Computer Program of Linear Regression for "Probacent" Model Predicting Human Tolerance to Total Body Irradiation

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ABSTRACT

A clear and exact quantitative relationship between dose of radiation and mortality in humans is still not known because of lack of human data thatwould enable to determine LD_{50} for humans in total body irradiation. The death rate equation derived from the "probacent"-probability equation of survival probability was employed in the author's previous study to construct the general formula of LD_{50} as a function of dose rate and duration of exposure, using an analytical method of least maximum difference principle. In this study, a computer program of least sum of squares described in the author's previous publication is used to construct a formula of LD_{50}. There is a remarkable agreement among values of computer-program-of-linear-regression-derived, least-maximum-difference-derived and reported LD_{50}. The results suggest that the computer program of linear regression seems to be simple, accurate, convenient and preferable than the previously used least maximum difference principle, and the formula of LD_{50} is better fitting the reported data on LD_{50} in total body irradiation in humans. The computer program of linear regression described in this study may be helpful in biomedical research.

Keywords: Computer Program;Linear Regression; Total Body Irradiation; Lethal Radiation Dose; Formula of LD_{50}; Formula of Mortality; Safety in Radiotherapy; Radiation Hazard and Injury; Global Safety.

1. INTRODUCTION

A clear and exact quantitative relationship between dose of radiation and mortality in humans is still not known because of lack of human data that would enable to determine LD_{50} for humans in total body irradiation. Analysis of human data has been primarily from radiation accidents, radiotherapy and the atomic bomb victims [1-9].

Consequently, laboratory animals have been used to investigate the relationship between radiation exposure and biomedical effects in total body irradiation, and further to possibly derive a general predictive mathematical formula expressing a dose-effect curve [1. 10-12]

The Gompertz model (1825) is one of the well-known mathematical expression among mortality models in the literature that are used to describe mortality and survival data of a population [13, 14].

On the basis of experimental observations on animals, clinical applications on patients and theoretical statistical reasoning, the author developed a general mathematical model of "probacent"-probability equation that may be applicable as a general approximation method to make useful predictions of probable outcomes in a variety of biomedical phenomena [15-18].

The model of the "probacent"-probability equation was constructed experimental studies on animals to express survival probability in mice exposed to *g*-force in terms of magnitude of acceleration and exposure time [15, 19]; and to express a relationship among intensity of stimulus or environmental agent (such as drug [15, 16, 20], heat [21], pH [22], electroshock [21, 23]), duration of exposure and biological response in animals.

The model was applied to data in the literature to express carboxyhemoglobin levels of blood as a function of carbon monoxide concentration in air and duration of exposure [24,25]; to express a relationship among plasma acetaminophen concentration, time after ingestion and occurrence of hepatotoxicity in man [26, 27]; to predict survival probability in patients with malignant melanoma [28, 29]; to express survival probability in patients with heart transplantation [30, 31]; to express a relationship among age, height and weight , and percentile in Saudi and US children of 6-16 years of age (32, 33]; to predict the percentile of heart weight by body weight from birth to 19 years of age [34, 35]; and to predict the percentile pf serum cholesterol leveld by age in adults [36, 37].

The model was applied to the United States life tables, 1992 and 2001 reported by the National Center for Health Statistics (NCHS) to construct formulas expressing survival probability, death rate and life expectancy in US adults, men and women (17, 38-40].

The formula of survival probability is expressed by the following "probacent"-probability **Eq. 1:**

$$P^r = \mathrm{A} - \mathrm{B} \log T \qquad (1a)$$

$$S = 10/\sqrt{2\pi}\int_{-\infty}^{P} \exp[-(P - 50)^2/200]dP \qquad (1b)$$

Where T = time after biomedical insult, diagnosis of cancer or age; P = *"probaent"* (abbreviation of probability percentage) = relative biological amount of reserve for survival; "probacent" (P) of 0, 50 and 100 corresponds to mean-5 SD, mean and mean+5 SD, respectively; the unit of "probacent" is 0.1 SD. In addition, 0, 50 and 100 "probacents" seem to correspond to 0, 50 and 100 percent probability in mathematical prediction problems in terms of percentage. Therefore, it seems to the author that survival probability can be used to predict probabilities in general biomedical phenomena. "probacent" (P) values are obtainable from a list of conversion of percent probability into "probacent" that was published by the author (Table 6 of Re. [15] and Table 4 of Ref. [16]). r, A and B are constants; A is an intercept and B a slope; r represents a curvature (a shape of curve) and expressed by the following equation:

$$r = \log(\mathrm{A} - \mathrm{B} \log T)/\log P$$

If the value of *r* becomes equal to one, **Eq. 1** represents a log-normal distribution. **Eq. 1** is considered to be fundamentally based on the Gaussian normal distribution.

In computation of **Eq. 1b** with computer programs, a formula of approximation is used because the computer cannot execute integral [15, 16, 41]. Matthematical transformation of formula of integral, **Eq. 1b** to the formula of approximation is described in the author's book [41,42].

Eq. 2 representing death rate or hazard rate is derived from **Eq. 1** expressingsurvival probability [40].

$$(\log D)^c = a + b \log T \qquad (2)$$

where *D* represents death rate in percentage (mortality probability); *T* is time or age; c, a and b are constants; c represents a curvature (a shape of curve) like r in **Eq. 1a**; a is an intercept and b a slope.

Eq. 2 was applied to express death rates in US total elderly population [17, 40]. It was found to better express death rates in US total elderly population than the Gompertz, the exponential and the Weibull distributions [17].

Mehta and Joshi successfully applied **Eqs. 1 and 2** to use model-derived data as an input for radiation risk evaluation of Indian adult population in their study [43].

Eq. 2 was applied to predict mortality probability and LD_{50} in ionizing total body irradiation in humans as a function of dose rate and duration of exposure [18]. The formula of LD_{50} was constructed from a mathematical analysis based on a least maximum-difference principle described in MATERIALS AND METHODS to minimize deviations, without employing statistical analysis of least sum of squares. Computer programs of least sum of squares are openly available [44, 45].

However to my knowledge, there seem to be no computer programs of linear regression in the literature that express a "probacent" model equation best fitting reported data.

The purpose of this study is to design a computer program of linear regression of least sum of squares for construction of a best fitting equation of LD_{50} in total body irradiation in humans.

2. MATERIALS AND METHODS

Data shown in a table of animal-modelpredictions of lethal radiation doses to humans published by Cerveny, MacVittie and Young [1] are used to construct a predictive formula expressing a relationship among dose rate in rad/min, duration of exposure in minutes and mortality in ionizing total body irradiation in humans.

The data are based on an extensive study of mortality resulting from radiation exposure and a compilation of animalexperimental data published by Jones, Morris, Wells andYoung at the Oak Ridge National Laboratory [2].

The data shown in Table 1 are lethal doses of LD_{50} based on animal-model predictions without subsequent medical treatment. The data are plotted on a log-log graph paper as illustrated in Figure 2 for a better mathematical analysis. The straight line representing LD_{50} indicates that the value of constant c in Eq. (2) is one.

2.1. Computer Program of Linear Regression

A close look at the data points in Figure 2 in graphic inspection suggests that the line connecting data points appears to reveal a straight line, and that it indicates the value of constant c in **Eq.2**is one. If the line is not straight and curved, the c value would be not one. In this study, c=1. A four-step approach is taken to construct the best-fitting computer-program-derived **Eq. 2** in analyzing data (see the author's previous publication [46].

The first step of compute-assisted mathematical analysis:

Two sets of data on dose rate (*D*) and duration of exposure (T) obtained from the reported data [1] are used to determine a value of the constant a in Eq. 2. Two sets of data are chosen from the beginning and ending areas of the data in Table 1 and Figure 2.

(1) *D*=50 rad/min, and*T*=3.72 min.

(2) *D*=1, and *T*=275 min

log 50 = a + b log 3.72 (3)

log 1 = a + b log 275 (4)

The value of constant a is derived from **Eqs. 3 and 4.**

a = 2.21766 (5)

The second step of computer-assisted mathematical analysis:

Enter a number as a constant b value in the computer program, starting from -1 because the line goes downward in Figure 2, and then numbers, -0.9, -0.8, -0.7, ... The sum of squares would be gradually decreasing. When the computer-generated line touches the data line, the sum of squares become minimum, theleast sum, ideally zero. After passing the data line, the sum of squares with a decreasing b value would suddenly begin to increase and continue to increase further more.

The third step of computer-assisted mathematical analysis:

If the sum of squares suddenly starts increasing after preceding gradual decease at a number N of b value, then enter two numbers, a slightly smaller N_1 and a slightly larger N_2than N; and calculate the sums of squares for each of N_1 and N_2. Then enter N_1 or N_2 in **Eq. 2** that has the smallest sum among N, N_1 and N_2 as the b value in the program. Repeat this third step, entering a number with a smaller number than the preceding number, N_3, N_4, N_5 or N_6 .... , and calculate sums, then compare them.

The fourth step of computer-assisted mathematical analysis:

Repeat the third step until a number N_k that has a satisfactory and seemingly least sum of squares is obtained. **Eq. 2** with values of 2.21766 for the constant a and $N_k$for the constant b would be the best fitting equation. Eq. (6) is finally constructed as the best fitting equation in this study.

$$\text{Log } D = 2.21766 - 0.909089 \log T \quad (6)$$

Figure 1 illustrates the computer program of linear regression for "probacent" model, **Eq. 6**in which LD_{50} is a function of dose rate *D* and duration of exposure *T* in ionizing total body irradiation in humans.

```
10   lprint
20   lprint "Sum of squares in linear regression for Eq. 6."
30   lprint "This program is for B=-0.909089."
40   lprint
50   lprint "B",tab(16);"Dose rate",tab(28);"Time",tab(56);"Sum of squares"
60   lprint tab(16);"rad/min",tab(28);"min",
70   lprint
80   read D,R
90   B=-0.909089
100  T=10^((log(D)/log(10)-2.21766)/B)
110  Z=T-R
120  'Z stands for differenc at dose rate D.
130  ZZ1=ZZ1+Z^2
140  'ZZ1 stands for sum of squares added up at dose rate D.
150  lprint B,tab(15);D,tab(27);T,tab(55);ZZ1
160  goto 80
170  data 50,3.72,20,10.2,10,21.8,5,46.8,2,128.5,1,275
```

```
Sum of squares in linear regression for Eq. 6.
This program is for B=-0.909089.

B              Dose rate    Time                        Sum of squares
               rad/min      min
-0.909089      50           3.7201477900139159843       0.0000000218418882132
-0.909089      20           10.1928380090917450155      0.0000513159556581403
-0.909089      10           21.8488615559384267376      0.0024387676043821454
-0.909089      5            46.8341349940772252481      0.0036039654250343482
-0.909089      2            128.3209104143624407212     0.0356770451088670268
-0.909089      1            275.0623333633464816954     0.0395624932949515345
```

LEGEND FOR FIGURE 1.

Figure 1 illustrates the computer program of linear regression for the “probacent”-model , Eq. (6) in which LD_{50} is a function of dose rate D and duration of exposure T in ionizing total body irradiation in humans. Results of execution of the program for 2.21766 of an a value and 0.909089 of a b value in **Eq. 6**are shown beneath the legend of the program in Figure 1 and Tables 1 and 2.

2.2. Least Maximum-Difference Principle

In analysis of the least maximum-difference, random different numbers are substituted as the constant b value in **Eq. 2**. This method was used in the author’s previous study [18] to minimize deviations without employing a computer program of linear regression. **Eq. 7**was constructed by this analytical method.

$$\text{Log } D = 2.21767 - 0.90913 \log T \qquad (7)$$

2.3. Description of the Computer Program

The program was written in UBASIC for IBM PC microcomputer and compatibles for **Eqs. 6 and 7**. A representative computer program is illustrated in Figure 1 to calculate the sum of squares, $\sum(E - O)^2$ with the values of a = 2.21766 and b = -0.909089 in **Eq. 6.**

2.4. Statistical Analysis

A chi-goodness-of-fit test (logrank test) [47] is used to test the fit of mathematical model to the reported data [1]. The differences are considered statistically significantwhen $p < 0.05$.

3. RESULTS

Table 1 shows comparison of the relationship among dose rate, duration of exposure and LD_{50} revealed in the analysis by the computer program of linear regression of least sum of squares and the least maximum difference principle. Values of duration of exposure or LD_{50} in each analytical method are very close.

Table 1. Comparison of values of duration of exposure and LD_{50} derived from computerprogram of linear regression and least maximum difference principle in total bodyirradiation in humans.

Dose rate (rad/min)		50	20	10	5	2	1
Duration of exposure (minutes)	Computer program of linear regression	3.72	10.2	21.8	46.8	128.3	275.1
	Least maximumdifferenceprinciple*	3.72	10.2	21.8	46.8	128.5	275.0
LD_{50}** (rad)	Computer program of linearregression	186.0	203.9	218.4	234.2	256.6	275.1
	Least maximumdifferenceprinciple	186.0	203.9	218.4	234.1	256.6	275.0
	Reported*** values	186	204	218	234	257	275

* Ref. [18].
** LD_{50} represents a radiation dose that causes a 50% fatality.
*** Ref. [1]

Table 2 shows comparison least sum of squares $\sum(E-O)^2$ and least maximum difference $|(E-O)|$ in each analytical method. Values of least sum of squares and least maximum difference in both methods are very close but the values derived from the computer program of least sum of squares are slightly smaller than those derived from the least maximum difference principle, suggesting the slightly better fit of **Eq. 6** than **Eq. 7**.

Chi-square test *p* values are >0.995 in each of the two analytical methods, suggesting a remarkable agreement between both analytical methods.

The above observed results seem to indicate that the analytical method of the computer program of linear regression seems to be simple and accurate in determining values of constants, a and b of **Eq. 2.**

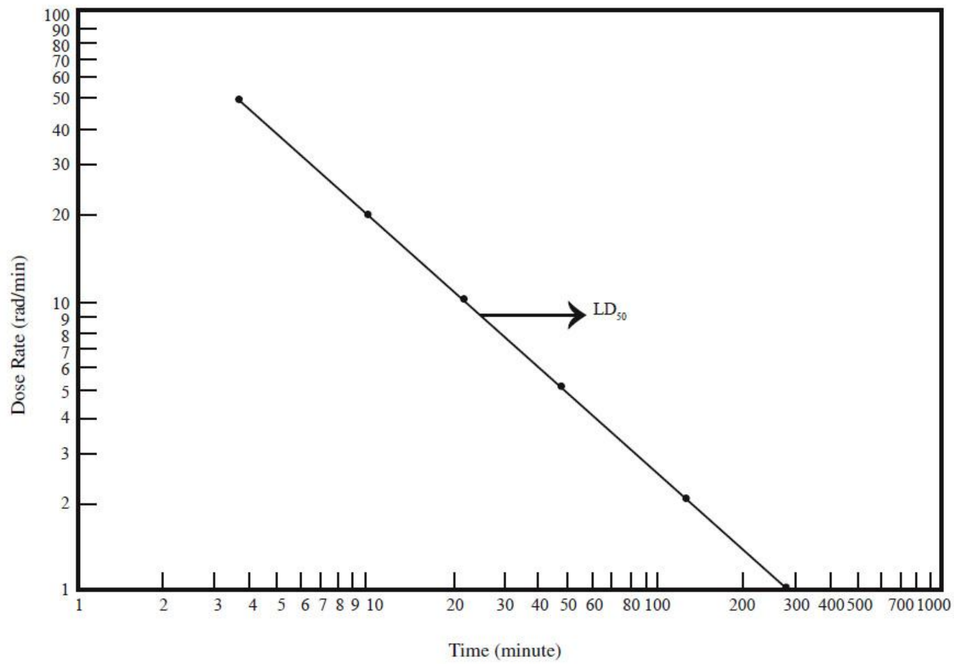
Figure 2 illustrates the relationship between dose rate and duration of exposure for LD_{50} of human tolerance in ionizing total body irradiation.

Table 2. Comparison of values of least sum of squares and least maximum difference derived from computer program of linear regression and least maximum difference principle in total body irradiation in humans.

	Computer-program-of linear-regression derived	Least-maximum-difference-principle derived*
Used "probacent" model equation	log *D*=2.21766-0.909089	log *D*=2.21767-0.90913
Least sum of squares $\sum(E-O)^2$	0.0396	0.0445
Least Maximum difference $|(E-O)|$	0.179	0.204
p-value	> 0.995	> 0.995

* Ref. [18].

E and O stand for values from computer program of linear regression and observatopn (reported value), respectively.



Legend for Figure 2.

Figure 2 illustrates the relationship between dose rate and duration of exposure for LD_{50}. The illustration seems to the author that the distributions of animal-model-predicted lethal dose of LD_{50} appear to be very closely represented by the straight line of the computer program of linear regression.

4. DISCUSSION

Comparison of data shown in Table 1 indicates a remarkable agreement between both values of duration of exposure and LD_{50}obtained from the computer program of linear regression and the least maximum-difference principle.

Comparison of least sum of squares and least maximum difference shown in Table 2 reveals that the computer program of linear regression gives smaller values of least sum of squares and least maximum difference than the least maximum-difference principle, suggesting more accuracy and better fit with the computer program of linear regression.

The computer program of linear regression seems to be preferable to the least maximum-difference principle to minimize the deviation.

Values of LD_{50} in Table 1 is a function of dose rate *D* and duration of exposure *T*:

$$LD_{50} = D \times T \qquad (8)$$

The values of LD_{50}, 1.860-2.751 Gy shown in Table 1 are considerably close to LD_{50} published in the literature: 2.45 Gy (Langham, 1967), 2.86 Gy (Lushbaugh et al. (1967), 2.65-2.70Gy (Bond and Robertson, 1957) [48], 2.3-2.6 Gy (Fujita, Kato and Schull, 1989) [49]. If it is taken into consideration that LD_{50} is a function of *D* and *T* as shown in **Eq. 8,** there seems to be a remarkable agreement betweenthe computer-program-derived and the reported, estimated LD_{50} values [48, 49].

The author feels that in the variety of biological phenomena, r and c values in **Eqs. 1** and**2** are, if applicable, generally greater than one or less than one but not one, indicating a curved line when plotted on a X-Y graph paper. The r and c values are relatively rarely one, indicating a straight line on a graph paper or otherwise approximately straight as seen Figure 2. The phenomena seem to be analogous to the light path in physics that light path is actually curved when passing through a gravitational field of space but appears straight [50, 51]. Results of this study suggest that the data-point-connecting line is not a truestraight line ($c \neq 1$), nonlinear and probably curved because the least sum of square for **Eq. 7** is not zero. Therefore, **Eqs. 6 and 7** represent an approximation method.

If the *r*value becomes to equal to one, **Eq. 1** represents a lognormal distribution. If the c value in **Eq. 2** that is derivable from **Eq. 2** [40] becomes essentially similar to the Weibull distribution [13]. Weibull distribution is a generalized exponential distribution [13]. If the base of a logarithm is one, the lognormal distribution becomes a normal distribution ($\log_1 1^n = n$) [41, 52].If the logarithm of one as its base is taken for X axis of time, the Gompertz distribution might be similar to the Weibull distribution. Therefore, it seems to the author that the Gompertz distribution might be a specific form of “probacent”-probability equation. A normal distribution is likewise a specific form of the “probacent”-probability equation.

“probacent” can be a dependent variable versus an independent variable such as time or age as seen in survival probability and life expectancy in US total adult population (NCHS) [17, 40]. “probacent” can be a dependent versus two independent variables such as intensity of stimulus or harmful agent and duration of exposure like dose of radiation and duration of exposure in total body irradiation [18], and like dose of drug and time after administration [16, 17]. In case of two independent variables**, Eq. 1** can make a prediction of probability of occurrence of response in subjects in variousbiological phenomena. The original and ultimate purpose of the author’s studies has been to find a general mathematical model, probably a mathematical law hidden in nature that might calculate the probability of safe survival in humans and other living organisms exposed to any harmful or adverse circumstances or conditions, overcoming the risk [15, 41].

The “probacent”-probability does not predict a single definite result or response for an individual observation in biodynamicbiological phenomena. Instead, if the same observations are made on a large number of similar population, each of who had the same condition at the start, the model would predict the possible outcomes, the approximate biomedical events in quantities under observations, but it could not predict the occurrence of the specific event in an individual.Thus, the “probacent” probability would introduce an unpredictability in biomedicine like an uncertainty principle of Werner Heisenberg in quantum mechanics [50, 51].

However, if the probability is 0 or 100 %, it might be able to predict that an individual exposed to a harmful or adverse circumstance under observation wouldbe most likely safe or riskywith a considerable certainty.

The computer program of nonlinear, curved regression for **Eq. 1** enables users easily calculate sums of least squares by using a formula of approximation, eliminating a need for consultation of table of normal frequency or percentile in books of statistics and mathematics.

5. CONCLUSIONS

In this study, a computer program of linear regression is designed to determine values of constants, a and b in **Eq. 2,**in order to construct thebest fitting "probacent" model equation. **Eq. 6** that expresses LD_{50} in total body irradiation in humans.**Eq. 6** seems to be better fitting and more accurate than **Eq. 7**thatwas constructed by the least maximum-difference principle in the author's previous study [18] as shown in Tables 1 and 2.

The general formulas of LD_{50}**, Eq. 6** and **Eq. 12**of the author's previous study [18] that represents a general formula of mortality probabilityfor dose-effect curve [18] might be of help for safety in radiotherapy, and further prevention of radiation hazard and injury.

The computer programs of linear and nonlinear, curved regressions for a "probacent" mathematical model may be useful in biomedical research.

The computer programwould need further improvements to enable users to readily construct the best-fitting equation of 'probacent" mathematical model.

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REFERENCES

[1]Cerveny, T.J., MacVittie, T.J. and Young, R.W. (1989) Acute radiation syndrome in humans. In. R.J. Walker and T. J. Cerveny, Eds.,*Medical Consequences of Nuclear Warfare,* TMM Publications, Office of the Surgeon General, Falls Church, pp. 15-36.

[2] Jones, T.J., Morris M.D., Wells, S.M. and Young, R.W. (1986) Animal mortality resulting from uniform exposures to photon radiation: Calculated LD_{50} and a compilation of experimental data. Oakridge National Laboratory, Oak Ridge.

[3] Nenot, J. (2009) Radiation accidents over 60 years. *Journal of Raddiological Protection,* **29,** 301-320.

[4] Abrahamson, S., Bender, M. A., et al. (1993) Health effect models for nuclear war plant accident consequence analysis. US Government Printing Office, Washington, DC.

[5] Donnelty, E.H.,Nemhauser, J. B. Smith M., et al. (2010)Acute radiation syndrome: Assessment and Management. *Southern Medical Journal,* **103,** 541-544.

[6] Department of Radiology, University of Illinois (1990) Acute effects of whole body irradiation: Lesson from Chernobyl.http//:www.uie.edu//com/uhrd/manuscript/section4.html

[7] Bavorstock, K.F., Ash, P.J.D. (1983) A review of radiation accidents involvinf whole body exposure and the relevance to the $LD_{50/60}$ for man. British Journal of Radiology, **56**, 837-849.

[8] Warren, S. (1961) The pathology of ionizing radiation. Thomas Publisher, Springfield.

[9] VanMiddlesworth, L. (1989) Effects of radiation on the thyroid gland. *Advanced Internal Medicine*, **34**, 265-284.

[10] Sacher, G.A. (1956) On the relation of radiation lethality to radiation injury and its relevance for prediction problem. *19th International Congress of Radiology,* 23-30 July, 1959, 1223-1232.

[11] Travis, E.L., Peters, L.G., Thommas, H.G., et al. (1985) Effect of dose-rate on total body irradiation: Lethality and pathologic findings. *Radiotherapy and Oncology,***4**, 341-351.

[12]Komarova, E.A., Kondratov, R.V., Wang, K., et al. (2004) Dual effect of p53 on radiation sensitivity in vivo: p53 promotes hematopoietic injury, but protects from gastro-intestinal syndrome in mice. *Oncology* ,**23**,3265-3271.

[13] Lee, E.T. and Wang, J.W. (2003) Statistical methods for survival data. John Wiley $ Sons, Hoboken, 8-197.
[14] Gompertz, B. (1994) Prametric models. *Statistical Methods in MaedicalResarch,* Blackwell Science, Cambridge, 482-483.
[15] Chung, S,J. (1960) Stidies on a mathematical relationship between stree and response in biological phenomena. *Journal of the National Academy of Sciences, Republic of Korea,* **2**, 115-162.
[16] Chung, S,J. (1986) Computer-assisted predictive mathematical relationship among metrazol and time and mortality in mice. *Computer Methods and Programs in Biomedicine,* **22**, 275-284.
[17] Chung, S.J. (2007) Computer-assisted predictive formulas expressing survival probability and life expectancy in US adults, men and women, 2001. *Computer Methods and Programs in Biomedicine,* **86**, 197-209.
[18] Chung, S.J. (2011) Predictive formulas expressing relationship among dose rate, duration of exposure and mortality probability in total body irradiation in humans. *Journal of Biomedical Science and Engineering,***4,** 497-505.
[19] Chung, S.J. (1959) Stidies of positive radial acceleration on mice. *Journal of Applied Physiology,***14**, 52-54.
[20] Boak, H. and Chung, S.J. (1962) Studies on a relationship between dose, time and percentage of occurrence of response and a method of evaluation of combined action in drugs. *The New Medical Journal,* **5**, 35-82.
[21] Kim, C.C. and Chung, S.J. (1962) Studies on a relationship between stress, duration of exposure and percentage of response in goldfish in single, double and triple stresses of acceleration, electroshock, heat, chemical and osmotic stimuli. *Republic of Korea Theses of Catholic Medical College,* **5**, 257-336.
[22] Cho, D.W. and Chung, S.J. (1961) Studies of tolerance of Paramecium caudatum to hydrogen and hydroxyl ions. *Bulletin of Yamaguchi Medical School,* **8**, 151-160.
[23] Chung, S.J. (1989) Computer-assisted mathematical relationship amonf electroshock voltage and duration and occurrence of convulsion in mice. *Computr Methods and Programs,* **28**, 23-30.
[24]Forbes, W.H., Sergent, F. and Roughton, F.J.W. (1988) The risk of carbon monoxide uptake by normal men. *American Journal of Physiology,* **143**, 594-608.
[25[Chung, S.J. (1988) Formula predicting carboxyhemoglobin resulting from carbon monoxide exposure. *Veterinary and Human Toxicolocy,***30**, 528-532.
[26] Prescott, L.F., Roscoe, P., Wright, N. and Brown, S.S. (1991) Plasma paracetamol half-life and hepatic necrosis in patients with paracetamoloverdosege. *Lancet,***1**, 519-522.
[27] Chung, S.J. (1989) Computer-assisted predictive mathematical relationship among plasma acetaminophen concentration, time after ingestion and occurrence of hepatotoxicity in man. *Computer Methods and Programs in Biomedicine,***28**, 37-43.
[28] Popescu, N.A., Beard, C.M., Winkelman, P.J., O'Brien, P.C. and Kurland, L.T. (1990) Cutaneous malignant melanoma in Rochester, Minnesota: Trends in incidence and survivorship, 1950 through 1985. *Clinical Proceedings,***65,** 1293-1302.
[29] Chung, S.J. (19940 Formula expressing a relationship among lesion thickness and time after diagnosis and survival probability in patients with malignant melanoma.*International Journal of Biomedical Computing,***37**, 171-180.
[30] Kirklin, J.R., NaftelD.C., Kirklin, Jw. Blackstone, E.H., White-Williams, C. and Bourge, R.C. (1988) Pulmonary vascular resistance and the risk of heart transplantation. *Journal of Heart Transplantation,***7**,331-336.
[31] Chung, S,J, (19930 formula predicting survival probability in patients with heart transplantation. *International Journal f Biomedical Computation,* **32**, 211-221.
[32] Magbool, G., Kaul, K.K., Corea, J.R., Osman, M. and Arfaj, A. (1993) Weight andheight of Saudi children six to 16 years from the Eastern Province.*Annal of Saudi Medicine,* **13**, 344-349.

[33] Chung, S.J. (1994) Formulas exoressing relationship among age, height and weight, and percentile in Saudi and US children 6-16 years. *International Journal of Biomedical Computing,* **37**, 259-272.
[34] Sholz, D.C., Kitzman, D.W., Hagen, P.T., Ilstrup, D.H. and Edwards, W.D. (1988) Age-related changes in normal human hearts during the first 10 decades of life. Part I. (Growth): A quantitative anatomic study of 200 specimens from subjects from birth to 19 years old. *MayoClinic Proceedings,* **13,** 126-136, 637.
[35] Chung, S.J. (1990) Formulas predicting the percentiles of heart weight by body weight in subjects from birth to 19 years of age. *International Journal of Biomedical Computing,***26**, 257-269.
[36] Feinleib, M. (1986) Total serum cholesterol levels of 20-70 years of age; United States, 1976-1980. US Department of Health and Human Services publicatin (PHS). *The National Health Survey,* **11**, 86-1686.
[37] Chung, S.J. (1990) Formulas predicting the percentile of serum cholesterol levels by age in adults. *Archives of Pathology and Laboratory Medicine,* **114**, 869-875.
[38] The National Center for Health Statistics (1993) Annual survey of births,
41, 1-36.
[39] Arias, E. (2004) United States life tables, 2001. *National Statistics Report,* **52,** 1-40.
[40] Chung, S.J, (1995) Formulas expressing life expectancy, survival probability and death rate in life tables at various ages in US adults. *International Journal of Biomedical Computung,* **39,** 209-217.
[41] Chung, S.J. (2009) Seeking a New World: A New Philosophy of Confucius and Kim Hang. Bloomington, Indiana,68-76, 153.
[42] Hastings, J.C. (1955) Approximation for Digital Computer. Princeton University Press, Inc., New Jersey, 185.
[43] Mehta,S.C. and Joshi, H.C. (2004) Model based point estimates of survival/death rate: An input for radition risk evaluation in Indian context. Indian Journal of Nuclear Medicine, **19**, 16-18.
[44] Cottingham, K.L. (2013) Simple linear regression & replicated regression in SAS. http://www.dartmouth.edu/-bio129/computerlabs/CE1handout.
[45] Naula, S.C. (1991) Comparison of computer programs for simple linear regression. *Journal of Statistical Computation and Simulation,* **39,** 63-68.
http://www.tandfonline.com/do/abs/10.1080/00949659
[46] Chung, S.J. (2011) Computer program of nonlinear, curved regression for "probacent"-probability equation in biomedicine. *Journal of Biomedical Science and Engineering,* **4**, 620-630.
[47] Dixon, W.J. and Massey, J.F.J. (1957 *Introduction to Statistical Analysis,* McGraw-Hill, New York, 192-204, 226-227.
[48] Levin, S.G., Young, R.W. and Stohler, R.L (1992) Estimation of median human lethal dose computed from data on occupants of reinforced concrete structure in Nagasaki, Japan. *Health Physics,* **63**,522-531.
[49] Fujitan, S. Kato, H. and Schull, W.J. (1989) The LD_{50}associated with exposure to the atomic bombing of Hiroshima. *Journal of Radiological Research (Tokyo),***30**, 359-381.
[50] Hawking, S.W. (1988) *A Brief History of Time. Bantom Books,* 32-32, 53-61.
[51] Suplee, C. (1999) *Physics in 20th Century,* Hany N. Abrams, Inc., New York, 82.
[52] Chung, S.J. (2010) *The Book of Right Change: A New Philosophy of Asia,* Bloomington, Indiana, 10.
[53] Chung, S.J. (2012) Computer-assisted formulas predicting cancer mortality risk after exposure to acute low dose ionizing radiation in humans. Journal of Biomedical Science and Engineering, 5, 176-185