

Evaluation of the In Press NCRP Wound Model Using USTUR Case 0262 Data

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INTRODUCTION

The highly anticipated NCRP wound model is currently in press and is due to be published in 2007. Concepts and approaches incorporated in this model have been presented at several recent internal dosimetry meetings. Previous dosimetric analyses of wound cases have not included 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 have been represented purely empirically, for example as multi-phased exponential retention components. The new NCRP model incorporates specific clearance pathways, based upon animal experimental data for various radionuclides, with an emphasis on solution chemistry that has been extrapolated to humans. Therefore, specific tests of its applicability to the human metabolic system are needed. This study discusses the applicability of the conceptual NCRP wound model to evaluating human plutonium contaminated wound data.

USTUR CASE 0262

Case 0262 was a U.S. Transuranium and Uranium Registries whole body donor. He had two prior inhalations of refractory ²³⁹PuO₂, and a Pu puncture wound to the skin of the thumb obtained while working with Pu materials in a glovebox. James et al. (in press) carried out a full biokinetic analysis of this case by solving the combined respiratory tract, wound, axillary lymph node and systemic Pu biokinetic model shown in Figure 1. In this model, the uptake and retention of Pu in the wound and associated axillary lymph node is treated entirely empirically in terms of several exponentially cleared compartments. The wound/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 ($\chi^2 = 42.7$), including the measured distribution of Pu between the wound, axillary lymph nodes, and major body organs. The study showed that only 40% of the Pu 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/axillary lymph node into the blood occurred extremely slowly (49% at $6 \times 10^{-5} \text{ d}^{-1}$ and 37% at $5 \times 10^{-6} \text{ d}^{-1}$). 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 ²³⁹Pu wound contamination consisted of a mixture of refractory ²³⁹PuO₂ and a more soluble Pu form.

This study examines the application of the new, mechanistic NCRP wound model to the evaluation of the USTUR Case 0262 (human) data. The NCRP (in press) wound model categorizes radionuclide materials into retention categories based on their solubility: weak, moderate, strong, avid, colloid, particle, or fragment. Each of these categories has been assigned two or three absorption rate coefficients and associated fractions. In this study, each of NCRP's 'default' categories of wound absorption behavior was implemented in the IMBA Professional Plus Version 4.0.28 bioassay analysis software (http://hss.energy.gov/CSA/CSP/sqa/central_registry/IMBA/imba.htm), and the software was used to determine how well NCRP's recommended parameter values represent the measured bioassay data, wound/axillary lymph node, and systemic retention.



Figure 1. Combined biokinetic model of wound site, axillary lymph node, respiratory tract and systemic plutonium solved by James et al. (in press) for USTUR Case 0262.

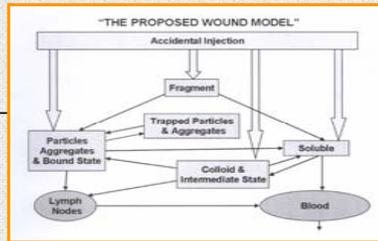


Figure 2. The NCRP (in press) biokinetic model of radionuclide translocation from a wound site as published by Guilmette and Durbin (2003). This model is set to replace empirical wound absorption models such as that shown in Figure 1.

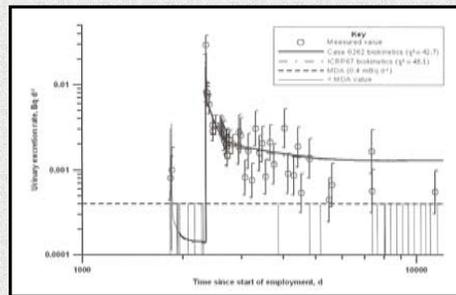


Figure 3. Optimum fit to the urinary excretion data for USTUR Case 0262 obtained by James et al. (in press) by varying retention parameters in the Figure 1 biokinetic model to minimize the total chi-square-sum ($\chi^2 = 42.7$).

METHODS

To evaluate the utility of the NCRP (in press) wound model retention coefficients in predicting the Case 0262 data, no prior assumption was made about the 'absorption category' of the Pu material. Instead, the default parameters for each absorption category (weak, moderate, strong, avid, particle and fragment) were entered into the IMBA wound module as six different 'hypothetical' intake regimes, and IMBA was allowed to find the combination of material types yielding an optimum 'fit' to the data (Figure 4). For this study, the two prior ²³⁹PuO₂ inhalations were ignored since James et al. (in press) shows that these contributed very little to the long term urinary excretion.

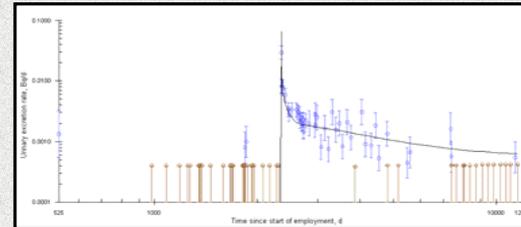


Figure 4. Fit to the Case 0262 urinary excretion data obtained by letting the IMBA software apportion the Pu deposited at the wound site between six 'hypothetical' NCRP categories of wound absorption behavior.

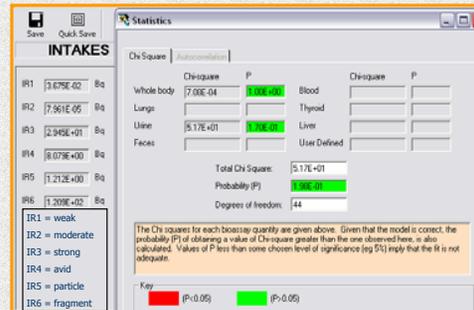


Figure 5. Fitted apportionment of NCRP wound absorption categories from Case 0262 data, and the resulting statistical parameters.

RESULTS

Figure 4 shows the fit to Case 0262's urinary excretion data (and whole body content at death) given by hypothetical combinations of the NCRP (in press) wound absorption categories. For this study, we ignored the translocation pathway between the wound site and axillary lymph node (which, in the James et al. analysis, accounted for 45% of the initially deposited Pu).

Figure 5 shows the apportionment of NCRP Pu wound absorption behavior determined by the IMBA software to give the 'best' (maximum likelihood) simultaneous fit to the Case 0262 urinary excretion and whole body retention data, and the statistical parameters of this fit. The overall sum of chi-squared is 51.7, indicating a highly significant statistical 'fit.'

The fitted apportionment between the various NCRP wound absorption categories is about 19% 'Strong,' 5% 'Avid,' 1% 'Particle,' and 76% 'Fragments.' In other words, the wound absorption of 'refractory' ²³⁹PuO₂ particles is best represented by NCRP's default absorption parameters for 'Fragments.'

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