FNG & Bilim Tıp Dergisi 2018;4(3):115-122
doi: 10.5606/fng.btd.2018.019

Original Article / *Özgün Makale*

Detecting the optimal patient-specific radiation dosimetry in Yttrium-90 microsphere therapy

Yitriyum-90 mikroküre tedavisinde hastaya spesifik optimal radyasyon dozimetrisinin belirlenmesi

Handan Tanyıldızı[1,3], Mustafa Demir[2], Baki Akkuş[3]

[1]*Altınbaş Universitesi, Vocational School of Health Services, Medical Imaging Techniques Program, İstanbul, Turkey*
[2]*Department of Nuclear Medicine, Istanbul Universitesi Cerrahpaşa Medical Faculty, İstanbul, Turkey*
[3]*Department of Physics, Istanbul University, Science Faculty, İstanbul, Turkey*

ABSTRACT

Objectives: This study aims to detect the maximum permissible activity (MPA) in patients with unresectable liver metastasis and hepatocellular carcinoma treated with Yttrium-90 (Y-90) microspheres and to evaluate the absorbed radiation doses with patient-specific dosimetry methods.

Materials and methods: A total of 31 patients (20 males, 11 females; mean age 47±0.2 years; range, 32 to 62 years) were applied dosimetry. Empiric, body surface area (BSA), Medical Internal Radiation Dose (MIRD) and partition internal dosimetry models were used to calculate the MPA to deliver the maximum absorbable dose to the tumor while reducing the absorbed dose by the critical organs.

Results: Mean Y-90 activity was 57483±7.7 megabecquerel (MBq) for empiric model, 1806.04±1.37 MBq for BSA, 1649.60±1.3 MBq for MIRD, and 1658.71 MBq for partition. Mean absorbed dose calculated according to empiric model was 40.14±0.20, 197.62±0.45 and 7.39±0.08 gray (Gy) for normal liver, tumor and lung, respectively. Mean absorbed dose calculated according to BSA was 33.61±0.18, 167.83±0.41, 6.39±0.08 Gy for normal liver, tumor and lung, respectively. Mean absorbed dose calculated according to MIRD was 29.63±0.17, 125.62±0.36 and 5.67±0.07 Gy for normal liver, tumor and lung, respectively. Mean absorbed dose calculated according to partition model was 29.82±0.17, 126.72±0.36 and 5.72±0.07 Gy for normal liver, tumor and lung, respectively.

Conclusion: Since the MPAs calculated according to empiric and BSA models will lead to organ toxicity by forming high amounts of absorbed doses at critical organs, these models are not appropriate approaches for dosimetry. On the other hand, MIRD and partition models are the most successful methods for internal dosimetry applications.

Keywords: Internal dosimetry; radionuclide therapy; Yttrium-90.

ÖZ

Amaç: Bu çalışmada, Yitriyum-90 (Y-90) mikroküreler ile tedavi edilen rezeke edilemeyen karaciğer metastazlı ve hepatosellüler karsinomlu hastalarda maksimum izin verilebilir aktivite (MPA) belirlendi ve absorbe edilen radyasyon dozları hastaya spesifik dozimetri yöntemleriyle değerlendirildi.

Gereç ve yöntemler: Toplam 31 hastaya (20 erkek, 11 kadın; ort. yaş 47±0.2 yıl; dağılım, 32-62 yıl) dozimetri uygulandı. Tümöre maksimum absorbe edilebilir dozu vermek amacıyla MPA'yı hesaplarken kritik organlar tarafından absorbe edilen dozu azaltmak için empirik, vücut yüzey alanı (BSA), Medikal İnternal Radyasyon Dozu (MIRD) ve partitisyon internal dozimetri modelleri kullanıldı.

Bulgular: Ortalama Y-90 aktivitesi empirik model için 57483±7.7 megabekerel (MBq), BSA için 1806.04±1.37 MBq, MIRD için 1649.60±1.3 MBq ve partitisyon için 1658.71±1.31 MBq idi. Empirik modele göre hesaplanan ortalama absorbe edilen doz normal karaciğer, tümör ve akciğer için sırasıyla 40.14±0.20, 197.62±0.45 ve 7.39±0.08 gray (Gy) idi. BSA'ya göre hesaplanan ortalama absorbe edilen doz normal karaciğer, tümör ve akciğer için sırasıyla 33.61±0.18, 167.83±0.41 ve 6.39±0.08 Gy idi. MIRD'ye göre hesaplanan ortalama absorbe edilen doz normal karaciğer, tümör ve akciğer için sırasıyla 29.63±0.17, 125.62±0.36 ve 5.67±0.07 Gy idi. Partitisyon modeline göre hesaplanan ortalama absorbe edilen doz normal karaciğer, tümör ve akciğer için sırasıyla 29.82±0.17, 126.72±0.36 ve 5.72±0.07 Gy idi.

Sonuç: Empirik model ve BSA modeline göre hesaplanan MPA'lar kritik organlarda yüksek miktarlarda absorbe edilen dozlar oluşturarak organ toksisitesine yol açacağından, bu modeller dozimetri için uygun yaklaşımlar değildir. MIRD ve partitisyon modelleri ise internal dozimetri uygulamaları için en başarılı yöntemlerdir.

Anahtar sözcükler: İnternal dozimetri; radyonüklid tedavi; Yitriyum-90.

Received: May 05, 2018 ***Accepted:*** June 27, 2018

Correspondence: Handan Tanyıldızı, PhD. Altınbaş Üniversitesi Sağlık Hizmetleri Meslek Yüksekokulu, Tıbbi Görüntüleme Teknikleri Programı, 34217 Bağcılar, İstanbul, Turkey. Tel: +90 212 - 604 01 00 e-mail: handan.tanyildizi@altinbas.edu.tr

Atıf:
Tanyıldızı H, Demir M, Akkuş B. Detecting the optimal patient-specific radiation dosimetry in Yttrium-90 microsphere therapy. FNG & Bilim Tıp Dergisi 2018;4(3):115-122.

Since there are two different arteries supplying blood to the liver and 80-100% of tumor cell's blood nourishment flow from the right hepatic artery,[1] the directed transarterial perfusion of radioactive microspheres leads to serious damage in unresectable tumors, which consequently increase morbidity and mortality.[2-7]

The widespread use of radioembolization requires debates on the amount of the optimal dose to be delivered to the patient similar to radiotherapy where the main purpose is to maximize the dose absorbed by tumor tissues and to reduce the dose absorbed by normal tissues. Possible vascular shunting from the hepatic artery to the lung will increase risks for lung irradiation and occurrence of lung tissue damage. Pre-dosimetry is highly recommended to calculate the maximum permissible activity (MPA) of Yttrium-90 (Y-90) taking into account the optimum effective dose for the tumor tissue and safe low doses for critical organs such as lungs and normal liver tissue to protect them from exposure to radiation and cellular toxicity.

According to previous publications on radiotherapy, the maximum tolerable dose has been limited to 35 gray (Gy) on the condition that the liver/tumor uptake ratio does not exceed 30%,[8] and lung absorbed dose is up to 12 Gy.[9]

It is well-known that Y-90 is a high-energy beta-emitter that may damage normal tissues of the liver and lungs. Shunting among lungs and liver, which opens a passage for microspheres to leak inside the lungs, may cause significant impairment in the lung tissue. Therefore, prior to Y-90 radioembolization, therapy simulation using technetium 99mTc macro aggregated albumin (Tc-99m-MAA) is recommended for pre-dosimetry to confirm the administered activity that would accumulate in the target tumor and limit the absorbed doses by normal liver tissue and lungs. Thus, in this study, we aimed to detect the MPA in patients with unresectable liver metastasis and hepatocellular carcinoma treated with Y-90 microspheres and to evaluate the absorbed radiation doses with patient-specific dosimetry methods.

MATERIALS AND METHODS

The study was conducted at İstanbul University, Cerrahpaşa Medical Faculty between February 2012 and June 2014 and included 31 patients (20 males, 11 females; mean age 47±0.2 years; range, 32 to 62 years) who underwent pre-dosimetry to determine MPA to ensure successive treatment with no side effects to the critical organs. Patients' mean height was 1.6±0.04 m, mean weight was 73.6±0.2 kg, mean tumor volume was 355.2±0.6 cm^3, and mean liver volume was 1,942.2±1.4 cm^3. The study protocol was approved by the İstanbul University, Cerrahpaşa Medical Faculty Ethics Committee. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Dosimetry models

Empiric model

The empiric method suggests a standard amount of activity given in accordance with the tumor size in the liver. The applicable amount of standard activity for liver and tumor volumes has been shown in detail.[10]

Body surface area model

Body surface area (BSA) is a new version of empiric method. It is basically calculated using the weight (kg) and height (m) values of the patient.[11]

Medical internal radiation dose model

Medical Internal Radiation Dose (MIRD) model application dictates presence of essential parameters, for instance liver and tumor mass, normal liver tissue and tumor uptake in order to calculate absorbed dose of normal liver and tumor as reported by Gulec at al.[12] On the other hand, the MPA of Y-90 intended to be applied may be consistent with the prescribed tolerable dose of the liver and lungs:

$$DOSE_{liver}\,(rad) = \frac{Activity_{total}\,(mCi)\times 184{,}000\times UPTAKE_{liver}}{m_{liver}\,(g)} \quad \text{Eq.1}$$

$$DOSE_{tumor}\,(rad) = \frac{Activity_{total}\,(mCi)\times 184{,}000\times UPT\ TLR_{tumor}}{m_{tumor}\,(g)} \quad \text{Eq.2}$$

$$DOSE_{lungs}\,(rad) = \frac{Activity_{total}\,(mCi)\times 184{,}000\times SF}{m_{lungs}\,(g)} \quad \text{Eq.3}$$

To evaluate the m_{liver} parameter, total liver volume was calculated over computed tomography scan using OsiriX software (Pixmeo, Switzerland) and then multiplied by soft tissue density.[13] To evaluate the m_{tumor} parameter, the Cavalieri principle was used. This principle is considered an accurate method to calculate the volume of

irregular objects[10,14-16] with reliable geometric data obtained from patients' Tc-99m-MAA single-photon emission computed tomography images for tumors.

The formation of arteriovenous connection with pulmonary system produces lung shunting involving a flow of microspheres into the inner layers of lungs exposing it to radiation. Thus, the fraction of Tc-99-MAA leaking into lungs is typically estimated by drawing a region of interest over the lungs and liver on the planar images as shown in the following function:[12]

$$SF = \frac{Counts_{lungs}}{Counts_{lungs}+Counts_{liver}} \quad Eq.4$$

For a patient to be accepted ideal and appropriate to undergo Y-90 radioembolization, the lung shunting fraction (SF) must not exceed 20%.[15] To assess tumor to liver uptake ratio plays a major role in accomplishing Y-90 MPA, in which the borders of tumor and normal liver are pointed out optically and tumor/liver ratio (TLR) is determined as:[17]

Table 1. Doses determined by empiric model

Patient No	Activity (MBq)	Normal liver (Gy)	Doses tumor (Gy)	Lung (Gy)
1	54,000	25.68	116.78	4.73
2	67,500	44.92	109.86	9.95
3	54,000	17.03	144.23	10.63
4	54,000	43.08	162.12	6.96
5	54,000	65.67	158.12	8.53
6	54,000	8.34	155.46	9.30
7	54,000	41.54	301.10	5.15
8	54,000	28.96	143.89	15.93
9	54,000	52.48	125.18	4.58
10	67,500	63.28	163.50	4.96
11	54,000	39.78	200.29	9.18
12	54,000	47.69	104.67	4.39
13	54,000	45.92	252.07	7.33
14	54,000	21.84	51.86	5.91
15	81,000	47.76	108.95	6.82
16	81,000	46.54	108.58	9.57
17	54,000	21.84	211.42	6.74
18	54,000	19.10	127.08	5.09
19	54,000	34.04	187.22	8.03
20	67,500	60.02	141.23	10.88
21	54,000	28.21	1,156.78	9.94
22	67,500	63.26	229.57	5.10
23	54,000	38.32	120.42	3.33
24	54,000	75.73	317.10	8.02
25	54,000	33.25	89.40	8.41
26	54,000	48.52	199.70	6.60
27	54,000	55.01	119.50	4.30
28	54,000	38.24	93.75	7.73
29	54,000	18.56	251.05	5.59
30	54,000	27.25	294.66	10.13
31	54,000	42.45	180.57	5.29
Mean±SD	57,483±7.7	40.14±0.2	197.62±0.45	7.39±0.08

MBq: Megabecquerel; Gy: Gray; SD: Standard deviation.

$$\text{tumor/liver ratio (TLR)} = \frac{\text{Maximum tumor counts}}{\text{Liver average counts}} \quad \text{Eq.5}$$

Partition model

In the partition model, the radiation dose of a functional organ with a mass of m (g) and an activity of A_0 (GBq) is calculated using the MIRD principles with a simplification.[18]

Statistical analysis

Microsoft Excel 2010 software was used for statistical analysis.

RESULTS

The amount of activity determined by the empiric model and the normal liver, tumor and lung doses to be formed are shown in Table 1. Mean normal liver, mean tumor, and mean lung doses were calculated as 40.14±0.20 Gy, 197.62±0.45 Gy, and 7.39±0.08 Gy, respectively, when mean 57,483±7.7 megabecquerel (MBq) activity was given according to empiric model. Normal liver doses shown in Table 1 were found to be well above the reference liver dose.[19] Lung dose limit[20] exceeded in one patient.

Table 2. Doses determined by body surface area model

Patient No	Activity (MBq)	Normal liver (Gy)	Doses tumor (Gy)	Lung (Gy)
1	1,702.54	21.88	99.50	4.03
2	2,353.97	42.34	103.55	9.38
3	1,808.03	15.41	130.51	9.62
4	1,898.12	40.93	154.02	6.62
5	1,493.32	49.08	118.18	6.37
6	1,616.9	6.75	125.80	7.53
7	1,539.2	32.06	232.40	3.98
8	2,016.5	29.28	145.47	16.10
9	1,761.2	46.25	110.34	4.04
10	1,513.3	38.35	99.10	3.01
11	1,909.57	38.02	191.44	8.77
12	1,705.7	40.72	89.39	3.75
13	1,783.4	41.02	225.18	6.54
14	1,875.9	20.52	48.71	5.55
15	2,120.1	33.81	77.13	4.83
16	2,223.7	34.56	80.63	7.11
17	2,027.6	22.16	214.55	6.84
18	1,646.5	15.75	104.76	4.19
19	1,949.9	33.24	182.84	7.84
20	1,657.6	39.86	93.78	7.22
21	1,550.3	22.89	938.39	8.06
22	1,790.8	45.38	164.68	3.66
23	1,816.7	34.91	109.69	3.03
24	1,546.6	58.69	245.73	6.22
25	2,060.9	34.33	92.31	8.68
26	1,724.2	41.90	172.44	5.70
27	1,798.2	49.57	107.68	3.87
28	1,539.2	29.46	72.22	5.96
29	1,764.9	16.40	221.91	4.94
30	1,872.2	25.58	276.63	9.51
31	1,920.3	40.84	173.74	5.09
Mean±SD	1,806.04 ±1.37	33.61±0.18	167.83±0.41	6.39±0.08

MBq: Megabecquerel; Gy: Gray; SD: Standard deviation.

The amount of activity determined by the BSA model and the normal liver, tumor and lung doses to be formed are shown in Table 2. Mean normal liver, mean tumor, and mean lung doses were 33.61±0.18 Gy, 167.83±0.41 Gy, and 6.39±0.08 Gy, respectively, when mean 1,806.04±1.37 MBq activity was given according to the BSA model. Normal liver doses shown in Table 2 were found to be well above the reference liver dose.[19] Lung dose limit[20] exceeded in one patient. The quantities of activity planned for the BSA model produced high radiation doses in critical organs.

The amount of activity determined by the MIRD model and the normal liver, tumor and lung doses to be formed are shown in Table 3. When mean 1,649.60±1.31 MBq activity was given according to the MIRD model, mean normal liver, mean tumor, and mean lung doses were calculated as 29.63±0.17 Gy, 125.62±0.36 Gy, and 5.67±0.07 Gy, respectively. Normal liver doses shown in Table 3 were close to the reference liver dose.[19] No radiation doses exceeded the maximum dose of 12 Gy for the lungs.[20]

Table 3. Doses determined by medical internal radiation dose model

Patient No	Activity (MBq)	Normal liver (Gy)	Doses tumor (Gy)	Lung (Gy)
1	2,257	29.01	131.92	5.34
2	2,220	39.93	97.66	8.84
3	1,805.6	15.39	130.34	9.61
4	1,850	39.89	150.11	6.45
5	1,202.5	39.52	95.16	5.13
6	1,628	6.80	126.67	7.58
7	1,443	30.00	217.46	3.72
8	1,480	21.45	106.59	11.80
9	1,517	39.84	95.04	3.48
10	1,572.5	39.84	102.94	3.13
11	1,498.5	29.83	150.22	6.88
12	1,665	39.74	87.23	3.66
13	1,295	29.76	163.38	4.75
14	2,738	29.94	71.07	8.09
15	2,479	39.51	90.12	5.64
16	2,571.5	39.93	93.17	8.21
17	2,027.6	22.16	214.56	6.84
18	1,665	15.92	105.90	4.24
19	1,757.5	29.94	164.68	7.06
20	1,646.5	39.57	93.11	7.17
21	370	5.22	214.22	1.84
22	1,184	29.99	108.83	2.42
23	1,554	29.81	93.66	2.59
24	777	29.45	123.32	3.12
25	2,368	39.40	105.95	9.96
26	1,239.5	30.10	123.89	4.09
27	1,443	39.73	86.31	3.11
28	2,072	39.66	97.22	8.02
29	1,110	12.03	162.72	3.62
30	1,295	15.14	163.70	5.63
31	1,406	29.87	127.07	3.72
Mean±SD	1,649.6±1.31	29.63±0.17	125.62±0.36	5.67±0.07

MBq: Megabecquerel; Gy: Gray; SD: Standard deviation.

Table 4. Doses determined by partition model

Patient No	Activity (MBq)	Normal liver (Gy)	Doses tumor (Gy)	Lung (Gy)
1	2,297.7	29.53	134.30	5.44
2	2,197.8	39.52	96.66	8.75
3	1,828.91	15.58	131.99	9.73
4	1,853.14	39.95	150.34	6.46
5	1,208.79	39.72	95.64	5.16
6	1,628.37	6.80	126.68	7.58
7	1,438.56	29.90	216.75	3.71
8	1,498.5	21.71	107.90	11.94
9	1,498.5	39.35	93.87	3.44
10	1,558.44	39.48	102.00	3.10
11	1,498.5	29.83	150.19	6.88
12	1,648.35	39.33	86.34	3.62
13	1,498.5	34.43	189.02	5.49
14	2,747.25	30.03	71.30	8.12
15	2,497.5	39.79	90.77	5.68
16	2,567.43	39.86	93.00	8.20
17	2,027.97	22.16	214.55	6.84
18	1,668.33	15.95	106.09	4.25
19	1,758.24	29.95	164.72	7.06
20	1,658.34	39.85	93.76	7.22
21	370.12	23	214.25	1.84
22	1,178.82	29.85	108.34	2.41
23	1,558.44	29.89	93.91	2.60
24	789.21	29.91	125.23	3.17
25	2,397.6	39.89	107.25	10.08
26	1,228.77	29.84	122.79	4.06
27	1,448.55	39.87	86.62	3.12
28	2,057.2	39.38	96.53	7.96
29	1,110.08	10.31	139.46	3.10
30	1,293.70	17.64	190.76	6.56
31	1,408.59	29.92	127.28	3.73
Mean±SD	1,658.72±1.31	29.82±0.17	126.72±0.36	5.72±0.07

MBq: Megabecquerel; Gy: Gray; SD: Standard deviation.

The amount of activity determined by the partition model and the normal liver, tumor and lung doses to be formed are shown in Table 4. Mean normal liver, mean tumor, and mean lung doses were 29.82±0.17 Gy, 126.72±0.36 Gy, and 5.72±0.07 Gy, respectively, when mean 1,658.72±1.31 MBq activity was given according to the partition model. The doses indicated in bold in Table 4 exceeded the maximum accepted 30-35 Gy liver dose.[19] No radiation dose exceeded the maximum dose of 12 Gy for the lungs.[20]

DISCUSSION

In this study, we aimed to perform patient-specific radiation dosimetry to determine the parameters required for the diagnosis of primary or metastatic liver cancer for an effective treatment.

In the field of Y-90 microspheres therapy, a great number of dosimetric models have been developed gradually starting from empiric, BSA, MIRD and partition models, and finally Monte Carlo simulation.[12,21-25] When MPA values calculated with empiric model were given to

patients, liver absorbed dose was higher than 30-35 Gy in 18 patients. Moreover, there was one patient whose lung absorbed dose was above the reference dose. With empiric model, the calculated MPA will deliver large absorbed doses to the critical organs, leading to organ toxicity in late stages. Therefore, we concluded that empiric model is not an appropriate dosimetry approach. Additionally, it does not allow patient-specific dosimetry.

Regarding MPA determined by the BSA model, the liver absorbed dose was higher in eight patients, and the lung absorbed dose was above the reference dose in one patient. Consequently, BSA model failed to be a suitable dosimetry model due to the calculated high absorbed doses that cause organ toxicity.

Since MIRD and partition models are mainly based on more scientific regulations compared to the previous models, they have great advantages to promote optimum Y-90 dosimetry.[11] The tumor, liver, and lungs masses, SF, TLR, and liver and tumor uptakes are the most essential parameters needed to achieve precise calculations for MPA of Y-90. Moreover, our cases did not have any dose higher than the reference doses. When the SF is high, it can keep the absorbed dose of lungs within the acceptable limits. Additionally, there is no theoretical limit for calculated activity.

In all dosimetry models used, it is assumed that the amount of activity given for treatment is homogeneously distributed throughout the tumor. However, it is known that dead areas such as necrosis may be present in the tumor. In addition, necrosis areas were ignored while tumor volume was calculated. In the next study, it is aimed to do dosimetry with the Monte Carlo method, which gives new and near-realistic results to remove all these limitations.

In conclusion, MIRD and partition models were found to be optimal dosimetry models. Based on the mean normal liver and lung dose values in our study, the amount of activity planned to be given according to the MIRD model has produced radiation doses that can be tolerated in critical organs. The MIRD model offers patient-specific dosimetry and is useful for routine Y-90 microsphere dosimetry calculations.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Breedis C, Young G.The blood supply of neoplasms in the liver. Am J Pathol 1954;30:969-77.
2. Yip D, Allen R, Ashton C, Jain S.Radiation-induced ulceration of the stomach secondary to hepatic embolization with radioactive yttrium microspheres in the treatment of metastatic colon cancer. J Gastroenterol Hepatol 2004;19:347-9.
3. Kennedy AS, Coldwell D, Nutting C, Murthy R, Wertman DE Jr, Loehr SP, et al. Resin 90Y-microsphere brachytherapy for unresectable colorectal liver metastases: modern USA experience.Int J Radiat Oncol Biol Phys 2006;65:412-25.
4. Kennedy AS, McNeillie P, Dezarn WA, Nutting C, Sangro B, Wertman D, et al.Treatment parameters and outcome in 680 treatments of internal radiation with resin 90Y-microspheres for unresectable hepatic tumors. Int J Radiat Oncol Biol Phys 2009;74:1494-500.
5. Sato K, Lewandowski RJ, Bui JT, Omary R, Hunter RD, Kulik L, et al.Treatment of unresectable primary and metastatic liver cancer with yttrium-90 microspheres (TheraSphere): assessment of hepatic arterial embolization.Cardiovasc Intervent Radiol 2006;29:522-9.
6. Gulec SA, Fong Y. Yttrium 90 microsphere selective internal radiation treatment of hepatic colorectal metastases. Arch Surg 2007;142:675-82.
7. Geschwind JF, Salem R, Carr BI, Soulen MC, Thurston KG, Goin KA, et al.Yttrium-90 microspheres for the treatment of hepatocellular carcinoma. Gastroenterology 2004;127:194-205.
8. Austin-Seymour MM, Chen GT, Castro JR, Saunders WM, Pitluck S, Woodruff KH, et al. Dose volume histogram analysis of liver radiation tolerance.Int J Radiat Oncol Biol Phys 1986;12:31-5.
9. McCammon R, Schefter TE, Gaspar LE, Zaemisch R, Gravdahl D, Kavanagh B. Observation of a dose-control relationship for lung and liver tumors after stereotactic body radiation therapy. Int J Radiat Oncol Biol Phys 2009;73:112-8.
10. SIR-Spheres®. Available from: http://www.radmed.com.tr/usr_img/sir_spheres/pdf/package_insert_sirtex.pdf. [Access: April 2005]
11. SIR-Spheres® Y-90 resin microspheres, (CR2189). Available from: https://www.sirtex.com/media/155126/ssl-us-13.pdf [Access: February 2017].

12. Şahin B, Aslan H, Ünal B, Canan S, Bilgic S, Kaplan S, Tumkaya L. Brain volumes of the lamb, rat and bird do not show hemispheric asymmetry: a stereological study, Image Anal Stereol 2001;20:9-13.
13. Güleç SA, Mesoloras G, Stabin M. Dosimetric techniques in 90Y-microsphere therapy of liver cancer: The MIRD equations for dose calculations. J Nucl Med 2006;47:1209-11.
14. Mayhew TM, Olsen DR.Magnetic resonance imaging (MRI) and model-free estimates of brain volume determined using the Cavalieri principle. J Anat 1991;178:133-44.
15. Pakkenberg B. Stereological quantitation of human brains from normal and schizophrenic individuals. Acta Neurol Scand Suppl 1992;137:20-33.
16. Mackay CE, Pakkenberg B, Roberts N. Comparison of compartment volumes estimated from MR images and physical sections of formalin fixed cerebral hemispheres. Acta Stereol 1999;18:149-59.
17. Gandhi SJ, Babu S, Subramanyam P, Shanmuga Sundaram P.Tc-99m macro aggregated albumin scintigraphy - indications other than pulmonary embolism: A pictorial essay. Indian J Nucl Med 2013;28:152-62.
18. Synder WS, Ford MR, Warner GG, Watson SB. "S" absorbed dose per unit cumulative activity for selected radionuclides and organs NM/MIRD. New York: Society of Nuclear Medicine; 1975.
19. Austin-Seymour MM, Chen GT, Castro JR, Saunders WM, Pitluck S, Woodruff KH, et al. Dose volume histogram analysis of liver radiation tolerance. Int J Radiat Oncol Biol Phys 1986;12:31-5.
20. McCammon R, Schefter TE, Gaspar LE, Zaemisch R, Gravdahl D, Kavanagh B. Observation of a dose-control relationship for lung and liver tumors after stereotactic body radiation therapy. Int J Radiat Oncol Biol Phys 2009;73:112-8.
21. Gulec SA, Mesoloras G, Dezarn WA, McNeillie P, Kennedy AS. Safety and efficacy of Y-90 microsphere treatment in patients with primary and metastatic liver cancer: the tumor selectivity of the treatment as a function of tumor to liver flow ratio. J Transl Med 2007;5:15.
22. Weber DA, Eckeman KF, Dillman LT, Ryman JC. MIRD: radionuclide data and decay schemes. New York: Society of Nuclear Medicine; 1989.
23. Snyder WS, Ford MR, Warner GG, Watson SB. 'S,' absorbed dose per unit cumulated activity for selected radionuclides and organs MIRD Pamphlet 11 (Reston, VA: Society of Nuclear Medicine) 1975;1-258.
24. Jabbari K. Review of fast monte carlo codes for dose calculation in radiation therapy treatment planning. J Med Signals Sens 2011;1:73-86.
25. Ho S, Lau WY, Leung TW, Chan M, Ngar YK, Johnson PJ, et al. Partition model for estimating radiation doses from yttrium-90 microspheres in treating hepatic tumours. Eur J Nucl Med 1996;23:947-52.