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ASSESSMENT OF PLUTONIUM EXPOSURES FOR AN EPIDEMIOLOGICAL STUDY OF US NUCLEAR WORKERS

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An ongoing case–control study evaluating the association between workplace external radiation exposures and leukaemia mortality required an assessment of internal plutonium exposures as a potential confounder. Of the study participants, 1092 were employed at four Department of Energy sites where plutonium-bearing materials were processed or stored. Exposures were assessed by first categorising exposure potentials based on available bioassay data, then estimating doses for workers in the highest categories using recent recommendations of the International Commission on Radiological Protection. Given the aetiology of leukaemia, equivalent dose to active bone marrow was chosen as the exposure variable. There were 556 workers each with at least one plutonium bioassay result, assigned to one of three evaluation categories. Dose estimates were made for 115 workers resulting in a collective equivalent dose of 2.1 person-Sv for 2822 exposure-years, compared with 29.8 person-Sv estimated from photon exposures. Modelling uncertainties were examined by comparison of results from independent analyses and by Monte Carlo simulation.

INTRODUCTION

The National Institute for Occupational Safety and Health (NIOSH) is conducting a multi-site case–control study to evaluate the relationship between protracted workplace external radiation exposure and leukaemia mortality. Study subjects (1269) were radiation workers, hired before the late 1970s, selected from the Portsmouth Naval Shipyard (PNS) in Kittery, Maine and four Department of Energy (DOE) nuclear facilities: Hanford Site, Savannah River Site (SRS), Oak Ridge National Laboratory (ORNL) and the Los Alamos National Laboratory (LANL). The study design excluded sites that had substantial groups of workers with the potential for internal exposures[1]. However, some workers were potentially exposed to plutonium during work involving nuclear weapons production. To investigate whether these exposures may confound a relationship between leukaemia mortality and external exposures, study subjects were categorised by the exposure potential and dose estimates were calculated for those who were most likely to be exposed. Owing to the aetiology of leukaemia, the equivalent dose to the haematopoietic bone marrow was estimated.

BACKGROUND

Previous studies of nuclear workers have used several methods for conducting retrospective plutonium exposure assessments. In a study of mortality among plutonium workers at the Rocky Flats Plant, Wilkinson *et al.*[2] separated workers into dichotomous categories using a systemic plutonium deposition of 74 Bq, as did Wiggs *et al.*[3] in a mortality study of white male workers at LANL. The threshold was chosen because systemic burdens <74 Bq were not considered reliably measured by urine bioassay[2,3]. More recently, studies of plutonium workers at the Russian Mayak facilities have used multiple body burden categories[4,5].

Wing *et al.*[6] used job titles, work areas and time periods to assign exposure categories while investigating an association of plutonium-related work and mortality at Hanford. Using work histories and information on facility processes and health physics monitoring practices, Wing *et al.*[6] assigned workers to three exposure categories: (1) minimal potential for exposure to plutonium; (2) non-routine or limited potential for exposure to plutonium and (3) routine potential for exposure to plutonium.

Omar *et al.*[7] used plutonium bioassay sample data and the standard metabolic models described in ICRP Publication 48[8] to estimate doses to plutonium workers at the Sellafield plant in UK. This approach allowed for summation of external and internal doses for use in the epidemiological analysis. Most recently, Brown *et al.*[9] assessed the annual equivalent dose to the lung for workers in a case–control study of lung cancer mortality at a major US plutonium processing facility. Brown *et al.* used bioassay data to metabolically model effective intakes and organ equivalent doses according to the

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dosimetry methods described in ICRP Publication 30. The ICRP has now revised its earlier recommendations, providing improved dosimetric models[10].

Except for Wing *et al.*, these studies relied on actual bioassay data or subsequent estimates obtained from bioassay data to assess plutonium exposures. Historically, operating facilities developed bioassay methods suitable to the physical and chemical form of the plutonium being produced or handled at their sites. However, chemists and health physics staff within DOE facilities would occasionally share experiences, resulting in some general similarities in analytical methods among facilities and across time. This is particularly true of urine excretion collection, chemical extraction and radioactivity determination during the developmental years of plutonium bioassay. Therefore, urine sample data were selected as the most consistent basis for the plutonium exposure assessment.

METHODS

Study subject selection

The study population consists of radiation workers selected as cases or controls in an epidemiological study of the association of leukaemia mortality and external ionising radiation exposures. Cases were defined from the population of monitored workers with a minimum of 30 d employment at one or more of the study sites. Four age-matched controls for each leukaemia case were randomly selected from risk sets defined from the cohort of workers using incidence density sampling[11]. Radiation exposure was assessed only to the date the control reached the index case age at death (cut-off date). In instances in which matched controls were selected more than once, exposures were assessed to the latest cut-off date assigned in the present analysis.

Records review

Plutonium urinalysis methods and all available bioassay data pertaining to the study subjects were assembled and coded into a relational database. Data were available in both hard copy and electronic format, with hard copy data chosen as the primary record source for all facilities except LANL. Records for LANL study subjects were mostly provided electronically with some additional hard copy information available in medical records. Therefore, electronic records from LANL were adopted as the primary record source and the medical records were used for comparison purposes only.

Historical documentation, dosimetry records and medical records were evaluated to discover information pertaining to known incidents or confirmation of plutonium deposition. Site records were reviewed to glean information on most prevalent plutonium compounds, bioassay methods, sample collection frequencies, chemical extraction and recovery, counting techniques, reporting requirements and detection levels. This information was used to develop thresholds for evaluation category assignments, and to examine bounds for assumptions and generalisations necessary to normalise exposures across facilities.

Category assignment

Study subjects were separated into four evaluation categories based on the distribution of available bioassay data. Detection and reporting thresholds were considered in the category definition to limit potential data misclassification. Category III consists of study subjects having at least one plutonium excretion result >17 mBq d^{-1} ($\sim$1.0 d.p.m. per 24 h excretion volume). Category II contains study subjects with sample results between 17 and 1.7 mBq d^{-1}. Category I contains the remainder of the study subjects with bioassay results ≤ 1.7 mBq d^{-1}. A fourth category (Category IV) comprised workers with no available bioassay data. For this study, exposures to workers within Category IV were assumed *de minimus*.

Dosimetry

The equivalent dose to active bone marrow was assessed for all study subjects with detectable plutonium urinary excretion ≥ 1.7 mBq d^{-1} (i.e. Categories II and III). Given low expected doses and the uncertainties associated with bioassay at or near detection levels, exposures to Category I workers were not quantified for the epidemiological analysis. Several study subjects were identified with multiple depositions involving various routes of entry and plutonium isotopic composition. The dose assessment performed for these workers required evaluation of several intake scenarios. The dose estimates were calculated using a computer spreadsheet that incorporated plutonium retention functions, excretion functions and dose conversion coefficients developed from the computer program Integrated Modules for Bioassay Analysis (IMBA) from the software package IMBA Expert OCAS Edition[12].

Intakes and subsequent doses were calculated from urine bioassay data using recent ICRP biokinetic models and available data regarding plutonium solubility, isotopic composition, date and route of exposure and remedial actions taken (i.e. tissue excision and/or chelation). Current ICRP default parameters were maintained for aerosol and deposition parameters, particle transport parameters[13], GI-tract parameters[14], biokinetic model parameters[15,16], radiation weighting factors[10] and

tissue weighting factors[10,17]. Any additional assumptions needed for the dose assessment were based on the observed patterns of excretion and knowledge of source term and work assignments. A deposition of a single plutonium isotope, either ^{239}Pu or ^{238}Pu depending on source term information, was assumed unless information in site records suggested otherwise. In lieu of source term information, ^{239}Pu was assumed.

Additionally, three general assumptions were made unless contradicting information was available. First, the route of entry was assumed to be inhalation since it was the pre-dominant pathway for recorded exposures. Second, intakes were assumed to occur 3 d prior to their associated first 'positive' bioassay sample because records suggest that incident sampling usually began the shift following the incident and, at times, up to 3 d could be required to collect a sufficient sample for analysis. The associated first positive sample is the sample used to indicate a potential intake or the first sample following a known incident. Third, the inhaled materials exhibited solubility best characterised by 50% Type M (moderate rate of absorption into blood) and 50% Type S (slow absorption). This assumption was based on the examination of facility records that suggested the most prevalent form of plutonium among work locations was moderately soluble (Type M) and that some oxides could be present. The solubility assumption was applied only when materials were unknown and a 'best-fit' excretion curve could not be determined. The range of uncertainty associated with the solubility assumption was tested by varying the solubility and comparing results from IMBA. For equivalent dose to active bone marrow from plutonium uptake, an overestimate of $<10\%$ was observed when assuming a 1:1 ratio of Type M and Type S materials for an uptake of solely Type M material.

The general assumptions also provided a means to compare bioassay categories. Each category may include workers with a large range of bone marrow doses from incorporated plutonium. For perspective, the exposure categories can be related to estimated doses using the standard assumptions. For example, the 50 y committed equivalent dose to bone marrow per excretion was 0.78 mSv per mBq d^{-1} assuming recent ICRP default parameters and (1) each bioassay result represents total daily excretion from a single uptake; (2) the route of entry was inhalation; (3) the bioassay data collection occurred 3 d following intake and (4) the inhaled material was 50% Type M and 50% Type S fresh weapons grade plutonium. Under these conditions, Category III corresponds to a committed equivalent dose to the active marrow >13.0 mSv and Category II is between 13.0 and 1.3 mSv as indicated in Table 1.

Table 1. Exposure categories based on bioassay data.

Exposure category	Pu excreta level (x)	Minimum H_{rbm} (50 y) (mSv)
I	Monitored, but $x < 1.7$ mBq d^{-1}	0
II	1.7 mBq d$^{-1} \leq x < 17$ mBq d^{-1}	1.3
III	$x \geq 17$ mBq d^{-1}	13
IV	Non-monitored	Unknown

Table 2. Isotopic composition (wt%) of four grades of plutonium.

Isotope	Weapons grade[a]	Reactor grade[a]	Commercial grade[a]	Heat source[b]
^{238}Pu	0.05	0.10	1.00	90.00
^{239}Pu	93.10	84.80	55.00	9.10
^{240}Pu	6.00	12.00	26.00	0.60
^{241}Pu	0.80	3.00	13.00	0.03
^{242}Pu	0.05	0.10	5.00	<1.00

[a]Nominal plutonium mixtures immediately following separations[18]
[b]Nominal plutonium mixture for isotopic heat source from DOE-STD-1128-98 (see Table 2.1[19])

Tests were performed to ensure that spreadsheet calculations were comparable with results from IMBA given identical input data. Estimates of annual doses were compared with the results of reference cases processed using IMBA. The reference cases consisted of a series of models used to determine the annual doses to active bone marrow from an inhalation of weapons grade plutonium (Table 2). Activity fractions were determined from the plutonium weight percentages reported by Carbaugh[18] and the DOE[19] allowing for decay and subsequent build-up of ^{241}Am after 10 y.

Recorded penetrating dose estimates from photon exposures were extracted from available site records for comparison with plutonium dose estimates. The external dose values were adjusted from the recorded results only by conversion to SI units. It is understood that these dose estimates best represent whole-body exposures and are likely to overestimate doses to the active bone marrow[20]. Additional uncertainties in dose estimates across facilities and time are likely to result from exposures to heterogeneous radiation fields, calibration methods, dosemeter design and the dosemeter energy response characteristics[21–23]. Also, some study subjects received radiation exposures from sources other than photons or internally deposited plutonium. Although important for the final epidemiological study, these uncertainties are not addressed at this time given the simple comparisons intended.

Table 3. Assumptions used in Monte Carlo simulation of plutonium depositions.

	Variable[a]	Distribution	Distribution assumptions
1	Plutonium mixture	Single point (discrete)	Where the likelihood of observation varies such that weapons grade is observed 70% of the time, fuel grade 20% and commercial grade 10%
2	Age of mixture	Triangular	Time (t) = 0 is assumed most likely and the maximum mixture age is 10 y
3	Intake date	Uniform	From the date of the first bioassay sample following an assumed intake to 7 d prior
4	Insoluble fraction	Triangular	The fraction of Type S materials (f_s) varied from zero to unity with zero most probable. The fraction of Type M materials is assumed equal to the quantity $1-f_s$
5	Sample yield	Normal	Where the arithmetic mean is unity with a 95% confidence interval of 0.8–1.2 (±20%)
6	Sample background counts	Normal	Where the arithmetic mean is assumed equal to the total background counts of the counting system and the standard deviation is equal to the square root of the arithmetic mean
7	Reagent background count rate	Normal	Where the arithmetic mean is assumed equal to 0.01 c.p.m. (assigned by site analyst) with a 95% confidence interval of 0.008–0.012 c.p.m. (±20%).
8	Sample gross counts	Normal	Where the arithmetic mean is equal to the total gross counts of the sample and the standard deviation equals the square root of the arithmetic mean
9	Bioassay reported result	Normal	Where the arithmetic mean is assumed equal to the reported values with a 95% confidence interval of ±40%

[a]Variables 6, 7 and 8 were preferred when actual counting system data were available. In lieu of counting data it was assumed that the bioassay results were subject to 40% error (Item 9)

Statistical methods

Two sets of dose estimates for workers in Category III were calculated independently by two dosimetrists, one using IMBA and the other using the computer spreadsheet calculations. Each dosimetrist had access to dosimetry records, medical records and site historical information, and was free to independently adopt any modelling assumptions in support of their dose calculations. The paired-samples, formed by subtracting the spreadsheet dose calculation (primary estimate) from the IMBA dose calculation (secondary estimate), were examined to evaluate the precision of the dose estimates and to investigate the validity of any assumptions that were adopted in calculating dose. Any large variations in paired-samples were examined by both dosimetrists for the presence of errors in data input or modelling assumptions. Differences in results were resolved to provide a final set of dose estimates.

A sensitivity analysis was conducted using Monte Carlo simulation[24] to examine the effects of varying certain dose estimating parameters and investigate the associated range of uncertainty. Five study subjects (Cases A–E), comprising single and multiple depositions, were selected for the sensitivity analysis to study a range of exposure conditions. Uncertain parameters were prescribed for each intake and varied though simulation trials using the parameter distributions described in Table 3. The distributions of each variable were constructed from assumptions based on records review and the dosimetry results for the study subjects. For example, the solubility type was assumed to be a mixture of Type S and Type M, which was modelled as a triangular distribution that varied by the fraction of Type S between zero and unity with zero most probable. This assumption was consistent with the records review and study subject excretion data indicating moderately soluble materials were most prevalent among recorded exposures. Each computer simulation consisted of 100 000 trials, varying all uncertain parameters randomly and simultaneously for each trial. Forecasts were made of cumulative doses and doses associated with each successive deposition for cases involving multiple intakes. Resulting dose distributions were examined and an uncertainty

parameter (K) was estimated for forecasted results such that $K = S^{1.96}$, where S is the geometric standard deviation of the forecasted distribution.

The reported cumulative doses from external whole-body exposures were compared with the cumulative bone marrow dose by cross-tabulation methods to examine the association between internal and external exposures. Workers were grouped by dose quartiles corresponding to exposure type. Interrelationships among quartiles were examined by cross tabulation.

RESULTS

Site characterisation

Early bioassay methods for measuring plutonium in urine were first reported by Healy[25] for Hanford, Farabee[26] for the Clinton Laboratory (ORNL) and Langham *et al.*[27] for Los Alamos. In general, urine was first digested using nitric acid, followed by plutonium extraction and quantifying. Most early extraction methods used precipitation with bismuth phosphate ($BiPO_4$) or co-precipitation using $BiPO_4$ followed by lanthanum fluoride (LaF_3). Later, solvent extraction, using thenoyltrifluoroacetone (TTA) or Tri-isooctylamine (TIOA), and ion-exchange methods were used. Beginning in the 1940s, alpha activity was quantified by gas-flow proportional counters. By the 1950s, gross alpha determination was improved via electrodeposition techniques, autoradiography and scintillation equipment. Batches of urine samples were analysed in concert with spiked samples. Large variability existed in chemical yields (recoveries), introducing significant errors in quantifying any one sample determined by batch recovery methods. Perhaps the most significant improvement occurred in the 1970s when alpha spectrometry was introduced for alpha energy detection enabling the use of plutonium isotopic tracers to uniquely determine the chemical yield of each sample.

Hanford

Routine plutonium urinalyses began at Hanford in 1946 using LaF_3–TTA extraction and gross alpha counting by gas-flow proportional counters. Early plutonium recoveries were reportedly between 80 and 90%[25]. The analysis was tailored to detect $\sim$11 mBq d^{-1}[25]. By June of 1949, improvements in counting methods had resulted in a sample detection limit of 5.5 mBq d^{-1}. Electrodeposition and autoradiography began in December 1952, which were reported to improve recoveries to 95% resulting in a detection level of 3 mBq d^{-1}[28,29]. By March 1953, methods were in place to routinely detect plutonium in urine at levels $>$1.7 mBq d^{-1}[29]. In October 1983, LaF_3–TTA extraction was replaced by anion-exchange columns and the chemical yield was established for each sample separately by the use of a ^{242}Pu tracer and alpha spectrometry[18].

Work histories indicate that $\sim$60% of the exposure-years associated with Category III exposures to Hanford study subjects involved work assignments in the Plutonium Finishing Areas (234–5 and 231) located in the 200 West Area. During processing, exposures to moderately soluble forms of plutonium were most common[30]. However, other less soluble forms were identified at Hanford, including an extremely insoluble form thought to originate from processes involving fired plutonium oxides[30].

SRS

Between 1952 and 1959, plutonium was extracted from nominal 1.5 litres urine samples by $BiPO_4$–LaF_3 co-precipitation. In 1959, an average recovery of $74\% \pm 23\%$ was reported using nitric acid/hydrogen peroxide dissolution and ion-exchange methods[31]. TIOA liquid extraction replaced the ion-exchange chemistry in 1966. This method also used direct evaporation on planchets instead of electrodeposition. In or around 1981, a new co-precipitation technique was introduced along with alpha spectrometry for routine plutonium bioassay. Special samples continued to be processed by TIOA until anion-exchange extraction and alpha spectrometry methods were fully implemented in 1988[32].

Autoradiography with $BiPO_4$–LaF_3 co-precipitation resulted in a reported sensitivity of 0.6 mBq per 1.5 litres of urine ($\sim$0.6 mBq d^{-1}). From 1964 to 1988, gross alpha counting was performed using solid-state surface-barrier detectors. The surface-barrier detectors greatly simplified bioassay methods but resulted in a slight increase in reported sensitivity at 1.7 mBq d^{-1}. Alpha spectrometry enabled separate reporting of ^{238}Pu (0.8 mBq d^{-1}) and ^{239}Pu (1.2 mBq d^{-1}) for routine samples in the early 1980s and for all samples by 1988[32].

Work history records and incident reports indicate that most study subjects with positive plutonium bioassay results were exposed while assigned to the plutonium separations areas. Approximately 70% of the exposure-years occurred in the 200F and 200H Separations Areas, and 46% of the exposure-years were associated with 221-F B-line activities. Both insoluble and moderately soluble forms of plutonium were prevalent in these areas[33]. However, incident data suggest most exposures were the result of handling plutonium nitrate solutions.

LANL

A plutonium urinalysis programme began at LANL in 1944. At first, the technique consisted of

evaporation, drying, and gross alpha counting by gas-flow proportional counters and was designed to detect an excretion of ~33.3 mBq d^{-1}[27,34]. By 1945, radiochemical separation used cupferron in chloroform followed by precipitation with LaF_3[35]. An average plutonium recovery of 82.3% ± 19.4% was reported. In October 1949, the separation procedure was changed to a $BiPO_4$–LaF_3 co-precipitation with radiochemical recovery of 67% ± 21%[35]. Bioassay records indicate these methods resulted in reported urine assays approaching 1.7 mBq d^{-1} by 1950. TTA/co-precipitation and autoradiography procedures (recovery 70.7% ± 17.2%) similar to those used at Hanford were introduced in 1957 and increased measurement sensitivity to ~0.83 mBq d^{-1}[35,36]. Between 1963 and 1981, an alkaline earth phosphate precipitation and ion-exchange method was primarily used with a reported average recovery of 84% ± 14%[37]. Between January 1967 and June 1971, plutonium urine assays were performed by either gross alpha counting or alpha spectrometry. Alpha spectrometry was used following June 1971[36]. Following 1981, precipitation was by alkaline earth phosphate or oxalate procedures[38].

Work histories indicate >82% of the Category III exposure-years were the result of early plutonium operations in DP West, which included plutonium purification, fluorination, reduction (to metal) and recovery. Of these operations, plutonium recovery activities involving high concentrations of plutonyl nitrate were a likely source of most early exposures[39].

ORNL

Beginning in 1947, ORNL used $BiPO_4$–LaF_3 co-precipitation methods with reported recoveries between 87 and 94%[26]. Between 1957 and 1964, sample treatment and separation of plutonium was done using $BiPO_4$–LaF_3 co-precipitation or by a co-precipitation series using calcium oxalate, lanthanum hydroxide and lanthanum fluoride[40]. The reported recovery for the latter method was ~100%[41]. Chemical separation by ion-exchange began in 1964, with reported recoveries of 93% ± 3%[42]. All ORNL methods employed gross alpha counting techniques until the onset of spectrometry methods in 1989.

Work histories indicate that most ORNL study subjects were exposed in the Separations Building (3019), the High Level Radiochemical Laboratory (4501 and 4505) or Transuranic Facility (7920). Approximately 43% of the exposure-years involved work in analytical or process chemistry job assignments. Plutonium-related incidents identified in study subject dosimetry records suggested uptakes of moderately soluble compounds were most prevalent.

Table 4. Plutonium exposure category assignments.

Category[a]	Hanford	SRS	LANL[b]	ORNL	Total
Person-years					
I	2240	725	303	148	3416
II	63	46	66	77	252
III	17	4	42	5	68
Persons					
I	290	90	31	31	442
II	20	18	15	23	76
III	15	4	16	4	39
Number of samples	3758	1425	961	596	6740
Monitored workers[c]	325	112	62	58	557 (556 actual)
Non-monitored workers[d]	189	95	111	184	579 (536 actual)

[a]Where x is the urine bioassay result in mBq d^{-1} and categories are defined as follows: Category I, $0 \le x < 1.7$; Category II, $1.7 \le x < 17$; and Category III, $x \ge 17$
[b]Includes study subject with employment at both LANL and ZIA
[c]One worker was monitored at both LANL and Hanford
[d]Data from facility workers but without facility plutonium monitoring data. There are 43 instances of multiple facility employment

Dosimetry evaluation

Medical and dosimetry records were used to identify 556 workers who participated in urine bioassay programmes during study eligibility. The results from 6771 bioassay samples, between 1945 and 1996, formed the basis for the category assignments listed in Table 4. Most available urine sample data (55.5%) pertained to Hanford employees followed by SRS (21.0%), LANL (14.2%) and ORNL (9.3%). Hanford also conducted the highest percentage of worker monitoring (63.2%) followed by SRS (54.1%), LANL (35.8%) and ORNL (24.0%). There were no plutonium-monitored workers at PNS and the monitored population for the plutonium assessment was among the 1092 workers with DOE employment.

Of the 556 workers with bioassay data, only 115 workers had at least one daily urine sample >1.7 mBq d^{-1}. Quantitative dose assessments were performed for these workers from 254 separate plutonium depositions between 1945 and 1975 (Table 5). Best fits of urine data to excretion curves using IMBA resulted mostly in assumptions of moderately soluble materials or mixtures with slight contributions from Type S materials. There were three uptakes modelled by IMBA that had associated excretions more indicative of Type S than Type M. The least soluble of these were two separate uptakes during fires. However, there were no study subjects

identified with urine data best-fit by IMBA to 100% Type S materials. There were 46 workers with multiple depositions and 69 workers with a single deposition. The most prevalent route of entry was inhalation (95.7%) followed by wound contamination (4.3%). The distribution of the cumulative equivalent doses to bone marrow was highly skewed, with arithmetic mean and median values of 18.4 and 5.6 mSv, respectively. Cumulative doses were summed for a collective dose of 2.1 person-Sv. LANL workers contributed most to the collective dose (43.4%), followed by Hanford (34.4%), ORNL (13.2%) and SRS (9.0%).

Figure 1 compares cumulative dose estimates reported by the two dosimetrists for 41 study subjects. The paired-sample distribution shows a slight positive bias with an arithmetic mean of 1.4 mSv (±3.1 mSv). However, a paired-sample *t*-test indicates the mean value was not significantly different from zero ($P = 0.36$). The distribution of the ratios of spreadsheet estimates to IMBA estimates appears log–normal with arithmetic mean and median values of 1.19 and 1.11 mSv, respectively, and 95% of the data between 0.69 and 1.91 mSv (Figure 2). Most of this variation resulted from differences in assumed dates of intake. The overall bias appears to result from the assumption of different absorption types. Type M materials were most often assumed using IMBA and a mixture of 50% Type M and 50% Type S was the default assumption for the spreadsheet calculations.

Table 5. Frequency of acute plutonium depositions by facility.

Bin range	Hanford	LANL	ORNL	SRS	Totals
1945–1949	12	13	3	0	28
1950–1954	14	21	26	0	61
1955–1959	15	12	14	9	50
1960–1964	10	6	4	12	32
1965–1969	12	5	14	15	46
1970–1974	1	4	3	22	30
1975–1979	0	0	0	7	7
Facility totals	64	61	64	65	254

Monte Carlo simulation

Table 6 summarises the statistics from Monte Carlo simulation of Reference Case E. The case involved multiple plutonium inhalation exposures between 1948 and 1951. Using the standard set of assumptions (without simulation), the estimated cumulative 50 y equivalent dose was 20.0 mSv from six intakes ranging from 25.9 to 259 Bq. The simulation distribution appears log–normal with geometric mean and geometric standard deviations of 23.9 and 1.29 mSv, respectively. The uncertainty factor (K) was estimated to be 1.66 resulting in an interval of 14.4–39.6 mSv (95% CI).

The cumulative dose distribution was sensitive to the number of individual intakes identified for each subject. The change in the cumulative dose distribution with intake number was investigated for Case E and demonstrates that the uncertainty decreases as the number of intakes per case increases (Table 6). Similar results were obtained with simulations involving four other cases (Table 7).

The intake date assignment was most often the greatest source of variance in exposure estimates. For example, >87% of the total variance for

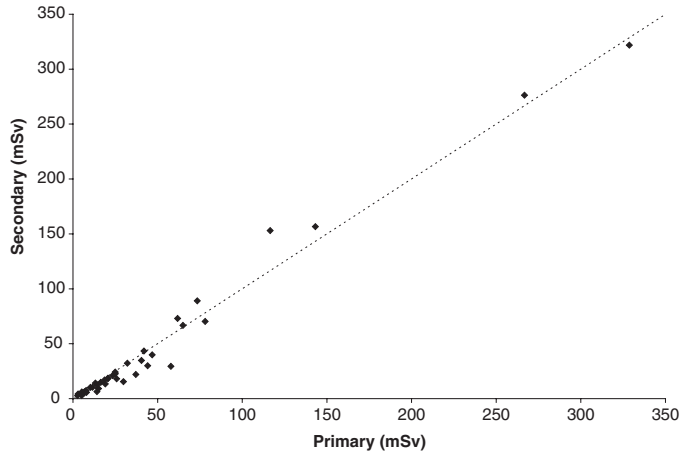

Figure 1. Comparison of spreadsheet (primary) and IMBA (secondary) cumulative dose estimates for the highest exposed category ($n = 41$).

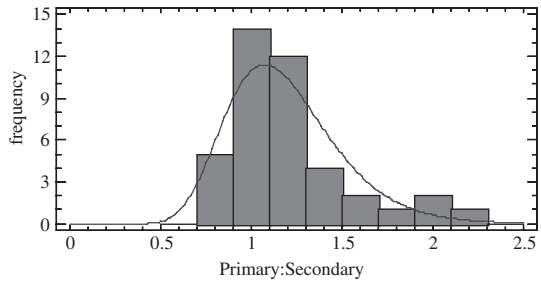

Figure 2. Histogram of the ratio of spreadsheet (primary) dose estimates to IMBA (secondary) dose estimates for the highest exposed category. The line indicates the fit to a log–normal distribution.

Reference Case A was associated with the assigned date of intake. Unfortunately, exposure dates were rarely found in historical exposure records unless an incident was confirmed. However, records indicate that it was common practice among facilities to request a 24 h sample following a suspected uptake. In addition, workers associated with an elevated potential for plutonium uptake received routine bioassay more frequently (i.e. weekly or biweekly) than others less exposed. Therefore, the current assumption of varying the date of intake uniformly over 7 d appears adequate for workers with the highest exposure potential (Category III). Dose estimates are expected to be less certain for Category II workers given that the frequency of bioassay monitoring

Table 6. Statistics from Monte Carlo simulation of Case E with varying number of total depositions (10^5 trials).

Statistics	Intake 1	Intakes 1 and 2	Intakes 1–3	Intakes 1–4	Intakes 1–5	All intakes (1–6)
Mean (mSv)	7.8	13.1	17.3	21.1	23.4	24.3
Median (mSv)	6.6	12.3	16.6	20.6	23.0	23.9
Standard deviation (mSv)	5.5	6.5	6.6	6.7	6.5	6.2
Variance	30.6	42.0	44.1	45.3	41.9	38.3
Skewness	1.28	0.92	0.74	0.62	0.58	0.61
Kurtosis	5.86	4.84	4.47	4.22	4.28	4.46
Coefficient of variability	0.71	0.49	0.38	0.32	0.28	0.25
2.5% Percentile (mSv)	1.4	3.6	6.4	9.6	12.1	13.6
97.5% Percentile (mSv)	20.9	27.8	31.9	35.7	37.3	37.7
Estimated uncertainty factor (K)	4.03	2.86	2.25	1.94	1.76	1.66

Table 7. Reference case cumulative dose statistics from Monte Carlo simulation.

Case ID	A	B	C	D	E
Number of depositions	1	2	4	6	6
Arithmetic mean (mSv)	4.8	6.7	16.7	16.8	24.3
Geometric mean (mSv)	3.8	5.9	15.8	16.2	23.6
Geometric standard deviation (mSv)	2.1	1.7	1.4	1.3	1.3
Standard deviation (mSv)	3.3	3.2	5.8	4.5	6.2
Variance	10.9	10.5	33.9	20.1	38.3
Skewness	1.26	0.93	0.85	0.52	0.61
Kurtosis	7.45	5.96	5.61	4.03	4.46
Coefficient of variability	0.68	0.48	0.35	0.27	0.25
Estimated uncertainty factor (K)	4.29	2.77	2.01	1.71	1.66
Contribution to variance from intake date variables (%)	87.2	84.9	80.8	80.9	74.7
Percentiles (%)					
0.0	0.3	0.9	3.2	4.5	7.0
2.5	0.9	1.9	7.3	9.0	14.8
5.0	1.1	2.2	8.4	10.0	16.4
50.0	4.2	6.3	16.2	16.5	27.1
95.0	10.9	12.6	27.0	24.6	42.7
97.5	12.5	14.0	29.7	26.4	46.6
100.0	69.0	70.6	108.9	70.9	79.2

Table 8. Cumulative external photon dose (mSv) by plutonium bioassay categories.

Plutonium bioassay[a]	*N*	Arithmetic mean	Median	5th Percentile	95th Percentile
Non-monitored (Category IV) excluding PNS	510	7.7	0.75	0.0	30.5
All sites non-monitored (Category IV)	681	12.8	1.2	0.0	57.8
Category I	441	38.4	11.0	0.1	214.8
Categories II and III	115	78.0	34.2	0.3	319.3

[a]Where x is the urine bioassay result in mBq d^{-1} and categories are defined as follows: Category I, $0 \leq x < 1.7$; Category II, $1.7 \leq x < 17$; Category III, $x \geq 17$; and Category IV, plutonium urine bioassay data not available

was often insufficient to accurately estimate a date of intake in the absence of incident data.

Under the general assumptions for a single uptake, a negative bias was observed for cumulative doses estimated from uptakes of ^{239}Pu without the presence of ^{241}Pu components. For single uptakes of weapons grade plutonium (Hanford mixture), the bias ranged from 1.6 to 17.0% for equivalent doses to the bone marrow integrated over 1–50 y. The bias increases with time since exposure and with the age of the inhaled plutonium mixture. For this study, the bias was not expected to significantly influence analysis results and further correction was not made. However, bias factors representing the ratio of the cumulative bone marrow dose from ^{239}Pu uptakes to doses from Hanford weapons grade plutonium were determined for mixtures at $t = 0$, 5 and 10 , where t is the years aged prior to exposure. These factors could be easily applied to existing dose calculations if corrections are warranted.

External and internal dose comparison

Records of cumulative external exposures to penetrating photon radiation were tabulated for 1237 study subjects among the 1269 workers selected for study. Of the 1237 workers with external exposures, 1066 were exposed among the DOE facilities and 171 had records of photon exposures at PNS. There were 32 study subjects without evidence of internal or external exposures, of which 26 were employed at the DOE facilities.

Most external exposures resulted from work at a single facility, although two-facility exposures were common to 42 workers and one worker's exposure was divided among three facilities. The cumulative dose distribution for each facility was highly skewed with median doses ranging from 0.6 mSv at LANL to 8.1 mSv at SRS. The distribution of cumulative doses for all facilities combined was also highly skewed with arithmetic mean and median values of 28.0 and 4.8 mSv, respectively. The collective dose from recorded photon exposures was 34.6 person-Sv (29.8 person-Sv excluding PNS) compared with 2.1 person-Sv estimated from internal plutonium exposures.

Table 8 shows the results of examining cumulative dose from external sources for workers grouped by bioassay categories. On average, higher external doses were observed with increasing internal dose categories, indicating an association between internal and external exposures. Workers were assigned to external photon exposure groups based on dose quartiles where the upper and lower quartiles were 18.7 and 0.4 mSv, respectively. Similar assignments were made for the internal plutonium exposures where the upper and lower quartiles were 14.4 and 2.0 mSv, respectively. Table 9 shows a comparison of dose quartiles by cross-tabulation. Of the 115 plutonium-exposed workers, 64 (56%) and 6 (5.2%) were in the upper and lower external exposure quartiles, respectively.

DISCUSSION

This study describes plutonium exposure assessment conducted within the context of an epidemiological study of the association between (primarily) external ionising radiation and leukaemia. It was expected at the outset of the study that plutonium would comprise a relatively small component of the collective dose to bone marrow for these study subjects, and it was observed that internal exposures, which were estimated for 9.3% of all workers (11% of DOE workers) with recorded photon exposures, contributed 2.1 person-Sv (6.1%) to the collective dose. While this contribution may seem trivial, a comparison of the dose distributions shows that internal exposures may be strongly related to external exposures and that the cumulative external dose from gamma and X-ray exposure is greater for workers with exposures to plutonium. For example, the median value of the cumulative external dose distribution for workers with estimated internal doses ($n = 115$) was 34 mSv compared with 4.9 mSv reported as the median for the 1066 DOE workers with recorded external exposures. Similar trends have been shown in other studies[2,3]. Thus neglecting internal dose from plutonium may present a source of bias that can lead to dose category misclassification and may skew the epidemiological dose–response assessment for leukaemia induced in

Table 9. Internal and external exposure cross-tabulation matrix.

	Photon exposure by quartiles[a]				Row totals
	1st	2nd	3rd	4th	
Plutonium exposure by quartiles[a]					
1st	1 (0.87)	2 (1.74)	10 (8.70)	15 (13.04)	28 (24.35)
2nd	0 (0.00)	4 (3.48)	13 (11.30)	12 (10.43)	29 (25.22)
3rd	3 (2.61)	2 (1.74)	6 (5.22)	18 (15.65)	29 (25.22)
4th	2 (1.74)	3 (2.61)	5 (4.35)	19 (16.52)	29 (25.22)
Column totals	6 (5.22)	11 (9.57)	34 (29.57)	64 (55.65)	115 (100.00)

Each cell contains observed frequency of workers in plutonium quartiles and percentage of total table represented by that cell (parentheses)
[a]Where workers with cumulative dose (x) are assigned by dose quartiles

the workplace. Researchers evaluating risks of leukaemia (or other cancers such as lung, bone or liver) at facilities with greater potential for plutonium exposure may find these methods to be helpful. Other methods of addressing missed dose from plutonium in epidemiological studies of external radiation and cancer (for example by excluding workers potentially exposed to internal radiation; Cardis and Kato[43]) may result in insufficient statistical power to detect associations between low-level workplace exposure and risk.

Limitations

Retrospective dose reconstruction from available bioassay data is a complex process requiring several steps to complete. With each step, some uncertainty in the estimate is introduced. Some of this uncertainty arises from a lack of knowledge about the exposure because such information was not entered into historical records. Other uncertainties are associated with the bioassay sampling procedures and the physicochemical characteristics and specific biokinetics of the particular contaminant involved. Additionally, there are analytical variabilities that introduce uncertainty in any exposure estimate based upon bioassay measurements. Boecker *et al.*[44] estimated an overall geometric standard deviation of 3.4 ($K \sim 11.0$) for 'modern' plutonium urine bioassay methods with appropriate exposure characterisation. This estimate was not inclusive, but results from the propagation of error from radiochemical analysis, day-to-day variability, background interference and modelling uncertainty. Potentially large sources of uncertainty not considered by Boecker *et al.* were sample collection and exposure time. Moss *et al.*[45] reported log–normal variations in LANL plutonium urinary data with a geometric standard deviation of 1.9 ($K \sim 3.5$) stemming from sample contamination, collection, analytical errors and metabolic variations.

For this study, uncertainty was examined by Monte Carlo simulation of certain parameters necessary for dose assessment. However, the simulation was limited to a few key modelling assumptions to examine the potential influence each may have on the final dose estimate within the range of variability assigned. Although efforts were made to provide reasonable estimates of the uncertainty in each assumption, data were not available to preclude subjective assignments. In addition, insufficient data were available to examine other sources of uncertainty, both within and among study facilities. Therefore, the simulation results are not a suitable substitute for an in-depth uncertainty analysis. Future research is needed to examine the uncertainty and potential bias that may result from the different techniques used among facilities and across time.

Models describing the biokinetics and transport of plutonium in the body indicate that only a small fraction of plutonium that is inhaled or ingested is excreted in urine following intake[13,15]. Therefore, the challenges presented in monitoring occupational exposure using urinalysis are to (1) collect a sample soon after exposure when models predict that plutonium excretion is greatest, (2) extract plutonium from the sample using a radiochemical method that is reliable and efficient and (3) detect plutonium extracted from the urine with the most sensitive and reliable instruments. Present day bioassay programmes utilise a sampling protocol that combines sample collection frequency with radiochemical methods having sufficient sensitivity to reliably detect exposures at or below current standards. However, early plutonium standards were less stringent, so ultra sensitive bioassay methods were not required. Although early bioassay monitoring programmes were sufficient to evaluate known incidents of exposure, where samples would be collected soon after intake when urinary plutonium excretion was expected to be high, some exposures that might

influence the results of the epidemiological study are likely to be undetected.

Estimates of bone marrow equivalent dose from plutonium were compared with exposures from other radiation sources. Unlike whole-body irradiation, alpha-emitting radionuclides in bone (^{226}Ra) or on bone surfaces (^{239}Pu) partially irradiate trabecular marrow, leaving a considerable fraction of healthy marrow unirradiated. Spiers and Vaughan have suggested that this difference may explain the marked absence of bone marrow neoplasms in human and animal studies of internally deposited alpha-emitters[46]. These studies indicate that certain bone-seeking alpha-emitters are not leukaemogenic agents. At the very least, bone marrow doses from exposures originating internally are largely dissimilar to exposures from whole-body penetrating radiation, making comparisons uncertain.

Assuming dose comparisons are appropriate, a potentially significant source of uncertainty results from the choice of the radiation weighting factor (w_r). The estimates of equivalent dose (H_T) were derived from absorbed dose (D) calculations using radiation weighting factors recommended by the ICRP to adjust for the relative biological effectiveness (RBE), where $H_T = Dw_r$ and $w_r = 20$ for alpha radiation[10]. This is consistent with the recommendations of the NCRP, which concluded that the biological effectiveness of internally deposited alpha-emitters relative to beta-emitters ranges from 15 to 50 for the induction of bone sarcomas, liver chromosome aberrations and lung cancers[47]. However, animal and human studies suggest that the leukaemia induction from internally deposited alpha-emitters is rare when compared with that of bone sarcoma[48]. Based on these observations, the US Environmental Protection Agency (EPA) has recommended an effective radiation weighting factor for leukaemia and alpha-emitters deposited in and on mineral bone of essentially unity[49]. The appropriateness of this assumption for plutonium workers in the leukaemia case–control study will be evaluated in the proposed epidemiological analyses, by examining the relative goodness-of-fit of statistical models of dose–response assuming different radiation weighting factors for plutonium.

CONCLUSION

A study of leukaemia risks associated with occupational exposure to protracted low-dose ionising radiation involved several dozen workers known to have worked with or around plutonium compounds. Although the primary epidemiological focus of the study is the effects of external radiation exposures, there is a need to assess the potential for missed bone marrow dose from internal exposures to plutonium given its relatively high exposure-to-dose relationship.

Similarities in general plutonium bioassay methods among DOE facilities provided a means to identify potential significant plutonium exposures for workers within a multi-facility cohort. Relating the plutonium bioassay data to exposure potential and then separating workers into evaluation categories enabled exposure assessors to identify a population for further examination. Doses were then estimated for 115 workers using urine bioassay data, facility-specific exposure information and current dosimetry techniques. The resulting dose distribution was highly skewed, with arithmetic mean and median values of 18.4 and 5.6 mSv, respectively. A comparison with the results from independent analyses by two dosimetrists suggests an appropriate use of methods and assumptions. Despite large uncertainties inherent to records-based internal dose assessment, a Monte Carlo simulation of key parameters in the dose calculations indicated a range of dose estimates that was appropriate for the proposed epidemiological study.

Exposures from internally deposited plutonium were limited to DOE-employment and contributed $\sim$2.1 person-Sv to the collective dose to bone marrow. Although this collective dose was relatively small ($<$10% of the collective dose of both internal and external sources), individual worker internal exposures were, to a degree, correlated with external exposures. Over half of the 115 plutonium-exposed workers had corresponding external exposures in the upper quartile range.

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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