Gonadal Dose Measurement in Diagnostic Nuclear Medicine Using Thermoluminescent Dosimeters

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Instead of using the Medical Internal Radiation Dose Committee (MIRD) concept to calculate the gonadal dose during diagnostic examination using radiopharmaceuticals, measurements of gonadal doses using thermoluminescent dosimeters were studied. The results obtained are comparable with that calculated using the MIRD concept. Five frequently used examinations were investigated, viz., liver, brain, thyroid, bone scintigraphy and cholestigraphy. The calibration of thermoluminescent dosimeters are fully described, and the experimental techniques are also fully presented.

Key Words: Medical Internal Radiation Dose Committee, gonadal dose, thermoluminescent dosimeter, liver, brain, thyroid, bone, chole, scintigraphy

1. Introduction

Internal dose such as for diagnostic purposes from radiopharmaceuticals is subject to the system of dose limitation, i.e., a system of justification, optimization and limitation as far as the radiation exposure or dose is concerned. The detailed description can be found in the Publication No. 26 of the International Commission of Radiological Protection issued in 1977.

The assessment of the dose received by the patient's organs and tissues plays an important role in determining the risk involved in the examination. Generally, absorbed dose per unit administered activity for the most frequently used radiopharmaceuticals and methods are calculated according to the Medical Internal Radiation Dose Committee (MIRD) concept. The data are given for critical or investigated organs, ovaries, testes, and red bone marrow. To estimate the radiation dose to the patient is to multiply the tabulated dose values per unit activity with the corresponding mean or the actually administered activity.

In the present work the authors have gathered from their own extensive experience in the medical applications of thermoluminescent dosimeters (TLD) and from the experience of others the latest knowledge of dose assessment as well. The TLDs were applied to measure the gonadal doses in various scintigraphic examinations, e.g., liver, brain, thyroid, bone, and gall bladder scintigraphy.

2. Experimental

Before injection with ^{99m}Tc -labeled radioactive agent, the weight and height of each patient were recorded. The TLDs were taped onto the proper positions as shown in Fig. 1. This followed the general practice for measuring gonadal dose in radiotherapy¹⁾. After injection ^{99m}Tc -labeled agent, scintiphotos were recorded with an Elscint Dymax LF scintillation camera. The activity of ^{99m}Tc -labeled radioactive agent was checked with an EON CAL-1 calibrated radioactivity assayer.

The TLD $\text{CaSO}_4:\text{Dy}$ powder of 80 mg was encapsulated in a black polyethylene capsule with 3 mm internal diameter, 1 mm wall thick-

Fig. 1 The positions of TLD's on patients.

ness and 20 mm length. For each reading it took 17.25 ± 0.40 mg $\text{CaSO}_4:\text{Dy}$. The powders were measured with the Harshaw 2000 B&C TLD reader. The one mm wall thickness is sufficient to establish electronic equilibrium for the 0.142 MeV γ -ray emitted from $^{99\text{m}}\text{Tc}$. The reader stability is $\pm 0.8\%$. The total error of the reader system in mR is within $\pm 5\%$. The calibration factors for TLDs include reader stability, and fading and energy dependence of TLDs²⁾.

In this experiment the response to γ -ray of $^{99\text{m}}\text{Tc}$ is 20% higher than that of ^{60}Co in terms of absorbed dose. The response is also linear with absorbed dose with the dose ranges of this experiment.

Since the half-life of $^{99\text{m}}\text{Tc}$ is rather short (6.02 h) the exposure rates (mR/h) decrease rather rapidly and follow the simple exponential decay law. The mean life of $^{99\text{m}}\text{Tc}$ is 8.7 h

which was used as the base line in dose measurement and calculation.

3. Results and Discussion

3.1 Liver scintigraphy

The study started shortly after injecting $92.5 - 222$ MBq (2.5 - 6 mCi) $^{99\text{m}}\text{Tc}$ -phytate. For the 93 male patients measured, the average gonadal dose is 19 ± 5 mrad/mCi-mean life or 30 ± 8 mrad/mCi for complete decay, while for the 45 female patients measured, the average gonadal dose is 18 ± 5 mrad/mCi-mean life or 28 ± 8 mrad/mCi for complete decay. Bioassay was also performed for the 138 patients. The items included GOT (glutamic oxaloacetic transaminase), GPT (glutamic pyruvic transaminase), bilirubin, and ALK-Pase (alkaline phosphatase), and the position ($x \downarrow$) and dimension of liver were also determined in order to find the correlation between gonadal dose and liver position and dimension as well. The results are shown in Tables 1 and 2. The function, position, and dimensions of liver bear no direct effect on gonadal dose as shown in Tables 1 and 2.

MIRD lists the S factors (rad/ $\mu\text{Ci h}$) of 4.5×10^{-7} for the liver to ovaries and 6.2×10^{-8} to testes, and 7.3×10^{-6} for the gall bladder to ovaries and 4.7×10^{-6} to testes.

It is obvious that ovaries have higher dose than tests based on the S factors alone and other factors are neglected when either liver or gall bladder is the source organ.

Table 1 The relationship between liver function and gonadal dose

		Male		Female	
		n	Dose (mrad/mCi-mean life)	n	Dose (mrad/mCi-mean life)
GOT (IU/l)	<50	50	18.79 ± 5.27	22	17.36 ± 5.11
	50 - 100	7	18.29 ± 3.87	6	18.49 ± 4.09
	>100	11	18.47 ± 5.46	4	13.87 ± 2.42
GPT (IU/l)	<50	52	18.75 ± 5.30	27	17.20 ± 4.68
	50 - 100	9	17.39 ± 5.08	3	18.66 ± 6.76
	>100	7	20.60 ± 3.45	2	13.98 ± 4.12
Bilirubin (mg/dl)	<1.5	55	19.14 ± 4.98	28	17.63 ± 4.84
	1.5 - 3.0	7	17.80 ± 5.43	2	(15.20)
	>3.0	3	15.08 ± 8.50	2	(12.15)
ALK-Pase (IU/l)	<100	47	18.92 ± 5.22	23	17.66 ± 5.15
	>100	19	18.60 ± 5.16	7	15.94 ± 3.92

Remarks: n =number of patients, 1 mrad=10 μGy , 1 mCi=37 MBq

(± 1 S.D.)

Table 2 The relationship between the position and dimensions of liver and gonadal dose

	Size(cm)	Male		Female	
		<i>n</i>	Dose (mrad/mCi-mean life)	<i>n</i>	Dose (mrad/mCi-mean life)
$x\downarrow$	0-10	76	18.49±5.07	35	18.03±4.98
	>10	14	21.24±3.75	7	18.28±4.34
Width	12-19	59	18.73±5.25	29	18.34±4.77
	20-27	33	18.72±4.83	10	15.42±4.87
Length	<15	55	17.94±5.57	32	17.89±4.85
	>15	36	19.09±4.03	12	17.91±4.87

Remarks: $x\downarrow$ =the distance between the lowest border of the liver and the xyphoid process on the sagital line. (± 1 S.D.)

3.2 Brain thyroid, and bone scintigraphy

The study started shortly after injection 555-925 MBq (15-25 mCi) free ^{99m}Tc ($^{99m}\text{TcO}_4^-$) for brain scintigraphy, 370-555 MBq (10-15 mCi) free ^{99m}Tc for thyroid scintigraphy, and 555-925 MBq (15-25 mCi) ^{99m}Tc -ppi (pyrophosphate) for whole-body bone scintigraphy; the Elscint Dymax LF scintillation camera was used to take the pictures of brain, thyroid, and bone, respectively. The activity of ^{99m}Tc was checked with an EON CAL-1 calibrated radioactivity assayer.

The gonadal doses for brain, thyroid, and bone scintigraphy are shown in Table 3.

Since the majority of the radiopharmaceuticals used in nuclear medicine are excreted *via* the urinary tract, the patient voiding schedule as related to the measured absorbed doses would be certainly as important as the contribution from the thyroid gland as a function of thyroid function.

For the 49 thyroid patients measured, they are grouped in two according to the thyroid function, i.e., T_3 (triiodothyronine) and T_4 (thyroxine) level and FTI (free thyroxine index) by RIA (radioimmunoassay) measurement. The

Table 3 Gonadal dose for brain, thyroid, and bone scintigraphy

Organ	Male		Female	
	<i>n</i>	(mrad/mCi)	<i>n</i>	(mrad/mCi)
Brain	34	25±8	16	28±7
Thyroid	12	18±4	37	22±5
Bone	21	34±9	24	27±8

Remarks: *n*=number of patients.

Table 4 Thyroid function and gonadal dose

Function test	Male		Female	
	<i>n</i>	(mrad/mCi)	<i>n</i>	(mrad/mCi)
T_3 (ng/dl)				
	<150	3 18±3	15	20±6
	>150	2 20±2	6	21±6
T_4 (μg/dl)				
	<8	3 18±3	15	21±6
	>8	2 20±2	6	20±4
FTI				
	<2.4	3 18±3	15	20±6
	>2.4	2 20±2	6	22±5

results are shown in Table 4.

For the 45 bone patients, they are grouped in three according to having or without metastasis at the pelvic bones, sacroiliac joint, hip joint, etc. The results are shown in Table 5.

It is concluded that the gonadal dose is independent of thyroid function. The same conclusion may also be drawn in bone scintigraphy if presence of metastasis or not. Since the gonad is far away from brain and thyroid, the experimental results are consistent with expectation.

Table 5 Metastatic bone lesion and gonadal dose

Metastasis	Male		Female	
	<i>n</i>	(mrad/mCi)	<i>n</i>	(mrad/mCi)
Without metastasis	6	33±4	6	28±7
Metastasis at pelvic region	1	40±0	3	23±4
Other metastasis	10	37±12	8	26±11

3.3 Cholescintigraphy

The study started shortly after injecting 111–185 MBq (3–5 mCi) ^{99m}Tc -HIDA (N-(2, 6-dimethylphenylcarbamoylmethyl)iminodiacetic acid). For the 40 male patients measured, the average gonadal dose is 48 ± 19 mrad/mCi-mean life, while for the 25 female patients measured, the average gonadal dose is 48 ± 17 mrad/mCi-mean life. No significant difference in gonadal doses between both sexes have ever been detected.

A good indicator of liver function is the serum bilirubin value. It is categorized in two groups, i.e., bilirubin value greater or less than 1 mg/dl. In the similar way, the biliary-to-bowel transit time of ^{99m}Tc -HIDA is also categorized in two groups, i.e., the excretion time greater or less than 60 min. The purpose of grouping was to observe the variation of gonadal dose in both sexes. It is interesting to note that no significant variation in gonadal dose was observed in male patients; however, the variation is significant in female patients as shown in Table 6.

Since the female gonad is situated intra-abdominally and the male gonad extra-abdominally, the female patients have in general higher gonadal dose even in both sexes having normal liver function and biliary-to-bowel transit time.

The decrease in hepato-cellular function or the blockage of bile flow would cause higher bilirubin value. The absorption and excretion of ^{99m}Tc -HIDA is then reduced and delayed, the transit time is thus longer, and the quantity of excretion is hence less as shown in Tables 6 and 7. Therefore hepatic dysfunction would cause a lower gonadal dose for female patients.

Table 6 Gonadal dose as a function of bilirubin value and biliary-to-bowel transit time

Bilirubin	Male		Female	
	<i>n</i>	(mrad/mCi)	<i>n</i>	(mrad/mCi)
<1 mg/dl	16	47 ± 13	9	60 ± 17
>1 mg/dl	22	49 ± 24	6	40 ± 14
Transit time				
<60 min	29	49 ± 21	18	53 ± 15
>60 min	10	44 ± 13	5	30 ± 8

n=number of patients

Table 7 Relationship between bilirubin value and biliary-to-bowel transit time

Bilirubin (mg/dl)	Transit time (h)			
	<i>n</i>	Male	<i>n</i>	Female
<1	18	0.7 ± 0.6	8	0.5 ± 0.1
>1	20	1.7 ± 1.7	6	1.9 ± 1.7

The liver function is related to the biliary-to-transit time as shown in Table 7, and the female gonadal dose is significantly affected by the radioactive agent excreted into the gut as discussed above. So, the detection duration of gonadal dose by TLD should be long enough to cover the biliary-to-bowel transit time. In this study, the detection duration was apparently longer than the biliary-to-bowel transit time, and the lower gonadal dose for female patients with poorer liver function could not be caused by an inadequate detection duration as shown in Tables 8 and 9.

Furthermore, assuming the quantity of HIDA excreted to the bowel were definite, then the longer the transit time, the lower the gonadal dose due to radioactive decay. Thus the more severe the hepatic dysfunction, the lower the gonadal dose should be. However, as the opposite the result of the present study revealed that the poorer the hepatic function, the lower the female gonadal dose.

Finally, the quantity of kidney excretion is also taken into account. When the hepato-cellular function is decreased, the quantity of kidney excretion is increased, and the activity

Table 8 Relationship between bilirubin value and detection time

Bilirubin (mg/dl)	Detection time (h)			
	<i>n</i>	Male	<i>n</i>	Female
<1	17	2.7 ± 0.8	8	2.5 ± 0.6
>1	20	3.0 ± 0.8	6	3.5 ± 0.8

Table 9 Relationship between excretion time and detection time

Excretion time (min)	Detection time (h)			
	<i>n</i>	Male	<i>n</i>	Female
≤60	29	2.7 ± 0.8	19	2.6 ± 0.6
>60	11*	3.4 ± 0.7	5**	3.3 ± 0.8

* Average 3.5 ± 1.3 h (male)

** Average 2.8 ± 1.1 h (female)

may accumulate in the bladder which would enhance the gonadal dose. However, contrary to the fact observed from this investigation, the female gonadal dose is less for the poor liver function. It is thus noted that the kidney excretion would not compensate enough to cause an increased gonadal dose.

Using the MIRD formalism and biological data, the absorbed dose to gonads is due to activity in the organ of interest as well from activity in organs at a distance. The TLD method dose not measure absorbed dose from activity in the gonads, e.g., non-penetrating radiation emitted in the gonads.

Based on the ICRU Report 32, an example is given to calculate the dose to the liver and to the ovaries by intravenous administration of ^{99m}Tc sulfur colloid³⁾ (ICRU 79). The absorbed fraction at the ovaries is 1.8×10^{-5} . The mean energy of penetrating radiation per nuclear transformation of the parent nuclide in the liver is $263 + 2.5 + 0.5 \text{ g mrad}/\mu\text{Ci h}$ and $37 \text{ g mrad}/\mu\text{Ci h}$ for non-penetrating radiation. The latter is 0.139 or 13.9% in the liver. In the ovaries the mean energy of penetrating radiation per nuclear transformation is $264 \text{ g mrad}/\mu\text{Ci h}$. If the mean energy of non-penetrating radiation remains the same as $37 \text{ g mrad}/\mu\text{Ci h}$, then it is about 0.14 or 14%. The TLD method may underestimate the dose measured by 14% at most.

In calculation using MIRD concept, the absorbed fraction of ^{99m}Tc -labeled agent in various organs or tissues relies on literature survey⁴⁾⁻¹¹⁾. Table 10 lists the results obtained from MIRD formulation, this measurements, and measurements done by other investigators. In the calcu-

lation, the total body as a target organ is taken into account in addition to ovaries and testes.

4. Summary

Thermoluminescent dosimeters $\text{CaSO}_4:\text{Dy}$ were used to determine the gonadal dose of 138 patients administered with ^{99m}Tc for liver testing. For the 93 male patients with average age $53 \pm 14 \text{ y}$, height $165 \pm 6 \text{ cm}$, weight $56 \pm 9 \text{ kg}$, the gonadal dose is $19 \pm 5 \text{ mrad/mCi}$ at 1 mean life, or $30 \pm 8 \text{ mrad/mCi}$ for complete decay. For the 45 female patients with average age $49 \pm 16 \text{ y}$, height $155 \pm 5 \text{ cm}$, weight $52 \pm 8 \text{ kg}$, the gonadal dose is $18 \pm 5 \text{ mrad/mCi}$ at 1 mean life, or $28 \pm 8 \text{ mrad/mCi}$ for complete decay. Bioassay was also performed for the determination of liver function and no significant results related to gonadal dose have ever been detected.

Same dosimeters $\text{CaSO}_4:\text{Dy}$ were used to determine the gonadal dose of 50 patients during brain scintigraphy. For the 34 male patients with average age $50 \pm 17 \text{ y}$, height $166 \pm 6 \text{ cm}$, and weight $64 \pm 12 \text{ kg}$, the gonadal dose was $25 \pm 8 \text{ mrad/mCi}$ at 1 mean life. For the 16 female patients with average age $39 \pm 13 \text{ y}$, height $156 \pm 5 \text{ cm}$, and weight $53 \pm 8 \text{ kg}$, the gonadal dose was $28 \pm 7 \text{ mrad/mCi}$ at 1 mean life. The difference in gonadal doses between sexes is not significant.

Similar procedures were performed to determine the gonadal dose of 49 patients during thyroid scintigraphy. For the 12 male patients with average age $41 \pm 13 \text{ y}$, height $168 \pm 5 \text{ cm}$, and weight $67 \pm 8 \text{ kg}$, the gonadal dose was $18 \pm 4 \text{ mrad/mCi}$ at 1 mean life. For the 37 female patients with average age $37 \pm 16 \text{ y}$, height $156 \pm$

Table 10 Comparison of gonadal doses (mrad/mCi)

Organ	Liver	Brain	Thyroid	Bone	Gall bladder	Remarks
Agent	-phytate	$^{99m}\text{TcO}_4^-$	$^{99m}\text{TcO}_4^-$	-ppi	-HIDA	
mCi	2.5 - 6	12 - 25	10 - 15	15 - 25	3 - 5	
Ovaries	28 ± 8	28 ± 7	22 ± 5	27 ± 8	47 ± 17	The authors
Testes	30 ± 8	25 ± 8	18 ± 4	34 ± 9	48 ± 19	
Ovaries	12	30	30	15	8	12)
Testes	3	9	9	15	2	
Ovaries	23		15	23	68	MIRD
Testes	19		15	23	40	

(10 mCi=370 MBq)

6 cm, and weight 49 ± 7 kg, the gonadal dose was 22 ± 5 mrad/mCi, at 1 mean life. According to the radioimmunoassay data of thyroid function, male and female patients were grouped in two, and no significant difference in gonadal dose had ever been detected even though the T_4 , T_4 , T_3 uptake, and FTI values of patients may vary.

The examination procedures were also applied in whole-body bone scintigraphy. For the 21 male patients with average age 49 ± 16 y, height 168 ± 7 cm and weight 60 ± 11 kg, the gonadal dose was 34 ± 9 mrad/mCi at 1 mean life. For the 24 female patients with average age 43 ± 16 y, height 156 ± 6 cm and weight 51 ± 8 kg, the gonadal dose was 27 ± 8 mrad/mCi at 1 mean life. No significant increase in gonadal dose had ever been detected even the metastasis region occurred at the pelvic bones, sacroiliac joint, and hip joint. $\text{CaSO}_4:\text{Dy}$ were used to determine the gonadal doses of 65 patients administered with $^{99\text{m}}\text{Tc-HIDA}$ for hepatobiliary images. For the 40 male patients aged 49 ± 12 y (mean $\pm$ S.D.), heighted 166 ± 5 cm and weighed 54 ± 8 kg, the gonadal dose was 48 ± 19 mrad/mCi at 1 mean life. For the 25 female patients aged 45 ± 17 y, heighted 155 ± 6 cm and weighed 48 ± 8 kg, the gonadal dose was 47 ± 17 mrad/mCi at 1 mean life. There was no significant difference in gonadal doses between sexes.

Regarding the duration of detection of gonadal doses by thermoluminescent dosimeters, that was longer than the biliary-to-bowel transit time in most patients, we found that the gonadal doses in female patients, with serum bilirubin level greater than 1 mg/dl or the biliary-to-bowel transit time by HIDA imaging longer than 1 h, were significantly less than those with bilirubin level less than 1 mg/dl or with a shorter biliary-to-bowel transit time. For male patients there was no significant difference between the two cases mentioned above. Even in patients with normal liver function by blood biochemical analysis, the gonadal dose for female was sig-

nificantly higher than that for male; that may be due to the difference of gonadal location, i.e., intra-abdominal organs for female and extra-abdominal organs for male.

The gonadal doses obtained using TLDs as mentioned above are comparable with that calculated using the MIRD concept.

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要 旨

核医学診断時における
生殖腺線量の熱ルミネセンス線量計による測定

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放射性医薬品を用いた診断のさいの生殖腺被曝線量を求めるにあたって MIRD の概念を用いるかわりに, 熱ルミネセンス線量計を用いての生殖腺線量の測定を行った。得られた結果は MIRD の概念を用いての計算値と比較した。臨床的に検査頻度の高い, 肝, 脳, 甲状腺, 骨, 胆道シンチグラムの 5 検査を調査した。熱ルミネセンス線量計の測定法および実験技術を完全に記載した。