A method for tracking a case under chelation using urinary excretion measurements

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1 Introduction

A considerable effort has been made to generate methods and biokinetic models for interpreting the urinary excretion of plutonium under the influence of DTPA [1-9]. The approaches have evolved from empirical [1, 2] to mechanistic [3] and most recently leaning towards pharmacokinetic approaches associating biokinetic compartments from the latest accepted plutonium systemic models [10] with those having more influence on the enhancement of the urinary excretion [4, 5, 6, 9]. In addition, work has been published with practical applications for estimating the influence of the excretion enhancement factor on internal dose estimates [7].

Several methods mentioned above focus on estimates of intake, dose, and efficacy of the chelation therapy only after all urine samples have been collected and/or the effect of chelation has subsided (typically taken to be 100 days). The need for early provisional estimates soon after the administration of DTPA has been proved urgent. The estimates can be refined as more bioassay samples are collected and analysed. The method described below has been developed for intake of plutonium by wounds, but it can be extended to other routes of intake and other radionuclides as well.

2 The proposed method

We propose a mechanistic method for tracking the intake and dose estimates and the efficacy of chelation therapy comprising single or multiple treatments, using the available information from Los Alamos National Laboratory (LANL) cases and a simplified wound model [8, 11, 12].

The wound simulation uses a numerical ordinary differential equations solver [13] applied to the latest plutonium systemic model [10], with one unit of activity initially deposited in the wound. A table containing the predicted activities in urine and in the whole body for the unperturbed case (without chelation) is generated and stored. As the chelation treatments occur, the enhanced excreted activity is calculated against the corresponding values from the unperturbed case, accounting for activities already removed in previous treatments. It uses a pre-established average enhancement factor and a two-term exponential function, like that proposed in the Hall model [2], with coefficients for rapid and slow removal of the chelate and short- and long-term retention half-lives of the chelate

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from LANL cases. These parameters will be refined as more bioassay data is collected. The solver is then stopped and the additional activity to be added to the enhanced excretion is selectively removed from the compartments that show the greatest availabilities for removal, i.e., higher transfer rates back to blood and higher activity values. This process is dominated by the amounts in blood, urinary bladder, renal tubules, and rapid-turnover soft tissue. The solver is then restarted, taking into account the delayed effects of each treatment for each subsequent day. Activities in compartments and the corresponding number of nuclear transformations are calculated for later comparison against the results from the unperturbed cases to account for the averted dose.

As real bioassay results become available, a maximum likelihood method is used to fit the intake using the available samples. In this way, preliminary estimates can be made before sufficient bioassay results are available to produce a final, more precise, estimate.

3 Further studies

We intend to study excretion patterns from related cases to assess additional input parameters for the method. We also intend to apply this method to inhalation cases and to other radionuclides using, whenever possible, available information from similar cases to assess input parameters.

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