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A Clinical Trial Of The Evaluation Of Environmental Exposure In Yttrium 90 Radioembolization

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Abstract

The aim of this study is to measure the dose rate of two different forms of Y-90 microsphere used for radioembolization and to evaluate the results according to radiation safety regularities. 19 patients were enrolled in study (Age:61±1.5, F/M:12/7). As a result of the evaluation of the physicians, 7 patients were treated with TheraSphere and 12 patients were treated with SIR-Sphere. Dose rate measurements were taken at the stage of activity preparation, injection, radioactive wastes and discharge of patients using an electronic dosimeter (ED). The staff was exposed to dose rate of 1.3×10^{-4} µSv/MBq.h during activity preparation stage, 2.4×10^{-4} µSv/MBq.h in injection stage for Therapshere application. For SIR-spheres application, the staff was exposed to dose rate of 24.5×10^{-4} µSv/MBq.h during activity preparation stage, 10.1×10^{-4} µSv/MBq.h in injection stage. The average amount of dose received per operation was calculated 0.92±0.48 µSv in TheraSphere and 3.22±0.89 µSv in SIR-Spheres. For discharge of the patients, the average dose rate recorded from 1 m was found 4.0±0.28 µGy/h for TheraSphere and 3.2±0.15 µGy/h for SIR-Spheres. The dose rate of radioactive wastes measured from the surface of the container which contained the radioactive wastes generated after the application was 0.5±0.1 µSv/h for TheraSphere and 1.1±0.08 µSv/h for SIR-Spheres. It is emphasized that Y-90 Therasphere application provides radiation safety more than SIR-Spheres because of its closed system, even so both applications shows low dose rate around the patient and short-term storage of radioactive wastes after application would be sufficient.

Keywords: Exposure, radioembolization, yttrium 90, radiation protection.

1. INTRODUCTION

The use of microspheres filled with a beta-emitting radionuclide, typically Y-90, has only become clinically relevant since the middle-1980s [1]. The application of microspheres to the liver requires an interventional-technical procedure in the field of multidisciplinary as radiology and nuclear medicine departments and it is described in literature [2,3]. In a typical Y-90 microsphere treatment, the aim is to deliver the maximum dose to tumor without causing toxical damage to the liver parenchyma [4]. In addition, the amount of Y-90 activity administered to the patient can be calculated with a patient spesific dosimetry including several parameters such as volume of tumor and normal liver tissue, lung shunt fraction, tumor to liver count ratio, etc.

Y-90 filled microspheres are used in two different forms as glass in Therasphere and resin in SIR-Sphere. Although some production features

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are different, their basic physical properties are similar and they do the same physical interactions in the tissue. Y-90 has a physical half-life of 64.2 hours, and it decays to stable Zirconium 90. Y-90 emits pure high-energy beta rays (energy maximum, 2.27 MeV; mean, 0.9367 MeV) [5]. Irradiation from Y-90 microspheres is essentially confined to the liver because of 3.8 mm mean range and approximately 10-mm maximum range of β-particles in soft tissue [6]. However, the physical interactions that take place in the path length of the electrons within the tissue, leads to emit Bremsstrahlung radiation whose energy range from 20 to 500 keV [7].

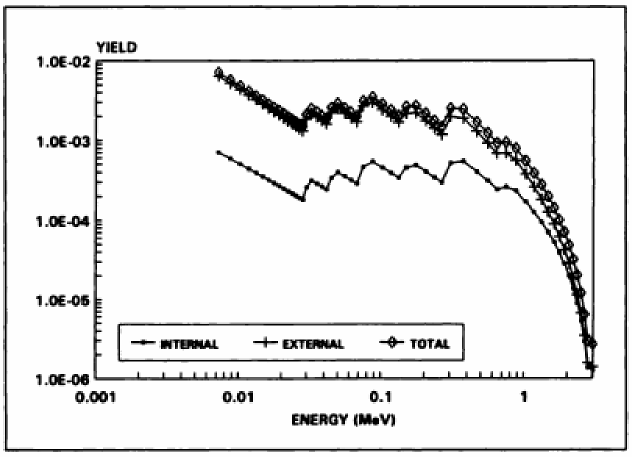

Figure 1. Bremmstrahlung spectrum of Y-90 microspheres formed along their range in the tissue [8].

Bremsstrahlung radiation is scattered at four different stages as Y-90 microsphere activity preparation, injection, patient and radioactive wastes. In all stages, medical staff who provide the care to the patient are exposed to the risk of Bremsstrahlung radiation. Therefore it is important to monitor dose rate measurements.

According to the recommendations based on Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) and adopted by the Turkish Atomic Energy Authority (TAEK), the patients undergone radionuclide therapy discharged when the dose rate taken from 1 m far from patient between 25-40 μSv/h [9]. This condition was determined by the European Atomic Energy Community (EURATOM) as 20-40 μSv/h [10]. Radioactive wastes generated after injection should be placed in a plastic container labeled with a warning sign containing information about the type of radionuclide and the amount of activity. The plastic container's storage was carried out according to the recommendations published by International Atomic Energy Agency (IAEA) [11].

In this study, we aimed to measure the dose rate of Bremmstrahlung radiation released into the environment in two different forms of Y-90 microsphere therapy, to assess the results in terms of national and international radiation safety regularities and to evaluate the radiation protection conditions.

According to the measurement results, the radiation doses that health workers will be exposed per process will be calculated. It will also be tested whether the radiation protection rules applied during the process are sufficient.

2. MATERIAL AND METHODS

This study included 19 patients who applied to Cerrahpasa Medical Faculty/ Nuclear Medicine Department/ Radionuclide Therapy Service for Y-90 radioembolization and all radiation measurements that occur throughout the operation. All dose rate measurement was done in four different stages with using an electronic dosimeter (Polimaster PM1621 model, energy range 10keV-20MeV). ED is a suitable for detecting and monitoring radiation in the areas of nuclear facility. It gives instantaneous radiation exposure and very useful in non routine work in which radiation level vary considerably and may be quite hazardous e.g. Y-90 radioembolization. This detector is filled with gas. Radiation produced ionization in gas resulting positive and negative ions are produced inside the detector volume. Ions drift to the electrodes due to the applied voltage between electrodes. In an outer circuit the current is measured which is proportional to the number of ion pair produced per second.

2.1. Activity Preparation

The first measurement was taken from 0, 0.5 and 1 m from the activity vial isolated by lead shielding considered as a reference for the stage of Y-90 Theraspheres and SIR-Spheres activity preparation in hot lab. Total operation time was recorded for activity preparation.

2.2. Injection

The second measurement was taken over the liver after the injection in the interventional radiology department. Total operation time was recorded for injection.

2.3. Radioactive Wastes

The third measurement was taken from the plastic container surface (0 cm) containing radioactive waste generated after Y-90 application. The measurements were used to determine transport and storage conditions.

2.4. Discharge

Discharge of the patient means the return of the patient into the community and so the radiation dose level must be taken under control. According to the national and international regulations, the measurement was taken at a distance of 1 m from the patients to be discharging dose rate.

2.5. Annual Dose Calculation and Radiation Protection Instrumentation

The total body dose absorbed per application was calculated by multiplying the staff dose rate (μSv/h) at the working distance with recorded and application time (h). The contribution rate of the dose absorbed per application to annual dose was determined.

The precautions taken during the application for radiation protection are detailed in Table 1.

3. RESULTS

The change in the dose rate of Y-90 activity during stage of preparation and injection across variable distances (cm) was shown in Tables 2 and 3 for Theraspheres and SIR-Spheres therapy.

In Therasphere, the dose rates irradiated from Bremsstrahlung radiation were quite low in the stage of preparation and injection. While the average amount of activity injected into the patient was 3596.4±8.56 MBq. In this context, staff was exposed to 1.3×10^{-4} μSv/MBq.h in the stage of preparation and 2.4×10^{-4} μSv/MBq.h in the stage of injection.

In SIR-Spheres application, staff was exposed to 24.5×10^{-4} μSv/MBq.h in the stage of preparation and 10.1×10^{-4} μSv/MBq.h in the phase of injection. According to these results, the dose rates due to Bremsstrahlung radiation were found low in the phase of preparation and injection. Unlike the other measurements, it was seen that the measurement taken from 0 m was 24 μSv/h in the stage of preparation and 162 μSv/h in the stage of injection in the application indicated by the number 9.

By considering the staff has worked during Y-90 avtivity loading from an average distance of 50 cm and with a total time of 0.5 h in the stage of preparation and injection, the average effective dose taken by staff per an application was calculated 0.92±0.48 μSv for TheraSphere and 3.22±0.89 μSv for SIR-Spheres.

The dose rate measurements recorded from radioactive wastes generated after application with TheraSpheres and SIR-Spheres application were given in Tables 4 and 5.

The mean dose rate measurement taken from the liver after Therasphere injection was found 19.75±0.63 μSv/h and the mean dose rate 1 m from patients after 24 h at discharging time was 4±0.28 μSv/h. These dose rate measurements found to be lower than previously reported values [12]. The dose rate measured from the surface of the plastic container including collected radioactive waste in Therasphere therapy was found 0.5±0.1 μSv/h. In light of these results, it was observed that the dose rate measurements of radioactive waste were obtained below 1 μSv/h.

The mean dose rate measurement taken from the liver after SIR-Spheres injection was 44.85±0.95 μSv/h and the mean dose rate from 1 m to patients after 24 h at discharging was found 3.2±0.15 μSv/h. These dose rate measurements were found to be lower than previously reported values [12]. The dose rate measured from the surface of the plastic container including radioactive waste generated SIR-Spheres application was found 1.1±0.08 μSv/h.

Statistical analysis was performed with t-test (Student's t-test) to determine whether there was a difference in dose rate measurements recorded from the surface of the plastic container for Theraspheres and SIR-Spheres application. There was a significant difference between the measurements of radioactive wastes for Therasphere and SIR-Spheres (P: 0.001287).

4. DISCUSSION

Y-90 radioisotope in the treatment of primary and metastatic liver tumor is increasingly used due to its clinical suitability and encouraging results after treatment. It is also advantageous to be safer in sense of radiation protection, unlike in other Peptide Receptor Radionuclide Therapy (PRRT) which has beta and high energy gamma rays such as Lu-177, I-131. In the field of radiation protection related to Y-90 are emphasized mainly the calibration procedures and the treatment method in the literature, on the other hand, the exposed doses to staff have been reported rarely [12-14]. Our results were found to be consistent with the work of Aubert et al. [13] which is about absorbed radiation dose of exposed to staff per application.

Y-90 microsphere treatment is performed approximately twice a week in our clinic, an average of 96 patients are treated per year. Considering the annual patient population, the dose contribution of Y-90 applications showed very low percentage to the annual permissible dose (0.44% for Therasphere and 1.5% for SIR-Spheres) for staff.

A comparative study was carried out by evaluating the environmental dose rate measurements between the Theraspheres and the SIR-Spheres. The environmental exposure level varied in both Y-90 applications in terms of our results, in the phase of preparation and injection, the environmental exposure resulting from SIR-Spheres application are higher than TheraSphere application. The reason for this difference is probably attributed to the open system of SIR-Spheres, therefore contamination probability had increased when the activity fraction was done in the laboratory.

External dose rate limits have not been yet established due to biodistribution of Y-90 and its pure beta emitting inside the body. According to the ICRP 2009 report, a limit was not shown because the Y-90 dose rate was too low [15]. On the other hand, in the study reported by R. Smart et al., the dose rate at 1 m distance from a patient given 4400 MBq Y-90 microsphere activity was found to be approximately 5 μSv/h [16].

It was observed that the average dose rates measured at 1 m distance from patients at discharging were below 4 μSv/h and the dose rates measured from radioactive wastes generated after the applications both Therasphere and SIR-Spheres were below 1 μSv/h as our results are compatible with the study reported by Cremonesi M. et al [17] and literature listed. Eventually, the environmental exposure doses originated from both SIR-Sphere and TheraSphere application are in compliance with the legislation.

In our study, it was enlighted that the staff was generally exposed to low doses, but when they performed an applicationt with SIR-Spheres, they received about 3.5 times more dose than TheraSphere.

5. CONCLUSION

In SIR-Spheres applications, slightly higher levels of environmental exposure were observed due to contamination. Contamination can be summarized as misinterpreting the activity, spreading the activity while dividing the activity, and not releasing the wastes generated during the division process. Nonetheless, the staff of interventional radiology and nuclear medicine were exposed to low doses in both SIR-Spheres and Theraspheres applications. Further, radioactive wastes collected after SIR-Spheres application should be stored for 3 days -during this time the dose will be further reduced by half-time-, while that of Therasphere was not necessary to store before disposing.

Considering the instrumentation used in applications, it was found that using plexy material shielding to protect the environmental exposure providing more radiation protection against large-scaled beta paricles as Y-90. It was also observed that the use of hot cell and lead aprons greatly reduce the absorbed dose from Bremmstrahlung.

REFERENCES

[1]. Dezarn Wa, Cessna Jt, Dewerd La, Feng W, Gates Vl, Halama J, Et Al. “Recommendations Of The American Association Of Physicists In Medicine On Dosimetry, Imaging, And Quality Assurance Procedures For 90y Microshere Brachytherapy In The Treatment Of Hepatic Malignancies”, *Med Phys* 2011; 38(8):4824-45.

[2]. Ariel Im, Padula G, “Treatment Of Symptomatic Metastatic Cancer To The Liver From Primary Colon And Rectal Cancer By The Intra-Arterial Administration Of Chemotherapy And Radioactive Isotopes”, *J Surg Oncol* 1978;10:327–336.

[3]. Ariel Im, Padula G, “Treatment Of Asymptomatic Metastatic Cancer To The Liver From Primary Colon And Rectal Cancer By The Intra-Arterial Administration Of Chemotherapy And

Radioactive Isotopes", *J Surg Oncol* 1982;20:151–156.

[4]. Howells Cc, Stinauer Ma, Diot Q, Westerly Dc, Schefter Te, Kavanagh Bd, Et Al. "Normal Liver Tissue Density Dose Response In Patients Treated With Stereotactic Body Radiation Therapy For Liver Metastases". *Int J Radiat Oncol Biol Phys* 2012;84(3):E441-6.

[5]. Murthy R, Nunez R, Szklaruk J, Erwin W, Madoff Dc, Gupta S, Et Al. "Yttrium-90 Microsphere Therapy For Hepatic Malignancy: Devices, Indications, Technical Considerations And Potential Complications", *Radiographics* 2005;25(1):S41-55.

[6]. Gulec Sa, Mesoloras G, Stabin M. "Dosimetric Techniques In 90y-Microsphere Therapy Of Liver Cancer: The Mird Equations For Dose Calculations", *J Nucl Med* 2006;47(7):1209-11.

[7]. Shen S, Denardo Gl, Yuan A, Denardo Da, Denardo Sj. "Planar Gamma Camera Imaging And Quantitation Of Yttrium-90 Bremsstrahlung". *J Nucl Med* 1994;35(8):1381-9.

[8]. Stabin Mg, Eckerman Kf, Ryman Jc, Williams Le. "Bremsstrahlung Radiation Dose In Yttrium-90 Therapy Applications". *J Nuci Med* 1994;35:1377-1380.

[9]. "Discharge Of Patients Undergoing Treatment With Radioactive Substances Radiation Protection Series Publication No. 4", *Australian Radiation Protection And Nuclear Safety Agency* (Arpansa), 2002

[10]. https://Ec.Europa.Eu/Energy/Sites/Ener/Files/Documents/097_En.Pdf

[11]. http://Www-Pub.Iaea.Org/Mtcd/Publications/Pdf/Pub1254_Web.Pdf

[12]. Sarfaraz M, Kennedy As, Cao Zj, Sackett Gd, Yu Cx, Lodge Ma, Et Al. "Physical Aspects Of Yttrium-90 Microsphere Therapy For Nonresectable Hepatic Tumors". *Med Phys* 2003;30:199–203.

[13]. Aubert B, Guilabert N, Lamon A, Richard M. "Which Protection Against Radiation For New Protocols Of Internal Radiotherapy By Yttrium 90?" *Proceedings Of The 6th European Alara Network Workshop*. 2002; 34(7): 47–9.

[14]. Tosi G. "Report On One Accident Occurred In A Nuclear Medicine Department In Italy". *Proceedings Of The 6th European Alara Network Workshop*. 2002; 34(7): 225-244.

[15]. ICRP Safety Reports Series No:63, Release Of Patients After Radionuclide Therapy. 2009; ISBN:978–92–0–108909–0, Issn 1020–6450.

[16]. Edmonds J, Smart R, Laurent R, Butler P, Brooks P, Hoschir R, Et Al. "A Comparative Study Of The Safety And Efficacy Of Dysprosium-165 Hydroxide Macro-Aggregate And Yttrium-90 Silicate Colloid In Radiation Synovectomy —A Multicentre Double Blind Clinical Trial", *Rheumatology* 1994; 33(10): 947-953.

[17]. Cremonesi M, Ferrari M, Paganelli G, Rossi A, Chinol M, Bartolomei M, Et Al. "Radiation Protection In Radionuclide Therapies With (90) Y-Conjugates: Risks And Safety". *Eur J Nucl Med Mol Imaging* 2006;33(11):1321-7.

APPENDICES

Table 1. Devices and instruments used for radiation protection in the different phases of therapy

Phases of therapy	Devices/instruments	Purpose
Hot Lab.	Hot cell	To shield Y-90 β- rays and bremsstrahlung
	Latex gloves	To avoid contamination
	Long tongs	To handle the Y-90 vial and reduce dose rate
	Polymethylmethacrylate cylindrical case	To shield Y-90 vials and syringes
	Lead aprons	To reduce the exposure to bremsstrahlung
	Electronic dosimeter	To monitor the dose rate outside the vial
Activity Administration	Infusion system	-
	Latex gloves	To avoid contamination
	Lead aprons	To reduce the exposure to bremsstrahlung
	Electronic dosimeter	To monitor the dose rate outside the vial and the radioactive waste
Patient hospitalisation	Lead aprons	To reduce the exposure to bremsstrahlung
	Electronic dosimeter	To monitor the spreading dose rate from patient at 1 meter

Table 2. Dose rate measurement in Y-90 Theraspheres therapy

Patient No	Activity (MBq)	Time (h)	Distance (cm)	Stage of Preparation (µSv/h)	Stage of Injection (µSv/h)
1	2397.6	0.5	0	11.7	4.2
			50	1.2	1.8
			100	0.7	0.9
2	4695.3	0.5	0	28.7	2.8
			50	1.5	2.5
			100	0.9	0.9
3	2997.0	0.5	0	1.8	3.8
			50	0.4	1.2
			100	0.2	0.4
4	3496.5	0.5	0	22	2
			50	1.5	1.3
			100	0.7	1
5	4095.9	0.5	0	24.4	3.8
			50	1.4	2.5
			100	0.3	0.7
6	2497.5	0.5	0	10	10
			50	1.5	4
			100	0.1	1.6
7	4995.0	0.5	0	6.7	4.1
			50	2.1	2.9
			100	0.4	0.6
Mean±SD.:	**3596.4±8.56**	**0.5**	**0**	**15**	**4.4**
			50	**1.4**	**2.3**
			100	**0.47±0.10**	**0.87±0.13**

Table 3. Dose rate measurement in Y-90 SIR-Spheres therapy

Patient No	Activity (MBq)	Time (h)	Distance (cm)	Phase of Preparation (μSv/h)	Phase of Injection (μSv/h)
1	1295	0.5	0	23	80
			50	7.8	4
			100	2.3	1.5
Continues...					
2	1554	0.5	0	45	27
			50	7.1	1
			100	2	0.6
3	1480	0.5	0	41	60
			50	5.6	4
			100	0.8	0.13
4	1295	0.5	0	21	16
			50	6.2	1
			100	1.7	0.8
5	1295	0.5	0	27	17
			50	8.2	1.4
			100	1.3	0.7
6	1665	0.5	0	31	72
			50	6.3	9
			100	2.4	2.1
7	1554	0.5	0	49	56
			50	6	7
			100	1.8	1.1
8	1665	0.5	0	35	31
			50	4.3	3.5
			100	1.4	0.9
9*	**1480**	**0.5**	**0**	**24**	**162**
			50	7.6	1.9
			100	2.6	0.6
10	1295	0.5	0	38	21.3
			50	18	5.6
			100	8	2.2
11	1480	0.5	0	28	34
			50	18	8.8
			100	6	2.7
12	1110	0.5	0	25	18.5
			50	9	3
			100	3	0.8
Mean±SD.:	**1464.14±5.46**	**0.5**	**0**	**32.2**	**49.6**
			50	**8.7**	**4.2**
			100	**3.6±0.27**	**1.48±0.17**

* Application that is thought to be contamination.

Table 4. Dose rate measurements which are taken from patients and their radioactive wastes in Y-90 Therasphere therapy

Patient No	Activity (MBq)	Discharge Measurement (μSv/h)	Dose rates taken from liver after injection (μSv/h)	Dose rate of radiactive wastes (μSv/h)
1	2397.6	3.8	28	0.4
2	4695.3	2.7	14.4	0.28
3	2997.0	6.4	17	0.39
4	3496.5	5.2	18	0.28
5	4095.9	3.8	24	1.7
6	2497.5	3.9	20.1	0.23
7	4995.0	2.4	16.8	0.29
Mean±SD.	**3596.4±8.56**	**4±0.28**	**19.75±0.63**	**0.5±0.1**

Table 5. Dose rate measurements which are taken from patients and their radioactive wastes in Y-90 SIR-sphere therapy

Patient No	Activity (MBq)	Discharge Measurement (μSv/h)	Dose rates taken from liver after injection (μSv/h)	Dose rate of radiactive wastes (μSv/h)
1	1295	4.6	58	1.1
2	1554	3.1	22.3	1.3
3	1480	2.6	20	1.5
4	1295	2.2	19	1.2
5	1295	3.7	32	1
6	1665	4.5	60	1.3
7	1554	3.7	55	1.1
8	1665	3.2	52	1.2
9	1480	2.8	37	0.9
10	1295	2.6	35	0.9
11	1480	2.9	42	1.2
12	1110	2.5	33	1
Mean:	**1464.14±5.46**	**3.2±0.15**	**44.85±0.95**	**1.1±0.08**