Measurement of ^{153}Sm-EDTMP bone uptake by whole-body scintigraphy and its application to individualized treatment dosimetry of bone metastasis

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Abstract To calculate a safe and effective ^{153}Sm-EDTMP therapy dose, a whole-body scintigraphy technique for prospective individual dosimetry was developed and the results were compared with 5 h urine collection method in 20 patients with bone metastases. Anterior and posterior whole-body images were obtained 10 min and 5 h after intravenous injection of 740 MBq ^{153}Sm-EDTMP and the bone uptake value was determined. There is a close correlation between the bone uptake value obtained from the whole-body scintigraphy and 5 h urine collection method (r=0.93). The radiation absorption dose to red marrow was limited to 1.4 Gy and the administered activity calculated from bone uptake value by whole-body scintigraphy was 1.40~2.27 GBq (mean 1.90 GBq). If the activity was calculated according to the standard body weight of 37 MBq·kg^{-1}, the administered activity would be 1.75~2.41 GBq (mean 2.18), the radiation absorption dose to red marrow would be 1.37~2.27 Gy (mean 1.63 Gy), but at these doses significant myelotoxicity would be anticipated, thus emphasizing the need for individual prospective dosimetry.

Keywords Samarium-153-EDTMP, Dosimetry, Whole-body scintigraphy
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1 INTRODUCTION

Samarium-153 ethylenediaminetetramethylene phosphonic acid (^{153}Sm-EDTMP) is effetive in the palliation of painful bony metastases[1]. Pain relief is seen in 60%~90% of patients treated with ^{153}Sm-EDTMP, and the onset of pain relief generally begins within 1 week of administration. The critical organ in ^{153}Sm-EDTMP therapy is the red bone marrow and myelotoxicity can be a significant side effect of the administration of therapeutic activities of ^{153}Sm-EDTMP[2]. There is an increase in the incidence and severity of myelotoxicity with increasing administered activity. Clinical trial indicated that it is prudent to limit the red marrow radiation absorbed dose to 1.4 Gy (1400 mGy),

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doses excess 2 Gy can cause significant myelosuppression[3,4]. We have developed a whole-body scintigraphic technique which is simple, accurate to calculate prospectively a safe and effective dose of ^{153}Sm-EDTMP in individual patients to palliate bone cancer pain without myelotoxicity.

2 MATERIALS AND METHODS

2.1 Patients

20 patients (10 males, 10 females) with multiple painful bony metastases from prostate (n=2), lung (n=2), breast (n= 6), NPC (n=4), colon (n=1), kidney (n=1), unknown cause (n=4). All patients had platelet and leukocyte counts within the normal range ascertained by whole blood profiles performed just before administration of ^{153}Sm-EDTMP (from Nuclear Dynamics Institute of China, Sichuan).

2.2 Whole body scintigraphy

Each patient received approximately 740 MBq ^{153}Sm-EDTMP intravenously as a sub-therapeutic activity, which is used to calibrate the gamma camera in counts and to determine the retained bone activity at 5 h. Ten minutes following injection of ^{153}Sm-EDTMP, anterior and posterior whole-body images were obtained using a dual-head, large field-of-view gamma camera (Elscint APEX SPX SPECT). The start time of imaging, the length of the scan and the number of steps were recorded. An acquisition of 3 min per step was used. A background scan was acquired when the patient had left the room, using the same geometry. Five hours later, the patient was instructed to totally void urine, another whole-body scan was obtained using acquisition parameters and patient-camera geometry identical to the 10 min scan.

2.3 Calculation of bone uptake value

Total whole-body counts (C_{T}) in each study were determined by summing the counts in the anterior (C_{A}) and posterior (C_{P}) projections:

$$C_{\mathrm{T}} = C_{\mathrm{A}} + C_{\mathrm{P}}$$

The total count was corrected for background (C_{B}) and radioactive decay (D_{F}) from the time of injection:

$$C_{\mathrm{T}} - C_{\mathrm{B}} = C_{\mathrm{NET}}$$

$$C_{\mathrm{NET}}/D_{\mathrm{F}} = C_{\mathrm{CORR}}$$

Where $D_{\mathrm{F}} = e^{-0.693t/2776.2}$ and t is the elapsed time in minutes from injection to commencement of imaging.

The corrected total count from the 5 h whole-body scan (C_{CORR5h}) was divided by the corrected total count from the 10 min whole-body scan (C_{CORRinit}). Bone uptake value = ($C_{\mathrm{CORR5h}}/C_{\mathrm{CORRinit}}$)× 100%.

2.4 Calculation of the bone uptake value by urine collection

During the period of whole-body scintigraphy, the urine volume excreted over 5 h was collected. The total urinary activity was determined, corrected for radioactive decay from the time of injection and subtracted from the activity injected to get the activity retained in bone at 5 h.

2.5 Calculation of the therapy activity (A_{TH})

The ^{153}Sm-EDTMP therapy dose was calculated according to the following formula[5,6].

$$A_{\mathrm{TH}} = \frac{D_{\mathrm{RM}}(\mathrm{mGy})}{0.5 \times B_{\mathrm{u}} \times T_{\mathrm{p}}/0.693 \times (S_{\mathrm{T}} + S_{\mathrm{C}}) \times 70/W}$$

Where D_{RM}=absorbed dose of red marrow (1400 mGy in the present study),

T_{p} = physical half life of ^{153}Sm (46.27 h),

S_{T} ="S" factor of trabecular bone,

S_{C} ="S" factor of cortical bone,

$S_{\mathrm{T}} + S_{\mathrm{C}}$=0.353 mGy/MBq·h[5],

W=patient's standard weight (22.5× height^2),

B_{u} = bone uptake value.

2.6 Statistical analysis

Bone uptake value obtained by whole-body scintigraphy and by urine collection were compared by calculating the Pearson correlation coefficient and by Paired-Samples t test. Absorbed doses of red marrow were compared by Paired-Samples t test.

3 RESULTS

There was a close correlation between the bone uptake value at 5 h, calculated by whole-body scintigraphy and by the urine collection method (Table 1). The Pearson correlation coefficient was 0.93. There was no significance of bone uptake value determined by both methods (t=1.3958, p=0.1789).

The maximum therapy activity administered within the limit of bone marrow absorbed dose of 1.4 Gy in 20 patients ranged from 1.40 to 2.27 GBq (Table 2).

There was a significant difference of therapy activity between individualized dosimetry calculated by bone uptake value and that estimated from administration of 37 MBq ^{153}Sm-EDTMP per kilogram body weight (t=4.075, p= 0.001). There was also a significant difference of red marrow radiation absorbed dose between the two methods (t=4.030, p=0.001).

Table 1 Bone uptake value (B_u) in 20 patients 5 h after the administration of 740 MBq ^{153}Sm-EDTMP: Whole-body (WB) scintigraphy compared with the urine collection (UC)

Patient	Height/m	Standard weight/kg	B_u% of injected activity		% Difference
			WB	UC	
1	1.60	57.6	47.2	47.3	0.2
2	1.56	54.8	45.5	45.1	0.9
3	1.60	57.6	59.0	66.3	12.4
4	1.67	62.8	53.5	62.6	-17.0
5	1.70	65.0	55.2	53.3	3.4
6	1.60	57.6	43.0	45.1	-4.9
7	1.64	60.5	50.1	53.7	7.2
8	1.50	50.6	52.3	47.8	8.6
9	1.70	65.0	56.9	63.7	-12.0
10	1.65	61.3	62.3	65.3	-4.8
11	1.45	47.3	35.7	31.6	11.5
12	1.62	59.0	50.9	55.3	-8.6
13	1.62	59.0	57.4	61.3	6.8
14	1.65	61.3	74.3	76.1	-2.4
15	1.68	63.5	57.8	58.2	-0.7
16	1.57	55.2	50.1	46.8	6.6
17	1.56	55.0	49.8	52.2	-4.8
18	1.68	63.5	63.8	65.2	-2
19	1.60	57.6	49.2	46.4	5.7
20	1.70	65.0	52.6	48.2	8.4

4 DISCUSSION

We believe that individual prospective dosimetry of ^{153}Sm-EDTMP is imperative. Bone uptake value of ^{153}Sm-EDTMP varies widely from 40%~95% between patients and in the same patient at different times as bone metastatic lesion progresses[2]. In this study, bone uptake value varies from 35.7%~74.3%. Therefore, the percentage of bone uptake is difficult to predict on the basis of patient height and weight before treatment.

Myelotoxicity is the only significant side-effect and the incidence and severity increase with increasing administered activity. Moderate-to-severe haematological toxicity has been reported at the supplier's recommended administered activity of 37 MBq·kg^{-1} [3,4].

Because of the unpredictability of bone uptake value of ^{153}Sm-EDTMP in patients with bone metastases, several investigators have suggested that individualized dosimetry can and should be performed using a sub-therapeutic activity of ^{153}Sm-EDTMP[2,7] taking advantage of the complete urinary clearance by 5 h post-injection with negligible non-osseous uptake.

In the past, we determined the bone uptake value by urine collection method, but it has some disadvantages: (1) It requires meticulous care in ensuring that all urine

is collected, the loss of even a small amount can introduce a significant error into the calculations. (2) It is inconvenient for patients to collect all their urine for 5 h and this can be an extra burden to staff. (3) Handling radioactive urine is a hazard for staff and carries the potential for a radiation spill. (4) Errors may also be introduced during urine volume and activity measurements.

Table 2 *Individualized dosimetry by whole-body scintigraphy compared with theoretical* marrow dose estimated from administration of 37 MBq ^{153}Sm-EDTMP per kilogram body weight

Patient	Individualized dosimetry		37 MBq·kg^{-1} dosimetry	
	Administered activity/GBq	Marrow dose/Gy	Activity /GBq	Marrow dose/Gy
1	2.10	1.43	2.10	1.43
2	2.00	1.37	2.00	1.37
3	1.66	1.40	2.13	1.80
4	1.99	1.40	2.32	1.63
5	2.00	1.40	2.41	1.69
6	2.27	1.40	2.13	1.31
7	2.05	1.40	2.24	1.53
8	1.62	1.38	1.87	1.60
9	1.94	1.40	2.41	1.74
10	1.67	1.40	2.27	1.90
11	2.25	1.40	1.75	1.09
12	1.97	1.39	2.18	1.55
13	1.74	1.40	2.18	1.75
14	1.40	1.39	2.27	2.27
15	1.86	1.40	2.35	1.77
16	1.87	1.39	2.04	1.53
17	1.87	1.39	2.04	1.53
18	1.69	1.40	2.35	1.95
19	1.99	1.41	2.13	1.50
20	2.10	1.40	2.41	1.61
$\bar{x}$	1.90	1.40	2.18	1.63

A major merit of ^{153}Sm is the 103 keV gamma emission. Bone scans using ^{153}Sm-EDTMP show excellent visualization of bone metastases and concordance with scans using ^{99}Tcm-MDP. This gamma emission permits quantitative imaging and affords the opportunity of using whole-body imaging for dosimetry calculations.

The whole-body scintigraphy method was validated against the urine collection method in 20 patients and the bone uptake value, determined by both methods showed excellent correlation (r=0.93). The sources of error are fewer in whole-body scintigraphy and we believe this new method is more simple and suitable for routine clinical practice. It should be assured that the bladder is completely empty and urinary activity is therefore

not counted as part the retained bone activity when doing 5 h ^{153}Sm-EDTMP bone scan. In addition, repeat ^{153}Sm-EDTMP bone scans performed when patients return for further treatment can be used to monitor their progress without a requirement for additional ^{99m}Tc bone scans. In this study, we limited the radiation absorption dose for red marrow to 1.4 Gy. The administered activity calculated from bone uptake value by whole-body scintigraphy was 1.40~2.27 GBq (mean 1.90 GBq). If we calculate activity according to standard body weight of 37 MBq.kg^{-1}, the administered activity would be 1.75~2.41 GBq (mean 2.18), then the radiation absorption dose for red marrow would be 1.37~2.27 Gy (mean 1.63 Gy), at such doses myelotoxicity should be anticipated, thus the need for individual prospective dosimetry should be emphasized.

In conclusion, this study applied the whole-body scintigraphy in the measurement of bone uptake value to calculate prospectively a safe and effective dose of ^{153}Sm-EDTMP in individual patients to palliate bone cancer pain without obvious myelotoxicity.

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