Tumor Dosimetry on SPECT ^{186}Re -HEDP Scans: Variations in the Results from the Reconstruction Methods Used

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ABSTRACT

The aim of this work was to estimate tumor-absorbed doses delivered from the administration of fixed activities of ^{186}Re -HEDP for the treatment of bone metastases from prostate cancer. The variations and reproducibility in the estimated absorbed dose owing to the reconstruction algorithm used (OSEM vs. FBP) were also analysed. For this aim, correction methods for scatter and attenuation were kept identical, whereas the same calibration data and thresholding techniques were used to obtain quantification. This study was carried out in spinal and pelvic lesions of 7 patients. For comparison, the absorbed doses, based upon the maximum and the mean voxel count, were calculated, resulting in the absorbed dose (maximum): 60 Gy ($\sigma = 30$ Gy) and 33 Gy ($\sigma = 15$ Gy) for OSEM and FBP, respectively, and absorbed dose (mean): 26 Gy ($\sigma = 12$ Gy) and 17 Gy ($\sigma = 7$ Gy) with OSEM and FBP, respectively. We concluded that the administration of fixed activity resulted in a range of absorbed doses, and we showed that, despite using the same approach, the choice of the reconstruction algorithm can result in differences higher than 50% in the estimated tumor-absorbed doses. In conclusion, the need for a standardization of the methodology used for the calculations is emphasized by this work, especially when comparisons between patients and different centers are of interest.

Key words: absorbed dose, bone dosimetry, ^{186}Re -HEDP

INTRODUCTION

^{186}Re -HEDP is a bone-targeting agent comprised of ^{186}Re , a medium-energy beta-emitter ($E_{\text{max}} = 1.07$ MeV, half-life 89.3 hours) with the additional emission of a gamma ray ($E_{\gamma} = 137$ keV, 9% abundance), and HEDP is a diphosphonate compound that targets bone.

According to the Medical Internal Radiation Dose (MIRD) formalism, the mean absorbed dose, $\tilde{D}_{t \leftarrow s}$, to a target t from a source s , is given by the product of the cumulative activity, $\tilde{A}_s$, in

the source with the $S_{t \leftarrow s}$ factor, as shown in Equation 1:

$$\tilde{D}_{t \leftarrow s} = \tilde{A}_s \times S_{t \leftarrow s} \quad (1)$$

The cumulated activity is the integral of the activity over time curve, which for tumor dosimetry, is determined from nuclear medicine images. Therefore, its accuracy relies on the accuracy of image quantification. Sophisticated methods have been developed and implemented for reconstructing, correcting, and analyzing single-photon emission computed tomography (SPECT) data for dosimetric purposes in targeted radionuclide therapy, mainly addressing ^{111}In and ^{131}I .^{1,2} These methods could be applied to other radioisotopes, such as ^{186}Re , but in any case, are

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seldom incorporated into clinical practice owing to their burden in time and resources.

The $S_{t \leftarrow S}$ factor represents the absorbed dose per decay and is mass dependent. Tabulated factors for reference organs are often used that can be found in the literature.^{3,4} Bone dosimetry is very challenging, as the tumors tend to build along the bone structures, and their volumes and shapes are not easily obtained.

This paper reports on tumor-absorbed doses delivered from the administration of fixed activities of ^{186}Re -HEDP in patients with bone metastases from prostate cancer. The aim of this study was to investigate the range of the calculated absorbed doses and to analyze variations in their estimation when only the algorithm for the reconstruction was altered (i.e., FBP or OSEM).

MATERIALS AND METHODS

Data Acquisition

Data from 7 patients participating in a fixed-activity (5000 MBq of ^{186}Re -HEDP), phase II trial were analyzed. The eligibility criteria for the selection of the patients, as well as the therapeutic procedure, were those used for the phase I activity escalation study described, in detail, elsewhere.⁵ SPECT data were acquired for the thorax and the pelvic region for each patient at ~ 0.5 , ~ 4 , ~ 24 , ~ 48 , and ~ 72 hours postadministration. A dual-headed gamma camera, the FORTE HP (ADAC; Philips Medical Systems, Ltd., Reigate, UK) scanner, was used for all acquisi-

Figure 1. Example of time activity curve fitted with two exponentials showing the uptake and decay phases observed in all time activity curves.

Figure 2. Histogram of lesion absorbed doses calculated based on the max (A) and the mean (B) voxel count using images reconstructed with FBP and OSEM.

tions. A low-energy, high-resolution collimator was used, providing parallel-beam geometry. Data were acquired at 64 projection angles for each head in a 128^2 matrix. Step and shoot mode was used, with 20 seconds per angle for an acquisition time. Three windows were set at the main peak at 137 keV (15%), below the main peak at 119 keV (7%), and above the main peak at 156 keV (6%).

A range of phantoms with known activities was scanned in the FORTE system, using the identical acquisition settings as for the patient scans. The phantom assembly for each scan was comprised of a water-filled cylinder of 11 cm height (H) and a diameter (D) of 19 cm, with either cylindrical inserts of H = 10 cm and D = 1, 2, 3, 4, or 5 cm, which will be referred to in this paper as shape 1, or with H = D = 1, 1.5, 2, 3, 4, or 5 cm, which will be referred to in this paper as shape 2.

Estimation of Tumor-Absorbed Dose

The SPECT data were reconstructed with FBP and OSEM (8 subsets and 8 iterations) into three-dimensional images of cubic voxels, with a size of 4.6 mm. Prior to the reconstruction, the data were corrected for scatter using the triple-energy window method.⁶ Linear attenuation correction was performed, with an attenuation coefficient of $\mu = 0.142 \text{ cm}^{-1}$ applied to elliptical outlines. All reconstructions and corrections were performed on the commercial system, HERMES (Hermes Medical Solutions; Stockholm, Sweden).

A mean value of percentage threshold over the maximum count was estimated from the phantom data for FBP: $38\% \pm 3.1\%$; and for OSEM: $33\% \pm 1.9\%$; by taking into consideration volumes larger than 6 cc. For smaller inserts, no recovery of the volume was achieved owing to resolution effects, which limited our analysis to

large lesions, mainly spinal and pelvic. For each lesion, a calibration factor was obtained from the reconstruction of the phantom, better approximating the lesion size, using the same filtering parameters as for the patient data. The time activity curves represented MBq/cc by taking into account the voxel size. Following the reconstruction, all images for each region were registered to the scan obtained ~ 24 hours after administration.

The time activity curves were fitted with two exponential phases, and the cumulated activity was calculated as the sum of the analytical integral of the exponential phases fitted to the last measured point, plus the integral to infinity from the last measured point. This last part was obtained by the extrapolation of a linear fit to the points over 24 hours in a log-linear plot. Figure 1 shows an example of a time activity curve fitted with two exponentials.

The tumor S-factor used was $0.184 \text{ Gy/MBq} \times \text{hours}$. The value was derived from tabulated data provided by MIRD⁷ of specific absorbed fractions for organs, considered as sources of uniform activity, and extrapolated to 1 g of mass. A density of 1 g/cc was assumed for the tumors.

RESULTS

Table 1 shows the calculated absorbed doses based on the mean and maximum voxel count for the 20 lesions examined, calculated with FBP and OSEM. The mean values are also plotted as a histogram in Figure 2. The results show large intra- and interpatient variations in the estimated lesion absorbed doses. The absorbed doses calculated with OSEM were substantially higher than those calculated with FBP, which is not fully understood.

Table 1. Summary of Lesion-Absorbed Doses

	FBPmax	FBPmean	OSEMmax	OSEMmean
Mean (Gy)	26	17	60	33
Std (Gy)	12	7	30	15

Reproducibility of time activity curves was studied for a random sample of patients. Figure 3 shows an example of time activity curves for a patient produced from single- and double-headed gamma-camera data based on the mean and maximum voxel counts. The time activity curves show positive reproducibility.

DISCUSSION AND CONCLUSIONS

This paper assessed the dosimetric results obtained when clinically suitable methods were applied to a set of patients treated with a fixed activity of ^{186}Re -HEDP. The methods used, although they did not incorporate absolute quantification, were reproducible and allowed for comparisons. Large intra- and interpatient variations were observed in the estimated tumor-absorbed doses.

It was surprising that the results changed considerably if the reconstruction algorithms FBP or OSEM were used, despite the fact that all other

steps in the process were kept similar. Considering that the true tumor-absorbed doses were unknown, this study resulted in the observation that the calculated values were different, but no conclusions could be drawn as to whether one set of results was more accurate than the other. In order to understand these variations, simulated data should be used, and this will be part of future studies.

The need for standardization of the methodology used for the calculations is emphasized by this work, especially when comparisons between patients and different centers are of interest.

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REFERENCES

1. He B, Du Y, Song X, et al. A Monte Carlo and physical phantom evaluation of quantitative In-111 SPECT. *Phys Med Biol* 2005;50:4169.
2. Dewaraja YK, Wilderman SJ, Ljungberg M, et al. Accurate dosimetry in ^{131}I radionuclide therapy using patient-specific, three-dimensional methods for SPECT reconstruction and absorbed-dose calculation. *J Nucl Med* 2005;46:840.
3. Stabin MG. MIRD: Personal computer software for internal dose assessment in nuclear medicine. *J Nucl Med* 1996;37:538.
4. Snyder WS, Ford MR, Warner GG, et al. "S" absorbed dose per unit cumulated activity for selected radionuclides and organs. (MIRD Pamphlet No. 11, revised) New York: The Society of Nuclear Medicine, 1975.
5. O'Sullivan JM, McCready VR, Flux GD, et al. High-activity rhenium-186 HEDP with autologous peripheral blood stem cell rescue: A phase I study in progressive hormone refractory prostate cancer metastatic to bone. *Br J Canc* 2002;86:1715.
6. Shao L, Freifelder R, Karp JS. Triple-energy window scatter correction technique in PET. *IEEE Trans on Nucl Sci* 1994;13(4):641.
7. Snyder WS, Ford MR, Warner GG. Estimates of specific absorbed fractions for photon sources uniformly distributed in various organs of a heterogeneous phantom. (MIRD Pamphlet No. 5, revised New York: The Society of Nuclear Medicine), 1978.