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A TEST OF THE NCRP WOUND MODEL DEFAULT RETENTION FUNCTION PARAMETERS USING THREE U.S. TRANSURANIUM & URANIUM REGISTRIES PLUTONIUM-CONTAMINATED WOUND CASES

by

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To the Graduate Faculty:

The members of the committee appointed to examine the thesis of Liesl Germann find it satisfactory and recommend that it be accepted.

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DISCLAIMER

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LIST OF ABBREVIATIONS

CINDY = Code for Internal Dosimetry

CIS = Colloid and Intermediate State

DOE = The U.S. Department of Energy

DTPA = Diethylene triamine pentaacetic acid

GI = Gastrointestinal

ICRP = The International Commission on Radiation Protection

IMBA = Integrated Modules for Bioassay Analysis

LOD = Limit of Detection

MDA = Minimum Detectable Activity

NCRP = National Council on Radiation Protection

NIOSH = The National Institute for Occupational Safety and Health

PABS = Particles, Aggregates and Bound States

TPA = Trapped Particles and Aggregates

USTUR = United States Transuranium & Uranium Registries

ABSTRACT

The new NCRP Report No. 156 biokinetic wound model's default retention equation parameters were largely derived from animal experimental data that have been extrapolated to humans. In order to test the NCRP parameters' ability to predict the systemic uptake of plutonium in human wound cases, this study applied the model's retention coefficients for plutonium solution chemistries (particle, fragment, colloid, avid and strong retentions) to three USTUR human plutonium-contaminated wound cases, Case 0262, Case 0151 and Case 0334. The Case 0262 plutonium material was determined to be 24% soluble plutonium, composed of strongly- and avidly-retained plutonium, and 76% highly insoluble plutonium categorized as fragment. The chi-square for this optimum fit series was a statistically significant $\chi 2 = 52.3$; $p = 0.18$. However the questionable category assignment of "fragment" indicates that slower retention parameters may be necessary for the plutonium particle category. The Case 0151 plutonium material varied from 56% to 77% strongly-retained, with the remainder being avidly-retained. A statistically significant fit was obtained with a chi-square of 25.4 ($p = 0.33$). The Case 0334 plutonium material was almost entirely strongly-retained with a statistically significant optimum fit chi-square of 62.6 ($p = 0.13$). These results indicate that the NCRP wound model default retention equation parameters accurately predict plutonium uptake in humans from wounds when the bioassay data are sufficient to determine the mixture of absorption categories.

Section 1 INTRODUCTION

1.1 Overview

The highly anticipated National Council on Radiation Protection (NCRP) Report No. 156 entitled, Development of a Biokinetic Model for Radionuclide-Contaminated Wounds for Their Assessment, Dosimetry and Treatment was published in late 2007. This NCRP publication represents the first formal attempt to develop a conceptual model of radionuclide behavior in a wound and its associated lymph nodes in the manner of those already published by the International Commission on Radiation Protection (ICRP) for the inhalation and ingestion intake pathways. The NCRP wound model incorporates a new mechanistic model for wounds with transfer rates between compartments that reflect the time-dependent nature of radionuclide absorption into systemic circulation via the blood.

Previous dosimetric analyses of wound cases did not include specific representations of the mechanisms of particle retention and absorption from the wound site nor particle transfer to associated lymphatic tissue. Rather, the kinetics of systemic uptake were represented purely empirically, for example as multi-phased exponential retention components. Recently, new interest in radionuclide-contaminated wounds generated by Gulf War depleted uranium shrapnel wound cases has led to the formal development of a biokinetic wound model by the NCRP (Guilmette et al., 2003). This new NCRP wound model provides an important tool for use in dosimetry calculations that includes a wound-specific biokinetic model together with experimentally supported absorption and translocation rates for a variety of radionuclides and chemical forms.

1.2 Significance

Due to a historical lack of human radionuclide-contaminated wound cases free from confounding treatments such as chelation or additional intakes, usually inhalations, much of the data that contributed to the formulation of the NCRP wound model's retention function parameters originated from animal experiments and has been extrapolated to humans. Data drawn from experiments with animals have often been heavily relied upon in scientific studies such as internal wound dosimetry where human *in vivo* trials are considered impractical and unethical, but correlations made between animal physiological response and human physiological response have occasionally proved inaccurate. Therefore, specific tests of the NCRP wound model retention functions' applicability to the human metabolic system must be carried out.

Work conducted by process and other workers in the past at Hanford, Rocky Flats and other United States Nuclear Weapon-program sites resulted in a large number of accidental radionuclide-contaminated wounds. Relevant bioassay, radiochemistry and health physics data for many of these accidental wound cases are available from the U.S. Transuranium and Uranium Registries (USTUR). The USTUR historical human radionuclide-contaminated wound subjects are ideal cases with which to test the NCRP wound model's applicability to the human metabolic system. Empirical analyses using these cases will help isolate weaknesses in Report No. 156's published retention functions and allow for adjustments to the wound model that will bring it more in line with the realities of human systemic radionuclide uptake biokinetics.

It is likely that the NCRP Report No. 156 wound model will become the principal guidance document for the internal dosimetry of wounds in the U.S., and perhaps

internationally as well, should it be adopted by the International Commission on Radiological Protection (ICRP) in the future.

1.3 Purpose

The purpose of this study is to evaluate the systemic uptake predictive ability of the NCRP wound model's default retention equation parameters in human plutonium wound cases by applying the model's retention functions for plutonium solution chemistries including particle, fragment, colloid, avid and strong retentions to actual human plutonium-contaminated wound cases from the U.S. Transuranium and Uranium Registries (USTUR). This analysis provides specific empirical dosimetric tests of the largely animal data-derived NCRP wound model's applicability to human plutonium-contaminated wound biokinetics.

1.4 Hypothesis

Due to the statistical fit obtained with the NCRP default parameters to the USTUR Case 0262 data in the preliminary study conducted to test the NCRP wound model plutonium uptake predictive ability (Germann et al., 2007), it is expected that the NCRP default wound retention function parameters will adequately predict the transfer of plutonium in selected human wound cases when used in combination with the IMBA dosimetric software's solving ability.

Null hypothesis (H_0): *The NCRP Report No. 156 wound model's default retention equation parameters accurately predict the systemic uptake of plutonium in human plutonium-contaminated wound cases.*

Alternate hypothesis (H_1): *The NCRP Report No. 156 wound model's default retention equation parameters do not accurately predict the systemic uptake of plutonium in human plutonium-contaminated wound cases.*

The null hypothesis is considered supported if the NCRP wound model's default retention equation parameters for plutonium solution chemistry yield statistically significant maximum likelihood chi-square (χ^2) fits at the 95% confidence level ($p > 0.05$) to bioassay and health physics data from all selected USTUR plutonium contaminated wound cases. The alternate hypothesis is considered supported if statistically significant fits to the bioassay and health physics data in the selected USTUR plutonium-contaminated wound cases are not obtained when using the NCRP wound model's default retention functions for plutonium solution chemistry.

Section 2 BACKGROUND

2.1 Plutonium

Plutonium, atomic number 94, is a radioactive element in the actinide series of elements. It is often referred to as a transuranic element since it falls in the group of elements above uranium in the Periodic Table (atomic number 92 and above). Plutonium has chemical properties similar to the lanthanide elements between atomic numbers 89 and 103. Although the majority of available plutonium is anthropogenic, it is also created naturally on earth in small quantities as a result of neutron capture by uranium.

Plutonium has 15 isotopes (Table 1), the most common of which are ^{238}Pu, ^{239}Pu, ^{240}Pu, and ^{241}Pu. It is thought that there are a few kilograms of primordial (very long-lived) ^{244}Pu in the earth's crust (IPCS, 1983).

Table 1. Common plutonium isotopes.

Isotope	*Decay Mode*	*Half-Life*	*Principal Energies (keV)*	*Intensity*
^{238}Pu	Alpha	87.7 years	5.59	0.716
			5.55	0.283
			5.45	0.001
^{239}Pu	Alpha	2.41×10^4 years	5.24	0.739
			5.23	0.152
			5.19	0.107
^{240}Pu	Alpha	6.56×10^3 years	5.26	0.734
			5.21	0.265
			5.11	0.0009
^{241}Pu	Beta	14.4 years	5.24×10^{-3}	1.0
^{244}Pu	Alpha	8.0×10^7 years	4.59	0.805
			4.55	0.194

(adapted from IPCS, 1983)

^{238}Pu, ^{239}Pu, and ^{240}Pu decay by alpha emission and they emit low energy x-rays during the alpha decay process. The isotope ^{241}Pu decays by isobaric transition to ^{241}Am, which eventually undergoes alpha decay. Common man-made sources of plutonium isotopes include nuclear weapon production, nuclear bomb testing, and nuclear reactors. It is estimated that one nuclear reactor-produced megawatt of electrical energy generates 1.2 x 10^{12} Bq of $^{239+240}Pu$, 4.0 x 10^{12} Bq of ^{238}Pu, and 2.1 x 10^{14} Bq of ^{241}Pu (IPCS, 1983).

Plutonium has four valence states in aqueous solution: 3, 4, 5, and 6. Four is the most common valence state, but it can only exist in solution if it is strongly complexed since plutonium captures oxygen rapidly. Plutonium dioxide (PuO_2) is the most common form of plutonium and is a highly insoluble compound.

2.2 Hanford Site Plutonium

The Hanford Site was a nuclear weapons plutonium production facility established as part of the Manhattan Project during 1943 in Washington State. Hanford was home to several plutonium-producing nuclear reactors and generated plutonium for the manufacture of U.S. nuclear weapons until the site was decommissioned during the 1980's. The National Institute for Occupational Health and Safety (NIOSH) Dose Reconstruction Project developed a technical document detailing the various types and forms of radioactive materials used at the Hanford Site. This document also summarized the internal dosimetry procedures employed during the facility's operational years. It is recorded within the NIOSH report that ^{238}Pu, ^{239}Pu, ^{240}Pu, ^{241}Pu and ^{242}Pu were present in the plutonium compounds handled by Hanford workers. The isotope ^{242}Pu was determined to contribute insignificantly to dose. Two types of plutonium mixtures were generated, a weapons grade plutonium with

6% ^{240}Pu and a fuel grade plutonium with 12% ^{240}Pu. About 92% of the weapons grade plutonium mixture and about 84% of the fuel grade plutonium mixture was ^{239}Pu, with the remainder comprised of small amounts of ^{238}Pu, ^{241}Pu, ^{242}Pu and ^{241}Am. As the goal of the Hanford Site was to produce weapons grade plutonium, it is expected that Hanford workers had the potential of exposure to plutonium mixtures at all stages in the refinement process. The decay schemes for ^{239}Pu and ^{240}Pu are provided in Appendix A and Appendix B, respectively.

2.3 Plutonium Biokinetics

As stated above, most plutonium isotopes emit alpha particles and low energy x-rays and they therefore pose little external danger to biological tissue. However, if plutonium is introduced internally to a biological organism through ingestion, inhalation or injection, substantial dose can result in the target organs and tissues. During 1993, the ICRP published an updated version of its ICRP Publication 56 (1989) actinide biokinetic model (Figure 1) in ICRP Publication 67 (1993). Though questions have been raised recently regarding the model's accuracy in predicting the early behavior of plutonium in the liver and skeleton, it has largely been found to be in agreement with long-term retention, excretion and distribution patterns (Leggett et al., 2005).

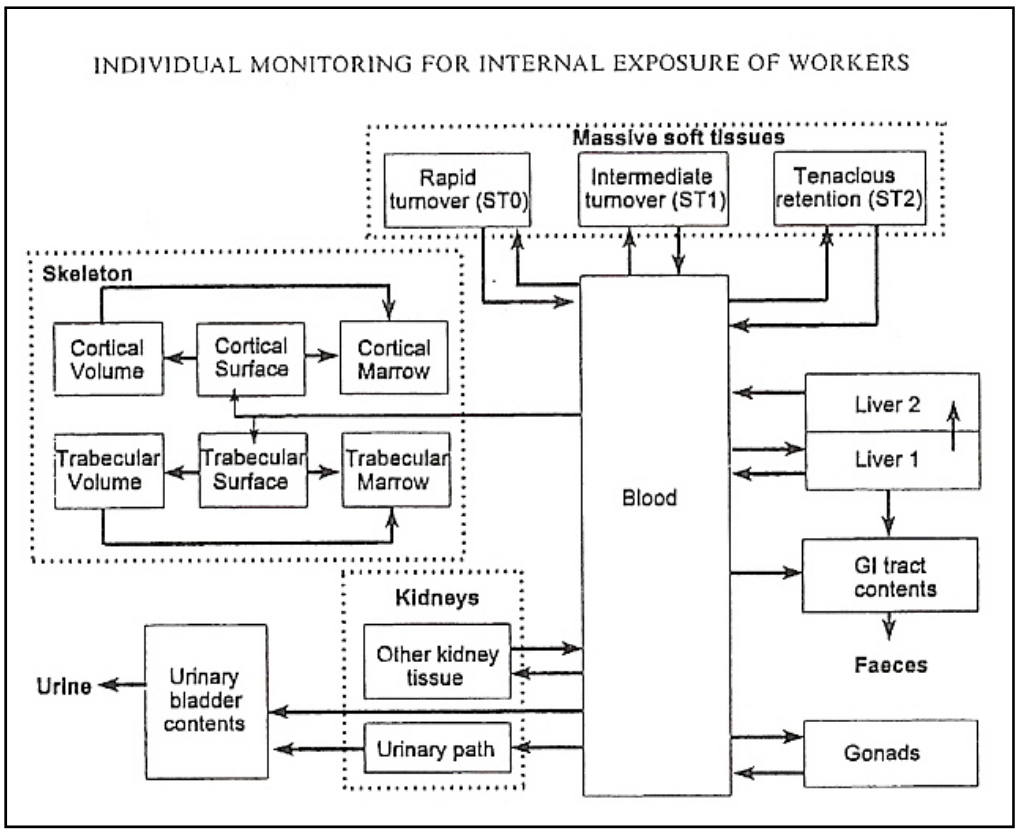


Figure 1. General ICRP 67 actinide biokinetic model (from reprint in ICRP 78).

The ICRP 67 biokinetic model provides an actinide-specific compartmental model, with its associated transfer rates, which is the standard for internal dosimetry of plutonium intakes today. Actinide radionuclide transport is modeled as a series of first order processes between compartments that represent the plutonium target organs of the body. Activity transfer rates into each organ from the transfer compartment (blood) are determined using the assumed deposition fraction in that organ, DF:

$$Organ\ Transfer\ Rate = \frac{0.693}{T_b} \bullet DF \qquad \text{(Equation 1)}$$

where T_b is the overall biological half-time of elimination from the blood and DF is the deposition fraction. The structure of the ICRP 67 biokinetic model takes into account the recycling of activity that occurs between compartments.

The ICRP 67 plutonium biokinetic model considers the blood a uniformly mixed compartment into which plutonium enters the biological system after an uptake and is distributed among the various organs and tissues. Using this approach, it should be understood that uptake fractions implicitly account for the competing rates and mechanisms among various organs. The massive soft tissues rapid turnover compartment (ST0) receives 30% of the blood plutonium with a removal half-time of 1 day, while the intermediate turnover (ST1) and tenacious retention (ST2) compartments receive 12.5% and 2% of the blood plutonium, respectively. ST1 has a moderate removal half-time of 2 years and ST2 covers the strongly retained activity with a removal half-time of 100 years.

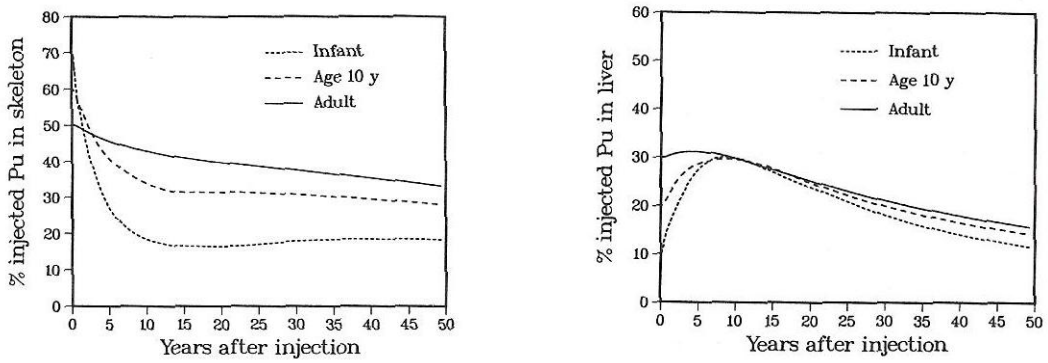


Figure 2. The retention of plutonium in the human skeleton and liver in years post injection (from ICRP 67, 1993).

The ICRP 67 model determines that 80% of the blood plutonium is initially transferred to the skeleton and liver (Figure 2). Plutonium activity transferred into the skeleton is assumed to deposit 60% on the trabecular bone surfaces and 40% on the cortical bone surfaces. Plutonium deposits first on the bone surfaces then moves to the bone marrow through resorption and eventually to the bone volumes when new bone is formed. The plutonium activity in the bone is slowly returned to the transfer compartment from the bone

marrow over a period of months (removal half-life of 0.25 years). The ICRP 67 liver is divided into a two section organ that includes a moderate retention compartment, Liver 1, with a removal half-time of 1 year, and a strong retention compartment, Liver 2, with a removal half-time of 9 years. Activity enters Liver 1 after which it is divided between Liver 2 and the gastrointestinal (GI) tract. These divisions of plutonium activity between the two compartments of the liver and the GI tract are determined considering the competing mechanisms and their composite transfer rates.

Other organ systems relevant to the plutonium biokinetic model include the kidneys and gastrointestinal tract. Kidneys in the ICRP 67 model lose plutonium activity to both the blood and urine. Bladder contents are considered as a separate compartment. About 2% of the blood plutonium and 50% of the activity from intermediate soft tissue is transferred to the bladder. The urinary path receives 1% of the transfer compartment plutonium and 0.5% goes to other kidney tissues. Two percent of the plutonium activity in the blood, plus 7% of the activity leaving the ICRP 67 Liver 1 compartment are transferred to the GI tract.

2.4 Wound Biology and Repair

The skin is comprised of three distinct layers, the hypodermis at the base, the dermis or structural support of the skin and the thin, epidermal layer on top. The hypodermis contains fibroblasts, adipose tissue and macrophages that separate the skin from the underlying muscle. The dermis is a dense collection of collagen and other connective tissues with two layers, the reticular and papillary layers, which gives the skin its strength. Finally, the epidermis is the outer protective layer comprised of five layers where skin cells are

produced, keratinized, and slowly pushed up to the surface where they die and are eventually sloughed off.

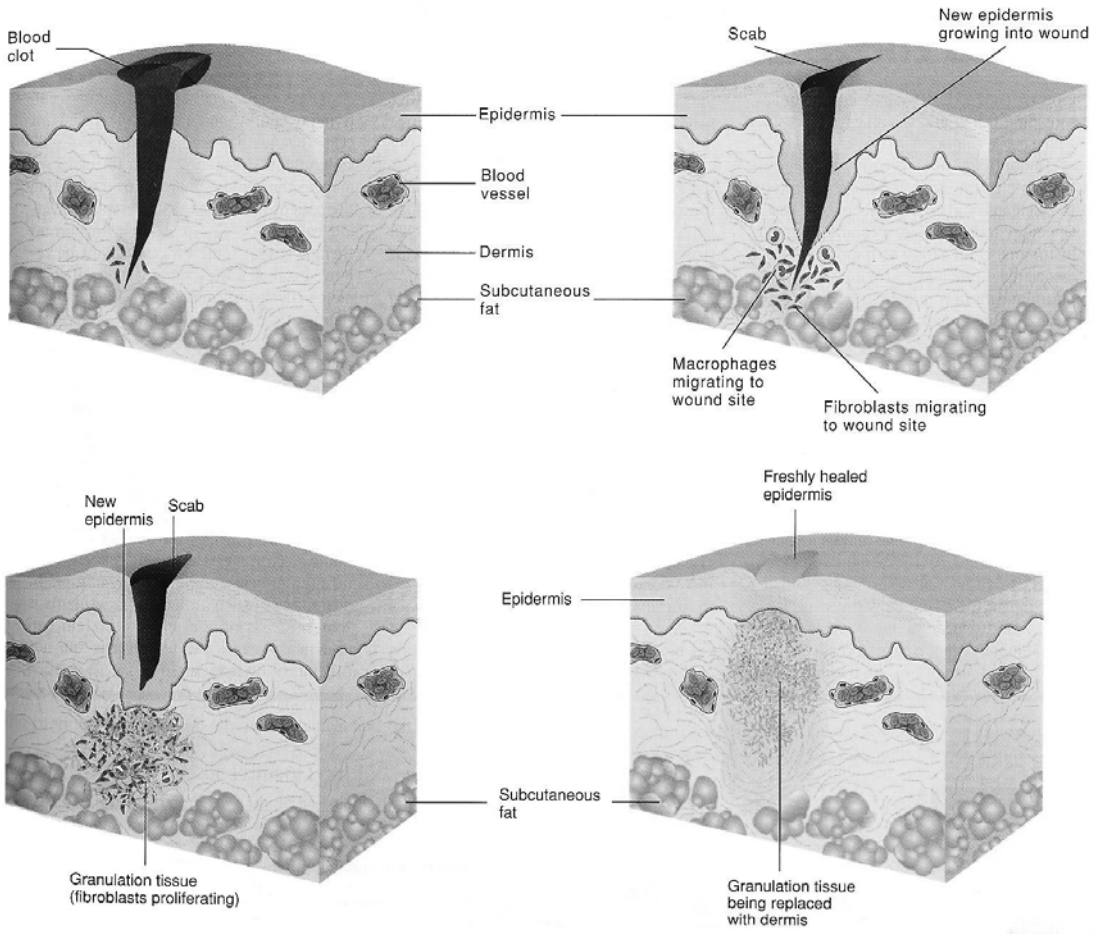


Figure 3. The steps involved in skin wound repair (from Seeley et al., 2000).

When the skin experiences a laceration or injection of a foreign body, tissue cleansing and repair proceeds rapidly in three stages: inflammation, scab formation and the creation of new granulation tissue (Figure 3). Inflammation occurs following the release of wound mediators such as histamines and kinins that stimulate pain receptors, dilate blood vessels and increase blood vessel permeability. This osmotic pressure change allows more white blood cells and water to enter the cells surrounding the wound and causes inflammation.

Simultaneously, clotting proteins cross into the damaged tissue and form a fibrin clot that unites the two edges of the wound. Fibroblasts, collagen-producing cells, move into the clot and gradually replace the fibrin clot with granulation tissue to make a scar. Capillaries grow inside the clot and the fibroblasts continue to multiply, producing ever more collagen with which to contract the wound and allow the new epidermal tissue to join and replace the scab (Seeley, 2000).

The inflammation and immunological response to a wound is begun by the introduction of small white blood cells from the red bone marrow called neutrophils, which are attracted by the histamines and kinins released by damaged tissue. The neutrophils release enzymes and oxygen compounds that kill damaged tissue and invading foreign bodies. During the later stages of immune response, monocytes present in the hypodermis and dermis combine with additional monocytes crossing into the wound from the blood. These immune system cells enter the damaged tissue, enlarge and become macrophages that engulf and digest larger foreign particles, bacteria and dead tissue. Macrophages also secrete growth factors that stimulate granulated tissue production. On occasion, the foreign material introduced into the skin through a wound consists of colloids, fragments or particles that are indigestible by macrophages. The phagocytosis of these materials sometimes results in the death of the macrophage and its ingestion by another macrophage. In this way, the elements of the foreign material are slowly digested and released into systemic circulation via the blood. Often the injection of such material also results in chronic inflammation or a total encapsulation of the material within the wound (Guilmette et al., 2007).

2.5 Wound Modeling

Many radionuclide-contaminated wounds have occurred in the years that humans have been using radionuclides for scientific and industrial purposes, and at least 2000 wounds have been analyzed and published (Ilyin, 2001). Most of these wounds involved actinide contamination incurred by nuclear weapons industry workers; 90% occurred in the hands and arms, especially the fingers, and 90% of the finger wounds were puncture wounds (Ilyin, 2001). A majority of actinide-contaminated wound cases were treated through surgical excisions and/or chelation treatments with diethylene triamine pentaacetate acid (DTPA) in order to minimize uptake or increase excretion of plutonium in the injured party's urine (Ilyin, 2001).

It was recognized early on by dosimetrists looking at bioassay data from contaminated wound cases that radionuclide intakes via the wound route of entry had the potential for slow "feed" into the system over time (Lagerquist et al., 1972), and that the biokinetics of radionuclide transport from wounds was likely very different from that of inhalations or ingestions. Tissue responses involved in the wound repair system such as inflammation, immune cell activities and cell regeneration enhance the importance of radionuclide chemical properties in transport (Guilmette et al., 2003). In addition, the injected radionuclide concentrations involved in wound accidents are usually on the order of micrograms to grams, much higher than the picogram per particle concentrations encountered in the typical inhalation intake (Guilmette et al., 2003).

Despite recognizing the uniqueness of radionuclide retention in wounds, prior to the publication of the NCRP Report No. 156 Wound Model in 2007, modeling of radionuclide transport from wounds into systemic circulation had been largely ignored by the internal

dosimetry scientific community (Guilmette et al., 2003). Widely used dosimetry systems such as ICRP 2 and ICRP 30 did not provide models for evaluating uptakes from the wound route of entry; radionuclide uptakes from wounds were simply assumed to be an injection into the blood compartment. As recently as 1989, Carbaugh stated that 50-year Committed Dose Equivalents were difficult to estimate with any certainty due to the potential for long-term very slow transport of material from wounds, a phenomenon still not very well understood at that time.

Various methods were employed to model the uptake of radionuclide activity into systemic circulation in wound cases. The general biokinetic model created by Johnson and Carver (1981) combined the ICRP 66 lung model, the ICRP 79 gut model and an organ model comprised of several compartments. Their model assumed a blood transfer compartment into which all uptakes dumped before dispersing out to the organs. Though uptake from a wound was included as a compartment in the model, it was predicted to deposit directly into the blood transfer compartment like an injection, and no transfer rates from wound to blood were provided. The ICRP 67 biokinetic model for plutonium (1993) similarly postulated a blood transfer compartment into which inhalation and ingestion activity enters, but no formal description of the wound route of entry was described. Lagerquist et al. (1972) assumed a wound site "reservoir" for their analysis of a plutonium and americium puncture wound case in order to account for changing transport rates from the wound into the blood. Falk et al. (2006) created a biokinetic wound model from the Code for Internal Dosimetry (CINDY) program and the IMBA dosimetric software for their analyses of five Rocky Flats wound cases. They hypothesized a 3 or 4 compartment, exponentially-

cleared wound model that included a "permanent" compartment for potentially non-transported activity.

The retention functions for these postulated wound compartments to the blood in dosimetry programs such as CINDY and IMBA are largely determined empirically through a tedious iteration process (Falk et al. 2006, LaBone 2005, James et al. 2008b). Initially hypothetical absorption fractions and uptake rates are entered and the program uses a statistical technique to calculate the value of intake that gives a "best-fit" to the bioassay data. The goodness of fit is evaluated qualitatively by eye or quantitatively by calculating the chi-square (χ^2) statistic. Manual (iterative) adjustments are then made to the assumed wound retention parameters in order to improve the fit. To assist dosimetrists with the iteration process, LaBone (2005) suggested an equation for the selection of preliminary parameters that includes short half-time retention and long half-time retention components:

$$R(t) = 0.9e^{\frac{-\ln 2}{1\,day}\cdot t} + 0.1e^{\frac{-\ln 2}{150\,days}\cdot t} \qquad \text{(Equation 2)}$$

LaBone suggests that the only two compartments be used for simplicity and that the soluble fraction be given the greatest weight since it is most important to dose.

While the iteration process provides bioassay data-driven retention functions for the uptake of radionuclide activity into systemic circulation, it is both time-consuming and somewhat arbitrary since the number of compartments used and the modeling of material transferred between the compartments are not based on the real biokinetic processes involved in wound foreign-body response.

2.6 The NCRP Biokinetic Wound Model

The NCRP Report No. 156 biokinetic wound model represents the first formal attempt to develop a conceptual model of radionuclide behavior in a wound and its associated lymph nodes. The general compartmental structure is comprised of five wound compartments that lead to systemic uptake into the blood or clearance to the lymph nodes (Figure 4). The five wound site compartments were conceived in order to account for the various radionuclide physical forms and the biochemical and chemical processes encountered in workplace settings.

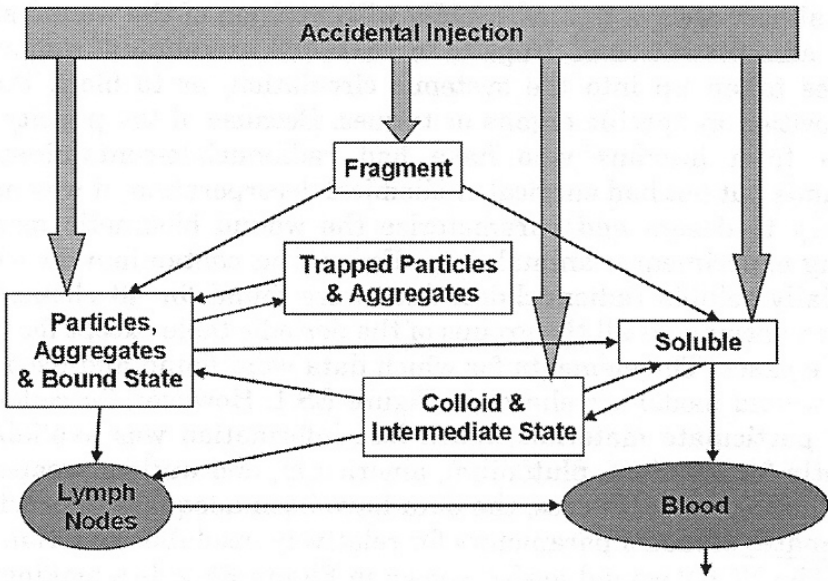


Figure 4. The general NCRP biokinetic model of radionuclide translocation from a wound site as published in NCRP Report No. 156 (2007).

These compartments are derived from the physical forms and solution properties of the entering radionuclides. The four NCRP categories of solution chemistry chemical bonding are: weak, moderate, strong, and avid. The three categories of "physical" particle retention include a colloid category and two "solid" categories, particle and fragment. A "particle" is

defined by NCRP Report No. 156 as any material up to 20 μm in size, and a "fragment" is defined as any material above 20 μm. Transfer between compartments is described by first-order kinetics and estimates of the transfer rates are provided in this report (Appendix D).

Soluble radionuclide compounds may enter the wound and be immediately transferred to the blood or a fraction may enter the Colloid and Intermediate State (CIS) compartment. The transfer of radionuclides in soluble compounds to the CIS compartment is driven by the element's tendency to hydrolyze at neutral pH. A hydrolyzing element will effectively bind to the tissue at the wound site by forming insoluble hydroxides. A fraction of the activity in the CIS compartment will return to the soluble state. An additional fraction of the activity in the CIS compartment will be altered by chemical reactions and transformed into bound states in the Particles, Aggregates and Bound State (PABS) compartment. The remainder of the activity in the CIS compartment is transported to the lymph nodes by macrophages.

Radionuclides associated with insoluble compound forms enter directly to the Fragment or PABS compartments. Fragments can be slowly dissolved into particles then carried to the lymph nodes for long-term retention by macrophages together with a fraction of the other PABS materials. The activity associated with the PABS materials can be dissolved over time back into a soluble form and eventually these materials are cleared into the blood. The NCRP biokinetic model also includes a Trapped Particles and Aggregates (TPA) compartment to account for material that is encapsulated or sequestered in the wound due to inflammation.

2.7 The NCRP Wound Model Plutonium Categories

NCRP Report No. 156 places various forms of plutonium into five of its physical radionuclide categories. Two of these are solution categories: strong and avid; and three are physical forms: colloid, particle and fragment. In solution, the NCRP wound model categorizes the plutonium $^{238}Pu^{4+}$ tetravalent cation as a strongly-retained radionuclide. Plutonium-238 is a much more soluble form of plutonium than ^{239}Pu since it has a significantly shorter half-life of 87.7 years and emits great amounts of energy that can break the chemical bonds with ^{238}Pu compounds. Plutonium materials with a large percentage of ^{238}Pu are assumed to be transferred into systemic circulation at a faster rate than insoluble forms of plutonium. The more insoluble $^{239}Pu^{4+}$ cation, however, can act as a strongly- or avidly-retained material, depending upon the mass of plutonium introduced into the wound site. Guilmette et al. (2003) showed that retention of plutonium in wounds increased with increasing plutonium mass, and this formed the basis of categorizing materials with greater than 3.2 μg (7,347 Bq) of ^{239}Pu as avidly-retained in the NCRP wound model. A separate category was created for colloidal forms of plutonium, and plutonium metal and oxides are included in the particle or fragment categories, with a particle being any material up to 20 μm in size and a fragment being any material above 20 μm.

2.8 The NCRP Default Retention Function Parameters

To simplify use of the biokinetic wound model in practical health physics dose assessments, the NCRP included default biokinetic retention equation parameters in its Report No. 156 (Table 2). These values represent the fractions and transfer rates in "equivalent" non-recycling exponentially-cleared compartments.

Table 2. NCRP Report No. 156 wound model default retention equation parameters.

Radionuclide Category	*Wound Retention Equation Parameters*					
	a_1 (%)	λ_1 (d^{-1})	a_2 (%)	λ_2 (d^{-1})	a_3 (%)	λ_3 (d^{-1})
Weak	55	55	40	6.0	5.0	0.1
Moderate	55	55	35	0.5	10	0.02
Strong	50	1.0	30	0.03	20	0.001
Avid	19	37	81	0.001	---	---
Colloid	15	3.0	8	0.055	77	7×10^{-4}
Particle	5	0.05	95	4×10^{-4}	---	---
Fragment	0.5	0.009	99.5	6.5×10^{-6}	---	---

The default retention parameters are NCRP's empirical fits to data from the same studies involving the injection or implantation of radionuclides in experimental animals that form the basis of the conceptual biokinetic wound model. As simplified versions of radionuclide transfer between the wound model compartments, the default parameters do not take into account lymph drainage, and therefore the use of these parameters for radionuclide forms such as insoluble materials with considerable lymph node transport is likely to overestimate blood absorption and urinary excretion. Also, the default parameters were determined largely from intramuscular wound studies and therefore model deep puncture wounds better than shallow wounds (NCRP, 2007). The NCRP predicts that these default parameters will be most useful in dose assessment cases where little information is available about the form of the radionuclide introduced into the wound.

2.9 U.S. Transuranium & Uranium Registries

The U.S. Transuranium & Uranium Registries program is a collection of medical records, exposure histories, and tissue samples from volunteer donors who were involved in accidental exposures to actinide elements during their employment in U.S. nuclear materials

production from the 1940s through the 1970s. The USTUR currently has approximately 500 active registrants previously employed at Department of Energy (DOE) sites throughout the United States. The USTUR database includes health physics records, organ tissue radiochemical analyses, bioassay data, and autopsy information relating to intakes of plutonium or other actinides for each registrant. To protect the anonymity of its registrants, the USTUR refers to each donor using an assigned case number.

The USTUR's mission is to use these real-life occupational case data to better understand the effects of transuranic elements on the human body and to assess the current biokinetic models' accuracy in predicting intakes and doses (James and Brooks, 2006).

2.10 IMBA Dosimetric Software

The Integrated Modules for Bioassay Analysis (IMBA) Professional Plus software is a bioassay data and internal dose assessment program initially developed by the United Kingdom's National Radiation Protection Board (now the Health Protection Agency) in collaboration with ACJ & Associates, Inc. IMBA is designed to calculate intakes from bioassay measurements and predicting bioassay results after a known intake, as well as determining the resulting effective doses and equivalent organ doses for the ICRP 68 reference worker.

ICRP 67's biokinetic plutonium model is used by IMBA to estimate intakes from plutonium urine excretion measurements and provide bioassay predictions following a known plutonium intake. Since this is a recycling system of compartments, IMBA utilizes a special module called NRPB_DIS that takes into account both the parent's activity and that of its progeny over time when solving the biokinetic system.

IMBA allows users to load ICRP default dosimetric and systemic compartmental models such as the ICRP 30 gastrointestinal tract model and the ICRP 66 lung model and solves these in conjunction with entered bioassay and health physics data. In the future, IMBA's developers plan to include the NCRP wound model and associated retention functions, but until that time, intakes received via wounds are calculated by means of a generic wound model into which the NCRP empirical retention equation parameters (a_i and λ_i) may be entered. The retention functions are defined within IMBA by a sum of exponential terms according to the formula:

$$R(t) = a_1 e^{-\lambda_1 t} + a_2 e^{-\lambda_2 t} + \ldots \qquad \text{(Equation 3)}$$

where a_i and λ_i are user defined and represent the absorption fraction and uptake rate (d^{-1}), respectively.

2.11 Two Prior Plutonium Wound Analyses Relevant to this Study

James et al. (2008b) carried out a full biokinetic analysis of USTUR Case 0262, a registrant with two inhalations of refractory $^{239}PuO_2$ and a plutonium puncture wound to the skin of the thumb obtained while working with plutonium materials in a glovebox. The biokinetic wound model approach used involved empirically treating the uptake and retention of plutonium in the wound and associated axillary lymph node in terms of several exponentially cleared compartments. The wound and axillary lymph node absorption rate constants were varied iteratively, together with several rate constants in the ICRP 66 lung model and the ICRP 67 biokinetic model to obtain an optimum fit to all of the Case 0262 data ($\sum\chi 2 = 42.7$). It was observed after considering the data generated by this study that

only 40% of the plutonium initially deposited in the skin wound was absorbed into the body over the 33 years following the accident. Most of the absorption from the wound and axillary lymph node into the blood occurred extremely slowly (49% at 6 x 10^{-5} d^{-1} and 37% at 5 x 10^{-6} d^{-1}). However, the other 14% was absorbed quite rapidly in two absorption phases of 0.5 d^{-1} and 0.012 d^{-1}, respectively. Therefore, James et al. concluded that Case 0262's ^{239}Pu wound contamination consisted of a mixture of refractory $^{239}PuO_2$, and a more soluble plutonium form. In addition, they showed that the two inhalations prior to the wound contributed very little to the long term urinary excretion.

When the NCRP Report No. 156 wound model became available in its final draft form in early 2007, a preliminary study was conducted by Germann et al. (2007) using USTUR Case 0262 and the NCRP default retention equation parameters. The empirical fractions and rates for six NCRP categories of wound absorption behavior, weak, moderate, strong, avid, particle and fragment were implemented in the IMBA Professional Plus Version 4.0.28 bioassay analysis software to determine how well the NCRP's recommended overall absorption rates represented the measured bioassay data, wound and axillary lymph node, and systemic retention. The result was a highly significant statistical fit ($\sum\chi^2 = 51.7$) that was very close to the fit obtained using an unrestricted choice of absorption rates ($\sum\chi^2 = 42.7$) in James et al. (2008b). IMBA assigned 76% of the calculated intake activity to the NCRP "fragment" category and 18% of the intake activity to the "strong" category.

Section 3 MATERIALS AND METHODS

3.1 Overview of Method

The USTUR plutonium-contaminated wound cases were surveyed for cases free from confounding inhalations, chelations and concurrent wounds. Case 0262 was already known to be an appropriate case for this study, so this case plus two additional cases were chosen for analysis. The case bioassay and health physics data were entered into the dosimetry software IMBA and various combinations of the NCRP recommended default retention fractions and half-times for relevant plutonium chemistry categories (strong, avid, colloid, particle and fragment) were used to obtain an "optimum" fit to the data that minimized the chi-square and autocorrelation coefficient statistical tests.

3.2 USTUR Case Selection

The approximately 150 USTUR cases that involved plutonium wound accidents were examined for a second and third case suitable for evaluation using the NCRP wound model default retention parameters. Several criteria were used for selection of the cases in order to minimize confounding factors.

First, it was important that the wounds involved a measurable uptake of plutonium above the minimum detectable activity (MDA) limit of the analysis method used at the time of the wound incident. According to the NIOSH Dose Reconstruction Project (2005) report for the Hanford Site, plutonium in-urine bioassays after 1952 were performed by a combination of electrodeposition, α-spectrometry and nuclear track emulsion. The MDA of an activity detection method is defined as the smallest concentration of radioactivity in a

sample that can be detected with a 5% probability of erroneously reporting a false negative when operating at the critical level (L_C). The L_C represents the limit at which the detection method reports false positives at less than a 5% probability. The MDA is derived from the critical limit and the limit of detection (LOD), which is calculated using the equation (adapted from Knoll, 2000):

$$LOD = 2.706 + 4.653\sigma_{NB} \qquad \text{(Equation 4)}$$

where 2.706 is a value derived from the critical level and σ_{NB} is the standard deviation of the net background counts. The MDA, then, is the activity equivalent of the LOD and is calculated with the formula (adapted from Knoll, 2000):

$$MDA = \frac{LOD}{\varepsilon \cdot t_{count} \cdot CF} \qquad \text{(Equation 5)}$$

where CF = conversion factors for activity units, ε = detector efficiency for the particular type of radiation and t_{count} = sample counting time. The variation of the MDAs over time for U.S. principal weapons sites were recently reported by the NIOSH Dose Reconstruction Project and are reproduced in Appendix E for the Hanford Site.

Second, cases in which the registrant received chelation treatment such as diethylene triamine pentaacetic acid (DTPA) were eliminated from consideration since transuranic chelating agents bind to plutonium and alter its chemical properties such that its excretion rate is greatly enhanced and the half-time of plutonium circulating in the blood reduced (Carbaugh, 1989; NIOSH, 2005). These chemical changes to the plutonium atom render the default ICRP 67 biokinetic model for plutonium an inappropriate representation of treated plutonium excretion rates (James et al., 2008a).

Third, two cases were selected that did not involve confounding prior or overlapping plutonium inhalations or wounds since in cases of multiple plutonium intakes the observed plutonium activities in urine excretion samples become combined. If a USTUR registrant had experienced a plutonium inhalation prior to a wound, the inhalation was modeled using the ICRP 66 lung model to determine whether the inhalation activity in the body had dropped to below detectable limits before the wound occurred. Inhalations shown in this way to be non-confounding were regarded as safe to ignore in the wound analysis. USTUR registrant cases with concurrent plutonium inhalations or wounds were not considered for analysis.

After careful review of the case files, Case 0151 and Case 0334 were chosen for analysis in addition to Case 0262, as they met all of the above criteria. Both Case 0151 and Case 0334 involved excisions of the plutonium-contaminated skin shortly after the accident. Though excisions likely remove a large amount of the activity at the wound site, the bioassay data in both cases clearly indicated a measurable uptake of plutonium into systemic circulation, so it is expected that the excisions only reduced the potential total uptake activity and did not affect the subsequent translocation of activity from the wound to systemic circulation.

3.3 Plutonium Solution Chemistry and Retention Functions

Five of the seven NCRP Report No. 156 radionuclide retention categories were used in the USTUR plutonium-contaminated wound case analyses. These included strong and avid retention for solution chemistries, and the colloid, particle and fragment categories for solid material. The NCRP wound model categorizes soluble plutonium materials that contain only ^{238}Pu or less than 3.2 μg (7347 Bq) of ^{239}Pu as "strongly-retained." As the NCRP notes

that the main difference between the strong and avid categories is mass of plutonium, plutonium materials with masses of ^{239}Pu greater than 3.2 μg (7,347 Bq) fall into the "avidly-retained" radionuclide category. The colloid category was also evaluated in order to account for the possibility of nitrate plutonium forms. Both of the solid categories, particle and fragment, were included in the case analyses with the fragment category representing the slowest clearance rate category.

3.4 USTUR Case Analysis

Case analysis was performed using IMBA Professional Plus Version 4.0.28 bioassay analysis software. The IMBA software models systemic circulation of plutonium from the blood to the relevant target organs and tissue, and its removal from the body through excretion using the ICRP 67 actinide biokinetic model. This software is capable of determining the total plutonium activity deposited in a wound when absorption fractions and uptake rates into the blood are defined in the generic wound model module. The default NCRP wound model parameters suggested for plutonium material chemistries were entered into IMBA for each case simultaneously as multiple intake regimes. In this way, no assumptions were made about the relative fraction of each category of the plutonium material, and IMBA was allowed to determine these fractions in order to obtain an "optimum" fit to the bioassay data. Following this preliminary analysis, the different NCRP parameters were entered into IMBA in various combinations until a minimum chi-square "optimum" fit to the data was achieved for each case.

Case bioassay and health physics data, including a whole body count for Case 0262, recorded in the case files were converted into SI units and entered into IMBA for analysis.

The limit of detection values determined whether or not a bioassay data point was considered "real" or less than the limit of detection in the case analysis. The limits of detection were taken to be one-half the minimum detectable activity for measured urine data reported in a Hanford technical document created by the NIOSH Dose Reconstruction Project. These values are date-specific and are given in Appendix E. A data point was only excluded as an outlier from the analysis when documented as such by the on-duty health physicist at the time of the incident (i.e., when noted in the case files).

3.5 Statistics

The IMBA Professional Plus software package employs the maximum likelihood method as its default bioassay data fitting routine. The maximum likelihood method determines a best estimate of an intake by first calculating the excretion function per unit intake that fits the data, then evaluating the probability of the intake given the bioassay data. Since the mean (μ) of the real parent distribution is unknown, a second experiment-derived distribution with an estimated mean (μ') is assumed and its standard deviation (σ') is set equal to the parent's standard deviation (σ). In this case, the probability of observing a value x_i is given by (Bevington et al., 2003):

$$P(\mu') = \left(\frac{1}{\sigma\sqrt{2\Pi}}\right)^N \exp\left[-\frac{1}{2}\Sigma\left(\frac{x_i - \mu'}{\sigma}\right)^2\right] \qquad \text{(Equation 6)}$$

When the individual probabilities for a set of N data points are multiplied, the above equation becomes (Bevington et al., 2003):

$$P(\mu') = \left(\frac{1}{\sigma\sqrt{2\pi}}\right)^{N} \exp\left[-\frac{1}{2}\sum\left(\frac{x_i - \mu'}{\sigma}\right)^2\right] \qquad \text{(Equation 7)}$$

The probabilities $P(\mu')$ of obtaining the experimental set of bioassay observations with different parent population means are compared. The case which results in the highest probability is considered the best estimate of a fit (Bevington et al., 2003) since the experimental data mean and standard deviation (μ', σ') are approximately equal to the parent distribution mean and standard deviation (μ, σ).

A benefit of the maximum likelihood method is that it allows data less than the limit of detection to be considered in an intake calculation in an unbiased manner since these data points are not arbitrarily assigned a value of 0, or as also commonly done MDA/2, but rather are given a probable value between 0 and the limit of detection based on the measurement error distribution curve. A test of the method's non-bias using Monte Carlo simulations showed that good estimates of the true intake result even when the number of < LOD data points are numerous (James et al., 2005; Marsh et al., in press).

A statistically significant maximum likelihood chi-square test (χ^2) at the 95% confidence level ($p > 0.05$) indicated a "good" fit to the data and the minimized chi-square situation for each case was considered the "optimum" fit. The chi-square statistic describes the goodness of fit to a set of data by measuring the disparity between observed data points and the predicted curve. The general equation for chi-square is (Knoll, 2000):

$$\chi^2 = \frac{1}{\mu'}\sum_{i=1}^{N}\left(x_i - \mu'\right)^2 \qquad \text{(Equation 8)}$$

where μ' is the experimental data mean and x_i is a particular value in the data set. A chi-square of zero results when the predicted function perfectly matches the expected data points,

however, since a perfect match is highly unlikely (considering measurement error), good agreement is considered to exist when the chi-square value is approximately equal to the number of degrees of freedom (the expectation value). When used in conjunction with the maximum likelihood method, the chi-square is essentially the sum in the exponential of Equation 7 above. By minimizing this sum (χ^2) the probability $P(\mu')$ that the parent distribution and the experimental distribution match is maximized.

Since the chi-square statistic does not detect a non-random scatter bias around the fit, another statistic was also applied to the data; the autocorrelation coefficient described in Puncher et al., 2006. The autocorrelation coefficient (ρ) is calculated using the following formula:

$$\rho = \frac{\sum_{i=1}^{N-1} R_i R_{i+1}}{\sum_{i=1}^{N} R_i^{\,2}} \qquad \text{(Equation 9)}$$

where N = the number of residuals, R_i = the ith residual in N residuals and ρ is a value between -1 and 1. The autocorrelation coefficient is expected to be close to zero in totally random conditions and a ρ close to 1 or -1indicates a less random scatter of data points around the fitted function. This statistic can expose a poor model fit to data resulting from non-randomness in bioassay data residuals and has been found to be an effective tool in bioassay analysis (Puncher et al., 2006). The autocorrelation test thereby provides a more stringent evaluation of the fit to the case data than the chi-square test alone.

3.6 Estimation of Error in the Urine Data

IMBA uses the ICRP 68 Reference Worker to estimate the average excretion rate over a specified time period. Since the NIOSH report for Hanford reports that most Hanford urine samples were simulated 24-hour samples, a period of one day was entered into the IMBA collection period column for USTUR case urine measurements in the analyses. Simulated 24-hour samples were not true 24-hour samples because they were collected over two evening through morning periods. This method of urine collection produced about 75% of the Reference Worker real 24-hour urine (Bihl, 2003). In addition, Moss et al. (1968) determined that true 24-hour samples had a geometric standard deviation of 1.1, but samples collected in the Hanford method exhibited greater variability with a geometric standard deviation of 1.9.

For comparative purposes, the urine data errors in the Case 0262 analysis were left at the errors generated empirically by James et al. (2008b) to reflect scatter in the data points. James et al. used a value of 2.4 for all urine samples less than the limit of detection and this value was extended to Cases 0151 and 0334. The error assumption used for urinary excretion rate measurements above the limit of detection in Case 0151 and Case 0334 was 1.8. As mentioned above, Moss et al. experimentally determined that a geometric standard deviation of 1.9 was associated with simulated 24-hour samples. The most conservative error value used by James et al. (2008b) for "real" urine measurements above LOD was 1.8 and since this value was very close to Moss et al.'s error assumption, a geometric standard deviation of 1.8 was assumed for the "real" urine measurement values in this study. The error distribution in all case analyses was assumed to be lognormal.

Section 4 RESULTS AND DISCUSSION

4.1 USTUR Case 0262

The Case 0262 registrant was an engineer at the Hanford Site for about 30 years who suffered two suspected inhalations of weapons grade plutonium and a subsequent puncture wound to the left thumb while working in a glove box. The exact isotopic composition and form of the plutonium mixture involved in the puncture wound was unknown. Urine samples immediately following the two inhalations showed measurable plutonium, however analysis of the case conducted by James et al. (2008b) showed that the two inhalations contributed very little to the long term urinary excretion, so the inhalations were ignored and the urinary data entered into IMBA represented only the puncture wound time period from the date of the accident through the following 25 years. A whole body count of $^{239+240}$Pu that was taken using a low-energy planar Ge (LEGe) detector at the autopsy was also included in the IMBA data set.

Several series of NCRP plutonium category combinations were implemented in IMBA for a Case 0262 total chi-square sum comparison and the lowest chi-square series are reported in Table 3. Series 1 included all five of the radionuclide categories suggested by NCRP for plutonium chemistries: strong, avid, colloid, particle and fragment. The total intake activity calculated by IMBA was 159 Bq, with the greatest apportionment to the fragment and strongly-retained categories, 121.7 Bq and 31.2 Bq respectively. The avid category received a smaller apportionment of 6.3 Bq. The total chi-square sum for Series 1 was 52.3 ($p = 0.18$).

Table 3. IMBA Professional Plus analysis results for Case 0262.

Radionuclide Category	Intake Activity Apportionment (Bq)		
	Series 1	Series 2	Series 3
Strong	31.2	31.2	35.9
Avid	6.3	6.4	
Colloid	4.0×10^{-5}		
Particle	0		
Fragment	121.7	121.7	122.9
$\Sigma\chi^2$ (probability)	52.3 (0.18)	52.3 (0.18)	55.5 (0.12)
Total ρ (probability)	9.5×10^{-2} (0.21)	9.5×10^{-2} (0.21)	0.12 (0.15)

As the colloid and fragment categories contributed insignificantly to the total intake activity in Series 1, for Series 2 they were eliminated from the analysis. The resulting total chi-square sum remained an unchanged statistically significant 52.3 ($p = 0.18$). The final set of NCRP default retention categories, Series 3, comprised only the strong and fragment categories and produced an increase in the total chi-square sum to 55.5 ($p = 0.12$) due to the loss of the avid category.

All three plutonium category combinations obtained fits to the Case 0262 bioassay data with statistically significant total chi-square sums and autocorrelations coefficients. Series 1 and 2 had the same chi-square value ($\Sigma\chi^2 = 52.3$), but since Series 2 had a slightly higher urine chi-square and autocorrelation statistical probability, it is considered to be the optimum fit series. The chi-square for this optimum fit series was 52.3 ($p = 0.18$) and the autocorrelation coefficient was 0.1 ($p = 0.21$). A graphical fit of the optimum solution to the Case 262 bioassay data is shown in Figure 5.

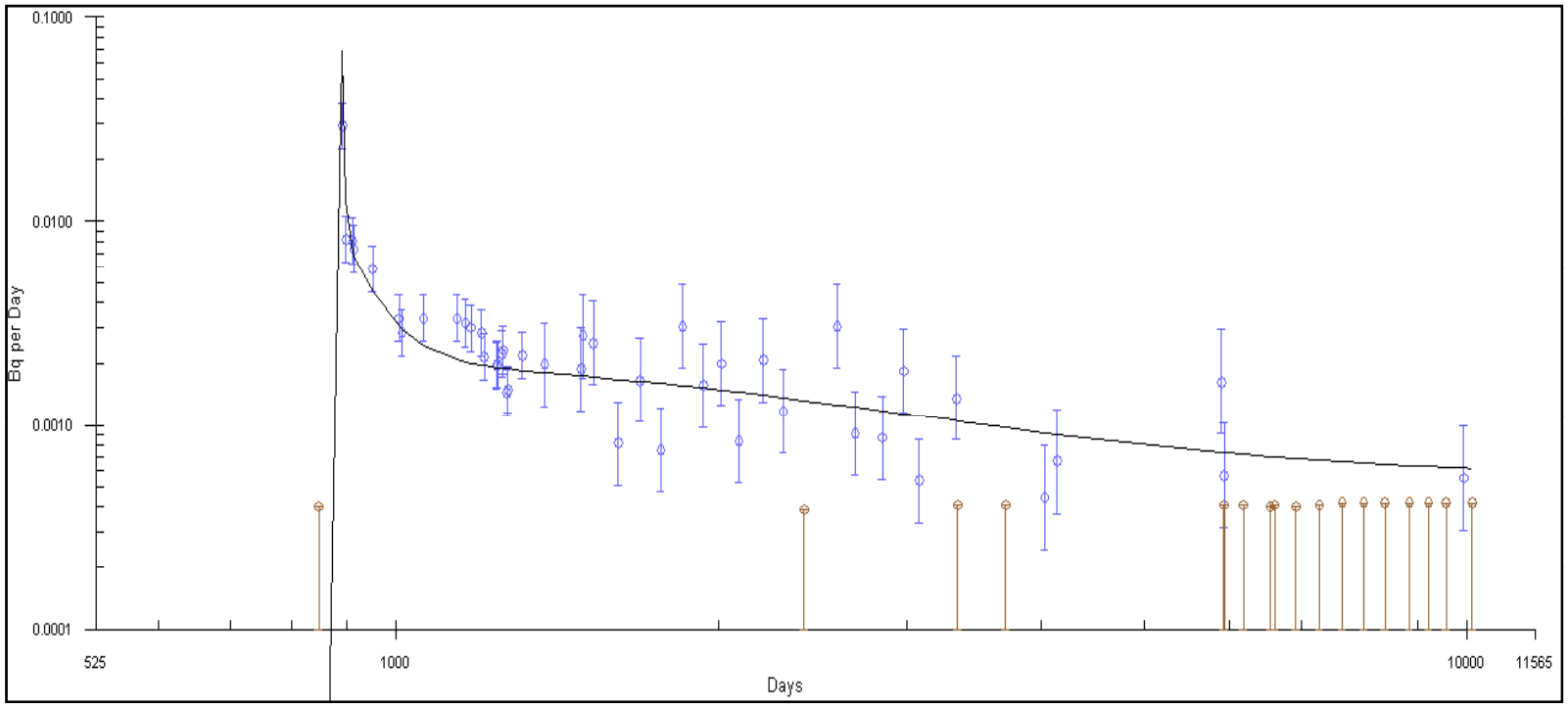


Figure 5. The optimum fit to the Case 0262 bioassay data generated by IMBA (Series 2).

The NCRP default retention parameters did not provide as good a fit to the urine data ($\Sigma\chi^2 = 52.3$) as the iterative process employed by James et al. (2008b) to fit the measured organ contents ($\Sigma\chi^2 = 42.7$). This is almost certainly due to the fact that the fit for this study was constrained by the three retention functions (strong, avid, fragment) provided by the NCRP. Nevertheless, the fit has a statistically significant chi-square and autocorrelation coefficient which demonstrates that the NCRP default parameters adequately modeled the bioassay data for Case 0262 when no assumptions were made about the plutonium material type.

The apportionment of intake activity assigned by IMBA indicates that the plutonium material involved in the puncture incident was 24% soluble plutonium, composed of strongly-retained (20%) and avidly-retained (4%) plutonium, and 76% highly insoluble plutonium categorized as fragment. This is consistent with the findings of James et al. (2008b) who found 14% of the plutonium material to be soluble. The unusual mixture of soluble and highly insoluble plutonium is probably a result of the environment in which the puncture took place. The Hanford Site processed plutonium for a diverse range of applications (Bihl, 2003), so it is not unreasonable to expect that the plutonium present in Hanford Site glove boxes included a variety of plutonium forms at different stages in the refinement process, some of which may have been residual from prior activities.

The fragment retention function received full apportionment for the insoluble component of the mixture, while the particle retention category contributed nothing to the fit of the Case 0262 data set. This is surprising since the fragment default parameters were primarily derived from experiments with depleted uranium over 20 μm in size. It is unlikely that that the registrant was working with fragmentary plutonium in the Hanford glove box;

rather, the plutonium material was likely to have been a particle form of $^{239}PuO_2$ as suggested by James et al. (2008b). Though the fit to the data was good, the questionable category assignment indicates that slower retention parameters may be necessary for the particle category in order to account for more insoluble forms of $^{239}PuO_2$. This underestimation of the particle retention function time-span is likely the result of the short life-span of the animals used in the experiments from which the wound model particle retention functions were derived.

4.2 USTUR Case 0151

The Case 0151 registrant was a pipefitter at the Hanford Site for about 30 years. In the 1950s, while working with a soluble form of plutonium through the gloves of a process hood, the registrant received a small puncture wound to the left ring finger. A survey of the wound and inside surface of the surgical glove indicated contamination of about 500 dpm and urine samples taken after the incident showed measurable amounts of plutonium. An excision was performed to remove the embedded contamination, but no chelation agents were administered. The health physicist at Hanford estimated the worker received an uptake of about 37 Bq of plutonium.

Several series of NCRP plutonium category combinations were implemented in IMBA for a Case 0151 total chi-square sum comparison and the three lowest chi-square series are reported in Table 4. Series 1 included all five of the radionuclide categories suggested by NCRP for plutonium chemistries: strong, avid, colloid, particle and fragment. The total intake activity calculated by IMBA was about 25 Bq, with the greatest apportionment to the soluble avid- and strongly-retained categories, 14.5 Bq and 10.3 Bq

respectively, and small apportionments to the three insoluble categories. The total chi-square sum for Series 1 was a statistically significant 27.0 ($p = 0.26$). However, the autocorrelation coefficient was not significant at 0.31 ($p = 3.3 \times 10^{-2}$).

Table 4. IMBA Professional Plus analysis results for Case 0151.

Radionuclide Category	Intake Activity Apportionment (Bq)		
	Series 1	Series 2	Series 3
Strong	10.3	10.3	10.2
Avid	14.5	14.6	14.6
Colloid	2.6×10^{-4}		
Particle	8.3×10^{-5}		
Fragment	4.4×10^{-3}	6.0×10^{-4}	
$\Sigma\chi^2$ (probability)	27.0 (0.258)	26.9 (0.261)	26.9 (0.259)
Total ρ (probability)	0.31 (3.3×10^{-2})	0.31 (3.4×10^{-2})	0.30 (3.3×10^{-2})

In Series 2, the colloid and particle categories were eliminated from analysis and the result was a slightly lower chi-square sum of 26.9 ($p = 0.26$). As expected, the removal of the fragment category from the analysis in Series 3 had no effect on the fit to the Case 0151 data. In Series 2 and 3, the sum of chi-squares was statistically significant while the autocorrelation coefficient remained below the 95% confidence level. Though the chi-square results for all three series analyses were comparable, Series 2 is considered the optimum fit to the Case 0151 data due to its slightly higher chi-square probability of 0.261. The graphical fit of the optimum solution to the Case 0151 bioassay data is shown in Figure 6.

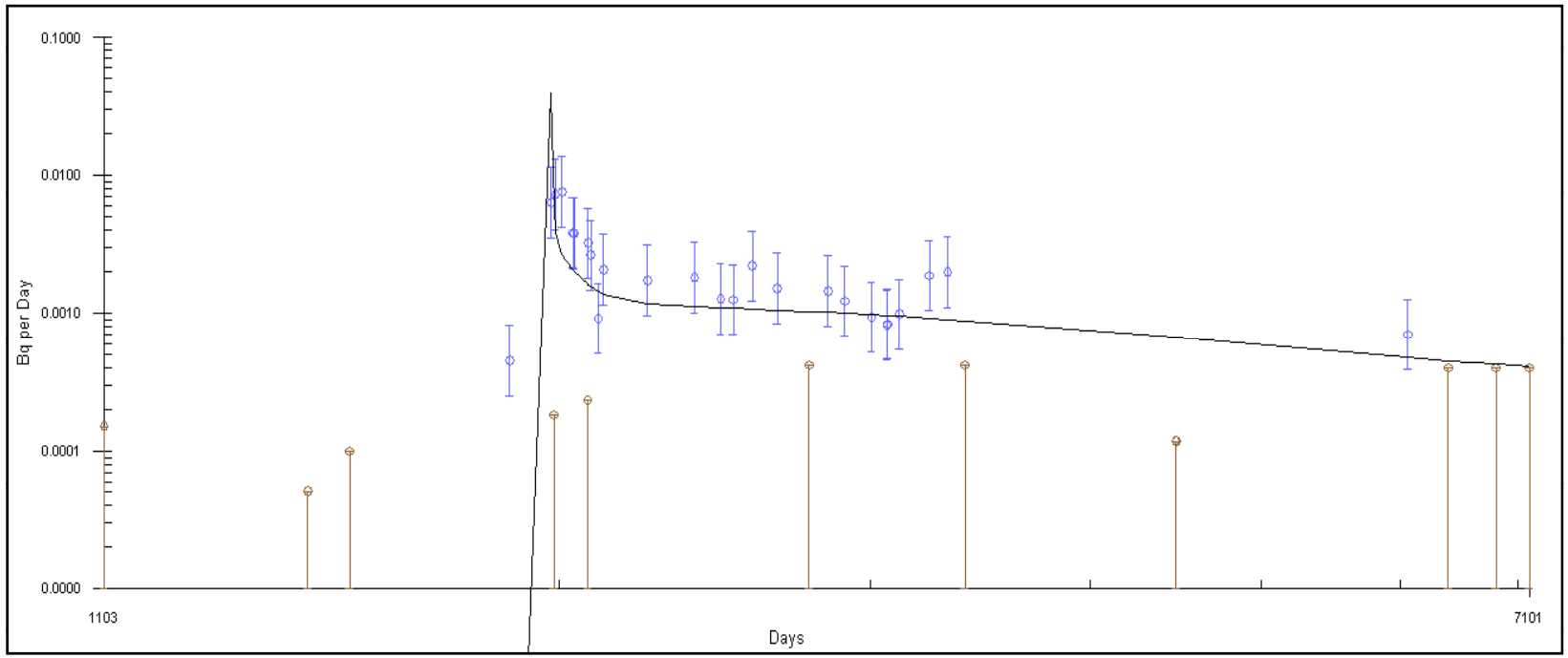


Figure 6. The optimum fit to the Case 0151 bioassay data generated by IMBA (Series 2).

A visual examination of the graphical solution for the Case 0151 optimal fit provides a clue as to the non-significant autocorrelation coefficient result. Several less than LOD urine measurements are present among the "real" urine data points; two of which occur within 4 months of the wound incident. IMBA is forced to drag the fit to the data set downward in order to include these points, resulting in a fit curve with too many data points above the curve.

The urine data for Case 0151 included a sample taken 7 days after the wound accident that was less than the limit of detection and was called "obviously not valid" by the health physicist who wrote the incident report. No technical justification was provided by the health physicist for this opinion, beyond the incongruity of a urine measurement below LOD immediately following a high plutonium measurement on day 2. Given the statistically non-significant autocorrelation coefficient results in the Case 0151 analysis reported above, a second set of analyses were performed for this case with the day 7 data point considered as an outlier and excluded from the IMBA calculations. This allowed an examination of the effect of this data point's removal on the fit to the data and the intake activity apportionment. The three lowest chi-square series results are given below in Table 5.

Table 5. IMBA Professional Plus analysis results for Case 0151 (with exclusion of outlier).

Radionuclide Category	Intake Activity Apportionment (Bq)		
	Series 1	Series 2	Series 3
Strong	14.03	17.57	17.51
Avid	10.71	6.52	6.58
Colloid	0		
Particle	0	2.3×10^{-5}	
Fragment	0		
$\Sigma\chi^2$ (probability)	25.4 (0.33)	25.6 (0.32)	25.6 (0.32)
Total ρ (probability)	0.24 (6.5×10^{-2})	0.23 (7.4×10^{-2})	0.23 (7.4×10^{-2})

Removal of the day 7 urine measurement from the IMBA intake calculation resulted in a lower chi-square fit to the data in all three series. In addition, all three outlier series yielded fits to the urine data with statistically significant autocorrelation coefficients. Series 1 yielded a statistically significant sum chi-square of 25.4 ($p = 0.33$), representing a slight decrease from the non-outlier Series 1 chi-square of 27.0 ($p = 0.258$). This was also the minimum chi-square fit to for the outlier series of analyses and was therefore considered the optimum fit to the data. The improved autocorrelation coefficient in the Case 0151 data fit as a result of removing the day 7 data point indicates that the original health physicist's assessment of the day 7 urine measurement as "invalid" was correct. A graphical fit of the optimum outlier solution to the Case 0151 bioassay data is shown in Figure 7.

The apportionment of intake activity assigned by IMBA indicates that the plutonium material involved in the Case 0151 puncture wound incident was a more soluble form of plutonium composed primarily of strongly- and avidly-retained plutonium. The percentage of total intake activity for the strongly-retained form varied from 56% to 77%, depending on the series parameters included in the analysis, with the remainder being avidly-retained. It is clear that the plutonium material involved in Case 0151 was more soluble than the plutonium material for Case 0262 since neither of the slow retention categories, particle and fragment, received an apportionment of the intake activity significant enough to affect the fit in any of the series analyses, either with or without the day 7 urine measurement. It is likely that the mass of the ^{239}Pu that contaminated the wound was small enough that the compound acted as a primarily soluble radionuclide. As stated previously, NCRP Report No. 156 categorizes material containing masses of ^{239}Pu under 3.2 μg as strongly-retained.

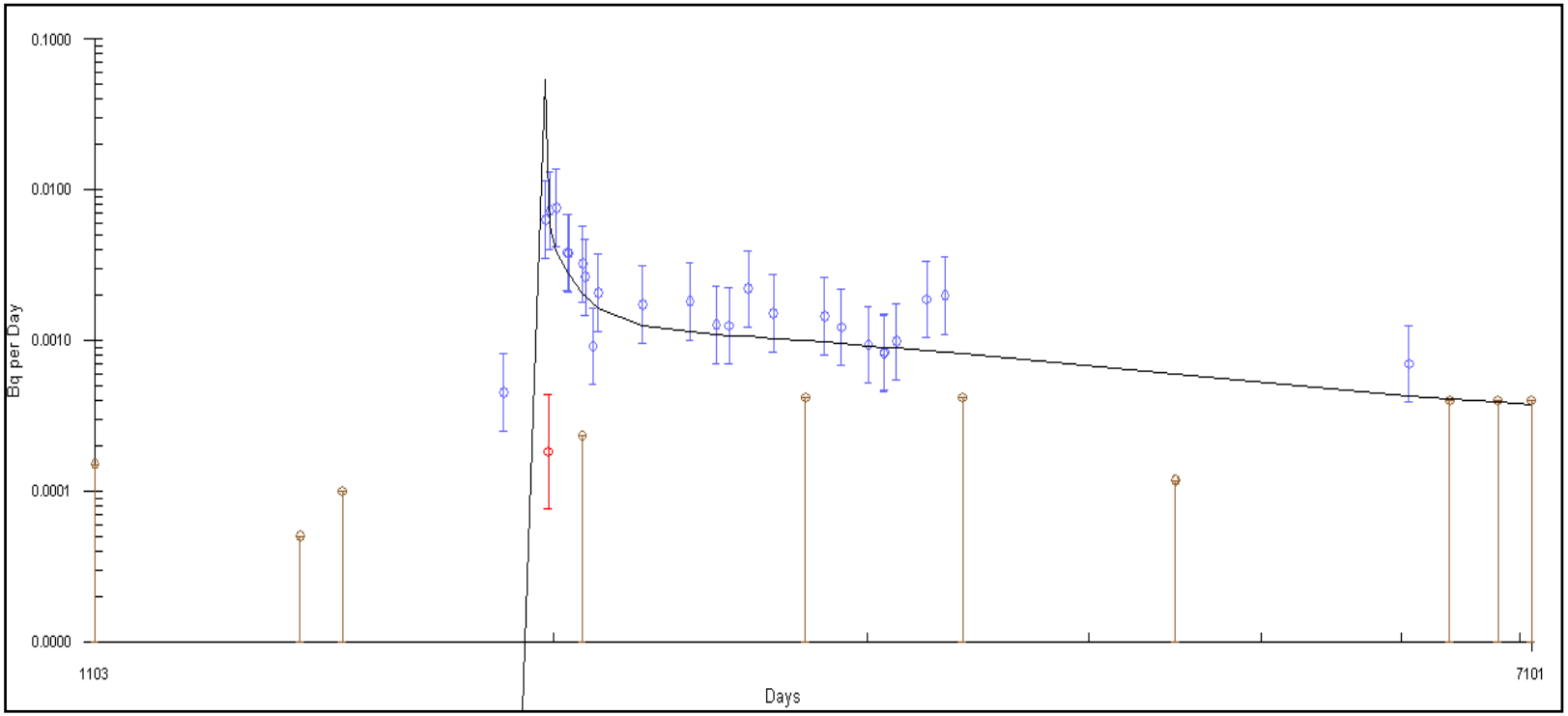


Figure 7. The optimum fit to the Case 0151 bioassay data generated by IMBA with the outlier excluded (Series 1).

The results of both sets of analyses for Case 0151, with and without the day 7 possible outlier, indicate that the NCRP default retention parameters can provide a statistically significant fit to urine measurement data for a wound contaminated with a more soluble form of plutonium when no assumptions are made about the material type. Though only the autocorrelation coefficients for the series of data fits that excluded the day 7 urine measurement were statistically significant, the chi-squares for all series analyses performed were above the 95% confidence level.

4.3 USTUR Case 0334

The Case 0334 registrant was employed at the Hanford Site for about 30 years. In the 1950s, this worker received a puncture wound to the right little finger while working through the gloves of a process hood. A survey of the inside of the inner gloves worn by the employee yielded a count of about 10,000 dpm. Two excisions were performed in the two days following the accident, but no chelating agents were administered. Urine samples taken after the incident showed measurable amounts of plutonium. Since another suspected intake incident was reported to have occurred to this registrant 6 years after the little finger puncture accident, the urine data used for the Case 0334 analysis in this study included urine measurements taken from the beginning of the year in which the puncture wound occurred up to the year of the second intake incident.

Several series of NCRP plutonium category combinations were implemented in IMBA for a Case 0334 total chi-square sum comparison and the four lowest chi-square series are reported in Table 6.

Table 6. IMBA Professional Plus analysis results for Case 0334.

Radionuclide Category	Intake Activity Apportionment (Bq)			
	Series 1	Series 2	Series 3	Series 4
Strong	156.7	164.7	159.3	159.3
Avid	1.13×10^{-4}	0	6.0×10^{-5}	
Colloid	0			
Particle	0	0		
Fragment	0			
$\Sigma\chi^2$ (probability)	63.8 (0.11)	62.6 (0.13)	63.3 (0.12)	63.3 (0.12)
Total ρ (probability)	0.41 (6.0×10^{-4})	0.40 (8.9×10^{-4})	0.40 (7.0×10^{-4})	0.40 (7.0×10^{-4})

IMBA was able to produce a statistically significant fit to all four of the best-fit series for Case 0334, including Series 1 which included all five of the radionuclide categories suggested by NCRP for plutonium chemistries: strong, avid, colloid, particle and fragment. The "optimum" fit series, Series 2, exhibited a minimum chi-square of 62.6 ($p = 0.13$), a value slightly lower than the resulting chi-squares in the other three series. The graphical fit of the optimum solution to the Case 0334 bioassay data is shown in Figure 8.

The total intake activities estimated by IMBA for the various Case 0334 analyses were in the range of 157 to 165 Bq, with all of the activity in the "optimum" fit attributed to the strongly-retained category. The plutonium material involved in this wound incident was clearly a more soluble form of plutonium than the material in Case 0151 since the apportionment of activity did not include an avid, or longer-retained component.

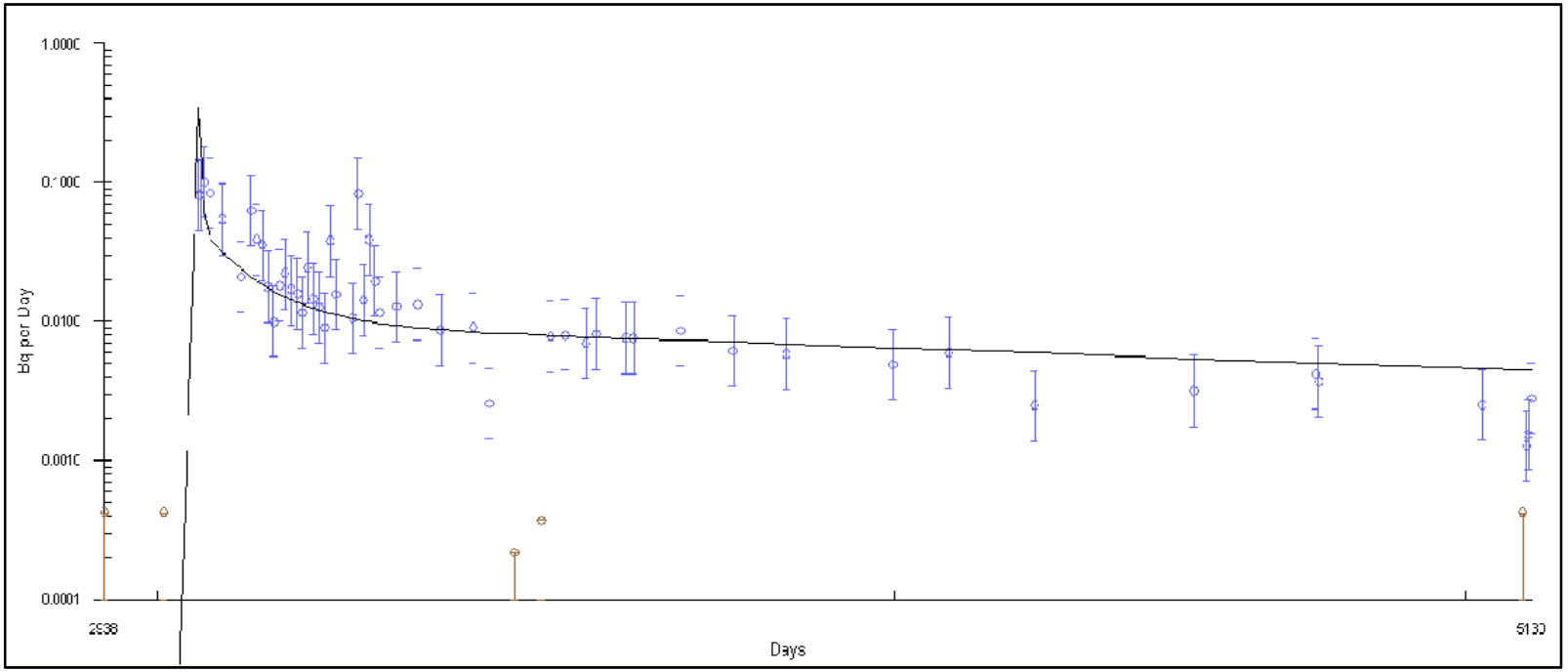


Figure 8. The optimum fit to the Case 0334 bioassay data generated by IMBA (Series 2).

Though all four of the best-fit series for Case 0334 had statistically significant chi-squares, none of the series resulted in fits with statistically significant autocorrelation coefficients. As mentioned above, the autocorrelation statistical test is a stringent evaluation of a data fit that exposes non-randomness in bioassay data residuals. It was demonstrated in the Case 0151 analysis that one outlier can greatly affect the statistical significance of the autocorrelation coefficient in a fit to bioassay data. The relatively high degree of scatter in the urine excretion measurements in Case 0334 likely explains the inability of IMBA to produce fits to these series with statistically significant autocorrelation coefficients. Three of the Case 0334 urine excretion measurements taken at day 164, day 199, and day 213 lie far above the fit generated by IMBA. Though the case records do not indicate it, the autocorrelation coefficient statistical test result combined with a visual evaluation of the bioassay graph (Figure 1) reveals a second intake activity peak, likely a plutonium inhalation event, that cleared rapidly and contributed insignificantly to the total dose.

4.4 Further Discussion of Results

The three USTUR plutonium-contaminated wound cases used in this study included a primarily insoluble plutonium material and two soluble plutonium materials and allowed for an evaluation of the NCRP wound model default retention equation parameters' ability to model intakes involving both types of plutonium chemistries. Since no assumptions were made about the form of plutonium contaminating the wounds, the dosimetric software IMBA was allowed to assign a portion of the intake activity to the five sets of plutonium default retention parameters as needed to obtain a fit to the case bioassay data. It was therefore

possible to quickly determine the composition of the plutonium material introduced into the wound by looking at the intake activity apportionments, provided a "good" fit was obtained.

A statistically significant chi-square was achieved in USTUR Case 0262 ($\Sigma\chi^2 = 52.3$, $p = 0.18$) Case 0151 ($\Sigma\chi^2 = 27.0$, $p = 0.26$) and Case 0334 ($\Sigma\chi^2 = 62.6$, $p = 0.13$) using all five of the default NCRP plutonium categories as separate intake regimes. Though the removal of selected categories during the analysis of Case 0151 resulted in a lower "optimized" chi-square, the difference was so small as to be negligible. In Case 0262 the Series 1 and "optimized" Series 2 were essentially identical, and in Case 0334 the "optimized" Series 2 fit chi-square was only slightly lower than the Series 1 fit chi-square. These results indicate that a statistically valid fit to human plutonium-contaminated wound case bioassay data is possible using the NCRP default retention parameters even without the necessity of reducing the number of chemistry categories. Since a statistically significant chi-square at the 95% confidence level was obtained in the fits to the bioassay data for all three USTUR cases analyzed, the null hypothesis is considered supported.

Section 5 CONCLUSION

5.1 Summary of Results

These results show that the range of retention rates encompassed by the NCRP default categories, when used with a formal statistical method to determine the relative contribution of each category, is adequate to represent the wound absorption behavior in the three USTUR cases tested. These default retention functions can adequately model systemic uptake from plutonium-contaminated wounds in humans provided that comprehensive bioassay data are available. Statistically significant fits to the bioassay data were obtained in each case using the NCRP wound model default retention parameters. These results substantiate the NCRP's prediction that the default parameters will be useful in dose assessment cases where little information is available about the form of the radionuclide introduced into the wound since in all three of the USTUR wound cases used in this study, no specifics about the contaminating plutonium chemical form, beyond general historical information about Hanford plutonium material, were known.

In addition, the Case 0262 analysis indicated that slower retention parameters may be necessary for the particle category in order to account for more insoluble forms of plutonium under 20 μm. This underestimation of the particle retention function time-span is likely the result of the short life-span of the animals used in the experiments from which the wound model particle retention functions were derived.

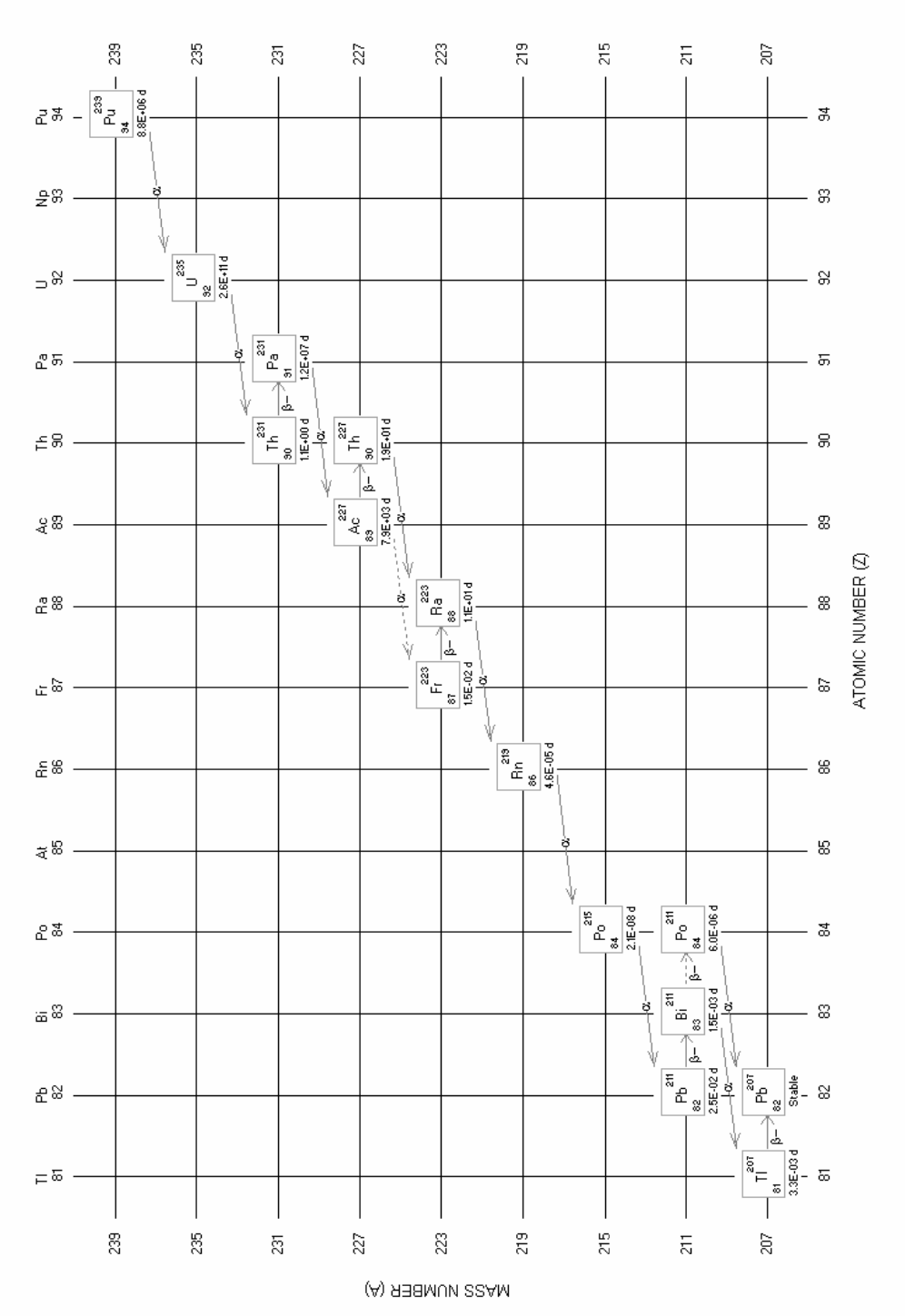
5.2 Future Work

In the future, it would be useful to conduct additional tests of the NCRP Report No. 156 wound model's default retention equation parameters ability to predict the systemic uptake of plutonium in human wound cases. This study involved an analysis of only three of the numerous and varied human plutonium-contaminated wound cases available in the USTUR database, so there are further opportunities to continue the evaluation of the NCRP wound model with additional cases that involve wounds contaminated by an array of plutonium materials, chemistries and activities. In particular, it would be beneficial to use additional wound cases to assess the need for a longer set of retention equation parameters for the NCRP wound model's particle category, as suggested by the Case 0262 results.

In addition, the scope of this study did not include an evaluation of NCRP Report No. 156's default transfer rates for the transport of radioactive material between the wound model biokinetic compartments, so a study that assessed the modeling ability of these transfer rates between the wound compartments and the blood for human plutonium-contaminated wound cases would also be useful to wound dosimetry.

APPENDIX A

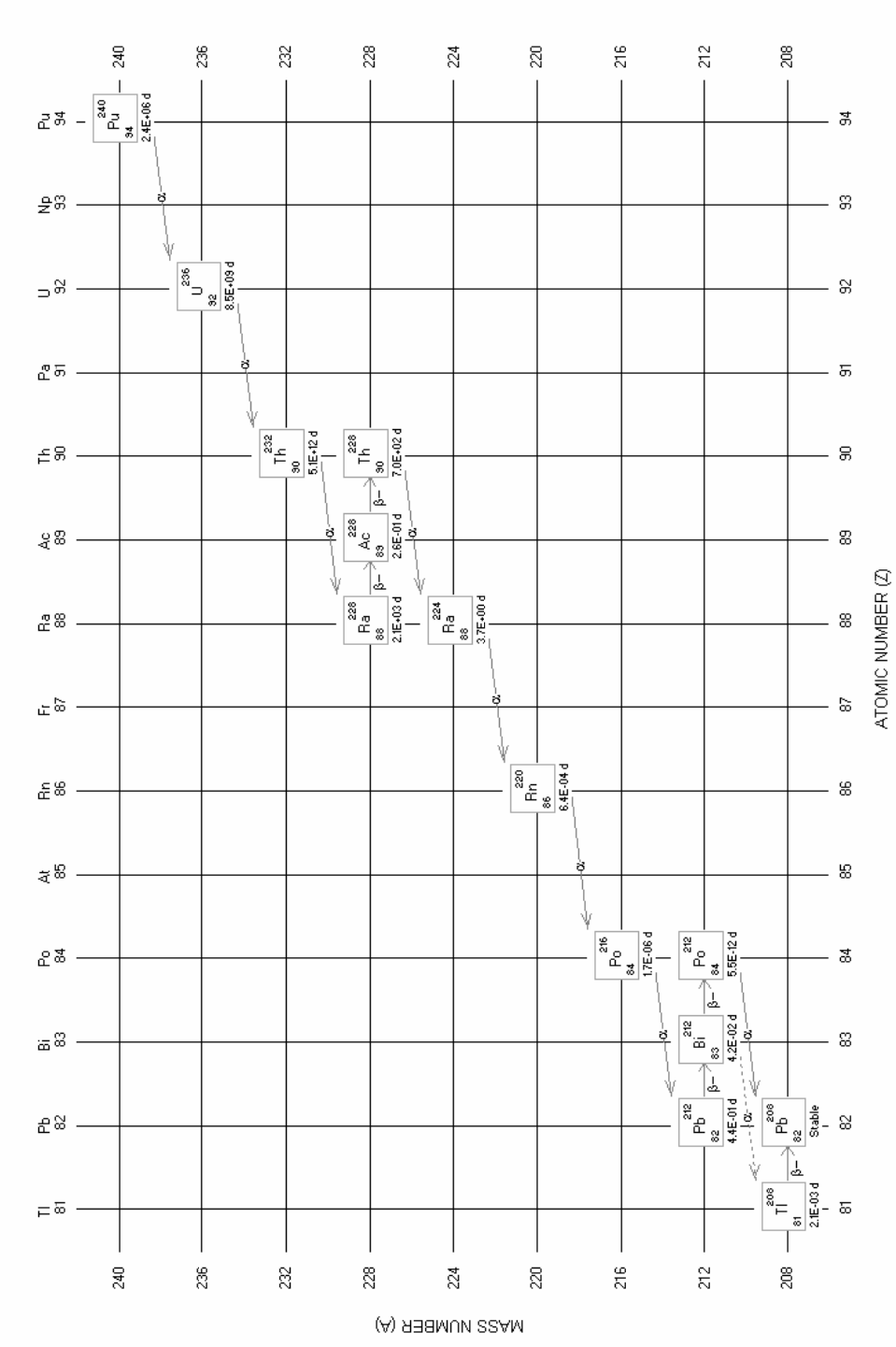
Plutonium-239 Decay Scheme



(Decay scheme from IMBA Professional Plus software)

APPENDIX B

Plutonium-240 Decay Scheme



(Decay scheme from IMBA Professional Plus software)

APPENDIX C

Adult Transfer Rates (d^{-1}) for the ICRP 67 Plutonium Model

Source and Target	*Transfer Rate (d^{-1})*
Blood to Liver 1	0.1941
Blood to Cortical Surface	0.1294
Blood to Trabecular Surface	0.1941
Blood to Urinary Bladder Content	0.0129
Blood to Kidney (urinary path)	0.00647
Blood to Other Kidney Tissue	0.00323
Blood to ULI Contents	0.0129
Blood to Testes	0.00023
Blood to Ovaries	0.000071
Blood to ST0	0.2773
Blood to ST1	0.0806
Blood to ST2	0.0129
ST0 to Blood	0.693
Kidneys (urinary path) to Bladder	0.01386
Other Kidney Tissue to Blood	0.00139
ST1 to Blood	0.000475
ST 1 to Urinary Bladder Contents	0.000475
ST2 to Blood	0.000019
Trabecular Surface to Volume	0.000247
Trabecular Surface to Marrow	0.000493
Cortical Surface to Volume	0.0000411
Cortical Surface to Marrow	0.0000821
Trabecular Volume to Marrow	0.000493
Cortical Volume to Marrow	0.0000821
Cortical/Trabecular Bone Marrow to Blood	0.0076
Liver 1 to Liver 2	0.00177
Liver 1 to Small Intestine	0.000133
Liver 2 to Blood	0.000211
Gonads to Blood	0.00019

(Adapted from ICRP 67, 1993)

APPENDIX D

Default Transfer Rates between Compartments for the Various Radionuclide Categories of the NCRP Biokinetic Wound Model

Transfer Compartments	*Weak*	*Moderate*	*Strong*	*Avid*	*Colloid*	*Particle*	*Fragment*
Soluble to blood	45	45	0.67	7.0	0.5	100	---
Soluble to CIS	20	30	0.6	30	2.5	---	---
CIS to soluble	2.8	0.4	2.4×10^{-2}	0.03	2.5×10^{-2}	---	---
CIS to PABS	0.25	6.5×10^{-2}	1.0×10^{-2}	10	5×10^{-2}	---	---
CIS to lymph nodes	2×10^{-5}	2×10^{-5}	2×10^{-5}	2×10^{-5}	2×10^{-3}	---	---
PABS to soluble	8×10^{-2}	2×10^{-2}	1.2×10^{-3}	0.005	1.5×10^{-3}	2×10^{-4}	0.0
PABS to lymph nodes	2×10^{-5}	2×10^{-5}	2×10^{-5}	2×10^{-5}	4×10^{-4}	3.6×10^{-3}	0.004
PABS to TPA	---	---	---	---	---	4×10^{-2}	0.7
TPA to PABS	---	---	---	---	---	3.6×10^{-3}	5×10^{-4}
Lymph nodes to blood	---	---	---	---	3×10^{-2}	6×10^{-4}	3×10^{-2}
Fragment to soluble	---	---	---	---	---	---	0.0
Fragment to PABS	---	---	---	---	---	---	8×10^{-3}

Adapted from NCRP Report No. 156 Wound Model, 2007.

APPENDIX E

Routine Plutonium Urinalysis Detection Levels for the Hanford Site

Adapted from the NIOSH Dose Reconstruction Project, 2003.

Period	*MDA (dpm/sample)*	*Decision Level (dpm/sample)*	*Measured Radionuclide*
Before June 1949	0.96	0.66	Total Pu alpha
6/1949 - 11/1952	0.33		Total Pu alpha
12/1952 - 1/27/53	0.18		Total Pu alpha
1/28/53 - 3/26/53	0.15		Total Pu alpha
3/27/53 - 11/06/53	0.05		Total Pu alpha
11/07/53 - 12/04/53	0.07		Total Pu alpha
12/53 - 4/55	0.057		Total Pu alpha
5/55 - 8/55	0.027		Total Pu alpha
9/55 - 9/55	0.04[a]		Total Pu alpha
10/55 - 9/30/83	0.05	0.025	Total Pu alpha
10/01/83 - 12/31/83	0.035	Not established 0.018 assumed	Each Pu-238, Pu-239
1/02/84 - 4/88	0.02		Total Pu alpha
5/88 - 5/90	0.02	0.01	Total Pu alpha
6/90 - 11/91	0.03	0.015	Total Pu alpha
11/91 - 4/2000	0.02	0.01	Total Pu alpha
5/2000 - 8/2001	0.02	X_b[b] + 2.05 x TPU[c]	Total Pu alpha
9/2001 - present	0.02	2 x TPU[c]	Total Pu alpha

[a] this value was most likely a decision limit rather than a real MDA

[b] mean of blanks

[c] total propagated uncertainty

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