

Cumhuriyet Medical Journal

cmj.cumhuriyet.edu.tr

Founded: 2004

Available online, ISSN:1305-0028

Publisher: Sivas Cumhuriyet Üniversitesi

Comparison of Dosimetry Results Before 90Y Microembolization Treatment with 99mTc MAA and After 90Y PET/CT Treatment

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Research Article	ABSTRACT
Research Article History Received: 06/02/2024 Accepted: 02/04/2024	ABSTRACT Radioembolization with Yttrium-90 (90Y) microspheres stands as an effective treatment option for liver tumors. The suitability of a patient for this treatment is routinely determined through dosimetry based on Technetium- 99m Macro Aggregated Albumin (99mTc MAA) SPECT/CT images. This study aims to compare pre-treatment (pre) dosimetry results with 99mTc MAA and post-treatment (post) dosimetry results after 90Y microsphere therapy in patients seeking liver tumor treatment. Eleven patients undergoing liver tumor treatment were randomly included in the study. In 99mTc-MAA dosimetry, the calculated treatment activity was 1.3-6.2 GBq (mean 3.2±1.4), tumor dose was 125.1-527.5 Gy (mean 264.7±139.4), and liver dose was 19.4-38.8 Gy (mean 31.9±5.8). Post-dosimetry using PET/CT images after 90Y microsphere therapy revealed a tumor dose of 156.2- 480.4 Gy (mean 266.5±102.9) and a liver dose of 20.6-37.4 Gy (mean 29.1±5.2). The doses exhibited good conformity for both tumor and normal liver tissue (p=0.85716 and p=0.53526, respectively). In conclusion, PET/CT-based post-dosimetry with 90Y microspheres proved to be an effective method in determining liver
	parenchymal tissue and tumor doses.

Keywords: 90Y microsphere therapy, dosimetry, 99mTc MAA, radionuclide therapy, 90Y microembolization

⁹⁰Y Mikroembolizasyon Tedavisinde ^{99m}Tc MAA ile Tedavi Öncesi ve ⁹⁰Y PET/BT Tedavi sonrası Dozimetri Sonuçlarının Karşılaştırılması

Araştırma Makalesi

ÖZ

Süreç

Geliş: 06/02/2024 Kabul: 02/04/2024 Karaciğer tümörleri tedavisinde Yitriyum 90 (⁹⁰Y) mikroküreler ile yapılan radyoembolizasyon etkili bir tedavi seçeneğidir. Hastanın tedaviye uygunluğu rutinde ^{99m}Tc Makro Albümin Agregat (MAA) SPECT/BT görüntüleri üzerinden yapılan dozimetri ile belirlenir. Bu çalışmada, karaciğer tümör tedavisi için başvuran hastalarda ^{99m}Tc MAA tedavi öncesi (pre) dozimetri sonuçları ile ⁹⁰Y mikroküre tedavi sonrası (post) dozimetri yapılarak sonuçlarının karşılaştırılması amaçlandı. Çalışmamıza karaciğer tümör tedavisi için başvuran ve rastgele seçilmiş 11 hasta dahil edildi. ^{99m}Tc-MAA dozimetri ile hesaplanan tedavi aktivitesi 1.3-6.2 GBq (ortalama 3.2±1.4), tümör dozu 125.1-527.5 Gy (ortalama 264.7±139.4) ve karaciğer dozu 19.4-38.8 Gy (ortalama 31.9±5.8) bulundu. ⁹⁰Y mikroküre tedavisinden sonra çekilen PET/BT görüntülerinden yapılan dozimetride tümör dozu 156.2-480.4 Gy (ortalama 266.5±102.9), karaciğer dozu 20.6-37.4 Gy (ortalama 29.1±5.2) bulundu. Dozlar, tümör ve normal karaciğer dokusu için iyi bir uyum gösterdi (p=0.85716 ve p=0.53526, sırasıyla). Sonuçta ⁹⁰Y mikroküreler ile PET/BT'ye dayanan post dozimetrinin karaciğer parankim doku dozunu ve tümör dozunu belirlemdi.

Anahtar Kelimeler: 90Y mikroküre tedavisi, dozimetri, 99mTc MAA, radyonüklid tedavi, 90Y mikroembolizasyon

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How to Cite: Taşlıyurt Ö, Yeyin N, Demir M. Comparison of Dosimetry Results Before 90Y Microembolization Treatment with 99mTc MAA and After 90Y PET/CT Treatment, Cumhuriyet Medical Journal. 2024; 46(2): 104-109.

Introduction

The majority of patients diagnosed with hepatocellular carcinoma (HCC) and secondary liver cancer are not eligible for curative surgical resection, and systemic chemotherapy alone rarely results in prolonged survival. Additionally, the excessive sensitivity of liver parenchymal tissue to radiation limits the achievement of desired doses in external radiotherapy. Hence, liver tumors are often characterized as having a poor prognosis in terms of radiotherapy. However, in contemporary medicine, radioembolization techniques have been developed and introduced into clinical practice as a novel treatment option.¹

Radioembolization, also known as Yttrium-90 (90Y) microsphere therapy, involves delivering microspheres labeled with 90Y, emitting pure beta radiation, to the tumor microcirculation via intra-arterial administration.² 90Y microsphere therapy is a form of brachytherapy, also referred to as radioembolization, transarterial radioembolization (TARE), or selective internal radiation therapy (SIRT). It constitutes a targeted treatment for both primary and secondary liver tumors.³

Yttrium-90 labeled microspheres, emitting pure β radiation, are delivered to liver tumors through microcirculation in the hepatic arteries. Particles emitted by the 90Y isotope, with a physical half-life of 2.67 days, have a maximum energy of 2.27 MeV and an average energy of 0.93 MeV. Beta particles with 0.93 MeV energy penetrate up to 11 mm within the tissue. The physical half-life of 90Y is 64.1 hours, with 94% of the radiation dose delivered within the first 11 days. Trapped within the tumor, 90Y-labeled microspheres allow for radiation of the tumor while preserving healthy liver tissue. Furthermore, the short distance covered minimizes the need for post-treatment radiation protection measures. There are two types of 90Y microspheres: resin microspheres with a diameter of 20 to 60 mm and glass microspheres with a diameter of 20-30 mm.^{4,5}

In patients with normal liver and kidney functions, predosimetry, known as hepatopulmonary angiography, is performed with Technetium-99m Macro Aggregated Albumin (99mTc-MAA) SPECT/CT before 90Y treatment to assess vascular anatomy. This allows determination of the hepatopulmonary shunt ratio and identification of any extrahepatic leakage into the intestinal system. While maximizing the radiation dose to the tumor, efforts are made to ensure that the dose to the liver parenchyma outside the tumor does not exceed 50-70 Gy. Additionally, by adjusting the tumor dose if necessary, based on the identified lung shunt ratio, efforts are made to keep the average lung dose below 35 Gy. Thus, pre-dosimetry allows for the estimation of the dose delivered to the tumor and normal liver, enabling the assessment of the optimal therapeutic 90Y activity.6,7,8 Through 99mTc-MAA dosimetry, the distribution of 90Y microspheres in the liver and tumor can be predicted in advance. In contrast, post-dosimetry reveals the actual biodistribution of 90Y microspheres, aiding in the optimization of treatment planning. For instance, post-treatment dosimetry can be used to detect tumors that are being exposed to less radiation than is ideal, hence highlighting the necessity of additional adjuvant therapies or re-super-selective radioembolization. Alternatively, if it is thought that the previous treatment resulted in excessive radiation exposure,

post-treatment dosimetry can select high-risk individuals for re-radioembolization. Lastly, in order to ascertain dose-response and dose-toxicity connections, quantitative post-treatment dosimetry data are essential.⁵

The aim of this study is to compare pre-dosimetry results with 99mTc-Macro Aggregated Albumin (MAA) and postdosimetry results after Yttrium-90 (90Y) microsphere therapy in patients seeking liver tumor treatment.

Materials and Methods

This retrospective study examined a total of 11 patients (5 males, 6 females) with metastatic or primary liver cancer who underwent treatment with 90Y microspheres at the Department of Nuclear Medicine, Istanbul University-Cerrahpasa, Faculty of Medicine. Patients who had undergone pre-treatment 99mTc-MAA scintigraphy and post-treatment 90Y PET/CT imaging were included in this study. This study has been approved by the local Ethics Committee of Cerrahpaşa Faculty of Medicine, Istanbul University-Cerrahpaşa, in accordance with the Helsinki Declaration (No: 83045809-604.01.02-). Informed consent has been obtained from all participating patients.

As a pre-treatment exclusion criterion, patients with a hepatopulmonary shunt ratio greater than 20% after the administration of 99mTc-MAA were not included in this study. The inclusion criterion involved patients with a hepatopulmonary shunt ratio below 20% who were deemed to benefit from 90Y microembolization therapy by the clinician.

99mTc MAA Imaging

Following the administration of 99mTc-MAA, threedimensional (3D) SPECT/CT and two-dimensional (2D) wholebody planar scintigraphy were performed using the Siemens Simbia T16 model SPECT/CT imaging device. Images were acquired using the triple energy window technique with a 140 keV and 20% window for the photopic energy of 99mTc radionuclide to correct for scatter.

For pre-dosimetry, 185 MBq (5 mCi) of 99mTc-MAA was administered in the interventional radiology department. Whole-body (WB) scintigraphy was performed with clinical protocol-compliant parameters of 256x1024 pixels, 15 cm/s speed, 128x128 pixels, 32 frames, and 30 s/frame. Calculations of dosimetry were carried out using the Simplicit90Y[™] software program. The Simplicit90Y[™] software (Mirada Medical LTD., Oxford, UK) determined the lung shunt ratio and regions of interest (ROIs) for the liver, lungs, and any area of interest in the body using 2D whole-body images.

For the 99mTc-MAA dosimetry, volumes of interest (VOIs) were drawn for the entire liver, perfused tissue, tumor, and any necrotic areas using SPECT/CT images. The prescribed tumor dose was determined while keeping the entire liver tolerance dose at a limit of 35 Gy. An average of 3.2±1.4 GBq of 90Y was administered to patients based on the predosimetry obtained with 99mTc-MAA.

90Y PET/CT Imaging

90Y microsphere activities were administered to patients in interventional radiology for radioembolization treatment. After radioembolization, patients were admitted to the leadshielded nuclear medicine treatment room. The next day, 90Y PET/CT imaging was performed using the GE Discovery model 710 device.

Each bed position took 15 minutes to acquire (for a total of 30 minutes). To adjust for attenuation, a low-dose CT scan (120 kVp, 40 mAs) was acquired. With a 5 mm full-width at half-maximum Gaussian filter, PET images were reconstructed using standard Poisson ordered subset expectation maximization, which included resolution recovery, time-of-flight data, and adjustments for attenuation, randoms, and scatter.

Dosimetry Calculations

Calculations of dosimetry were carried out using personalized software, Simplicit90Y[™] (Mirada Medical LTD., Oxford, UK), utilizing three-dimensional volumetric data. The dosimetry calculation process involved registering the images obtained from patients (whole-body, SPECT/CT, or PET/CT), segmenting SPECT or PET images, and determining the dosimetry calculations of the defined areas of interest (VOIs).⁹ Since the Simplicit90Y[™] program could not perform the reconstruction of SPECT or PET images, digital imaging and communication in medicine (DICOM) formatted reconstructed image data were utilized.¹⁰ In the 11 included patients, VOIs were drawn for the entire liver, perfused area, and tumor based on segmentation with SPECT/CT and PET/CT images.

Statistical Analysis: SPSS program was used for statistical analysis, p<0.05 was considered significant. The Mann-Whitney U test was employed to determine if there was a statistically significant difference between the pre- and post-treatment dosimetric results in this study.

Results

Patient data and dosimetric calculations following the administration of 99mTc-MAA were evaluated using the Simplicit90YTM software based on scintigraphic images (Figure 1). From the 99mTc-MAA images, the liver volume ranged from 928.3 to 3394.9 cm³ (mean 1623±732), tumor volume ranged from 70.9 to 592.8 cm³ (mean 339.4±227.4), the calculated amount of 90Y activity ranged from 1.3 to 6.2 GBq (mean 3.2±1.4), tumor dose ranged from 125.1 to 527.5 Gy (mean 264.2±139.4), and liver parenchyma dose ranged from 19.4 to 38.8 Gy (mean 31.9±5.8) (Table 1).

Patient data post 90Y microsphere treatment was evaluated through PET/CT images, and dosimetric calculations were performed using the Simplicit90Y^M software (Figure 2). The tumor volumes ranged from 168.8 to 793.1 cm³ (mean 405.6±232.8), 90Y tumor doses ranged from 156.2 to 480.4 Gy (mean 266.5±102.9), and 90Y liver doses ranged from 20.6 to 37.4 Gy (mean 29.1±5.2) (Table 2).



Figure 1: Short-axis, coronal, and sagittal cross-sectional views of the tumor in the liver from left to right in a SPECT/CT image taken after the administration of 99mTc-MAA in a patient. Yellow, blue, and red colors respectively indicate liver, lung, and tumor.



Figure 2: Short-axis, coronal, and sagittal cross-sectional views from left to right of PET/CT images taken after 90Y microsphere treatment, showing tumors in the patient's liver. Yellow, blue, and red colors respectively indicate liver, lung, and tumor.

	Liver	Tumor	90Y		Liver parenchyma dose
PatientNo	volume(cm ³)	volume(cm ³)	activity(GBq)	Tumor dose (Gy)	(Gy)
1	1824.3	165.2	3.7	129.7	36.3
2	2165.2	755.3	3.52	125.1	38.8
3	928.3	70.9	2.6	225.3	36.4
4	2221.4	592.8	3.4	186.2	29.6
5	1326.9	262.3	6.2	527.5	23.1
6	1340.1	466.4	3.2	143.6	32.1
7	1284.5	126.2	2.5	169.8	34.4
8	1196.3	300.1	1.3	321.3	33.6
9	1050.9	557.4	3.2	235.1	19.4
10	1119.8	151.2	1.3	380.2	32.4
11	3394.9	175.3	4.3	462.1	34.9
Mean±SD	1623±732	339.4±227.4	3.2±1.4	264.2±139.4	31.9±5.8

Table 1: Liver and Tumor Volumes, and Doses Calculated from 99mTc-MAA Images

Table 2: Dosimetric results calculated from PET/CT Images in patients treated with 90Y microsphere	Table 2: Dosimetric results calculated from PET/CT Images in	n patients treated with 90Y microspheres
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Patient no	Tumor volume (cm ³)	⁹⁰ Y tumor dose (Gy)	⁹⁰ Y liver dose (Gy)
1	202.4	222.6	37.4
2	793.1	196.2	28.2
3	196.2	201.5	29.4
4	659.3	190.8	22.5
5	202.2	480.4	24.2
6	639.4	213.8	34.7
7	335.4	156.2	29.8
8	442.1	334.6	28.5
9	616.4	213.3	20.6
10	168.7	322.1	33
11	206.7	400.1	32.6
Mean±SD	405.6±232.8	266.5±102.9	29.1±5.2







Figure 4: Correlation between pre-and post dosimetry results for tumor doses

The correlation of pre and post dosimetry results for the liver is shown in Figure 3, and the correlation graph of pre and post dosimetry results for tumor doses is shown in Figure 4.

The evaluation of liver and tumor doses in pre and post dosimetry was subjected to the Mann Whitney-U test. No significant difference was found between 99mTc-MAA and 90Y tumor doses (p=0.85716) for tumor doses. Similarly, no significant difference was observed between 99mTc-MAA and 90Y liver doses (p=0.53526).

The limitations of this study

In this study, it is recommended to increase the number of patients for the comparison of pre- and postdosimetry and to evaluate the comparison using parametric tests. Additionally, due to the relatively small number of patients and the patient-specific nature of dosimetric calculations, heterogeneous distributions were observed in liver and tumor doses.

Discussion

The significance of personalized dosimetry in nuclear medicine for liver tumor radioisotope treatment is increasing day by day. Currently, investigating the differences or similarities between pre- and postdosimetry remains a subject of research. However, there can be some variations between the calculated absorbed doses through dosimetry. The main reasons for these differences can be attributed to catheter differences, microsphere structure, and the number and structure of injected radioactive particles. Liver tumors can be successfully treated with 90Y radioembolization. In this study, pre-dosimetry with 99mTc-MAA SPECT/CT and post-dosimetry with 90Y PET/CT were performed on 11 patients to determine tumor and liver doses.

When reviewing studies on tumor doses, Martin et al., in a study on 79 patient data, reported not only a

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compatibility in terms of absorbed average doses but also in dose distribution between 99mTc-MAA dosimetry and 90Y microsphere PET/CT dosimetry. However, it was found that the doses absorbed by the tumor were 26% higher in pre-dosimetry than in post-dosimetry. The researchers found that the average absorbed doses of healthy liver were 49.47 ± 22.18 Gy and 54.53 ± 19.78 Gy for pre- and post-dosimetry, respectively. Overall, nontumor liver doses showed a stronger correlation with tumor-free liver compared to the tumor, which was explained by increased heterogeneity of the microsphere within the target structure and a greater dose gradient in the tissue of the tumor.¹¹ Knesaurek et al. determined that the tumor doses of 16 patients were 234.72±172.54 Gy and 314.07±197.02 Gy for 99m Tc-MAA SPECT/BT and 90 Y PET/BT, respectively. An average difference of 25% was found for tumor dose, with a reported linear correlation between tumor doses at the level of r=0.71. Additionally, they demonstrated that the mean values of postdosimetry 90 Y PET/CT dose results were slightly higher compared to pre-dosimetry values of 99m Tc-MAA SPECT/BT. They suggested that these differences might stem from variations in regions of interest (ROI), especially when the catheter tips in 99m Tc-MAA and 90 Y studies are positioned very similarly and away from major bifurcation points. They noted the importance of this situation, particularly for tumors smaller than 10 cm³. The researchers also found that the normal liver doses were 42.02±22.36 Gy and 49.85±24.88 Gy for 99m Tc-MAA SPECT/BT and 90 Y PET/BT, respectively, with a linear correlation between the respective doses at r=0.86.12 In our study, no significant difference was found in tumor doses between pre and post microsphere dosimetry (p=0.85716). Additionally, consistent with the literature, a strong correlation of R²=0.8913 was found among tumor doses.

Yoo Sung Song et al. found a close correlation between doses absorbed by the tumor in 99mTc-MAA SPECT/CT and

90Y PET/CT dosimetry (r=0.64). However, the average tumor doses in pre-dosimetry 99mTc-MAA SPECT/CT were significantly lower than those in post-dosimetry 90Y PET/CT (135.4±64.2 Gy vs. 185±87.8 Gy). According to these researchers, the absorbed doses by the tumor and liver were 62.6±38.2 Gy and 45.2±32 Gy for 90Y PET/CT and 99mTc-MAA SPECT/CT, respectively (p=0.02).¹³ Kao et al. compared tumor doses obtained from 99m Tc-MAA SPECT/CT pre-dosimetry with those from 90 Y PET/CT post-dosimetry in 23 patients. They found an excellent association between the outcomes of 99m Tc-MAA and 90 Y PET/CT for average tumor doses (+3.8% low median relative error with a 95% confidence interval ranging from -1.2% to +13.2%).14 Our study yielded similar results to previous studies, with no significant difference found in tumor doses between pre and post microsphere dosimetry (p=0.85716). In our 90Y PET/CT post-dosimetry results, the tumor dose was found to be 156.2-480.4 Gy (mean 266.5±102.9 Gy). When examining the correlation of liver parenchymal tissue doses, a relationship with R²=0.4776 at a low level was found, despite very small differences between pre- and post-dosimetry values (p=0.53526).

Conclusion

In radioembolization treatment, pre-treatment dosimetry with 99mTc-MAA SPECT/CT can be effectively used as a conservative method for planning activity to calculate the dose that was given to both the tumor and the healthy liver tissue. It was concluded that the dosimetry performed with 99mTc-MAA SPECT/CT before treatment is compatible with the dosimetry performed with PET/CT imaging after treatment.

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