RESEARCH ARTICLE

Automatic detection of osteoporosis based on hybrid genetic swarm fuzzy classifier approaches

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Objectives: This study proposed a new automated screening system based on a hybrid genetic swarm fuzzy (GSF) classifier using digital dental panoramic radiographs to diagnose females with a low bone mineral density (BMD) or osteoporosis.

Methods: The geometrical attributes of both the mandibular cortical bone and trabecular bone were acquired using previously developed software. Designing an automated system for osteoporosis screening involved partitioning of the input attributes to generate an initial membership function (MF) and a rule set (RS), classification using a fuzzy inference system and optimization of the generated MF and RS using the genetic swarm algorithm. Fivefold cross-validation (5-FCV) was used to estimate the classification accuracy of the hybrid GSF classifier. The performance of the hybrid GSF classifier has been further compared with that of individual genetic algorithm and particle swarm optimization fuzzy classifiers.

Results: Proposed hybrid GSF classifier in identifying low BMD or osteoporosis at the lumbar spine and femoral neck BMD was evaluated. The sensitivity, specificity and accuracy of the hybrid GSF with optimized MF and RS in identifying females with a low BMD were 95.3%, 94.7% and 96.01%, respectively, at the lumbar spine and 99.1%, 98.4% and 98.9%, respectively, at the femoral neck BMD. The diagnostic performance of the proposed system with femoral neck BMD was 0.986 with a confidence interval of 0.942–0.998. The highest mean accuracy using 5-FCV was 97.9% with femoral neck BMD.

Conclusions: The combination of high accuracy along with its interpretation ability makes this proposed automatic system using hybrid GSF classifier capable of identifying a large proportion of undetected low BMD or osteoporosis at its early stage.

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Introduction

Osteoporosis is a skeletal disease characterized by a reduction of bone mass resulting in impaired bone architecture.¹ It is associated with the thinning and

increased porosity of the cortical bone, and reduced connectivity of the trabecular bone structures, which increase bone fragility and risk of fractures.² The most commonly used method for screening osteoporosis is the measurement of bone mineral density (BMD) by dual-energy X-ray absorptiometry.³ Although BMD is

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Figure 1 A digital dental panoramic radiograph of a 61-year-old female, with marked boxes on the right and left sides showing the region of interest (ROI).

a significant predictor of fracture risk, it is a generic factor and does not differentiate between the cortical and trabecular bones or predict much about the internal structure of the bone.⁴ However, dental radiography is a great tool to observe the alterations of the mandibular cortex as well as the trabecular bone.⁵

Computer-assisted image analysis is useful to visualize and evaluate the bone architecture directly from the dental panoramic radiograph (DPR), thus reducing human intervention.^{6,7} Various regression models have been proposed earlier for osteoporosis.^{5,8,9} However, these models require strong assumptions to predict the relationship between disease risk and each risk factor. In recent years, use of classifier systems like multi-layer perceptron,¹⁰ Bayes classifier,¹¹ random forest classifier,¹² multilayer feed-forward neural network¹³

and support vector machine (SVM) based on cortical^{14,15} or trabecular bone features^{16,17} has been developed for the detection of a low BMD or osteoporosis. Although all these classifiers delivered an acceptable diagnostic accuracy, they did not explain the input variables involved, the interpretations of experimental results or how they produced a predicted outcome. Therefore, these screening systems possess very little flexibility in developing an accurate diagnostic system and are imprecise in updating the associated model.

Lately, fuzzy logic is in trend and has been proven to efficiently solve this problem in several medical diagnoses.^{18–20} The combination of computer-assisted diagnostic tools and interpretable rules certainly help early diagnosis of a low BMD or osteoporosis. To our knowledge, the only method available for osteoporosis

Figure 2 The original region of interest (a), skeleton image (b), trabecular segments (c) and thinning of trabecular segments (d).

Figure 3 The block diagram of the proposed system. BMD, bone mineral density; DPR, dental panoramic radiograph; GS, genetic swarm; MF, membership function; RS, rule set.

assessment based on DPRs is the medical expert system proposed by Arifin *et al.*²¹ They reported that their fuzzy neural network-based computer-aided system effectively identified post-menopausal females with suspected low BMD. In their study, the interpretable rules required for the system were collected from oral radiologists. The diagnostic decisions depend on the experience, expertise and perception of the practitioner.²² As complexity of the system increases, it is not easy to follow a particular path for diagnosis. Hence, owing to the difficulties associated with the derivation of the rule base from experts, researchers developed inductive learning algorithms which derive knowledge directly from the data, thus minimizing human intervention and increasing the reliability and performance of the system. In light of these factors, this study has adopted genetic swarm (GS) optimization algorithm,^{23,24} which combines the strengths of genetic algorithms (GAs) with those of particle swarm optimization (PSO), for designing a fuzzy classifier to diagnose a low BMD or osteoporosis. GA²⁵ and PSO²² are the best known evolutionary algorithms used in several medical diagnoses.^{22,26–28}

This study focused on developing an automatic osteoporosis diagnostic system that surpassed the defects

of existing learning algorithms. The objective of the study was to propose a hybrid genetic swarm fuzzy (GSF) classifier for obtaining simple and interpretable knowledge for a low BMD or osteoporosis from the geometrical attributes of the mandibular cortical and trabecular bone on dental radiographs and also to evaluate the performance of the hybrid GSF classifier compared with that of individual GA and PSO fuzzy classifiers.

Methods and materials

This study involved 141 female subjects within the age range 45–92 years (64.3 ± 11.2 years) who visited Kyungpook National University Hospital, Daegu, Korea, between February 2007 and April 2012. Each subject underwent both digital DPR and BMD evaluation during their visit. Of the 141 patients, 120 patients and 21 patients were classified as normal and as having a low BMD or osteoporosis, respectively, based on lumbar spine BMD, whereas 121 patients and 20 patients were determined to be normal and as having a low BMD or osteoporosis, respectively, based on femoral neck BMD. All digital DPRs were acquired using the same digital panoramic equipment (OP-100D; Imaging Instrumentarium, Tuusula, Finland) at 12 mA and 17 s; the voltage was modified between 60 and 70 kV, using automatic exposure control. Images were stored in joint photographic experts group format with a matrix of 2972×1536 -pixel resolution.

BMD evaluation was performed on the lumbar spine (L2–L4), femoral neck or both by using dual-energy X-ray absorptiometry (GE Healthcare, Madison, WI). The patients were classified as normal (T-score ≥ -1.0), osteopenic (T-score between -1 and -2.5) or osteoporotic (T-score ≤ -2.5) at each skeletal site according to the World Health Organization guidelines.²⁹ The study protocol was approved by the Institutional Research Board of Kyungpook National University Hospital.

Assessment of the mandibular cortical bone

The inferior mandibular cortical width was measured continuously both to the right and left sides (300×300 pixels) of the mandibular cortex at every point between the upper and lower boundaries of the cortical bone (Figure 1). The procedure was similar to the one designed by a previous study.⁶ Briefly, the system used the eight-neighbourhood distance function and dynamic programming to estimate the diameter and optimal path of the segmented cortical bone, respectively. The cortical margins were obtained as the envelope of the disc outlined by each pixel on the trace and its radius equalled the pixel value. Furthermore, the distance between the boundaries of the cortex was measured using a second-order polynomial function. The cortical fractal dimension (C.FD) was measured on the segmented image of the cortical bone for either side as described in

Figure 4 Membership functions.

Table 1 Multiple regression analysis of the significant attributes of the mandibular cortical and trabecular bones based on femoral neck bone mineral density

Attributes	Unstandardized		Standardized		p-value	95% confidence interval	
	B	Standard error	B	t		Lower bound	Upper bound
C.Wi	0.392	0.038	0.4353	5.66	0.0001 ^a	0.2637	0.6069
C.FD	0.3081	0.0026	0.0266	3.82	0.0003 ^a	0.0128	0.0405
Tb.Wi	0.6826	0.0041	0.1105	11.01	0.0001 ^a	0.0907	0.1304
Tb.FD	0.1423	0.0075	0.035	1.7	0.0913	−0.0059	0.0767
Tb.N	0.6067	0.0276	0.5504	9.01	0.0103 ^b	0.4339	0.6788
Tb.Sp	0.73	0.0039	0.0937	12.62	0.0001 ^a	0.079	0.1084
Tb.E	0.159	0.062	0.033	3.2	0.117	0.0252	0.0421
Tb.Ao	0.1852	0.0231	0.917	2.832	0.1582	0.728	1.178
Tb.Ec	0.250	0.028	0.310	3.48	0.056	0.148	0.501
Tb.L	0.3807	0.0028	0.247	4.28	0.082	0.113	0.336

C.FD, cortical fractal dimension; C.Wi, cortical width; Tb.Ao, trabecular angular orientation; Tb.E, trabecular Euler number; Tb.Ec, trabecular eccentricity; Tb.FD, trabecular fractal dimension; Tb.L, trabecular segment length; Tb.N, trabecular number; Tb.Sp, trabecular separation; Tb.Wi, trabecular width.

$R = 0.779$, $R^2 = 0.607$, adjusted $R^2 = 0.601$, standard error of the estimate = 0.7228.

^a $p < 0.01$ significant difference.

^b $p < 0.05$ significant difference.

a previous study.¹⁵ The mean mandibular cortical width and C.FD values from both sides of the mandibular cortex were used in this study.

Assessment of the trabecular bone

A computer-aided diagnostic system that automatically measures the trabecular bone pattern of the mandible on DPRs similar to a previous study was employed.³⁰ The area to the left (250×150 pixels) of the mandible, inferior to the first premolar, was assigned as the region of interest because of its sharpness. In brief, the morphological skeleton of the trabecular bone was extracted from the original image by the combinations of image-processing methods such as median filter, Radon transformation, erosion and dilation. Finally, an average filter followed by the traditional thinning algorithm was applied to acquire the trabecular bone into line segments of one-pixel width (Figure 2). The trabecular fractal dimension was measured on the segmented image, which is an indicator of the complexity of the trabecular bone structure.¹⁵ In addition, the following attributes were extracted from the segmented image based on structural anisotropy and mechanical properties of the trabecular bone:

- (I) trabecular width or trabecular thickness: the mean distance across individual trabeculae, represented in micrometres

- (II) trabecular number: the number of trabecular plates per unit distance
- (III) trabecular separation: the mean distance between trabeculae, represented in micrometres.
- (IV) trabecular Euler number: the difference between the total number of skeletons in the image and the number of holes in those skeletons. It is an indicator of the connectedness of a trabecular bone structure.
- (V) Trabecular angular orientation: the angle between the horizontal axis and the major axis of the ellipse whose second moments are same as the line segment. It provides a measure of bone strength and stiffness.
- (VI) Trabecular eccentricity: an elliptic parameter indicating a circular shape by lengthening, which was estimated using the following equation:

$$E_c = \frac{\sqrt{(L_M^2 - L_m^2)}}{L_M} \quad (1)$$

where L_M and L_m are lengths of the major (longest diameter of an ellipse) and the minor (shortest diameter of an ellipse) axes, respectively. A higher eccentricity value represents an elongated shape, while a lower value represents a circular shape of the trabecular bone structure.

Table 2 Correlation analysis of the significant attributes of mandibular cortical and trabecular bones based on femoral neck bone mineral density

Correlation analysis	C.Wi	C.FD	Tb.Wi	Tb.FD	Tb.N	Tb.Sp	Tb.E	Tb.Ao	Tb.Ec	Tb.L
Analysis of variances										
p-value	0.0001	0.0003	0.0001	0.093	0.0103	0.0001	0.117	0.1582	0.056	0.082
Sum square	3.3863	0.0127	0.2184	0.0224	5.5325	0.157	1.042	2.101	3.023	0.523
Sign	^a	^a	^a		^b	^a				

C.FD, cortical fractal dimension; C.Wi, cortical width; Tb.Ao, trabecular angular orientation; Tb.E, trabecular Euler number; Tb.Ec, trabecular eccentricity; Tb.FD, trabecular fractal dimension; Tb.L, trabecular segment length; Tb.N, trabecular number; Tb.Sp, trabecular separation; Tb.Wi, trabecular width.

F-value = 32.457, adjusted $R^2 = 0.601$.

^a $p < 0.01$ significant difference.

^b $p < 0.05$ significant difference.

Table 3 Genetic swarm control parameters

Parameter	Value
Population size	30
Cross-over probability	0.9
Mutation probability	0.1
Swap probability	0.5
weight min/max	0.4/0.9
C1/C2	2/2
Maximum generation	100

max, minimum; min, minimum.

(VII) Trabecular segment length (Tb.L): the number of pixels contained in the segment.

Fuzzy classifier design for screening osteoporosis

Fuzzy classifier has proved to be significantly useful in medical diagnosis for both the quantitative and qualitative evaluation of medical data and consequently in deriving accurate results.^{26–28} A fuzzy classifier is simply a classifier that includes a set of fuzzy membership function (MF) and rule set (RS). It consists of if–then rules characterized by the MF and is adopted and fired using the inference mechanism to derive the output. The basic steps in designing a classifier for identifying a low BMD or osteoporosis using DPR are partitioning of the input attributes to generate initial MF and RS followed by classification using a fuzzy inference system based on the generated MF and RS. The process is continued by repeated tuning of MF and RS using the GS algorithm until optimal classification performance is achieved. The block diagram of the proposed automatic osteoporosis screening on DPR using the hybrid GSF classifier system is shown in Figure 3. Each extracted attribute is fuzzified into three linguistic terms (low, medium and high) based on their measurements as shown in Figure 4. It is to be noted that a trapezoidal MF is assigned to low (l) and high (h) and triangle MF is assigned to medium (m). Each linguistics term is represented by three MF points and hence, each extracted and fuzzified attribute consists of nine MF points represented as $P_1, P_2, P_3, P_4, P_5, P_6, P_7, P_8$ and P_9 . The first and last points (P_1 and P_9) are fixed and represent the minimum and maximum values of the input variables, respectively. The remaining MF points are developed between the dynamic ranges with limits such as $[P_1, P_9]$ for P_2 , $[P_2, P_9]$ for P_3 , $[P_2, P_3]$ for P_4 , $[P_4, P_9]$ for P_5 , $[P_5, P_9]$ for P_6 , $[P_5, P_6]$ for P_7 and $[P_7, P_9]$ for P_8 . The general form of a fuzzy if–then rule in developing an RS is defined as

$$R_i : \text{if } [I_1 \text{ is } 0/(l/m/h)_{I_1}], [I_2 \text{ is } 0/(l/m/h)_{I_2}] \text{ and } I_n \text{ is } [0/(l/m/h)_{I_n}] \text{ then class } C_m \quad (2)$$

where “ R_i ” denotes rule selection that can take either 0 or 1 to select or deselect the rule, respectively. $I_1, I_2, I_3 \dots I_n$ are input variables representing a random integer value among 0, 1, 2 and 3 for denoting “none” (0), “low” (1), “medium” (2) and “high” (3). The output “ C_m ” represents 1 (healthy) and 0 (osteoporosis) class

labels. The newly generated initial MF and RS are fed to the fuzzy inference system to perform data classification. The inference system that performs qualitative reasoning through fuzzy implication operations has been used to classify the input into corresponding output classes.³¹ In this study, the GS algorithm is adopted for optimal acquisition of knowledge from the selected attributes of mandibular cortical and trabecular bones such that PSO is responsible for tuning the continuous points of MF, while GA is responsible for framing the discrete number of RS. Each MF point along with the corresponding RS is evaluated with the objective criterion of minimizing error and the number of rules. It is defined as

$$\text{Minimize } \text{Obj} = (T_s - C_s) + R_s \quad (3)$$

where T_s is the total number of samples, C_s is the number of correctly classified samples and R_s is the selected number of rules. The optimization of MF and RS using the GS algorithm is presented in Appendix A.

Statistical analyses

This study has used 10 input attributes and 1 class attribute. The significant attributes of the mandibular cortical and trabecular bones derived from DPR were selected by correlation and multiple regression analysis (SPSS® v. 17.0; IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL) in order to reduce the complexity for the next stage.^{32,33} The attribute “class” was considered a dependent variable and the remaining 10 attributes were considered independent variables while using BMD from both the lumbar spine and femoral neck. The level of significance was set at $p < 0.05$ for these experiments. The selected significant attributes were used as input for the fuzzy classifier model. The sensitivity and specificity were calculated to provide an indication of the overall performance of the model. The positive-predictive value, negative-predictive value, accuracy and the likelihood ratio for a positive risk result were also evaluated. The diagnostic accuracy of the proposed diagnostic system in identifying females with low skeletal BMD was evaluated by exercising receiver-operating curve analysis to calculate the area under the curve (AUC). The fivefold cross-validation method was applied to ensure the consistency and generalization of the prediction model produced by the GS algorithm. It is used to reduce bias in the machine learning algorithms. In fivefold cross-validation, the data are randomly separated into k equal subsets. While $k-1$ subsets are used as training data for the determination of the model parameters of the classifier, other subsets are used as data for testing the performance of the trained classifier. The experiment was repeated five times separately using different members of the training and testing data possessing different compositions from those of the other experiment. The average of these five different compositions of classification performance was evaluated. The performance of a hybrid GSF classifier

Figure 5 The optimal membership functions of the (a) cortical width, (b) cortical fractal dimension, (c) trabecular width, (d) trabecular number and (e) trabecular separation with lumbar spine bone mineral density.

has been further compared with individual GA fuzzy and PSO fuzzy classifiers.

Results

Table 1 shows five significant attributes of the mandibular cortical and trabecular bones on DPR calculated

by multiple regression analysis on the basis of femoral neck BMD, which included the cortical width, C.FD, trabecular width, trabecular number and trabecular bone separation ($p < 0.05$). Table 2 shows similar experimental results from the correlation and regression analysis. It displays the magnitude of variance by sum of square and correlation analysis, which were obtained from the magnitude of intersection between the

Figure 6 The optimal membership functions of the (a) cortical width, (b) cortical fractal dimension, (c) trabecular width, (d) trabecular number and (e) trabecular separation with femoral neck bone mineral density.

attributes, *i.e.* the “Class” and 10 other attributes. Similar significant attributes on the basis of lumbar spine BMD are not shown in the table. These five significant attributes of the mandibular cortical and trabecular bones derived from DPR were used as input for the hybrid GSF classifier. The GS algorithm extracts knowledge in the form of MF and RS from the data for the fuzzy inference system to perform classification. Hence, each attribute was partitioned to generate the

initial MF and RS. The generated RS was evaluated by allowing each rule at a time to perform classification of all the 141 data in this study. Based on the objective criterion as described above in Equation (3), the GS algorithm iteratively optimized the MF and RS for maximizing the accuracy and minimizing the number of rules. As seen in Figure 4, 9 MF points represented an input attribute and hence, a total of 45 (5×9) MF points were generated. The size of the newly generated initial RS was

Table 4 Indicative rules for low bone mineral density (BMD) or osteoporosis with lumbar spine and femoral neck BMD

<i>Skeletal region</i>	<i>Rules</i>
Lumbar spine BMD	If C.Wi is medium, Tb.Wi is medium and Tb.N is high, then normal If Tb.Sp is low, Tb.N is medium, C.Wi is high and C.FD is high, then normal If C.FD is low, Tb.Sp is low and Tb.N is medium, then normal If C.FD is low, C.Wi is high and Tb.N is high, then normal If C.Wi is low, C.FD is low, Tb.Wi is medium and Tb.Sp is high, then osteoporosis If C.Wi is low, Tb.N is low, Tb.Wi is low and C.FD is medium, then osteoporosis
Femoral neck BMD	If C.FD is low, Tb.Sp is low, Tb.Wi is medium, Tb.N is high, and C.Wi is high, then normal If C.Wi is low, C.FD is low and Tb.N is high, then osteoporosis If Tb.N is low, Tb.Wi is low and Tb.Sp is high, then osteoporosis

C.FD, cortical fractal dimension; C.Wi, cortical width; Tb.N, trabecular number; Tb.Sp, trabecular separation; Tb.Wi, trabecular width.

fixed to contain a maximum of 10 if–then rules. Since each rule requires 7 design variables (1 or 0 for rule selection, 5 input attributes and 1 or 0 for output class), a total of 70 (7×10) design variables represented the complete RS. The GS algorithm was found to yield better classification results with different values for the control parameters which are presented in Table 3. It was observed that the MF points tuned by the GS were optimized after 50 iterations and allocated evenly within the boundaries of each linguistic term to attain an acceptable classification accuracy at both lumbar spine and femoral neck BMDs. The optimal MF graphs for the five significant attributes of the mandibular cortical and trabecular bones on DPR with lumbar spine and femoral neck BMD are shown in Figures 5 and 6, respectively. The ranges of values are also plotted in the graphs. During each generation, the ranges of each MF points were evolved and tuned simultaneously along with the RS. Furthermore, when the tuned MF and the RS were fed into the fuzzy classifier, the highest classification accuracy of 96.0% with minimum number of six rules at the lumbar spine BMD, 98.9% with minimum number of three rules at the femoral neck BMD was observed. The evolved optimal rules based on the ranges of values acquired from the attributes of DPR at lumbar spine and femoral neck BMD for classifying normal females from those with a low BMD or osteoporosis are

shown in Table 4. The sensitivity and specificity of the hybrid GSF classifier model predictions for classification were 95.3% and 94.7%, respectively, with lumbar spine BMD and 99.1% and 98.4%, respectively, with femoral neck BMD and are presented in Table 5. The diagnostic performance of the proposed system with femoral neck BMD resulted in a higher performance of AUC (0.986) with a confidence interval of 0.942–0.998 for identifying females with a low BMD or osteoporosis than that with lumbar spine BMD 0.962 with a confidence interval of 0.912–0.983. In addition, the mean accuracy measured using the geometrical attributes of the mandibular cortical and trabecular bones for the lumbar spine and the femoral neck BMD were 94.3% and 97.9%, respectively, using the hybrid GSF classifier model as shown in Tables 6 and 7. The performance of the GA fuzzy and PSO fuzzy classifiers was inferior to that of the proposed hybrid GSF classifier, as shown in Figure 7. The complex operations of GA took more iterations for optimizing MF and RS at both lumbar spine and femoral neck BMDs. In addition, the MF and RS generated by GA were not suitably modified in each iteration, resulting in lower accuracy and more rules than the GS algorithm. Although the simplified operations of PSO took lesser iterations than the GS algorithm for optimizing MF and RS, it delivered a poor classification accuracy and more number of rules than the hybrid GS algorithm owing to the small inertia weight and early premature convergence of the global best position over a period of iterations.

Discussion

This study has newly proposed an automated screening system using a hybrid GSF classifier model based on the geometrical attributes of the cortical and trabecular bone of the mandible acquired from DPR for discriminating females with a low BMD or osteoporosis from normal females. In both skeletal sites, high classification results were obtained compared with conventional classifiers, with an accuracy of 96.0% at the lumbar spine and 98.9% at the femoral neck. Furthermore, a hybrid GSF classifier based on the DPR built in this study provides diagnostic knowledge and explanation ability in terms of the most relevant and interpretable rules with high classification performance (0.986), especially at the femoral neck BMD for the diagnosis of a low BMD or osteoporosis. The ranges of values of each linguistic term for every input attributes derived

Table 5 Diagnostic performance of the hybrid genetic swarm fuzzy classifier in classifying females with low lumbar spine and femoral neck bone mineral density at 95% confidence interval

<i>Skeletal region</i>	<i>Sensitivity (%)</i>	<i>Specificity (%)</i>	<i>Positive-predictive value (%)</i>	<i>Negative-predictive value (%)</i>	<i>Accuracy (%)</i>	<i>Likelihood ratio (+) (%)</i>	<i>Prevalence (%)</i>
Lumbar spine	95.3 (76.2–99.8)	94.7 (90.5–98.6)	80.0 (59.3–93.2)	98.1 (95.3–99.9)	96.0 (90.3–99.5)	22.86 (9.6–54.2)	14.89 (9.5–21.7)
Femoral neck	99.1 (83.2–100)	98.4 (94.2–99.8)	91.2 (70.8–98.9)	99.4 (96.7–100)	98.9 (92.0–100)	60.5 (15–239)	14.18 (8.9–21)

Table 6 Classification performance of the hybrid genetic swarm fuzzy classifier using fivefold cross-validation with lumbar spine bone mineral density

<i>Fold</i>	<i>Tr—composition range</i>	<i>Tr—size</i>	<i>Te—composition range</i>	<i>Te—size</i>	<i>CC</i>	<i>Accuracy (%)</i>
Fold 1	29–141	113	1–28	28	26	92.86
Fold 2	1–29 and 57–141	113	29–56	28	27	96.43
Fold 3	1–56 and 85–141	113	57–84	28	27	96.43
Fold 4	1–84 and 113–141	113	85–112	28	26	92.86
Fold 5	1–112	112	113–141	29	27	93.1

CC, correctly classified; Te, testing data; Tr, training data.

from the MF were manually examined by the oral radiologists (KHH and MSH). Furthermore, the significance of different combinations of input attributes and their linguistic terms found in each rule produced by the GS algorithm in determining normal and a low BMD or osteoporosis was also verified based on the number of correctly classified samples from the total number of samples. The structural parameters such as thickness, number and separation of the trabecular bone were found to be related to osteoporotic subjects and the reported ranges of values for identifying a low BMD or osteoporosis were almost similar to the linguistic terms associated with each attribute in this study.³⁴ Furthermore, several studies^{6,7,21,35,36} suggested the cut-off threshold of cortical width as the most appropriate threshold for referral for bone densitometry and it is also similar to the ranges of values obtained from MF in this study.

Till date, there has been only one study that developed a fuzzy expert system for the diagnosis of osteoporosis using the attributes of the mandibular cortical bone.²¹ It was reported that MF was generated by using the thresholding method and integrated the RS based on expert knowledge in decision-making. Generation of knowledge-based interpretable rules for the classifier model is one of the most difficult and time-consuming part, since it involves acquiring specific knowledge from a group of medical experts.²⁰ Furthermore, in a complete fuzzy expert system, both MF and RS are dependent on each other and need to be tuned simultaneously. However, the study by Arifin *et al*²¹ focused only on tuning of the MF and not on the RS and hence could not be accounted as a complete fuzzy expert system. However, in this study, the GS algorithm generates both the MF and RS simultaneously and can be considered reasonable without any bias towards any particular linguistics. Furthermore, it is to be noticed that the rules obtained using DPR for both normal and

a low BMD or osteoporotic subjects are very simple, comprise the most significant attributes, are comprehensible and consequently would justify the decisions. Moreover, the sensitivities and specificities from this study are much higher than 84.0% and 74.7% reported in the study by Arifin *et al*.²¹ This vast difference in the detection performance is reasonable because the present system with GS algorithm tries to find solutions closer to the global optimum and hence, the average error of GS is much smaller than that of other techniques.²³ Furthermore, the difference in sensitivity and specificity may be due to the difference in outcomes; Arifin *et al*²¹ had used the outcome of cortical bone parameters, whereas the present study uses cortical as well as trabecular bone parameters. Incorporating more input variables of cortical as well as trabecular bones on DPR with a suitable definition of a fuzzy MF and RS has led to a better performance in identifying post-menopausal females with suspected low BMD.²¹

Several methods proposed previously for osteoporosis classification are based on “black box” approaches such as SVM and neural networks. In our previously proposed SVM model,³⁷ the average and variance of the mandibular cortical width were utilized for differential diagnosis, which resulted in a much lower sensitivity and specificity of 90% and 69.6%, respectively, with femoral neck BMD. Chang *et al*¹³ obtained a lower sensitivity (57.9%) and higher specificity (68.9%) from a multilayer feed-forward neural network using feature selection. Our newly proposed diagnostic system using optimized GSF classifier modelling has achieved a higher sensitivity and specificity especially with femoral neck BMD for determining females with normal and osteoporotic subjects compared with existing systems. Moreover, merging the genetic operations with swarm operations in the fuzzy classifier is the uniqueness of this study and it attempts introducing comprehensive RS and well-tuned MF along with the highest

Table 7 Classification performance of the proposed hybrid genetic swarm fuzzy classifier using fivefold cross-validation with femoral neck bone mineral density

<i>Fold</i>	<i>Tr—composition range</i>	<i>Tr—size</i>	<i>Te—composition range</i>	<i>Te—size</i>	<i>CC</i>	<i>Accuracy (%)</i>
Fold 1	29–141	113	1–28	28	28	100
Fold 2	1–29 and 57–141	113	29–56	28	28	100
Fold 3	1–56 and 85–141	113	57–84	28	28	100
Fold 4	1–84 and 113–141	113	85–112	28	28	96.43
Fold 5	1–112	112	113–141	29	27	93.1

CC, correctly classified; Te, testing data; Tr, training data.

Figure 7 Performance comparisons of a hybrid genetic swarm fuzzy classifier with individual genetic algorithm (GA) and particle swarm optimization (PSO) fuzzy classifiers for the (a) number of iterations, (b) number of rules in the rule set and (c) classification accuracy. BMD, bone mineral density.

classification accuracy. On the other hand, in an artificial neural network, learned knowledge is not transparent to the user and is concealed in several connections, thus rendering it incomprehensible.

The combination of textures and mandibular cortical width based on the SVM model classifier contributed to a better assessment of osteoporosis compared with the use of only individual measurements¹⁵ and reported a 96.8% accuracy, which is lower than our present result with femoral neck BMD. The study by Mantzaris et al³⁸ applied probabilistic neural networks based on the clinical characteristics of patients, which proved to be an effective potential soft computing technique for the evaluation of osteoporosis risk. It reported a 96.6% accuracy that is almost equal to the 96.0% accuracy with lumbar spine BMD in the present study. Another retrospective study by Testi et al¹¹ introduced Bayes classifier based on the clinical characteristics and geometric parameters of the proximal femur for hip fracture and reported an 82.0% accuracy, which is much lower than our present result. Another study implemented image processing and artificial intelligence-based techniques using trabecular bone features for osteoporosis and osteoarthritis and reported

100% success in classifying these two populations by using a GA.²⁸ However, that study employed various attributes, clinical factors and classifier models, which are different from ours and hence might not be directly comparable with ours. Furthermore, these approaches possess an inherent and practical drawback of opacity in their knowledge-based classification decisions, whereas our hybrid GSF classifier model can represent the interactions and relationships that exist between different attributes on DPR in a simple way owing to its symbolic formulation. This is a significantly important feature in developing support systems for medical decisions and will be immensely helpful to clinicians in diagnosis.

Recently, an osteoporosis prediction model using the multilayer perceptron has incorporated a new data preprocessing method.¹⁰ They have reported an increased classification performance with an AUC of 0.951 for 15 hidden layers, which is similar to the AUC of 0.962 at lumbar spine BMD and slightly lower than the AUC of 0.986 at femoral neck BMD evaluated in this study. The AUC (0.631) for the wrapper-based feature selection method was found to be higher than that without it (0.489) for identifying females with osteoporosis,¹³

which is in accordance with our finding that pre-processing using the statistical method to select significant features was useful in this study. Moreover, the optimization method increases the potential of discrimination for the diagnostic system up to the highest AUC of 0.962 at the lumbar spine and 0.986 at the femoral neck BMD. The limitation of this study is the use of a small number of representative training data in order to extract valid rules and create a reliable fuzzy model. Further studies with a large number of subjects, and different skeletal sites using different panoramic equipment, should be performed to evaluate the accuracy and RS of the proposed hybrid GSF classifier system for the diagnosis of a low BMD or osteoporosis based on the cortical and trabecular bone architecture. However, the present classifier model based on DPR can absorb the strengths of GA and PSO for validating a diagnostic system. Furthermore, employment of alternative global optimization techniques and additional information such as clinical characteristics could be introduced along with radiographic measurements to generalize the interpretable rules and linguistic variables.

To our knowledge, this is the first study to be carried out on optimization of this rule base. This is also the

first study to propose a low BMD or osteoporosis classification model using a hybrid GS optimization-based fuzzy classifier based on geometrical attributes of the mandibular cortical and trabecular bones from DPR. Our results reveal that the hybrid GSF classifier model using the attributes of the DPR has a notable performance accuracy and high efficiency in discriminating low BMD or osteoporosis from normal subjects. Compared with existing osteoporosis diagnostic models, our GSF classifier model has the following advantages: (1) efficiency in producing an acceptable classification accuracy along with reasonable interpretability of the results; (2) automatic selection of training parameters to generate both MF and RS; and (3) good discrimination performance with the small but different members of training and testing data. Moreover, this method strongly suggests that the attributes of both the mandibular cortical as well as the trabecular bone are potentially involved in designing the optimal RS for discriminating osteoporosis-related structural changes found in DPR. Taken together, the hybrid GSF classifier is a promising model for low BMD or osteoporosis diagnosis and a suitable classifier technique for early detection of undetected osteoporosis, which can also be incorporated into the automated diagnostic system.

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Appendix A

In this appendix, we provide the optimization method using the GS algorithm.

Using PSO, an adaptable velocity is randomly initialized for each MF point (treated as particle position). At each iteration step, the individual best position p^i and the global best position p_k^g are computed for each particle based on this measure. The new velocity and position of each particle is updated by the following equations:

$$v_{k+1}^i = \omega v_k^i + c_1 \times r_1 \times (p^i - x_k^i) + c_2 \times r_2 \times (p_k^g - x_k^i) \quad (A1)$$

$$x_{k+1}^i = x_k^i + v_{k+1}^i \quad (A2)$$

where v_k^i is the velocity of the particle i at iteration k , v_{k+1}^i is the velocity of the particle i at iteration $k + 1$, x_k^i is the position of the particle i at iteration k (previous MF point), x_{k+1}^i is the position of particle i at iteration $k + 1$ (new MF point), ω is the inertia weight (ranges from 0.4 to 1.4), r_1 and r_2 are random numbers between (0, 1), c_1 is the self-confidence factor (ranges from 1.5 to 2) and c_2 is the swarm confidence factor (ranges from 2 to 2.5).

GA attempts to optimize the generated RS using three operations repeatedly. Tournament selection, being the first operation, aims to select the best RS based on the objective criterion using Equation (3). Then, a BLX- α crossover is applied using Equations (A3–A5) between randomly selected if–then rules (parents) from

the initially generated RS, which gives rise to the new if-then rules (child).

$$Y = \begin{cases} e_1 + r \times (e_2 - e_1): & \text{if } u^{\min} \leq y \leq u^{\max} \\ \text{repeat sampling :} & \text{otherwise} \end{cases} \quad (\text{A3})$$

$$e_1 = u_1 - \alpha(u_2 - u_1) \quad (\text{A4})$$

$$e_2 = u_2 + \alpha \times (u_2 - u_1) \quad (\text{A5})$$

where $u^{\min}$ and $u^{\max}$ are the lower and upper bounds of the RS and u_1 and u_2 are the minimum and maximum of the randomly selected parent if-then rules from RS, respectively. While e_1 and e_2 denote the resultant child if-then rules, r and α are uniform random numbers between 0 and 1. Depending on the measurements of two parent if-then rules, the newly generated if-then rule (child) may be either close or far away from the parent. Finally, a non-uniform mutation operation is

applied, which also generates a new if-then rule by the equation

$$x'_k = \begin{cases} x_k + \Delta(t, \text{UB} - x_k), & \text{if a random } \beta \text{ is } 0 \\ x_k + \Delta(t, x_k - \text{LB}), & \text{if a random } \beta \text{ is } 1 \end{cases} \quad (\text{A6})$$

where LB and UB are the lower and upper bounds of the RS, x_k is a parent if-then rule, x'_k is a child rule and t is the value of the current iteration. The discrimination function $\Delta(t, y)$ is evaluated as:

$$\Delta(t, y) = y \left(1 - \gamma \left(1 - \frac{t}{T} \right)^b \right) \quad (\text{A7})$$

where γ is a random number between 0 and 1, T is the maximal iteration and b is a system parameter that determines the degree of dependency on the iteration number. This repeated process increases the probability of generating an optimized RS closer to its predecessor than a random choice.