Dosimetry and prescription in liver radioembolization with ^{90}Y microspheres: 3D calculation of tumor-to-liver ratio from global ^{99m}Tc–MAA SPECT information

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Abstract

Dosimetry in liver radioembolization with ^{90}Y microspheres is a fundamental tool, both for the optimization of each treatment and for improving knowledge of the treatment effects in the tissues. Different options are available for estimating the administered activity and the tumor/organ dose, among them the so-called *partition method.* The key factor in the partition method is the tumor/normal tissue activity uptake ratio (*T/N*), which is obtained by a Single-Photon Emission Computed Tomography (SPECT) scan during a pre-treatment simulation. The less clear the distinction between healthy and tumor parenchyma within the liver, the more difficult it becomes to estimate the *T/N* ratio; therefore the use of the method is limited. This study presents a methodology to calculate the *T/N* ratio using global information from the SPECT. The *T/N* ratio is estimated by establishing uptake thresholds consistent with previously performed volumetry. This dose calculation method was validated against three-dimensional voxel dosimetry, and was also compared with the standard partition method based on freehand regions of interest (ROI) outlining on SPECT slices. Both comparisons were done on a sample of 20 actual cases of hepatocellular carcinoma treated with resin microspheres. The proposed method and the voxel dosimetry give very similar results. Differences are found in several cases when comparing with results derived from the ROI method. Differences in the *T/N* ratio imply more difference in tumor dose that in normal liver dose. Dispersion of values is greater in the ROI-based method than in the other two. The process is very simple and avoids the subjectivity inherent to manual distinction between tumor/normal liver tissue interfaces. Dosimetry results obtained with the new method are equivalent to those provided by voxel dosimetry. Compared to the use of ROIs, it also provides greater simplicity and – most importantly – greater reproducibility.

Keywords: Radioembolization, Microspheres, Partition Method, Y90 dosimetry

Introduction

Transarterial liver radioembolization (TARE) is a form of nuclear medicine radiotherapy in which microspheres loaded with yttrium-90 are delivered to the tumor via the hepatic artery. It leverages the liver's dual blood supply to deposit a large quantity of radiation dose to the tumor without damaging the healthy parenchyma. The administered activity and the dose estimation are determined during a pre-treatment simulation involving the administration of macroaggregated albumin marked with ^{99m}Tc (^{99m}Tc -MAA), carried out according to the planned treatment, and in an immediately subsequent SPECT scan (Dezarn *et al.*, 2011).

In the case of resin spheres, the prescription methods currently available are: (I) Empirical Method, not personalized and already in disuse; (II) Body Surface Area (BSA) method, which includes patient size and liver size in an empirical equation for the calculation of activity, but does not take into account the absorbed dose; (III) Partition Method, which considers the different uptake of healthy and diseased tissue *(Ho et al., 1996; Sirtex SIR-Spheres® Package Insert; Kennedy et al., 2012).*; and finally (IV) Three-Dimensional (3D) Dosimetry, which has several possibilities in development, although it is still not widespread in practice and little clinical data is available (Dezarn *et al.*, 2011; O'Doherty, 2015). The latter two are based on the MIRD schema, so they are not only prescription methods but also dose estimation methods. This dose estimation is needed to obtain a personalized prescription and treatment planning in nuclear medicine therapy and is becoming increasingly demanded (Chiesa *et al.*, 2017). Given that 3D dosimetry is not quite established in routine clinical practice, the most sophisticated method in use is usually the partition method, and it is increasingly prevalent in hospitals throughout the world. The resin microspheres manufacturer (SIR-Spheres®, Sirtex Medical) suggests using the partition method in especially favorable anatomies (Sirtex *SIR-Spheres®* Package Insert). The Partition method is described and validated for cases where it is possible to clearly identify the border between the healthy parenchyma and the tumor (Ho *et al.*, 1996; Ho *et al.*, 1997a; Ho *et al.*, 1997b).

To perform the calculations, it is necessary to know: (I) lung shunt fraction (*LSF*), fraction of the activity injected into the patient that migrates to the lungs; (II) liver and tumor masses, obtained by volumetry in radiological imaging, (III) lung mass, usually replaced by the standard value of 1 kg; and (IV) the tumor/normal tissue ratio (*T/N*), as defined in equation (1)(Dezarn *et al.*, 2011; Sirtex *SIR-Spheres®* Package Insert; Giammarile *et al.*, 2011; Gulec *et al.*, 2006).

$$T/N = \frac{\left(\frac{A_{Tumor}}{m_{Tumor}}\right)}{\left(\frac{A_{NormalLiver}}{m_{NormalLiver}}\right)} \quad (1)$$

Where A_{Tumor} and $A_{NormalLiver}$ are tumor and healthy liver activity, and m_{Tumor} and $m_{NormaLiver}$ are the masses of the tumor and the healthy liver, respectively.

No single benchmark method exists to calculate the *T/N* ratio (Arbizu *et al.*, 2014), and recent proposals of objective observer-independent methods are conditioned by segmentation(Garin *et al.*, 2012; Lam *et al.*, 2015; Kao *et al.*, 2012; Garin *et al.*, 2013). In the standard procedure a comparison between the quotient defined in equation (1) and a normalized ratio of counts of two regions or volumes of interest on the SPECT images was performed, including tumor and healthy liver, respectively. This measure is manual and therefore presents a high degree of uncertainty, depending greatly on the criterion of the particular user performing this.

When both the partition and BSA methods are applicable, the former is considered a better choice, but presents serious limitations which impede its widespread use(Kao *et al.*, 2011). It is customary to employ the partition method only in patients selected for presenting especially clear healthy-diseased parenchyma interfaces. Only experience and knowledge of the equations of the model, its meaning and its scope, can determine the most appropriate method for each patient.

This study presents a new method, based on the partition method, by estimating the *T/N* ratio from the global information provided by the gamma camera imaging of ^{99m}Tc -MAA. The validity of the new method was studied in cases treated with radioembolization, comparing its results against those obtained through 3D dosimetry at the voxel level.

Methods

Estimating the tumor/normal tissue uptake ratio

In a practical way, *T/N* ratio it is often likened to the ratio of SPECT counts per unit surface area or volume, between tumor and normal liver (Dezarn *et al.*, 2011). For a 3D analysis, distinction between healthy and diseased tissue is needed, but this is complex on both a conceptual and technical level. For the method proposed herein, segmentation based on the SPECT count thresholds is considered valid. All voxels with counts below a lower threshold T_l are identified as nonirradiated region; voxels with counts

above an upper threshold T_2 are identified as tumor; and the rest, located between the two thresholds, is identified as treated healthy liver.

The SPECT voxel value spectrum, between a minimum (m) and a maximum (M), on an arbitrary scale, is defined by the parameters of acquisition and reconstruction. It is assumed that each voxel number of counts is proportional to the ^{90}Y activity deposited in it. This way, total counts of the study correspond to the total administered activity. Similarly, the sum of counts of all the voxels with $T_1 \leq i < T_2$ corresponds to the activity in the normal liver, and the sum of counts of all the voxels with $i \geq T_2$ corresponds to the activity in the tumor. The grey level histogram of the 3D matrix shows the frequency of voxels, f_i, that are assigned each value of spectrum i, from $i=m$ to $i=M$ (figure 1). Thus, the sum of counts of a range (a, b) is:

$$Counts(a,b) = \sum_{i=a}^{b} i \cdot f_i \tag{2}$$

Given that the sum of counts in each voxel is proportional to the activity contained in it, where k is the proportionality constant, the activity in the volumes of interest can be determined:

$$A_{Total} = k \cdot \sum_{i=\mathrm{m}}^{M} i \cdot f_i \tag{3}$$

$$A_{NormalLiver} = k \cdot \sum_{i=T_1}^{T_2-1} i \cdot f_i \tag{4}$$

$$A_{Tumor} = k \cdot \sum_{i=T_2}^{M} i \cdot f_i \tag{5}$$

Knowing the voxel volume, V_{voxel}, and the number of voxels between the thresholds, healthy liver and tumor volume can be expressed as:

$$V_{NormalLiver} = V_{voxel} \cdot \sum_{i=T_1}^{T_2-1} f_i \tag{6}$$

$$V_{Tumor} = V_{voxel} \cdot \sum_{i=T_2}^{M} f_i \tag{7}$$

Optimal thresholds for each patient were chosen so as to verify equations (6) and (7). That is, threshold values were selected so that the volume of all the voxels with counts over T_1 and T_2 include the volume obtained in the previous liver and tumor volumetry, respectively.

On first approximation, the mass densities of the tumor and the healthy parenchyma can be considered equal. This allows for the identification of the ratio of masses from the *T/N* definition in the ratio of the volumes defined in equations (6) and (7). When applying the theoretical definition of the *T/N* ratio (equation (1)), the 3D *T/N* uptake ratio, T/N_{3D}, can be defined as:

$$T/N_{3D} = \frac{\left(\frac{\sum_{i=T_2}^{M} i \cdot f_i}{V_{voxel} \cdot \sum_{i=T_2}^{M} f_i} \right)}{\left(\frac{\sum_{i=T_1}^{T_2-1} i \cdot f_i}{V_{voxel} \cdot \sum_{i=T_1}^{T_2-1} f_i} \right)} \quad (8)$$

The T/N_{3D} estimation method should be valid in all cases for which the following conditions are verified: (I) clear uptake of activity throughout the entire liver or in one of lobes; (II) the most marked uptake foci located in the areas with tumor presence in diagnostic imaging; and (III) absence of significant extrahepatic leaks.

The T/N_{3D} ratio thus calculated does not differ conceptually in any respect to the *T/N* ratio commonly used in the partition method. It is simply a more realistic way of calculating the parameter, which is then included in the model's dose calculation without modification.

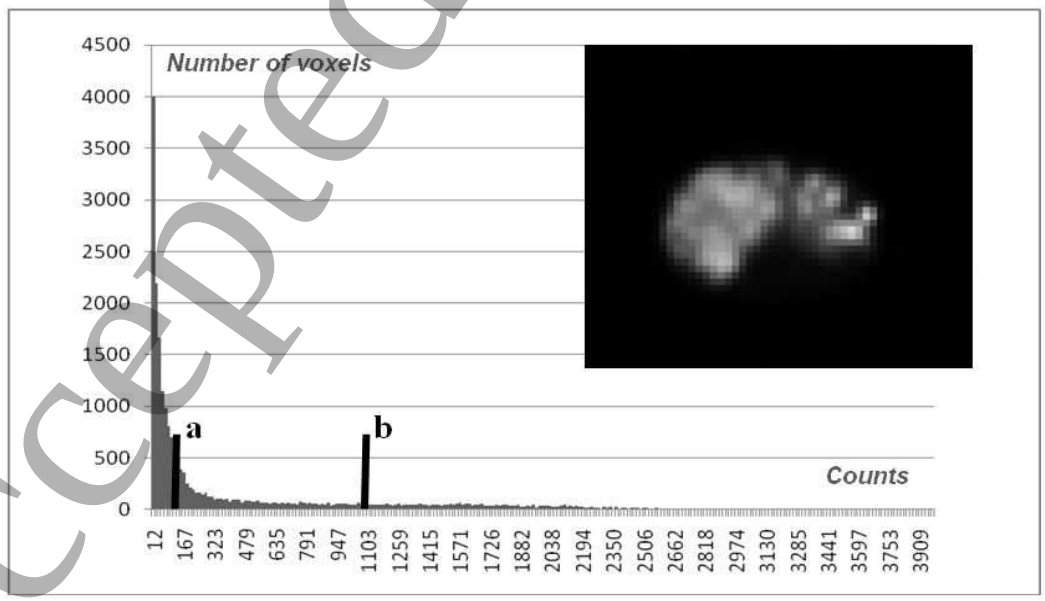

Figure 1 Grey level histogram of ^{99m}Tc-MAA SPECT image (axial slice shown in upper right inset). Vertical lines mark the range of values (a, b) in which the sum of counts should be obtained.

Selected cases

The proposed calculation method was implemented retrospectively in a group of 20 cases of hepatocellular carcinoma treated with resin spheres at our centre between August 2011 and October 2015. For comparative purposes, the *T/N* ratio was estimated for this group with two other methods (ROI drawing on axial slices of SPECT and with voxel dosimetry). Only cases for which the tumor was sufficiently identifiable as to calculate the *T/N* ratio using ROIs in a reliable manner were selected. Table 1 shows the characteristics of the 20 cases that met the criteria.

Case	$V_{Total\ Liver}$ (cm^3)	V_{Tumor} (cm^3)	*LSF*
1	1490	25	11%
2	1399	189	4%
3	863	52	8%
4	863	52	5%
5	1056	20	2%
6	2538	8	6%
7	2050	28	3%
8	1248	4	3%
9	1327	10	6%
10	1845	355	3%
11	1356	15	7%
12	772	115	7%
13	1027	15	8%
14	1683	17	8%
15	1006	10	6%
16	1385	30	2%
17	1907	38	7%
18	1407	47	6%
19	1427	77	7%
20	1107	172	10%

Table 1 Anatomical data of selected cases for *T/N* and dose calculation.

SPECT-CT acquisition was conducted using an Infinia Hawkeye 4 (General Electric Healthcare) model dual-head gamma camera. LEHR (Low Energy High Resolution) collimators were used, and ^{99m}Tc energy peak was selected. 64 projections (64 x 64, 25 s per projection) were acquired. Attenuation correction was applied. Images were reconstructed with the OSEM (ordered subset expectation maximization) algorithm. Liver and tumor volumetry were carried out using the diagnostic CT scans. Lung shunt fraction was calculated based on planar gamma camera imaging according to the standard procedure (Dezarn *et al.*, 2011; Giammarile *et al.*, 2011).

Comparison between methods

In the new method proposed in this study, the T/N_{3D} ratio was calculated using the 3D voxel matrix of SPECT, according to the definition of equation (8). Each voxel belongs to one and only one of the three distinct subsets: tumor voxels, healthy liver voxels and all other voxels. The thresholds which verified the conditions established by equations (6) and (7) were chosen to delimit the subsets, T_1 and T_2, respectively. Optimal thresholds were obtained for each patient by an iterative computation process as explained below:

An initial test threshold t_0 was established as the maximum value of the spectrum *(M)*. Next, a test liver volume V_0 was computed by summing up the volume of all the voxels with counts $i > t_0$ and a comparison with the known volume $V_{TotalLiver}$ was made. Successive test thresholds t_j were then selected and associated test volumes V_j were calculated for the next iterations:

$$t_j = t_{j-1} + (M/2^j) \quad \text{if} \quad V_{j-1} < V_{TotalLiver} \tag{9}$$

$$t_j = t_{j-1} - (M/2^j) \quad \text{if} \quad V_{j-1} > V_{TotalLiver} \tag{10}$$

After *"n"* iterations (being *n* the number of the image bits), the definitive liver volume $V_n = V_{TotalLiver}$ was obtained, from which the optimal threshold $T_1 = t_n$ was established. The same process was repeated for achieving a T_2 threshold to fit a known tumor volume (V_{Tumor}). Both the T/N_{3D} value and its corresponding threshold were computed with in-house software specifically developed to this end with the Python programming language (Python Software Foundation).

The second way of estimating the *T/N* ratio was the traditional method using ROIs (T/N_{ROI}). The counts in 5 ROIs representative of healthy tissue and another 5 with tumor foci were measured on axial slices of the SPECT.

The third way to estimate the *T/N* ratio was the voxel S-value approach (VSV), carried out using a convolution of the ^{99m}Tc-MAA activity matrix with a kernel for ^{90}Y, in accordance with the following equation (Dezarn *et al.*, 2011; Bolch *et al.*, 1999):

$$\mathbf{D} = \tilde{\mathbf{A}} \otimes \mathbf{K} \tag{11}$$

Where $\mathbf{D}$ is the absorbed dose matrix, $\tilde{\mathbf{A}}$ is the matrix of accumulated activity obtained from the ^{99m}Tc-MAA, and **K** is the spatial distribution of *S* factors at the voxel level, which acts as the convolution kernel. The count transformation in activity is performed by normalizing the value of each voxel (C_i) with respect to the total counts in the treated liver, according to the equation (12) (Sarfaraz *et al.*, 2004):

$$A_i = A_{Total} \frac{C_i}{(C_{Total} - C_{Background})} \tag{12}$$

Where A_i is the administered activity in each voxel, A_{Total} is the total activity in the liver (administered activity minus lung shunt), C_{Total} is the sum of counts of all SPECT voxels, and $C_{Background}$ is the sum of counts of all voxels outside the treated volume (i. e., outside the liver and tumor, including all the voxels outside the patient). The employed kernel was downloaded from the *S values for voxel dosimetry* online database(Lanconelli *et al.*, 2012). It was used corresponding to ^{90}Y with a spacing of 2.21 mm. Manipulation of DICOM files, transformation of counts in accumulated activity and convolution were carried out with in-house software developed with the Python programming language(Mañeru *et al.*, 2015). Once the spatial dose distribution was known, the tumor was identified by locating the area with the highest dose until the known tumor size was reached. Of the remaining volume, the normal liver was identified, in turn, by locating the area with the highest dose until the healthy parenchyma size was reached. The calculation of the *T/N* (T/N_{VSV}) ratio is reduced to the quotient between the mean dose in the tumor and in the healthy liver.

Voxel dosimetry was considered the most reliable of the three methods of dose estimation, and so T/N_{VSV} was used as the reference in the comparison.

Results

The T/N_{3D} ratio was estimated according to the new method for the selected cases. Likewise, the *T/N* ratio was estimated using ROIs on the SPECT (T/N_{ROI}) and voxel dosimetry (T/N_{VSV}). Table 2 shows the thresholds and the *T/N* ratio values obtained. Relatively little spread can be seen in the *T/N* ratio values; the range of all the values of the three methods is between 1.7 and 7.5. VSV method has a range between

1.7 and 5.7, with an average value of 3.5. Eighty percent of the values are between 2 and 5, in accordance with both theoretical expectations and expectations based on comparison with other publications (Gulec *et al.*, 2009; Campbell *et al.*, 2009). The value obtained by the ROI method moves significantly away from the other two in a number of cases, although on average there is not much difference (3% difference between the 3D method and the VSV method, and 7% difference between the ROI method and the VSV method, in both cases providing a higher value). Figure 2 illustrates all this in a graph.

	Threshold		***T/N***		
Case	T_1	T_2	***3D***	***ROI***	***VSV***
1	1310	32700	5.71	7.50	5.68
2	1900	10700	2.84	2.45	2.72
3	5000	24000	2.54	2.02	2.46
4	4300	28500	2.71	2.93	2.64
5	1760	32760	4.14	5.69	4.11
6	680	10300	5.53	3.10	5.12
7	1265	7950	3.36	2.32	3.26
8	2025	16350	3.33	3.27	3.30
9	1765	9800	2.49	2.31	2.42
10	1218	5180	2.66	3.09	2.62
11	900	7900	4.88	3.58	4.65
12	1555	3515	1.91	2.08	1.88
13	2240	17500	3.71	3.18	3.50
14	1173	16100	4.76	4.85	4.66
15	2620	28000	4.63	4.79	4.49
16	1010	14850	3.67	4.62	3.47
17	815	11320	4.79	6.35	4.66
18	1510	10200	3.67	5.93	3.52
19	1150	9920	3.90	3.59	3.80
20	2865	6820	1.73	2.07	1.72

Table 2 Thresholds values used for the calculation of T/N_{3D} and values of the *T/N* ratio obtained through the three methods.

Knowing lung shunt, liver and tumor volumes and the *T/N* ratio, the partition method equations are used to immediately deduce the mean doses to the tumor and the healthy liver. Figures 3 and 4 contain the

dosimetry results with the new method and the two used for comparison, expressed in units of dose /activity (Gy/GBq).

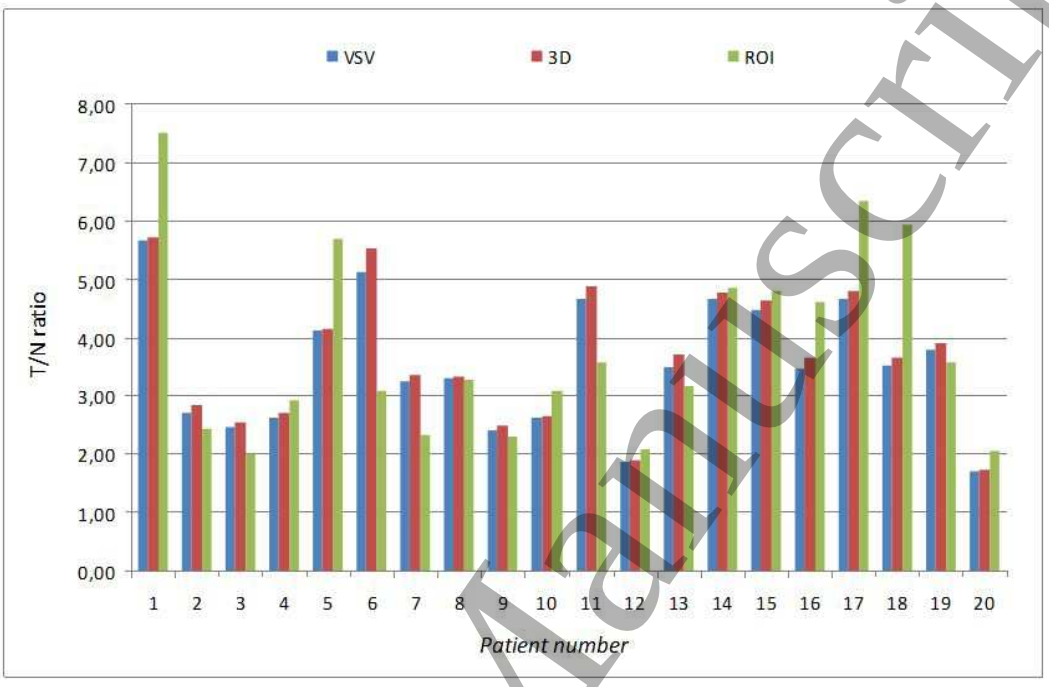

Figure 2 Values of the *T/N* ratio obtained in the three compared methods

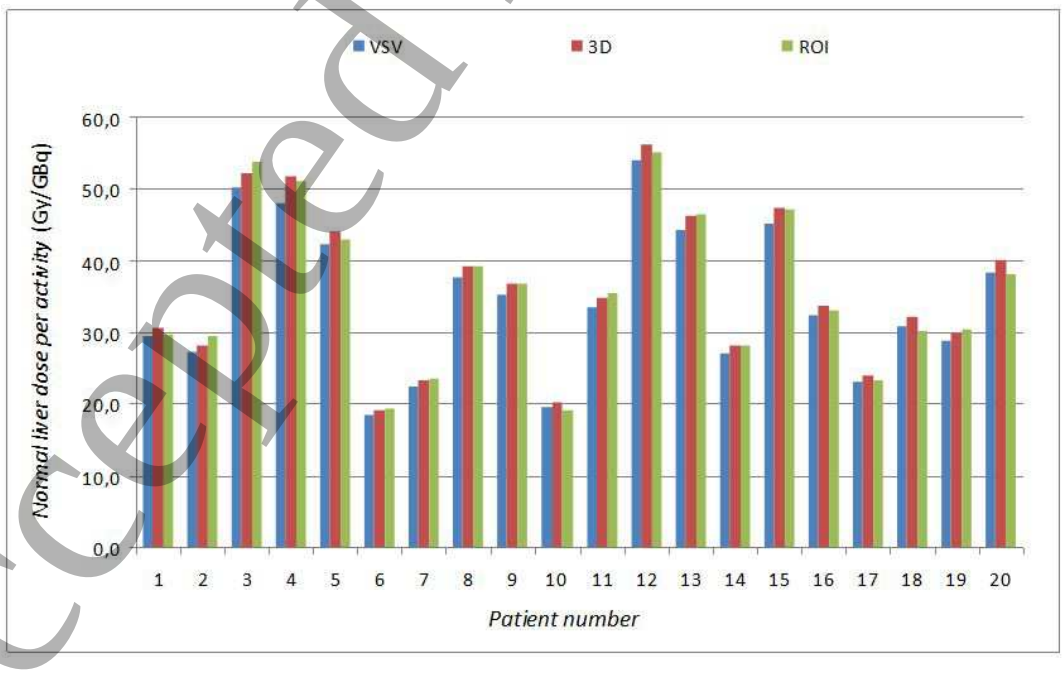

Figure 3 Dose per unit of ^{90}Y activity administered in healthy liver.

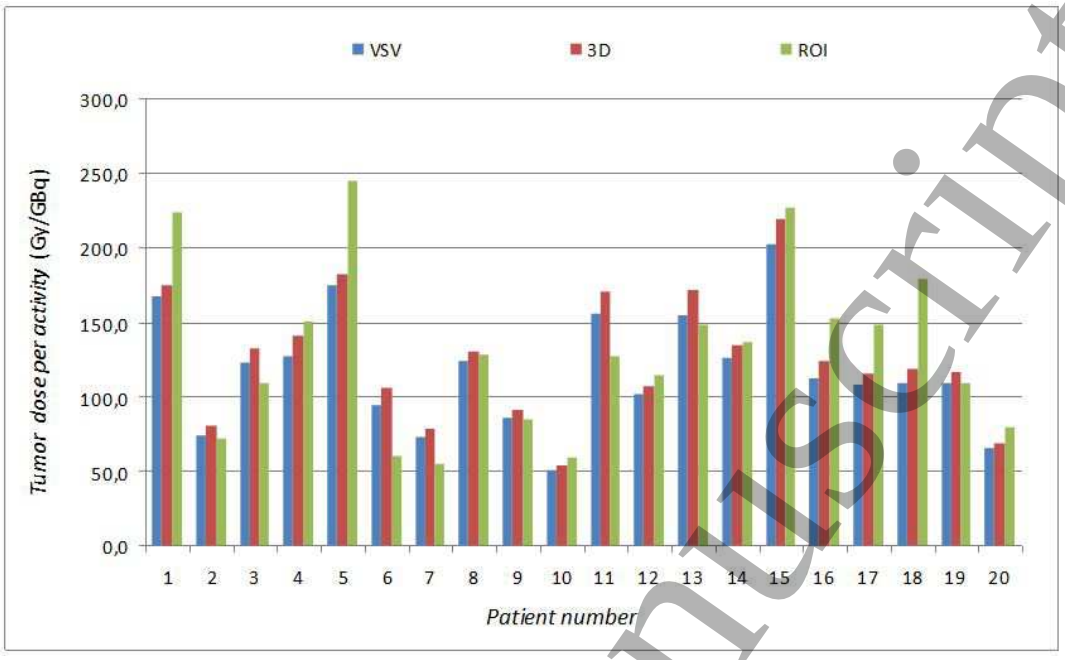

Figure 4 Dose per unit of ^{90}Y activity administered in tumor.

Discussion

The partition method assumes the validity of the simulation with ^{99m}Tc-MAA, although the identification of the behavior of the macroaggregates with that of the microspheres remains a controversial topic today (Ulrich *et al.*, 2013; Wondergem *et al.*, 2013; Lam *et al.*, 2015; Chiesa *et al.*, 2014). However, according to the current state of the art, there is no other alternative but to accept this equivalence, and it is considered generally valid (Garin, 2015; Braat *et al.*, 2015; Garin *et al.*, 2015).

The only current possibility for calculating the *T/N* ratio before treatment is by extracting the information from the ^{99m}Tc-MAA SPECT. The limitations of this simulation completely condition any calculation derived from it. The activity distribution in the liver is not uniform, consistent with the local differences of microsphere concentration. Different areas are supplied by different blood vessels, each with its own blood flow (Uliel *et al.*, 2012). Each lesion has a specific uptake, sometimes in different ways within the same patient. Even within large lesions, areas of different uptake appear due to the different vascularization or the lack thereof in the case of necrosis. This distribution, full of gradients and local maxima and minima, is not easy to simplify by dividing the total liver volume into 2 separate areas (healthy and sick). It is even more difficult to do so with a small number of ROIs, which should be identified with representative parts from both areas, excluding from the analysis the rest of the activity

map. Using these ROIs leaves aside most of the information contained in the SPECT, which is already limited in itself. Only a calculation of the *T/N* ratio using the complete SPECT, as proposed in this study, will include all the details provided by the ^{99m}Tc-MAA SPECT in the resulting value. In this way, the *T/N* ratio and the partition method can be brought to a higher level of accuracy. The mean dose values obtained will be as true to reality as the applied division between the healthy and diseased areas. For this work, this division was based on a previous volumetry derived from diagnostic CT images. However, other alternatives can also be considered. We believe that direct VOI drawing on SPECT-CT images presents several practical problems. A CT gamma camera cannot always provide images with the same quality as those obtained when diagnostic equipment is used. Registration between both CT images is possible, although a perfect anatomical coincidence is difficult: internal movements and changes in the position of the patient can result in significant differences. Nevertheless, the size of the liver and of the tumor will be the same despite liver deformations, and thus a reliable volumetry can be always taken as valid. The threshold selection from grey-level histograms is another possible alternative. The latter is a very useful segmentation technique in nuclear medicine imaging; unfortunately, the ^{99m}Tc-MAA SPECT images analysed in this work did not show any pattern as to allow the determination of a threshold value in the histogram. All these considerations led us to accept the volumetry data as a robust start point for segmentation.

The new partition method (based on T/N_{3D}) and the reference (T/N_{VSV}) give very similar results. The differences found, both in the *T/N* ratio and in the absorbed dose, are minimal compared to other uncertainties of the process. We therefore present the T/N_{3D} ratio calculation as a very reliable method for estimating the mean dose. A detailed analysis of the results shows that the T/N_{3D} ratio is slightly higher than T/N_{VSV} in all cases. To some extent, this could be due to the difference caused by using the local energy deposition approach respect instead of a convolution method (Pasciak *et al.*, 2014). The use of the partition method (T/N_{3D}) implies acceptance of local deposition, and consequently does not consider the difference between a defined tumor focus and several dispersed foci. In the first case, the high uptake voxels would be near each other, and the dose scattered from these areas would contribute mainly to the rest of the next high activity voxels. In contrast, in the case of dispersed foci, a greater number of high activity voxels would contribute to the dose in the voxels considered to be healthy tissue. The size of the tumor, the tumor grouping or dispersal and the voxel size are factors that would determine the amount of this effect, which is not easy to model. The partial volume effect will therefore be different for different

distributions of activity. On the other hand, the way to estimate the background in the voxel dosimetry calculation (equation (12)) introduces a normalization in the calculation of the dose distribution that can also have an influence on this systematic difference between the value pairs of the *T/N* ratio.

It also shows that, on average, $T/N_{3D} < T/N_{ROI}$, being the most marked difference in cases in which the standard method offers higher values for the *T/N* ratio. The cause of this behavior should be associated with the characteristics of the tumor distribution, but a cause-effect relationship between the initial data (administered activity and tumor and organ volumes) and this difference has not be found. Given that it is more pronounced in cases with a higher value for T/N_{ROI}, it seems reasonable to ascribe this deviation to the limitations of the ROI-based method in more extreme cases. Because of this, a more accurate tumor dose estimation should be expected when using this method.

We have seen that the major differences in the T/N ratio do not necessarily imply appreciable differences in the dose to the healthy liver, while the values of the dose to the tumor are more influenced by the variation of the T/N ratio. This suggests that any errors in the estimation of the T/N ratio can have significant influence in the calculation of doses to the tumor but little influence in the calculation of doses to healthy tissue. The risk of toxicity in normal hepatic tissue is the main parameter determining the administered activity in patients who undergo radioembolization. With this in mind, it may seem that the proposed method does not improve the accuracy of normal liver dose; however, the comparison with the standard T/N estimation was performed only in special cases (those for which the drawing of the ROI is feasible). The potential candidate cases for using the described methodology are all those that comply with conditions (I), (II), and (III), that is, more than the ones that are normally considered suitable for the use of the partition method. A better understanding on the absorbed dose in tumor and healthly liver will enable more personalized treatments. A growing number of patients for whom the alternative is the BSA method could benefit with such a personalized treatment planning via the partition method.

The dispersion of values of any of the three dosimetric parameters, represented by the standard deviation is greater in the ROI-based method than in the other two. It is thus clear that the dose data calculated from T/N_{ROI}, in addition to deviating more from the reference value, are less reproducible than those calculated from T/N_{3D}. This is particularly striking when applying the ROI method in such a controlled manner as was done in this study, where a uniform criterion was followed to contour ROIs. Different people, in different centers, with different tools, will increase the real dispersion in the estimate of T/N_{ROI}. In this context, the presented method for estimating the tumor-to-liver uptake ratio as T/N_{3D} is extremely

reproducible, because it only has the liver and tumor volumes as variables. It is true that they are not always easy to measure, but that challenge is also present in the standard ROI method (Ilhan *et al.*, 2015). More reproducibility is a great advantage since it shortens the learning curve, prevents human error and allows for a more reliable exchange of data between centers.

Implicitly, using the new method based on T/N_{3D} implies accepting tumor and liver segmentation based on uptake thresholds in the ^{99m}Tc-MAA SPECT. The delimitation of volumes from thresholds has a very solid conceptual foundation in the field of radioembolization; the requirement that the areas of higher uptake coincide with the areas of the highest tumor activity is precisely one of the reasons this therapy is effective (Kao *et al.*, 2012; Uliel *et al.*, 2012). The other major requirement, the absence of extrahepatic leaks, is a cause of contraindication for the treatment, for which reason it is also a fully justified condition (Lau *et al.*, 2012; Kennedy *et al.*, 2007). In the case of existing low uptake necrotic zones, the method proposed here is an advantage since the calculation does not ever include them in the tumor (and not even in the healthy liver if signal is small enough).

The described method is based on the ^{99m}Tc-MAA as a surrogate of the behavior of the microspheres, but this does not preclude it from being similarly applicable to the post-treatment dosimetry based on PET (Braat *et al.*, 2015; Srinivas *et al.*, 2014; Pasciak *et al.*, 2014).

Conclusion

We present a new method for calculating the activity uptake ratio between the tumor and the healthy tissue, taking into account the full influence of the SPECT scan prior to treatment. The results obtained with this method, in terms of mean dose in tumor and liver, are comparable to those achieved with the VSV method which can be considered as a reference. If the prescription of treatment is performed using the mean dose in the tumor, as is usually done in practice, the simplicity and reproducibility of the proposed method makes it an excellent option for calculating the administered activity.

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