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Estimation of Thorium Deposited in Thorotrast Patients by CT Scanner in Comparison with Whole Body Counter

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Thorotrast/CT scanner/Whole body counter/Dosimetry

The deposits of thorium dioxide in Thorotrast patients are observed in the reticulo-endotherial system, such as liver and spleen. The amounts of deposits in patients can be estimated by a whole body counter, but hospitals which have the apparatus are few. In this study the method for the estimation of thorium dioxide deposited in Thorotrast patients by a computed tomography (CT) scanner was examined and established. A relationship between the activity of Th-232 per volume and the CT number was determined with CT phantom experiments. The activity of Th-232 per volume of the spleen and the liver of Thorotrast patients were estimated by the relationship and their absorbed dose rates were evaluated. The estimates by the CT scanner were compared with those by the whole body counter. The estimates by the CT scanner of the activity per volume which is related to the absorbed dose rate was more accurate than that by the whole body counter. In the case of CT scanner, the distribution of thorium deposited in the body was obtained.

INTRODUCTION

Thorotrast, a colloidal solution containing 24–26% of thorium dioxide was intravascularly injected to patients, mainly wounded soldiers, for angiography from about 1930 to 1945 in Japan.[1, 2] The colloidal particles of thorium dioxide are selectively taken into the reticulo-endotherial system such as liver, spleen and lymph nodes, and could hardly be excluded from the body.[3–5] The tissues deposited by thorium dioxide are irradiated with alpha-, beta- and gamma-rays from Th-232 and its daughter nuclides for a long period. Malignant liver tumor, leukemia and liver cirrhosis have been reported in Thorotrast patients, and the cause was considered to be the internal irradiation mainly by alph-rays.[6–7]

To analyze the relationship between the internal irradiation and its biological effects, it is necessary to evaluate the thorium burden in Thorotrast patients. The absorbed dose rate

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can be estimated from the Th-232 activities measured with a whole body counter.[8, 9] However, general hospitals have the apparatus are few. In this work the method for the estimation of Th-232 in Thorotrast patients by a computed tomography (CT) scanner was examined and established. The estimates were compared with those obtained by the whole body counter.

MATERIALS AND METHODS

1. *Thorotrast*

Colloidal Thorotrast solution (Testagar and Co. Inc.) was purchased in 1962. By the spectroscopy of alpha- and gamma-rays, it was assumed that the Thorotrast solution was produced 3 years before the purchase.[10]

2. *The Measurements by the CT Scanner*

A General Electric CT scanner (type: CT/T 8800) was used in this study. The voltage was constant, 120 kV, and the current was variable according to the size of an object and the thickness of slice. The display matrix was 320 x 320 of pixels, and the pixel size was 1.3 mm by 1.3 mm. The CT number was adjusted to 0 for water and to −1000 for air. The obtained CT number for the normal liver and the spleen was around 40–50.

A CT phantom was designed for the experiments with the CT scanner. The phantom was cylindrical with 30 cm diameter by 14 cm length made of polypropylene filled with water (Fig. 1). In the phantom 20 polyethylen capsuls which contained varying concentration of Thorotrast diluted in 5% dextrin solution up to 3.3×10^3 pCi/cm^3 (122 Bq/cm^3) were arranged. The size of the capsul was 1 cm diameter and 4 cm length. A CT image of each capsul contained 64 pixels which were considered to be statistically enough. To check the changes of CT numbers by a beam hardening effect of X-ray, the capsuls contained the various concentration of Thorotrast were arranged on inner circle and outer circle, respectively, as shown in Fig. 1 and the experiments with a smaller size of a phantom, 19 cm diameter, were performed. Most of adults have a diameter of 19 cm to 30 cm of their abdomin.

3. *The Measurements by the Whole Body Counter*

The details of the whole body counter has been described in a previous report.[11] Briefly, the measurement room has an iron wall of 20 cm thickness. The inner side of the wall is lined with 0.3 cm lead and 0.3 cm Lucite plate. Gamm-rays from Thorotrast was measured with a pair of 20 cm diameter NaI (Tl) scintillation detectors coaxially positioned above and below the couch. The distance between the detectors was 50 cm, and the position of the axis of detectors was set on the liver and the spleen of the patient.

An Alderson phantom (type: OSP-150) which contained models of liver nad spleen was filled with water and was used for the experiments with the whole body counter. The liver model had a volume of 1400 cm^3 and contained 22.33 nCi (826.2 Bq) of Th-232. The spleen model had a volume of 150 cm^3 contained 13.64 nCi (504.7 Bq) of Th-232. The position of the Alderson phantom and models of liver and spleen for the measurements by the whole body counter is shown in Fig. 2. The estimation of the activity of Th-232 was performed by the

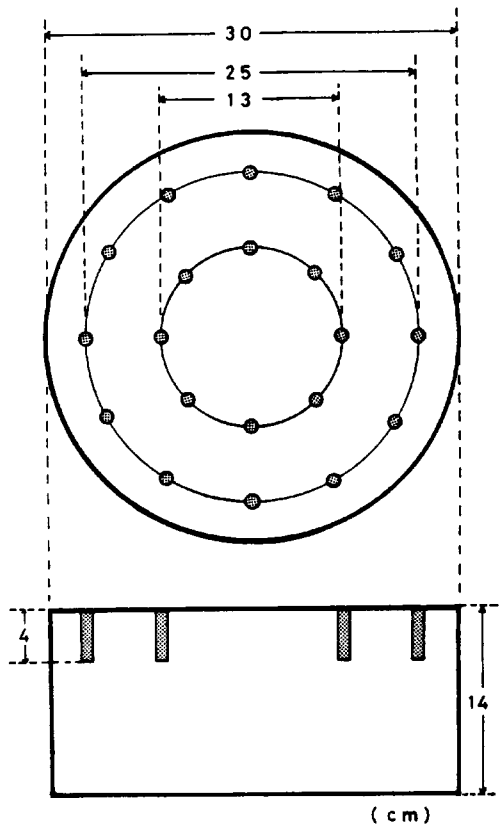

Fig. 1. The diagram of the CT phantom for the experiment with the CT scanner. The size of the phantom is 30 cm diameter by 14 cm height. The capsuls indicated by dotted circles contained varying concentrations of Thorotrast, and were arranged on two circles.

measurement of gamma-rays from Ac-228, a daughter nuclide of Th-232: its gamma-ray energy is 0.911 and 0.969 MeV. The energy range for the measurements of the photo-peak was 0.86–1.15 MeV. The obtained activity of Ac-228 was converted to the activity of Th-232, being divided by the Th-228/Th-232 ratio of 0.40. The values of Ac-228/Th-232 ratio were taken from the Ac-228/Th-232 ratio,[12] for the half life of Ac-228 is very short (6.1 hr) compared with that of its daughter, Th-228 (1.9 yr).

The counting efficiency for gamma-rays emitted from the liver and the spleen differs between upper and lower detectors by the different position of these organs in the human body. When the total activity of Ac-228 in the liver and the spleen is denoted by A_1 and A_s, respectively, the counting rate of gamma-rays by the upper detector C_u and by the lower detector C_1 are expressed as,

$$\begin{aligned} C_u &= \epsilon_{u,1} A_1 + \epsilon_{u,s} A_s \\ C_1 &= \epsilon_{1,1} A_1 + \epsilon_{1,s} A_s \end{aligned} \qquad (1)$$

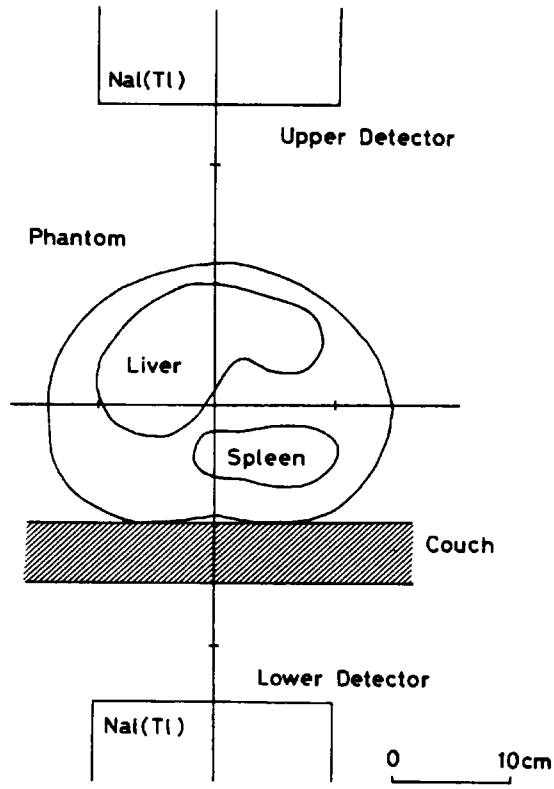

Fig. 2. The arrangement of the Alderson phantom for the measurement with the whole body counter.

Where $\epsilon_{u,1}$ and $\epsilon_{u,s}$ are the gamma-ray counting efficiency of the upper detector for Ac-228 in the liver and the spleen, respectively, and $\epsilon_{1,1}$ and $\epsilon_{1,s}$ are of the lower detector. And,

$$A_l = (\epsilon_{1,s} Cu - \epsilon_{u,s} C_l)/(\epsilon_{u,1} \epsilon_{1,s} - \epsilon_{u,s} \epsilon_{1,1})$$
$$A_s = (\epsilon_{u,1} C_l - \epsilon_{1,1} C_u)/(\epsilon_{u,1} \epsilon_{1,s} - \epsilon_{u,s} \epsilon_{1,1}) \quad (2)$$

The values for the parameters were obtained with the Alderson phantom; $\epsilon_{u,1}$ = 10.39 cpm/nCi, $\epsilon_{u,s}$ = 4.75 cpm/nCi, $\epsilon_{1,1}$ = 9.99 cpm/nCi, $\epsilon_{1,s}$ = 24.05 cpm/nCi.

As a position of spleen of the phantom was close to the lower detector, the value of the efficiency of lower detector for spleen, $\epsilon_{1,s}$ wsa five times larger than that of upper one, $\epsilon_{u,s}$ in contrast with the equality of their values for liver, $\epsilon_{1,1}$ and $\epsilon_{u,1}$.

RESULTS AND DISCUSSION

1. The Estimation of the Activity of Th-232 by the CT Scanner

The CT numbers of varying concentrations of thorium dioxide in the CT phantom were estimated and the results are shown in Fig. 3. The concentration of thorium dioxide was expressed by the activity of Th-232 per volume (pCi/cm^3). Though CT images of each capsul

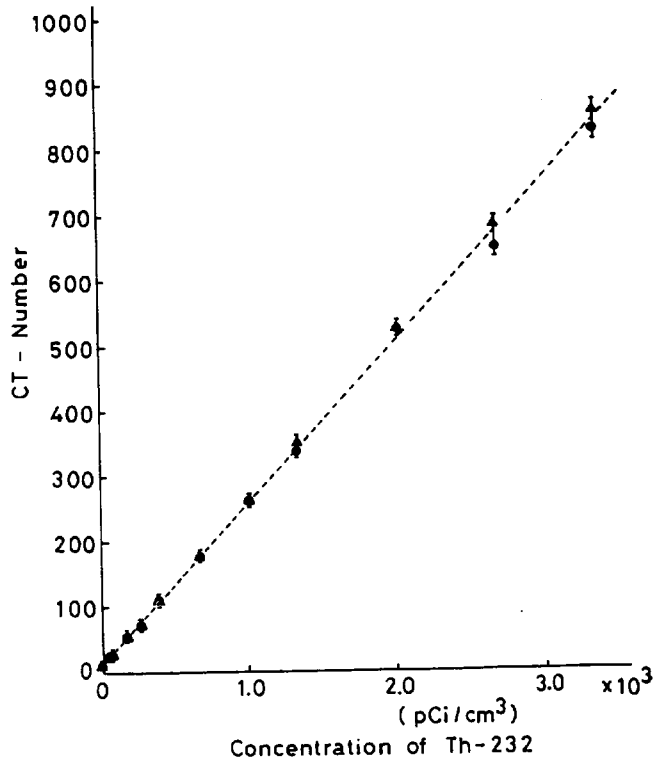

Fig. 3. The CT numbers against the concentration of Th-232. The concentration of Th-232 is expressed by pCi/cm^3. Closed circles and triangles are for Thorotrast capsuls on the inner and outer circles in the phantom, respectively. The dotted line is a regression line by the least square method.

of the phantom contained 64 pixels, the CT number was evaluated from 25 pixels near the center of the capsul to avoid the edge-effect. Circles and triangles are for capsuls located on the inner circle and on the outer circle of the CT phantom, respectively (see Fig. 1), and vertical bars indicate one standard deviation. The difference of the CT numbers for thorium dioxide between the inner circle and the outer circle was about 4%. Experiments with a smaller size of a CT phantom, 19 cm diameter, was performed, and the obtained CT numbers were the same to those indicated in Fig. 3 within 5% errors (data not shown). As these differences were not significant compared with the standard deviation of CT numbers in each capsul, it was considered that the change of CT numbers by the beam hardening effect of X-ray was not observed. The relationship between the CT number C_t and the activity of Th-232 per volume D_t (pCi/cm^3) was obtained by the least squre method,

$$C_t = 2.47 \times 10^{-1} D_t + 8.8 \quad (3)$$

Eq. (3) indicates that the increase of CT numbers which was the difference between with and without thorium deposited was proportional to the activity of Th-232 per volume. And,

$$D_t = (C_t - 8.8)/2.47 \times 10^{-1} \quad (4)$$

The value of 8.8 indicates the CT number for 5% dextrin solution without Thorotrast. Thus, the activity of Th-232 per volume was obtained by the difference of the CT numbers with and without thorium deposited was divided by a constant value, 2.47×10^{-1} Therefore, substituting C_p and C_n on the measurements of patients for C_t and 8.8, respectively, the activity of Th-232 per volume of organs of each patient, D_p (pCi/cm^3), can be obtained.

$$D_p = (C_p - C_n)/2.47 \times 10^{-1} \quad (5)$$

where C_p and C_n are the CT numbers for the organ which contains and does not contain Thorotrast, respectively. The values for C_n were obtained from normal subjects.

Seven cases of Thorotrast patients were examined (Table 1). Scans were done at 10 mm intervals, with 10 mm of collimation throughout the abdominal region. The liver and the spleen were viewed on 11 or 12 sections and 4 to 8 sections of tomograph, respectively. Fig. 4 is a typical CT scanning image of patient 1, showing high CT number in the liver and the spleen due to the deposits of Thorotrast. The deposits in lymph nodes in abdominal region are also observed and a histogram of CT numbers of the overall pixels in lymph nodes obtained from all tomographic sections of patient 1 are shown in Fig. 5. The overall mean with the

Table 1. CT numbers of liver and spleen obtained from Thorotrast patients and normal subjects.

Subjects	Age	Sex	Thorotrast injected		CT number	
			Amount (ml)	Location	Liver (mean ± SD)	Spleen (mean ± SD)
Patient 1	67	M	12	left femoral artery	63 ± 23	67 ± 25
2	63	M	*	left femoral artery	65 ± 18	70 ± 30
3	64	M	20	left femoral artery	52 ± 13	52 ± 12
4	71	M	*	right femoral artery	74 ± 16	158 ± 64
5	62	M	*	right femoral artery	76 ± 24	97 ± 40
6	56	M	*	left femoral artery	46 ± 16	139 ± 48
7	71	M	*	aorta abdominalis	64 ± 44	109 ± 37
Normal 1	29	M			43 ± 10	38 ± 10
2	41	M			54 ± 11	37 ± 9
3	63	M			54 ± 9	46 ± 11
4	17	F			44 ± 11	36 ± 9

*Injected amounts were not known.

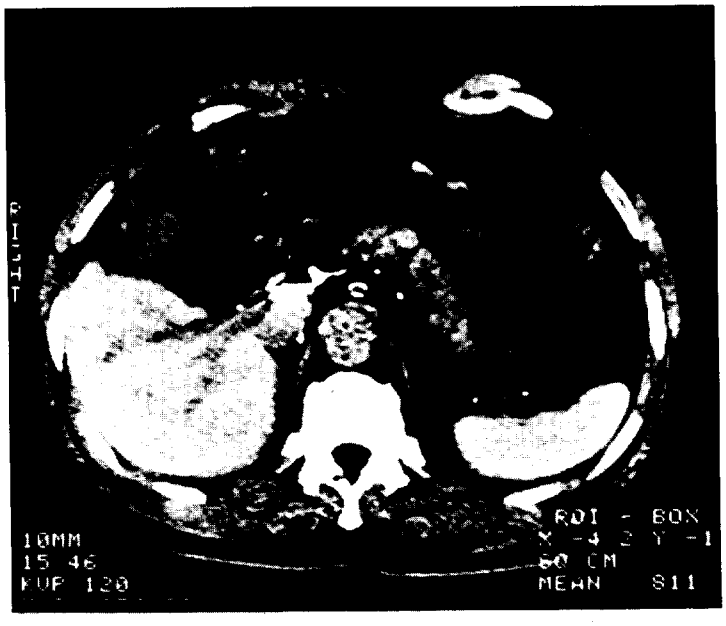

Fig. 4. A typical CT scanning image of patient 1. The liver and the spleen showed high CT numbers.

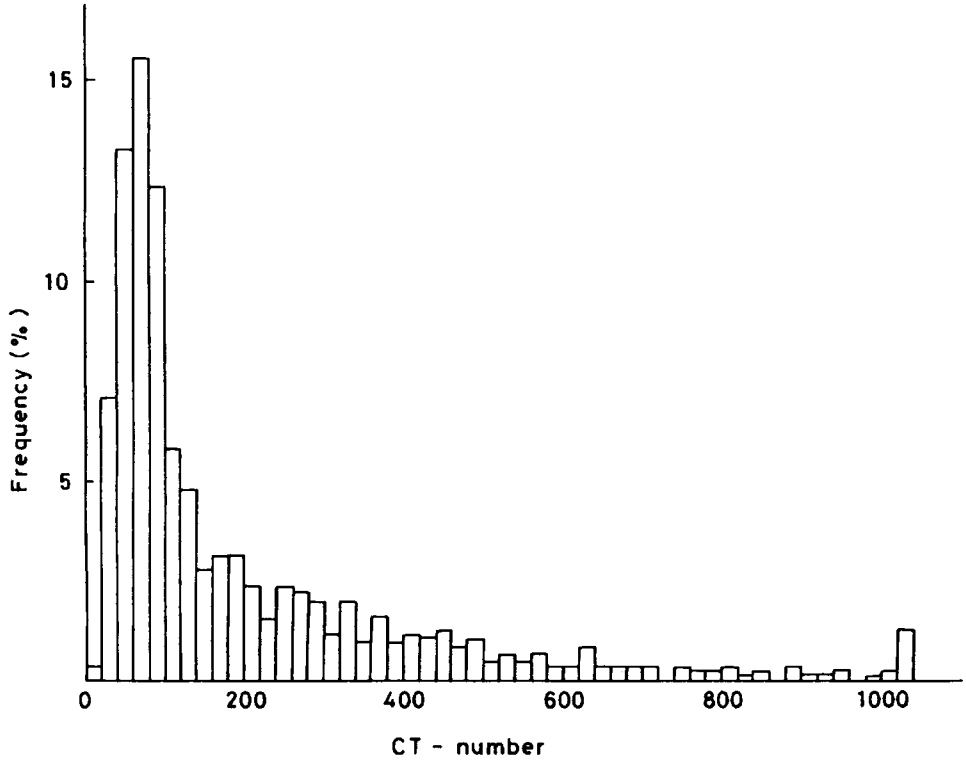

Fig. 5. The distributions of the CT number of the lymph nodes of patient 1. Few CT numbers above 1000 which are saturated numbers are shown in the lymph nodes.

standard deviation (SD) of the CT number were 199 ± 210. And few of the CT numbers were distributed above 1000 which was a saturated CT number of the scanner. On evaluation of thorium deposited for liver or spleen, therefore, the CT numbers in the area of the lymph nodes and the artifact near them were excluded to avoid the error.

The distributions of the CT numbers were compared between patient 5 and normal subject 1 in Fig. 6 for the liver, and between patient 4 and normal subject 1 for the spleen in Fig. 7. The distributions of the CT numbers in both Fig. 6 and Fig. 7 were taken from all tomographic sections of the organ. In Fig. 6, the numbers of pixels and the overall mean ± SD of CT numbers were 77504 and 75 ± 24, and 79287 and 43 ± 10 for patient 5 and normal subject 1, respectively. In Fig. 7, those were 4556 and 158 ± 64, and 7672 and 38 ± 10 for patient 4 and normal subject 1, respectively. The CT numbers for the patient showed higher values and distributed wider than those of the normal subject. The CT numbers in the organ of patients distributed below 350. In Table 1 the overall mean CT numbers with their SD for the liver and the spleen are summarized. With eq. (5) the activity of Th-232 per volume in patients were estimated. Each C_p was the overall mean CT numbers in all tomographic sections of the liver or spleen for each patient. The values for C_n were obtained by being averaged the overall mean CT numbers of 4 normal subjects: 49 for the liver and 39 for the spleen. Obtained D_p

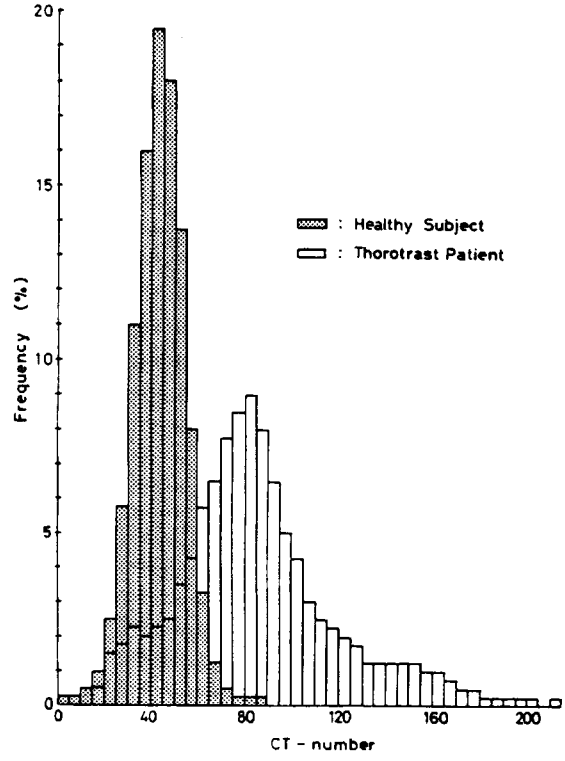

Fig. 6. The distributions of the CT number of the liver. Open and dotted histograms are of patient 5 and healthy subject 1, respectively.

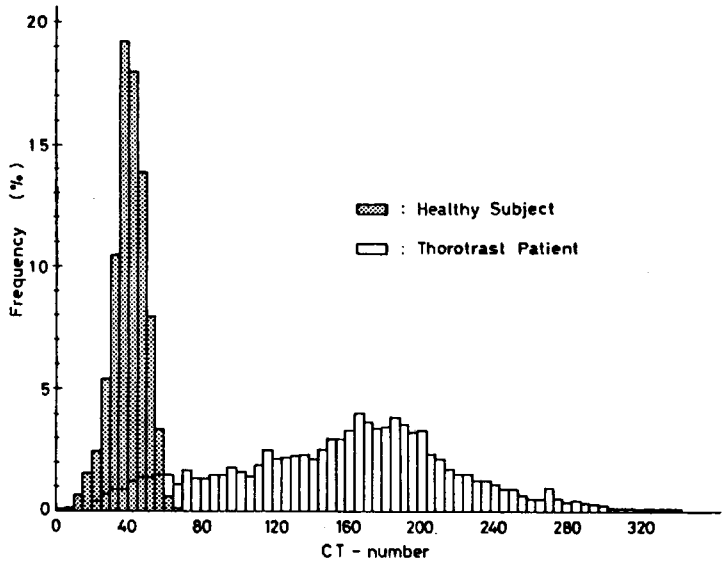

Fig. 7. The distributions of the CT number of the spleen. Open and dotted histograms are of patient 4 and of healthy subject 1, respectively.

Table 2. Activity of Th-232 per volume and the dose rate for liver and spleen estimated by CT scanner.

	Liver		Spleen	
Patients	Activity of Th232 per volume (pCi/cm^3)	Dose rate (cGy/week)	Activity of Th-232 per volume (pCi/cm^3)	Dose rate (cGy/week)
1	57	0.11	113	0.23
2	65	0.13	126	0.26
3	12	0.02	53	0.11
4	101	0.20	482	0.98
5	109	0.22	235	0.48
6	0	0	405	0.83
7	61	0.12	283	0.58

was average value for whole organ. The estimated activity of Th-232 per volume is summarized in Table 2. Patient 6 showed no deposit of Thorotrast in the liver.

2. Estimation of the Absorbed Dose Rate of Th-232 in Thorotrast Patients by CT Scanner

For the evaluation of radiation hazard of Thorotrast patients, the absorbed dose rate in the organs were estimated from the activity per volume, which was directly obtained by the CT scanner. The absorbed dose rate from the activity of Th-232 per unit volume was derived as follows. The dose rate in an organ R is given by

$$R = E/M \tag{6}$$

where E is the total energy of all alpha-rays emitted from Th-232 and its daughter nuclides in a week in the organ, and M is the mass of the organ. E is expressed by

$$E = 60 \times 60 \times 24 \times 7\ nf\ \Sigma k_i b_i e_i \tag{7}$$

where $60 \times 60 \times 24 \times 7$ is a value of one week expressed in seconds, n is the activity of Th-232 in the organ, f is the average self absorption coefficient of alpha-rays in Thorotrast aggregates. k_i is the activity ratio of i-th daughter nuclide to Th-232, b_i and e_i are the emission rate and the average energy of the alpha-rays of i-th daughter nuclide, respectively. From eqs. (6) and (7),

$$R = 60 \times 60 \times 24 \times 7\ nf\ (\Sigma k_i b_i e_i)/\rho V \tag{8}$$

where ρ and V are the density and the volume of the organ, respectively, and n/V can be obtained from D_p in eq. (5).

In the present work, the values of parameters in eq. (8) were used of previously published data: results obtained by Kaul et al.[12] for f and k_i, Table of Isotopes[13] for b_i and e_i. And the dose rate R in cGy/week became

$$R = 2.01 \times 10^{-3}\ D_p$$

for the liver, and

$$R = 2.04 \times 10^{-3}\ D_p$$

for the spleen. The estimated dose rate for the patients is shown in Table 3.

Table 3. Comparison of the estimates by CT scanner and whole body counter.

	CT scanner					Whole body counter		
	Liver		Spleen		Sum of	Liver	Spleen	Sun of
Patients	Volume (cm^3)	Activity (nCi)	Volume (cm^3)	Activity (nCi)	activity (nCi)	Activity (nCi)	Activity (nCi)	activity (nCi)
1	1230	68	125	14	82	142	49	191
2	1270	83	41	5	88	89	20	109
3	1070	13	47	2	15	–	–	–
4	1230	124	77	37	161	171	38	209
5	1310	143	23	5	148	174	20	194
6	1350	0	130	53	53	–	–	–
7	1200	73	25	7	80	103	16	119

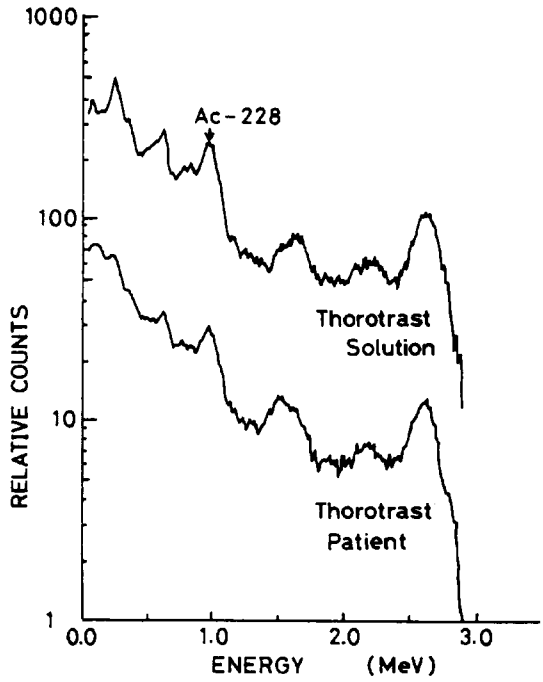

Fig. 8. Spectra of gamma-rays from the Thorotrast solution and patient obtained by the whole body counter. The upper curve is of the Thorotrast solution, and the lower curve is of the Thorotrast patient 4.

3. The Estimation of the Activity of Th-232 by the Whole Body Counter

In Fig. 8 a typical spectrum of gamma-rays from patient 4 is shown. Photo-peaks of Pb-212 (0.24 MeV), Ac-228 (0.91 MeV) and T1-208 (2.62 MeV), which are daughter nuclides of Th-232, were recognized in the Figure. The gamma-ray spectrum for Thorotrast solution is also presented in the Figure for a comparison. Both spectra were identical. The gamma-rays from Ac-228 in organs were counted and the activity was evaluated by eq. (2). An activity of Th-232 was estimated by being divided the activity of Ac-228 by an activity ratio of Ac-228 to Th-232 in living tissues, 0.4 which was taken from Kaul et al.[12] The estimated activity in the liver and the spleen is tabulated in Table 3. For two cases, patients 3 and 6, in which a large amount of Thorotrast was deposited in inguinal region where Thorotrast was injected, gamma-rays from that region made difficult to estimate the activity in the liver and the spleen, although the estimation by the CT scanner was possible (see Table 1).

4. The Comparison of the Th-232 Activity Estimated by the CT Scanner and the Whole Body Counter

For the comparison of the activity per volume estimated by the CT scanner with the activity estimated by the whole body counter. The results obtained by the CT scanner was multiplied by the organ volume. The volume of organs was determined by the pixel size and the number of pixels obtained from the CT images. The results are shown in Table 3. The

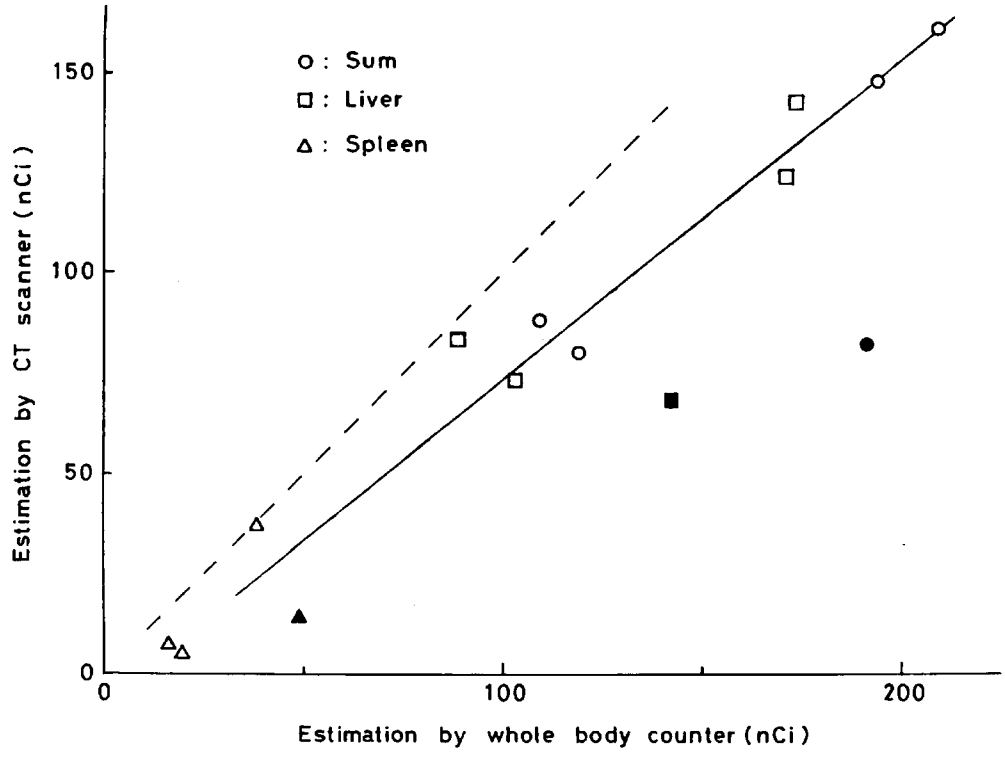

Fig. 9. The relationship of the activity of Th-232 estimated by the CT scanner and that by the whole body counter. Where, □, △ and ○ show the activity for the liver, for the spleen and summed up for the liver and the spleen, respectively. Patient 1 who had much deposits of Thorotrast in lymph nodes and excluded from the analysis is showed by the solid symboles. The broken line shows a relationship Y = X and solid line shows the relationship obtained by the least square method for the activity summed up for the liver ad the spleen, excluding patient 1; $Y_a = 0.796\ X_a - 6.37$, where Y_a and X_a were estimates by the CT scanner and those by the whole body counter.

activity of Th-232 of the liver and of the spleen were summed and compared the estimates by the CT scanner with those by the whole body counter as shown in Fig. 9. A linear regression equation by the least square method was obtained and

$$Y_a = 0.602\ X_a + 12.91 \tag{9}$$

where Y_a and X_a are the activity summed up for the liver and the spleen by the CT scanner and that by the whole body counter, respectively. The correlation coefficient between the estimates by the CT scanner and the whole body counter was 0.713. A relationship of $Y_a = X_a$ between the estimates by the CT scanner and those by the whole body counter should be obtained when both estimates were accurate for the activity of Th-232. However, the estimates by the whole body counter were larger than those by the CT scanner by 47% at the average value for 5 patients. In the estimation by the CT scanner, the activity in organs other than

the liver and the spleen such as lymph nodes were excluded from the calculation, while in that by the whole body counter, gamma-rays of the overall abdominal region were counted without identification of organs. Thus, the results by the whole body counter were overestimated for the sum of the liver and the spleen. To prevent a such kind of the overestimation by the whole body counter, therefore, patient 1 which had much deposits of Thorotrast in lymph nodes compared with other 4 cases was eliminated from the analysis. The regression equation for 4 patients was obtained and

$$Y_a = 0.796\, X_a - 6.37 \tag{10}$$

where, the value of intercept of −6.37 indicates the underestimation of the CT scanner to the whole body counter, for the latter measures the deposits of Thorotrast not only in the lymph nodes but also in the liver and spleen. However, the value of 6.37 nCi was not considerable. The value of inclination of 0.796 also indicates the underestimation of the CT scanner. In the estimation of the whole body counter, the steady state activity ratio of Ac-228/Th-232 in organs of survival patients was required for conversion from the direct measured value of Ac-228. As the metabolism of daughter nuclides in living tissues differs patient to patient, the ratio of Ac-228/Th-232 which was taken from the average value of privious study[12], 0.40 might be inaccurate for the cases chosen in this study. When the ratio of the CT scanner to the whole body counter, 0.796 was resulted from the differences of the activity ratios, 0.50 would be obtained as the activity ratio of Ac-228/Th-232 for our cases. However, the discrepancy of the activity ratio between 0.40 and 0.50 was not large. It was considered that the estimates by the whole body counter agreed well with those by the CT scanner in permissible errors. The correlation coefficient was 0.98 and which also indicates that the estimates by the CT scanner consist with those by the whole body counter.

The activity of Th-232 estimated by the CT scanner and by the whole body counter are compared for the liver and for the spleen in Fig. 9. When patient 1 was excluded by the above reason, the relationships became;

$$\begin{aligned} Y_l &= 0.706\, X_l + 10.97 \\ Y_S &= 1.543\, X_S - 22.76 \end{aligned} \tag{11}$$

where Y_l and X_l are activity of Th-232 for the liver estimated by the CT scanner and by the whole body counter, respectively; Y_S and X_S are for the spleen. The values of parameters of eq. (11), 0.709 and 1.543, indicate that the whole body counter overestimated the activity in liver and underestimated the activity in spleen. The counting efficiency of the detector changes when the distance between the detector and the organ varies. The values of the counting efficiency for eq. (2) were determined from the position of the models of liver and spleen of the Alderson Phantom shown in Fig. 2. As the position of the organs differs patient to patient, the values of the parameter should be changed. However, the constant values for the parameters were used for each patient in the usual method by the whole body counter. This

might be the reason of overestimation or underestimation.

The correlation coefficients were 0.947 and 0.968 for the estimation for the liver and spleen, respectively.

CONCLUSION

On the whole body counter, the existence of Th-232 can be clearly noticed by counting the gamma-rays from the daughter nuclides and detected the radioisotopes in abdominal region almost independently the position when the counts of both detectors are summed. Therefore, the overall activity in a body can be measured exactly and was agreed with the activity of Th-232 summed up for the liver and the spleen estimated by the CT scanner. However, in the estimation of the activity of each organ, the results showed the disagreement of two methods, for the reason the whole body counter has the following defects:

1) It is difficult to estimate accurate activity in the liver and the spleen, since the parameters used in eq. (2) might change when the geometry of those organs of each patient differs from that of the Alderson phantom shown in Fig. 2.
2) It is not possible to measure accurately the gamma-rays from the liver and spleen when thorium deposits exist in other organs.

It could be concluded that the estimates of Th-232 in each organ by the CT scanner are more accurate than those by the whole body counter, for the distribution of thorium deposits in the abdominal region is directly obtained from the CT images. Moreover, using the direct values from CT scanner, the absorbed dose rate can be estimated without the values of organ volumes while in the whole body counter, the volumes of organ are required and taken from the average values of Japanese or determined by the CT scanner. Therefore the estimated dose by the whole body counter would include their uncertainty.

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