Radiation Safety Issues in Y-90 Microsphere Selective Hepatic Radioembolization Therapy: Possible Radiation Exposure from the Patients

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Abstract

Purpose The purpose of this study was to estimate the possible external radiation dose to other individuals from patients treated with Y-90 resin microspheres for unresectable hepatocellular carcinoma.

Methods We designed the study prospectively to estimate the possible radiation dose to other individuals from patients who had been treated with Y-90 microspheres for unresectable hepatocellular carcinoma. We estimated the total effective dose equivalent (TEDE) using two methods: ‘theoretical’ TEDEs according to the administered activity and ‘measured’ TEDE based on the ‘measured’ ambient radiation exposure rate. We compared the results from each method to determine when we can release patients from confinement at the earliest time complying with the patient release criteria.

Results A total of 20 administrations of Y-90 resin microspheres were done in 18 patients. The average administered

activity was 1.2 ± 0.77 (0.28–2.97) GBq. The ‘theoretical’ TEDEs were in the range of 0.8–10 μ Sv. The ‘measured’ TEDEs were in the range of 2.31–185 μ Sv. The measured TEDEs tend to be higher than the theoretical TEDEs. The values of theoretical and measured TEDE were both far less than 1 mSv, the upper limit at which the licensee can release a patient without any written documents.

Conclusion The effective dose equivalent caused by the Y-90 microsphere administered patient is very low. It is safe in terms of radiation safety to the other individuals when Y-90 microsphere radioembolization therapy is done with dose less than 3 GBq. Because the measured TEDE tends to be higher than the theoretical TEDE, it is recommended to use ‘measured’ TEDE for determining patient release.

Keywords Radiation safety · Y-90 microsphere · Selective hepatic radio-embolization therapy · Liver tumor · Hepatocellular carcinoma

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Introduction

Transarterial chemoembolization (TACE) is the major treatment option for the unresectable primary or secondary liver malignancies. Although the majority of the technique is based on bland embolization and chemoembolization techniques, yttrium-90 (Y-90) microsphere radioembolization therapy (RET) represents an alternate transarterial embolization option. There are ample data that support the use of Y-90 microspheres for primary and metastatic liver tumors [1–4]. Meanwhile, the patient who has been administered radioisotopes acts as a radiation source to others: caring healthcare personnel, family members and also to non-related individuals in streets, commuters and public places. The radiation safety and

protection is one of the major issues in the treatment of disease by administration of radioisotopes such as I-131 or Y-90 [5, 6].

Yttrium-90 is a pure beta-emitter, with a decay energy of 0.94 MeV and the average penetration depth in human tissue is 2.4 mm. In the form of microspheres, it is suitable for selective arterial injection. The physical half-life of Y-90 is 64.2 h. The radiation exposure from a ‘radioactive’ patient who has been implanted with pure beta-emitters is very limited, unless the patient has an open wound that could make a possible leak from the body [7].

The external radiation exposure by a pure beta-emitter such as Y-90 is mainly from bremsstrahlung radiation. The radiation safety issues in using Y-90 radioisotope have already been well evaluated with Y-90-labeled Zevalin (ibritumomab tiuxetan) treatment and it is well recognized that Y-90 Zevalin therapy can be safely done on an outpatient basis using only universal precautions [8]. The typically administered dose of Y-90 Zevalin is 777–1,110 MBq (21–30 mCi), with a maximum of 1,184 MBq [8, 9]. A study showed that the family members who had close contact with patients who had been treated with Y-90 Zevalin had a minimal radiation exposure of 3.5 mrem (0.035 mSv) [10]. On the other hand, the maximum administering dose of Y-90 microspheres is up to 3 GBq, much higher dose than Zevalin. The biodistribution of microspheres after liver RET is mainly localized and confined to embolized liver; somewhat different from Zevalin therapy, in which the administration is via systemic circulation.

Therefore, careful consideration needs to be given in determining when the patient can be released from medical confinement, and patient release must follow the national and regional regulations. The Atomic Energy Act of the Republic of Korea limits the maximum permissible dose to nonoccupational exposure to 5 mSv. The Public Notification (Go-Si) No. 2008-45 of Ministry of Education, Science and Technology stipulated that medical use of radioisotopes must comply with this regulation [11, 12]. According to this regulation, the licensee may release patients if it can be demonstrated that the total effective dose equivalent (TEDE) to another individual from exposure to a released patient is not likely to exceed 5 mSv (500 mrem). In addition, licensees must provide a released patient with written instructions on recommended actions to maintain the dose to other individuals as low as reasonably achievable if the dose to any other individual is likely to exceed 1 mSv (100 mrem).

The purpose of this study was to focus on radiation safety considerations after the treatment of patients with Y-90 microspheres. We serially measured the radiation exposure emitting from the patients after the Y-90 microsphere implantation. We carefully evaluated the possible radiation exposure dose by bremsstrahlung radiation to other individuals on the basis of measured exposure rates and administered activity, respectively. We calculated the total effective dose

equivalent (TEDE) based on the ‘measured’ radiation exposure rate at the time of patient release as well as estimated ‘theoretical’ TEDE according to the administered activity for each consecutive patient. We compared the results by each method to evaluate which method can estimate the real TEDE more reasonably and to determine when we can release patients from confinement at the earliest time complying with the patient release criteria.

Materials and Methods

Study Design

We designed the study to estimate the possible external radiation dose to other individuals from the patient who treated with Y-90 microspheres (SIR-Sphere, SIRTex, Lane Cove, Australia) for unresectable hepatocellular carcinoma. SIR-Spheres are resin-microspheres of approximately 35 μm (microns) in diameter containing Y-90. Yttrium-90 is produced by neutron bombardment of Y-89 in a commercial reactor, yielding a pure beta emitter with an average decay energy of 0.94 MeV. The average penetration depth of Y-90 beta emission in human tissue is 2.4 mm, and a maximum range of 1.1 cm. It is assumed that 1 GBq (27 mCi) of Y-90 delivers a total dose of 50 Gy/kg in tissue. No significant amount of Y-90 leaches from the microspheres, and it decays to stable zirconium-90 with a half-life of 2.67 days (64.2 h). The microspheres are suspended in sterile, pyrogen-free water for injection [7, 13].

The major inclusion criteria of selective injection of Y-90 microsphere are: (1) patients with primary hepatocellular carcinoma which is unresectable, (2) Child-Pugh class A or B with total bilirubin less than 2.0 mg/dl, and (3) ECOG (Eastern Cooperative Oncology Group) performance scale 0–1. From December 2008 to June 2009, a total of 18 patients were enrolled (Table 1). If the liver to lung shunt is more than 20%, the patient is excluded from the study. The liver to lung shunt is measured with Tc-99 m macroaggregated albumin (MAA) hepatic angiography imaging. This study was approved by Internal Review Board of our institution, and all the patients gave informed consent to perform the study.

Calculation of Administering Activity and Administration of Dose

We calculated the administration activity of Y-90 microspheres by the partition model [14]. Tc-99 m MAA intra-arterial angiography is done for evaluation of the distribution of microspheres, measurement of tumor-to-normal-liver ratio and liver-to-lung shunt fraction. We determined the volume of treatment according to the selected position of the microcatheter. Three days to 1 week before Y-90 microsphere injection, all

Table 1 Summary of patient data

Patient no.	Age	Sex	Diagnosis	Child class	Total bilirubin (mg/dl)	Albumin (g/dl)	Tumor volume (ml)	Volume of Treatment (ml)	Liver lung shunt (%)	Injected dose (GBq)
1	77	F	HCC	A	0.54	3.8	310	1,220	4.4	1.84
2	53	M	HCC	B	1.08	3.1	5	520	5.1	0.28
3 ^a	72	M	HCC	A	0.71	4.0	110	960	4.8	0.92
4 ^a	60	M	HCC	A	0.65	3.6	1000	1,550	7.9	2.97
5	42	M	HCC	A	1.06	4.1	674	1,666	9.1	2.86
6	55	M	HCC	A	1.27	3.7	20	460	6.2	0.4
3 ^b	72	M	HCC	A	1.38	3.5	120	1,400	4.8	0.69
7	72	M	HCC	B	1.51	3.3	30	770	4.3	1.08
8	63	M	HCC	A	0.66	4.4	65	1,050	6.5	0.81
9	77	M	HCC	A	0.72	4.0	110	1,450	10.0	0.89
10	64	M	HCC	B	1.00	3.0	163	1,370	8.4	1.7
11	57	M	HCC	A	0.60	4.2	61	510	5.7	0.67
12	70	F	HCC	B	0.84	2.9	15	550	4.7	0.52
13	70	M	HCC	A	0.37	3.9	68	965	3.8	0.98
14	66	M	HCC	A	0.94	4.2	84	885	1.9	1.35
15	79	M	HCC	A	0.84	4.2	110	700	5.7	0.79
16	65	M	HCC	B	0.87	3.6	5	280	6.7	0.23
17	84	M	HCC	A	0.33	4.1	50	615	5.7	0.81
18	73	M	HCC	B	0.58	3.1	103	1,200	8.1	1.47
4 ^b	60	M	HCC	A	0.28	3.6	660	1,220	7.9	2.08
Mean	66.55				0.81	3.72	188.2	967.1	6.09	1.2
SD	10.13				0.34	0.45	270.4	407.4	2.01	0.77

^a First injection^b Second injection

patients had Tc-99m macroaggregated albumin (MAA) hepatic angiography images taken, which were done by injection into the hepatic artery to evaluate perfusion to the liver during the evaluation angiographic study. The measurement of volume of the liver, tumor and lung is done using X-ray computerized tomography (CT). Based on the partition model, the target radiation absorbed dose to the tumor is set to 120 Gy.

The administering dose was prepared in the nuclear medicine department according to the preparation guide manual provided by the manufacturer [15]. Then the injection apparatus was delivered to the angiography-intervention room. The administration of Y-90 microspheres was done by an interventional radiologist. After completion of the injection, the radiation safety personnel checked carefully the room, the personnel involved and the equipment used during the procedure for possible radioactive contamination.

Measurement of Exposure from the Patients and Release Criteria

We measured ambient radiation exposure rate at 1 m from the patient using a survey meter (Victoreen Model 290, USA) during time periods of 0–3 h, 4–12 h, 13–24 h, and 25–72 h,

respectively, after administration. We also measured exposure rate at 10 cm from the upper abdomen and puncture site at the same time periods. The patient was kept in an isolation room until the decision was made whether the patient may be released from confinement.

It has not been fully established what amount of activity of Y-90 microspheres can be administered to release a patient without any confinement or instruction. The technical manual provided by the manufacturer recommended that patients only be released when the ambient dose equivalent rate at 1 m from the patient does not exceed 25 $\mu\text{Sv/h}$ [15]. This effective dose equivalent is equivalent to the ambient exposure rate of 2.5 mR/h. We initially set patient release criteria to the ambient exposure rate of 2.5 mR/h at 1 m from the patient: i.e., the patient can be released without a written document instruction from confinement if the ambient exposure rate at 1 m from the patient is less than 2.5 mR/h.

Estimation of Radiation Exposure

When a patient is administered a radioisotope for a therapeutic purpose, the accumulated external radiation exposure (dose equivalent) from an administered gamma-emitting radioisotope

until certain time can be calculated using specific gamma ray constant ($R \cdot \text{cm}^2/\text{MBq} \cdot \text{h}$) and physical half-life. The method of calculation is discussed in the United States National Council on Radiation Protection and Measurements (USNCRP) Report No. 37 and by other researchers [16–20]. The gamma-ray constants and physical half-lives for radionuclides typically used in nuclear medicine procedures are given in the United States Nuclear Regulatory Commission (USNRC) Regulatory Guide 8.39, Appendix A. However, Y-90 is a pure beta-emitter and the external beta-dose would be negligible. The USNRC Regulatory Guide does not list an exposure rate constant for beta-emissions [17], so it is reasonable to consider the exposure by bremsstrahlung radiation from the patient when one is dealing with Y-90.

After injection into the hepatic artery, microspheres become embolized in the microvasculature where the beta radiation from Y-90 provides a local radiotherapeutic effect. The microspheres are embedded in the tumor vasculature and permanently retained in the tumor tissue [7, 15]. Therefore, it can be assumed that the effective half-life of Y-90 microspheres is equivalent to the physical half life [17, 21, 22].

When an individual is likely to receive the maximum dose from exposure to the radioactive patient until the total decay of radioisotope, i.e. exposed until infinite time, the following equation can be used to estimate the total effective dose equivalent (TEDE) that an individual is likely to receive from exposure by bremsstrahlung radiation to a released patient:

$$D(\infty) = \frac{34.6 \Gamma_{br} Q_0 T_p E}{r^2}. \quad (1)$$

Where $D(\infty)$ is the TEDE from external exposure, attributable to bremsstrahlung radiation, to total decay (i.e., out to infinite time) in mSv; Γ_{br} is the specific bremsstrahlung constant for Y-90 in soft tissue ($1.52 \cdot 10^{-3} \text{ mSv} \cdot \text{cm}^2/\text{MBq} \cdot \text{h}$); Q_0 is the administered activity in MBq; T_p is the physical half-life of radioisotope in days (2.67 days for Y-90); E is the occupancy factor at 1 m (0.25); and r is distance from the patient in centimeters (1 m = 100 cm) [23–25].

When not in the company of the radioactive patient, an individual usually will be at a distance well beyond the index distance of 1 m. Because the exposure rate is rapidly decreasing by distance from the source, the exposure rate may be considered negligibly small for the distance farther than 1 m [18]. That is the reason why we only estimated radiation exposure at 1 m from the patient.

For a radionuclide with a physical half-life greater than 1 day and no consideration of biological elimination, it is assumed that the individual likely to receive the highest dose from exposure to the patient would receive a dose of 25% of the dose to total decay ($E=0.25$) at a distance of 1 m. Selection of 25% as the occupancy factor for

estimating the dose is based on measurements discussed in the supporting regulatory analysis and is conservative in most normal situations [17, 26]. Thus, Eq. 1 will be:

$$D(\infty) = \frac{34.6 \Gamma_{br} Q_0 T_p (0.25)}{(100 \text{ cm})^2} \quad (2)$$

The values of TEDE derived from these equations are based on the administered activity, so they are ‘theoretical’. It is desirable to compare the calculated exposure dose with the actual measured exposure rate. The ‘measured’ TEDE can be calculated using actual measured ambient exposure rate.

An exposure of $2.58 \cdot 10^{-4} \text{ C/kg}$ (1 R) will result in an absorbed dose of 1 cGy (1 rad) and an absorbed dose of 1 cGy (1 rad) will result in an effective dose equivalent of 1 cSv (1 rem). The quantities of exposure, absorbed dose, and effective dose equivalent can be used interchangeably [18–20]. Therefore, if we know the measured initial exposure rate, R_0 (R/h), from the patient at 1 m, then it is possible to estimate the ‘measured’ TEDE using measured initial ambient exposure rate until an individual is exposed to the patient to total decay. Because the exposure dose rate at 1 m is theoretically equal to $\Gamma Q_0/10,000 \text{ cm}^2$ [17, 23], Eq. 2 becomes

$$D(\infty) = 34.6 R_0 T_p (0.25) \quad (3)$$

We compared the ‘theoretical’ TEDE calculated using Eq. 2 with the ‘measured’ TEDE calculated using actual measurement of the ambient exposure rate and Eq. 3.

Results

Total 20 administrations of Y-90 SIR microspheres were done in 18 patients (Table 1). The average administered activity was 1.2 ± 0.77 (0.28–2.97) GBq (Table 2). The measurements of ambient exposure rates during the period of 0–3 h, 4–12 h, 13–24 h, and 25–72 h are listed in the Table 2. The average exposure rates from patients were as follows: measurements at 10 cm from patient’s abdomen during these time periods were 14.1 ± 16.1 , 8.23 ± 8.52 , 4.03 ± 3.67 , and $5.7 \pm 7.2 \text{ mR/h}$, respectively; measurements at 10 cm from the puncture site during these time periods were 3.38 ± 3.32 , 1.71 ± 1.4 , 1.4 ± 1.0 , and $1.42 \pm 1.2 \text{ mR/h}$, respectively; measurements at 1 m from the patient during these time periods were 0.33 ± 0.39 , 0.1 ± 0.07 , 0.12 ± 0.1 , $0.34 \pm 0.4 \text{ mR/h}$, respectively (Table 2 and Fig. 1).

The estimated ‘theoretical’ TEDE according to the administered activity was calculated using Eq. 2 and the values are listed in the Table 3. The values of theoretical TEDE at 1 m from the patient are in the range of 0.8–10 μSv . These values are only 0.08–1% of the maximum

Table 2 Serial post-administration measurement of radiation exposure rate from patient

Patient	0–3h (mR/h)			4–12h (mR/h)			13–24h (mR/h)			25–72h (mR/h)			Exposure rate at release (mR/h at 1m)	Time of patient release (h)
	10cm Abd	10cm Punc	1m	10cm Abd	10cm Punc	1m	10cm Abd	10cm Punc	1m	10cm Abd	10cm Punc	1m		
1							6	1.9	0.04				0.04	49:00
2							0.65	0.32	0.015				0.015	22:00
3 ^a									0.15				0.15	20:00
4 ^a	22	5.2		20	5.1					14	2.8	0.12	0.12	50:00
5	15	3.1		10	3.1		9.5	2.9	0.3				0.3	49:00
6				3.8	0.9					1.9	0.75	0.1	0.1	73:00
3 ^b				5.6	0.9	0.1							0.1	5:55
7							1.5	0.8	0.12				0.12	25:30
8										1.2	0.7	0.8	0.8	48:50
9							2.5	1.1	0.1				0.1	23:40
10				7.3	1.8	0.14							0.14	25:30
11				2.2	0.5	0.03							0.03	24:00
12				0.7	0.3	0.01							0.01	23:00
13				5.4	1.1	0.2							0.2	121:30
14	42	9.2		30	2.9	0.1							0.1	74:00
15	1.6	0.9		1.6	0.5	0.03							0.03	73:00
16	1.8	0.8	0.05										0.05	72:00
17	1.9	1.1	0.6			0.05							0.05	49:00
18				5.4	1.4	0.1							0.1	74:00
4 ^b				6.8	2.0	0.2							0.2	24:30
Mean	14.1	3.38	0.33	8.23	1.71	0.1	4.03	1.4	0.12	5.7	1.42	0.34	0.14	
SD	16.1	3.32	0.39	8.52	1.4	0.07	3.67	1.0	0.1	7.2	1.2	0.4	0.16	

Abd abdomen, Punc puncture site

^a First injection

^b Second injection

permissible effective dose equivalent of 1 mSv, the limit below which the licensee can release a patient without any written documents. This finding suggests that if an individual were continuously in contact with a patient for 25% of the time from administration of the isotope until its total decay, that individual would receive a TEDE far less than 1 mSv.

It is more realistic to calculate TEDE based on the actual measurement of ambient exposure rate than to theoretically estimate TEDE based on administered activity in the daily practical situation. In usual daily medical practice, it is easier to measure exposure rate in certain time intervals. The measured TEDE calculated using Eq. 3 is in the range of 2.31–185 μ Sv (Table 3), which is only 0.23–18.5% of the maximum permissible effective dose equivalent of 1 mSv. The measured TEDEs tend to be higher than the theoretical TEDEs and the ratio of measured to theoretical TEDE is from 1.28 to 65.99 (Table 3). It seems that this wide variety of difference of ratio is partly due to variation of tumor location and measurement geometry. Again the

measured TEDE is also far less than the maximum permissible TEDE of 1 mSv (Fig. 2).

Discussions

Patients who were administered radioisotopes for diagnostic or therapeutic purposes are radioactive for some period of time after administration and may expose other individuals and the environment to radiation. Calculation of radiation of the absorbed effective dose equivalent to other individuals is necessary for radiation safety concerns. Radioprotection precautions must consider the characteristics of administered radioisotopes [16, 27, 28]. Greater concerns should be exercised when dealing with therapeutic procedures.

In 1996, the USNRC issued a new regulation that allowed for the release of patients from medical confinement if the expected TEDE to individuals exposed to the patient is not likely to exceed 5 mSv. The radiation safety licensee should also issue documents to the patients explaining possible

Fig. 1 Exposure rate measurement at different time periods: **a** 10 cm from abdomen; **b** 10 cm from puncture site; **c** 1 m from the patient

restriction of activities to reduce possible radiation exposure to other individuals as low as reasonably achievable if the patient exposure to the other people is likely to exceed 1 mSv [6, 17, 18, 29].

The USNCRP recommended that the maximum permissible effective dose equivalent for the ‘non-pregnant adult family member’ should be limited to 5 mSv and for members of the general public, children and pregnant women to 1 mSv [30]. A ‘family member’ is any person who spends a considerable amount of time with the patient on a regular basis, providing support, comfort and care. A ‘member of the general public’ is any individual who is not a patient undergoing treatment, not a family member of such a patient, and not an occupationally exposed individual participating in the care and management of such a patient [18, 30]. Zanzonico et al. [18] suggested that

such standards for the family members of radionuclide therapy patients should not be as restrictive as those for members of the general public, since family members knowingly and willingly accept their radiation burden and radionuclide therapy is an infrequent event during the patient’s lifetime.

The Atomic Energy Act (Weon Ja Ryeok Beop) of the Republic of Korea also limits the maximum permissible absorbed dose by nonoccupational exposure to 5 mSv. The Public Notification (Gosi) No. 2008-45 promulgated by the Ministry of Education, Science and Technology (MEST) stipulated that medical use of radioisotopes must comply with this regulation [11, 12]. According to the MEST Public Notification No. 2008-45, the licensee may release patients if it can be demonstrated that the TEDE to another individual from exposure to a released patient is not likely to exceed 5 mSv (500 mrem). In addition, the licensee must provide a released patient with written instruction on the recommended modulation of actions to maintain the dose to other individuals as low as reasonably achievable if the dose to any other individual is likely to exceed 1 mSv (100 mrem) [11, 12].

Selective intra-arterial radioembolization therapy (SIRET) involves administration of Y-90 microspheres into the hepatic arterial circulation via the transarterial catheter, following which the radioactive microspheres preferentially target a hypervascular tumor within the liver. This results in the tumor receiving a high dose of radiation [1–4]. Recently, Y-90 resin microspheres have been approved by the United States Food and Drug Administration (USFDA) and also by the Korean Food and Drug Administration (KFDA) as medical devices. Once injected, they are permanently implanted into an hepatic tumor [7, 15]. Y-90 is a pure beta-emitter with average decaying energy of 0.93 MeV and the average penetration depth in human tissue is 2.5 mm. The physical half-life of Y-90 is 64.2 h. Because only beta-rays emit from the embolized Y-90 microsphere within the body, the radiation exposure from the patient is very limited unless the patient has an open wound that can make microspheres leak from the body [7].

Possible radiation exposure to other individuals from internally administered gamma-ray emitting radioisotopes is well recognized and there are ample reports [17, 18, 27, 28]. For the gamma-emitting radioisotopes, the TEDE can be calculated using the specific gamma-ray exposure rate constants and physical half-lives for radionuclides typically used in nuclear medicine are given in the USNRC Regulatory Guide 8.39, Appendix A [17].

Because the external exposure by Y-90 is not by gamma radiation and external beta-dose would be negligible, the specific gamma-ray exposure rate constant is not applicable in this situation. The USNRC Regulatory Guide does not even list a specific gamma-ray (exposure rate) constant for Y-90; as stated, the activity is not from beta-emissions [17]. High energy beta-emitters such as Y-90, however, can

Table 3 Calculation and comparison of TEDE using ‘theoretical’ and ‘measured’ calculation methods

Patient	Theoretical TEDE (μSv) ^a	Release time from administration	Measured exposure rate (mR/h) ^b	Total exposure (mR) ^c	Measured TEDE (μSv) ^d	Dm/Dt ratio ^e
1	6.3	49:00	0.04	0.924	9.24	1.47
2	0.9	22:00	0.02	0.346	3.46	3.85
3-1 ^f	3.2	20:00	0.15	3.464	34.64	10.83
4-1 ^f	10	50:00	0.12	2.771	27.71	2.77
5	10	49:00	0.3	6.929	69.29	6.93
6	1.4	73:00	0.1	2.310	23.10	16.50
3-2 ^g	2.4	5:55	0.1	2.310	23.10	9.62
7	3.8	25:30	0.12	2.771	27.71	7.29
8	2.8	48:50	0.8	18.476	184.76	65.99
9	3.1	23:40	0.1	2.310	23.10	7.45
10	5.9	25:30	0.14	3.233	32.33	5.48
11	2.4	24:00	0.03	0.693	6.93	2.89
12	1.8	23:00	0.01	0.231	2.31	1.28
13	3.4	121:30	0.2	4.619	46.19	13.59
14	4.7	74:00	0.1	2.310	23.10	4.91
15	2.8	73:00	0.03	0.693	6.93	2.47
16	0.8	72:00	0.05	1.155	11.55	14.43
17	2.8	49:00	0.05	1.155	11.55	4.12
18	5.2	74:00	0.1	2.310	23.10	4.44
4-2 ^g	7.3	24:30	0.2	4.619	46.19	6.33

^a Theoretical estimation of TEDE at 1 m by Eq. 2^b Actual measurement of ambient exposure rate at 1 m of patient at the time of release^c Calculation of total cumulative exposure to infinite time^d Estimation of measured TEDE at 1 m by Eq. 3^e Ratio of measured TEDE to theoretical TEDE^f First injection^g Second injection

produce sufficient in vivo bremsstrahlung. Several researchers postulated that external radiation exposure by Y-90 is generally ignored and patient restrictions are not required for radiation safety purpose. The USNRC regulatory guide did not apply the activity limits and dose-rate limits of patient release for pure beta-emitters such as Y-90 because, as it stated, of the minimal exposures to members of the public resulting from activities normally administered for diagnostic or therapeutic purposes [23].

However, these reports only considered the exposure in theoretical estimation [24, 25]. Yet the radiation dose from the bremsstrahlung radiation is not well recognized, the resulting radiation hazard may therefore be of some concern, at least theoretically, and should be systematically evaluated [25]. We believe that the contribution of such radiation should be carefully considered and clarified in regard to determining when the patient can be released from medical confinement, to meet the regulatory requirements.

We estimated theoretically the exposure dose rate by bremsstrahlung radiation using Eq. 2. For the calculation of

‘theoretical’ TEDE, it is necessary to know the ‘specific bremsstrahlung constant.’ The term ‘specific bremsstrahlung constant’ is a conceptual and thus artificial quantity analogous to the specific gamma-ray constant for photons and the bremsstrahlung constant is several orders of magnitude less than the specific gamma-ray constant [24, 25]. The theoretical values of TEDE based on administered activity are listed in Table 3. Using Eq. 3, we could estimate the TEDE that an individual is likely to receive from exposure to the radioactive patient at a distance of 1 m. The assumption of TEDE by using an occupancy factor, E , of 25% at 1 m is conservative in most normal situations because, when bremsstrahlung radiation emits from the body, it is largely attenuated by body tissue, so that the real measurement of exposure rate is quite low [17, 24, 26].

We observed in this study that the values of estimated theoretical TEDE at 1 m from the patient are in the range of 0.9–10 μSv (Table 3). These values are only 0.09–1.0% of the maximum permissible effective dose equivalent of 1 mSv. This finding suggests that if an individual were continuously

Fig. 2 Plot of measured TEDE according to the measurement of ambient exposure rate at the time of release

in contact with the patient for 25% of time from the day of isotope administration until total decay of the isotope, the individual would receive a TEDE far less than 1 mSv.

Because the radioisotope is confined in the patient's abdomen, there could be a significant attenuation of low energy bremsstrahlung radiation while traveling within the body. So, the actual radiation dose may be different from the theoretically calculated TEDE based on administered activity. The 'measured' exposure dose equivalent calculated by actual measurement of ambient exposure rate can be different from estimated 'theoretical' exposure dose [28]. According to our observation, the 'measured' TEDEs are generally higher than those of 'theoretical' TEDEs as the ratio of 'measured' TEDE to 'theoretical' TEDE (D_m/D_t ratio) is from 1.28 to 65.99 (Table 3). This wide variety of ratio seems to be partly due to variability of tumor location and measurement geometry. These results are contrary to the observation by Siegel et al. [27] and Willegagnon et al. [28], who dealt with gamma radiation and observed that measured TEDE is lower than theoretical TEDE. To our knowledge, this is the first report that compares the theoretical TEDE with measured TEDE in Y-90 microsphere RET. The reason

for the higher values for measured TEDE and wide variation of measurement is not clearly elucidated. We think that the reason for this contradiction and variation is partly because of the type of radiation, i.e., gamma-ray versus bremsstrahlung, and partly because of difference in the biodistribution. For the calculation of theoretical TEDE, it is assumed that biodistribution is even within the body, but for the measured TEDE, it directly represents the measurement of the ambient radiation exposure. Although the measured TEDE is higher than the theoretical TEDE, the measured TEDE is far less than the maximum permissible TEDE of 1 mSv.

Gulec and Siegel [24] reported that in all proposed situations of exposure to patients administered 3 GBq of Y-90 microspheres, the estimated bremsstrahlung doses were very small, in the range of 0.05–0.21 mSv to the total decay. It has been reported that at approximately 6 h after the administration of 2.1 GBq, the average activity of Y-90 microspheres, doses at 0.25, 0.5, and 1 m from patient's abdomen measured 18.8, 9.2, and 1.5 mSv/h, respectively [15]. This indicated that no patient restrictions are required for radiation safety purpose. Zanzonico et al. [25], postulated that the maximum allowable administered activity of Y-90, in terms of release criteria, is 1,420 GBq based on the assumption using Eq. 2.

In the present study, all the individuals were administered a dose of less than 3 GBq. The measured TEDE calculated using Eq. 3 is in the range of 0.002–0.18 mSv, i.e., 0.2–18% of the maximum permissible effective dose equivalent of 1 mSv (Table 3). Again, the measured TEDE is far less than the maximum permissible TEDE of 1 mSv in present study population of Y-90 microsphere therapy of less than 3 GBq. However, because the actual measured TEDE tends to be higher than the theoretical TEDE, as in this observation, it is a more conservative way to use values of measured TEDE in determining patient release.

In general, for patients treated with Y-90 microspheres of less than 3 GBq of activity, record keeping or issuing of an instruction document is not needed according to the NRC and Korean national regulation.

Conclusions

We measured the ambient radiation exposure rate from the patient after administration of Y-90 microspheres and estimated the total effective dose equivalent by exposure to the patients. The total effective dose equivalent caused by the Y-90 microsphere administered patient is very low, even from the time of administration. It is very safe in terms of radiation safety to other individuals when Y-90 microsphere administration therapy is done with doses of less than 3 GBq. Because the 'measured' TEDE tends to be higher than the 'theoretical' TEDE, it is recommended to use measured TEDE in determining patient release after Y-90 microsphere administration.

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