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Research Article

Assessment of A Software for Semi-Automatically Calculating the Bone Scan Index on Bone Scintigraphy Scans

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2. Key words

BSI; 99mTc-HMDP; Prostate cancer; Bone metastases; Prognosis prediction

1. Abstract

1.1. Aims: The incidence of bone metastases exceeds 85% in patients who die of prostate cancer. Therefore, it is important to diagnose bone metastases from prostate cancer using bone scintigraphy. We developed a software program that semi-automatically calculates the bone scan index (BSI) on 99mTechnetium-hydroxymethylene diphosphonate bone scintigraphy scans with a computer-aided diagnosis system (VSBONE® BSI). We examined whether the BSI obtained using this software could replace the extent of disease (EOD) score.

1.2. Methods: The subjects were 80 patients who were diagnosed with prostate cancer at our hospital and underwent bone scintigraphy. We analyzed the receiver operating characteristic (ROC) curve to determine the BSI cut off value between EOD groups. The cut off value was determined based on the maximum value of the sum of the sensitivity and specificity.

1.3. Results: When a BSI of 0.16 was used as the cut off value to distinguish between EOD 0 and 1-4, the sensitivity and specificity were 90.1% and 100%, respectively. When a BSI of 0.91 was used as the cut off value to distinguish between EOD 0-1 and 2-4, the sensitivity and specificity were 100% and 81.3%, respectively. When a BSI of 4.56 was used as the cut off value to distinguish between EOD 0-2 and 3-4, the sensitivity and specificity were 90.5% and 100%, respectively.

1.4. Conclusion: Our results suggest that the BSI can be calculated using this software.

3. Introduction

In recent years, the incidence of prostate cancer has increased in Japan due to an increasingly Westernized lifestyle [1]. Prostate cancer is the second most common cancer among Japanese men [2]. The most common form of metastasis from prostate cancer is bone metastasis, and the incidence of bone metastases exceeds 85% in patients who die of prostate cancer [3,4]. Therefore, it is important to diagnose bone metastases from prostate cancer using bone scintigraphy. Several studies have attempted to quantify bone metastases by bone scintigraphy with different results [5,6]. The semi-quantitative extent of disease (EOD) score is a convenient indicator and is useful for predicting the prognosis of prostate cancer [7,8]. In contrast, the bone scan index (BSI), a quantitative index, is also useful for predicting the prognosis of prostate cancer and judging the therapeutic effect [9, 10]; however, the BSI is difficult to calculate. In addition, both these indicators are subjective, and the results may vary greatly depending on the observer.

Recently, we developed a software program that semi-automatically calculates the BSI on 99mTechnetium-hydroxymethylene diphosphonate (99mTc-HMDP) bone scintigraphy scans using a computer-aided diagnosis system (VSBONE® BSI) (Nihon Medi-Physics Co., Ltd., Japan). [11-13]. We examined whether the BSI obtained using this software could replace the EOD score.

4. Materials and Methods

4.1. Patients

The subjects consisted of 80 patients who were diagnosed with prostate cancer at our hospital and underwent bone scintigraphy from February 2017 to April 2019 (mean age 76.5 ± 6.9 years).

We obtained written informed consent from all participants. This was a retrospective study that used nuclear medicine imaging data. This study follows the tenets of the Helsinki Declaration of 1975, revised in 1983 (Declaration of Helsinki: ethical principles for medical research involving human subjects). The patients' human rights were respected; the patients could refuse to participate in this study without experiencing any disadvantages related to medical treatment. This study was approved by the Ethics Committee of the Graduate School of Medicine, Osaka City University, under the name of "Validation of an automated diagnostic system for abnormal accumulation sites in nuclear medicine images, certification number 2019-40."

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4.2. Bone Scintigraphy

Whole-body anterior and posterior bone scan images were acquired within 3–5 hours of intravenous injection of 740 MBq 99mTc-HMDP. The imaging devices employed were an ADAC Forte and Philips Bright view X equipped with low-energy high-resolution collimators. The imaging parameters of the Forte were as follows: scan speed of 20 cm/min, 1024 × 1024 matrix, and a 140-keV photopeak with a 20% window. The imaging parameters of the Bright view X were as follows: scan speed of 20 cm/min, 1024 × 512 matrix, and a 140-keV photopeak with a 20% window.

4.3. Extent of Gisease Grade

The final assessment of each patient was made by two experienced radiologists in the field of bone scintigraphy and was used as the gold standard classification. The EOD categories as defined by Soloway et al. [7] were applied.

4.4. Bone Scan Index Analysis

VSBONE® BSI is a software program involving artificial intelligence with deep learning, developed to calculate BSI from 99mTc-HMDP bone scintigraphy scans [11, 12]. In the analysis protocol, VSBONE® BSI was used to perform skeletal anatomical structure recognition processing of bone scintigraphy images and to detect abnormal accumulation. Subsequently, using the analysis results, the VSBONE® BSI view software was used to calculate the BSI and output the data [11, 13].

To use the software, the user imports the Digital Imaging and Communications in Medicine (DICOM) data of the front and back images of bone scintigraphy into the personal computer in which the software is installed. The user selects target cases and processes them with VSBONE® BSI commands. When the process is completed, the VSBONE® BSI view command is automatically launched, and the process result is displayed. On the result screen, the area determined to have bone metastases is displayed in red as a "hot spot with high attention," and the area determined not to have bone metastases is displayed in blue as a "hot spot with low attention." Injection leakage and distribution in the bladder and kidney are not recognized as abnormal accumulation. If the result calculated by VSBONE® BSI is inconvenient, it is possible to edit the hotspot. Then, the report is completed and saved.

4.5. Statistical Analysis

A statistical software package (JMP SAS Institute., Cary, NC, USA) was used for all statistical analysis. The mean, standard deviation, median, and range of BSI for each EOD group were determined. Differences were evaluated by a two-tailed test and the significance level was set to 0.05. The area under the curve (AUC) was evaluated using receiver operating characteristic (ROC) curve analysis to determine the BSI cut off value between EOD groups. The cut off value was determined based on the maximum value of the sum of sensitivity and specificity.

5. Results

Of the 80 patients, 9 had no bone metastases (EOD 0) and 71 had bone metastases. Of the 71 patients with bone metastases, 23 were classified as EOD 1, 27 as EOD 2, and 21 as EOD 3-4. The site of bone metastasis was determined by other imaging diagnostic tools such as computed tomography (CT) and magnetic resonance imaging (MRI) or by follow-up observation.

The relationship between EOD scores and the BSI is shown in (Table and Figure 1). The average values of BSI classified according to EOD 0, 1, 2, and 3-4 are 0.00, 0.61, 2.51, and 10.89, respectively. There was no significant difference in BSI between the EOD 0 and EOD 1 groups, but there was a significant difference in BSI between the EOD 0 and EOD 2 groups, the EOD 0 and EOD 3-4 groups, the EOD 1 and EOD 2 groups, the EOD 1 and EOD 3-4 groups, and the EOD 2 and EOD 3-4 groups.

(Figure 2a) shows the ROC curve of BSI for discriminating between EOD 0 and 1-4. When a BSI of 0.16 was used as the cut off value, the sensitivity and specificity were 90.1% and 100%, respectively. (Figure 2b) shows the ROC curve of BSI for discriminating between EOD 0-1 and 2-4. When a BSI of 0.91 was used as the cut off value, the sensitivity and specificity were 100% and 81.3%, respectively. (Figure 2c) shows the ROC curve of BSI for discriminating between EOD 0-2 and 3-4. When a BSI of 4.56 was used as the cut off value, the sensitivity and specificity were 90.5% and 100%, respectively.

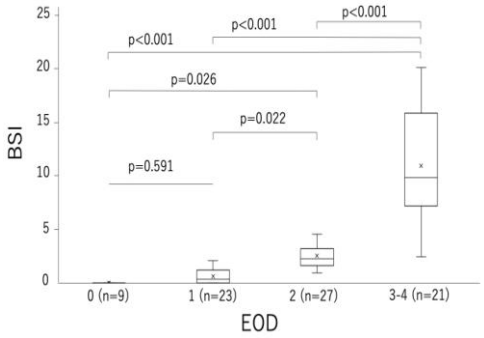

Figure 1
Box and whisker BSI plots for each EOD score
EOD: extent of disease, BSI: bone scan index

Table 1: Comparison of BSI and EOD score

	EOD			
	0 (n=9)	1 (n=23)	2 (n=27)	3-4 (n=21)
Mean (SD)	0.00 (0.01)	0.61 (0.69)	2.51 (1.14)	10.89 (5.37)
Medium	0	0.33	2.25	9.81
Min, Max	0, 0.02	0, 2.04	0.91, 4.52	2.43, 20.04

EOD: extent of disease, BSI: bone scan index, SD: standard deviation

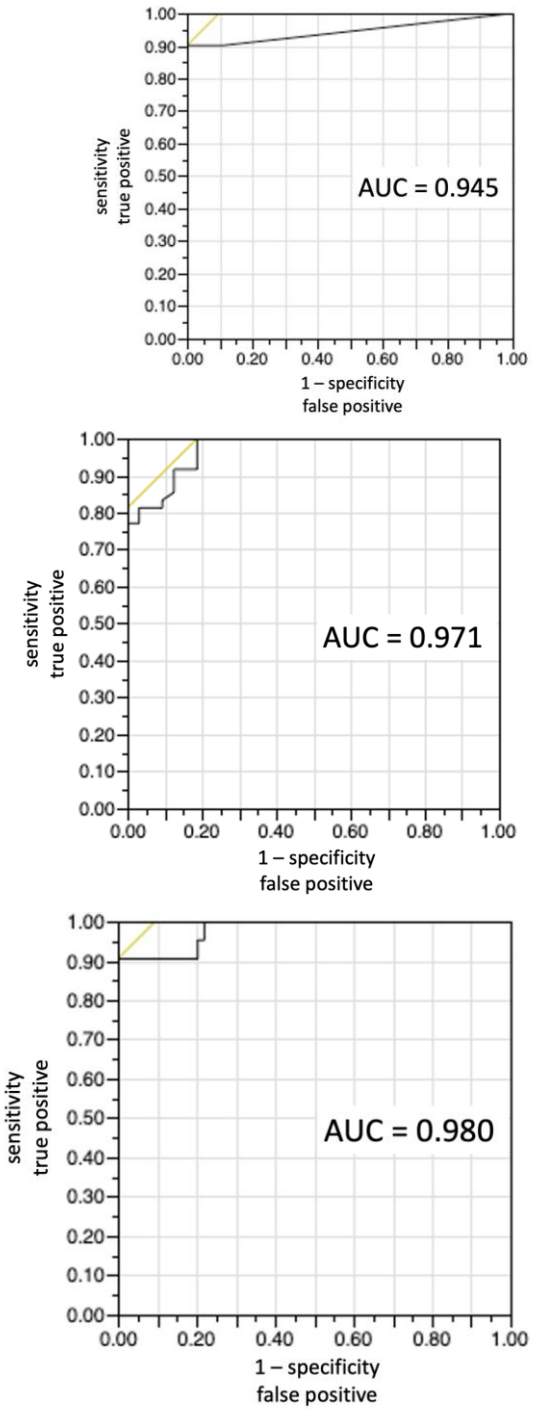

Figure 2: ROC curves for the BSIs to predict EOD score:
A: EOD 0 versus 1-4; **B:** EOD 0, 1 versus 2-4; **C:** EOD 0–2 versus 3,4.
ROC: receiver-operating curve, **BSI:** bone scan index, **EOD:** extent of disease, **AUC:** area under the curve

6. Discussion

Bone scintigraphy is an imaging modality used to detect bone metastases, determine the efficacy of treatment, and predict survival in patients with prostate cancer. EOD scores and the BSI are used as prognostic indicators. It has been reported that BSI more accurately reflects the state of bone metastasis than the EOD score [14]; however, the calculation of BSI is burdensome.

BONENAVI® (FUJIFILM Toyama Chemical Co., Ltd., Japan.) has already been used as a software for semi-automatically calculating the BSI from 99mTechnetium-methylene diphosphonate (99mTc-MDP) bone scintigraphy scans, using a computer-aided diagnosis system. Takahashi et al. reported that the sensitivity and specificity were 88.5-100% and 92.4-99.3%, respectively, when the BSI cut off value for EOD 1 was 0.05, the BSI cut off value for EOD 2 was 0.5, and the BSI cut off value for EOD 3-4 was 1.5 [15].

In this study, on analyzing 99mTc-HMDP bone scintigraphy scans using a computer-aided diagnosis system, the BSI cut off values for EOD 1, 2, and 3-4 were 0.16, 0.91, and 4.56, respectively. The sensitivity and specificity were 90.1-100% and 81.3-100%, respectively. It was difficult to make an accurate comparison owing to the variations in drugs and cases; however, VSBONE® BSI and BONENAVI® have high sensitivity and specificity.

7. Conclusion

Our results suggest that the BSI can be calculated using this software.

8. Acknowledgement

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