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Quantitative evaluation in tumor SPECT and the effect of tumor size: Fundamental study with phantom

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An experimental study with phantoms was performed in order to evaluate the effect of the tumor volume on the quantitative estimation in tumor SPECT. The ratio of mean count/pixel in the phantom to that of the background (T/N ratio) was well correlated with the size of the phantom: even when the concentration of the Tc-99m O_4^- solution of globular phantoms with diameters of 29, 37 and 46 mm was constant, the greater the size of the phantom, the higher was the T/N ratio. This study showed that we should understand that the T/N ratio was certainly affected by the reduction of the tumor size itself whenever we evaluate treatment response or assess tumor viability after treatment by reference to the T/N ratio.

Key words: tumor SPECT, partial volume effect, thallium index, T/N ratio

INTRODUCTION

IN THE MANAGEMENT of cancer treatment, sufficient functional evaluation of the tumor is not obtained only by morphological imaging methods such as CT and MRI. In contrast, the role of nuclear medicine in cancer diagnosis is to estimate functional aspects of the tumor, for example, to assess tumor viability or to evaluate treatment response. Quantification or numerical expression of the incorporation of radionuclides such as thallium-201, which accurately reflects the viable tumor burden,[1] into the tumor makes this functional evaluation more objective but it is very difficult to calculate the absolute uptake by the tumor. An easy and simple method usually available is to measure relative uptake by the tumor. For instance in thallium SPECT (single photon emission computed tomography) the ratio of average counts/pixel in the tumor to that in the normal background is expressed and used as the thallium index[2] or as the T/N ratio,[3] and it is generally believed that a high T/N ratio means the aggressiveness or the high malignancy of the tumor,[4] and a decrease in the T/N ratio after treatment indicates good treatment response.[5] Nevertheless, there are few data concerning whether the tumor volume affects the T/N ratio, and the influence of the partial volume effect[6] is not fully discussed in the quantification of tumor uptake. There certainly is a reduction in the size of the tumor when the treatment is very effective, so we should correctly understand that T/N ratio is certainly affected by the reduction in the tumor size whenever we evaluate treatment response by means of the T/N ratio.

In this manuscript, fundamental experiments with phantoms were performed in order to clarify the correlation between the quantitative parameters of tumor uptake and tumor volume in tumor SPECT. A simple and easy method for correcting the partial volume effect is also described.

MATERIALS AND METHODS

We used the SP-6 phantoms for measuring cubic volume (Fig. 1). Acrylic globular phantoms 29, 37 and 46 mm in diameter, which were filled with Tc-99m O_4^- solution at a constant concentration (407–518 KBq/m*l*), were fixed in a cylindar phantom 20 cm in diameter. The Tc-99m O_4^- solution was further diluted from a strength of 1/2 to a strength of 1/8 as a background to the globular phantom and a cylindar phantom was filled with it. The counts for the Tc-99m O_4^- solution inside and outside the globular phantom were obtained with a well-type scintillation counter as the target count (T) and background count (B),

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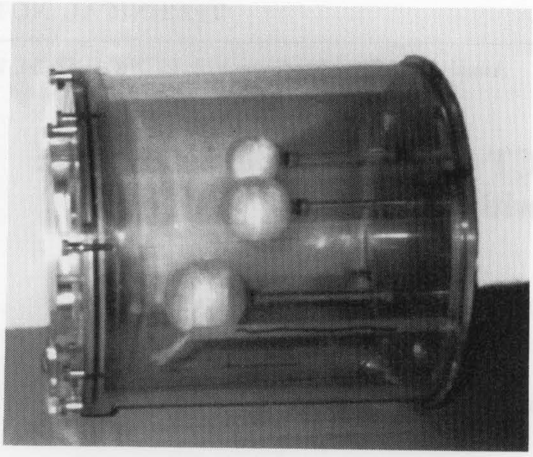

Fig. 1 The Sp-6 phantom which consists of three globular phantoms 29, 37 and 46 mm in diameter.

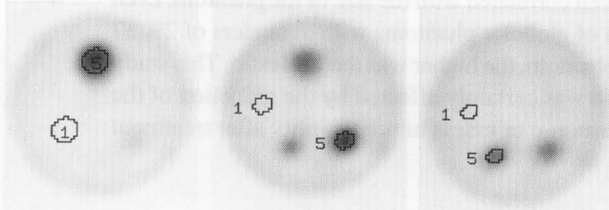

Fig. 2 The ROIs at the slice of the phantoms 46 mm (the left), 37 mm (the middle) and 29 mm (the right) in diameter. Automatic 80% cut off of the maximum count was used to set the ROI. Same ROI in size was also set at the background.

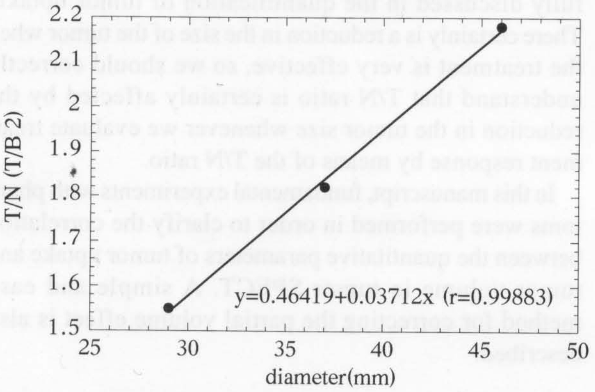

Fig. 3 Correlation between the T/N ratio and the diameter of the phantom when the actual T/B was set at 2.0. There was a linear correlation between the two parameters.

respectively, to calculate the actual T/B ratio. Actually measured T/B ratios were 2.0, 3.0, 3.9, 4.1, 5.0, 6.0, 7.9 and 8.1. The phantoms were scanned with a three-head rotating SPECT system (Toshiba GCA 9300A) with a low-energy parallel collimator. Data acquisition was performed with a 4° step angle, each step for 30 sec in a 128 × 128 matrix. Butterworth and Ramp filters were used for reconstruction in preprocessing and back-projection.

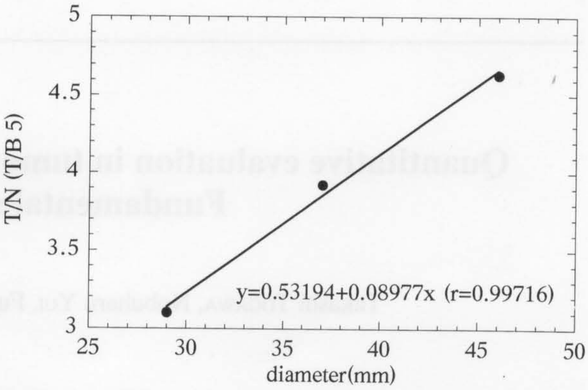

Fig. 4 Correlation between the T/N ratio and the diameter of the phantom when the actual T/B was set at 5.0. There was also a linear correlation between the two parameters.

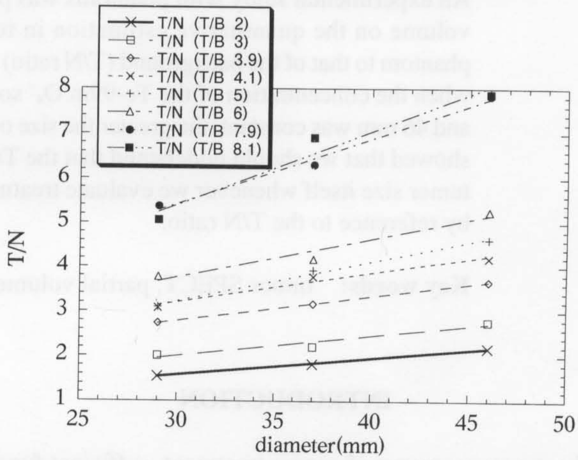

Fig. 5 Correlation between the T/N ratio and the diameter of the phantom when the actual T/B ranged from 2.0 to 8.1. The greater the diameter of the phantom, the higher the T/N ratio in each actual T/B was and there were linear correlations between T/N ratio and the diameter of the phantom.

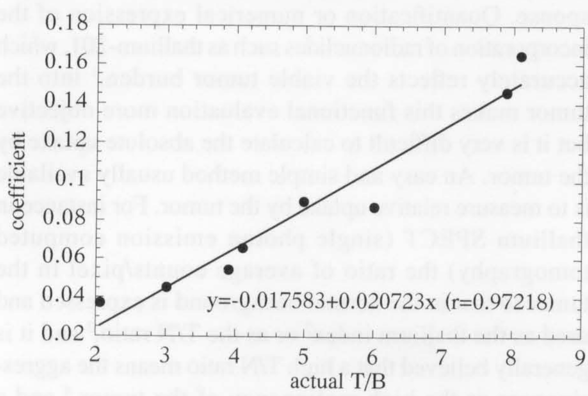

Fig. 6 Correlation between the correlative coefficient and the actual T/B. There was a linear correlation between the two parameters.

Scatter and attenuation corrections were not performed. Region of interest (ROI) was set on the globular phantom and on the background and automatic 80% cut off of the

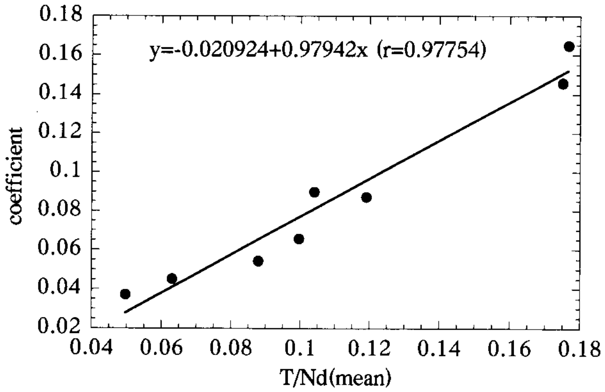

Fig. 7 Correlation between the correlative coefficient and T/N·d (mean value). There was a linear correlation between the two parameters.

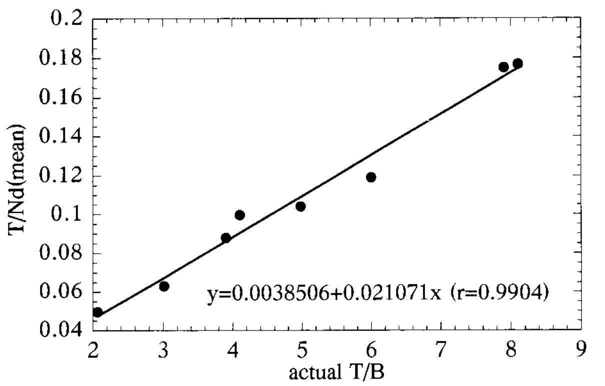

Fig. 8 Correlation between T/N·d (mean value) and the actual T/B. There was a linear correlation between the two parameters.

maximum count was used to set the ROI (Fig. 2). The numbers of pixels in the ROIs of phantoms 29 mm, 37 mm and 46 mm in diameter were 28.0 ± 2.0, 38.5 ± 2.5 and 68.0 ± 2.0, respectively. The mean counts/pixel for the ROI in the globular phantom (T) and in normal background (N) were measured three times, and the T/N ratio was expressed as the mean of three measurements. The T/N·d value, which was the T/N value corrected by the diameter (d) of the phantom, was also found.

RESULTS

The correlation between the T/N ratio and the diameter of the phantom when the actual T/B ratio was set to 2.0 is shown in Figure 3. T/N ratios of the phantoms 29, 37 and 46 mm in diameter were 1.55, 1.82 and 2.18, respectively. The greater the diameter of the phantom, the higher the T/N ratio was. There was a linear correlation between the two parameters (r = 0.998), and the correlative coefficient was 0.037. Similarly, the correlation when the actual T/B was 5.0 is shown in Figure 4. T/N ratios of the phantoms 29, 37 and 46 mm in diameter were 3.10, 3.92 and 4.63, respectively. The greater the diameter of the phantom, the higher the T/N ratio was. There was also a linear correlation between the two parameters (r = 0.997) and the correlative coefficient was 0.089, and Figure 5 shows the correlation when the actual T/B ranged from 2.0 to 8.1. The greater the diameter of the phantom, the higher the T/N ratio in each actual T/B was, and there were linear correlations between T/N ratio and the diameter of the phantom. Correlative coefficients were 0.037, 0.045, 0.054, 0.066, 0.090, 0.087, 0.146 and 0.165 when the actual T/B were 2.0, 3.0, 3.9, 4.1, 5.0, 6.0, 7.9 and 8.1, respectively. That is, in each T/B ratio, the correlative coefficient was a constant value regardless of the size of the phantom, so if the correlative coefficient was obtained we could predict the actual T/B ratio irrespective of the size of the phantom. Actually there was a statistically significant correlation between the correlative coefficient and the actual T/B ratio (r = 0.97), as shown in Figure 6: the higher the actual T/B ratio, the greater the correlative coefficient was. Figure 6 shows that if we obtained the correlative coefficient we could predict the actual T/B ratio irrespective of the size of the phantom. But because the number of lesion is either one or two in actual clinical cases, it is difficult to actually get a linear regression and to obtain its correlative coefficient in a patient unless there are multiple lesions such as brain metastases.

We have already reported T/N·d which was a simple parameter corrected by tumor diameter (d) to correct the partial volume effect.[3] Briefly, in brain metastases, the mean maximal diameter and maximum diameter at right angles of the tumor enhanced by Gd-DTPA on MRI was directly measured on MRI and was used to correct the T/N ratio. The correlation between T/N·d, which was corrected by the diameter (d) of the phantom, and the correlative coefficient is shown in Figure 7. There was a significant linear correlation between the coefficient and T/N·d (r = 0.977). It is therefore, possible to predict the correlative coefficient by calculating T/N·d. Furthermore, there was also a significant linear correlation between T/N·d and the actual T/B (r = 0.99), as shown in Figure 8. Figure 8 shows that T/N·d can predict the actual T/B unless correlative coefficient was not measured.

DISCUSSION

During and after cancer treatment by radiotherapy or chemotherapy, it is very important to objectively assess the extent of the tumor reduction or the decrease in tumor viability. Usually the changes in the tumor diameter or size before and after the treatments expressed on CT or MRI are helpful in judging the therapeutic effect, but when the tumor still remains or the size of the tumor has not changed even after the treatment, further functional evaluation by tumor imaging is needed. Visual or semiquantitative comparison of Tl-201[5] or Ga-67 uptake[7] by the tumor before and after the treatment has been tried to assess treatment response.

The ratio of uptake by the tumor to normal regions (T/N ratio) has usually been used for semiquantitaive evaluation, and the decrease in the T/N ratio after the treatment has been believed to show the effectiveness of the therapy,[8] but whether or not a reduction in tumor size after the treatment has an effect on the T/N ratio is not definitely known. It is generally thought that when the diameter of the lesion is twice that of the FWHM or more in any SPECT system, the lesion can be positively delineated.[9] Actually in order to correctly assess the accumulation in the lesion, the lesion needs to be two and a half times to three times as large as the FWHM. When quantitative evaluation was performed on a lesion smaller than 3 times that of the FWHM, the smaller the lesion was, the more the count of the lesion was underestimated. This so-called partial volume effect is one of the major reasons why the quantitative evaluation is difficult and inaccurate. The FWHM of the SPECT system we used in this study was 13 mm and the T/N ratio for the phantom with a diameter of 46 mm (3.5 times that of the FWHM) shows a count recovery of $96.7 \pm 6.2\%$ of the actual T/B ratio. In contrast, the count recovery was $81.3 \pm 7.2\%$ and $68.1 \pm 5.5\%$, respectively, even when the diameter was 37 mm (2.8 times that of the FWHM) and 29 mm (2.2 times that of the FWHM). The present study therefore showed that the count recovery was not very good even when the phantom size was greater than twice that of the FWHM.

Generally speaking, not only a partial volume effect but also attenuation correction and Compton-scatter are the major factors which have an influence on the quantitative estimation of tumor SPECT. Concerning the effect of attenuation correction on the thallium index, Kim et al.[2] stated that there was no statistical difference between nonattenuation-corrected and attenuation-corrected scans in the thallium index, but we have no data on Compton-scatter correction in quantifying the T/N ratio.

Concerning correction of the partial volume effect, no excellent correction method has yet been reported, but as a simple and easy corrective method, the T/N·d value, which was T/N value corrected by the diameter (d) of the tumor, was reported in lung cancer by Higashi et al.[10] and also in metastatic brain cancer by Togawa et al.[3] In this experiment, a significant correlation was shown between the diameter (X) of the phantom and the T/N ratio (Y), and the correlation was plotted in the equation $Y = \alpha X + \beta$. In this equation correlative coefficient α, which was constant regardless of the size of the phantom, could predict the actual T/B ratio. If correlative coefficient α is constant regardless of the size of the phantom, the actual T/B ratio can be estimated from the correlative coefficient. The correlative coefficient is expressed as $\alpha = (Y - \beta)/X$ and if β is smaller than Y, α approximates Y/X, that is, the correlative coefficient closely resembles T/N·d.

The present study with phantoms showed that this correction by T/N·d was useful and reliable to some degree from a fundamental viewpoint. Even when the actual T/B varied from 2.0 to 8.1, there was a significant linear correlation between T/N·d and the actual T/B ($r = 0.99$). It was showed that the actual T/B could be estimated by means of T/N·d when the size of the phantom was different, but the correction by d should be adapted to the tumor whose uptake was uniform, such as a globular phantom. The correction of the partial volume effect with T/N·d in an actual clinical case is limited only to a tumor which has a globular shape and the accumulation is uniform such as in a metastatic brain tumor.[3] This phantom study showed that we have to keep in mind the decrease in tumor size when we evaluate the therapeutic effect by means of the T/N ratio.

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