Evaluation of Dosimetric Parameters for Tumor Therapy with ^{177}Lu and ^{90}Y Radionuclides in Gate Monte Carlo Code

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ABSTRACT

Background: ^{90}Y and ^{177}Lu are two well-known radionuclides used in radionuclide therapy to treat neuroendocrine tumors.

Objective: This current study aims to evaluate, compare and optimize tumor therapy with ^{90}Y and ^{177}Lu for different volumes of the tumor using the criterion of self-absorbed dose, cross-absorbed dose, absorbed dose profile, absorbed dose uniformity, and dose-volume histogram (DVH) curve using Gate Monte Carlo simulation code.

Material and Methods: In our analytical study, Gate Monte Carlo simulation code has been used to model tumors and simulate particle transport. Spherical tumors were modeled from radius 0.5 to 20 mm. Tumors were uniformly designed from water (soft tissue reagent). The full energy spectrum of each radionuclide of ^{177}Lu and ^{90}Y was used in the total volume of tumors with isotropic radiation, homogeneously. Self-absorbed dose, cross-absorbed dose, absorbed dose profile, absorbed dose uniformity, and DVH curve parameters were evaluated.

Results: The absorbed dose for ^{90}Y is higher than ^{177}Lu in all tumors (p-value <5%). The uniformity of the absorbed dose for ^{177}Lu is much greater than ^{90}Y. As the tumor size increases, the DVH graph improves for ^{90}Y.

Conclusion: Based on self-absorbed dose, cross-absorbed dose, absorbed dose uniformity, and DVH diagram, ^{177}Lu and ^{90}Y are appropriate for smaller and larger tumors, respectively. Next, we can evaluate the appropriate cocktail of these radionuclides, in terms of the type of composition, for the treatment of tumors with a specific size.

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Keywords

Radionuclide Tumor Therapy; Gate Monte Carlo; Dosimetry; DVH; Lutetium-177; Yttrium-90

Introduction

Radionuclide radiation therapy is an important method for treating the disseminated tumors and metastases [1]. A major advantage of radionuclide therapy is that it treats not only primary large tumors and macro-metastases but also small tumors and micro-metastases [1, 2].

As tumor tissue absorbs radiopharmaceuticals, healthy tissue also absorbs them and irradiated, and radionuclide therapy planning thus aims is to deliver the highest absorbed dose to the tumor tissue and the least

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damage to the organ at risk [3-5].

^{90}Y and ^{177}Lu are two well-known radionuclides used in radionuclide therapy of neuroendocrine tumors. Based on the previous literature, ^{177}Lu and ^{90}Y have low and high energy beta particles, respectively, and also they are widely used for treating smaller and larger tumors [6-9].

In the clinical situation, the most serious part of treatment planning of radionuclide therapy is determining the measure of prescribed radioactive material for improving treatment, based on the maximum absorbed dose to the tumor tissues and the minimum absorbed dose to critical organs. Also, there are some limitations, including methods for estimating dose distribution in tumors and tissues around tumors. As a result, proper treatment planning is an accurate and fast method of dose estimation to optimize treatment planning. If the dosimetry technique adopted is not appropriate, we may experience an increase in the absorbed dose of around the tumor and an insufficient absorbed dose inside the tumor as a result of estimating the wrong dose, leading to cancer reversion and low utilization [4, 8, 10].

Evaluation of self-dose and cross-dose of tumors in radionuclide therapy is important to examine the treatment planning [9].

It is also important to study the tumor's absorbed dose profile to evaluate the tumor absorbed dose's flatness, which directly affects the optimal treatment [11].

Dose Volume Histogram (DVH) and external radiotherapy can be utilized to examine the treatment planning of radionuclide therapy [12].

It seems that the study of physical parameters can well evaluate treatment planning in radionuclide therapy. Therefore, the current study aims to evaluate, compare and optimize tumor therapy with ^{90}Y and ^{177}Lu for different sizes of tumors using the criteria of self-absorbed dose, cross-absorbed dose, absorbed dose profile, dose uniformity, and DVH curve, using Gate Monte Carlo simulation code.

Material and Methods

In this analytical study, Gate version 8.1 (based Geant4 package version 10.4) Monte Carlo simulation code has been used to model tumors and simulate particle transport. Spherical tumors were modeled from radius 0.5 to 20 mm (volume of 0.4 to 4000 mm^3) [13]. The dimension of an area outside the tumor is greater than three times the maximum range of each radionuclide for calculating the cross dose. Tumors were uniformly designed from water (soft tissue reagent). The total energy spectrum of ^{177}Lu and ^{90}Y radionuclides were used in the total volume of tumors with isotropic radiation, homogeneously [14]. The characteristics of these radionuclides are shown in Table 1. To achieve more accuracy, "standard physical processes" were used to perform the simulation, which included Photoelectric, Compton, Rayleigh Scattering, Gamma Conversion, Electron Ionization, Bremsstrahlung, and Multiple Scattering processes [9]. The output files from the simulation include the dose and dose uncertainty files. The absorbed dose, D_m, is calculated by energy deposited by equation 1.

(1) D_m = Energy deposited/Volume

D_m finally divided by the number of primary particles, and then the absorbed dose is eventually reported in Gy/Bq.s. The absorbed dose uniformity (flatness) inside the tumor (given from dose profile)is defined based on equation 2 [11, 15]:

$$(2)\ \%\text{flatness} = \frac{\text{Dosemax} - \text{Dosemin}}{\text{Dosemax} + \text{Dosemin}} \times 100$$

We also plot the relative Dose Volume Histogram (DVH) for all tumors and radionuclides.

Table 1: Characteristic parameters of ^{177}Lu and ^{90}Y.

Isotope	$T_{1/2}$ (day)	Average energy (Kev)	Maximum range (mm)
Yttrium-^{90}	2.67	935.3	11
Lutetium-^{177}	6.7	133.5	2.2

To achieve statistical uncertainty less than 5%, the number of primary particles for simulation was considered 10^9 and 10^8 for ^{177}Lu and ^{90}Y, respectively.

Results

Absorbed dose

The calculated self-absorbed dose for ^{177}Lu and ^{90}Y radionuclides are presented for all tumors in Table 2. The cross absorbed dose is also shown in Table 3.

Using the Mann-Whitney test, we analyzed the absorbed doses for ^{177}Lu and ^{90}Y radionuclides in all tumor sizes and concluded a substantial difference between absorbed doses for ^{177}Lu and ^{90}Y in all tumor sizes.

The absorbed dose for ^{90}Y is greater than ^{177}Lu (p-value <5%) in all tumor sizes.

The self-absorbed dose according to the tumor's dimension is presented in Figure 1, which is qualitatively observed that as the

Table 2: Self-absorbed doses (Gy/Bq.s) for ^{177}Lu and ^{90}Y in different sizes of tumors.

Radionuclide radius of tumors (mm)	^{90}Y	^{177}Lu
0.5	1.43E-08	1.349E-09
1	1.96E-09	1.84E-10
2	2.25E-10	2.41E-11
3	7.75E-11	7.27E-12
4	3.30E-11	3.10E-12
5	1.70E-11	1.50E-12
6	1.05E-11	9.27E-13
8	4.73E-12	3.94E-13
10	2.71E-12	2.03E-13
11	1.53E-12	3.06E-13
12	1.18E-12	1.18E-13
15	6.08E-13	6.08E-14
18	9.45E-13	3.54E-14
20	5.19E-13	2.59E-14

Table 3: (Cross-dose/total dose)×100 for ^{177}Lu and ^{90}Y different sizes of tumors.

Radionuclide radius of tumors (mm)	^{90}Y	^{177}Lu
0.5	0.0026	0.00062
1	0.0193	0.0044
2	0.139	0.028
3	0.369	0.085
4	0.786	0.184
5	1.387	0.328
6	2.044	0.518
8	3.778	1.038
10	5.541	1.726
11	6.289	1.072
12	7.515	2.552
15	10.475	3.995
18	7.008	5.612
20	10.256	6.748

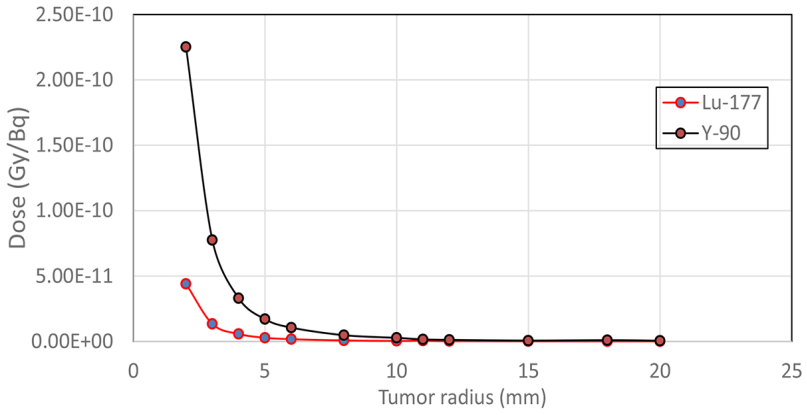

Figure 1: Absorbed dose for ^{177}Lu and ^{90}Y in different sizes of the tumors.

tumor size increases the difference of ^{177}Lu and ^{90}Y decreases. Figure 2 shows the ratio of cross absorbed dose to total-absorbed dose as a function of tumor size. By increasing tumor size, the delivered absorbed dose to the outside of the tumor increases for ^{177}Lu and ^{90}Y, but from one size onwards, this reduction is gradual, and the extra-tumor doses for ^{177}Lu and ^{90}Y are almost constant.

Flatness

Absorbed dose profiles of ^{177}Lu and ^{90}Y for a special tumor are shown in Figure 3 as an example. The absorbed dose flatness, which is a function of tumor size, is presented in Table 4. As seen, the flatness of ^{177}Lu is better than ^{90}Y. In addition, Figures 4 and 5 show the flatness values according to distance.

Table 5 shows Pearson coefficient values (showing the graph's slope) with the significant level for determining the amount of uniformity improvement with increasing tumor size. It is observed that as tumor size increases, the uniformity of the absorbed dose of ^{177}Lu and ^{90}Y improves. It is worth noting that the rate of ^{90}Y absorbed dose uniformity improves greater than that of ^{177}Lu (p-value= 0.05).

Dose Volume Histogram (DVH)

The relative volume as a function of relative dose diagrams for ^{177}Lu and ^{90}Y radionuclides and tumor with the sizes of 1, 10 and, 20 mm, as representatives of all tumor sizes, are shown in Figure 6. It is understandable that as the tumor size increases, the DVH graph improves for ^{90}Y as well. In smaller tumors, for ^{90}Y, energy is transferred to a smaller volume of tumor space than in larger ones.

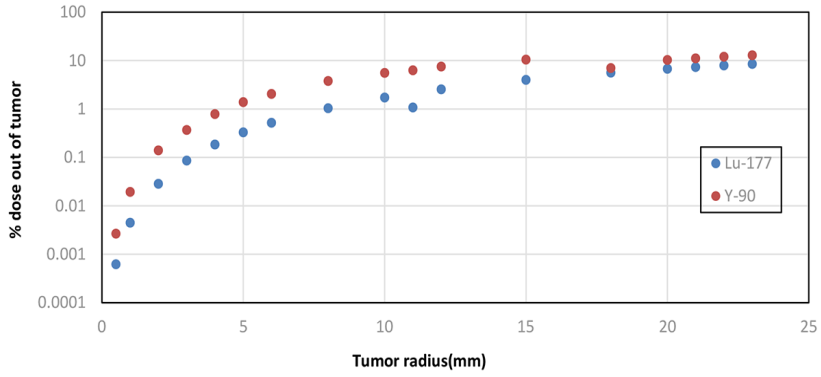

Figure 2: Graph of (Cross-dose/total-dose)*100 for different sizes of tumors.

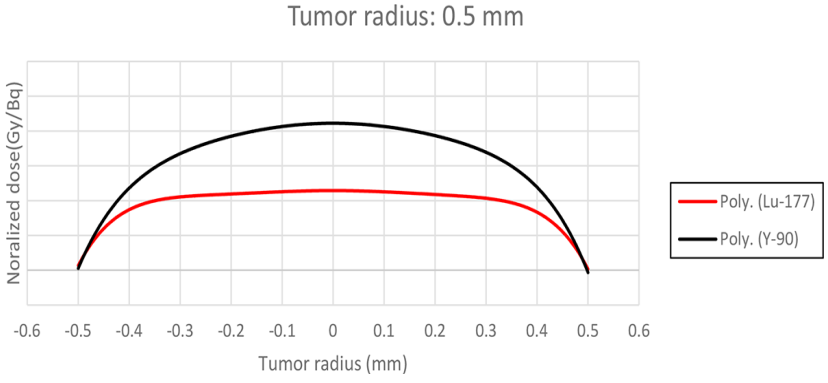

Figure 3: Dose profile of ^{90}Y and ^{177}Lu for 0.5 mm radius of tumor.

Table 4: Dose flatness inside the tumors for ^{177}Lu and ^{90}Y.

Radionuclide radius of tumors (mm)	^{90}Y	^{177}Lu
0.5	17.88	9.18
1	18.38	6.82
2	16.57	10.21
3	14.72	12.57
4	17.67	10.56
5	13.98	11.20
6	11.85	11.89
8	11.75	15.11
10	9.68	14.52
11	8.09	9.27
12	7.06	9.21
15	4.84	6.22
18	7.80	6.96
20	7.46	7.12

Discussion

For all tumors, the absorbed dose for ^{90}Y is more than ^{177}Lu, which because of the higher energy of beta particles in ^{90}Y compared to ^{177}Lu. This issue is in accordance with previous work such as Enger et al. [9] in 2008 and O. 'Donoghue et al. [13] in 1995.

Given that the absorbed dose profile was studied in the past, it seems that this parameter and the absorbed dose uniformity of the tumor can help to improve the treatment planning of radionuclide therapy.

Our study examined the absorbed dose uniformity and concluded that the flatness of ^{177}Lu is better than ^{90}Y, i.e. the absorbed dose variation for ^{177}Lu is less than ^{90}Y, and ^{177}Lu delivers a more uniform absorbed dose to the entire tumor volume and ultimately improves tumor treatment.

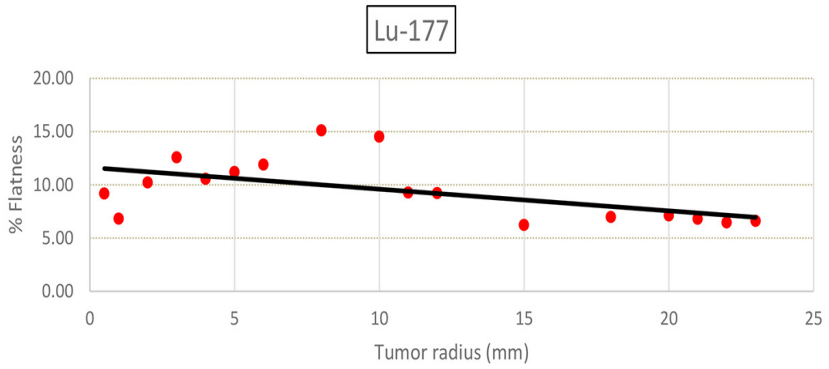

Figure 4: Dose flatness for ^{177}Lu as a function of tumor radius.

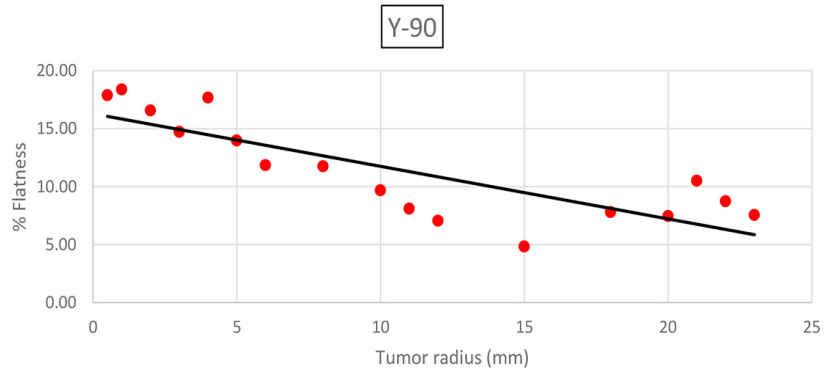

Figure 5: Dose flatness for ^{90}Y as a function of tumor radius.

Table 5: Pearson coefficient values and significant levels for correlation of absorbed dose uniformity with tumor radius for ^{177}Lu and ^{90}Y.

Radionuclide	Pearson coefficient	sig
^{177}Lu	-0.599	0.014
^{90}Y	-0.820	0.000

Figures 4 and 5 show the absorbed dose uniformity values inside the tumors for ^{177}Lu and ^{90}Y. Also, for determining the amount of uniformity improvement with increasing tumor size, Pearson coefficient values (showing the graph's slope) with a significant value are shown in Table 5. It is observed that with increasing tumor size, the absorbed dose uniformity of ^{177}Lu and ^{90}Y radionuclides improves, and it is noteworthy that the rate of ^{90}Y absorbed dose uniformity improves greater than that of ^{177}Lu. DVH can also be used to examine treatment planning in radionuclide therapy [12].

In our study, we also have drawn DVH curves for ^{177}Lu and ^{90}Y in all tumors. By evaluating the DVH curves, it can be realized that ^{177}Lu is more suitable than ^{90}Y for smaller tumors because ^{177}Lu transfers the energy of the beta particles to the larger space of the small tumors.

^{90}Y transfers a higher dose to the tumor, while covers less volume of the tumor. Moreover, it seems that with increasing tumor size, the DVH curve improves for ^{90}Y. Thus, ^{90}Y can be used to treat larger tumors; however, it should be mentioned that using ^{90}Y causes a non-uniform dose within the tumor and increases the dose to surrounding organs.

According to the obtained results, ^{177}Lu has better dose uniformity and DVH than ^{90}Y for smaller tumors, and also delivers lower absorbed dose to outside area of the tumors. The disadvantages of ^{177}Lu are unfavorable DVH for larger tumors and delivers low absorbed dose in all tumors. The benefits of ^{90}Y are more tumor dose, and more favorable DVH for larger tumors, and its disadvantage is less absorbed dose uniformity and a more dose outside of the tumor.

In terms of the impact of tumor size on physical parameters in tumor therapy, we can conclude that by increasing tumor size: 1- the absorbed dose difference between ^{177}Lu and ^{90}Y decreases, 2- the absorbed dose flatness improves, and 3- the DVH diagram for ^{177}Lu and ^{90}Y worsens and improves, respectively.

By examining the parameters of self-absorbed dose, cross-absorbed dose, absorbed dose uniformity, and DVH diagram, the results of our work support the strategy of using

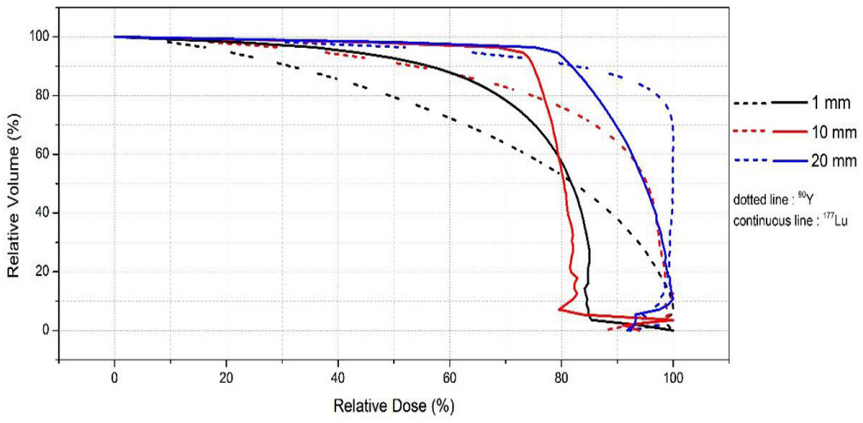

Figure 6: Relative dose volume histogram for tumors of 1, 10, and 20 mm in radius for ^{177}Lu, continuous line, and ^{90}Y, dotted line.

^{177}Lu and ^{90}Y for treatment of small and large tumors, respectively, in order to use the advantages of each radionuclide for better tumor treatment [4, 5, 16, 17].

Conclusion

In targeted radionuclide therapy, the physical parameters of self-absorbed dose, cross-absorbed dose, absorbed dose uniformity, and DVH diagram could be utilized to evaluate the treatment planning system. By examining these parameters, it can be concluded that ^{177}Lu and ^{90}Y are appropriate for smaller and larger tumors, respectively. In addition, we can evaluate the appropriate cocktail of these radionuclides, in terms of the type of composition, for the treatment of tumors with a specific size.

Conflict of Interest

None

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