Seminars in Applied Statistics for Radiation Cytogenetics and Biodosimetry

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Seminar V. Biological dosimetry – Dose response calibration

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Specific features of the LQM: alpha- and beta-coefficients; nonsense of negative values.

Curve fitting by Maximum Likelihood Estimate or Iteratively Reweighted Least Squared Method

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CABAS *versus* DoseEstimate in regard of calibration curve fitting.

The assessment of the goodness-of-fit of the dose response and the strength (accuracy) of the coefficients.

Influence of the overdispersion at different number of dose response points.

Expansion of the dose range: The interdependence of the LQ coefficients (a “see-saw” effect).

Influence of the number of cells scored and aberrations found at different dose points.

Dose response within the low dose range: 0,1 – 1,0 Gy acute γ-rays.

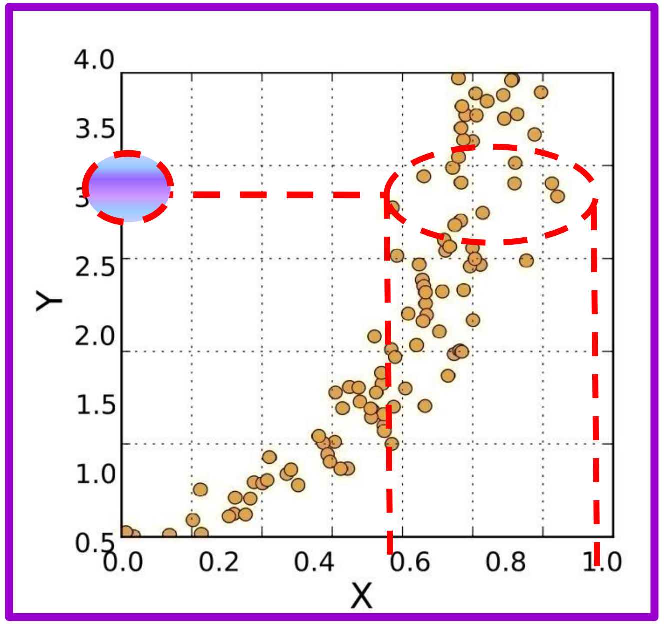
The initial linearity of the dose response at doses <0,1 Gy; minimum dose for the curvature.

The analysis of the published dose response data within the low dose range.

The overall inter-laboratory heterogeneity of the cytogenetic dose response data.

Calibration of the Dose Response in Radiation Cytogenetics

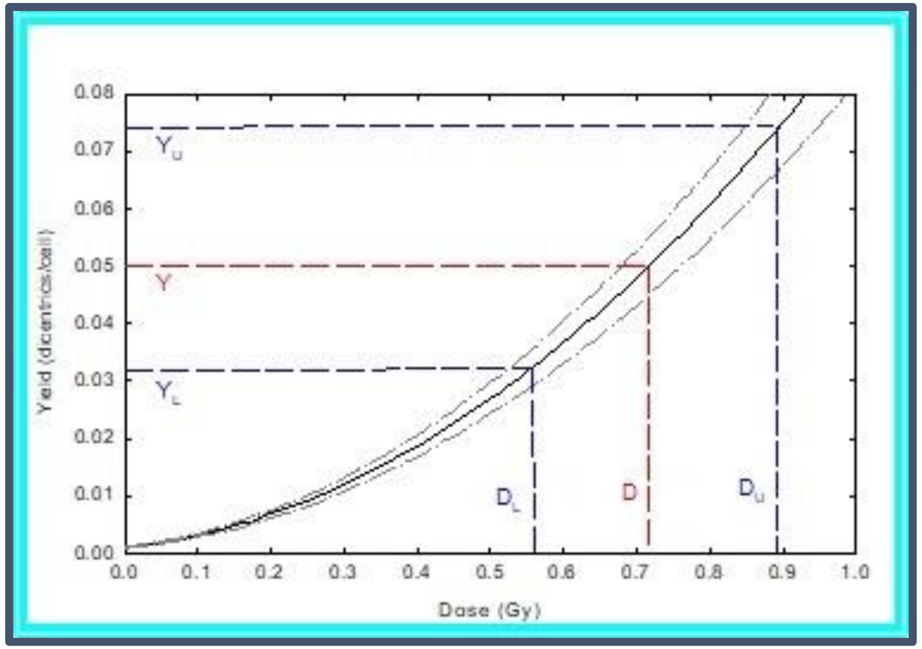
It is accepted that the yield of radiation-induced chromosome aberrations in peripheral blood lymphocytes shows a clear relationship with dose.



Raw *in vitro* calibration data

Why do we need a formal mathematical description of the dose response?

- Obviosly, to be able to assess the accumulated radiation dose with certain confidence, based on common sence and correct statistics.



Properly fitted dose response model

Choice of the Model for the Dose Response

For low LET radiation (X- or γ-rays) the overall relationship of the yields of chromosome aberrations (Y) to radiation dose (D) is a complex sigmoid, with a linear part within the range of very low doses up to 20-50 mGy and a saturation at doses >22-25 Gy.

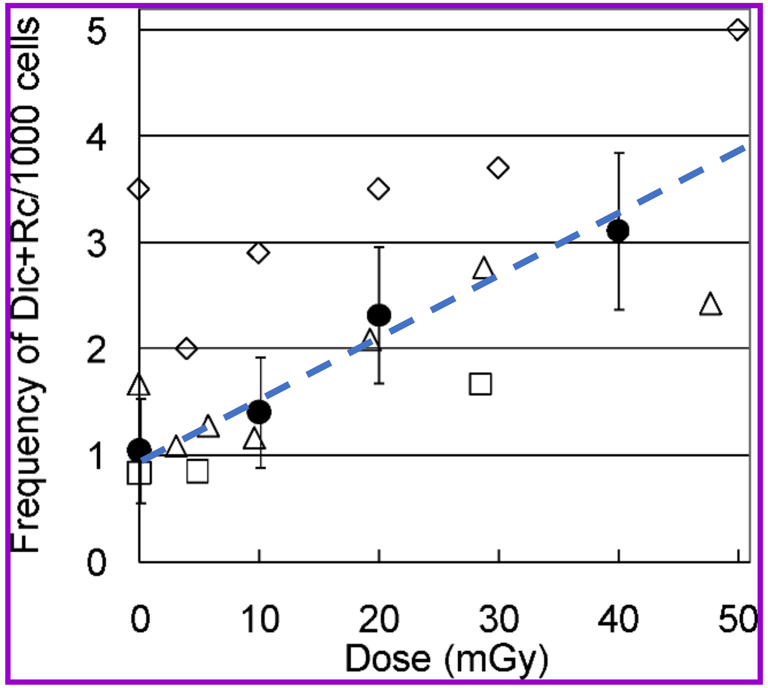
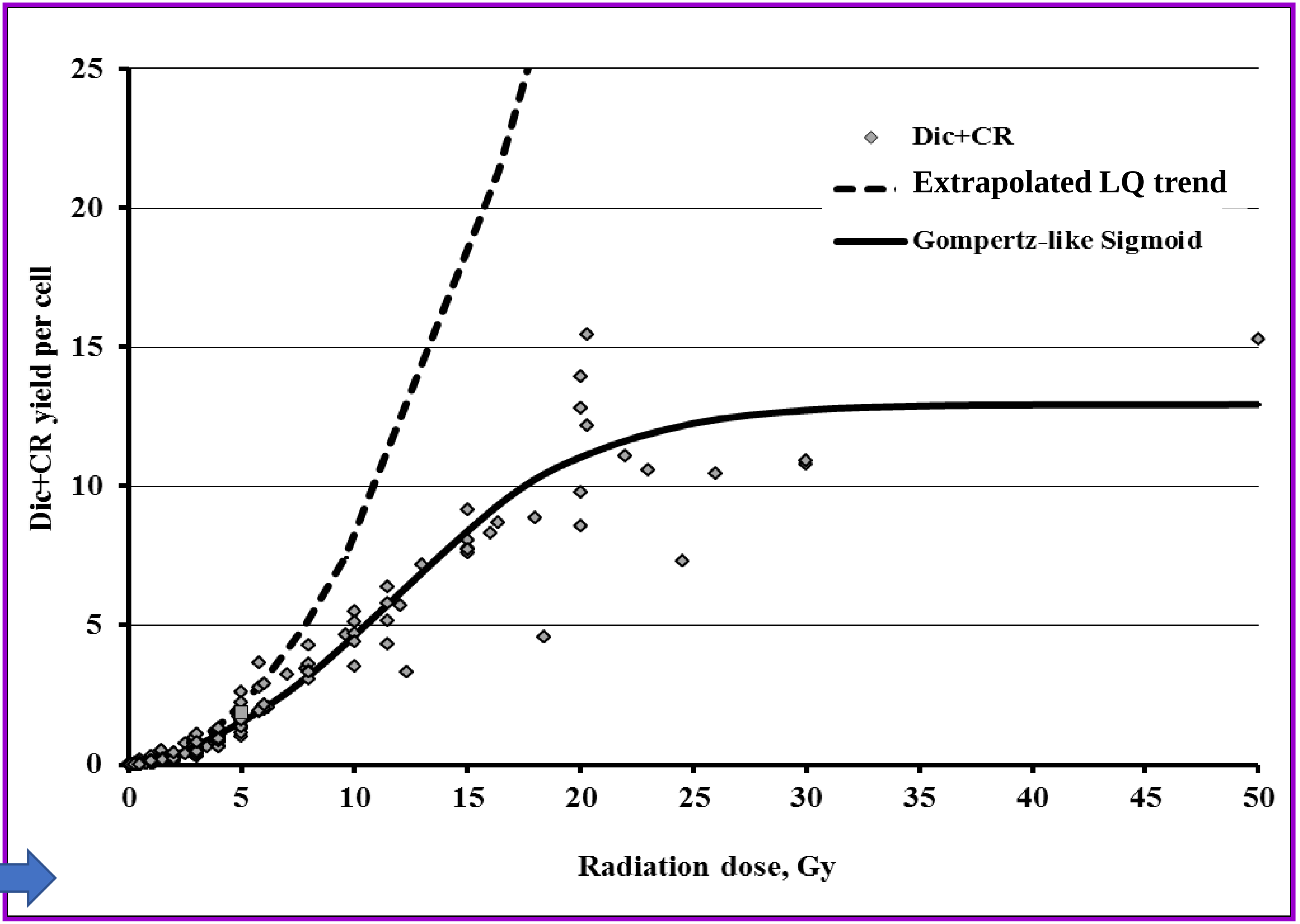


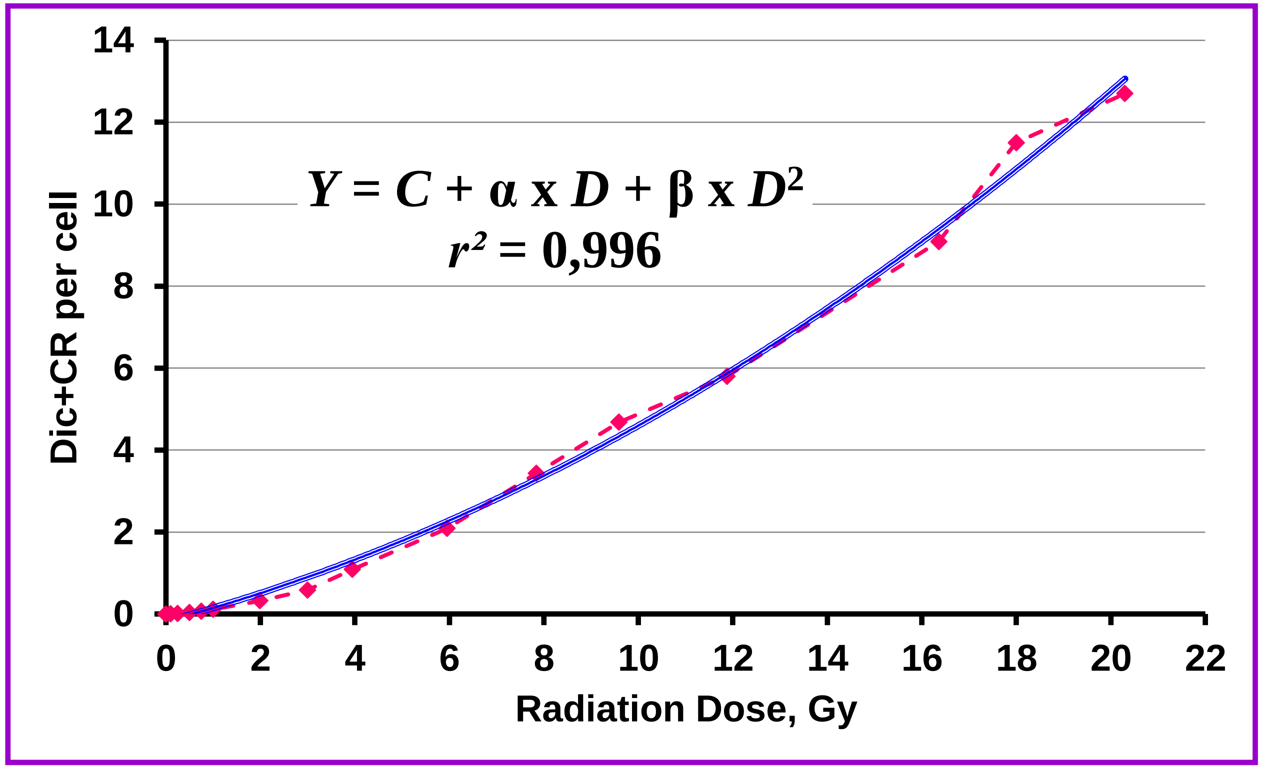
Fig. (modified) from Iwasaki et al, 2011;
DOI: 10.1667/RR2097.1

Pooled data from >30 publications presenting cytogenetic dose responses *in vitro*.



Linear Quadratic Model of the Dose Response

For practical biodosimetry the dose response can be approximated by the Linear-Quadratic equation. Best fit of the LQ model exists in between ~0.5 Gy and ~5.0 Gy, but it can be effectively used up to ~20 Gy.



Parameters of the LQ Model:

C – the background level of aberrations;

α – the linear coefficient: aberrations resulting from the interaction of DNA DSBs, caused by a single ionising track that traversed two double helices, breaking both;

β – the quadratic coefficient: aberrations produced by the interaction of DNA DSBs, each being caused independently in different sites by different ionising tracks.

ATTENTION: Negative coeffitients of the LQ dose response have NO SENSE!

Two main strategies of fitting dose response regression

Maximum Likelihood Estimation

The method of MLE is used for the estimation of the parameters of an assumed probability distribution, given some observed data. This is achieved by maximizing a likelihood function so that, under the assumed statistical model, the observed data is most probable. The point in the parameter space that maximizes the likelihood function is called the maximum likelihood estimate.

Iteratively Reweighted Least Squares

The method of IRLS is used to obtain the certain optimization of the objective functions, which suppose to have the form of a *p*-normal distribution, by an iterative method, in which each step comprises building a regression using the weighted least squares technique. IRLS is used to find the maximum likelihood estimates of a generalized linear model, as a way of mitigating the influence of outliers in an otherwise normally-distributed data set.

Both methods – MLE and IRLS – give the same result in regard of the mean values of dose response coefficients and their errors.

Iteratively Reweighted Least Squares (IRLS)

A common criterion for closeness is the sum of squares differences:

$$SSD = \sum_{i=1}^{n} \left(Y_0 - Y_f\right)^2$$

Standard procedure of the LQ regression analysis by the weighted Least Squares method:

$$Y = C + \alpha \text{ x } D + \beta \text{ x } D^2$$

$$\begin{cases} C w_i + \alpha \sum D w_i + \beta \sum D^2 w_i = \sum Y w_i; \\ C \sum D w_i + \alpha \sum D^2 w_i + \beta \sum D^3 w_i = \sum Y D w_i; \\ C \sum D^2 w_i + \alpha \sum D^3 w_i + \beta \sum D^4 w_i = \sum Y D^2 w_i. \end{cases}$$

Common approach is to minimize SSD with weights of data points by inverse of their variance (dispersion)

$$w = \frac{1}{\sigma_i^2} \longrightarrow SSD = \sum_{i=1}^{n} \frac{\left(Y_0 - Y_f\right)^2}{\sigma_i^2}$$

First coefficients are obtained by minimising the SSD via the equation, in which Y_o is the observed yield, Y_f the expected yield from a linear-quadratic model and the weighting factor is $w_i = 1 / (Y_0/N)$; where Y_0 is the yield of aberrations and N is the number of cells at each dose.
Then the coefficients are recalculated using as weighting factor $w = 1/(Y_f/N)$, obtaining new coefficients and new expected frequencies Y_f for each dose. This procedure is repeated with new weighting factors, $w = 1/(Y'_f/N)$ and so on, until the coefficients do not vary. Note that in the iterations the variances are based on the fitted means, not the real variance, e.g. Poisson overdispersion.

Manual fitting of the LQ Regression
by the Iteratively Reweighted Least Squares method in MS Excel

Original data

$w_i = 1 / (Y_0/N);$

Values to estimate using MS Excel

$$\begin{cases} C \times \Sigma w_i + \alpha \times \Sigma D_i w_i + \beta \times \Sigma D_i^2 w_i = \Sigma Y_i w_i; \\ C \times \Sigma D_i w_i + \alpha \times \Sigma D_i^2 w_i + \beta \times \Sigma D_i^3 w_i = \Sigma Y_i D w_i; \\ C \times \Sigma D^2_i w_i + \alpha \times \Sigma D_i^3 w_i + \beta \times \Sigma D_i^4 w_i = \Sigma Y_i D^2 w_i \end{cases}$$

	Dose, Gy	Cells scored	Dic+CR found	Yield	Weight, w_i	Dose*w_i	$(Dose^2)$*w_i	$(Dose^3)$*w_i	$(Dose^4)$*w_i	Yield*w_i	Yield*Dose *w_i	Yield*$Dose^2$ *w_i
	0,00	10000	10	0,0010	10000000	0,0000	0,0000	0,0000	0,0000	10000	0	0,0000
	0,10	2005	8	0,0040	502503,125	50250,3125	5025,0313	502,5031	50,2503	2005	201	20,0500
	0,25	1994	29	0,0145	137104,6897	34276,1724	8569,0431	2142,2608	535,5652	1994	499	124,6250
	0,50	920	31	0,0337	27303,2258	13651,6129	6825,8065	3412,9032	1706,4516	920	460	230,0000
	0,75	900	64	0,0711	12656,2500	9492,1875	7119,1406	5339,3555	4004,5166	900	675	506,2500
	1,00	1185	135	0,1139	10401,6667	10401,6667	10401,6667	10401,6667	10401,6667	1185	1185	1185,0000
Total	2,6000	17004	277	0,2383	10689968,9571	118071,9520	37940,6881	21798,6893	16698,4504	17004	3019	2065,9250
					Σw_i	$\Sigma D_i w_i$	$\Sigma D_i^2 w_i$	$\Sigma D_i^3 w_i$	$\Sigma D_i^4 w_i$	$\Sigma Y_i w_i$	$\Sigma Y_i D w_i$	$\Sigma Y_i D^2 w_i$

Manual fitting of the LQ Regression by the IRLS – the 1st iteration

$$\begin{cases} C \times 10689968{,}9571 + \alpha \times 118071{,}9520 + \beta \times 37940{,}6881 = 17004 \\ C \times 118071{,}9520 + \alpha \times 37940{,}6881 + \beta \times 21798{,}6893 = 3019 \\ C \times 37940{,}6881 + \alpha \times 21798{,}6893 + \beta \times 16698{,}4504 = 2065{,}9250 \end{cases}$$

$$\begin{cases} C + \alpha \times 0{,}01105 + \beta \times 0{,}00355 = 0{,}00159 \\ C + \alpha \times 0{,}32134 + \beta \times 0{,}18462 = 0{,}02557 \\ C + \alpha \times 0{,}57455 + \beta \times 0{,}44012 = 0{,}05445 \end{cases}$$

1. Simplyfy equations by dividing each part by the multiplier of C.
2. Use the 1st equation to express C via α and β: $C = 0{,}00159 - \alpha \times 0{,}01105 - \beta \times 0{,}00355$
3. Subtract the 1st equation from the 2nd equation: $\alpha \times 0{,}31029 + \beta \times 0{,}18107 = 0{,}02398$
4. Use the result to express α via β: $\alpha = 0{,}07728 - \beta \times 0{,}58356$
5. Re-write the 3rd equation substituting C and α by respective expressions containing β:

$$0{,}00159 - (0{,}07728 - \beta \times 0{,}58356) \times 0{,}01105 - \beta \times 0{,}00355 + (0{,}07728 - \beta \times 0{,}58356) \times 0{,}57455 + \beta \times 0{,}44012 = 0{,}05445$$

6. Find a solution for β, and then consequently for α and C: **β = 0,086460; α = 0,026823; C = 0,000988.**
7. Use the estimates of the coefficients in the LQ equation $Y = 0{,}000988 + 0{,}026823 \times D + 0{,}0886460 \times D^2$

to calculate the fitted aberration yields:

Dose, Gy	Expected Yield
0,00	0,000988
0,10	0,004535
0,25	0,013100
0,50	0,036014
0,75	0,069739
1,00	0,114271

8. Use the expected yield to calculate new weights $w_i = 1 / (Y_f/N)$, needed for the next iteration:

Weight, w_i
10126332,8618
442173,7789
152248,4023
25545,5822
12905,3283
10370,1067

Manual fitting of the LQ Regression by the IRLS – the 2nd iteration

	Dose, Gy	Cells scored	Dic+CR found	Yield	Weight, w_i	Dose*w_i	(Dose^2)*w_i	(Dose^3)*w_i	(Dose^4)*w_i	Yield*w_i	Yield*Dose *w_i	Yield*Dose^2 *w_i
	0,00	10000	10	0,0010	10126332,8618	0,0000	0,0000	0,0000	0,0000	10126,3329	0,0000	0,0000
	0,10	2005	8	0,0040	442173,7789	44217,3779	4421,7378	442,1738	44,2174	1764,2844	176,4284	17,6428
	0,25	1994	29	0,0145	152248,4023	38062,1006	9515,5251	2378,8813	594,7203	2214,2446	553,5611	138,3903
	0,50	920	31	0,0337	25545,5822	12772,7911	6386,3955	3193,1978	1596,5989	860,7751	430,3875	215,1938
	0,75	900	64	0,0711	12905,3283	9678,9962	7259,2472	5444,4354	4083,3265	917,7122	688,2842	516,2131
	1,00	1185	135	0,1139	10370,1067	10370,1067	10370,1067	10370,1067	10370,1067	1181,4046	1181,4046	1181,4046
Total	2,6000	17004	277	0,2383	10769576,0602	115101,3725	37953,0124	21828,7949	16688,9698	17064,7537	3030,0658	2068,8446
					Σw_i	$\Sigma D_i w_i$	$\Sigma D_i^2 w_i$	$\Sigma D_i^3 w_i$	$\Sigma D_i^4 w_i$	$\Sigma Y_i w_i$	$\Sigma Y_i D w_i$	$\Sigma Y_i D^2 w_i$

$$\begin{cases} C \times 10769576{,}0602 + \alpha \times 115101{,}3725 + \beta \times 37953{,}0124 = 17064{,}7537 \\ C \times 115101{,}3725 + \alpha \times 37953{,}0124 + \beta \times 21828{,}7949 = 3030{,}0658 \\ C \times 37953{,}0124 + \alpha \times 21828{,}7949 + \beta \times 16688{,}9698 = 2068{,}8446 \end{cases}$$

$$\Rightarrow \begin{cases} C + \alpha\ 0{,}01069 + \beta \times 0{,}00352 = 0{,}00158 \\ C + \alpha \times 0{,}32974 + \beta \times 0{,}18965 = 0{,}02633 \\ C + \alpha \times 0{,}57515 + \beta \times 0{,}43973 = 0{,}05451 \end{cases}$$

New coefficients: C = 0,000988; α = 0,027591; β = 0,085630. Repeat calculations of Y_f and w_i.

Manual fitting of the LQ Regression by the IRLS – the 3rd iteration

	Dose, Gy	Cells scored	Dic+CR found	Yield	Weight, w_i	Dose*w_i	(Dose^2)*w_i	(Dose^3)*w_i	(Dose^4)*w_i	Yield*w_i	Yield*Dose *w_i	Yield*Dose^2 *w_i
	0,00	10000	10	0,0010	10122670,0187	0,0000	0,0000	0,0000	0,0000	10122,6700	0,0000	0,0000
	0,10	2005	8	0,0040	435557,0009	43555,7001	4355,5700	435,5570	43,5557	1737,8833	173,7883	17,3788
	0,25	1994	29	0,0145	150632,2654	37658,0664	9414,5166	2353,6291	588,4073	2190,7401	547,6850	136,9213
	0,50	920	31	0,0337	25420,7723	12710,3862	6355,1931	3177,5965	1588,7983	856,5695	428,2848	214,1424
	0,75	900	64	0,0711	12885,1404	9663,8553	7247,8915	5435,9186	4076,9390	916,2767	687,2075	515,4056
	1,00	1185	135	0,1139	10375,7501	10375,7501	10375,7501	10375,7501	10375,7501	1182,0475	1182,0475	1182,0475
Total	2,6000	17004	277	0,2383	10757540,9479	113963,7580	37748,9213	21778,4514	16673,4503	17006,1870	3019,0131	2065,8956
					Σw_i	$\Sigma D_i w_i$	$\Sigma D_i^2 w_i$	$\Sigma D_i^3 w_i$	$\Sigma D_i^4 w_i$	$\Sigma Y_i w_i$	$\Sigma Y_i D w_i$	$\Sigma Y_i D^2 w_i$

$$\begin{cases} C \times 10757540{,}9479 + \alpha \times 113963{,}7580 + \beta \times 37748{,}9213 = 17006{,}1870 \\ C \times 113963{,}7580 + \alpha \times 37748{,}9213 + \beta \times 21778{,}4514 = 3019{,}0131 \\ C \times 37748{,}9213 + \alpha \times 21778{,}4514 + \beta \times 16673{,}4503 = 2065{,}8956 \end{cases}$$

$$\begin{cases} C + \alpha \times 0{,}01059 + \beta \times 0{,}00351 = 0{,}00158 \\ C + \alpha \times 0{,}33124 + \beta \times 0{,}19110 = 0{,}02649 \\ C + \alpha \times 0{,}57693 + \beta \times 0{,}44169 = 0{,}05473 \end{cases}$$

New coefficients: C = 0,000988; α = 0,027596; β = 0,085622. Repeat calculations of Y_f and w_i.

Manual fitting of the LQ Regression by the IRLS – the 4th iteration

	Dose, Gy	Cells scored	Dic+CR found	Yield	Weight, w_i	Dose*w_i	($Dose^2$)*w_i	($Dose^3$)*w_i	($Dose^4$)*w_i	Yield*w_i	Yield*Dose *w_i	Yield*$Dose^2$ *w_i
	0,00	10000	10	0,0010	10120770,3237	0,0000	0,0000	0,0000	0,0000	10120,7703	0,0000	0,0000
	0,10	2005	8	0,0040	435506,5723	43550,6572	4355,0657	435,5066	43,5507	1737,6821	173,7682	17,3768
	0,25	1994	29	0,0145	150623,5686	37655,8922	9413,9730	2353,4933	588,3733	2190,6136	547,6534	136,9133
	0,50	920	31	0,0337	25420,5081	12710,2541	6355,1270	3177,5635	1588,7818	856,5606	428,2803	214,1401
	0,75	900	64	0,0711	12885,3210	9663,9908	7247,9931	5435,9948	4076,9961	916,2895	687,2171	515,4128
	1,00	1185	135	0,1139	10376,0500	10376,0500	10376,0500	10376,0500	10376,0500	1182,0816	1182,0816	1182,0816
Total	2,6000	17004	277	0,2383	10755582,3438	113956,8442	37748,2089	21778,6082	16673,7519	17003,9977	3019,0007	2065,9248
					Σw_i	$\Sigma D_i w_i$	$\Sigma D_i^2 w_i$	$\Sigma D_i^3 w_i$	$\Sigma D_i^4 w_i$	$\Sigma Y_i w_i$	$\Sigma Y_i D w_i$	$\Sigma Y_i D^2 w_i$

$$\begin{cases} C \times 10755582{,}3438 + \alpha \times 113956{,}8442 + \beta \times 37748{,}2089 = 17003{,}9977 \\ C \times 113956{,}8442 + \alpha \times 37748{,}2089 + \beta \times 21778{,}6082 = 3019{,}0007 \\ C \times 37748{,}2089 + \alpha \times 21778{,}6082 + \beta \times 16673{,}7519 = 2065{,}9248 \end{cases}$$

$$\begin{cases} C + \alpha \times 0{,}01060 + \beta \times 0{,}00351 = 0{,}00158 \\ C + \alpha \times 0{,}33125 + \beta \times 0{,}19111 = 0{,}02649 \\ C + \alpha \times 0{,}57694 + \beta \times 0{,}44171 = 0{,}05473 \end{cases}$$

New coefficients: C = 0,000988; α = 0,027596; β = 0,085622. Coefficients are the same, as in the previous iteration.

Perform calculations of Y_f to estimate the goodness of fit.

Estimation of the goodness of fit by chi-squared test

$$Y = 0{,}000988 + 0{,}027596 \times D + 0{,}086522 \times D^2$$

Dose, Gy	Cells scored	Dic+CR found	Yield	Expected Yield	Expected Dic+CR	(Obs - Exp)	$(\text{Obs - Exp})^2$	/ Expected
0,00	10000	10	0,0010	0,00099	9,88066	0,11934	0,01424	0,00144
0,10	2005	8	0,0040	0,00460	9,23070	-1,23070	1,51463	0,16409
0,25	1994	29	0,0145	0,01324	26,39720	2,60280	6,77455	0,25664
0,50	920	31	0,0337	0,03619	33,29597	-2,29597	5,27146	0,15832
0,75	900	64	0,0711	0,06985	62,86222	1,13778	1,29453	0,02059
1,00	1185	135	0,1139	0,11421	135,33324	-0,33324	0,11105	0,00082
								$\Sigma\chi^2 = 0{,}60190$

Degrees of freedom: $df = n - k$ = 6 dose points – 3 fitted coefficients = 3

$\Sigma\chi^2 = 0{,}60190$; $df = 3$; $p = 0{,}8960$

CABAS

CABAS (and CABAS 2) – a freeware program that can:

- Fit chromosomal aberration data to a linear-quadratic equation <u>by maximum likelihood</u> and test the goodness of fit

- Calculate the dose and the uncertainty based on the scored frequency of aberrations

- Check if the aberration distribution is Poissonian and, in case it is not, calculate the dose received by the exposed part of the body

- Estimate the minimum number of cells necessary to detect a given dose of radiation

- Calculate the dose in the case of fractionated or protracted exposure to radiation

-**Estimate the odds ratio of zero dose versus a suspected dose**

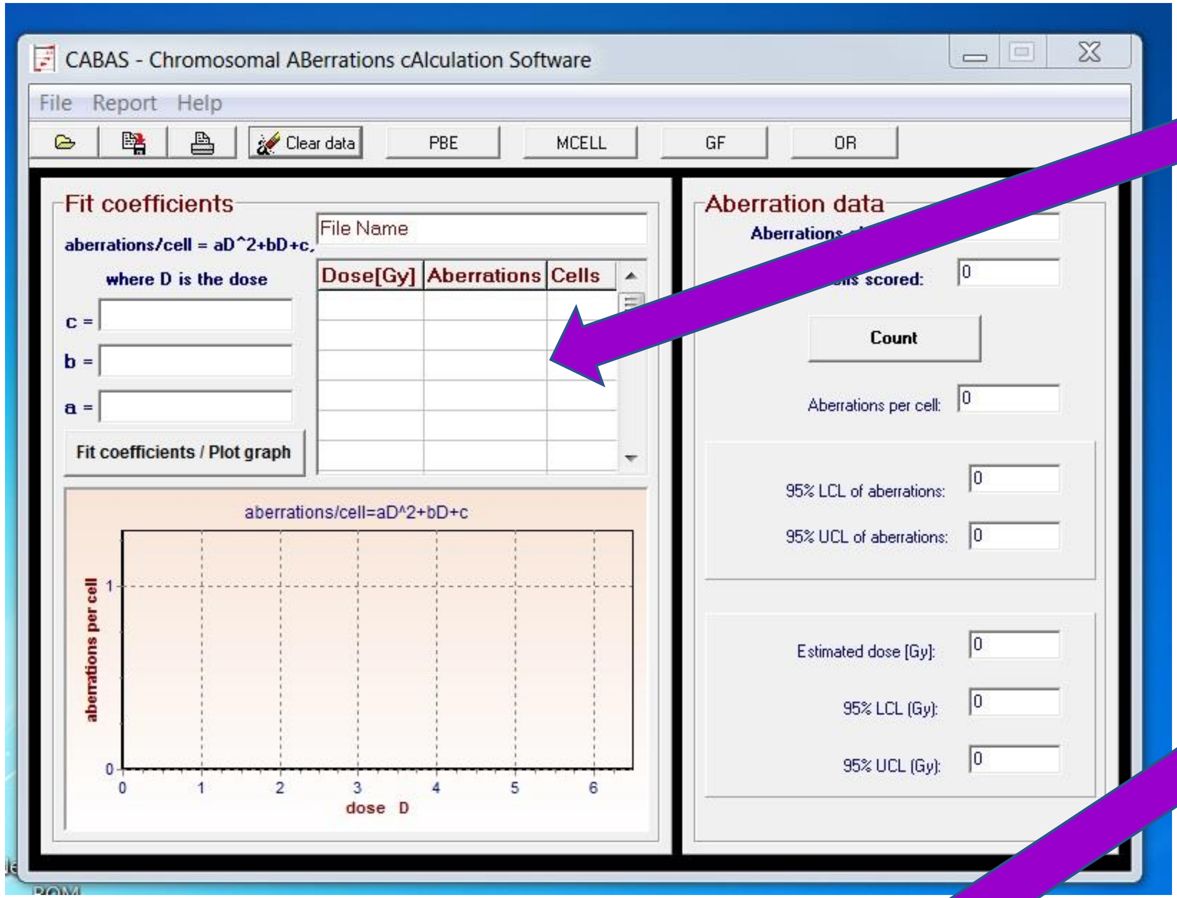
IMPORTANT NOTE:

All calculations in CABAS are based on the Poisson statistics.

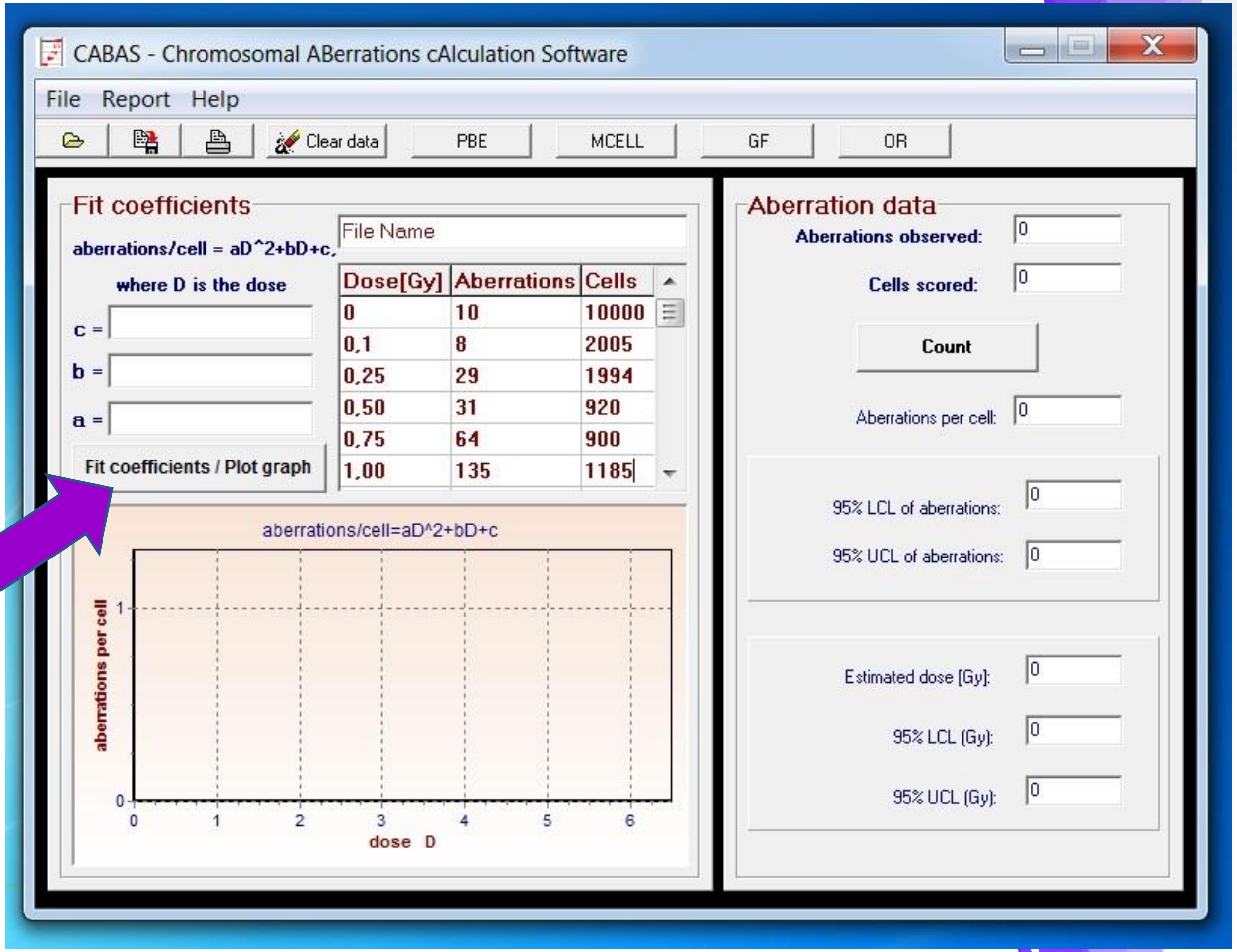
CABAS is intended for fitting dose response curves obtained with low LET radiation, where the distribution of ChAbs <u>should be</u> Poissonian.

CABAS doesn't accept the number of aberrations >300 in the sample for the calculation of the dose.

Example of the calibration curve fitting by CABAS_v.2.0



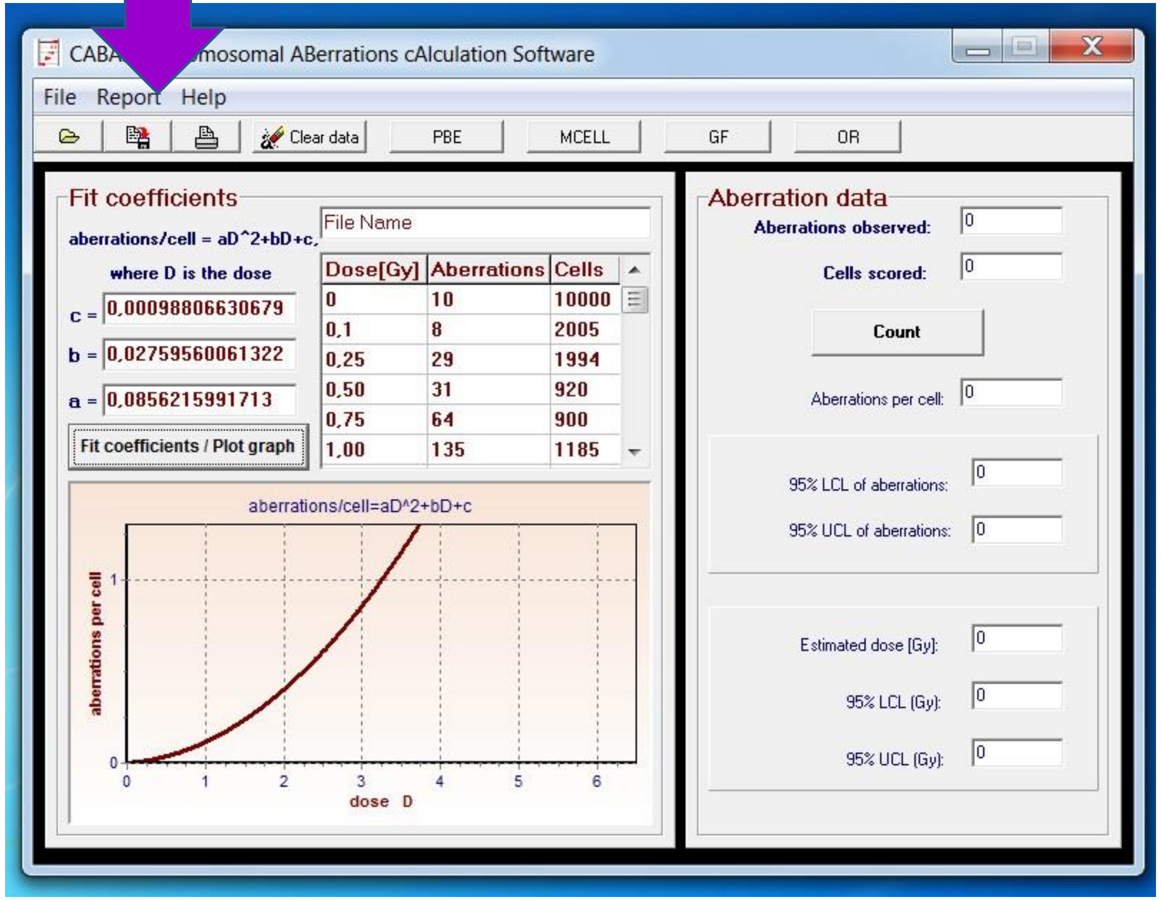
1. Input data into these columns

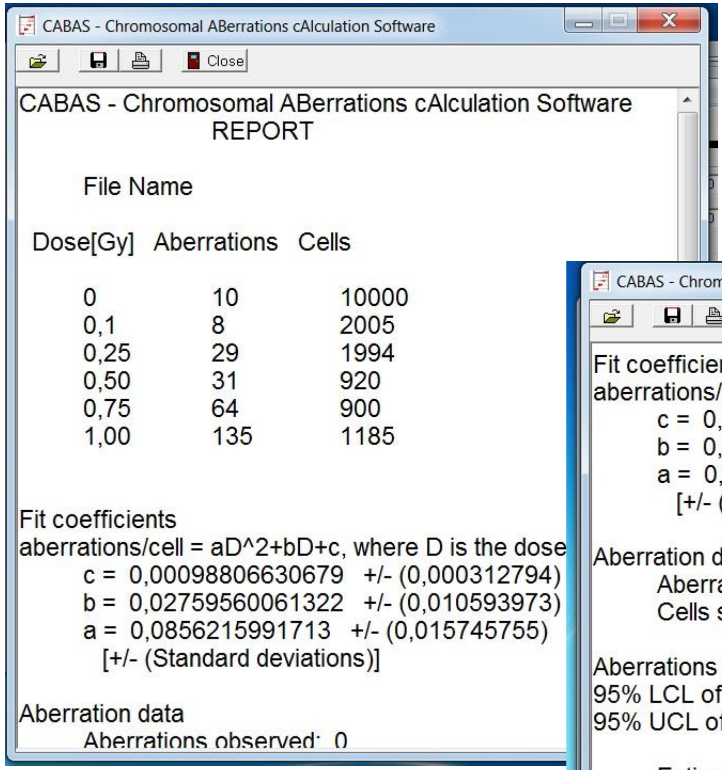


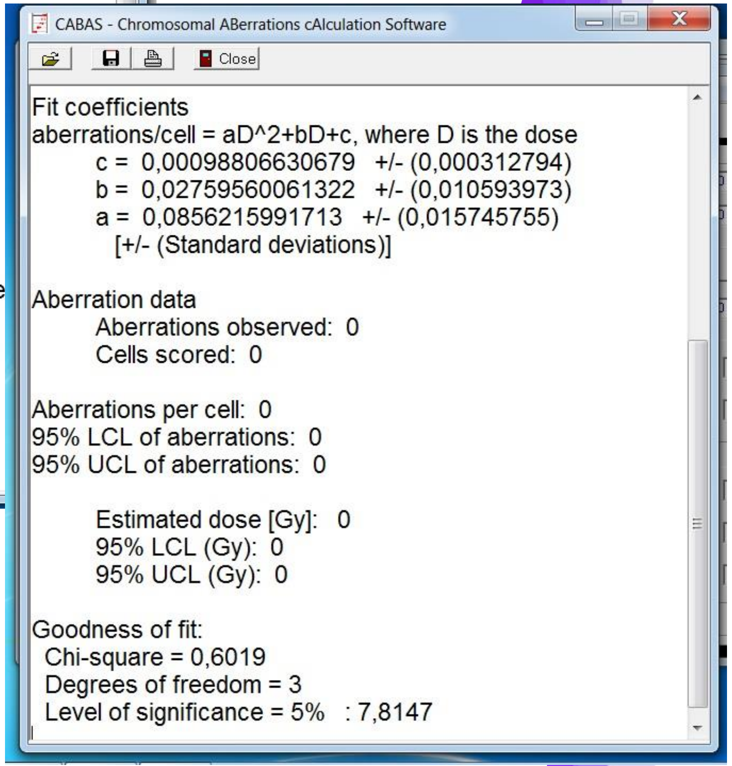
2. Press this button

Example of the calibration curve fitting by CABAS_v.2.0

Press "Report" to see coefficients with errors



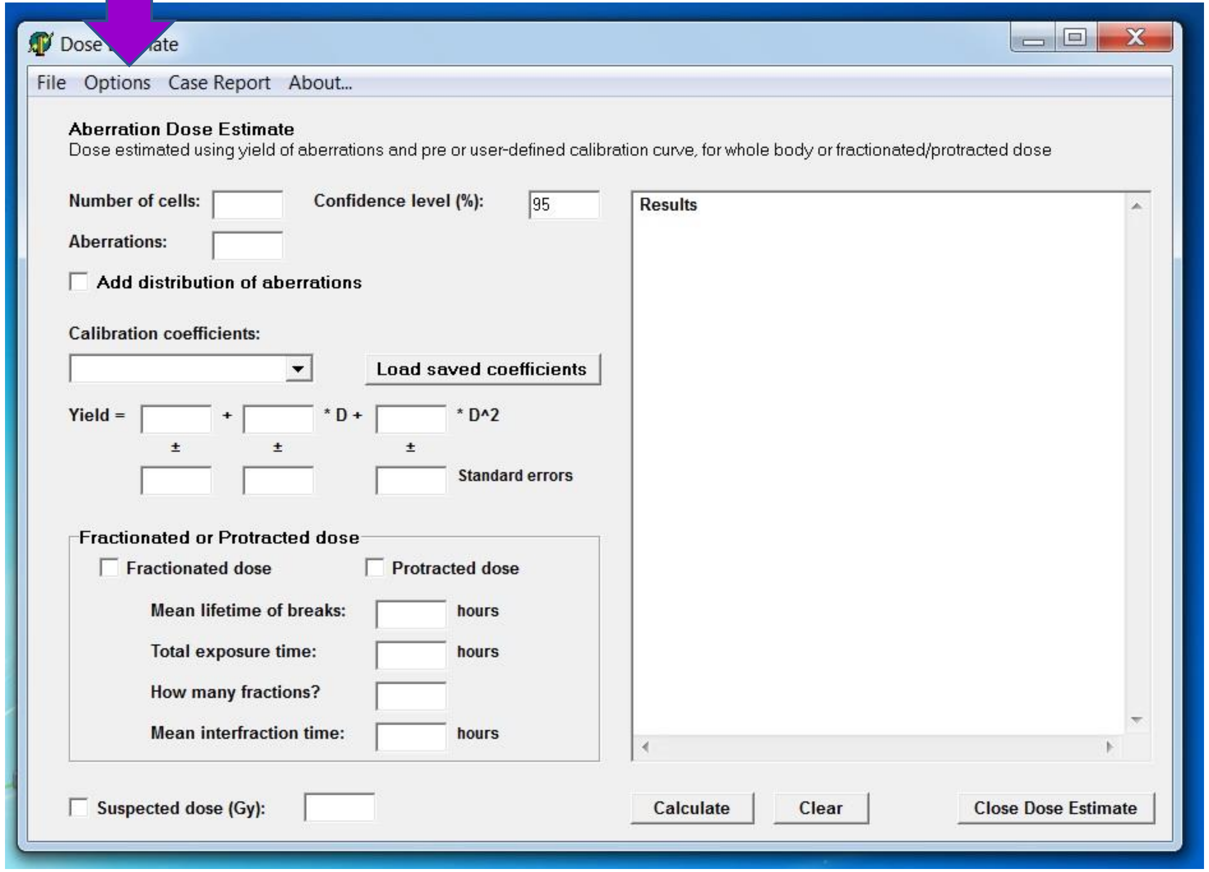




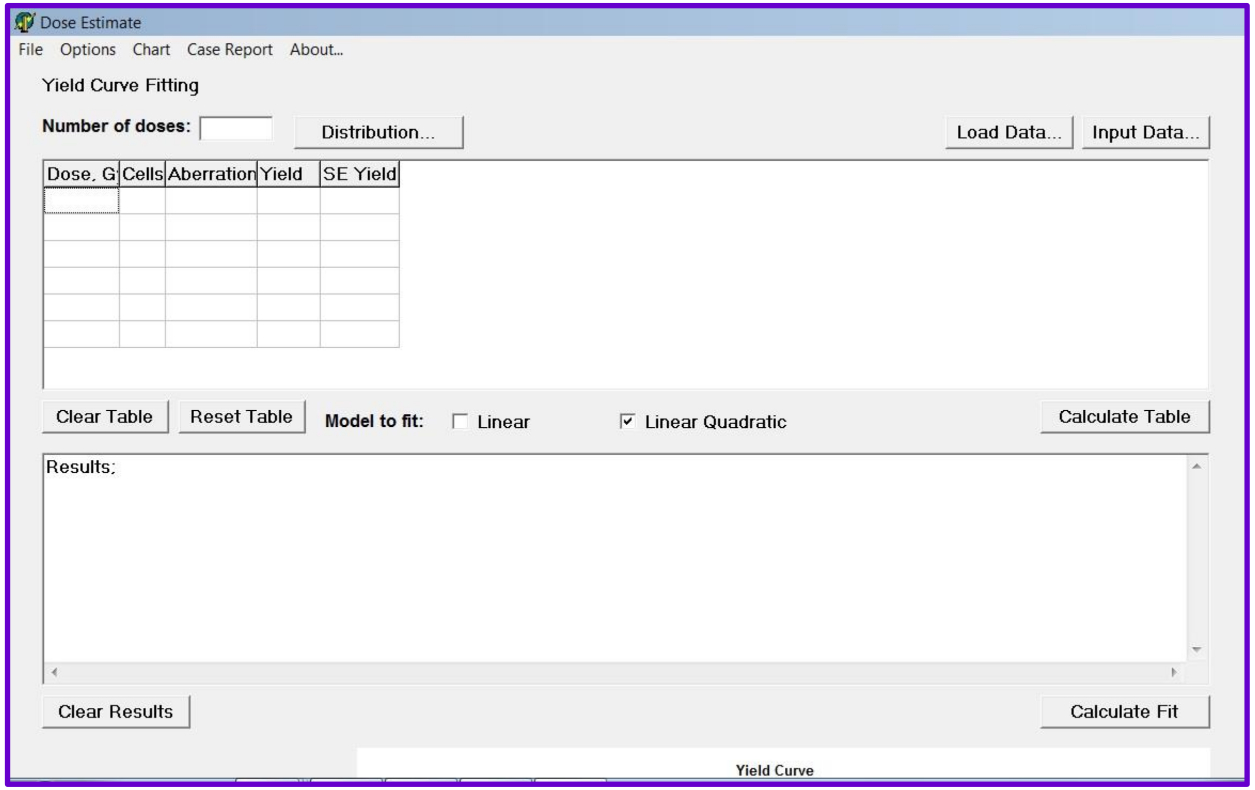
$$Y = 0{,}000988(\pm\ 0{,}000313) + 0{,}027596(\pm\ 0{,}010594)\times D + 0{,}085622(\pm\ 0{,}015746)\times D^2$$

DoseEstimate_v.5.1

Press "Options" and select "Yield curve fitting"



This screen will appear

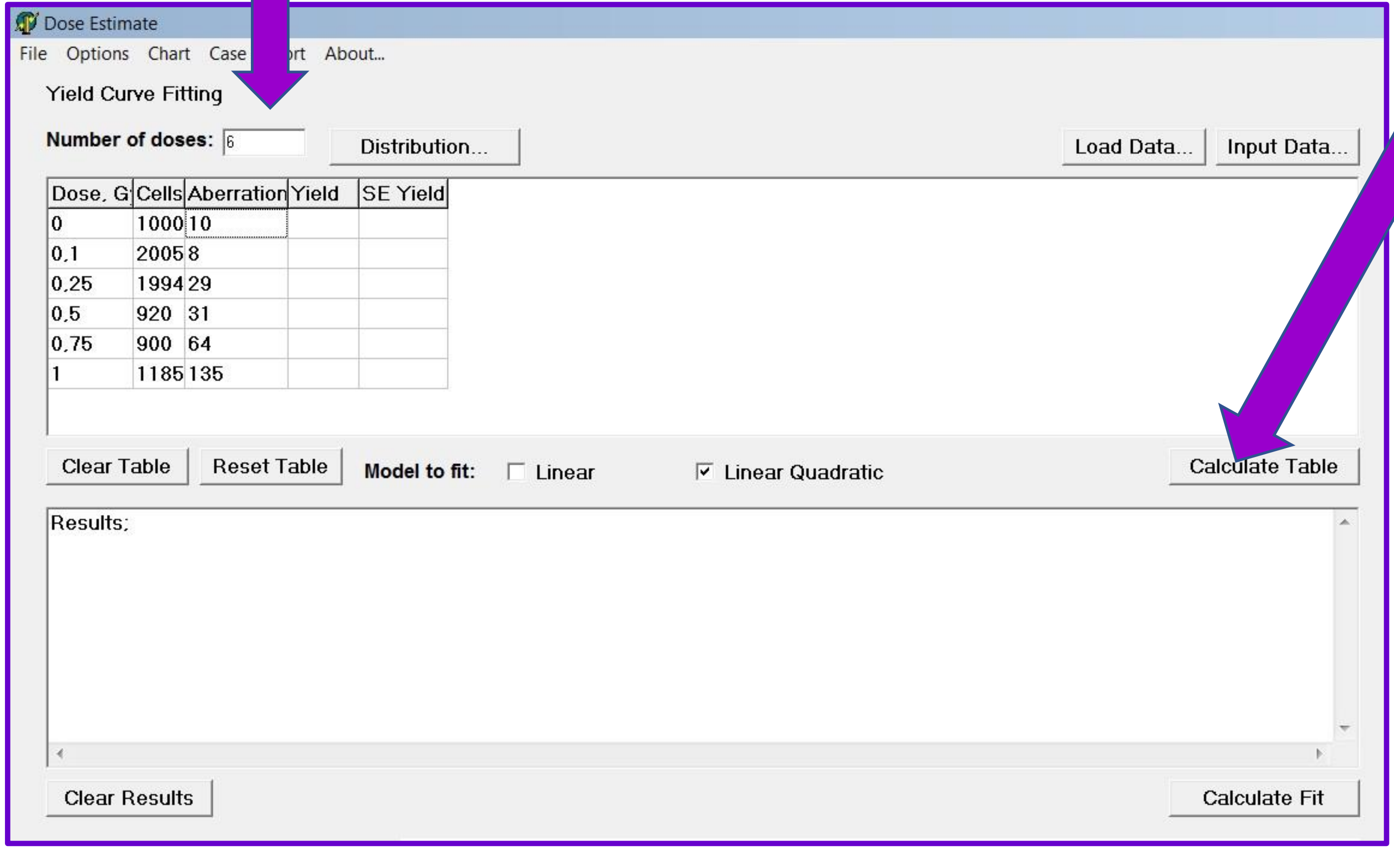


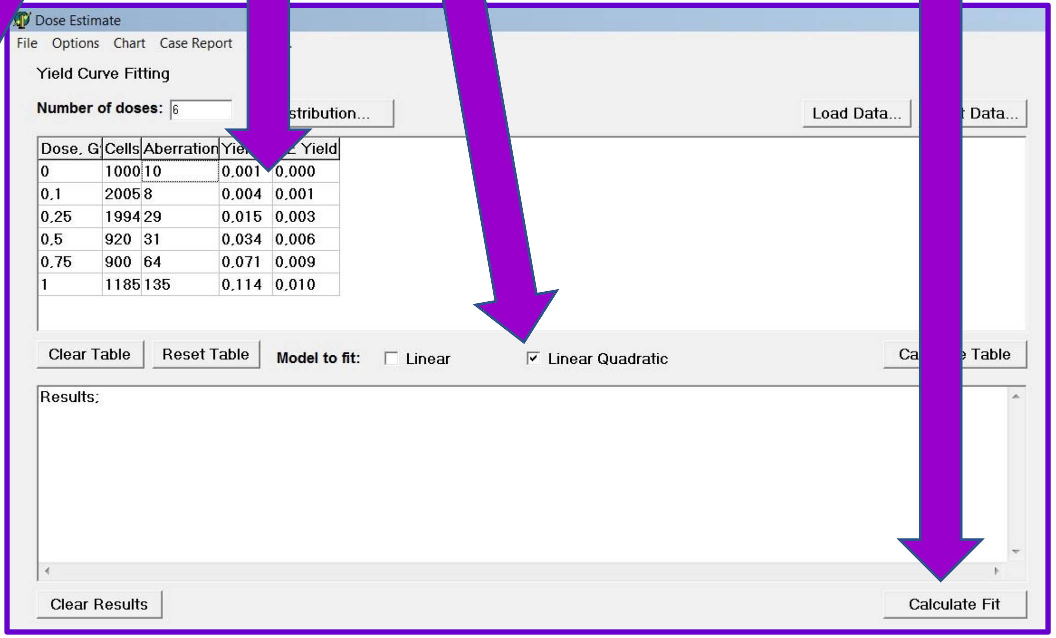
DoseEstimate_v.5.1

1. Input the number of dose points, including control. Then input data into the table: doses, cells and aberrations.

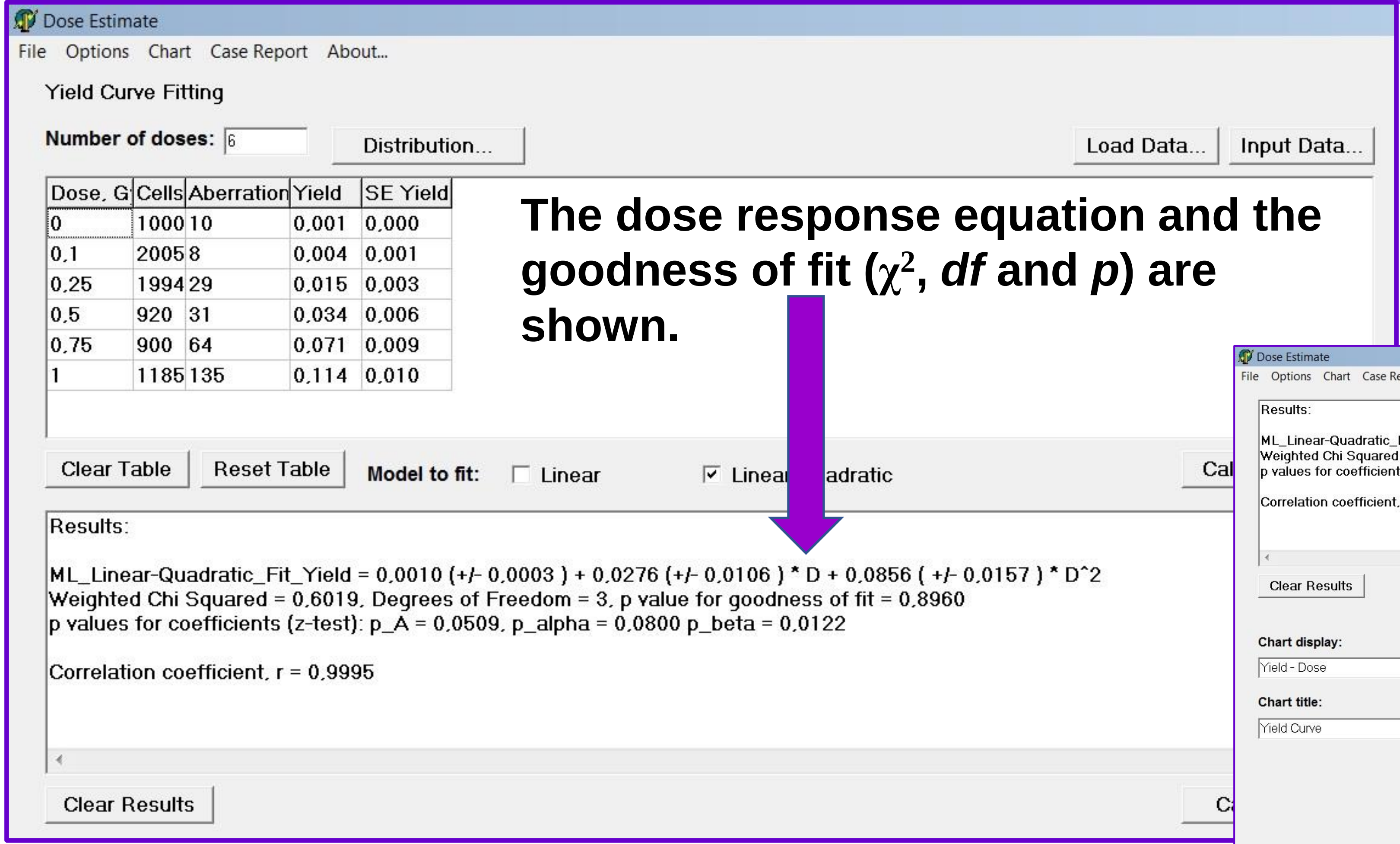
2. Press "Calculate Table", and the yield and SE will appear.

3. Select Linear Quadratic. Press "Calculate Fit".



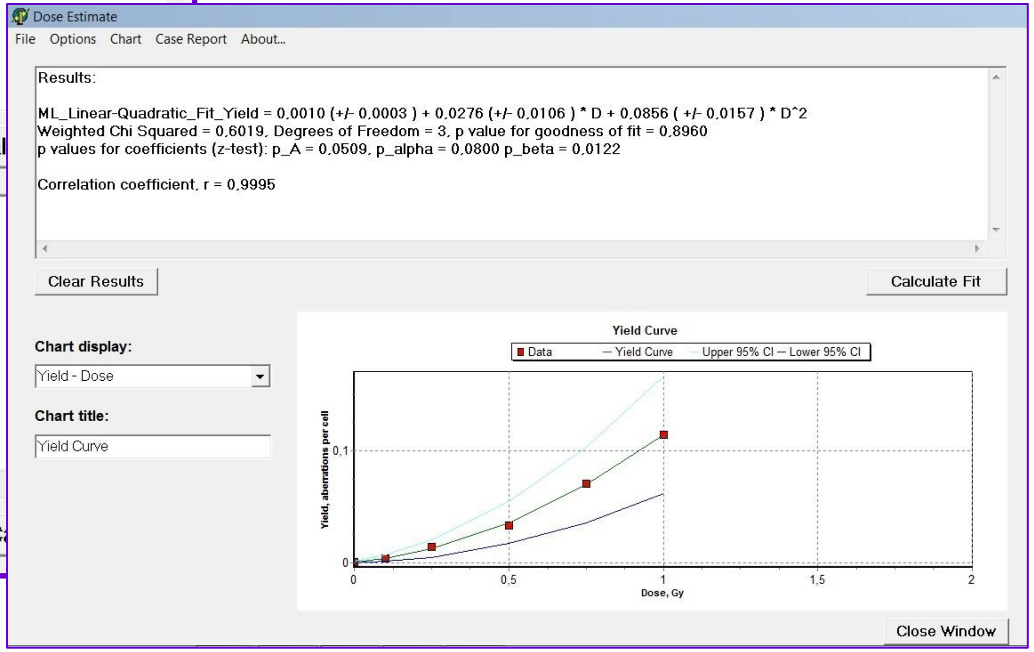


DoseEstimate_v.5.1



The dose response equation and the goodness of fit (χ^2, *df* and *p*) are shown.

Scroll down to see the graphic curve



Y = 0,0010 (± 0,0003)+0,0276(± 0,0106)×D+0,0856 (± 0,0157)×D^2

The assessment of the goodness-of-fit of the dose response

The *p* value of the χ^2 –test (χ^2 =0,6019; *df* = 3; *p*=0,8960) indicates that the fitted data points are not statistically different from the observed ones <u>confirming a good fit.</u>

$$Y = 0{,}0010\ (\pm\ 0{,}0003) + 0{,}0276(\pm\ 0{,}0106)\times D + 0{,}0856\ (\pm\ 0{,}0157)\times D^2$$

The significance of the linear and quadratic coefficients can be evaluated by the *F-test,* the ratio between each coefficient and its *SE*.

F =Mean / Error: C = 3,333 α = 2,604 β = 5,452
p = 0,1746 p = 0,2263 p = 0,0986

For each coefficient the *F* value must be higher than 9.275 (the cut off value for *F.05 [3, 3],* where *[3,3]* are the number of *df*).

Alternatively, the significance of the coefficients (their difference from zero) can be checked by the *t*-test, again using the ratio between each coefficient and its *SE*.

t =Mean / Error: C = 3,333 α = 2,604 β = 5,452
p < 0,05 p > 0,05 p < 0,05

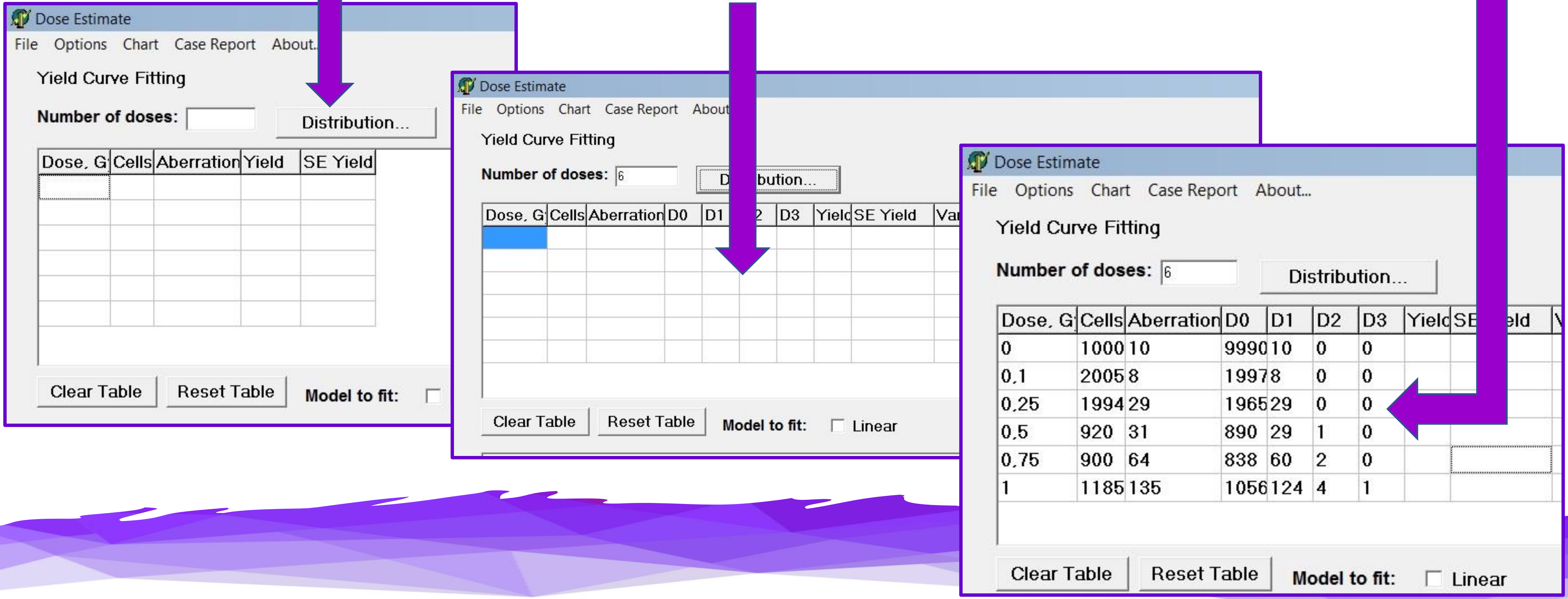
For each coefficient the *t* value must be higher than 3,18, or 5,84, or 12,92 (the cut off values for *t.05, or t.0.1, or t.001,* respectively, for *df* = 3).

The accuracy of the coefficients can be additionally estimated as the ratio of the error to the mean value.

Error/Mean: C = 30% α = 38% β = 18%

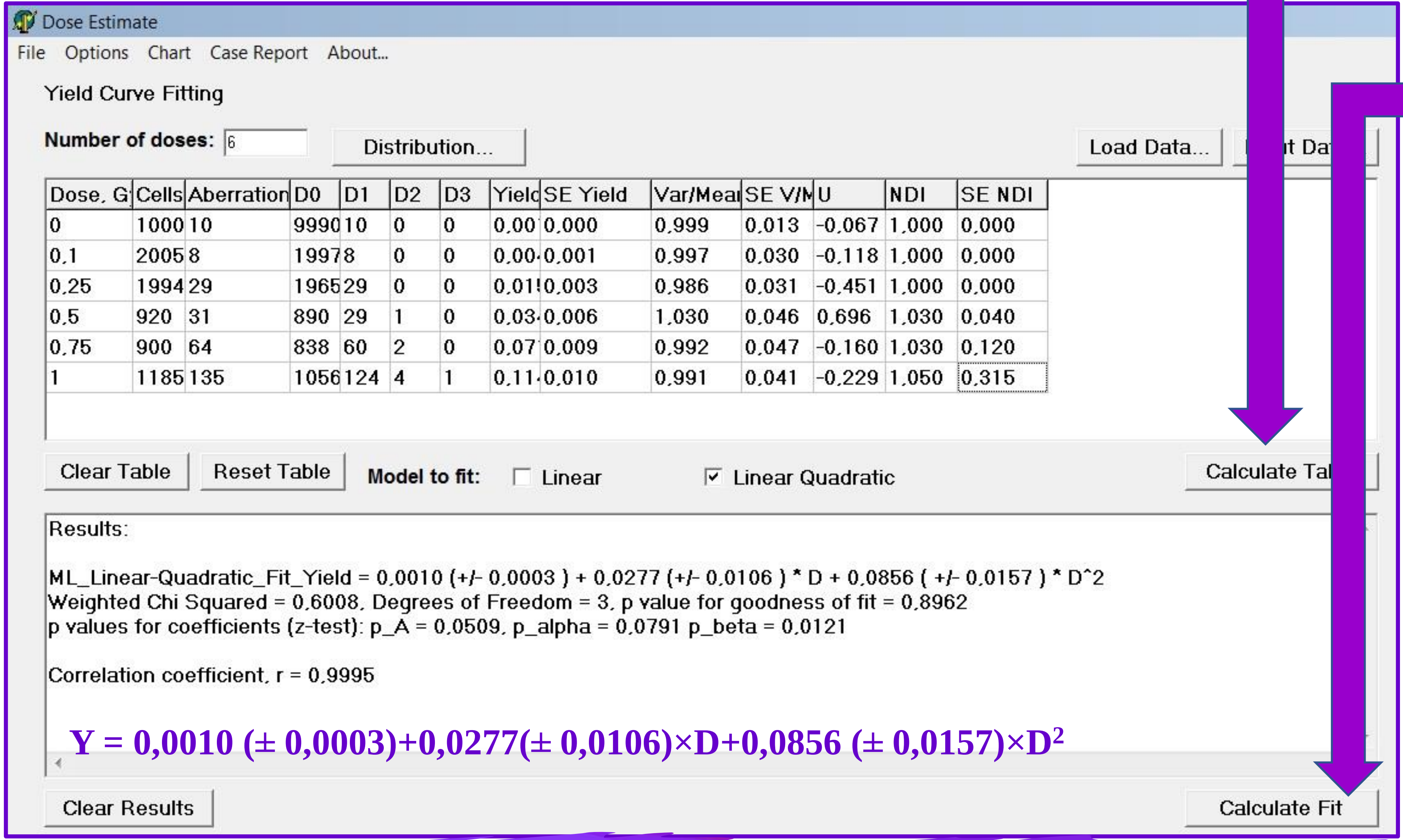
DoseEstimate_v.5.1 – Add aberration per cell distribution

Click on “Distribution”. Input the maximum number of aberrations observed in one cell in your dose response experiment. Then input data into the table: doses, total cells, total aberrations and cells with certain number of aberrations: 0, 1, 2, …, etc.



DoseEstimate_v.5.1 – with aberration per cell distribution

Press “Calculate Table”, and the yield, SE, dispersion index and u-test value will appear.



Dose, G	Cells	Aberration	D0	D1	D2	D3	Yield	SE Yield	Var/Mea	SE V/M	U	NDI	SE NDI
0	1000	10	990	10	0	0	0,00	0,000	0,999	0,013	-0,067	1,000	0,000
0,1	2005	8	1997	8	0	0	0,00	0,001	0,997	0,030	-0,118	1,000	0,000
0,25	1994	29	1965	29	0	0	0,01	0,003	0,986	0,031	-0,451	1,000	0,000
0,5	920	31	890	29	1	0	0,03	0,006	1,030	0,046	0,696	1,030	0,040
0,75	900	64	838	60	2	0	0,07	0,009	0,992	0,047	-0,160	1,030	0,120
1	1185	135	1056	124	4	1	0,11	0,010	0,991	0,041	-0,229	1,050	0,315

$Y = 0{,}0010\ (\pm\ 0{,}0003) + 0{,}0277(\pm\ 0{,}0106) \times D + 0{,}0856\ (\pm\ 0{,}0157) \times D^2$

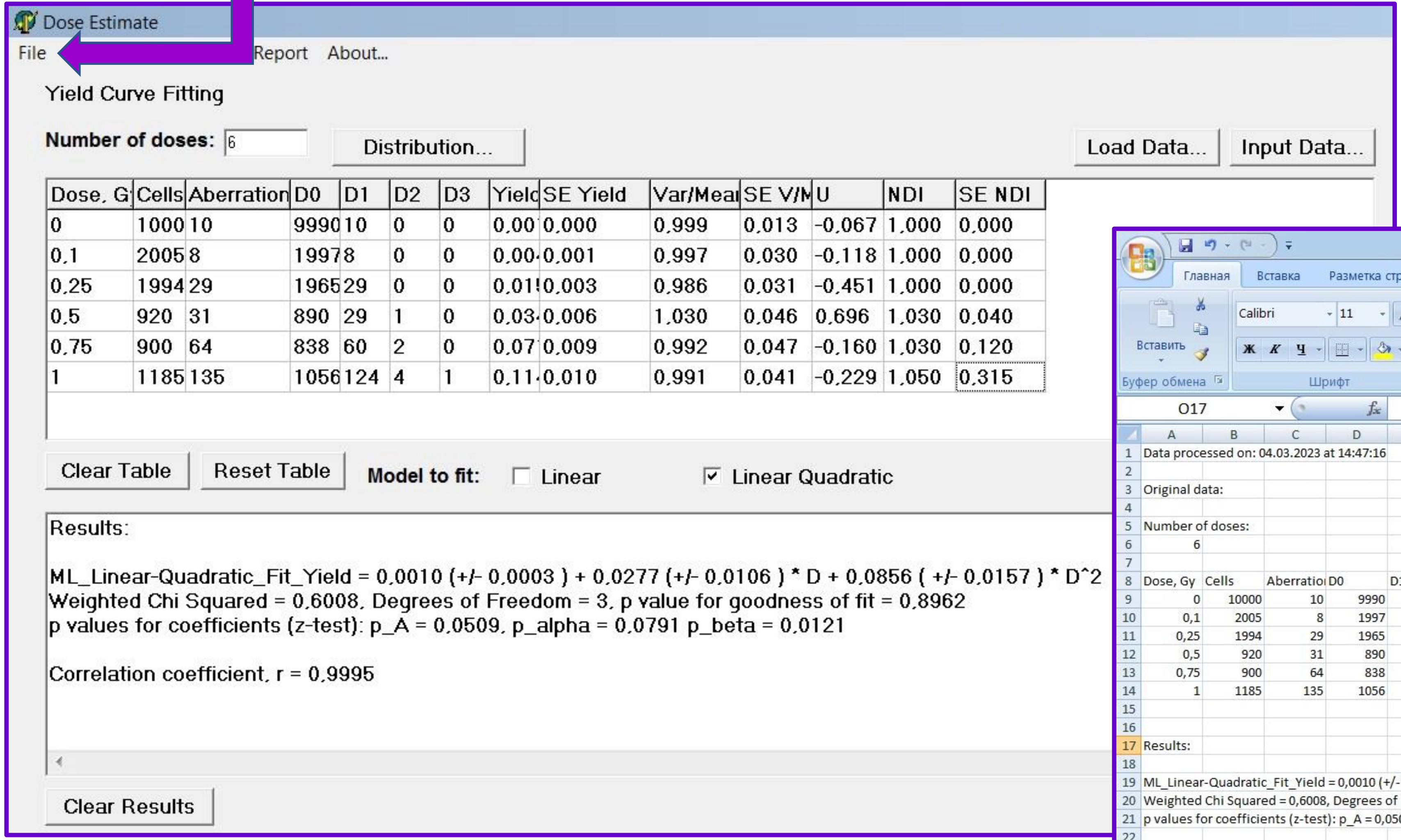
Press “Calculate Fit”. The dose response equation and the goodness of fit (χ^2, *df* and *p*) will be shown.

Aberration per cell distribution was close to the Poisson statistics ($\sigma^2/Y \approx 1$; $u<|1{,}96|$). The dose response equation and the goodness of fit (χ^2, *df* and *p*) remained the same.

DoseEstimate_v.5.1. The report on the curve fitting

Press "File", select "Save results", type file name.xls and save.

The resultant xls file contains tabulated data

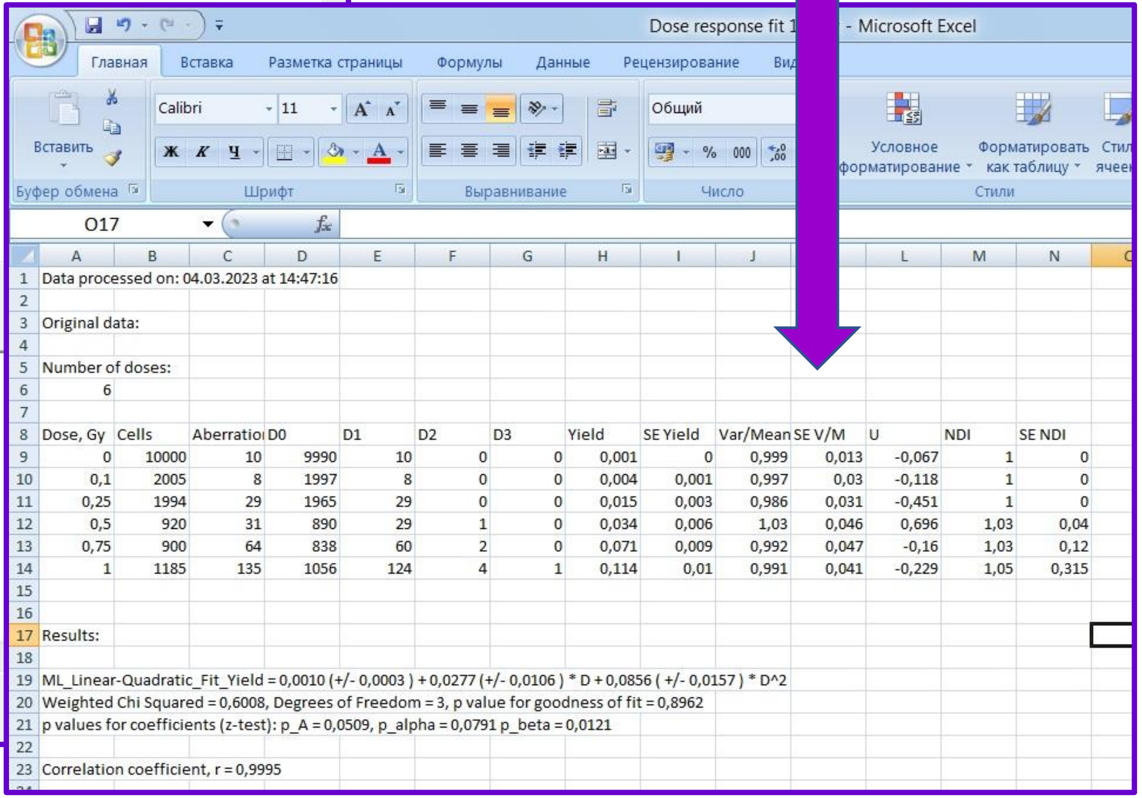


Dose, G	Cells	Aberration	D0	D1	D2	D3	Yield	SE Yield	Var/Mea	SE V/M	U	NDI	SE NDI
0	1000	10	9990	10	0	0	0,00	0,000	0,999	0,013	-0,067	1,000	0,000
0,1	2005	8	1997	8	0	0	0,00	0,001	0,997	0,030	-0,118	1,000	0,000
0,25	1994	29	1965	29	0	0	0,01	0,003	0,986	0,031	-0,451	1,000	0,000
0,5	920	31	890	29	1	0	0,03	0,006	1,030	0,046	0,696	1,030	0,040
0,75	900	64	838	60	2	0	0,07	0,009	0,992	0,047	-0,160	1,030	0,120
1	1185	135	1056	124	4	1	0,11	0,010	0,991	0,041	-0,229	1,050	0,315

Results:

ML_Linear-Quadratic_Fit_Yield = 0,0010 (+/- 0,0003) + 0,0277 (+/- 0,0106) * D + 0,0856 (+/- 0,0157) * D^2
Weighted Chi Squared = 0,6008, Degrees of Freedom = 3, p value for goodness of fit = 0,8962
p values for coefficients (z-test): p_A = 0,0509, p_alpha = 0,0791 p_beta = 0,0121

Correlation coefficient, r = 0,9995



1 Data processed on: 04.03.2023 at 14:47:16

3 Original data:

5 Number of doses:

6 6

	Dose, Gy	Cells	Aberratioi	D0	D1	D2	D3	Yield	SE Yield	Var/Mean	SE V/M	U	NDI	SE NDI
9	0	10000	10	9990	10	0	0	0,001	0	0,999	0,013	-0,067	1	0
10	0,1	2005	8	1997	8	0	0	0,004	0,001	0,997	0,03	-0,118	1	0
11	0,25	1994	29	1965	29	0	0	0,015	0,003	0,986	0,031	-0,451	1	0
12	0,5	920	31	890	29	1	0	0,034	0,006	1,03	0,046	0,696	1,03	0,04
13	0,75	900	64	838	60	2	0	0,071	0,009	0,992	0,047	-0,16	1,03	0,12
14	1	1185	135	1056	124	4	1	0,114	0,01	0,991	0,041	-0,229	1,05	0,315

17 Results:

19 ML_Linear-Quadratic_Fit_Yield = 0,0010 (+/- 0,0003) + 0,0277 (+/- 0,0106) * D + 0,0856 (+/- 0,0157) * D^2

20 Weighted Chi Squared = 0,6008, Degrees of Freedom = 3, p value for goodness of fit = 0,8962

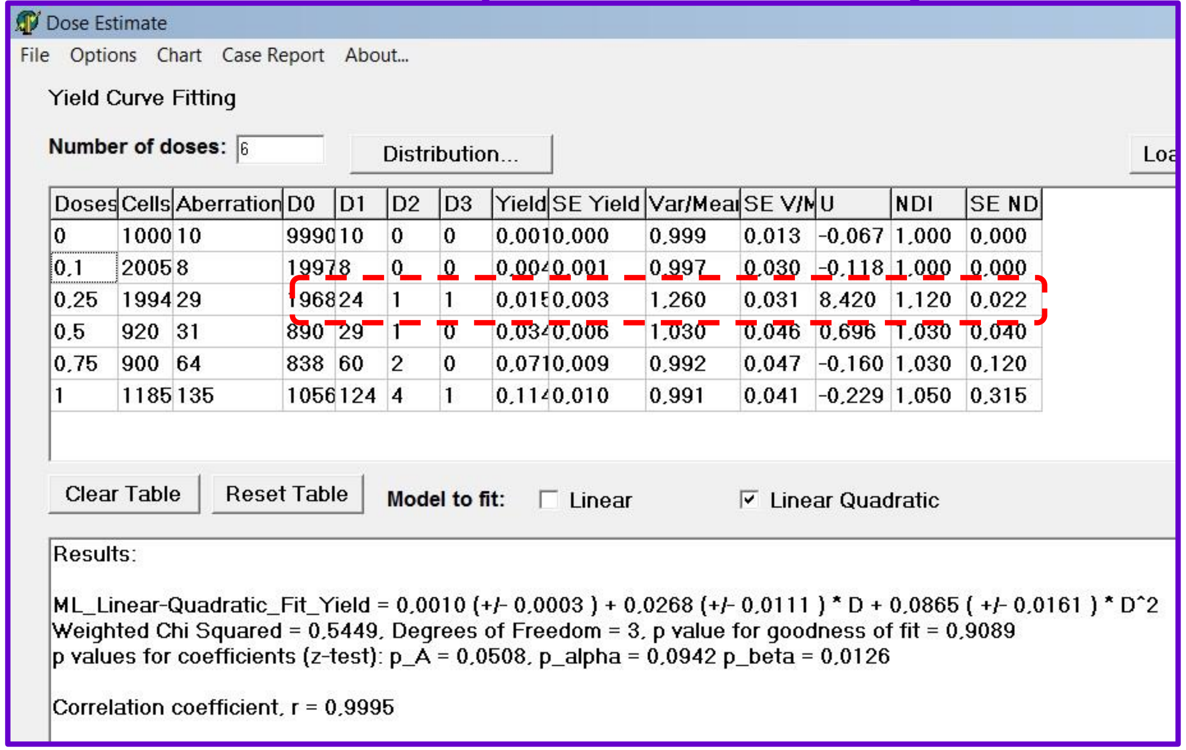
21 p values for coefficients (z-test): p_A = 0,0509, p_alpha = 0,0791 p_beta = 0,0121

23 Correlation coefficient, r = 0,9995

The effect of the overdispersion of AbCD on the dose response

If the AbCD is esentially overdispersed in compare to the Poisson statistics ($\sigma^2/Y>1$; $u>1{,}96$) on one or two experimental points, the small changes of the mean values of the dose response coefficients can take place, and the increase of the *SE* of coefficients is not very large.

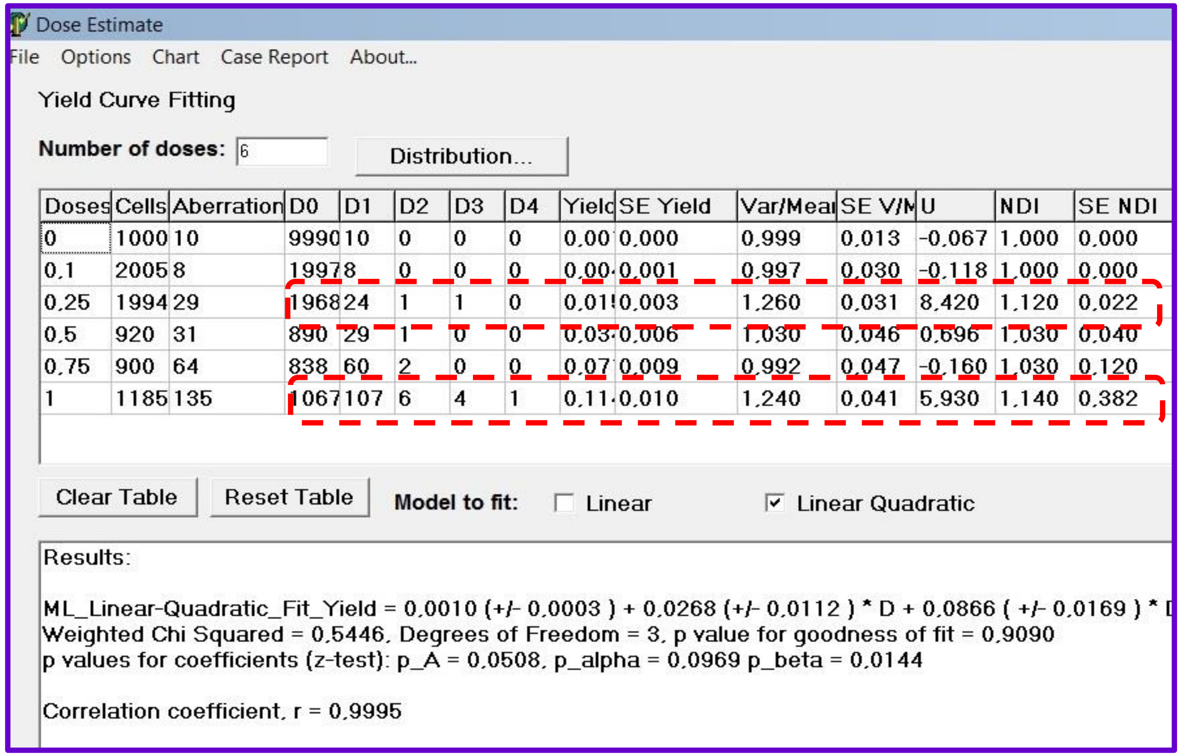
Overdispersion at 0,25 Gy



Doses	Cells	Aberration	D0	D1	D2	D3	Yield	SE Yield	Var/Mea	SE V/M	U	NDI	SE ND
0	1000	10	990	10	0	0	0,001	0,000	0,999	0,013	-0,067	1,000	0,000
0,1	2005	8	1997	8	0	0	0,004	0,001	0,997	0,030	-0,118	1,000	0,000
0,25	1994	29	1968	24	1	1	0,015	0,003	1,260	0,031	8,420	1,120	0,022
0,5	920	31	890	29	1	0	0,034	0,006	1,030	0,046	0,696	1,030	0,040
0,75	900	64	838	60	2	0	0,071	0,009	0,992	0,047	-0,160	1,030	0,120
1	1185	135	1056	124	4	1	0,114	0,010	0,991	0,041	-0,229	1,050	0,315

α=0,0268(± 0,0111) β=0,0865 (± 0,0161)

Overdispersion at 0,25 and 1,00 Gy



Doses	Cells	Aberration	D0	D1	D2	D3	D4	Yield	SE Yield	Var/Mea	SE V/M	U	NDI	SE NDI
0	1000	10	990	10	0	0	0	0,00	0,000	0,999	0,013	-0,067	1,000	0,000
0,1	2005	8	1997	8	0	0	0	0,00	0,001	0,997	0,030	-0,118	1,000	0,000
0,25	1994	29	1968	24	1	1	0	0,01	0,003	1,260	0,031	8,420	1,120	0,022
0,5	920	31	890	29	1	0	0	0,03	0,006	1,030	0,046	0,696	1,030	0,040
0,75	900	64	838	60	2	0	0	0,07	0,009	0,992	0,047	-0,160	1,030	0,120
1	1185	135	1067	107	6	4	1	0,11	0,010	1,240	0,041	5,930	1,140	0,382

α=0,0268(± 0,0112) β=0,0866 (± 0,0169)

The effect of the overdispersion of AbCD on the dose response

Dose Estimate

File Options Chart Case Report About...

Yield Curve Fitting

Number of doses: 6 Distribution... Load

Doses	Cells	Aberration	D0	D1	D2	D3	D4	Yielc	SE Yield	Var/Mea	SE V/M	U	NDI	SE NDI
0	1000	10	9991	8	1	0	0	0,00	0,000	1,200	0,013	14,800	1,110	0,001
0,1	2005	8	1998	6	1	0	0	0,00	0,001	1,250	0,030	8,350	1,140	0,002
0,25	1994	29	1968	24	1	1	0	0,01	0,003	1,260	0,031	8,420	1,120	0,022
0,5	920	31	892	26	1	1	0	0,03	0,006	1,230	0,046	4,920	1,110	0,052
0,75	900	64	843	52	3	2	0	0,07	0,009	1,210	0,047	4,520	1,120	0,160
1	1185	135	1067	107	6	4	1	0,11	0,010	1,240	0,041	5,930	1,140	0,382

Clear Table Reset Table **Model to fit:** ☐ Linear ☑ Linear Quadratic

Results:

ML_Linear-Quadratic_Fit_Yield = 0,0010 (+/- 0,0003) + 0,0275 (+/- 0,0118) * D + 0,0857 (+/- 0,0176) * D^2
Weighted Chi Squared = 0,4828, Degrees of Freedom = 3, p value for goodness of fit = 0,9227
p values for coefficients (z-test): p_A = 0,0633, p_alpha = 0,1025 p_beta = 0,0165

Correlation coefficient, r = 0,9995

$$Y = 0{,}0010\ (\pm\ 0{,}0003) + 0{,}0275(\pm\ 0{,}0118) \times D + 0{,}0857\ (\pm\ 0{,}0176) \times D^2$$

Clear Results

Even if the AbCD is esentially overdispersed ($\sigma^2/Y>1$; $u>1{,}96$) on all experimental points, the mean values of the dose response coefficients and the goodness of fit remained nearly the same, as they were in the scenario of the strict Poisson AbCD. However, a remarkable increase of the *SE* of coefficients is observed.

If the dispersion index (σ^2/Y) shows a clear dose-dependent trend, then follow the guidance of the IAEA Manual (2011).

Inverse interdependence of the LQ coefficients: the “see-saw” effect

Adding the next point – 2 Gy – leads to the changes of the LQ coefficients

Dose Estimate

File Options Chart Case Report About...

Yield Curve Fitting

Number of doses: 7 Distribution... Loa

Dose, G	Cells	Aberration	D0	D1	D2	D3	D4	Yielc	SE Yield	Var/Meai	SE V/M	U	NDI	SE NDI
0	1000	10	9990	10	0	0	0	0,00	0,000	0,999	0,013	-0,067	1,000	0,000
0,1	2005	8	1997	8	0	0	0	0,00	0,001	0,997	0,030	-0,118	1,000	0,000
0,25	1994	29	1965	29	0	0	0	0,01	0,003	0,986	0,031	-0,451	1,000	0,000
0,5	920	31	890	29	1	0	0	0,03	0,006	1,030	0,046	0,696	1,030	0,040
0,75	900	64	838	60	2	0	0	0,07	0,009	0,992	0,047	-0,160	1,030	0,120
1	1185	135	1056	124	4	1	0	0,11	0,010	0,991	0,041	-0,229	1,050	0,315
1,99	2095	675	1525	477	82	10	1	0,32	0,012	1,030	0,031	0,904	1,180	1,930

Clear Table Reset Table **Model to fit:** ☐ Linear ☑ Linear Quadratic

Results:

ML_Linear-Quadratic_Fit_Yield = 0,0009 (+/- 0,0003) + 0,0402 (+/- 0,0077) * D + 0,0623 (+/- 0,0056) * D^2
Weighted Chi Squared = 2,9680, Degrees of Freedom = 4, p value for goodness of fit = 0,7816
p values for coefficients (z-test): p_A = 0,0360, p_alpha = 0,0065 p_beta = 0,0004

Correlation coefficient, r = 0,9990

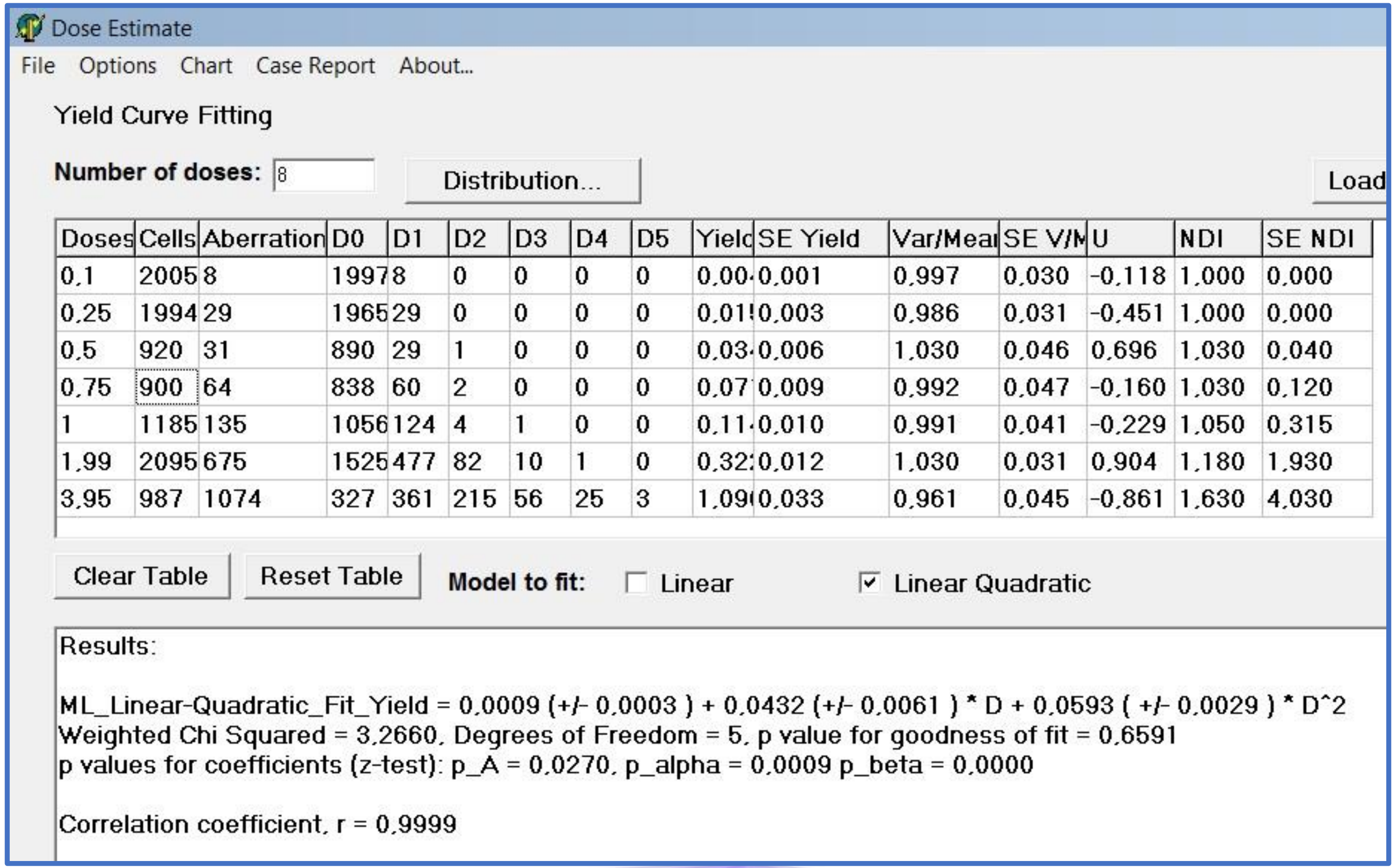
Up to 1 Gy:
α=0,0277(± 0,0106) β=0,0856 (± 0,0157)

Up to 2 Gy:
α=0,0402(± 0,0077) β=0,0623 (± 0,0056)

Coefficient α increases, coefficient β decreases

Inverse interdependence of the LQ coefficients: the “see-saw” effect

Adding the next point – 4 Gy – leads to further changes of the LQ coefficients



Doses	Cells	Aberration	D0	D1	D2	D3	D4	D5	Yield	SE Yield	Var/Mea	SE V/M	U	NDI	SE NDI
0,1	2005	8	1997	8	0	0	0	0	0,00	0,001	0,997	0,030	-0,118	1,000	0,000
0,25	1994	29	1965	29	0	0	0	0	0,01	0,003	0,986	0,031	-0,451	1,000	0,000
0,5	920	31	890	29	1	0	0	0	0,03	0,006	1,030	0,046	0,696	1,030	0,040
0,75	900	64	838	60	2	0	0	0	0,07	0,009	0,992	0,047	-0,160	1,030	0,120
1	1185	135	1056	124	4	1	0	0	0,11	0,010	0,991	0,041	-0,229	1,050	0,315
1,99	2095	675	1525	477	82	10	1	0	0,32	0,012	1,030	0,031	0,904	1,180	1,930
3,95	987	1074	327	361	215	56	25	3	1,09	0,033	0,961	0,045	-0,861	1,630	4,030

Up to 1 Gy:
α=0,0277(± 0,0106) β=0,0856 (± 0,0157)

Up to 2 Gy:
α=0,0402(± 0,0077) β=0,0623 (± 0,0056)

Up to 4 Gy:
α=0,0432(± 0,0061) β=0,0593 (± 0,0029)

Coefficient α increases, coefficient β decreases

Inverse interdependence of the LQ coefficients: the “see-saw” effect

Adding the next point – 6 Gy – leads to further changes of the LQ coefficients

Dose Estimate

File Options Chart Case Report About...

Yield Curve Fitting

Number of doses: 9 Distribution... Load Data...

Doses	Cells	Aberration	D0	D1	D2	D3	D4	D5	D6	D7	Yielc	SE Yield	Var/Mea	SE V/M	U	NDI	SE NDI
0,25	1994	29	1965	29	0	0	0	0	0	0	0,01	0,003	0,986	0,031	-0,451	1,000	0,000
0,5	920	31	890	29	1	0	0	0	0	0	0,03	0,006	1,030	0,046	0,696	1,030	0,040
0,75	900	64	838	60	2	0	0	0	0	0	0,07	0,009	0,992	0,047	-0,160	1,030	0,120
1	1185	135	1056	124	4	1	0	0	0	0	0,11	0,010	0,991	0,041	-0,229	1,050	0,315
1,99	2095	675	1525	477	82	10	1	0	0	0	0,32	0,012	1,030	0,031	0,904	1,180	1,930
3,95	987	1074	327	361	215	56	25	3	0	0	1,09	0,033	0,961	0,045	-0,861	1,630	4,030
5,95	352	737	39	86	104	72	35	10	5	1	2,09	0,077	0,879	0,075	-1,610	2,350	4,880

Clear Table Reset Table **Model to fit:** ☐ Linear ☑ Linear Quadratic Ca

Results:

ML_Linear-Quadratic_Fit_Yield = 0,0009 (+/- 0,0004) + 0,0502 (+/- 0,0070) * D + 0,0544 (+/- 0,0026) * D^2
Weighted Chi Squared = 9,2290, Degrees of Freedom = 6, p value for goodness of fit = 0,7204
p values for coefficients (z-test): p_A = 0,0492, p_alpha = 0,0004 p_beta = 0,0000

Correlation coefficient, r = 0,9990

Up to 1 Gy:
α=0,0277(± 0,0106) **β=0,0856 (± 0,0157)**

Up to 2 Gy:
α=0,0402(± 0,0077) **β=0,0623 (± 0,0056)**

Up to 4 Gy:
α=0,0432(± 0,0061) **β=0,0593 (± 0,0029)**

Up to 6 Gy:
α=0,0502(± 0,0070) **β=0,0544 (± 0,0026)**

Coefficient α increases, coefficient β decreases

The effect of the number of cells scored and aberrations found at different dose points

Doses	Cells	Aberrations
0	1000	1
0,10	1000	4
0,25	1000	15
0,50	1000	34
0,75	1000	71
1,00	1000	114
1,99	1000	322
3,95	1000	1090
5,95	1000	2090

1000 cells on each point:
α=0,0556 (± 0,0082)
β=0,0515 (± 0,0023)
Goodness of fit:
χ^2 **= 9,765; *df* =6; *p* =0,7116**

Doses	Cells	Aberrations
0	10000	10
0,10	10000	40
0,25	10000	150
0,50	10000	340
0,75	10000	710
1,00	10000	1140
1,99	10000	3220
3,95	10000	10900
5,95	10000	20900

10 000 cells on each point:
α=0,0556 (± 0,0082)
β=0,0515 (± 0,0023)
Goodness of fit:
χ^2 **= 97,650; *df* =6; *p* =0,0000**

Doses	Cells	Aberrations
0	10000	10
0,10	2500	10
0,25	667	10
0,50	294	10
0,75	141	10
1,00	88	10
1,99	31	10
3,95	9	10
5,95	5	10

10 aberrations on each point:
α=0,0339 (± 0,0108)
β=0,0625 (± 0,0131)
Goodness of fit:
χ^2 **= 1,434; *df* =6, *p* =0,9879**

Doses	Cells	Aberrations
0	100000	100
0,10	25000	100
0,25	6667	100
0,50	2941	100
0,75	1408	100
1,00	877	100
1,99	311	100
3,95	92	100
5,95	48	100

100 aberrations on each point:
α=0,0337 (± 0,0050)
β=0,0632 (± 0,0062)
Goodness of fit:
χ^2 **= 13,100; *df* =6, *p* =0,6805**

Shift of the dose range

Zero dose removed

Doses	Cells	Aberrations
0,10	25000	100
0,25	6667	100
0,50	2941	100
0,75	1408	100
1,00	877	100
1,99	311	100
3,95	92	100
5,95	48	100

100 aberrations on each point
C = <u>- 0,0018</u> (± 0,0008)
α=0,0529 (± 0,0070)
β=0,0540 (± 0,0049)
Goodness of fit:
χ^2 =2,735; *df* =5; *p* =0,7408

Low dose points removed

Doses	Cells	Aberrations
0	100000	100
0,75	1408	100
1,00	877	100
1,99	311	100
3,95	92	100
5,95	48	100

100 aberrations on each point
C = 0,0010 (± 0,0001)
α=0,0577 (± 0,0099)
β=0,0518 (± 0,0056)
Goodness of fit:
χ^2 =0,627; *df* =3; *p* =0,8902

High dose points removed

Doses	Cells	Aberrations
0	100000	100
0,10	25000	100
0,25	6667	100
0,50	2941	100
0,75	1408	100
1,00	877	100

100 aberrations on each point
C = 0,0010 (± 0,0001)
α=0,0244 (± 0,0048)
β=0,0910 (± 0,0115)
Goodness of fit:
χ^2 =3,6040; *df* =3; *p* =0,3075

Number of aberrations gradually decreased

Doses	Cells	Aberrations
0	100000	100
0,10	22500	90
0,25	5333	80
0,50	2059	70
0,75	845	60
1,00	439	50

C = 0,0010 (± 0,0001)
α=0,0240 (± 0,0048)
β=0,0924 (± 0,0132)
Goodness of fit:
χ^2 =2,9100; *df* =3; *p* =0,4057

Shift of the dose range

Number of aberrations gradually increased

Doses	Cells	Aberrations
0	10000	10
0,10	5000	20
0,25	2000	30
0,50	1176	40
0,75	704	50
1,00	526	60

C = 0,0010 (± 0,0003)
α=0,0259 (± 0,0090)
β=0,0882 (± 0,0169)
Goodness of fit:
χ^2 =1,0130; *df* =3; *p* =0,7982

Number of aberrations gradually increased & higher dose points consequently removed

to 0,75 Gy

Doses	Cells	Aberrations
0	10000	10
0,10	5000	20
0,25	2000	30
0,50	1176	40
0,75	704	50

C = 0,0010 (± 0,0003)
α=0,0254 (± 0,0100)
β=0,0899 (± 0,0234)
Goodness of fit:
χ^2 =1,0030; *df* =2; *p* =0,6055

to 0,50 Gy

Doses	Cells	Aberrations
0	10000	10
0,10	5000	20
0,25	2000	30
0,50	1176	40

C = 0,0010 (± 0,0003)
α=0,0259(± 0,0117)
β=0,0876 (± 0,0368)
Goodness of fit:
χ^2 =0,9987; *df* =1; *p* =0,3176

to 0,25 Gy

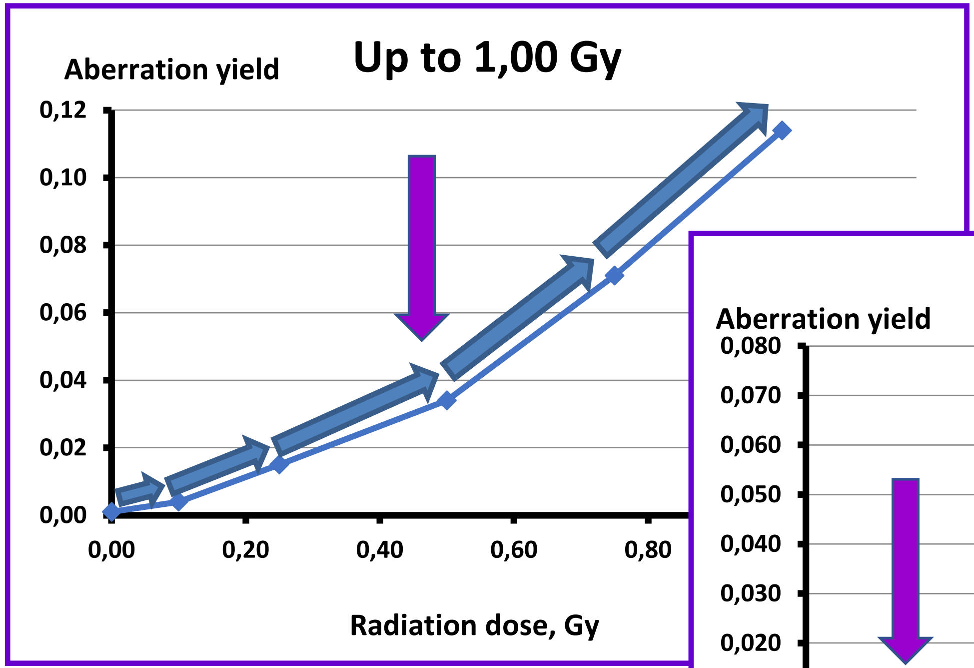
Doses	Cells	Aberrations
0	10000	10
0,10	5000	20
0,25	2000	30

C = 0,0010 (± 0,0003)
α=0,0127(± 0,0172)
β=0,1733 (± 0,0951)
Goodness of fit:
χ^2 =0,0000; *df* =0; *p* =???

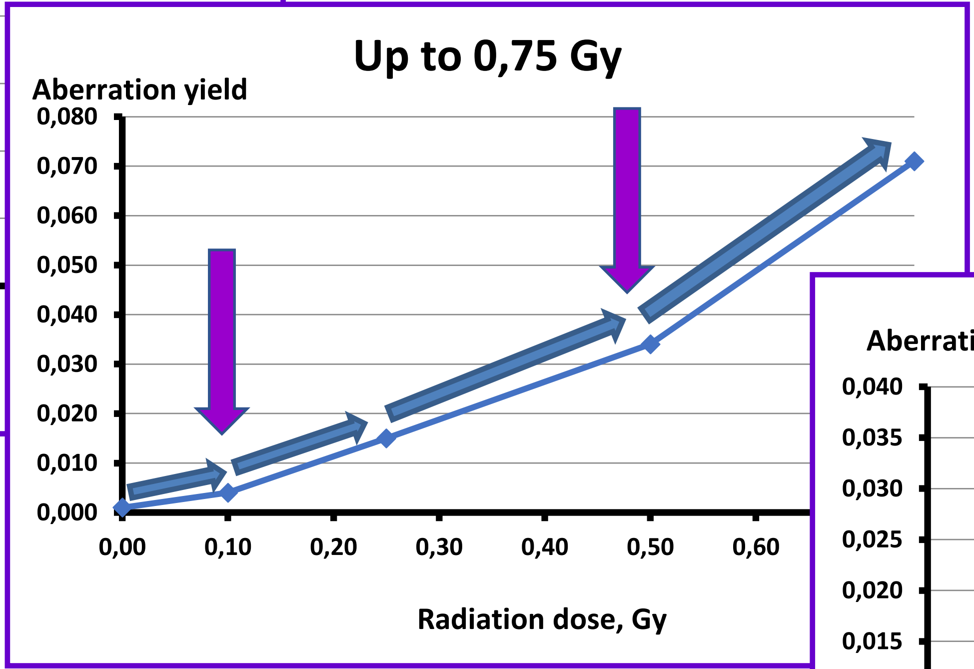
Alternative fit: Linear Model
Y = C + α x D
C = 0,0009 (± 0,0010)
α=0,0442(± 0,0095)
Goodness of fit:
χ^2 =3,279; *df* =1; *p* =0,0702

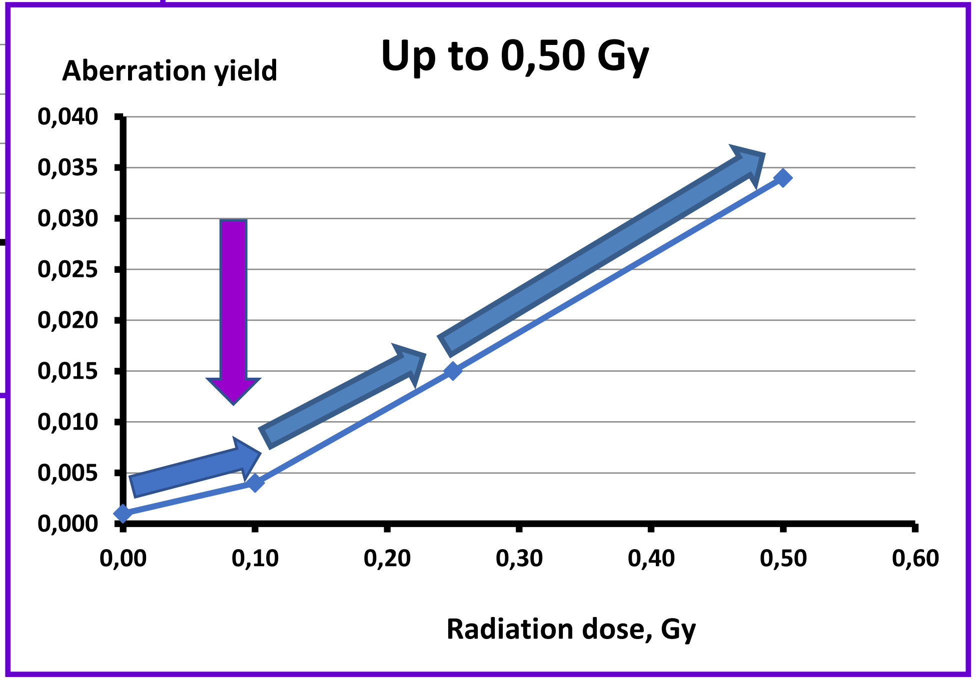
Linear Model is not very good!

Graphic analysis of the dose response within low dose range



"Angle" points are detected at 0,10 Gy and 0,50 Gy. The curvature is present within the entire dose range from 0,10 Gy to 1,00 Gy. Thus, the LQ model is valid, while a Linear dose response would be better applied at doses <0,1 Gy.





Iwasaki et al, 2011 (*Rad Res*; DOI: 10.1667/RR2097.1): 2 criteria for defining an upper dose limit for linear approximation: (1) A traversal of <1 ionization track per nucleus. (2) A contribution of βD^2 to the effect is negligible, e.g. the ratio $\beta D^2 / \alpha D < 0{,}10$. In both cases the limit is 30-50 mGy.

Fitting dose response from data found in the literature

Iwasaki et al, 2011 (*Rad Res*); DOI: 10.1667/RR2097.1

Dic+CR yields *in vitro;* ^{60}Co γ-rays

Doses, Gy	Cells	Aberrations	Yield
0,00	5748	6	0,00104
0,01	6414	9	0,00140
0,02	5608	13	0,00232
0,04	5782	18	0,00311
1,00	228	25	0,10965

Up to 1,0 Gy

$Y = 0{,}0010\ (\pm\ 0{,}0004)+0{,}0523(\pm\ 0{,}0211)\times D+0{,}0563(\pm\ 0{,}0309)\times D^2$

Goodness of fit: $\chi^2 = 0{,}4506$; *df* =3; *p* =0,9296

Up to 0,04 Gy: **Negative value of β !!!**

$Y = 0{,}0010\ (\pm\ 0{,}0004)+0{,}0584(\pm\ 0{,}0617)\times D - 0{,}1082(\pm\ 1{,}5670)\times D^2$

Linear Model fit:

$Y = 0{,}0010\ (\pm\ 0{,}0022)+0{,}0544(\pm\ 0{,}0203)\times D$

Goodness of fit: $\chi^2 = 0{,}2393$; *df* =2; *p* =0,8872

Golfier et al, 2009 (*Rad Prot Dosim*); DOI: 10.1093/rpd/ncp061

Dicentric yields *in vitro;* CT scanner X-rays 63 keV

Doses, Gy	Cells	Aberrations	Yield
0,00	4100	1	0,00024
0,025	4732	5	0,00106
0,05	4355	9	0,00207
0,10	4492	19	0,00423
0,30	3813	68	0,01783
0,60	2715	117	0,04309

Up to 0,6 Gy

$Y = 0{,}0002\ (\pm\ 0{,}0002)+0{,}0365(\pm\ 0{,}0085)\times D+0{,}0610(\pm\ 0{,}0199)\times D^2$

Goodness of fit: $\chi^2 = 0{,}4506$; *df* =3; *p* =0,9296

Up to 0,3 Gy:

$Y = 0{,}0002\ (\pm\ 0{,}0002)+0{,}0310(\pm\ 0{,}0113)\times D+0{,}0922(\pm\ 0{,}0477)\times D^2$

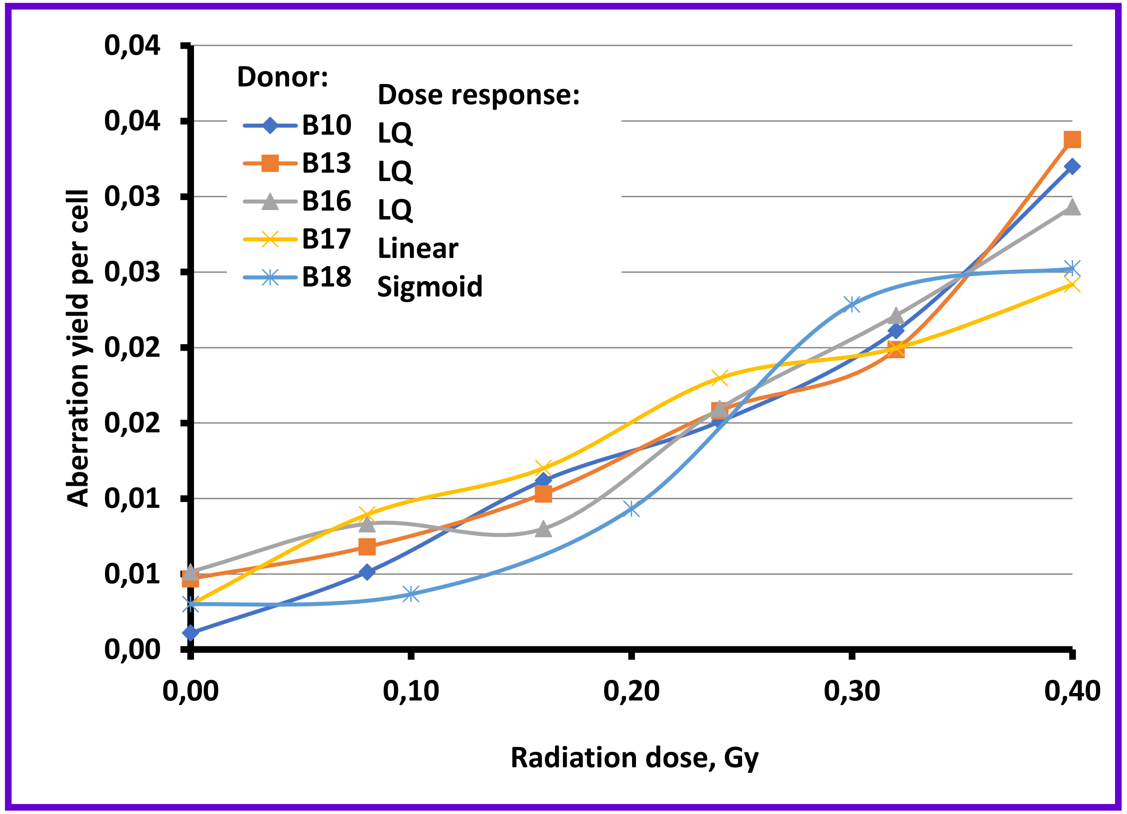
Goodness of fit: $\chi^2 = 4{,}093$; *df* =2; *p* =0,8153

As expected, if coefficient α decreases, then coefficient β increases

Fitting dose response from data found in the literature

Vorobtsova et al, 2001 (*IJRB*); DOI: 10.1080/09553000110075527

Dicentric yields *in vitro;* ^{60}Co γ-rays



5 donors; individual data input separately:

Y = 0,0036 (± 0,0008)+0,0325(± 0,0157)×D+0,0760 (± 0,0465)×D^2

Goodness of fit: χ^2 =9,3470; *df* =26; *p* =0,9999

3 donors with LQ dose response; individual data pooled

Doses, Gy	Cells	Aberrations	Yield
0,00	3161	12	0,0038
0,08	2596	18	0,0069
0,16	1618	16	0,0099
0,24	1479	23	0,0156
0,32	2362	50	0,0212
0,40	1743	56	0,0321

Y = 0,0039 (± 0,0011)+0,0214(± 0,0211)×D+0,1134(± 0,0620)×D^2

Goodness of fit: χ^2 =0,4506; *df* =3; *p* =0,9296

If individual data were input separately:

Y = 0,0039 (± 0,0011)+0,0214(± 0,0211)×D+0,1134(± 0,0620)×D^2

Goodness of fit: χ^2 =4,093; *df* =15; *p* =0,9974

Coefficients remained the same; goodness of fit depended on the degrees of freedom.

Fitting dose response from data found in the literature

Abe et al, 2018 (*JRR*); DOI: 10.1093/jrr/rrx052
Dicentic yields (centr-FISH) *in vitro;* ^{60}C0 γ-rays ; dose rate 26,26 mGy/min;
Duration of exposure at the highest doses 19 – 38 min
Individual data from 5 donors pooled together

Doses, Gy	Cells	Aberrations	Yield
0,00	10056	8	0,00080
0,01	10076	11	0,00109
0,02	10094	16	0,00159
0,05	10131	24	0,00237
0,10	10105	28	0,00277
0,20	10133	60	0,00592
0,50	10115	188	0,01859
1,00	10285	540	0,05250

Up to 1,00 Gy
Y = 0,0010 (± 0,0002)+0,0186(± 0,0036)×D+0,0329(± 0,0047)×D^2
Goodness of fit: χ^2 =2,0130; *df* =5; *p* =0,8473

Up to 0,20 Gy
Y = 0,0009 (± 0,0002)+0,0230(± 0,0103)×D+0,0063(± 0,0559)×D^2
Goodness of fit: χ^2 =1,7400; *df* =3; *p* =0,6280

Up to 0,10 Gy: **Negative value of β !!!**
Y = 0,0008 (± 0,0002)+0,0433(± 0,0192)×D – 0,2321(± 0,1947)×D^2
Linear Model fit:
Y = 0,0009 (± 0,0009)+0,0217(± 0,0058)×D
Goodness of fit: χ^2 =1,5520; *df* =3; *p* =0,6704

Up to 0,05 Gy
Linear Model fit:
Y = 0,0008 (± 0,0013)+0,0324(± 0,0110)×D
Goodness of fit: χ^2 =0,1455; *df* =2; *p* =0,9298

To comparable with
α=0,0544 (± 0,0203)
in Iwasaki et al, 2011

Heterogeneity of the cytogenetic dose response (literature data)

Shi et al, 2018 (*Rad Res*); DOI: 10.1667/RR14976.1

Dic+CR yields (PNA-FISH) *in vitro;* ^{137}Cs γ-rays ; dose rate 0,667 mGy/min; duration of exposure <u>30 – 120 min</u>

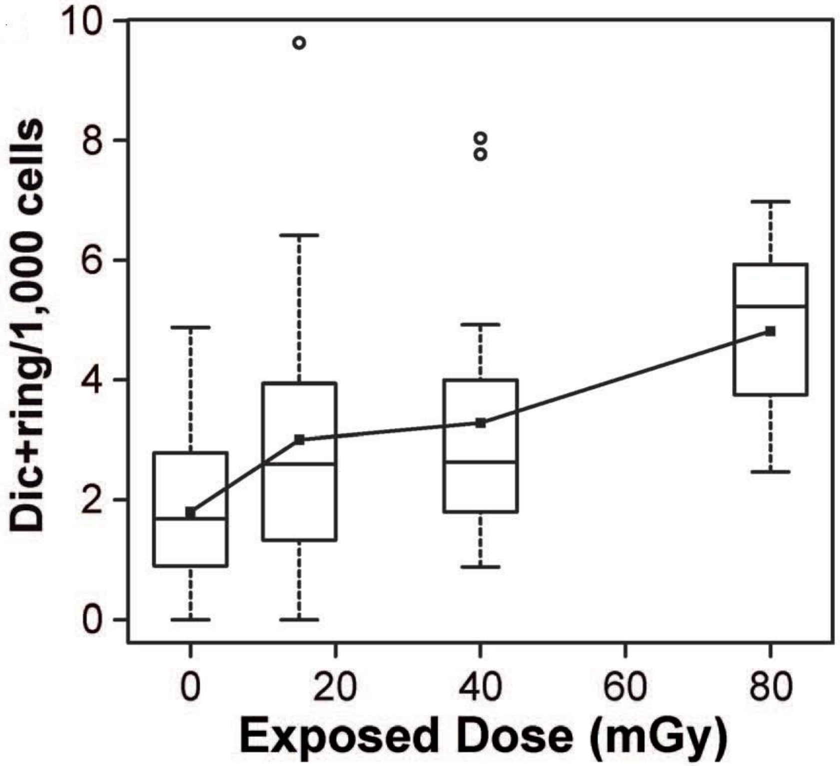


Fig. 3A. Box-plot of combined data from 15 donors

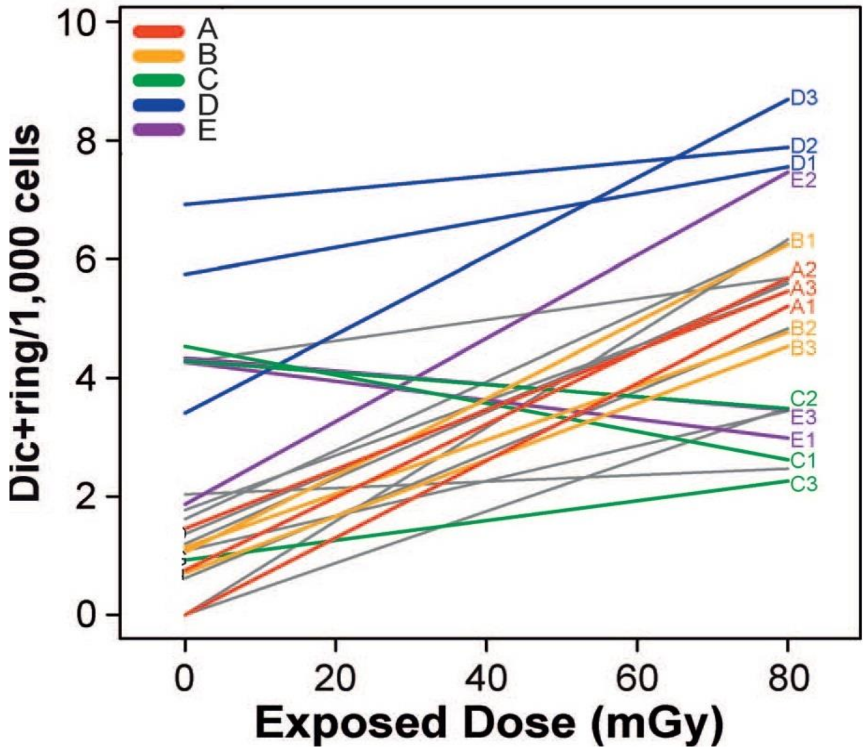
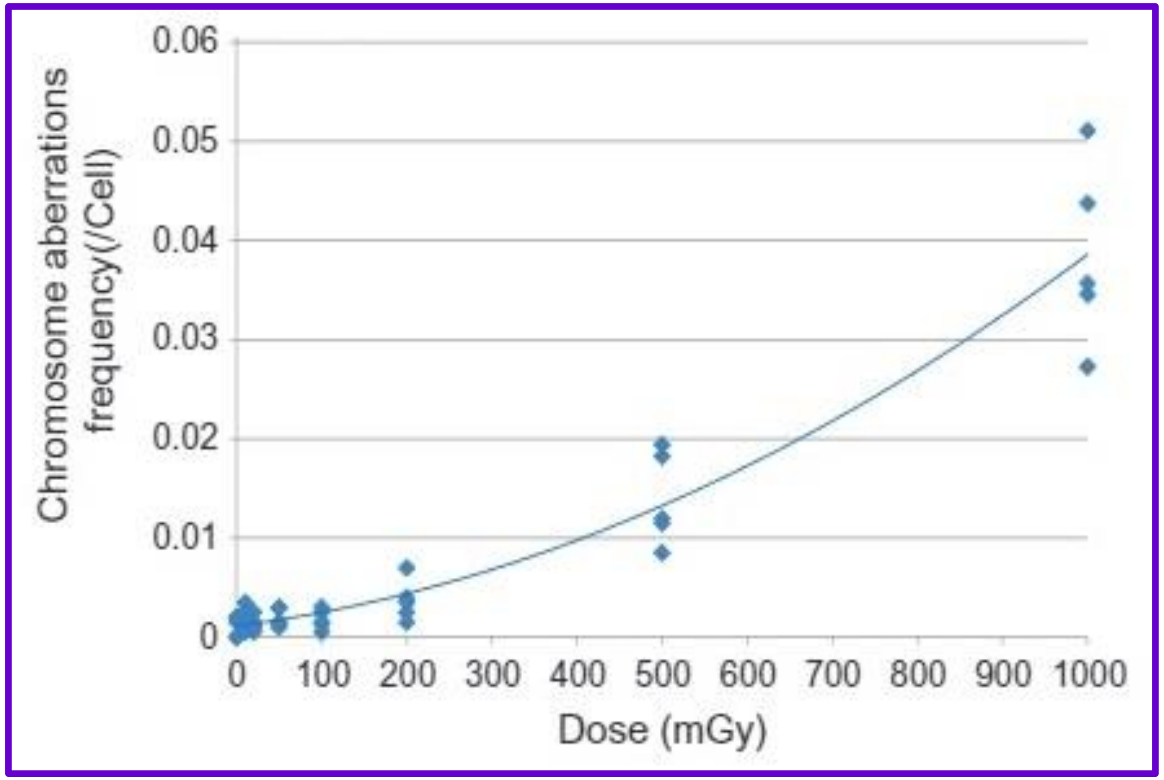


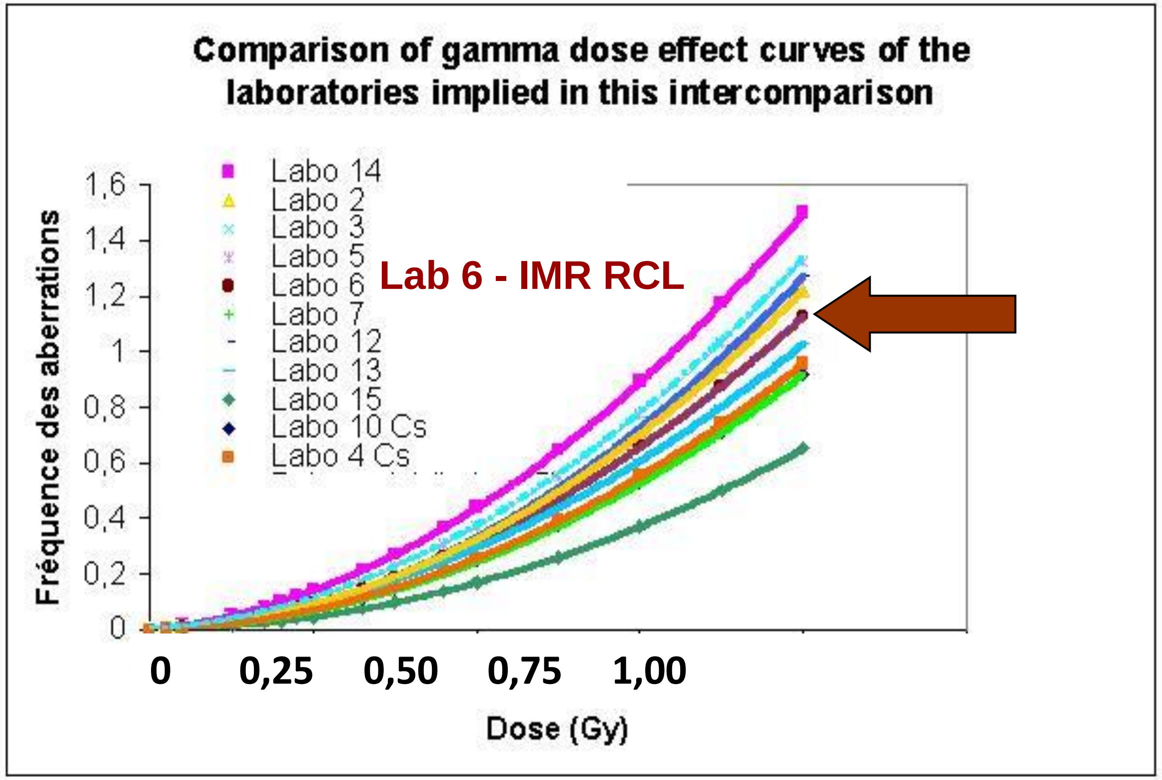
Fig. 3B. Individual data from 5 donors in 3 repeats

Heterogeneity of the cytogenetic dose response (literature data)

Abe et al, 2018 (JRR); DOI: 10.1093/jrr/rrx052
Dicentic yields (Giemsa) *in vitro;* ^{60}Co γ-rays

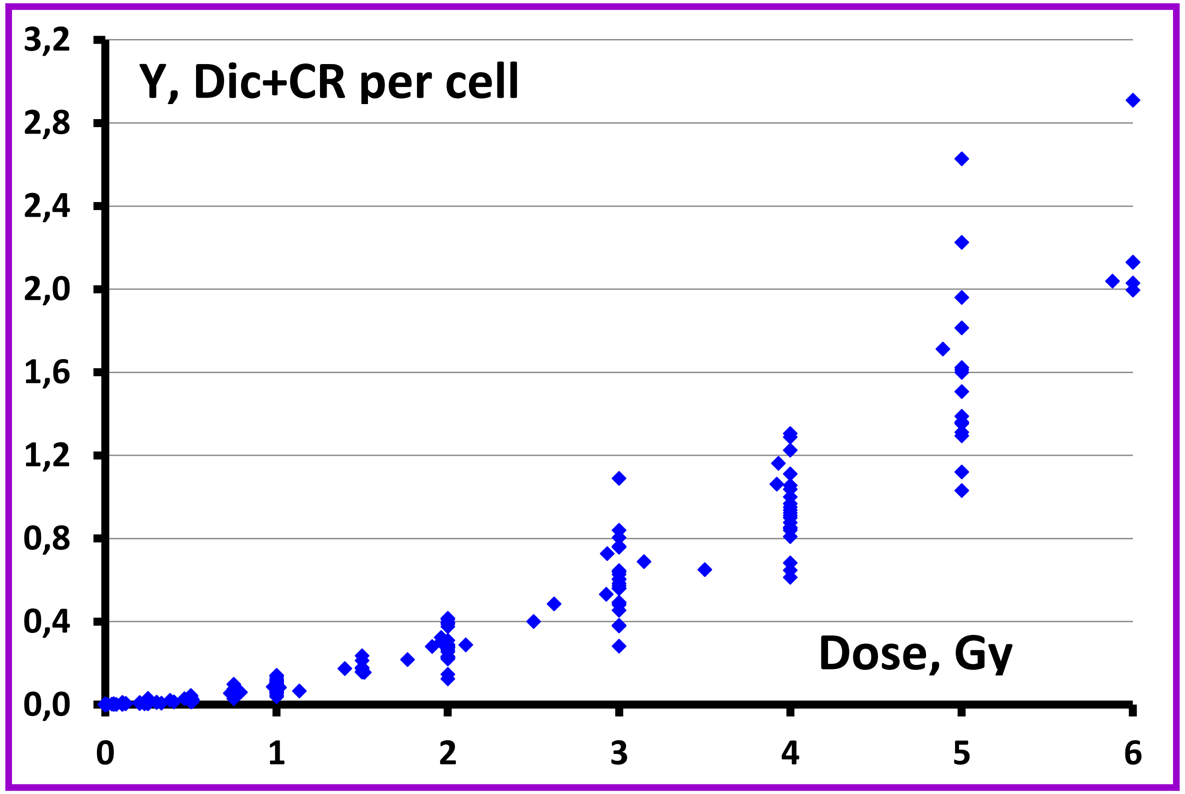


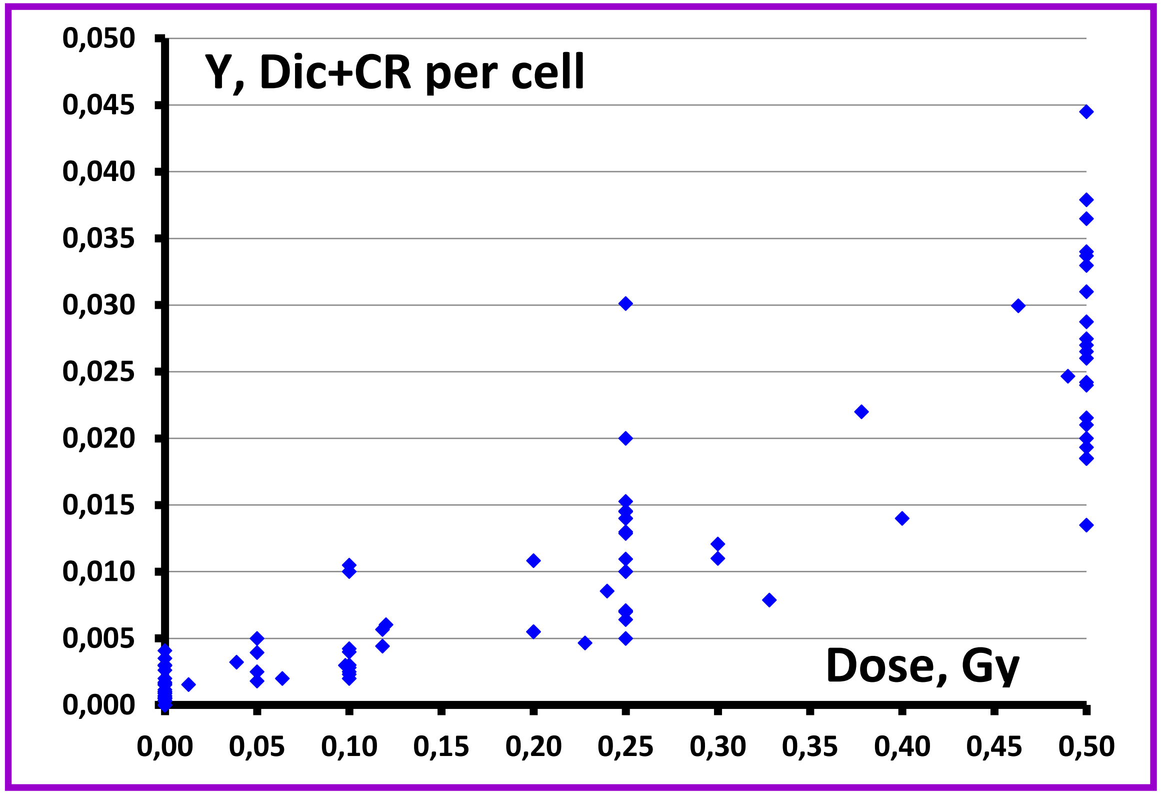
A spectrum of dose responses from different laboratories participating in the SILENE intercomparison (IRSN, France, 2002)



Heterogeneity of the cytogenetic dose response (literature data)

Vinnikov V., 2016; unpublished (part of the Report on the IAEA RC 17079 in the CRP E3.50.08).
Data combined from >30 research publications on Dic+CR yields *in vitro;* acute γ-rays





Variations of the radiation-induced aberration yields exist between labs and between donors.
This is NORMAL!!!

The methodology of the assessment of radiation dose from the aberration yield in different scenarios of exposure (and the respective capacities of CABAS and DoseEstimate) will be presented in the next lecture.

THANK YOU FOR YOUR ATTENTION!!!