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Effect of tumour involvement on activity determination of resin Yttrium-90 in selective internal radiation therapy of metastatic liver cancer

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Technical Note

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Abstract

Introduction: The study was aimed to evaluate the effect of tumour involvement on resin Yttrium-90 (Y90) activity determination for metastatic liver cancer treatment.
Methods: One hundred and two cases of resin Y90 microsphere treatment were retrospectively studied. Body surface area (BSA) method was used in the calculation of resin Y90 activity. The total activity (*TA*) was calculated as a summation of activities obtained from BSA-based calculation and tumour involvement (*TI*). *TI* and *TA* of each case were evaluated. The contributions of *TI* to *TA* were calculated with the ratio of *TI*/*TA*.
Results: The average contribution of *TI* to *TA* was 4·1%. The contributions were < 5·8% in 75% of the cases, < 2·2% in 50% of the cases and < 1·0% in 25% of the cases.
Conclusions: Overall the effect of tumour involvement on the activity determination was small. The activity calculation could be simplified by neglecting *TI* in 25% of the cases where the activity contribution from *TI* was less than 1%. Contouring tumour and liver structures for *TI* calculation could be avoided in these cases, and the efficiency of the workflow for resin Y90 procedures could be improved.

Introduction

Radioembolisation using Y90 microspheres, i.e., selective internal radiation therapy (SIRT), is a promising treatment modality for liver cancer treatment.[1] Glass based Y90 microsphere (Therasphere™, Boston Scientific, Boston, USA) was approved by the Food and Drug Administration as Humanitarian Device for treating hepatocellular carcinoma, as a neoadjuvant to surgery or transplantation.[2] Resin-based Y90 microsphere (SIR-Spheres™; Sirtex Medical Limited, NSW, Australia) was approved by the Food and Drug Administration for treating colorectal metastases.[3]

In resin based Y90 procedures, body surface area (BSA) method or partition model method is often used to determine resin Y90 activity for a treatment.[3–7] Although more advanced dosimetric methods have been proposed,[7–9] the BSA method, a semi-empirical method, because of its simplicity, is popularly used for resin Y90 procedures.

In the BSA method, Y90 activity is determined by two components: the BSA and tumour involvement. The BSA is calculated with a patient's height and weight, and the tumour involvement is calculated as the ratio between tumour volume and liver volume. To obtain the volumes, tumour and liver structures need to be contoured on 3D images (e.g., CT or MR). The contouring process usually is time-consuming, especially in the cases where there are multiple small tumours. In our institution, multi-departments are involved in Y90 procedures. Efficiency of Y90 procedure workflow (from activity calculation to delivery) often relies on the activity calculation process. In an emergent case, a quick turnaround from activity calculation to treatment delivery is needed. It is of interest to investigate how significant the contribution of tumour involvement is to the activity determination.

In this paper, a retrospective study was conducted to investigate the effect of tumour involvement on resin Y90 activity determination.

Methods

One hundred and two clinical cases were included in the study. The patients were treated in our institution in recent years. In our practice, the resin Y90 activities were determined using the BSA method. The activity (total activity *TA*) was calculated as[4]

$$TA(GBq) = BSA - 0.2 + TI \quad (1)$$

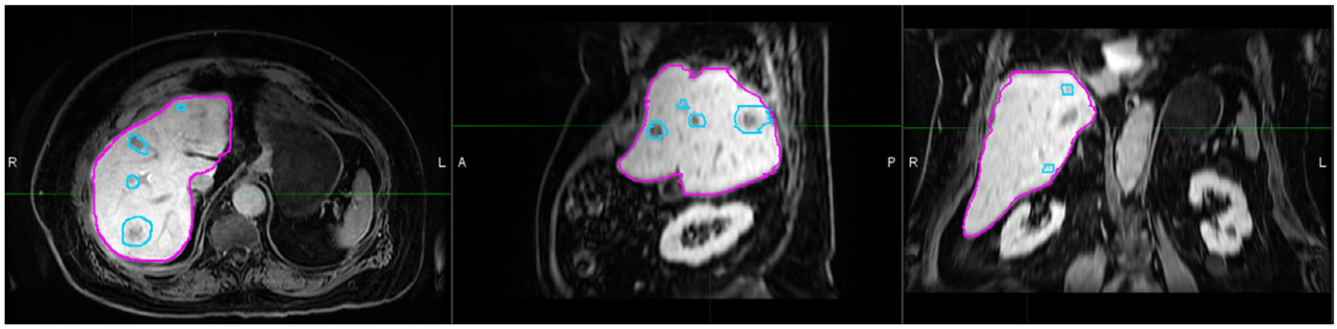

Figure 1. Tumour (cyan) and liver (magenta) structures contoured for activity calculation. The contribution of *TI* to total activity *TA* was 1% in this case.

where

$$BSA(m^2) = 0.20247 \times H(m)^{0.725} \times W(kg)^{0.425} \quad (2)$$

TI is tumour involvement, *H* is patient height (m) and *W* is patient weight (kg).

$$TI = \frac{V_T}{V_L} \quad (3)$$

V_T and V_L are tumour volume and liver volume, respectively. When *TI* is applied in Eq. (1) as a component of the TA, it has the unit of GBq.

In our practice, tumour and liver structures were contoured by oncologists on MR or CT images in MIM software (MIM Software Inc., Cleveland, OH, USA). The volumes were calculated in MIM. To limit normal liver dose and lung dose, a reduction factor F_{total} was applied to the TA. The default value was 25%. The treatments were lobar treatments. Y90 activities for each lobe (right or left lobe) treatment was calculated with *TA*, F_{total} and a lobe reduction factor F_{lobe}.

$$A(GBq) = TA \times (1 - F_{total}) \times (1 - F_{lobe}) \quad (4)$$

For a right lobe treatment, a lobe reduction factor of 30% was applied to the calculation. For a left lobe treatment, a lobe reduction factor of 70% was applied. The lobe reductions were made based on the approximation that right lobe and left lobe account for approximate 70% and 30% of liver volume (mass), respectively.

The partition model[4] was used to estimate normal liver dose D_{Liver} and lung dose D_{Lung}:

$$D_{Liver}(Gy) = \frac{49.67 \times \left(1 - F_{Lung}\right) \times A}{M_{iver} + M_{Tumor} \times (R - 1)} \quad (5)$$

$$D_{Lung}(Gy) = \frac{49.67 \times A \times F_{Lung}}{M_{Lung}} \quad (6)$$

F_{Lung} is lung shunt fraction, M_{Liver} and M_{Tumour} are total liver mass and tumour mass, respectively, and *R* is the uptake ratio of tumour and normal liver. F_{Lung} and *R* were obtained from Nuclear Medicine technetium-99m macro-aggregated albumin (^{99m}Tc MAA) studies. M_{Liver} and M_{Tumour} were calculated with liver volume and tumour volume, with an assumed density of 1·03 g/cm^3.[3,10] M_{Lung} was assumed to be 1 kg.[3]

Y90 is a daughter product of Sr90. Metyko et al's study[11] showed that the measured activity ratio between Sr90 and Y90 in SIR-Spheres was ~3×10^{-9}. The content of Sr90 in SIR-Spheres is negligible. Dose contribution of SIR-Spheres is primarily from Y90.

In our practice, tolerance doses of 35 Gy for liver and 8 Gy for lung were used. The tolerance doses were dose limits considered in the activity determination to limit the Y90 activity to avoid causing toxicities in the liver and lung. They were defined based on the literature recommendation[12] and our institutional discussion. Lau et al recommended the dose limits of 50 Gy and 20 Gy to normal liver and lung, respectively.[12] Considering that a default 25% reduction was applied to the calculated activity in our SIRT procedures, we used 35 Gy as the normal liver dose limit for a whole liver. We used a lower lung dose limit 8 Gy in our SIRT procedures. If accumulated normal liver dose and lung dose (i.e., the doses accumulated from both right lobe and left lobe treatments) were within the tolerances, the calculated activity *A* was then used for the treatment. If any of the doses exceeded the tolerances, the reduction factor F_{total} was adjusted to lower the dose to be within the tolerances.

To study the effect of *TI* on activity determination, we evaluated the *TI* and *TA* in the 102 cases. The ratio of *TI*/*TA* was calculated, which reflected the contributions of *TI* to *TA*.

Results

Figure 1 shows tumour (cyan) and liver (magenta) contours delineated in MR images in a case. Each tumour was contoured and all tumour volumes were added up to generate a total tumour volume. The total tumour volume and liver volume were used in the activity calculation. Although there were multiple tumours in this case, the *TI* was only 0·02. In the activity calculation, the contribution of *TI* to *TA* was only 1%.

Figure 2 shows a boxplot of *TI* and *TA* of the 102 cases. *TI* ranged from 0·003 to 0·383 GBq (mean: 0·075; standard deviation: 0·086), and *TA* ranged from 1·276 to 2·577 GBq (mean: 1·786; standard deviation: 0·259). Overall, the magnitudes of *TI* were very small compared to *TA*.

Figure 3 shows a boxplot of ratio of *TI* and *TA*. Among the 102 cases, the contributions of *TI* to *TA* ranged from 0·2% to 22·2%, with an average contribution of 4·1% (standard deviation 4·4%).The contributions were less than 5·8% in 75% of the cases, less than 2·2% in 50% of the cases, and less than 1·0% in 25% of the cases.

Table 1 lists the statistical results.

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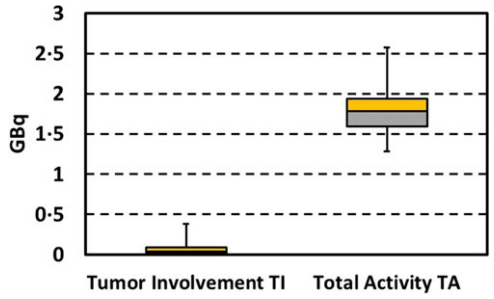

Figure 2. Tumour involvement *TI* and total activity *TA* of 102 cases.

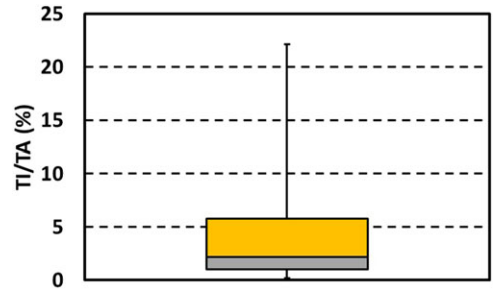

Figure 3. Ratio of tumour involvement *TI* and total activity *TA*, *TI/TA*, of 102 cases.

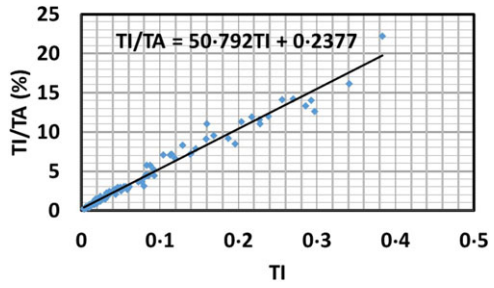

Figure 4. *TI/TA* as a function of *TI*.

Discussion

In the BSA method, tumour and liver structures need to be contoured in order to calculate *TI* for determining *TA*. Our study showed that in 25% of the 102 cases studied, *TI* contributed less than 1% to the *TA*. It is implied that the BSA method could be simplified, that is, *TI* could be neglected in the activity calculation in these cases, and contouring tumour and liver structures, which was time-consuming, could be avoided.

In our institution, multi-departments are involved in Y90 procedures: radiation oncologists contour tumour and liver structures for determining tumour involvement, medical physicists calculate Y90 activity using a patient's height and weight and tumour involvement, a lab prepares resin Y90 microsphere vials for treatment following a prescription based on the activity calculation, and interventional radiologists deliver the treatment. The efficiency of the procedure workflow (from activity calculation to delivery) often relies on the activity calculation process, which relies on the contouring process for tumour involvement determination. In emergent cases, a quick turnaround from activity calculation to treatment delivery is needed. If the structure contouring could be avoided with minimal activity deviations (< 1%) in an emergent case, the activity determination process could be expedited and the efficiency of the workflow for resin Y90 procedures could be improved. In the emergent cases where the volume contouring is avoided, lung dose still can be estimated because the lung dose calculation does not involve the liver and tumour volumes. In our practice, patients have treatments to right lobe and left lobe, respectively. The two treatments are about one month apart. If the volume contouring is avoided due to emergency (it will be in the first treatment if it happens), the liver and tumour will be contoured after the emergent procedure to estimate the normal liver dose of the first treatment. The activity of the second treatment will be adjusted if needed, to limit the total liver dose to be within the tolerance. As in other cases, both lung dose and normal liver dose will be estimated.

Table 1. TI, TA and TI/TA of the 102 cases

	Minimum	Maximum	Median	Mean	Standard deviation
TI (GBq)	0·003	0·383	0·036	0·075	0·086
TA (GBq)	1·276	2·577	1·785	1·786	0·259
TI/TA (%)	0·2	22·2	2·2	4·1	4·4

Figure 4 shows *TI/TA* as a function of *TI*. *TI/TA* varied almost linearly with *TI*. With the fitted linear curve, one can estimate the deviations caused by neglecting *TI* in the activity calculation. In our institution, radiology reports include an estimation of tumour involvement. The estimation of tumour involvement could be used with the curve to predict potential deviations caused by neglecting *TI* in the calculation. The prediction could be used to determine if *TI* can be neglected (i.e., structure contouring can be avoided) with minimal deviations or not.

Conclusions

The study showed that overall the effect of tumour involvement on the activity determination was small. *TI* could be neglected in the activity determination in 25% of the cases in the study where the activity contribution from *TI* was less than 1%. Avoiding contouring processes would bring improvement of the workflow efficiency in emergent situations where a quick turnaround from activity calculation to treatment delivery is needed.

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Conflict of interest. The authors declare none.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of Thomas Jefferson University and relevant national guidelines on human experimentation in USA and with the Helsinki Declaration of 1975, as revised in 2008.

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