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RESEARCH ARTICLE

Computer-aided diagnosis system for osteoporosis based on quantitative evaluation of mandibular lower border porosity using panoramic radiographs

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Objectives: A new computer-aided screening system for osteoporosis using panoramic radiographs was developed. The conventional system could detect porotic changes within the lower border of the mandible, but its *severity* could not be evaluated. Our aim was to enable the system to measure severity by implementing a linear bone resorption severity index (BRSI) based on the cortical bone shape.
Methods: The participants were 68 females (>50 years) who underwent panoramic radiography and lumbar spine bone density measurements. The new system was designed to extract the lower border of the mandible as *region of interests* and convert them into morphological skeleton line images. The total perimeter length of the skeleton lines was defined as the BRSI. 40 images were visually evaluated for the presence of cortical bone porosity. The correlation between visual evaluation and BRSI of the participants, and the optimal threshold value of BRSI for new system were investigated through a *receiver operator characteristic* analysis. The diagnostic performance of the new system was evaluated by comparing the results from new system and lumbar bone density tests using 28 participants.
Results: BRSI and lumbar bone density showed a strong negative correlation ($p < 0.01$). BRSI showed a strong correlation with visual evaluation. The new system showed high diagnostic efficacy with sensitivity of 90.9%, specificity of 64.7%, and accuracy of 75.0%.
Conclusions: The new screening system is able to quantitatively evaluate mandibular cortical porosity. This allows for preventive screening for osteoporosis thereby enhancing clinical prospects.
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Keywords: diagnostic imaging; osteoporosis; preventive screening; radiography; automated diagnosis

Introduction

Osteoporosis can be defined as “a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture”.[1] Women are particularly at risk as they display roughly four times the morbidity rate of males as a result from osteoporosis.[2,3] This outcome is likely arising from males having a higher peak bone mass compared to females

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(who also portray a rapid decline in sex hormones as a consequence of menopause).[4,5] A large-scale survey in the United States showed that about half of the post-menopausal females are found to have low bone density.[6] However, large segments of the population with no previous diagnosis of osteoporosis are currently at risk for osteoporotic fracture as they are asymptomatic until a fracture occurs.[6,7] Therefore, it is important to screen asymptomatic patients as osteoporotic fractures greatly increase morbidity and mortality risks.[8,9] In particular, vertebral fractures are the most common complication of osteoporosis and are associated with long-term morbidity and mortality.[10,11] Although BMD measurements are effective in predicting vertebral fractures, many patients are often asymptomatic until a fracture occurs, and BMD tests are typically not optimally performed.[12] Previous studies reported that, in patients having low skeletal bone mineral density (BMD), porosification can be observed in the lower mandibular cortical bone on panoramic radiographs.[13,14] Other studies have confirmed that investigating cortical bone porosity on panoramic radiographs is an effective way to screen for osteoporosis and can predict the occurrence of vertebral fractures.[12,13,15–27] Previously, in our institution (Department of Oral and Maxillofacial Radiology, Graduate School of Biomedical and Health Science, Hiroshima University), a computer-aided diagnosis (CAD) system was developed to screen for osteoporosis using dental panoramic radiographs in a semi-automated fashion.[28,29] The previous system was able to detect porotic changes, such as erosion and fissuring, on panoramic radiographs at the lower border of the mandibular cortex. An overview of this system is shown in Figure 1. Region of interest (ROI) extraction was semi-automated. The average co-ordinates of the mandibular inferior margin cortex just below the mental foramen, as specified in a previous study from our lab, were used.[29] Point 1 depicts the average co-ordinates of the mandibular inferior margin cortex from 100 subjects of this previous study. Point 2 can be defined as the point perpendicularly below or above Point 1 on the contour edge line. Referring to Point 2, a region of 400 × 100 pixels was extracted as a ROI. The flow diagram of the conventional CAD system is shown in Figure 2. As a result of these semi-automated image processing steps, if many "skeleton lines" occurred in the lower marginal cortical bone of the mandible, the patient would be diagnosed as suspected low-skeletal BMD. Although the system has high diagnostic accuracy, in some cases, false negatives emerge. One potential cause for this is that the skeleton lines after image processing occasionally become connected to one another and converted into a single pixel agglomeration (Figure 3). Therefore, it is essential to evaluate the panoramic radiographs in a qualitatively different way than merely based on the number of skeleton lines. In addition, although the presence or absence of linear bone resorption of the cortical bone can be assessed through conventional methods, its severity could not be further explored. If the morphology of skeleton lines can be quantified, a severity assessment would be made possible and diagnostic precision would be improved. The purpose of this study was fourfold, namely: (1) to redesign the CAD system, thereby enabling calculation of the linear bone

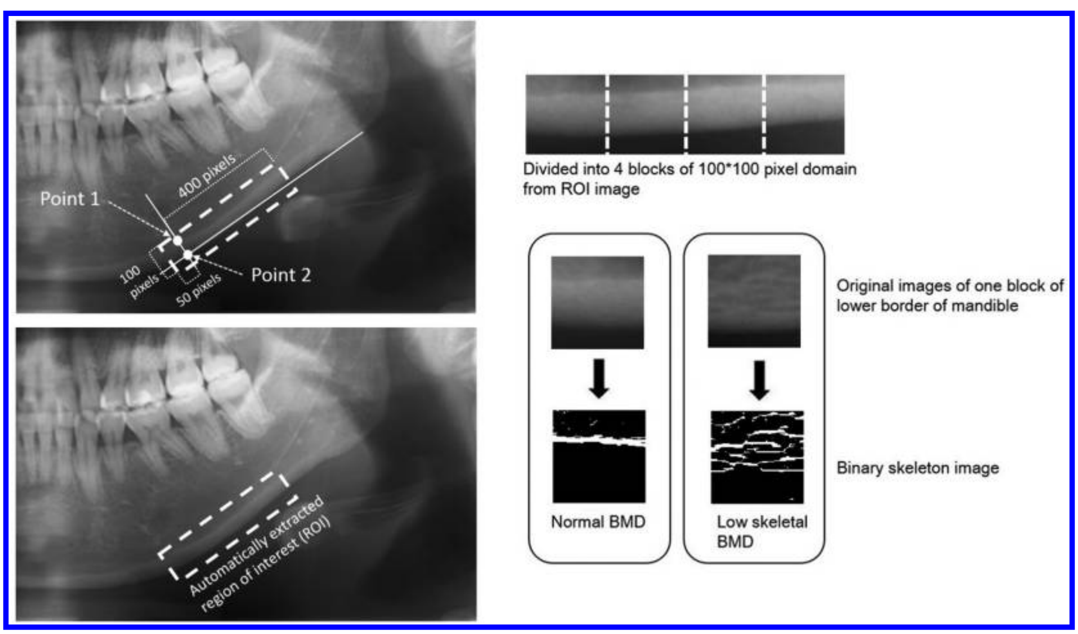

Figure 1 Image processing within the conventional CAD system. The cortical bone of the inferior border of the mandible immediately under the mental foramen is automatically extracted as a ROI with a size of 400 × 100 pixels, and divided into four blocks. The image in each blocks are converted into binary skeleton lines by mathematical morphological image processing (via the image processing toolbox in Matlab). If there were blocks converted into an abundance of skeleton lines, the patient was projected to have low skeletal bone mineral density. CAD,computer-aided diagnosis; ROI, region of interest.

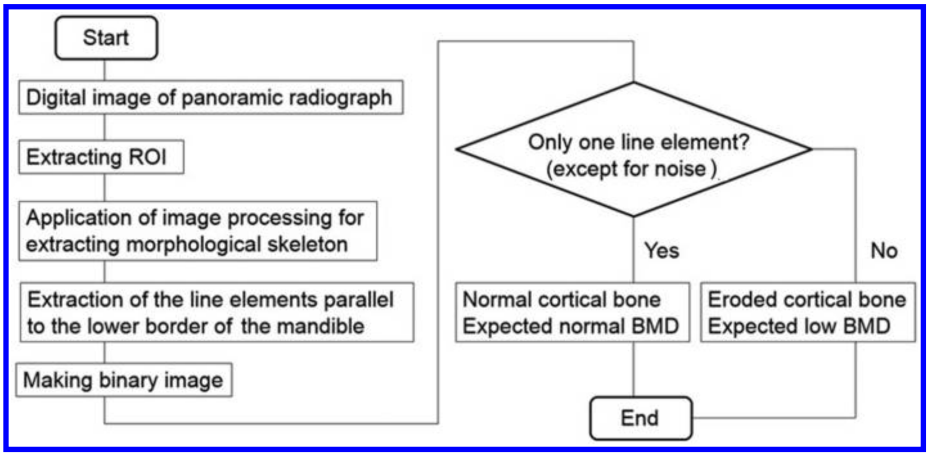

Figure 2 Flow diagram of a conventional CAD system. CAD,computer-aided diagnosis; ROI, region of interest.

resorption severity index (BRSI) based on the shape of skeleton lines after image processing, (2) to investigate whether the results of visual evaluation of the bone porosity and the BRSI are correlated, (3) to calculate the threshold value of the BRSI that is most suitable for identifying the bone resorption, and to measure diagnostic accuracy for vertebral osteoporosis using this threshold value, and (4) to investigate whether the BRSI correlates with lumbar spine bone density.

Methods and materials

Panoramic radiographs and bone mineral density assessment of the lumbar spine

The study was designed as a retrospective study using panoramic radiographs, BMD examination data, and other patient history data from patients included in a study that led to the development of an earlier version of the software.[29] Panoramic radiographs from 200 postmenopausal females aged 50 years or older, who visited our department between 2009 and 2011 were used in this study. It has been confirmed that these participants had no history of bone metabolic diseases and no history of use of drug intake that could affect bone metabolism. All participants agree to participate in this study. Conducting this research using data, including taking panoramic radiographs and BMD assessment through DXA, obtained from the participants has been approved by the Hiroshima University Clinical Research Ethics Committee in 2008. For each image, the lower border of the mandible just under or slightly distal to the mental foramen was defined as ROI. Extraction of ROI used the same method as the conventional software and was performed automatically.[29] Consequently, 136 ROIs were selected from both sides. These ROIs did not include radiopaque images other than the target mandible, such as the hyoid bone and a ghost image of the contralateral mandible. Figure 4 shows an example of a ROI including the hyoid bone. As indicated by the arrow, this image should not have been evaluated has been included in the evaluation (as it contains the hyoid bone). Therefore, such images were excluded from the subjects. Of all 200 participants, 68 females (mean age 64.1 ± 8.34) were selected. Of all selected 68 participants, 40 females were classified into Group A. The participants in Group A were used to define BRSI, to investigate whether the results of the visual evaluation of the bone porosity and the BRSI correlated, and to

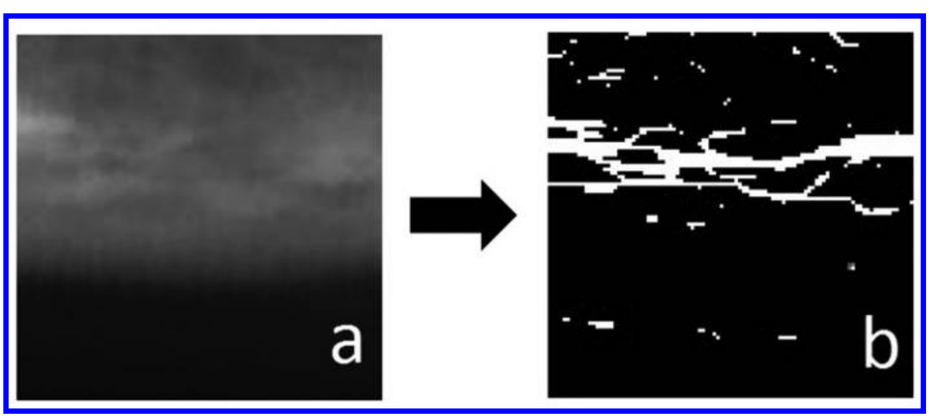

Figure 3 Example of a false-negative case in which all skeleton lines were connected after image processing.

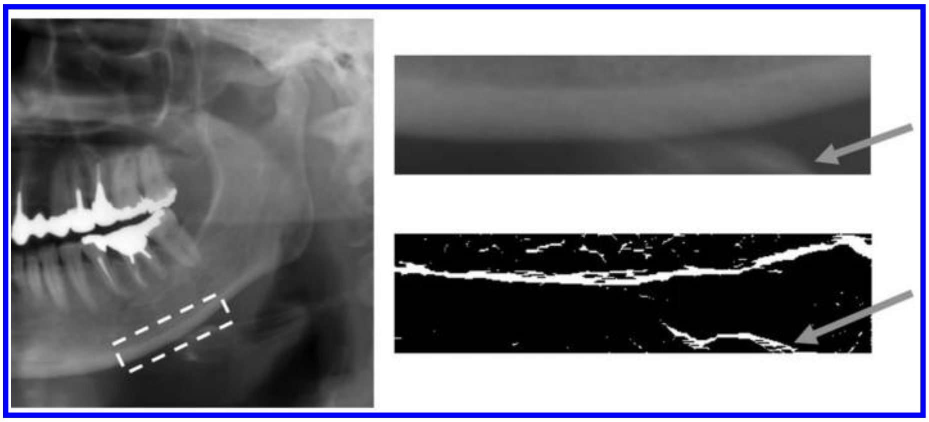

Figure 4 An example of a ROI including a part of the hyoid bone. ROI, region of interest.

calculate the BRSI threshold which closest matched the visual evaluation. The other 28 participants (mean age 58.6 ± 7.68) were also selected from 68 participants, and classified as Group B. The participants in Group B received a bone density test on the second to fourth lumbar vertebrae through dual energy absorptiometry (DXA) on the same day as their panoramic radiography examination. The absence of vertebral fractures was confirmed in all patients using lateral radiographs of the lumbar spine taken at the same time as the DXA measurement. Group B was used to assess the diagnostic accuracy by comparing the results of the osteoporosis diagnosis based on DXA to the results of the diagnosis acquired through the redesigned novel CAD system, and to evaluate the correlation between the BRSI and the lumbar vertebral bone density measurement as assessed by DXA. All panoramic radiographs were taken using Cypher® digital panoramic X-ray equipment (Asahi Roentgen, Kyoto, Japan). Furthermore, DPX-α® (Lunar Co., Madison, WI) was used for the BMD test. Based on the World Health Organization's diagnostic criteria, those with bone density below −2.5 standard deviation (SD) of the young adult mean (YAM) should be diagnosed as osteoporosis. Table 1 shows the results of bone density measurement of Group B.

Calculation method of linear bone resorption severity index

The images inside the ROIs were converted to skeleton lines by image processing based on mathematical morphology[30] and binarized in the same method as conventional CAD.[28,29] Figure 5 shows examples of 400 × 100 pixel regions of mandibular cortical bone as ROI which are converted into morphological skeleton lines. Within the binarized skeleton line, in the region where the thickness exceeded three pixels, internal bright areas were cut out and a 1-pixel margin was extracted. All the bright pixels of the image after this processing were decided to constitute the perimeter of the skeleton line. The total perimeter pixel length of all skeleton lines was defined as the BRSI. Therefore, the BRSI unit is a pixel. MATLAB 2010a in combination with the Image Processing Toolbox (MathWorks, Inc. Natick, MA) was used for all image processing and index calculation.

Visual classification of the mandibular cortical bone

The ROIs of panoramic radiographs of Group A were visually classified into two groups: those with and without linear bone resorption. Classification was performed by three evaluators (TN, SY, SH). Only if linear bone resorption was found by all evaluators an image would be classified as displaying bone resorption. If even one of the evaluators judged that there was no bone resorption, the image was classified as not showing bone resorption.

Statistical evaluation and CAD reconstruction

Based on the results of visual evaluation of images of Group A, the BRSI was calculated for each of the ROIs with and without the linear bone resorption group. Mann–Whitney's *U* test was used to assess whether there was a significant difference between the two groups' mean values. Receiver operator characteristic (ROC) analysis (which is a graphic illustration of the diagnostic capacity of a binary classification system through

Table 1 Result of bone density measurements of Group B

	The second to fourth lumbar vertebrae bone density	
	YAM ≥ −2.5SD	*YAM < −2.5SD*
Number of participants	17	11
Average BMD of the second to fourth lumbar vertebrae (g/cm^2)	1.040 ± 0.121	0.721 ± 0.094

BMD, Bone Mineral Density; YAM, young adult mean.

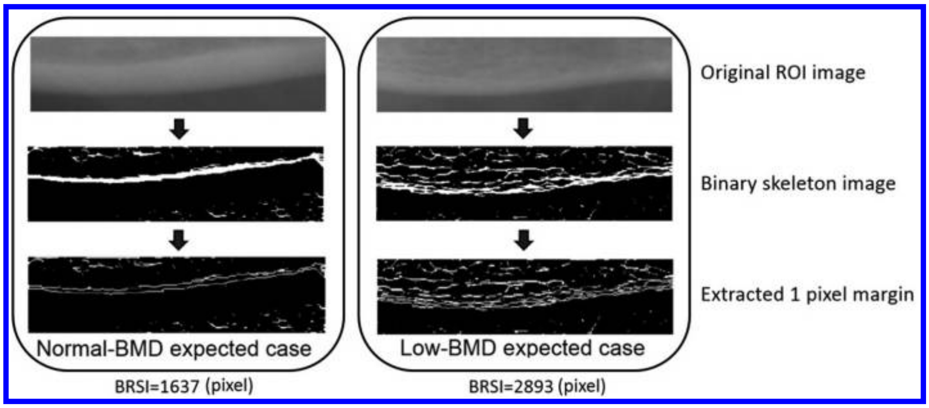

Figure 5 Comparison of binary skeleton images between normal- and low-BMD expected cases. The total perimeter length of the skeleton lines is predicted to be longer for low-BMD expected cases. The total perimeter length of all skeleton lines was coined the BRSI. BMD,bone mineral density; BRSI, bone resorption severity index; ROI, region ofinterest.

systematic variation of its discrimination threshold) was used to investigate the correlation between the visual assessment result and the BRSI. In addition, the optimal threshold value of BRSI that most closely approximated the visual assessment required when the system determines the presence or absence of bone resorption was obtained through ROC analysis. That is, we redesigned the CAD to indicate that the subject was suspected to have low vertebral bone mass if the input image exceeded the BRSI threshold.

Panoramic radiographs of Group B were diagnosed using the redesigned CAD to evaluate its diagnostic efficacy. The osteoporosis diagnosis based on the lumbar spine bone density measurement by DXA and diagnosis of CAD were compared, and the sensitivity, specificity, and accuracy were obtained. Furthermore, the correlation between BRSI and the lumbar vertebral bone density of the image of Group B was evaluated using Spearman's rank correlation coefficient.

p-Values of < 0.05 were considered to represent significant differences for Mann–Whitney's *U* test and Spearman's rank correlation coefficient. SPSS v 11.0 statistical software (SPSS Inc., Chicago, IL) was used for all statistical analysis. MATLAB 2010a in combination with the Image Processing Toolbox (MathWorks, Inc. Natick, MA) was used to redesign the existing CAD system.

Results

As a result of the visual evaluation, linear bone resorption images were observed in 33 out of 80 ROIs on both sides of the image within Group A. The mean of the ROI's BRSI's with and without visual linear bone resorption images were 2589.4 ± 311.5 and 1786.4 ± 240.7, respectively. Those with visual linear bone resorption showed significantly higher values ($p < 0.05$).

Figure 6 shows an ROC curve using the results of visual evaluation and BRSI. The area under the ROC curve was 0.983. Therefore, BRSI was strongly correlated with visual evaluation. It was found that the image with larger BRSI tended to be visually classified as linear bone resorption.

A part of the BRSI, sensitivity, and 1-specificity frequency distribution table is shown in Figure 7. The sensitivity-(1-specificity) is maximum when the BRSI threshold was 2198. Therefore, it was found that the threshold value of BRSI closest to the visual evaluation is 2198.

When the panoramic X-ray image of Group B was diagnosed using the obtained threshold value and compared with lumbar spine bone density measurement by DXA, the sensitivity, specificity, and accuracy were 90.9%, 64.7%, and 75.0%, respectively. When the same image was diagnosed through the conventional system, the sensitivity, specificity, and accuracy were 90.9%, 70.6%, and 78.6%, respectively. The redesigned new CAD system had slightly higher diagnostic accuracy, but with somewhat lower diagnostic efficacy than the conventional system. There was one more false-positive as compared to the conventional system. The Spearman's rank correlation coefficient between the BRSI and lumbar vertebral bone density in Group B was −0.563, indicating a strong negative correlation ($p < 0.01$).

Discussion

We devised the BRSI for CAD diagnosis based on the shape of the linear resorption image of the mandibular marginal cortical bone on panoramic radiographs. False negatives as shown in Figure 3 appeared slightly less frequently using this metric. In fact, the BRSI displayed in Figure 3 (originally incorrectly diagnosed as normal) exceeded the threshold (BRSI = 2908) and was therefore correctly diagnosed as suspected low BMD in the new system. As the BRSI had a strong correlation with the visual evaluation as well as a strong negative correlation with lumbar vertebral bone density, the higher the BRSI, the more linear bone resorption images appeared, and the suspicion that the lumbar spine had

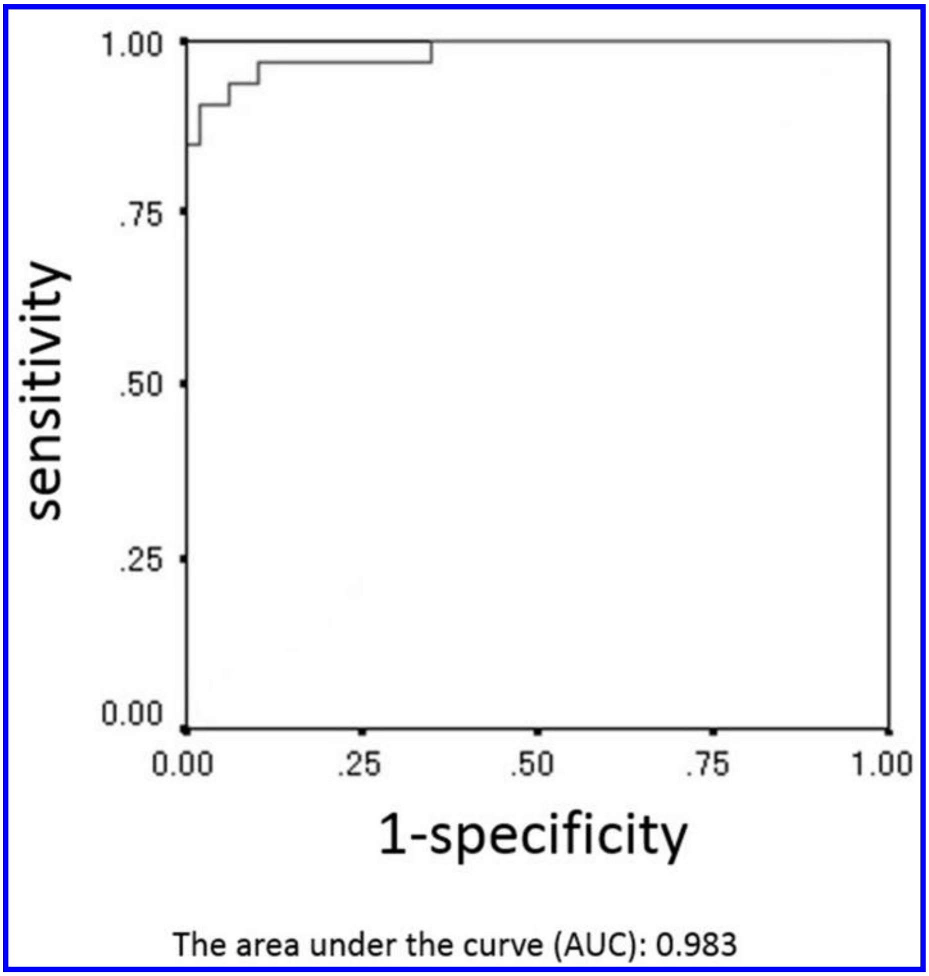

Figure 6 ROC curve from the comparison of visual evaluation results and BRSI. AUC,are under the curve; BRSI, bone resorption severity index; ROC, receiveroperating characteristic.

lower bone density increased. By using BRSI, we believe that osteoporosis screening using a panoramic radiographs can be performed quantitatively. If the BRSI is provided together with the diagnosis result, the clinical dentist can assess whether the value is close to the BRSI threshold value even if the diagnosis result of the CAD does not suspect low skeletal BMD. In such cases, the clinical dentist could still alert the patient to be cautious. Furthermore, if the BRSI value is much higher than the threshold value, the clinical dentist could confidently recommend that the patient should undergo a more accurate bone density test, such as DXA, at a medical hospital. Conversely, compared to the conventional system, the specificity and the accuracy of the novel CAD system were slightly decreased.[29] The reason was that there was one more false-positive compared to the conventional system. In this study, we used only cases in which structures other than the targeted lower jawbone cortical bone, such as the hyoid bone, were not included in the ROI. Therefore, the number of participants who could participate in this study was relatively small. The conventional system was designed using over 200 participants.[29] On the other hand, only 68 participants were included in the current study. It seems beneficial to appraise the system and evaluate its diagnostic accuracy using more participants in the future. In addition, it will be necessary to consider the evaluation method when radiopaque images other than the mandibular cortical bone is included in the ROI as shown in Figure 4. For example, conventionally, the ROI was divided into four blocks of 100 × 100 pixels, and the blocks including undesirable images were excluded from evaluation.[29] Although some manual operations will be required, it still qualifies as a beneficial endeavor. This system was designed using Cypher® digital panoramic X-ray equipment. Therefore, if the images are not compatible with this X-ray machine, automatic ROI selection and diagnosis will be difficult to perform (as the resolution and the characteristics of the image are different). In order to better disseminate the CAD system, it will be necessary to eliminate this machine model dependency. In addition, this study focused on detecting vertebral osteoporosis, and investigated the relationship between lumbar bone density and BRSI. Generally, to examine

BRSI (pixel)	Sensitivity	1-specificity
1277	1.000	1.000
1360	1.000	.980
1446	1.000	.959
1462	1.000	.939
2036	.970	.204
2043	.970	.184
2050	.970	.163
2067	.970	.143
2086	.970	.122
2094	.970	.102
2102	.939	.102
2119	.939	.082
2133	.939	.061
2152	.909	.061
2182	.909	.041
2198	.909	.020
2227	.879	.020
2284	.848	.020
2322	.848	.000
2339	.818	.000

Figure 7 A part of the frequency distribution table from the ROC analysis. BRSI,bone resorption severity index; ROC, receiver operating characteristic.

the presence of whole-body osteoporosis, a BMD measurement of the femoral neck is also performed.[31–33] Therefore, it may be necessary in the future to investigate whether BRSI also correlates with the BMD of femoral neck to improve our understanding of the relationship between skeletal bone densities. While these issues need to be resolved, the newly designed CAD system opens additional screening options to assess the presence of osteoporosis more effectively than before.

Conclusions

A novel CAD system using the BRSI to evaluate the porosity of the lower marginal cortical bone on panoramic radiographs quantitatively was designed. The visual evaluation for porosity in the lower border of the mandible and the BRSI were highly correlated. Therefore, it was concluded that the higher the

BRSI, the higher the mandibular porosity. The BRSI threshold value that was closest to the visual evaluation was obtained, and adopted for the new system. The new CAD had a high diagnostic accuracy close to that of the conventional system. A strong negative correlation was found between BRSI and bone density of lumbar spine. Therefore, it was considered that the higher the BRSI, the higher the possibility of low vertebral bone density. As the porosity of the mandibular cortical bone could now be displayed numerically by the new CAD system, objective and quantitative evaluation for osteoporosis screening has been made easier. Further improvements in diagnostic screening such as those reported in this paper will contribute to the prevention of bone fractures caused by osteoporosis.

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