Tritium Metabolism 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 experiment, the stable isotope of hydrogen, deuterium (D), was used as a substitute for tritium.

In FY 2013, volunteers were administered with 4 g of D-labeled and 0.4 g of ^{13}C-labeled leucine or 1 g of D-labeled and 0.1 g of ^{13}C-labeled alanine during lunches of four successive days. After the first administration, their urine and breath samples were collected for up to 16 weeks for analysis of D and ^{13}C, respectively, with mass spectrometers. All procedures of the experiment were approved by the IES Review Board for Human Subject Experiments, and written informed consents were obtained from all volunteers.

The D/H ratio data obtained for the urine samples were used to construct a model of metabolism of D ingested as leucine or alanine. 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 dividing ratio of ingested OBD to OBD_1, transfer rate constant between those compartments, and the excreting rate constant of FWD compartment were determined by a least square fitting method using the measured data. The excreting rate constant of D from the FWD was 7.6×10^{-2} d^{-1} for leucine and was 8.2×10^{-2} d^{-1} for alanine, which were comparable with that of the ICRP metabolic model, 7.1×10^{-2} d^{-1}. Although the degradation rate constants of OBD_1 and OBD_2 were not substantially different between leucine and alanine ($7.1\text{-}7.8 \times 10^{-3}$ d^{-1} and $7.6\text{-}8.2 \times 10^{-2}$ d^{-1}), the dividing ratio for ingested OBD to the OBD_1 having the fast degradation rate was smaller for leucine (5.2×10^{-1}) than for alanine (9.0×10^{-1}). Thus the cumulative exposure of the human body to D calculated by the model after a single oral intake during 50 y, which corresponds to the committed dose for tritium, was larger in leucine than alanine.

We calculated the cumulative exposure after a single oral intake of various compounds labeled by D or ^{13}C by using the model constructed in the present study and the model constructed previous to FY 2013. The obtained results were compared with the cumulative exposure by ICRP metabolic model for tritium. The comparison showed that our model for ^{13}C gave lower exposure than that of ICRP model, while higher exposure are obtained by our model for tritium than the ICRP one, showing the necessity for the further study.

Table 1 Dose of labeled compounds and isotopes

Subject group	Chemical formula of labeled compound	Dose to subjects (g person^{-1})		
		Labeled compound	D	^{13}C
Leucine-administered group	$(CD_3)_2CDCD_2CD(NH_2)COOH$	1.0	0.14	0
	$(^{13}CH_2)_2{}^{13}CH{}^{13}CH_2{}^{13}CH(NH_2){}^{13}COOH$	0.1	0	0.057
Alanine-administered group	$CD_3CD(NH_2)COOH$	1.0	0.086	0
	$^{13}CH_3{}^{13}CH(NH_2){}^{13}COOH$	0.1	0	0.042

Table 2B Alanine group parameters in the model

Parameter	Value
f_1	1.0±0.0
d	0.90±0.05
k_1	34±16
k_2	0.0071±0.0026
k_3	0.082±0.007

*: Each value is the mean±standard deviation.

Table 2A Leucine group parameters in the model*

Parameter	Value
f_1	0.97 ± 0.05
d	0.52 ± 0.07
k_1	7.8 ± 3.8
k_2	0.0078 ± 0.0056
k_3	0.076 ± 0.021

*: Each value is the mean±standard deviation.

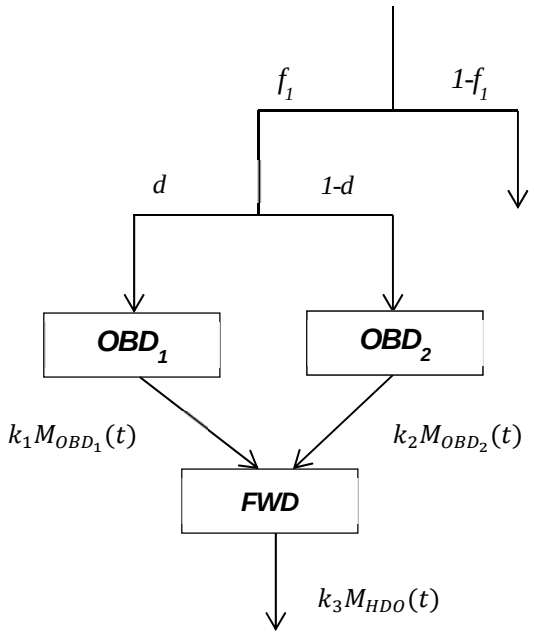

Fig. 1 Three-compartment model of metabolism of D ingested as amino acid

FWD, *OBD$_1$*, *OBD$_2$*: compartment names, *$M_{FWD}(t)$*, *$M_{OBD1}(t)$*, *$M_{OBD2}(t)$*: D amounts in each compartment (g). *k_1* to *k_3*: transfer rate constants.

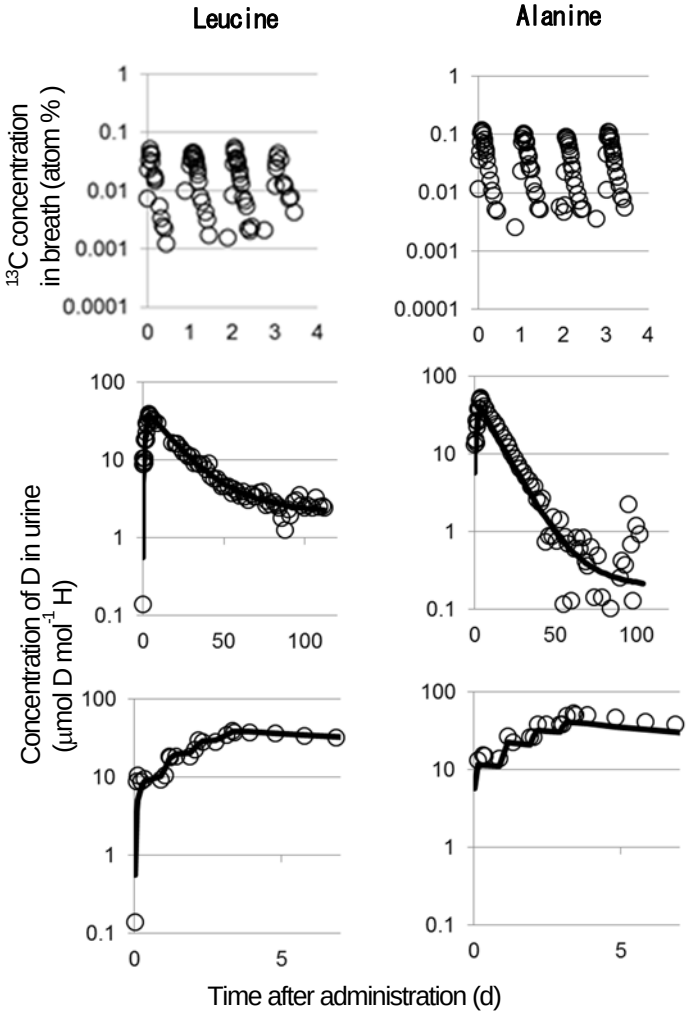

Fig. 2 Concentration of ^{13}C in breath CO_2 and D in urine water
Open circle: concentration after administration. Solid line: estimated values by the model.

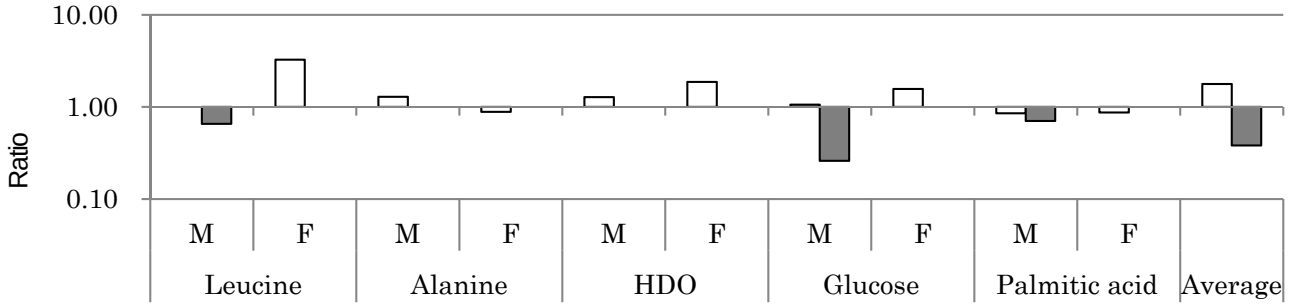

Fig. 3 Ratio of cumulative exposure to D or ^{13}C for 50 y after single dose by present three-compartment model to that by the ICRP model.

Cumulative exposure is the area under the retention curve of D and ^{13}C. Results reported through 2013 are included. M, male. F, female. Open bar, D. Filled bar, ^{13}C. The average was obtained by the assumption of representing Leucine F, Glucose F, and Palmitic acid F as protein, carbohydrate, and fat in the diet of Japanese given by the *Standard Table of Food Composition in Japan (5th revised edition)*, respectively.