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# Notes on the Effect of Dose Uncertainty[1]

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## Abstract

The apparent dose-response relationship between amount of exposure to acute radiation and level of mortality in humans is affected by uncertainties in the dose values. Some possible magnitudes of these effects are numerically demonstrated.

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It is apparent that one of the greatest concerns regarding the human data from Hiroshima and Nagasaki is the unexpectedly shallow slope of the dose response curve. This may be partially explained by uncertainty in the dose estimates. In the following, we will demonstrate some potential effects of dose uncertainty on the apparent dose-response relationship.

For purposes of demonstration, we shall assume a "real" $LD_{50}$ of 300 cGy. Also, suppose that the slope is such that the ratio $LD_{90}/LD_{10}$ is 1.9. This value is an estimate for 70 kg animals at a dose rate of 50 R/min based upon our earlier analysis of animal studies [1], and is consistent with estimates of other investigators. A final assumption is that the real dose response relationship follows a probit model. These assumptions lead to the "true" dose response model graphed in Figure 1. Our intention is that this hypothesized model be fairly consistent with most current estimates of the dose-response relationship in man; minor changes in the hypothesized model would induce small changes in what follows, but should not change the pattern or rough magnitude of results.

The central question is: What effect would the possible uncertainties in dose estimates have on the "apparent" dose response function? By apparent function, we mean the dose response function that would be observed based upon unlimited data — the result of a perfect analysis of a perfect and infinite data set, with the exception that dose values are subject to error. The first point to be addressed then is the type and magnitude of errors likely to be present in the data.

Although a number of potential sources for dose error exist, we shall consider two grouped sources. The first will be called "external" error, and includes primarily uncertainties in weapon yield and ground transport. The second will be called "interior" error, and includes building penetration, and personnel locations and orientations. External error in certain instances could be thought of as "common" error; if one person's dose estimate is 5% high because of uncertainty in weapon yield, then this should apply to all persons subject to the same exposure. Interior errors are perhaps more reasonably treated as random, in the sense that they create independent problems in each estimated dose. This treatment is, of course, at least somewhat over-simplified; external errors may be a bit different as they apply to different buildings, particularly if the location of the explosion epicenter is uncertain, and interior errors for two persons located near each other in the same building could well be correlated. However, this does not seem an unreasonable separation of common and individual errors for these purposes.

Some recent calculations have resulted in "educated guesses" of the possible magnitudes of these uncertainties for the data from the Chinzei and Shiroyama schools in Nagasaki [2]; these are about 15% for external uncertainty and about 20% for interior uncertainty. These figures represent uncertainty in internal doses as opposed to free-in-air calculations. Also, they are intended to represent the standard deviations associated with uncertainty sources. For example, if external

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error is really +15%, and interior error has a standard deviation of 20%, we can think of "apparent" dose as being the "real" dose multiplied by an unobservable random factor with a mean of 1.15 and a standard deviation of .20. This is the approach we've taken in the following calculations; details are given in the Appendix.

Table 1 shows the effects of -15%, 0%, and +15% external uncertainty combined with 20%, 30%, 40%, and 50% interior uncertainty on the value of the ratio $LD_{90}/LD_{10}$. Recall that we started with a "real" value of 1.9; the table shows the percentage increase of the "apparent" value. The uncertainties suggested in [2] suggest that this ratio shouldn't be inflated by more than about 30%. However, if interior uncertainty is as much as 50%, the apparent $LD_{90}/LD_{10}$ could be doubled.

Table 2 more directly addresses possible effects on the slope of the dose response curve. Entries in this table are percentage increases in the apparent interquartile range, i.e. $LD_{75} - LD_{25}$. Since "slope" in the middle region of the dose response curve can be expressed as the inverse of this quantity, a doubling of the interquartile range (increase of 100%) corresponds to a halving of the slope, and so forth. The uncertainties suggested by [2] indicate that the apparent interquartile range should be increased by no more than about 50% due to dose uncertainty. If interior uncertainty is closer to 50%, the interquartile range could be doubled.

It is clear that if the slope of the apparent dose response curve is significantly affected, then estimates of high and low lethal doses must be considered to be questionable. For example, if the slope is half what it should be, then the difference between apparent $LD_{90}$ and $LD_{10}$ is twice what it should be, and at least one of these apparent values must be considerably different than its real counterpart. However, it must be noted that uncertainties of this magnitude also have some effect on the apparent $LD_{50}$ as well. Table 3 contains percentage increases and decreases of the apparent $LD_{50}$ due to dose uncertainty; recall that we started with a true value of 300 cGy. Even based upon the suggested uncertainty values, there could be as much as a 20% error in the apparent $LD_{50}$ due to dose uncertainty.

One other point should be made about the potential effects of dose uncertainty. When a random component of dose uncertainty is present which is multiplicative in its action (e.g. 20% standard deviation), the *shape* of the dose response curve is also changed. Recall that we started with a symmetric probit model for the true dose response relationship — this seemed to us to be the model which performed "best" in most of the animal studies. Figure 1 shows the apparent dose response relationship which results from +15% external uncertainty and 40% interior uncertainty, along with the original true dose response curve for comparison. As noted above, the slope of the apparent curve is considerably flatter than that of the true curve, but note that the apparent curve is also skewed with a longer tail at the high-dose end. Hence the apparent curve actually looks more like, say, a log-probit model, even though the "real" dose response function in this hypothetical case is an untransformed probit model.

Considerable effort has been spent by investigators in calculating dose estimates for human radiation exposures. These calculations are often quite sophisticated, and account for considerable detail in geography, building structure, et cetera. However, the problem is extremely complex, uncertainties are present, calculated uncertainties are themselves uncertain, and the possible effects of these points on our final estimates need to be considered.

## References

[1] Morris, M.D. and Jones, T.D. (1987). "Prediction of the Mortality Dose-Response Relationship in Man due to Nuclear Radiation", Manuscript in preparation.

[2] Rhodes, W.A. (1987). Presentation at the Defense Nuclear Agency's $LD_{50}$ Workshop, March 9, 1987.

## Appendix

Every non-decreasing dose response function which either reaches or asymptotically approaches 0 for low enough dose and 1 for high enough dose corresponds to a distribution of tolerances in individuals. The probit model corresponds to a normal distribution of tolerances, the Weibull model to a Weibull distribution, et cetera. In choosing the probit model, we are actually claiming that each individual in the population has a "tolerance" dose — if he is exposed to a lesser dose he survives and if he is exposed to a greater dose he dies — and that these tolerance doses are normally distributed across the population. Since the uncertainties discussed in these dosimetry analyses have been expressed as percentage values, it is apparent that they can be represented by multiplicative factors. Hence the "apparent" tolerance for an individual is his "true" tolerance multiplied by a random variable with the mean chosen to be 1 plus common error in dosimetry, and a standard deviation equal to the random error. We have used the log-normal distribution to represent these multiplicative errors, due primarily to convention; a different distribution could have been used resulting in somewhat different results. So, the apparent distribution of tolerances is the distribution of the product of two random variable, $T \times E$. Here $T$ is normally distributed with mean of 300 rads and standard deviation of 73 rads (our true distribution of tolerances) and $E$ is log-normally distributed with mean of $1 + S$ and standard deviation of $R$, where $S$ is systematic error represented as a fraction and $R$ is the standard deviation of random error. The apparent dose response curve is then the cumulative distribution function of this product. For these results, this distribution was calculated by Monte Carlo simulation. A total of 10,000 independent normal values were generated, and each multiplied by a corresponding independent log-normal value. The resulting cumulative distribution of values should very closely approximate the function which would be found analytically (if it is actually possible to do so).

Table 1: Percentage Increases in Apparent $LD_{90}/ LD_{10}$.

| External Sources | Interior Sources | | | |
|---|---|---|---|---|
| | 20% | 30% | 40% | 50% |
| -15% | 28 | 59 | 99 | 151 |
| 0% | 20 | 44 | 75 | 111 |
| +15% | 16 | 34 | 58 | 86 |

Table 2: Percentage Increases in Apparent Interquartile Range.

| External Sources | Interior Sources | | | |
|---|---|---|---|---|
| | 20% | 30% | 40% | 50% |
| -15% | 16 | 39 | 64 | 83 |
| 0% | 28 | 52 | 76 | 98 |
| +15% | 41 | 64 | 87 | 111 |

Table 3: Percentage Changes in Apparent $LD_{50}$.

| External Sources | Interior Sources | | | |
|---|---|---|---|---|
| | 20% | 30% | 40% | 50% |
| -15% | -19 | -22 | -25 | -29 |
| 0% | -4 | -6 | -10 | -13 |
| +15% | +12 | +9 | +6 | +2 |

Fig 1: True and Apparent Dose Response Curves