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UNCERTAINTY MODELING OF RETENTION FUNCTION IN BIOKINETIC MODEL USING POLYNOMIAL CHAOS THEORY - DEVELOPMENT OF COMPUTATIONAL ALGORITHM

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ABSTRACT

Uncertainty analysis of the retention function of any radionuclide either ingested or inhaled plays a central role in the dosimetry of internally deposited radionuclide. The modeling approach presented in International Commission of Radiological Protection publication used exponential retention curves to calculate dose to the possible target or critical organs. Presence of large scatter or imprecision measurement of biokinetic model parameters demands uncertainty analysis of model for its better refinement. Uncertainty analysis of the retention function of a typical radionuclide say strontium is the focal theme of the paper. Uncertainties present in strontium retention function in biokinetic models arise from the assumptions of the biokinetic model, values of the model parameters, radiation weighting factor and tissue weighting coefficients. Mathematically, strontium retention function is expressed as the product of the parameters representing the fraction of strontium absorbed from the gastrointestinal tract, fraction initially retained in the skeleton, proportional to uptake rate, power function slope and strontium elimination rate. Uncertainty associated with a biokinetic model is expressed in terms of lower and upper bounds, A and B, such that there is judged to be roughly a 90% probability that the true central value is no less than A and no more than B. Uncertainty is expressed in terms of these bounds termed as uncertainty factor defined details in the paper. Polynomial chaos expansion method has been adopted to estimate the propagation of uncertainties in the parameters of the strontium retention function. The paper describes the details of polynomial chaos expansion technique to address the uncertainty propagation. Polynomial chaos expansion is an efficient simulation compared to traditional Monte Carlo.

Keywords: *Radionuclide, Retention function, Polynomial chaos expansion, Uncertainty factor.*

1.0 INTRODUCTION

Computational techniques for assimilating data in biokinetic models to understand the uncertainty of the retention function of any radionuclide either ingested or inhaled play a central role in the dosimetry of internally deposited radionuclide. Comprehensive uncertainty analyses of computational physics models are essential, especially when these models are used in decision making. This is especially true for internal dosimetry, where complex computer programs are often used to model and assess the internal dose received by the personnel. The systematic accounting of parametric uncertainty in internal dosimetry models is important, as this aid in the quantification of the degree of confidence in assessing the internal dose received by the personnel while working in radioactive area. Uncertainties are typically classified as aleatory and epistemic [1]. Aleatory uncertainty (also called probabilistic uncertainty) arises from randomness in the system whereas epistemic uncertainty arises due to the lack of knowledge (or ignorance). Epistemic uncertainties may also arise from assumptions introduced in the mathematical model and it can be possible to reduce using inference from experimental observations. Uncertainty that is explicitly recognized by a stochastic model is categorized as aleatory. Uncertainty of the model parameters and the model itself is epistemic. Hence the aleatory/epistemic split of the total uncertainty is model-dependent [2]. Uncertainties associated with the physical parameters of the biokinetic and dosimetric models are due to lack of sufficiency of relevant data or knowledge and error in the measurements of bioassay samples. The stages involved in the uncertainty quantification of a model generally include (a) estimation of uncertainties of model inputs, (b) estimation of uncertainty of the model output and (c) propagation of uncertainty in the model output. Monte Carlo methods are the most widely used techniques for statistical/probabilistic uncertainty analysis, with diverse applications. Given input uncertainty distributions (frequency or probability density data) these methods involve repeated generation of pseudo-random instantiations (sampling) of inputs followed by application of the model to these instantiations to yield a set of model responses. These model outputs are then further analyzed statistically.

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A traditional "uncertainty analysis or error analysis" typically focuses on uncertainty present in the data itself labeled as the "data uncertainty". Traditional method consists of (a) the characterization of uncertainty in model parameters/inputs via their probability density functions (pdfs) and (b) the propagation of these pdfs through model equations to obtain the pdf of selected output metrics[3]. A large number of sample realizations (10^6 or more) of model inputs are required to achieve an acceptable level of confidence about the model output uncertainty. The large numbers of realizations reduce the efficiency of the simulation even though it involves standard or Latin Hypercube sampling. In case of computationally intensive models, the time and resources required by these methods will be prohibitively expensive. However, number of simulations for adequate estimation of uncertainty of the model output can be substantially reduced as compared to conventional simulation, if the model uncertain inputs and output are expressed in the form of a series expansion of standard normal random variable (chaotic expansion); Output of the model then contains the coefficients which are calculated from a limited number of model simulations. The net result is to create a statistically equivalent polynomial approximation to the model outputs. This efficient simulation method presented in this paper is called as "Polynomial Chaos Expansion" (PCE)[3]. PCE is applied for quantification and propagation of the uncertainty of the strontium retention function as model output with a limited number of model run.

The selection of ^{90}Sr retention function as a model for carrying out uncertainty analysis using PCE is mainly due to its importance in radiation protection, as its yield is high during the fission of ^{235}U. When ^{90}Sr is released into the environment, it enters the human body through contaminated dietary foodstuffs, because it is absorbed by the gastrointestinal (GI) tract. Therefore, ingestion of ^{90}Sr is a major exposure pathway for both workers in nuclear industry and the members of the public. Once absorbed in the human body, ^{90}Sr migrates from body fluids to other organs and tissues, especially to bones and retains there for many years. Irradiation of bone tissue increases the risk of cancer such as leukemia or bone cancer. Accurate internal dose estimation is directly related to the quantitative analysis of cancer risk. The prime factor on which the estimation of internal dose due to contamination of ^{90}Sr depends is the intestinal absorption fraction, f_1. The relative uptake of strontium from contaminated food is not well known, i.e, highly uncertain. Similarly, elimination rate of strontium, percentage of the amount of strontium retained in the skeleton are also not well known. Hence, these uncertainties propagate in the retention function of the strontium and accordingly, accuracy in the estimated internal dose decreases. In fact, quantification of uncertainty of the retention function will dictate the amount of accuracy in internal dose, in the sense that, less the uncertainty more will be the accuracy. So, uncertainty analysis in this regard is an important issue.

The paper presents the development of algorithm to quantify the uncertainty associated with the retention function of Sr-90. The paper is organized in the following way. Section 2 presents the mathematical details of PCE. Section 3 describes the model used for computing uncertainty. Methodology of uncertainty analysis of the model output is described in section 4. Section 5 presents the results of uncertainty analysis of the model output and corresponding discussions. Finally conclusion is described in section 6.

2.0 MATHEMATICS OF POLYNOMIAL CHAOS EXPANSION

The Polynomial Chaos Expansion (PCE) approach has its foundation in the work of Wiener (1938)[4], who represented a Gaussian process as an infinite series of Hermite polynomials that take a vector of random variables as arguments. Ghanem and Spanos (1991)[5] used this representation to develop the stochastic finite element method. Xiu and Karniadakis (2002)[6] extended the theoretical framework to non-Gaussian process by using different polynomial basis functions. This generalized polynomial chaos approach was used to address the problem of heat transfer with random material properties by Wan et al. 2004[7].

The PCE is the representation of a random variable, more generally a stochastic process, with an infinite series of orthogonal polynomials that take a vector of independent and identically distributed (iid) random variables as arguments. Mathematically, PCE of a random process can be represented by

$$y_j = a_{j,0} + \sum_{i_1=1}^{n} a_{j,i_1}\Gamma_1(\xi_{i_1}) + \sum_{i_1=1}^{n-1}\sum_{i_2>i_1}^{n} a_{j,i_1 i_2}\Gamma_2(\xi_{i_1},\xi_{i_2}) + \ldots\ldots \quad (1)$$

where $\{a_{j,k} \mid k = 0, 1,\ldots, n-1\}$ are unknown coefficients to be determined with respect to the specified model used for uncertainty analysis, n represents the number of uncertain model inputs and $\Gamma_p(\{\xi\})$'s are defined to be multivariate Hermite polynomials in the p – dimensional sequence of uncorrelated standard normal random variables, $\{\xi_i\}$. The multivariate Hermite polynomials can be written as,

$$\Gamma_p(\xi_{i_1},..,\xi_{i_p}) = (-1)^p e^{\frac{1}{2}\xi^T\xi}\frac{\partial^p}{\partial\xi_{i_1}.....\partial\xi_{i_p}}e^{-\frac{1}{2}\xi^T\xi} \quad (2)$$

The inputs are represented as functions of identically independently distributed (iid) normal random variables $\{\xi_i | i=1,n\}$ and each ξ_i has zero mean and unit variance. These random variables are referred to as "Standard Random Variables (srvs)". Once the inputs are expressed as functions of these srvs, the output metrics can be represented as functions of the same set of srvs[8]. The minimum number of srvs needed to represent the inputs is defined as the "number of degrees of freedom" in input uncertainty. In practice, in the theory of PCE, the minimum number of simulations re

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quired for generating the sample points of the uncertain inputs from the respective pdf depends on the order of the Hermite polynomial and the number of uncertain inputs. Therefore, if n is the number of uncertain inputs and r be the order of the polynomial, the number of simulations required can be formulated as

$$N = \frac{(n+r)!}{n!\,r!} \tag{3}$$

Since the model outputs are deterministic functions of model inputs, they have at most the same number of degrees of freedom in uncertainty. So, the number of unknown coefficients to be determined for the fitted polynomial that represents the model output can be explicitly written using eqn. (3) as

$$N_2 = 1 + 2n + \frac{n(n-1)}{2}, \qquad \text{for } 2^{nd} \text{ order Hermite polynomial} \tag{4}$$

$$N_3 = 1 + 3n + \frac{3n(n-1)}{2} + \frac{n(n-1)(n-2)}{6}, \qquad \text{for } 3^{rd} \text{ order Hermite polynomial} \tag{5}$$

So, an explicit representation of 2nd order polynomial chaos expansion for three uncertain inputs can be written using equations (1-5) as:

$$y_2 = a_0 + a_1\xi_1 + a_2\xi_2 + a_3\xi_3 + a_4(\xi_1^2 - 1) + a_5(\xi_2^2 - 1) + a_6(\xi_3^2 - 1) + a_7\xi_1\xi_2 + a_8\xi_1\xi_3 + a_9\xi_2\xi_3 \tag{6}$$

So, according to the number of uncertain model inputs, n = 2, 3, and 4, the number of unknown coefficients to be determined in the polynomial chaos expansion can be obtained using equations (4) and (5) as {6, 10 and 15} and {10, 20 and 35} respectively. Number of unknown coefficients will guide the number of simulations. Thus for two uncertain model inputs, second order polynomial chaos expansion needs six simulations to estimate the unknown coefficients. For reference, the first few Hermite polynomials are given by

$H_0(\xi) = 1$, $H_1(\xi) = 2\xi$, $H_2(\xi) = 2(\xi^2 - 1)$ (7)

and the higher order Hermite polynomials can be generated using the recurrence relation given by

$H_{k+1}(\xi) = 2\xi\, H_k(\xi) - 2\,k\, H_{k-1}(\xi)$ (8)

2.1 Transformation of Model Inputs

Number of sample values for the model outputs will have to be generated on the basis of number of unknown coefficients. Therefore, for six unknown coefficients, six model outputs are to be generated for the specified model. Sampling points for generation of these outputs will be obtained from the model uncertain inputs for which inputs are to be transformed into standard normal random variables (srvs) [8]. In PCE, approach for transforming model uncertain inputs is based on the principle that random variables with well-behaved (square-integrable) probability density functions (pdfs) can be represented as functions of a set of srvs [8],[9]. Standard transformation of the uniform, normal, lognormal and gamma pdfs of model inputs in terms of srvs can be written as

Uniform [a,b] : $a + (b-a)\left\{\frac{1}{2} + \frac{1}{2}erf\left(\frac{\xi}{\sqrt{2}}\right)\right\}$

Normal (μ,σ): $\mu + \sigma\xi$ (9)

Lognormal (μ,σ): $\exp(\mu + \sigma\xi)$

Sample values of the output metrics (eqn. (6)) and the corresponding polynomial chaos expansion are finally arranged in the matrix form as $[\xi]\{a\} = y$, from which coefficient vector, {a} can be solved using singular value decomposition.

3.0 ALGORITHM and MODEL USED IN COMPUTATION

Algorithm developed for computing the uncertainty using polynomial chaos is based on efficient Monte Carlo simulation. Efficiency of the algorithm dictates on the basis of a substantial reduction in simulation compared to traditional Monte Carlo simulation. The model used to demonstrate our algorithm addresses the retention functions of strontium is used for uncertainty analysis. The whole body strontium retention in adult humans at time t days after acute oral administration can be represented by the combination of power and exponential functions [10] and the same is given by

$$R(t) = f_1\, P\, t^{-b} \exp(-\lambda t) \tag{10}$$

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where, f_1 (Gut absorption factor) is the fraction of strontium absorbed from the gastrointestinal tract, 'P' represents fraction initially retained in the skeleton, proportional to uptake rate, 'b' signifies the power function slope, and λ is the strontium elimination rate. This simplified model describes the time history of strontium content in bone relative to the ingested amount, but does not describe the uneven distribution through different bone tissues. It is known that for times greater than 100 days, almost all ingested strontium is incorporated in bone. Input parameters f_1, P, and t^{-b} of the model (eqn. (10)) are considered as uncertain and their uncertainties are described by the respective probability density function given in Table 1. This model retention function numerically coincides with the biokinetic model for adults used for ^{90}Sr-dose calculation [10].

Table 1 Uncertainty of Input Parameters of Model

Parameters	Description	Distribution	Alpha	Beta
f_1	Fraction of strontium absorbed from the GI tract	lognormal	0.38	2.06
P	Fraction initially retained in the skeleton	normal	0.79	0.05
b	Power-function slope	normal	0.18	0.04
λ	Strontium elimiantion rate	lognormal	2.36	1.88

Note: Alpha and Beta are GM and GSD for lognormal distribution and arithmetic mean and arithmetic standard deviation for normal distribution

3.1 Uncertainty Analysis of Model Input Parameters

The propagation of total uncertainty of the model output depends on the analysis of variability in all the inputs of the biokinetic model. Finally the model output is expressed as a function of time following intake. The model output being a function of the several inputs and each input being uncertain, the uncertainty analysis of the output is dependent on the resultant uncertainty analysis of the each input. In other words, it is desired to express the error propagation in the final output. Uncertainty analysis of the input parameters is expressed in terms of the respective probability density function. The estimated distributions for individual parameters of model are considered on the basis of the literature data [11]. According to Hollriegl, Li and Oeh [11], the probability function of the parameter, f_1, representing the fraction of ^{90}Sr absorbed from the gastrointestinal tract (GI) is represented by a lognormal curve with a geometric mean of 0.38 and a geometric standard deviation of 2.06. The diffusion process of radionuclide into the bone volume can be described by the power function, t^{-b}, that depends on the fraction initially retained in the skeleton (P). Likhtarev et al. [12] has studied that the parameters 'P' and 'b' are correlated and the correlation coefficient between them is 0.34 with a statistical significance at $p < 0.05$ level. Statistical analyses performed by Likhtarev et al [12] shows that the empirical distribution of P and b follow normal distribution. The arithmetic mean and the standard deviation of the normal distribution of P are 0.79 and 0.05 respectively and that of the parameter, b are 0.18 and 0.04 respectively. The distribution of the long term strontium elimination rate, λ, can be constructed on the basis of repeated measurements of ^{90}Sr body burden of large number of individual subjects. Least square fitting of these data and decay correction of ^{90}Sr jointly derive the individual elimination rates. Frequency distribution of the elimination rate parameter, λ, approximates to a lognormal distribution with GM as 2.36 and GSD as 1.88. The frequency distribution of this parameter does not differ significantly from lognormal. .

4.0 ANALYSIS OF UNCERTAINTY PROPAGATION OF MODEL OUTPUT

The polynomial chaos expansion is used to construct the response surface representing the model output. Propagation of the impact of parameter uncertainty through the model is evaluated using this response surface. Finally, uncertainties in strontium retention function resulting from individual variability in metabolic processes are evaluated by a Monte Carlo simulation of the generated response surface. Computer software MUUPOCE version 1.0 ("Model Uncertainty Using POlynomial Chaos Expansion") developed by authors is used to evaluate the uncertainty analysis of the model output. Execution of the process is schematically depicted in Fig. 1. Standard normal random variables (srvs) are generated corresponding to each input uncertain parameters. Thus 4 srvs are generated for model. Selection of Hermite polynomial as the basis of the expansion is due to domain variability ($-\infty$ to ∞) of the input parameters. Second order Hermite polynomials is selected from the point of simplicity in computation. Based on this second order polynomial and number of uncertain input parameters number of unknown coefficients is computed from eqn.(3). Thus for the present model, we need to estimate 15 unknown coefficients for constructing the representative polynomial chaos surface. Model output at the respective sampling points is computed using the variability of each uncertain input. Once the model output at the sampling points is generated and srvs are known, we obtain a matrix equation (eqn. (6)). Coefficients of the output approximation (a polynomial chaos surface) are estimated using the singular value decomposition method on this matrix.

The output representation in terms of srvs is directly used to construct its probability density function (PDF) and cumulative distribution function (CDF) by using Monte Carlo simulation. Statistical properties of the output, such as the mean, median, mode, skewness, kurtosis, individual moments, percentiles, and the correlations between the output and inputs are finally evaluated.

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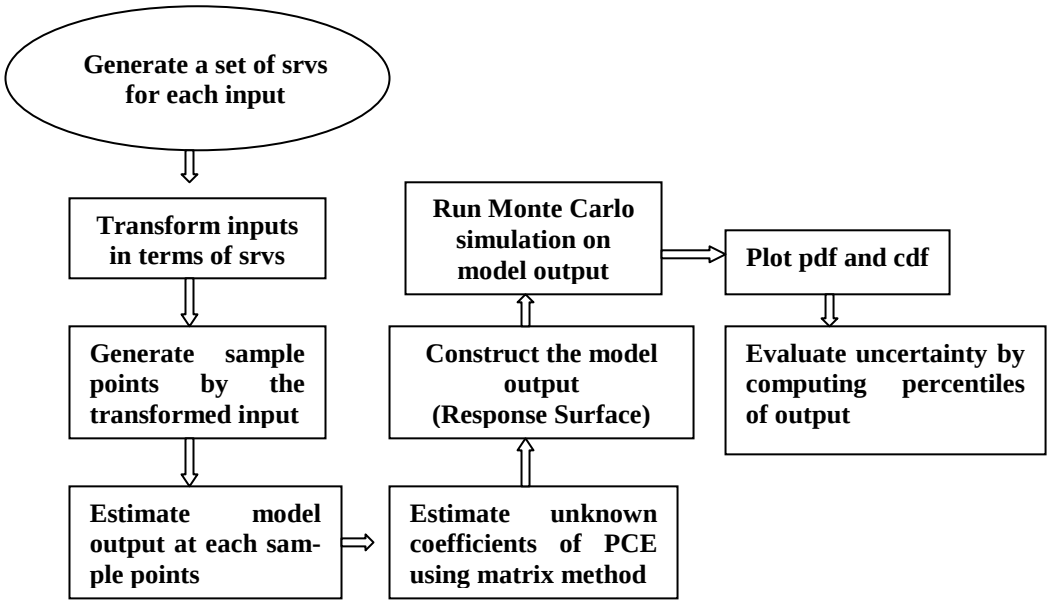

Fig 1. Schematic diagram of steps involved in PCE method

5.0 RESULTS AND DISCUSSION

5.1 Retention Function Model of ^{90}Sr

Uncertainties of input parameters of the present model are represented in terms of the corresponding PDF and they are shown in Figs. 2-5. PDF and CDF of the model output are generated for a time after intake, t = 0.02 y, 0.05 y, 0.08 y, 1 y and 5 y respectively and the frequency plots of the PDF for time after intake, t = 0.02y, 0.05y, 0.08y and 1 y are presented in Figs.6-9. Kolmogorov-Smirnov test has been applied on simulated outputs and it has been found that the ^{90}Sr body burdens are lognormal for these wide ranges of time after intake. Fig. 10 presents the cumulative probability plots of the retention function of ^{90}Sr for these varying times after intake values. Total uncertainty of the retention function of ^{90}Sr is then expressed in terms of the 5th (Lower Bound, A) and 95th percentiles (Upper Bound, B). Results of uncertainty of the retention function in terms of percentiles and the statistics of the represented response function for various times after intake values are shown in Table 2.

Table 2 Uncertainty Estimate of Retention Function of Sr-90

Time after intake (y)	Geometric Mean (GM)	Geometric SD (GSD)	5th percentile	95th percentile
0.02	2.14	1.91	0.165	1.955
0.05	1.81	1.65	0.130	1.53
0.08	1.65	1.53	0.109	1.31
1	1.06	1.09	0.0003	0.208
5	1.00	1.01	0.000	0.004

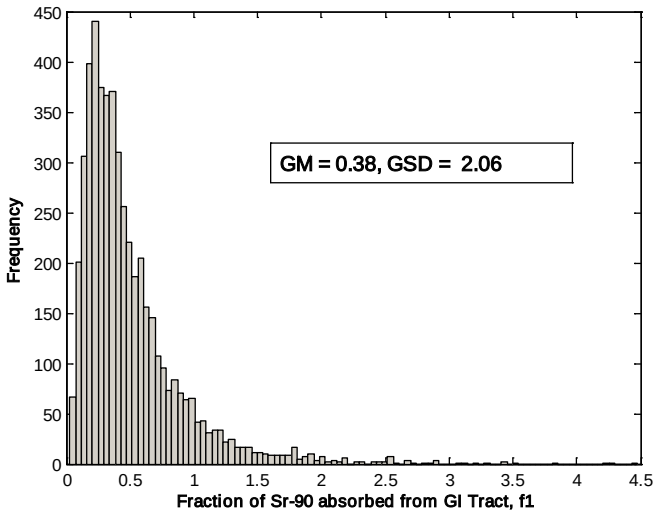

Fig 2. Frequency distribution of Input parameter, f_1

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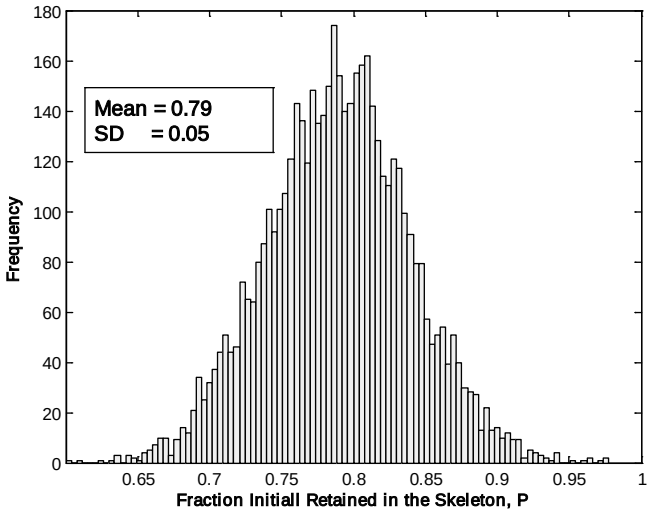

Fig 3. Frequency distribution of Input parameter, P

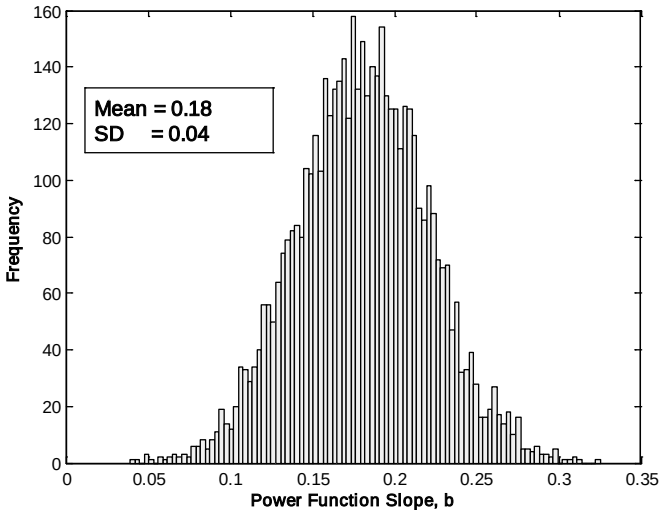

Fig 4. Frequency Distribution of Parameter b

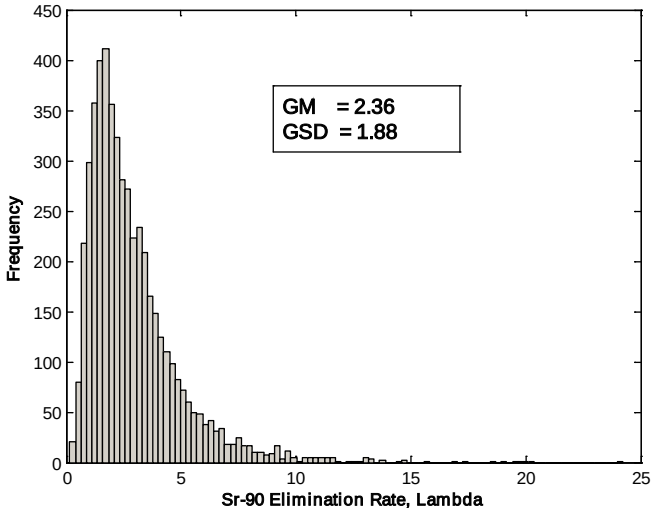

Fig 5. Frequency Distribution of Parameter λ

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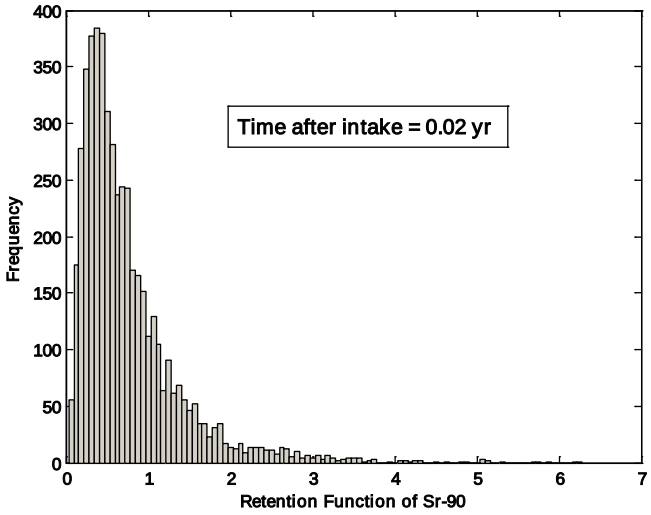

Fig 6. Frequency Distribution of Retention Function of Sr-90

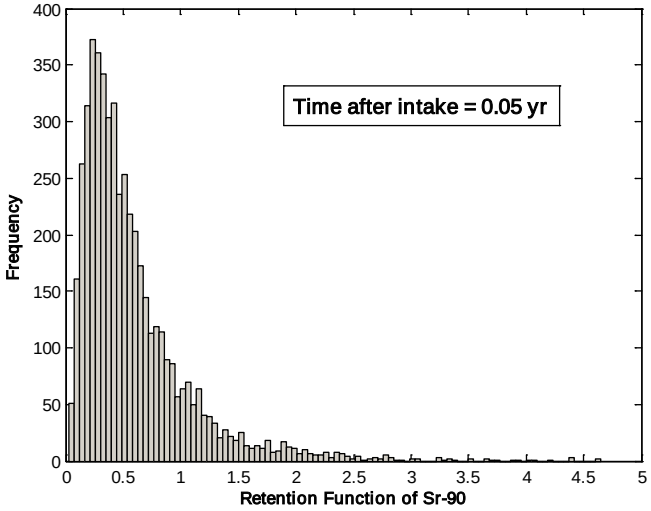

Fig 7. Frequency Distribution of Retention Function of Sr-90

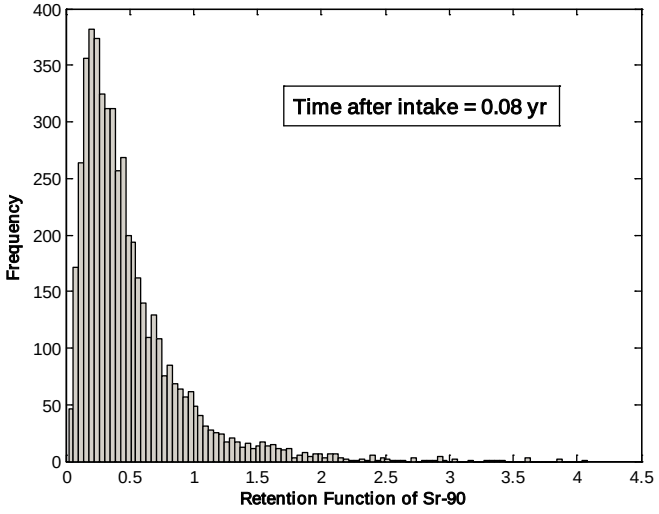

Fig 8. Frequency Distribution of Retention Function of Sr-90

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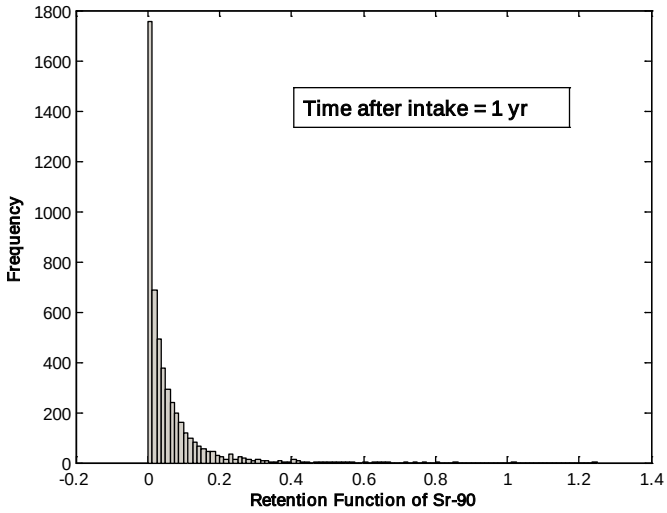

Fig 9. Frequency Distribution of Retention Function of Sr-90

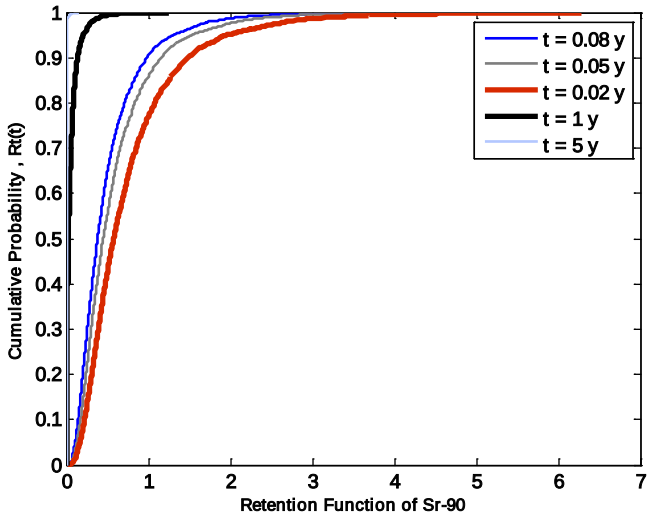

Fig 10. Cumulative Frequency Distribution of Retention Function of Sr-90 for various time after intakes

6.0 CONCLUSION

Uncertainty analysis of a simplified model of strontium retention is carried out. The computed distributions of individual body burdens are essentially lognormal for a wide range of time after intake, in a manner consistent with observed data on global fallout. Polynomial chaos expansion technique facilitates an efficient method for uncertainty propagation compared to traditional Monte Carlo. Domain range of input parameters can dictate the basis function of the response surface. Propagation of uncertainty of retention function of Sr-90 can be used as an input for computing the uncertainty in dose assessment.

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