose** and on the base of **spatial distribution (dose Map) for EB absorbed dose**.

- **Select “Use probability distribution”** or **“Use space distribution”** with a tick.
- **Click** the button **““SAL $\rightarrow D_{min}, D_{max}$ ””**.