3.3 ヒト体内におけるトリチウム代謝に関する調査研究

Tritium Metabolism in the Human Body

増田 毅, 松下 兼作, 多胡 靖宏, 久松 俊一
環境影響研究部
Tshuyoshi MASUDA, Kensaku MATSUSHITA, Yasuhiro TAKO, Shun'ichi HISAMATSU
Department of Radioecology

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 (7.1-7.8 $\times 10^{-3}$ d^{-1} and 7.6-8.2 $\times 10^{-2}$ 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.

1. 目的

大型再処理施設から排出されるトリチウムの一部は、農作物や海産物を介して経口摂取され、体外へ排出されるまでの間に内部被ばくを起こすと考えられている。内部被ばく線量を評価するためには、摂取したトリチウムの代謝排泄に関するデータが必要であるが、有機物として摂取した場合の代謝排泄に関するデータはほとんどない。そこで本調査では、人体内トリチウム代謝モデルの作成を目標としている。平成 25 年度は、アミノ酸として経口摂取した場合のトリチウム代謝モデルを作成するため、安定同位体である重水素(D)をトレーサーとして標識したロイシン及びアラニンを経口投与して代謝排泄データを得、モデルを作成したので報告する。

2. 方法

健常な日本人男性及び女性を被験者とし、標識ロイシン投与群には重水素標識ロイシン及び^{13}C標識ロイシンを、標識アラニン投与群にはD標識アラニン及び^{13}C標識アラニンを昼食時に4日間連続で経口投与した（Table 1）。投与7日前から投与開始112日後までの尿及び呼気を採取し、それぞれに含まれるD濃度及び^{13}C濃度を質量分析器により測定した。得られたデータにより、D代謝3コンパートメントモデル（Fig. 1）を作成しパラメータを得た（Table 2A, 2B）。

3. 成果の概要

標識投与後の尿中自由水D濃度及び呼気中二酸化炭素 ^{13}C 濃度のそれぞれ投与前 7 日間の平均値からの変化を Fig. 2 に示す。投与中 4 日間の尿での D 濃度は標識アラニン投与群の方が高かったが、その後標識アラニン投与群のD濃度は急速に低下し、一方、標識ロイシン投与群は D 濃度の低下が小さかった。モデルにより得られたパラメータを Table 2 に示す。速い代謝コンパートメント OBD_1 への分配率 d は標識アラニン投与群(0.90±0.05)が標識ロイシン投与群(0.52±0.07)より大きく、標識アラニン投与群での初期の速い代謝排泄はこのためと考えられた。得られた D 代謝パラメータから、経口摂取後 50 年の体内残留量曲線下面積を求め、ICRP モデルからのそれに対する比を求めたところ（Fig. 3）標識ロイシン中 D は標識アラニン中 D よりもより多い残留が推定された。呼気中二酸化炭素 ^{13}C 濃度データについては、H26 年度に作成する最終的なモデルの作成と検証に使用する。

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 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.

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.

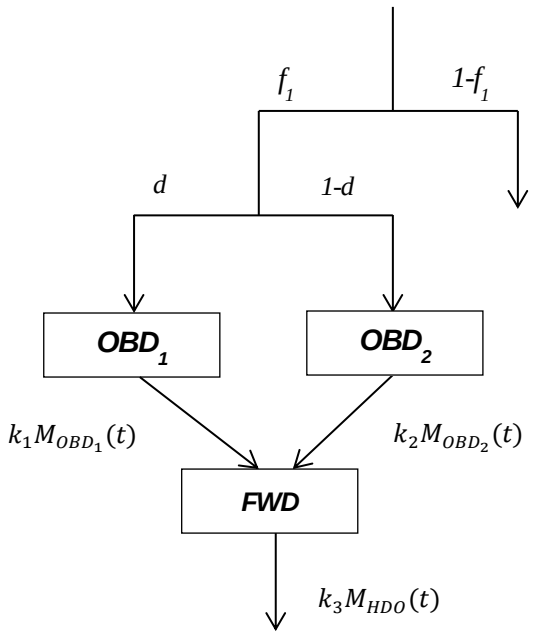

Fig. 1 Three-compartment model of metabolism of D ingested as amino acid

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.

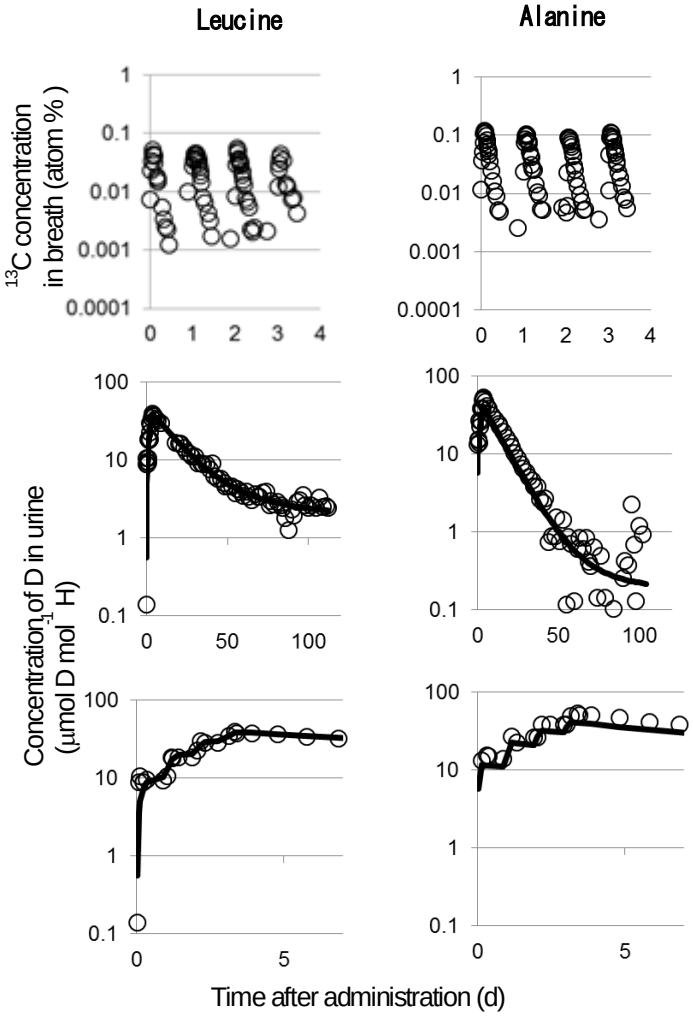

Fig. 2 Concentration of ^{13}C in breath CO_2 and D in urine water
Open circle: concentration after administration. Solid line: estimated values by the model.

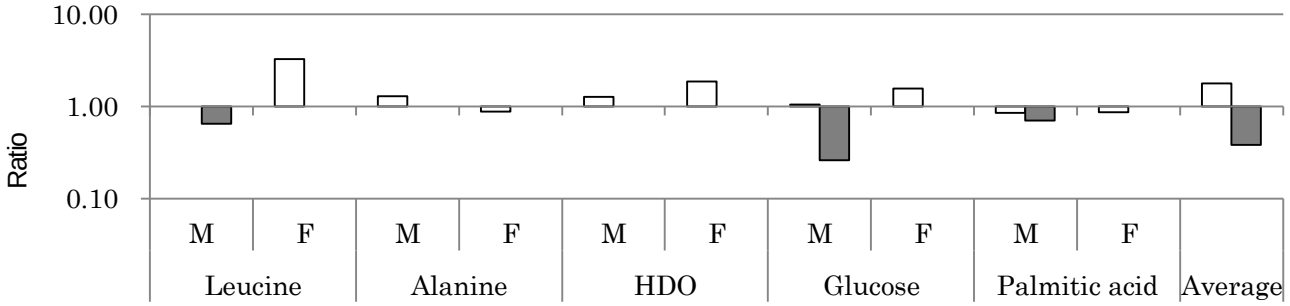

Fig. 3 Ratio of cumulative exposure to D or ^{13}C for 50 y after single dose by present three-compartment model to that by the ICRP model.

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.