Partition model for estimating radiation doses from yttrium-90 microspheres in treating hepatic tumours

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Abstract. A uniform distribution of yttrium-90 (\textsuperscript{90}Y) microspheres throughout the entire liver has always been assumed for dose calculation in treating hepatic tumours. A simple mathematical model was formulated which allows estimation of the activities of a therapeutic dose of \textsuperscript{90}Y microspheres partitioned between the lungs, the tumour and the normal liver, and hence the radiation doses to them. The doses to the tumour and normal liver were verified by intra-operative direct beta-probing. The percentage of activity shunted to the lung and the tumour-to-normal tissue ratio (T/N) were obtained from gamma scintigraphy using technetium-99m-labelled macroaggregated albumin (MAA) which simulates the \textsuperscript{90}Y microspheres used in subsequent treatment. The intrahepatic activity was partitioned between the tumour and the normal liver based on the T/N and their masses determined from computerized tomography slices. The corresponding radiation doses were computed using the MIRD formula. The estimated radiation doses were correlated with the doses directly measured using a calibrated beta-probe at laparotomy by linear regression. The radiation doses to the tumour and the normal liver, estimated using the partition model, were close to that measured directly with coefficients of correlation for linear regression: 0.862 for the tumours and 0.804 for the normal liver compartment (\textit{P}<0.001). The partition model permits a distinction between the radiation doses received by the tumour and normal liver to be made and the doses thus estimated are close to the actual doses received. The optimal doses to the tumour and normal liver and hence the required quantity of \textsuperscript{90}Y microspheres to be administered can be easily predetermined.

Key words: Partition model – Yttrium-90 – Radiation doses – Hepatic tumours


Introduction

Treating inoperable liver cancer with intra-arterial infusion of yttrium-90 microspheres was pioneered in the 1960s [1, 2]. Pure beta radiation from \textsuperscript{90}Y cannot penetrate soft tissue thicker than 11 mm, making direct measurement of the distribution of the microspheres within the liver impossible outside the body. The distribution of the microspheres throughout the entire liver has been assumed to be uniform in most studies [1–9], including a recent one [10]. It has been well established that \textsuperscript{90}Y microspheres of both the ceramic and the resin type are non-biodegradable. Once infused into the liver, they will stay in the microvasculatures of the tumour or the liver parenchyma and decay with the physical half-life of \textsuperscript{90}Y [1–9]. The radiation dose can thus be estimated using the MIRD formula [11] knowing the activity per unit mass. On the assumption of a uniform distribution the doses to tumour and normal liver are identical. Simulation using gamma-emitting ytterbium-169 microspheres to visualize the intrahepatic distribution of microspheres was attempted by Ariel and Pack [2]. Technetium-99m-labelled macroaggregated albumin (\textsuperscript{99m}Tc-MAA) for hepatic arterial perfusion scintigraphy [12] and assessment of arteriovenous shunting [13] became widely used in estimating the pulmonary shunting and intrahepatic distribution of \textsuperscript{90}Y microspheres [6–10, 14–16]. Estimation of the radiation dose to the tumour by a partition model has been mentioned by one of the research groups [8, 9], but it has not been formally expressed, verified or adopted in dose calculation [10]. Burton et al. [17–20] pioneered intraoperative administration of \textsuperscript{90}Y microspheres with direct beta-probing of the liver and tumour surface during laparotomy. The intraoperative dosimetry was further verified by liquid scintillation counting of liver biopsies containing \textsuperscript{90}Y microspheres.

In the present study, a partition model for estimating radiation doses to the lungs, hepatic tumours and normal liver is formulated and applied to patients receiving \textsuperscript{90}Y microspheres during laparotomy [16]. The validity of the model was verified by intraoperative dosimetry.
Materials and methods

Fourteen patients, including two recurrent cases, with inoperable hepatocellular carcinoma (HCC) and three patients with colorectal liver metastases but no extrahepatic disease were entered into the study. The whole group consisted of three females and 14 males. The median age was 50 years (range 18-74).

The patients were subjected to selective hepatic angiography (HAG) and 99mTc-MAA scan for assessment of the percentage of radioactivity shunted to the pulmonary system and the tumour-to-normal tissue ratio (T/N) of uptake of 99mTc-MAA within the liver. This technique has been reported previously [14-16].

Computerized tomography (CT) images of the abdomen were obtained with 1:1 magnification and 5 mm transaxial thickness. The tumours and normal liver were outlined on each section and the areas were digitised with reference to a phantom of a known area. The total area taken over all slices multiplied by the section thickness gave the volume. The mass of the tumour (M_T) and the mass of the normal liver (M_N) were obtained by multiplying the respective volume by the density (1.03 g/cm³) of soft tissue.

The partition model for estimation of radiation doses assumes the distribution of 90Y microspheres during the treatment is identical with the 99mTc-MAA particles during the diagnostic HAG. Although the 90Y microspheres are resin based while the 99mTc-MAA particles are composed of albumin, the two types of particles have a similar average size (90Y microspheres: 29-35 μm; 99mTc-MAA: 10-100 μm, average 30 μm). Between 6.6 and 23.1x10⁷ 90Y microspheres are injected in one treatment but the number of 99mTc-MAA particles required (3.0x10⁵) for the diagnostic scan is less than 1% of the number of 90Y microspheres.

It has been established that 90Y microspheres will be trapped inside the microvasculature and decay at the physical half-life of 90Y to infinity without biological degradation [1-10, 16-20]. From decay data of 90Y [21], an activity uptake of 0.037 MBq/novistic scan is less than 1% of the number of 90Y microspheres.

The estimated radiation doses to the tumour and the normal liver were readily computed by substituting the respective activity uptake A_T and A_N into Eq. 1.

The average radiation dose to the liver as a whole, with no distinction between tumour and normal tissue, was also computed by substituting the total intrahepatic activity uptake (A_T+A_N) and total liver mass (M_T+M_N) into Eq. 1 for comparison.

Activity of 90Y per unit mass was determined from the count rates directly measured over the tumour and normal liver surface by a calibrated beta-probe during laparotomy. Radiation absorbed dose calculations for these tissues assumed that the 90Y was removed from the tissues solely by radioactive decay. Details of this technique have been described elsewhere [14, 16]. The radiation doses to the tumours and normal liver estimated by the partition model were correlated with the data from intraoperative dosimetry.

Bremsstrahlung scans of the lung and liver were performed before the patients were discharged for confirmation of the distribution of the 90Y microspheres but not for dose calculation because of poor image quality [22].

Results

The patient characteristics, masses of tumour and normal liver, the percentages of lung shunting and T/N ratios determined from 99mTc-MAA images are shown in Table 1. The percentages of lung shunting varied between 2.2% and 15.0% (median 7.3%) and the T/N ratios from the 99mTc-MAA scan ranged from 3.0 to 13.6 (median 4.7).

The total activity of 90Y microspheres administered ranged from 2 to 7 GBq with a median of 3 GBq. The estimated activity of 90Y shunted into the pulmonary system varied between 0.044 and 0.798 GBq with a median of 0.219 GBq.

The activity of 90Y microspheres retained in the tumour (A_T) and the normal liver (A_N) was estimated using the partition model. The estimated radiation doses to the lung, the tumour and normal liver obtained by substituting the corresponding activity uptake and mass into Eq. 1 are listed in Table 2. The tumour dose and normal liver dose determined by direct beta-probing of the tumour and normal liver surfaces are listed in the final two columns.

The radiation dose to the tumour, as measured by the beta-probe, varied between 107 and 305 Gy (median 162 Gy) while that to the normal liver ranged from 15 to 77 Gy (median 26 Gy). For the lungs, only radiation doses estimated by the partition model were available. The values ranged between 2 and 40 Gy (median 11 Gy).

Correlations between the radiation doses determined by the partition model and the values obtained from intraoperative dosimetry for the tumours and the normal liver compartments are illustrated in Figs. 1 and 2. Coefficients of correlation for linear regression performed on the two independent sets of data were 0.862 for the tumours and 0.804 for the normal liver compartments (P<0.001). Thus the radiation doses estimated using the partition model are close to those measured by intraoperative beta-probing, although the two sets of readings are not identical.