

ELIMINATING BIAS IN ROUTINE BIOASSAY WHEN THERE IS AN UNKNOWN TIME OF INTAKE

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Abstract— Routine bioassay programmes sometimes find evidence of an unsuspected intake. If there were no workplace indicators of exposure or intake, it is necessary to assume a value for the time of intake. Under these circumstances, the International Commission on Radiological Protection (ICRP) continues to recommend using the midpoint of the interval between routine bioassay measurements (ICRP Publication 78, paragraph 106). The assumption of $T/2$ as the time of intake, where T is the interval between bioassay measurements, represents the *expectation value of the time of intake*, $\langle t \rangle$, assuming uniform probability of an intake at any given time. This assumption results in a modest bias, of the *expectation value of the intake*, $\langle I \rangle$, that would have been received by a population of workers who had uniform probability over time of intake. This underestimation leads to a negative or positive bias in dose estimates derived in this fashion. The bias is characterised for realistic, routine urinalysis programs for Pu, U and ^3H , as well as for *in vivo* measurements of ^{125}I , ^{131}I and ^{137}Cs . Simple numerical methods are presented for correcting the bias. The bias is greatest for radionuclides whose half-lives are short with respect to the interval between bioassay measurements. Since the primary concern is estimating intake rather than time, the assumed time of intake should be chosen as $t_{(I)}$ rather than $T/2$. The ICRP should consider revising some of the tables in its Publication 78 to reflect this.

INTRODUCTION

Routine bioassay programmes sometimes find evidence of an unsuspected intake. In order to infer the value of that intake, it is necessary to assume a value for the *time* of intake if there were no workplace indicators of exposure or intake. Under these circumstances, the International Commission on Radiological Protection (ICRP) continues to base its recommendations on the assumption of a single acute intake occurring at the midpoint of the interval between routine bioassay measurements (ICRP Publication 78, paragraph 106)⁽¹⁾. The assumption of $T/2$ as the time of intake, where T is the interval between bioassay measurements, represents the *expectation value of the time of intake*, $\langle t \rangle$, if one assumes a uniform probability of an intake at any given time.

This paper characterises the bias for routine urinalysis programs for Pu, U and ^3H , as well as for *in vivo* measurements of ^{125}I , ^{131}I and ^{137}Cs . A simple formula is presented for correcting the bias. In virtually all cases presented here, the ICRP Publication 78 assumption results in a modest bias in estimating *expectation value of the intake*, $\langle I \rangle$, that would have been received by a population of workers who had uniform probability of intake over the time between bioassay measurements. This leads to a negative or positive bias in effective dose estimates derived using the ICRP assumption.

THE PROBLEM

Unexpected intakes may be revealed by routine bioassay programmes. Such events usually have an unknown

time course of intake. Often one assumes that a single acute intake occurred at time t , during the interval T between bioassay results. The discussion that follows assumes that there have been no prior intakes by the individual in question that affect the measured quantity m .

The ICRP⁽¹⁾ recommends the assumption that t be the midpoint between bioassay samples, i.e. $T/2$. The ICRP recommendation amounts to the assumption that the unknown time of intake is the expectation value of t , $\langle t \rangle$, over the interval T given uniform probability of time of intake. The ICRP assumption leads to a bias whose size depends on intake retention function $\text{IRF}(t)$, i.e. (Bq in compartment/Bq of intake) or (Bq/day excreted/Bq of intake) for the bioassay compartment in question.

An alternative to the ICRP assumption of $t = T/2$ is to assume that the intake occurred at the time, $t_{(I)}$, at which the expectation value of intake, $\langle I \rangle$, occurs. In general, $t_{(I)} \neq T/2$, so $\langle I \rangle \neq I(\langle t \rangle) = I(T/2)$.

NUMERICAL APPROACH

Using the software package IMBA-Expert⁽²⁾, intake retention functions for appropriate bioassay compartments were evaluated for ^3H , ^{125}I , ^{137}Cs , ^{234}U and ^{239}Pu for days 1 through 365 following an acute inhalation intake. The ratio $\langle I \rangle / I(\langle t \rangle)$ should be 1 if the ICRP assumption that the intake occurred at $T/2$ is adequate.

If m represents the bioassay quantity measured, then an intake can be inferred from the *intake retention function*, $\text{IRF}(t)$, for that bioassay compartment:

$$I = \frac{m}{\text{IRF}(t)}$$

The discussion that follows assumes that there have been no prior intakes by the individual in question that

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affect the measured quantity m . Estimating $\langle I \rangle$ for an intake that may have occurred on any day from 1 to D requires estimating $\langle 1/IRF \rangle$, the expectation value of $1/IRF$ for this time period:

$$\begin{aligned} \langle I \rangle &= m \int_0^T \frac{dt}{IRF(t)} \left(\int_0^T dt \right)^{-1} \\ &\approx m \sum_1^D \frac{1}{IRF(d)} \left(\sum_1^D 1 \right)^{-1} = \frac{m}{D} \sum_1^D \frac{1}{IRF(d)} = m \langle 1/IRF \rangle. \end{aligned}$$

The quantity $\langle 1/IRF \rangle$ can be evaluated numerically. It is important to recognise that, in general, $\langle 1/IRF \rangle \neq 1/\langle IRF \rangle$.

MAGNITUDE OF THE BIAS

To evaluate the magnitude of the bias introduced by the $T/2$ assumption, one can evaluate

$$\frac{\langle I \rangle}{I(\langle t \rangle)} = \frac{\langle 1/IRF \rangle}{1/IRF(\langle t \rangle)}$$

The ratio on the right-hand side of this equation equals 1 if the $T/2$ assumption is adequate; the intake is underestimated if this ratio is greater than 1. Values of the ratio are shown in Table 1. The bias is most severe for radionuclides whose half-life is short compared with the interval between bioassay measurements, e.g., ^3H and ^{131}I . For uranium, doses may be underestimated by 10% for annual urinalysis.

DISCUSSION

The existence of large uncertainties elsewhere in the inference of dose from intake do not justify introducing an additional bias, whatever its size. One should be technically correct where possible and when it is not burdensome.

By using $t_{(D)}$ instead of $T/2$, as implemented in the expectation value of the reciprocal of the intake retention function over the time interval in question, one can avoid the bias. Modern software easily computes $t_{(D)}$, which results in an estimate of intake that is unbiased, i.e. correct on the average. Furthermore, it is fairer to workers to do the best job one reasonably can in inferring intake and dose from bioassay measurements.

Finally, even this solution doesn't solve the problem of using uncertain doses in a regulatory framework.

CONCLUSION

ICRP should consider revising its recommendation to assume an intake occurred at the midpoint of the time interval.

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Table 1. The ratio $\langle 1/IRF \rangle/[1/IRF(\langle t \rangle)]$ for some common radionuclides, bioassay compartments, and sampling intervals.

Nuclide	Type	Compartment	Days between bioassay results						
			7	15	31	61	91	183	365
^3H	F	Whole body	1.01	1.04	1.17	1.59	1.87	1.66	3.79
^{125}I	F	Thyroid	1.01	1.01	1.01	1.05	1.11	1.51	3.92
^{131}I	F	Thyroid	1.03	1.09	1.39	2.98	8.02	281	—
^{137}Cs	F	Whole body	0.96	0.97	0.98	1.00	1.01	1.06	1.24
U-nat	S	Urine	0.85	1.05	1.02	1.07	1.09	1.10	1.09
^{239}Pu	M	Urine	1.09	0.98	0.82	0.90	0.93	0.96	0.96

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