(Plenum Publishing Corporation, 1987)

CALIBRATION OF A RADIATION DETECTOR:

CHROMOSOME DOSIMETRY FOR NEUTRONS

Peter G. Groer

Center for Epidemiologic Research
Oak Ridge Assoc. Univs.
Oak Ridge, TN 37831

Carlos A. De B. Pereira

Operations Research Center
U. C. Berkeley
Berkeley, CA 94720

ABSTRACT

Calibrative densities for the unknown neutron dose D_f of an individual accidentally exposed to high doses (>20 rad) of neutrons are derived. These densities incorporate prior dose information (e.g., from a dosimeter reading, or from dose reconstruction efforts), information from an *in vitro* calibration experiment with neutrons of the same energy, and information from the number of dicentric chromosome aberrations y_f observed shortly (< 4 weeks) after exposure in a sample of n_f lymphocytes from the exposed individual. If Y, the number of dicentric aberrations induced by a known neutron dose d in n lymphocytes is assumed to be Poisson distributed ($Y \sim Po(n\alpha d)$) and if D_f and the parameter α are assumed to have gamma priors it is possible to give an analytic solution for the calibrative density $f(d_f|\mathcal{D})$. $\mathcal{D}$ consists of the calibration data and the observed aberrations in a sample of lymphocytes from the exposed individual. This density characterizes the remaining uncertainty about D_f after consideration of the prior information about D_f and α and of the data $\mathcal{D}$.

INTRODUCTION

After accidental exposures to low or high LET radiation it is desirable to obtain dose estimates for the accident victims. Estimation of doses is also mandated by regulations dependent on the

severity of the accident. Personal dosimeters and dose reconstruction by health physicists can provide initial information about the magnitude of the radiation doses. In this paper we take the view that this prior dose information should be combined with data on chromosome aberrations observed in a sample of lymphocytes from the accident victim(s) to reduce the uncertainty about the radiation doses to which the accident victims were exposed. Data on chromosome aberrations can be used to make inferences about radiation doses with the help of data from *in vitro* calibration experiments. In such experiments $n_i (i=1,2,\ldots N)$ lymphocytes are exposed *in vitro* to several fixed doses d_i and the resulting aberrations y_i are scored under the microscope. The resulting reduction in the dose uncertainty helps physicians to decide if and how the victim(s) should be treated.

DERIVATION OF THE CALIBRATIVE DENSITY

We are interested in obtaining an expression for the calibrative density[1] $f(d_f|\mathfrak{D})$. $\mathfrak{D}$ stands for all the data and consists of the following observed events:

$$\mathfrak{D} = \left\{(Y_1=y_1|D_1=d_1,n_1)\ldots.(Y_N=y_N|D_N=d_N,n_N),\ (Y_f=y_f|n_f)\right\}$$

The first N events correspond to the data from the "controlled" calibration experiment. In this experiment n_i cells are exposed to a neutron dose d_i which is accurately controlled by the experimenter. In the n_i cells so exposed y_i chromosome aberrations are observed. The last event consists of the observation of y_f chromosome aberrations in n_f cells of the accident victim who was exposed to an unknown neutron dose D_f . The subscript f is mnemonic for "future" and indicates that y_f is observed after the calibration experiment has been performed.

Derivation of the calibrative density for D_f , $f(d_f|\mathfrak{D})$ involves expressing this density in terms of other densities and probabilities using the rules of probability. First, we will give a general derivation without a specific model and priors. This derivation involves a model parameter α which will later be identified as the rate at which chromosome aberrations are produced after neutron irradiation.

$$f(d_f|\mathfrak{D}) = \int_0^\infty f(d_f,\alpha|\mathfrak{D})\, d\alpha$$
$$= \int_0^\infty f(d_f|\alpha,y_f,\mathfrak{D}')\, f(\alpha|y_f,\mathfrak{D}')\, d\alpha \qquad (1)$$

Where $\mathfrak{D}' = \mathfrak{D} - \{y_f|n_f\}$ stands for the calibration data and $\{y_f|n_f\}$ is abbreviated by y_f in Equ. (1). Since conditional on α, D_f is independent of $\mathfrak{D}'$, we can rewrite the last line of Equ. (1):

$$f(d_f|\mathfrak{D}) = \int_0^\infty f(d_f|\alpha,y_f)\, f(\alpha|y_f,\mathfrak{D}')\, d\alpha$$
$$= \int_0^\infty \frac{p(y_f|d_f,\alpha)\, f(d_f|\alpha)}{p(y_f|\alpha)} \cdot f(\alpha|y_f,\mathfrak{D}')\, d\alpha$$
$$= \int_0^\infty \frac{p(y_f|d_f,\alpha)\, f(d_f)}{p(y_f|\alpha)} \cdot \frac{p(y_f|\alpha,\mathfrak{D}')\ \ f(\alpha|\mathfrak{D}')}{p(y_f|\mathfrak{D}')}\, d\alpha$$
$$\propto f(d_f) \int_0^\infty p(y_f|d_f,\alpha)\, f(\alpha|\mathfrak{D}')\, d\alpha \qquad (2)$$

Equ. (2) states that the calibrative density is proportional to the prior density for D_f and the predictive density for a future number of chromosome aberrations y_f. The predictive distribution incorporates, of course, the information from the calibration experiment through the posterior distribution $f(\alpha|\mathfrak{D}')$. For the derivation of Equ. (2) we assumed that the prior for D_f does not depend on α. We proceed now to insert the appropriate model and the prior distributions used into Equ. (2) to obtain the special form of $f(d_f|\mathfrak{D})$ which applies to dose estimation after neutron irradiation.

In the literature on cytogenetic dosimetry (see e.g. Ref. 2) we found that a Poisson model for Y, the number of chromosome aberrations induced, is used for all types - high or low LET - of ionizing radiation. In the case of neutron exposure this model is:

$$Y|(\alpha,n,d) \sim Po(n\alpha d) \qquad (3)$$

In words the Poisson mean is proportional to the neutron dose d delivered to the n cells. This simple model neglects the background rate of chromosome aberrations. Since the background frequency is in

the range of 1 to 2 per thousand cells,[3] it can be neglected for doses of 20 rads and more. We judged gamma priors for α and D_f: $\alpha \sim Ga(a,b)$, $D_f \sim Ga(A,B)$. The gamma family of distributions is rich enough to be able to express a multitude of judgements about the uncertainty surrounding α and D_f and in addition it provides for the Poisson model the usual mathematical conveniences of a family of conjugate prior distributions.

Inserting the Poisson model for Y and the priors for α and D_f into Equ. (2) one finds:

$$f(d_f|\mathfrak{D}) \propto d_f^{\mathfrak{B}-1} (d_f + \mathfrak{a})^{-\mathfrak{b}} \exp(-Ad_f) \qquad (4)$$

where $\mathfrak{B} = B + y_f$, $\mathfrak{a} = a/n_f$ with

$$\mathfrak{a} = a + \sum_{i=1}^{N} n_i d_i \quad \text{and} \quad \mathfrak{b} = \sum_{i=1}^{N} y_i + y_f + b \ .$$

The mode of $f(d_f|\mathfrak{D})$ occurs at

$$d_M = \left[-\mathfrak{C} + \sqrt{(\mathfrak{C}^2 + 4A\mathfrak{a}(\mathfrak{B}-1)} \right] / 2A$$

with $\mathfrak{C} = A\mathfrak{a} + \mathfrak{b} + 1 - \mathfrak{B}$

In the following section we will use Equ. (4) for a particular calibration experiment and show graphs of $f(d_f|\mathfrak{D})$ for different observed y_f and n_f.

EXAMPLE

The example is based on a hypothetical radiation accident with a ^{210}Po-Be neutron source. Readout of the neutron dosimeter worn by the victim and subsequent calculations by Bayesian health physicists based on calibration data for the neutron dosimeter and the geometry of the accident yielded a calibrative density $f(d_f)$ for the unknown dose D_f to the lymphocytes of the victim which could be approximated by a $Ga(A = .1, B = 10)$. This gamma density becomes the prior for the subsequent analysis of dicentric chromosome aberrations in a

sample of lymphocytes from the victim. In $n_f = 104$ metaphases a cytogenetic technician scored $y_f = 64$ dicentric aberrations shortly after the accident. Based on calibration experiments with other types of radiation the prior distribution for α was judged to be $Ga(a = 1000 , b = 10)$. As stated already earlier $Y \sim Po(n\alpha d)$ is the statistical model. This model is thought to be valid for a wide range of neutron doses.[2] If this model, the gamma priors for α and

TABLE 1. Calibration data for Po-Be Neutrons (from reference 2)

dose d_i (rad)	Cells n_i	Dicentrics y_i
50	269	109
75	78	47
100	115	94
150	90	114
200	84	138
250	59	125
300	37	97

D_f and the calibration data[2] shown in Table 1 are used one obtains the calibrative density shown in Fig. 1 from Equ. (2). Fig. 1 shows also the prior density for D_f . Both densities are divided by $f(d_M|\mathfrak{D})$ where d_M is the modal dose. Fig. 2 shows $f(d_f|\mathfrak{D})$ for $y_f = 8$ dicentrics in $n_f = 13$ metaphases. This density is clearly wider than $f(d_f|\mathfrak{D})$ shown in Fig. 1. In practice the calibrative densities could be updated sequentially and scoring of metaphases could stop whenever the physician is satisfied by the obtained precision.

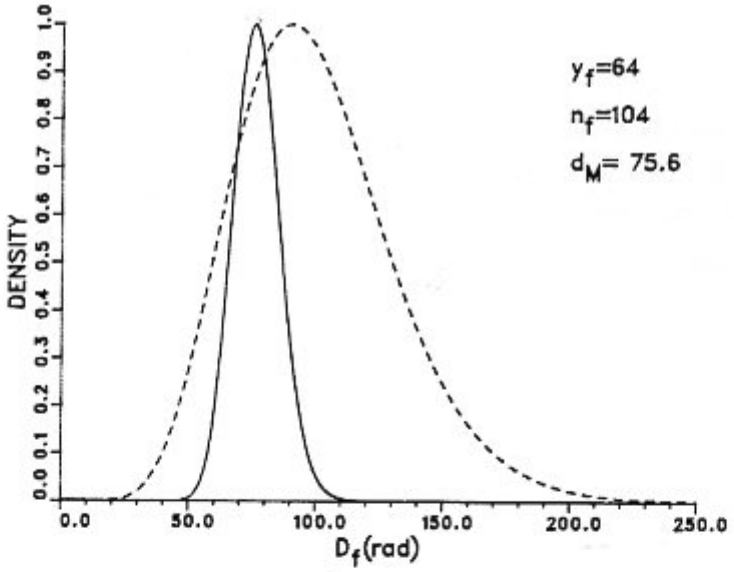

Fig. 1 : Prior and calibrative density for D_f with $y_f = 64$ and $n_f = 104$.

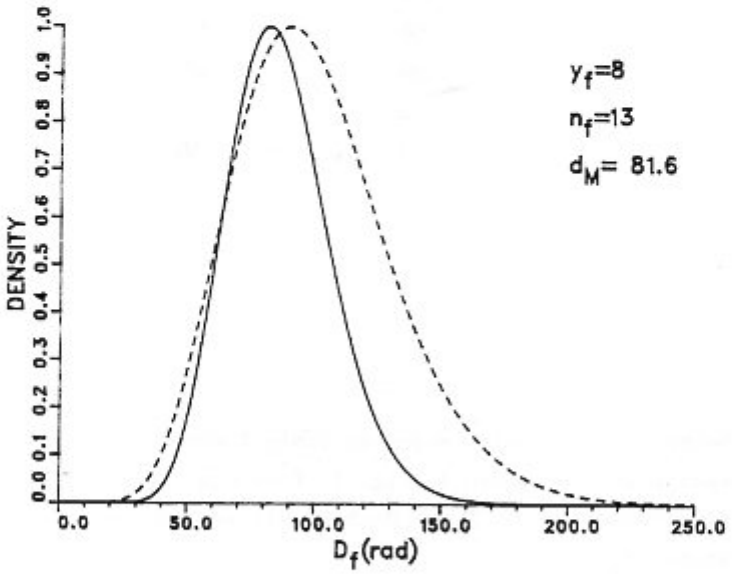

Fig. 2 : Prior and calibrative density for D_f with $y_f = 8$ and $n_f = 13$.

SUMMARY

We derived calibrative densities for the unknown neutron dose D_f of a hypothetical accident victim and pointed out that it is possible to obtain analytic solutions for this type of radiation if gamma priors and the "public" Poisson model from the cytogenetic literature are used. Our calculations neglected the small background frequency and are therefore only valid for doses which evidence a much greater number of aberrations. Incorporation of a background rate α_o into the analysis would extend the results to lower doses. This extension is presently under investigation. Another extension involves exposure to so-called low LET radiation like γ- and X-rays. For this case the public model[2] is $Y \sim Po[n(\alpha_o+\alpha d+\beta d^2)]$ and $f(d_f|\mathcal{D})$ cannot be given in closed form.

It is standard practice to estimate doses for accident victims by deterministic procedures using a maximum likelihood estimate for the model parameters. In our example this would give $\hat{d}_f = y_f/(n_f\hat{\alpha})$ as our estimate of the neutron dose. With this procedure the uncertainty about D_f cannot be specified and other information about D_f from a personal dosimeter or from dose reconstruction efforts cannot be incorporated.

ACKNOWLEDGEMENTS

We wish to thank Drs. Michael Bender, Gayle Littlefield and Julian Preston for teaching us the essentials of cytogenetic dosimetry. Without their knowledge, encouragement and patience this work would not have been possible. Support for this work was provided by the National Cancer Institute under interagency agreement 40-849-85, NCI No. Y01-CP-50512 with the U.S. Department of Energy and by contract No. DE-AC05-760R00033 between the U.S. Department of Energy Office of Energy Research and Oak Ridge Assoc. Univs.

REFERENCES

1. Aitchison, J., and Dunsmore, I.R., *Statistical Prediction Analysis*, Cambridge University Press, Cambridge (1975).

2. Edwards, A.A., Lloyd, D.C., and Purrot, R.J., 1979, "Radiation induced chromosome aberrations and the Poisson distribution," *Rad. and Environ. Biophys.*, 16:80.
3. Bender, M.A., Preston, R.J., Leonard, R.C., and Shelby, M.D., 1986, *Chromosomal aberration analysis in peripheral lymphocytes of a large control population*, unpublished manuscript, Brookhaven National Laboratory, Upton, New York.