Uncertainty Analysis of Strontium Retention in Humans Resulting from Individual Variability in Metabolic Parameters

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Abstract – Uncertainties in whole-body strontium retention resulting from individual variability in metabolic parameters are estimated by using parameter uncertainty analysis. Probability distributions, derived from literature data and historical Urals Research Center for Radiation Medicine results, were assigned to all parameters in simple biokinetic model. Uncertainties in parameters were propagated to probability distributions in strontium-body burden using the Monte-Carlo simulation. It is found that the calculated distributions of individual ^{90}Sr-body burdens are essentially lognormal for a wide range of time after intake. The model predictions are shown to be consistent with actual individual strontium-body burden measurements.

INTRODUCTION

The sources of uncertainty in dose-conversion factors per unit of radionuclide intake are connected with the biokinetic and dosimetric models used. If the biokinetic model takes into account the age- and sex-dependencies of metabolic parameters, the main source of uncertainty connected with this model will be the inter-individual biological variability in humans. This variability appears to be due in large part to individual differences in anatomical and physiological factors controlling the distribution and excretion of substances in the body.

The purposes of this work are to

- develop a traditional analysis of uncertainty of ^{90}Sr-body burdens according to the analysis of variability in each major factor in the biokinetic model and to propagate such uncertainties to the final product—body burden as a function of time following intake;
- analyze available experimental data of strontium-90 retention in human body and whole-body counter data of ^{90}Sr-body burden, obtained at Urals Research Center for Radiation Medicine (URCRM) for residents of the Techa River exposed to chronic irradiation as a result of releases of radioactive materials from the Mayak plutonium complex (Southern Urals, Russia);
- compare the above results—that of the traditional model approach and that of actual measured data;

MODEL DESCRIPTION

Simplified model representing the combination of power and exponential functions is used to describe the whole-body strontium retention in adult humans at time *t* days after acute oral administration:

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

where:

f_1 - fraction of strontium absorbed from the gastrointestinal tract;

P - fraction initially retained in the skeleton, proportional to uptake rate;

b - power function slope;

λ - 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 must be noted that for times greater than 100 days, almost all ingested strontium is incorporated in bone.) This simplified retention function numerically coincides with the biokinetic model for adults used for ^{90}Sr-dose calculations for residents of the Techa River (1).

PARAMETER UNCERTAINTY ANALYSIS

The analysis of variability in each major factor in the biokinetic model was used to propagate such uncertainties to the final product—body burden as a function of time following intake (Fig.1). The first step in parameter uncertainty analysis is to derive a probability function for the input values. The estimated distributions for individual parameters were based on literature data and historical URCRM results.

The database, established in URCRM, contains the unique results of individual ^{90}Sr whole-body measurements for more than 15,000 members of the Techa River Cohort (TRC). These data give a great opportunity for the purposes of this investigation as well as for the uncertainty evaluation of the calculated internal doses for the TRC members (2).

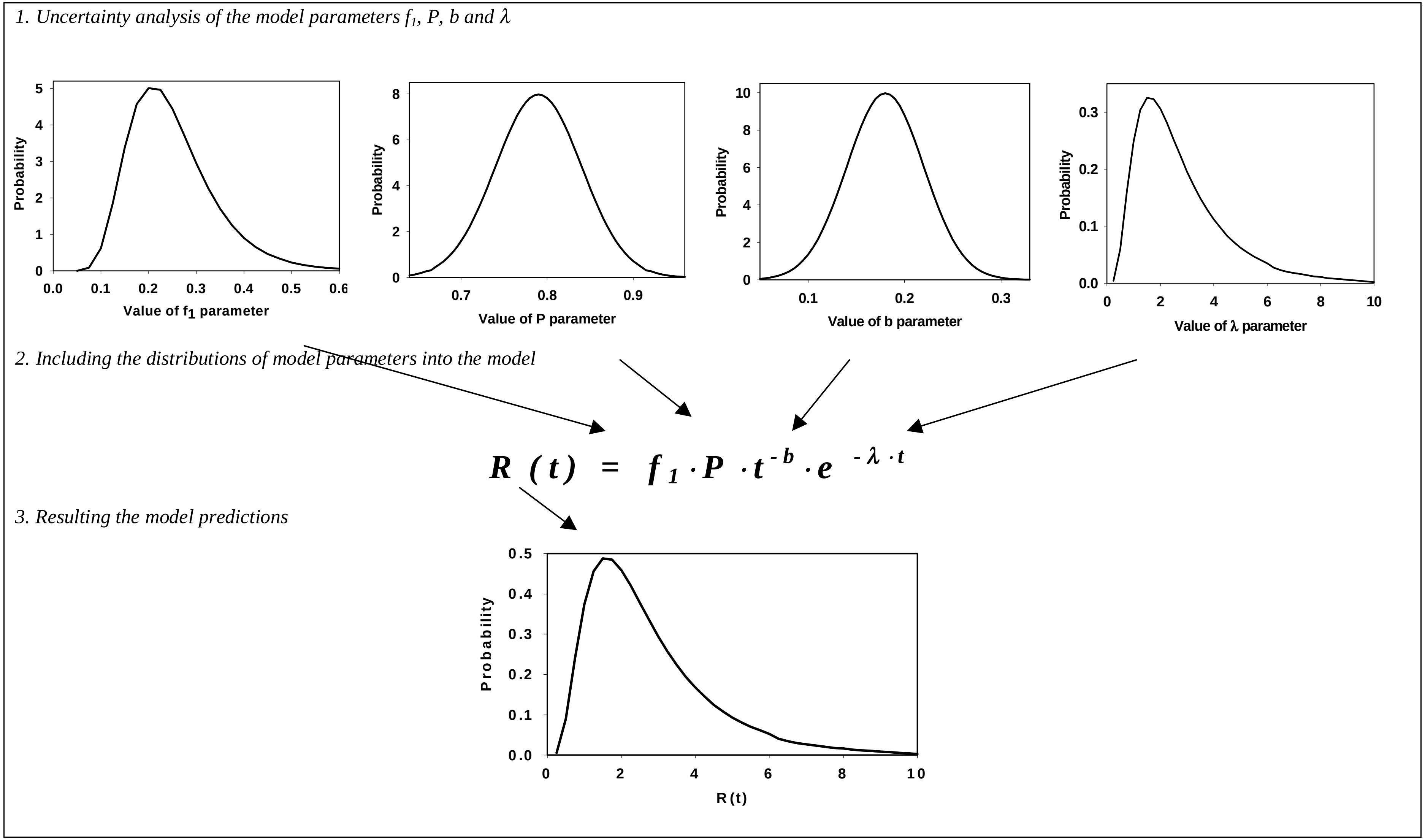

Figure 1. Uncertainty-analysis approach for the strontium-retention function.

The fraction of strontium absorbed from the gastrointestinal tract (f1)

Based on review of the available literature data (3-7), the reported range of gut absorption extends from 10.3% to 53.4% (8). According to Khursheed and Phipps (9), the f_1 distribution may be approximated as lognormal. For the study here, the ends of the reported range of the f_1 value indicated above have been used as the 1st and 99th percentiles of a lognormal distribution, respectively, to define a "high confidence range."

Fraction initially retained in the skeleton (P) and power-function slope (b)

The process of radionuclide diffusion into the bone volume, which can be described by the power function t^{-b}, depends on the fraction initially retained in the skeleton, *P*. Both of these parameters were extensively studied in 44 subjects by Likhtarev et al. (8). A correlation is expected to be observed between the parameters *P* and *b*. To check this assumption, the correlation coefficient has been calculated from the data of Likhtarev et al. The value of the correlation coefficient for the *P* and *b* parameters is 0.34, and the correlation between parameters is significant at the $p<0.05$ level.

Statistical analyses were performed on the data obtained by Likhtarev et al. (8). Figs. 2a and 2b indicate that the empirical distributions of *P* and *b* can be approximated as normal distributions.[1] For *P* the mean, $\overline{X}$ = 0.79 and standard deviation, $\sigma = 0.05$, and for *b* the mean, $\overline{X}$ = 0.18 and standard deviation, $\sigma = 0.04$. As a result of these analyses, correlated normal distributions for the *P* and *b* parameter are used in the Monte Carlo simulations described below. The parameters of each distribution are those shown in Figs. 2a and 2b.

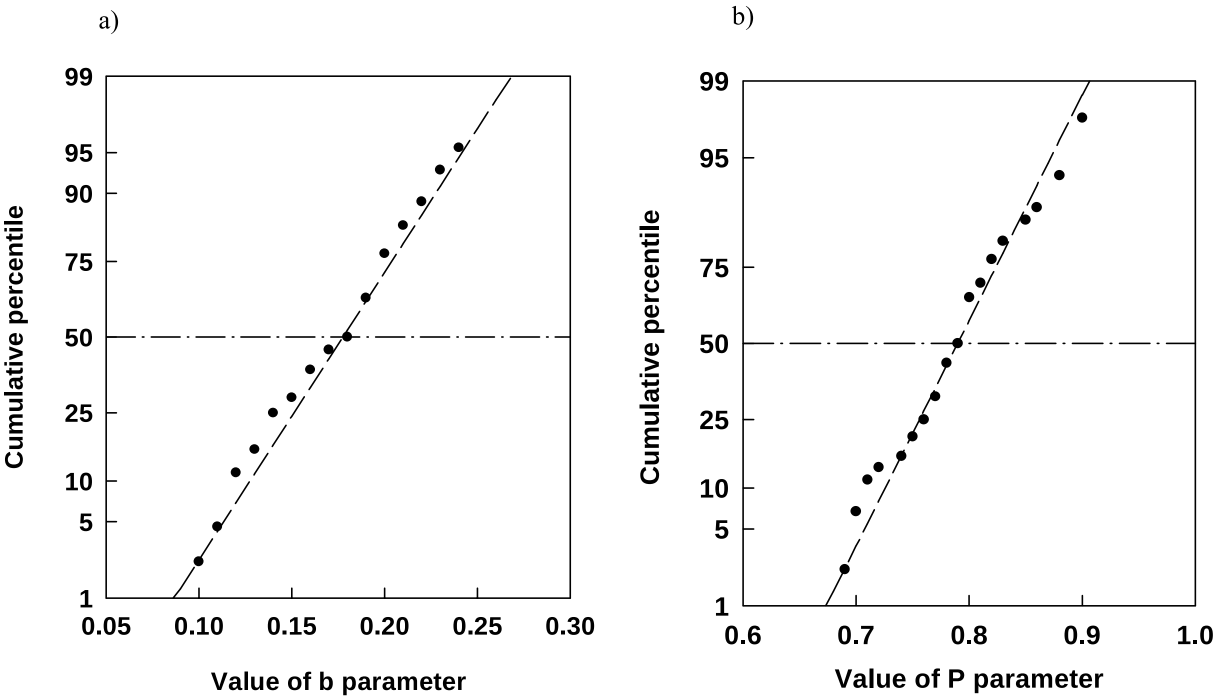

Figure 2. Empirical and modeled distributions of retention function parameter ***a)*** b, describing the slope of the power function, and ***b)*** P, describing the fraction initially retained in the skeleton.

Strontium elimination rate (λ)

The distribution for individual estimates of the long-term strontium-elimination rate was derived from repeated measurements of ^{90}Sr-body burden for residents of the Techa River. The ^{90}Sr-body burden was determined by measuring the bremsstrahlung of yttrium b-rays using phoswich detectors and a scanning-bed geometry in a specially shielded room (10). This study included measurements of 106 persons aged 30–40 years who were investigated with the whole body counter more than three times during the period 1974–1986. An exponential function was assumed to describe the decrease of ^{90}Sr-body burden with time. A least-squares technique was used for fitting, and the derived individual-elimination rates were corrected for radioactive decay of ^{90}Sr. The frequency distribution of the elimination parameter, λ, and its approximation to a lognormal distribution, are shown in Fig. 3 (11). The frequency distribution of this parameter does not differ significantly

[1] As confirmed by the results of both the chi-square and Kolmogorov-Smirnov tests.

from lognormal.[2] The geometric mean, $\bar{x}_g$ = 2.36 and the geometric standard deviation, σ_g = 1.88.

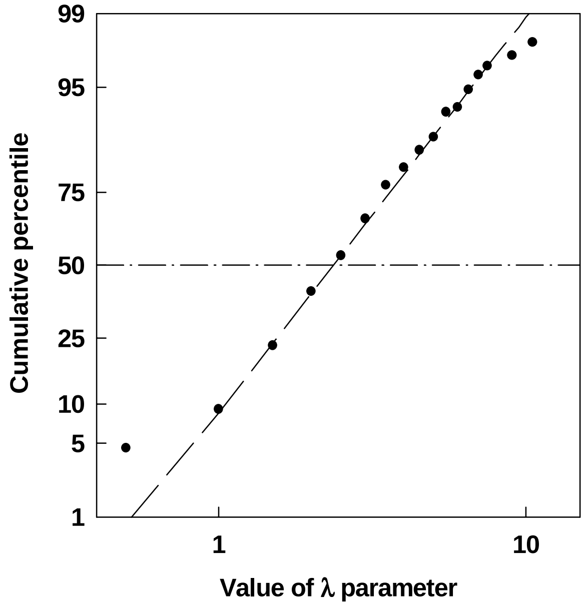

Figure 3. Empirical and modeled distribution of retention function parameter λ, describing the long-term elimination of ^{90}Sr from the body. This parameter is lognormally distributed.

MODELING RESULTS

Monte Carlo simulation was used to propagate the effects of parameter uncertainty through the model and to evaluate the uncertainty in strontium-body burden resulting from individual variability in metabolic processes (Fig. 1). The main results of simulations performed using Monte Carlo simulations are shown in Table 1. It is found that the calculated distributions of individual ^{90}Sr-body burdens are essentially lognormal for a wide range of time after intake (from 1 month to 40 y). Body-burden variations within a homogeneously exposed human population are predicted to be lognormally distributed with a geometric standard deviation increasing from 1.4 to 2.1 depending on the time after intake (Table 1). These results are consistent with data on global fallout (12), where a lognormal distribution with σ_g = 1.55–1.67 was found for ^{90}Sr concentration in human bones measured in 1964–1965.

Table 1. Results of stochastic modeling of individual variability of strontium retention (median and geometric mean are given in percent of ingested activity).

Time after intake, y	Median	Geometric mean	Geometric standard deviation
0.08	10.0	11.0	1.4
1	6.0	6.8	1.4
10	2.6	2.8	1.6
20	1.4	1.5	1.8
30	0.8	0.8	1.9
40	0.5	0.4	2.1

[2] According to Chi-square and Kolmogorov-Smirnov tests

COMPARISON OF MEASURED STRONTIUM-BODY BURDENS WITH PREDICTIONS FROM THE BIOKINETIC MODEL

To compare the model predictions with data on Sr-body burden measurements two data sets have been used:

- data of I.A.Likhtarev's experiment in homogeneous group of subjects (8) to compare the model predictions with data on short-term retention;
- data on ^{90}Sr-body burden measurements of the Techa River residents to compare the model predictions with data on long-term retention.

The short-term retention

The whole-body counter data of strontium retention were obtained on 44 healthy young adult males receiving strontium-85 by ingestion or injection during the first few months after acute intake.

Comparison of the model predictions corrected for radioactive decay of ^{85}Sr with data on short-term retention is shown in Fig.4. It is apparent that the model predictions are in reasonable agreement with observed values.

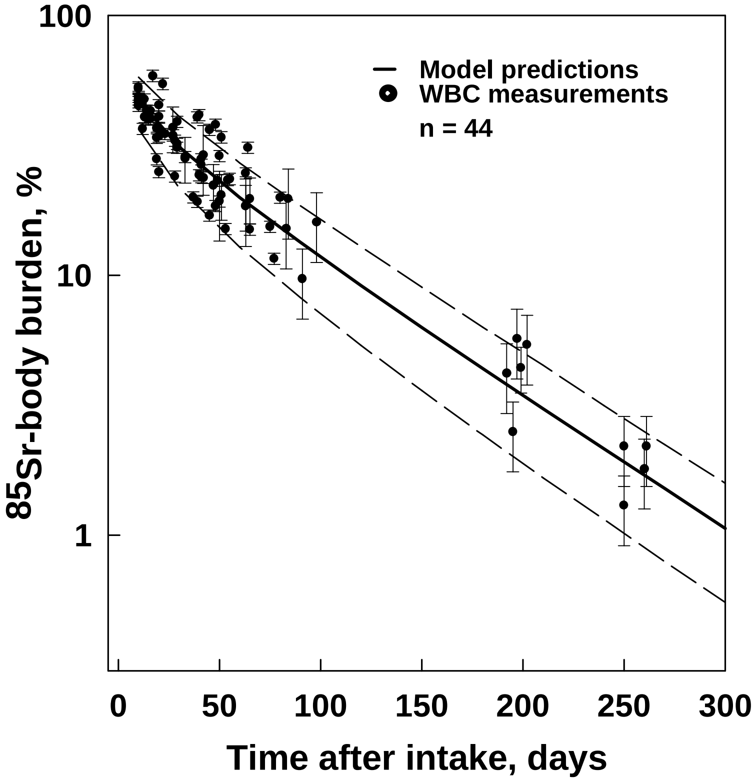

Figure 4. Comparison of modeled and measured ^{85}Sr-body burdens of adult males under Likhtarev study.

The long-term retention

Since 1974, residents of the Techa Riverside have been examined for their ^{90}Sr- and ^{137}Cs-body burdens with a specially developed whole-body counter (WBC). The use of the WBC has resulted in 31,800 individual measurements on 15,250 members of the Techa river cohort.

Variability of ^{90}Sr-body content for members of the Techa river cohort depends on many factors such as age, sex, source of drinking water (Techa River or wells), period of time over which a person lived on the contaminated river, the distance of the place of residence from the site of radioactive release, the time between the moment of WBC measurement and the period of major intake, and individual biological variability of metabolic parameters.

In this work and as the first step of the analysis of measured ^{90}Sr-body burdens, the distribution of body burdens is examined for the permanent (lived in the village during the entire period of the releases from 1949 to 1956) adult (born before 1929) residents of Muslyumovo village (located in the mid-Techa region). A further restriction is that these residents were measured by the WBC during the rather small time interval of 1978 through 1982.

Fig. 5 demonstrates the modeled distribution of ^{90}Sr-body burdens for adult permanent residents of Muslyumovo 30 years after the primary intake, compared to WBC measurements for this group. The value of σ_g is slightly larger for the experimental data set than for the modeled values. This can be interpreted as illustrating the predominant contribution of "individual variability of metabolic parameters" to the total uncertainty for this group of subjects. As can be seen from Fig. 5 about 10% of the lower values of the experimental results appear to deviate from a lognormal distribution. The cause of the deviation at low values is probably related to additional uncertainty in the measurement of low body burdens of ^{90}Sr.

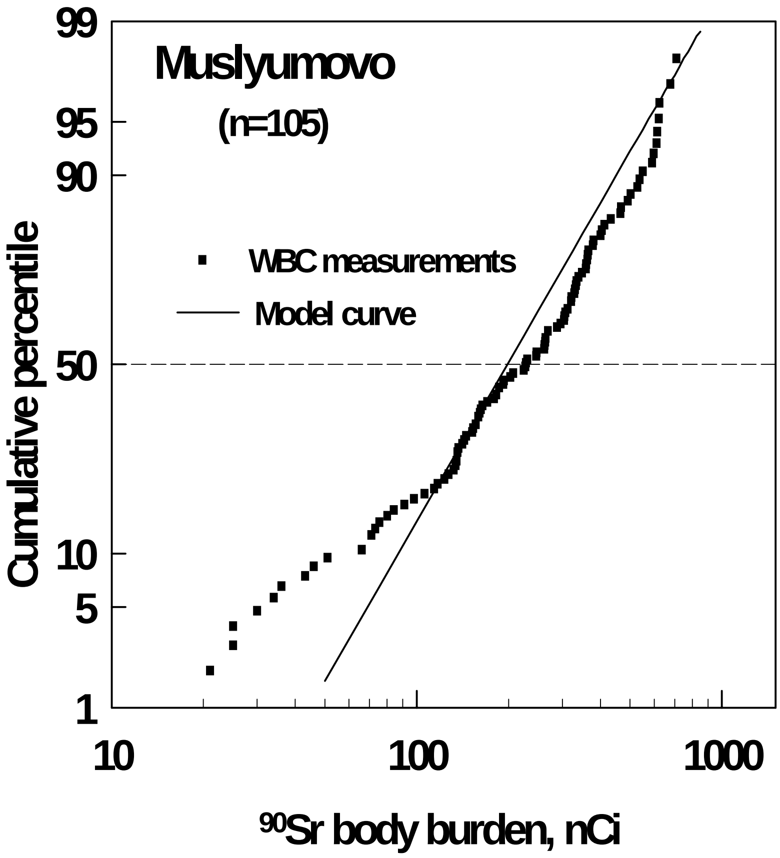

Figure 5. Comparison of modeled and measured ^{90}Sr-body burdens of adult permanent residents of the village of Muslyumovo 30 years after the major intake. Measurements were made with the SICH 9.1 whole-body counter (WBC) between 1978 and 1982.

CONCLUSION

A simplified model of strontium retention in the body was analyzed. The calculated 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. Measured body burdens for the village of Muslyumovo were compared to the calculated results; agreement was good, although the uncertainties for the measured values were slightly larger than predicted by the model. This agreement is taken to indicate that the major source of variation in body burdens of adult permanent residents of Muslyumovo is individual variation in metabolic parameters.

The results of this investigation will be used in the uncertainty evaluation of the calculated internal doses as the part within the framework of the Techa River Dosimetry System.

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