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NUCLEAR MEDICINE AND MOLECULAR IMAGING

ORIGINAL ARTICLE

A computer program to assess the bone scan index for Tc-99m hydroxymethylene diphosphonate: evaluation of jaw pathologies of patients with bone metastases using SPECT/CT

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PURPOSE

This study aimed to evaluate the jaw pathologies of patients with bone metastases using a computer program to assess the bone scan index (BSI) for Tc-99m hydroxymethylene diphosphonate (HMDP) with single-photon emission computed tomography/computed tomography (SPECT/CT).

METHODS

Ninety-seven patients with jaw pathologies (24 with bone metastases and 73 without) were evaluated. High-risk hot spots and BSI in the patients were evaluated using the VSBONE BSI (ver.1.1) analysis software for Tc-99m HMDP that scanned SPECT/CT and automatically defined the data. The two groups were compared using the Pearson chi-square test and Mann–Whitney U test for high-risk hot spots and BSI, respectively. A *P* value of <0.05 was considered statistically significant.

RESULTS

High-risk hot spot occurrence was significantly correlated to bone metastases [sensitivity, 21/24 (87.5%); specificity, 40/73 (54.8%); accuracy, 61/97 (62.9%); $P < 0.001$]. The number of high-risk hot spots was higher in patients with bone metastases (5.96 ± 10.30) than in those without (0.90 ± 1.50; $P < 0.001$). Furthermore, the BSI for patients with bone metastases (1.44 ± 2.18%) was significantly higher than for those without (0.22 ± 0.44%; $P < 0.001$).

CONCLUSION

A computer program that assessed BSI for Tc-99m HMDP may be useful in the evaluation of patients with bone metastases using SPECT/CT.

KEYWORDS

Bone, diagnosis, metastatic tumor, scintigraphy, single-photon emission-computed tomography

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Bisphosphonates are inhibitors of osteoclastic bone resorption and are useful in the treatment of osteoporosis and bone metastases of cancer. However, they are also implicated in the onset of medication-related osteonecrosis of the jaw (MRONJ).[1-4] Bone scintigraphy can demonstrate physiological changes in the bone and is useful for detecting MRONJ.[5,6] Furthermore, multimodal imaging techniques, such as scintigraphy, computed tomography (CT), and magnetic resonance imaging, are useful for the detection of MRONJ.[7-10]

The bone scan index (BSI) is based on a review of the bone scan, visually estimating the fraction of each bone involved, and summing this across all bones to determine the percentage of total skeletal involvement.[11,12] BSI can be used as a bone management tool to evaluate bone scintigraphy, e.g., by providing baseline-BSI[13,14] and response-BSI.[15,16]

Recently, a computer program called VSBONE BSI was developed that could scan bone scintigraphy and automatically define the BSI for Tc-99m hydroxymethylene diphosphonate

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(HMDP).[17,18] The VSBONE BSI software is a deep learning-based image interpretation system that performs skeletal segmentation and the extraction of hot spots of the bone metastatic lesion from a whole-body bone scintigram, followed by automated measurement of the BSI. This program is a computer-aided detection system for scintigraphy and is useful for screening bone metastases in prostate cancer. Furthermore, in recent years, single-photon emission CT/CT (SPECT/CT) has been applied for the evaluation of oral and maxillofacial lesions.[19-26] However, to the best of our knowledge, no reports have been published on BSI analysis aided by software for the jaw pathologies of patients with bone metastases using SPECT/CT. This study was performed to evaluate the jaw pathologies of patients with bone metastases using a computer program to assess BSI for Tc-99m HMDP with SPECT/CT.

Methods

The protocol was approved by the Ethics Committee of The Nippon Dental University (ECNG-R-400). After providing written informed consent, 97 patients with jaw pathologies [35 men and 62 women; mean age, 74.5 years (range, 43–92 years)] underwent SPECT/CT at our university hospital from October 2018 to July 2021. Informed consent was obtained from patients who participated in the clinical investigations. Among the jaw pathology patients, 24 patients with different cancers (eight with breast, six with lung, six with prostate, two with rectal, one with thyroid, and one with kidney cancers) and bone metastases had MRONJ with bone metastases of cancer; 73 patients were without bone metastases, including 46 with MRONJ with osteoporosis, 17 with chronic osteomyelitis, and 10 with osteoradionecrosis (Table 1). MRONJ patients were diagnosed in accordance with the 2014 American Association of Oral and Maxillofacial Surgeons position paper.[1] The histopathological diagnoses of jaw pathologies were obtained after sampling during surgery or biopsy performed in all cases at our university hospital, whereas osteoporosis and bone metastases were diagnosed and treated in another hospital.

Main points

- We evaluated the jaw pathologies of patients with bone metastases using a computer program to assess their bone scan index (BSI) for Tc-99m hydroxymethylene diphosphonate with single-photon emission computed tomography/computed tomography (SPECT/CT).
- Patients with bone metastases had a significantly higher BSI than those without bone metastases.
- The computer program could be useful for the evaluation of patients with bone metastases using SPECT/CT.

Whole-body bone SPECT/CT scans were obtained using a SPECT/CT scanner (Optima NM/CT 640, GE Healthcare, Tokyo, Japan) following our hospital's protocol.[19,20] Patients were administered an intravenous injection of 740 MBq of Tc-99m HMDP (Clear Bone Injectable; Nihon Medi-Physics, Tokyo, Japan) prior to the scan acquisitions. Anterior and posterior-view bone scans were acquired using a low-energy high-resolution collimator, the 140 keV photoenergy peak for Tc-99m, a scanning speed of 10 cm/min, and a 256 × 1024 matrix of 2.1 mm pixel size.

The SPECT/CT data were obtained using the MI software and workstation (Q. Volumetrix and Xeleris 4DR, GE Healthcare Japan, Tokyo, Japan). The evaluation of high-risk hot spots and BSI in the patients was performed using commercially available software for Tc-99m HMDP (VSBONE BSI v.1.0; Nihon Medi-Physics, Tokyo, Japan), which scanned SPECT/CT and defined the data automatically. We defined the high-risk hot spots as suspected bone metastases. Furthermore, true positives for osseous metastatic diseases were obtained by biopsy/pathologically in another hospital.

Statistical analysis

The high-risk hot spots and BSI of patients with/without bone metastases were compared using the Pearson chi-square test and Mann–Whitney U test, respectively. Statistical analyses employed the SPSS Statistics (v.26) software package (IBM Japan, Tokyo, Japan). A P value of <0.05 was considered statistically significant.

Results

The BSI for the jaw pathologies of patients with bone metastases evaluated by SPECT/CT is presented in Table 2. High-risk hot spots were significantly correlated to bone metastases [sensitivity, 21/24 (87.5%); specificity, 40/73 (54.8%); accuracy, 61/97 (62.9%); $P < 0.001$]. High-risk hot spot numbers in patients with bone metastases (5.96 ± 10.30) were significantly higher than in patients without bone metastases (0.90 ± 1.50, $P < 0.001$). Furthermore, the BSI of patients with bone metastases (1.44 ± 2.18%) was significantly higher than that of patients without bone metastases (0.22 ± 0.44%, $P < 0.001$). Figures 1 and 2 show MRONJ patients with and without bone metastases, respectively.

Table 1. The characteristics of jaw pathologies of patients, derived using a computer program to assess the bone scan index

Parameters	Bone metastases	
	With	Without
Number of patients	24	73
Age (years)		
Mean ± SD (range)	70.6 ± 7.1 (55 – 84)	75.8 ± 10.1 (43 – 92)
Sex		
Men	13	22
Women	11	51
Underlying disease		
MRONJ with bone metastases		
Breast cancer	8	
Lung cancer	6	
Prostate cancer	6	
Rectal cancer	2	
Thyroid cancer	1	
Kidney cancer	1	
MRONJ with osteoporosis		46
Chronic osteomyelitis of the jaw		17
Osteoradionecrosis of the jaw		10

SD, standard deviation; MRONJ, medication-related osteonecrosis of the jaw.

Table 2. The bone scan index of the jaw pathologies of patients with bone metastases, derived using single-photon emission computed tomography/ computed tomography

Parameters	Bone metastases		Total	*P* value
	With (n = 24)	Without (n = 73)	(n = 97)	
High-risk hot spots				< 0.001
Positive	21 (87.5%)	33 (45.2%)	54 (55.7%)	
Negative	3 (12.5%)	40 (54.8%)	43 (44.3%)	
High-risk hot spot numbers				< 0.001
Mean ± SD	5.96 ± 10.30	0.90 ± 1.50	2.15 ± 5.65	
Range	0 – 46	0 – 8	0 – 46	
Bone scan index (%)				< 0.001
Mean ± SD	1.44 ± 2.18	0.22 ± 0.44	0.52 ± 1.25	
Range	0.00 – 8.26	0.00 – 2.12	0.00 – 8.26	

SD, standard deviation.

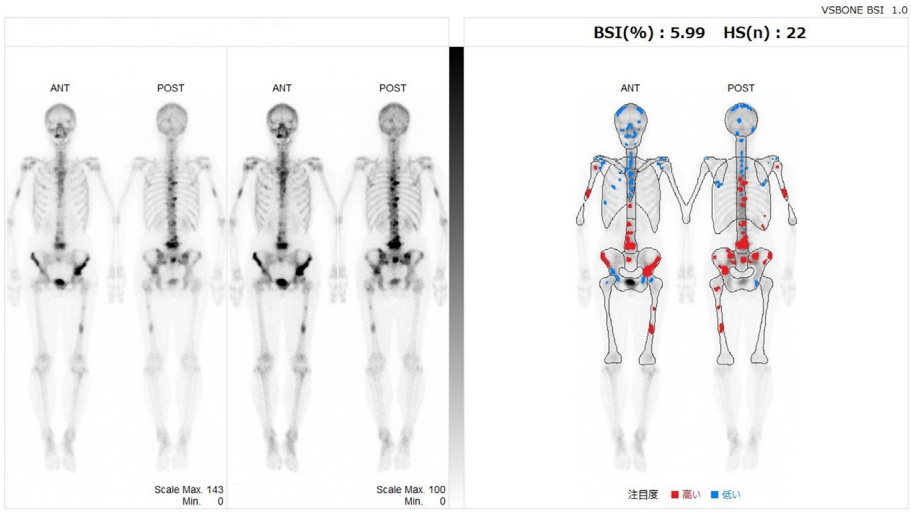

Figure 1. Medication-related osteonecrosis of the jaw of the right side of the maxilla in a 68-year-old woman with breast cancer and multiple bone metastases. The bone scan index and high-risk hot spot number (n) are 5.99% and 22, respectively. The red and blue areas indicate high-risk and low-risk hot spots, respectively.

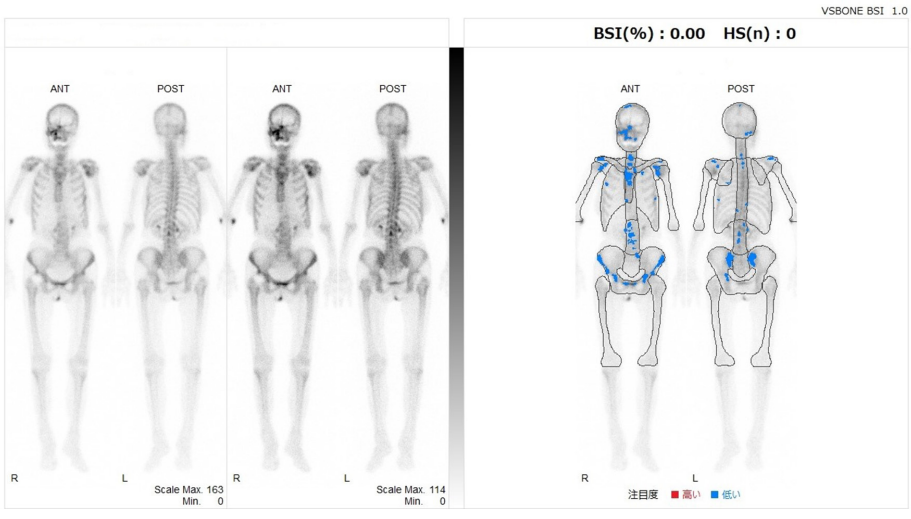

Figure 2. Medication-related osteonecrosis of the jaw of the right side of the maxilla in a 90-year-old woman with osteoporosis without bone metastases. The bone scan index and high-risk hot spot number (n) are 0.00% and 0, respectively. The red and blue areas indicate high-risk and low-risk hot spots, respectively.

Discussion

We investigated the performance of a computer program to assess BSI for Tc-99m HMDP in the jaw pathologies of patients with bone metastases via SPECT/CT. The results showed that high-risk hot spots were significantly correlated to bone metastases, and the BSI of patients with bone metastases was significantly higher than of those without. Planar bone scintigraphy is a standard radiological technique used to detect skeletal metastases in patients with prostate cancer.[27] Petersen et al.[28] evaluated the response of bone metastasis in prostate cancer, particularly the correlation between computer-assisted BSI responses and clinical response classification. The findings indicated that the BSI software should be useful for the evaluation of bone metastases.

Sabbatini et al.[13] showed that the BSI quantifies the extent of skeletal involvement caused by the tumor and allowed for the stratification of patients with a distinct prognosis for clinical trials. Kaboteh et al.[14] developed an automated method for calculating BSI that could be used to calculate the number of new lesions and changes in BSI of serial bone scans. Dennis et al.[15] retrospectively examined the serial bone scans of patients with castration-resistant metastatic prostate cancer enrolled in four clinical trials. Mitsui et al.[16] showed that the BSI reflected bone metastasis' response to chemotherapy. However, to the best of our knowledge, little has been published regarding the usefulness of BSI for the jaw pathologies of patients using SPECT/CT. Our results showed that high-risk hot spots were significantly correlated to bone metastases [sensitivity, 21/24 (87.5%); specificity, 40/73 (54.8%); accuracy, 61/97 (62.9%); $P < 0.001$). Furthermore, the BSI of patients with bone metastases (1.44 ± 2.18%) was significantly higher than that of patients without bone metastases (0.22 ± 0.44%, $P < 0.001$). We found that the BSI analysis software for Tc-99m HMDP could be useful for the evaluation of patients with bone metastases using SPECT/CT.

This study has several limitations. The sample was relatively small. The most interesting feature of BSI in cancer patients is the ability to detect and diagnose bone metastases early and perform follow-up procedures. However, the bone scan are not specific for malignant lesions or metastasis. There are numerous benign etiologies with a similar scintigraphic appearance as malignant lesions.[29,30] Therefore, diagnoses for malignant lesions or metastasis should be performed using multimodal imag-

ing. SPECT and SPECT/CT bone scans are at least twice as sensitive in detecting bone abnormalities, for malignant and benign etiologies. Based on scintigraphic appearance alone, it is not possible to differentiate between malignant and benign jaw pathologies.[29,30] A standardized uptake value (SUV) for the evaluation of jaw pathologies has been reported for Tc-99m HMDP SPECT/CT,[19,20,23-25] but further research in the jaw pathologies of patients is necessary to validate these results, particularly the relationship between BSI and SUV.

In conclusion, we evaluated the jaw pathologies of patients with bone metastases using a computer program to assess BSI for Tc-99m HMDP with SPECT/CT. The BSI of patients with bone metastases was significantly higher than that of patients without bone metastases. This computer program could be useful for the evaluation of patients with bone metastases using SPECT/CT.

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Conflict of interest disclosure

The authors declared no conflicts of interest.

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