Biokinetic Models for Pregnant and Lactating Women: Adaptation of ICRP Models for Epidemiological Studies of Exposed Southern Urals Populations

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ABSTRACT

A large number of individuals living along the banks of the Techa River (Southern Urals, Russia) were exposed from discharges of liquid radioactive wastes that occurred in 1949-1956 from the first Russian plutonium facility "Mayak". A unique database of measurements of ^{90}Sr in humans, compiled at the Urals Research Center for Radiation Medicine (URCRM) from long-term monitoring of the Techa River population, allows models developed by the International Commission on Radiological Protection (ICRP) to be adapted specifically for the studied population.

Development of population-specific models is an important prerequisite for reliably assessing internal doses for epidemiological studies of radiation risk. This paper presents the results of adapting ICRP biokinetic models for calcium (Ca) and strontium (Sr) in pregnant and lactating women from the studied population.

The maternal models were based on biokinetic models for Ca and Sr for an adult female that were developed recently for the Techa River population. Using ICRP methodology the models were adjusted to include foetal compartments for the period of pregnancy and to allow for changes in mineral metabolsim. Parameters of the foetal model specific to the Techa River population were estimated using ICRP approaches which account for Ca content in the maternal diet and in the blood and skeletal compartments of mother and foetus. For the period of lactation, the ICRP methodology was extended to consider a longer breastfeeding period in the rural Techa villages that includes exclusive and partial breastfeeding and corresponding changes in maternal mineral metabolism. Ca and Sr transfer to breast milk is determined on the basis of Ca content in maternal diet, skeleton and breast milk specific for the studied population. The models were validated using data on ^{90}Sr in foetuses and their mothers and measurements of ^{90}Sr-body burdens in pregnant and lactating women resident in the Techa River villages (*see Tolstykh et al*). The models were used to compute *in utero* doses from maternal ingestion of Sr radioisotopes at the Techa River (*Shagina et al*) and to calculate intakes of Sr radionuclides with breast milk by infants born in the Techa River villages.

These studies allow more reliable estimates of the internal doses received in early life to be used in epidemiological studies of the Techa River cohorts.

1. MATERNAL MODELS FOR Ca AND Sr

Age-dependent biokinetic models for Ca and Sr for females from the Techa River population (TBM) are used as a basis for the development of models for pregnant and lactating women. The model has the same structure as the ICRP model for Ca and Sr (ICRP 67, 1995) but model parameters for these elements were evaluated specifically for the studied population (***Fig.1***)

The major data set for evaluation of model parameters included measurements of ^{90}Sr-body burdens conducted at the URCRM since 1974 with the use of a specifically designed whole body counter SICH-9.1 (WBC) (Kozheurov 1994). More than 30,000 measurements were made between 1974 and 1997 on over 16,000 people who lived in the Techa riverside villages. ***Fig.2*** compares WBC data for females from the Techa River population with corresponding predictions obtained with TBM and ICRP models. Of the two models only the TBM is gender-dependent and its predictions are in good agreement with WBC data (***Fig.2***)

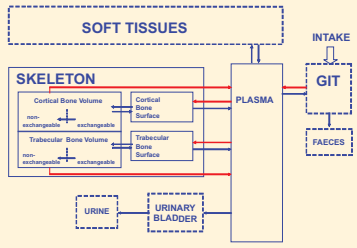

Fig.1. Structure of the ICRP biokinetic model for Ca and Sr (ICRP Publ. 67, 1995). Basic model parameters that determine Ca and Sr retention are shown in red. These parameters, as well as, the transfer from plasma to urinary bladder are modified for the periods of pregnancy and lactation (***Fig.3a-c***)

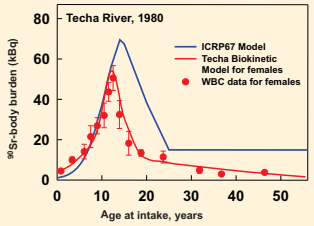

Fig.2. Retention of ^{90}Sr in the skeleton **30 years** after the beginning of the intake in females of different ages at intake in comparison with model predictions. WBC measurements were obtained in 1978-1982

2. MODIFICATION OF MATERNAL MODELS FOR PREGNANCY AND LACTATION

Published data on Ca metabolism during pregnancy and lactation were used to quantify changes in gastrointestinal absorption, urinary excretion and bone turnover for these periods relative to the non-pregnant and non-lactating baseline state (***Figs.3a-c)***

Analysis of URCRM archival data showed that the period of exclusive breastfeeding in the Techa River settlements in 1950s was 5-7 months (modelled as 6 months) and the total duration of breastfeeding was 13-17 months (modelled as 16 months).

Fig.3a. Modifying factor for gastrointestinal absorption of calcium and strontium during pregnancy, exclusive and partial breastfeeding

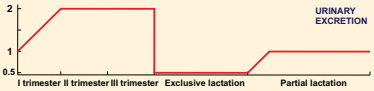

Fig.3b. Modifying factor for urinary excretion for calcium and strontium for period of pregnancy, exclusive and partial breastfeeding

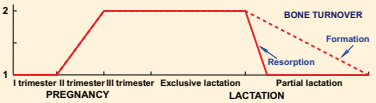

Fig.3c. Modifying factor for bone deposition and resorption of calcium and strontium for period of pregnancy, exclusive and partial breastfeeding

3. ADAPTATION OF THE FOETAL MODEL FOR THE TECHA RIVER POPULATION

The general approach for adapting the ICRP foetal and milk models to the studied population is described by (Shagina et al. 2007).

The structure of the ICRP foetal model (ICRP 88, 2002) was retained (Fig.4). However, parameters defining Ca exchange between maternal and foetal blood were calculated from data on Ca in the Urals population, and Ca transfer from foetal blood to foetal bone surface was fitted to Russian data on Ca content in the skeleton of foetuses aged 23-38 weeks (***Fig.5***).

Discrimination against Sr relative to Ca for placental transfer was evaluated from data of Borisov (1972). The Sr placental discrimination factor is assumed to remain at 0.6 from conception until the middle of the third trimester and then to increase to 0.95 at term.

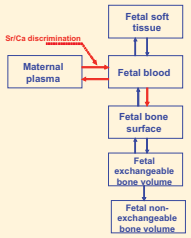

Fig.4. Structure of the ICRP foetal model. Parameters re-evaluated for the Techa River population are shown in red

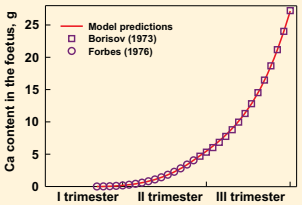

Fig.5. Fitting of the calcium transfer rate from foetal blood to foetal bone surface. Data of Forbes were used for foetal ages of 8-22 weeks, data of Borisov were used for foetal ages 23-38 weeks

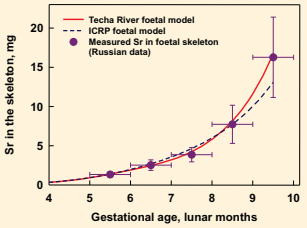

Fig.6. Comparison of model predictions with measurements of stable strontium in the foetal skeleton obtained by Borisov (1973)

4. ADAPTATION OF THE MODEL FOR TRANSFER TO THE BREAST MILK FOR THE TECHA RIVER POPULATION

The structure of the ICRP model for Ca and Sr transfer to breast milk (ICRP 95, 2004) was adopted for this work (**Fig.7**). Parameters defining Ca transfer to breast milk have been re-calculated from data on maternal Ca dietary intakes, Ca intakes with breast milk for the Urals population (Table 1) and maternal changes in mineral homeostasis (***Fig. 3a-c***).

Discrimination between Ca and Sr transfer from maternal blood to breast milk was obtained from URCRM data on ^{90}Sr concentration in breast milk and maternal skeleton obtained in studies of global fallout in the Urals and Russia (***Table 2***). The discrimination factor was found to be equal to 0.88 in contrast to the ICRP value of 0.4.

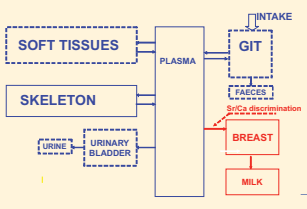

Fig.7. Modification of the TBM for a female of reproductive age for period of lactation. Fitted transfer rates for calcium and strontium are shown in red

Table 1. Data on Ca concentration in breast milk and breast milk excretion used for fitting Ca transfer rate from maternal blood to the breast milk for the Techa River population and comparison with ICRP reference values (ICRP 95, 2004)

Age, months *post partum*	Ca concentration in breast milk, mg/L	Mass of excreted breast milk, g/d	Ca excretion with breast milk, mg/d	Ca excretion with breast milk in ICRP model, mg/d
0 mo	250	800	200	250
6 mo	250	800	200	250
16 mo	180	200	36	-

Table 2. Statistical characteristics of the ratios of ^{90}Sr/Ca concentration in breast milk to that in the maternal skeleton obtained on the basis of measurements performed in the Southern Urals in 1966 (URCRM data)

	Statistical characteristics			
	Average	*5th*	*Median*	*95th*
Ratio of ^{90}Sr/Ca concentration in breast milk to that maternal skeleton	4.0	0.8	3.6	16,6

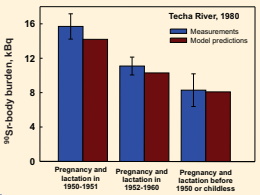

Fig. 8. Comparison of measured ^{90}Sr body burden in 1980 in three groups of women living in a Techa River settlement (see poster by *Tolstykh et al.*) with respective values obtained with models considered in present study

CONCLUSIONS

The biokinetic models described here for foetal and breast milk transfer will be used to provide improved estimates of *in utero* doses and of intakes of activity by the suckling infant from maternal ingestion of Sr isotopes at the Techa River. Reliable dose reconstruction is essential if credible assessments of radiation risk are to be made from epidemiological studies of the Techa River cohorts.

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