Development of Metabolic Model of Tritium in the Human Body

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Abstract

In the radiation safety assessment for nuclear facilities including the first commercial spent nuclear fuel reprocessing plant in Rokkasho, Japan, the internal dose of the public due to tritium has been estimated using the dose conversion factors based on the ICRP metabolic model of hydrogen in the human body. The ICRP metabolic model is very simple and is comprised of a free water tritium (FWT) compartment and organically bound tritium (OBT) compartment having biological half-lives of 10 and 40 d, respectively.

Although the biological half-life of tritium water (HTO) in the human body was examined in several cases such as accidental intakes or experimental administrations, actual data on the metabolism of OBT are quite limited. The objective of this research program is to establish experimentally the metabolism of tritium including OBT in the human body for more realistic dose estimation. In the present experiment, the stable isotope of hydrogen, deuterium (D), was used as a substitute for tritium.

Until FY 2013, D-labeled glucose, palmitic acid, and leucine were administered to volunteers as representative of carbohydrates, lipids, and proteins, respectively, followed by measuring the D/H ratio in their urine. A model for metabolism of each compound was constructed by using the urine D/H data. The model had a compartment of free water D (FWD) and two compartments of organically bound D (OBD_1 and OBD_2), which are separately connected to the FWD compartment. The OBD_1 and OBD_2 represent the compartments having fast and slow rates of degradation to the FWD, respectively. The parameters in the model were determined by a least square fitting method using the measured data. By combining the models for those compounds as representative of three major nutrients, we could predict the metabolism of D in foods from their proportion of the three major nutrients.

In FY 2014, D-labeled soybean was prepared and administered to volunteers. The urine excretion of D from the volunteers was measured to verify the prediction with the combined model and composition of three major nutrients in soybean. After soybean plants were exposed to 20% D_2O as soil water and atmospheric moisture for 3 weeks, soybeans were harvested and lyophilized. The dried soybeans were soaked in tap water to remove exchangeable OBD, and then lyophilized again. Volunteers were administered 8.5 to 11 g of lyophilized D-labeled soybean during lunches of four successive days. After the first administration, their urine samples were collected for up to 16 weeks for analysis of D concentrations with mass spectrometers. The first morning urine samples for 7 d before the administration were also collected and used as control samples of each volunteer. All processes of the experiment were approved by the IES Review Board for Human Subject Experiments, and written informed consents were obtained from all volunteers.

The estimated concentrations of FWD in urine by the combined model and the proportion of the three major nutrients of soybean, agreed relatively well with the observed values throughout the experimental period. We constructed a metabolic model of D-labeled soybean directly from the measured data and calculated cumulative D-burden after single D-labeled soybean ingestion for 50 y. The cumulative D-burden

obtained was 1.6 times smaller than the prediction by the combined model. On the other hand, the cumulative dose for 50 y after single dietary reference intakes for Japanese by the combined model was 1.3 times larger than the prediction by the ICRP model for OBT. Judging from the error in the soybean case, it was considered that the prediction by the combined model was roughly consistent with the ICRP model.

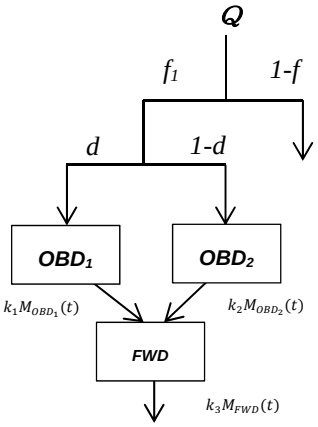

Fig. 1 Structure of the metabolic model for ingested deuterium.
Q: mass of administered deuterium. OBD_1, OBD_2, *FWD*: compartment of deuterium. f_1, *d*: distribution factor. k_n: elimination rate constant. *M*: mass of deuterium in each compartment.

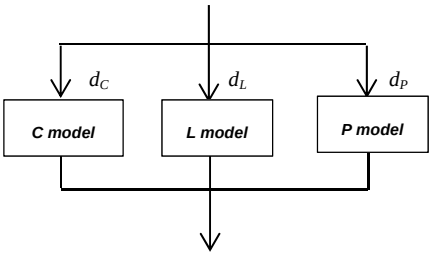

Fig. 2 Structure of the combined metabolic model for ingested deuterium in foods.
C model, *L model*, *P model*: submodel (Fig. 1) of ingested deuterium in carbohydrates, lipids, and proteins, respectively. d_c, d_L, d_P: proportion of carbohydrates, lipids, and proteins in food, respectively.

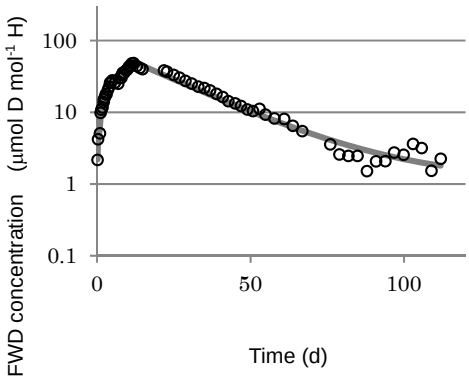

Fig. 3 An example of the typical time course of concentrations of free water deuterium in urine samples after the first administration of deuterium labeled soybean. The solid line shows the estimation by the model shown in Fig. 1.

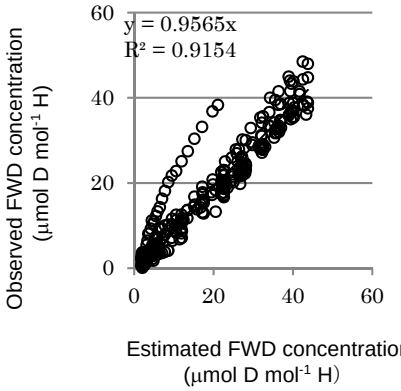

Fig. 4 Estimated and observed concentrations of free water deuterium in urine samples of all the male volunteers.