Paper:

Developing computer-aided osteoporosis diagnosis system using fuzzy neural network

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A thin or eroded cortex of the mandible detected on dental panoramic radiographs is independently associated with low skeletal bone mineral density (BMD) or osteoporosis in postmenopausal women. The purposes of this study were to develop new computer-aided diagnosis system that combines these two panoramic measures by using fuzzy neural networks (FNN) for identifying postmenopausal women with osteoporosis. Dental panoramic radiographs of 100 postmenopausal women who visited our clinic and had BMD assessments at the lumbar spine and the femoral neck were used in this study. Mandibular cortical width and shape were measured by computer-aided systems and used as the inputs. This system partitioned the input space into a set of subspaces using a novel fuzzy thresholding and constructed the fuzzy inference system incorporated with multi layer perceptron neural network. Our results show that the combination of cortical width and shape by using FNN can be used for the identification of postmenopausal women with osteoporosis in dental clinic. Dentists may identify postmenopausal women accurately by using the new FNN based system and refer them to medical professional for BMD testing.

Keywords: computer-aided; fuzzy neural network; osteoporosis; panoramic radiograph

1. INTRODUCTION

Osteoporotic fracture is a risk factor for subsequent long-term morbidity and mortality in elderly, especially postmenopausal women. It is estimated that over 200 million people worldwide have osteoporosis (1). The prevalence rates of osteoporosis according to World Health Organization criteria in the Japanese female population aged 50 through 79 years are estimated as 35.1% at the spine (2). Since bone mineral density (BMD) is one of the indicators predicting osteoporotic fractures, postmenopausal women with low skeletal BMD should be referred for BMD testing. However, it is likely that a large segment of postmenopausal women with low BMD will not have BMD testing if they do not have a deep concern of osteoporosis. In fact, the low response rate (42%) in postmenopausal women who were invited for BMD testing has been reported in the Canadian Multicentre Osteoporosis Study (3).

Postmenopausal women have many opportunities to visit dental clinics for oral care or treatment. A large number of dental panoramic radiographs (approximately 12 million in Japan and 17 million in the United States) are taken annually for the diagnosis and treatment of dental diseases, such as dental caries and periodontal disease, but not for the diagnosis of non-dental diseases in general dental practice (4,5). It would be very beneficial for postmenopausal women with undetected low BMD if the dentists can identify them by incidental finding on dental panoramic radiographs and refer them to medical professionals for BMD testing prior to the incidence of osteoporotic fractures.

Some investigators have suggested that a thin or eroded inferior cortex of the mandible detected on dental panoramic radiographs is useful for identifying postmenopausal women with low skeletal BMD or osteoporosis (6-16). We demonstrated that an eroded cortex was significantly associated with biochemical markers of bone turnover in Japanese postmenopausal women (13). However, a thin cortex was not associated with these markers, suggesting that cortical width may mainly reflect peak bone mass obtained in younger age. Horner et al. demonstrated the significant association between cortical width and skeletal BMD in 135 healthy peri-menopausal women aged 45-55 years (9). Two cortical measures, cortical width and shape (erosion), were independently investigated in identifying postmenopausal women with low BMD or osteoporosis in previous studies; however, the combination of two measures may contribute to an increase of diagnostic efficacy.

We recently developed two computer-aided diagnosis systems in which the dentists can semi-automatically measure cortical width or cortical shape (erosion) on digitized dental panoramic radiographs rapidly and accurately (17, 18). The diagnostic efficacy of these systems in identifying postmenopausal women with osteoporosis was almost similar to that of an experienced oral radiologist and that of a questionnaire based screening tool for osteoporosis. A large number of dental panoramic radiographs can be accurately analyzed in screening for osteoporosis if dental panoramic radiographs are gathered and digitized in some institutions or if these systems can be installed in digital dental panoramic machine that recently spreads over the world (19).

The purposes of this study were to develop new computer-aided diagnosis system that combines two cortical measures by using Fuzzy neural networks (FNN) and to confirm the diagnostic efficacy of new system in identifying postmenopausal women with osteoporosis. In comparison with the previous two computer-aided diagnosis systems applied individually, the new system achieved much superior diagnostic efficacy for identifying postmenopausal women with osteoporosis.

2. MATERIALS

Subjects and panoramic radiography

Of 531 women who visited our clinic for BMD testing between 1996 and 2001, 100 postmenopausal women aged 50 years and older with no previous osteoporosis diagnosis (mean 59.6 years; range 50 to 84 years) were randomly recruited for this study. Panoramic radiography was taken for all the subjects with informed consent at the time of BMD measurements of the lumbar spine (L2-L4) and the femoral neck. Skeletal BMD was measured by dual energy-x-ray absorptiometry (DXA, DPX-alpha, Lunar Co., Madison, WI, U.S.A.). The *in vivo* short-term precision error for the lumbar spine and the femoral neck BMD in our clinic was 1.0% and 2.8%, respectively. None of the subjects had any metabolic bone disease (hyperparathyroidism, hypoparathyroidism, Paget's disease, osteomalacia, renal osteodystrophy, or osteogenesis imperfecta), cancers with bone metastasis, significant renal impairment and had medications that affect bone metabolism such as estrogen. None had a history of smoking and had any bone destructive lesions in the mandible. All the subjects had no menstruation for at least 1 year. When using the definition of the Japanese Society for Bone and Mineral research (20), 54 of the 100 women presented a normal BMD (BMD more than 80% of Japanese young adult mean), 21 osteopenia (70–80%) and 25 osteoporosis (less than 70%) in the lumbar spine. Forty-seven had normal BMD, 24 osteopenia and 24 osteoporosis in the femoral neck. Five women did not have DXA of the femoral neck. The rate of women with osteoporosis in the lumbar spine in our study was similar to that (26%) in 1033 postmenopausal women aged 50 years and older in the Adult Healthy Study (AHS) cohort in Japan (21).

Since we need to identify women with osteoporosis, the output of this study will be osteoporosis group and normal group. Therefore, we assigned all women with osteoporosis as the member of osteoporosis group and combined those with normal and those with osteopenia as the member of normal group.

All panoramic radiographs were obtained with AZ-3000 (Asahi Co., Kyoto, Japan) at 12 mA and 15 seconds; the kV varied between 70 and 80. Screens of speed group 200 (HG-M, Fuji Photo film Co., Tokyo, Japan) and film (UR-2, Fuji Photo film Co., Tokyo, Japan) were used. The appearance of the mandibular inferior cortex was bilaterally clear in the radiographs. All radiographs were digitalized with the resolution of 300 dpi using a flatbed scanner (ES-8000, Epson, Japan).

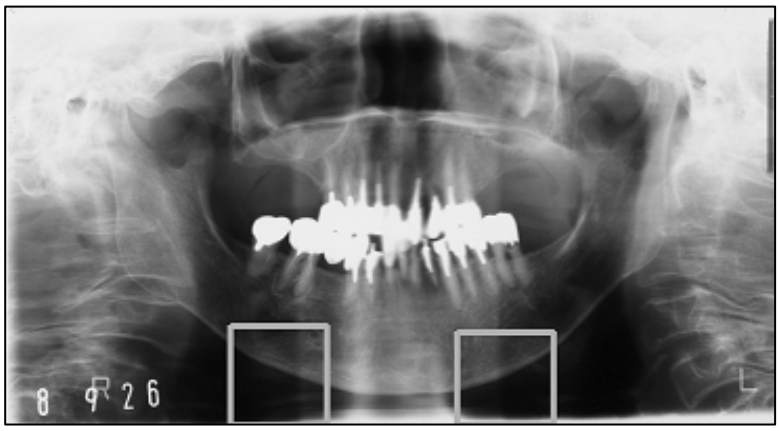

Figure 1. Dental panoramic radiograph.

3. DEVELOPMENT OF COMPUTER-AIDED SYSTEM

We recently have developed the computer-aided diagnosis system to measure the cortical width of the lower border of the mandible below the mental foramen on dental panoramic radiographs. The measurement steps for left and right cortex of the mandible mainly include identifying the area of interest as two boxes (Figure 1), followed with enhancing the original image, and selecting an appropriate point at which we can measure the width (Figure 2) on the right (a) and left (b) sides. Cortical width less than or equal to the specified cut off threshold is considered as having osteoporosis (BMD less than 70% of Japanese young adult mean), otherwise as having normal skeletal BMD (BMD more than or equal to 70% of Japanese young adult mean).

(a) (b)

Figure 2. Right and left cortical width.

We have also applied a set of image processing steps for extracting segments along the endosteal margin of cortex distally from mental foramen (17). The segments which are considered as noise-free are collected and their sizes are analyzed to distinguish normal from cortical erosion. Furthermore, we have removed all segment considered as noise and derived some statistically measurement of segments size, including minimum, average, and maximum of segments size, as well as the number of segments. The first two features have distribution that shown difference between normal BMD and osteoporosis, while the rest features seem not too useful since their distribution shared almost all of segments size. Thus, the minimum size and average size of segments are selected to be the input variables as well as the cortical width.

The details of the fuzzy neural network system employed to the identification were explained in our recent study (22). This system was run on Pentium 4 (CPU 1.80 GHz) with 1 GB of RAM.

3.1. Fuzzy Thresholding Method

The problem considered in this study may be stated in a precise way as that of finding a proper configuration of fuzzy membership function from the available training set. It is first necessary to know how many fuzzy membership functions each cortical parameter has. Determination of an optimum cut off threshold by previous studies in identifying postmenopausal women with osteoporosis indicated the importance of defining two different classes.

Thresholding is a simple but effective tool for separating data into two non-overlapping sets. Since thresholding is a well-researched field, there exist many algorithms for determining an optimal threshold of the image. An exhaustive survey of thresholding methods and their

categorization exists in literature (23). Several fuzzy thresholding methods have attempted to minimize the measure of fuzziness from a given histogram which contains an unknown mixed distribution of two classes. The measurement can be obtained from entropy, index of fuzziness, and index of nonfuzziness (24).

Inspired by the histogram thresholding algorithm (25), our previous report proposed a novel fuzzy thresholding method on the basis of histogram (22). This algorithm minimized a criterion function in which the index of fuzziness of a given partition is measured.

The method established low and normal linguistic variables modeled by two fuzzy sets. A criterions function than minimized fuzziness of both fuzzy sets to obtain an optimal cut off threshold. It was interesting to point out that the determined cut off threshold is not merely used to split two fuzzy sets but also to provide two fuzzy membership functions that correspond to osteoporosis and normal skeletal BMD fuzzy sets needed in the fuzzy inference system.

In the implementation of the histogram thresholding method on the basis of fuzziness degree comparison, we shall assume:

1. A given histogram consists of two fuzzy sets which correspond to the normal BMD and osteoporosis.
2. The membership degree of the least cortical measure achieves the maximum value for osteoporosis fuzzy set and the minimum value for the normal skeletal BMD fuzzy set.
3. The membership degree of the highest cortical measure achieves the maximum value for normal skeletal BMD fuzzy set and the minimum value for osteoporosis fuzzy set.

3.1.1. Two Linguistic Variables

Let us define *Low* and *Normal* linguistic variables modeled by two fuzzy sets of X, denoted by L and N with fuzzy membership function denoted by $\mu_L(x_i)$ and $\mu_N(x_i)$, respectively. The models reflect the compatibility measure of each cortical parameter in *low* and *high* regions. These fuzzy sets are formally defined as

$$L = \{(x_i, \mu_L(x_i))\} \text{ and } N = \{(x_i, \mu_N(x_i))\}, \text{ where } x_i \in X. \quad (1)$$

Given the minimum and maximum value are x_{min} and x_{max}, respectively, and the cut off threshold is t, then based on the assumption 2, the author uses Z-function for fuzzy set L and S-function for fuzzy set N. Since the fuzzy membership functions change with the change of parameter t which is assigned with any value ranged from x_{min} and x_{max}. The definitions are modified as

$$L = \{(x_i, \mu_L(x_i,t))\} \text{ and } N = \{(x_i, \mu_N(x_i,t))\}, \quad (2)$$

where $x_i \in X$ and $x_{\min} \le t \le x_{\min}$. Then fuzzy membership functions are defined as

$$\mu_L(x,t) = Z(x;t,x_{\min},x_{\max}) = \begin{cases} 1, & x \le x_{\min} \\ 1-2\{(t-x)/(t-x_{\min})\}^2, & x_{\min} < x \le (t+x_{\min})/2 \\ 2\{(t-x)/(t-x_{\min})\}^2, & (t+x_{\min})/2 < x < x_{\max} \\ 0, & x \ge t \end{cases} \quad (3)$$

$$\mu_N(x,t) = S(x;t,x_{\min},x_{\max})$$
$$= \begin{cases} 0, & x \le t \\ 2\{(x-t)/(x_{\max}-t)\}^2, & x_{\min} < x \le (t+x_{\max})/2 \\ 1-2\{(x-t)/(x_{\max}-t)\}^2, & (t+x_{\max})/2 < x < x_{\max} \\ 1, & x \ge x_{\max} \end{cases} \quad (4)$$

Parameter t which controls the S-function and Z-function is assigned with any possible value between x_{min} and x_{max}. Each assignment of parameter t and computation of fuzzy membership value of each cortical parameter in fuzzy subsets L and N is then followed by measuring the fuzziness.

3.1.2 Fuzziness Measurement

In the training set, the author has already classified the data into two groups labeled as *osteoporosis* and *normal* groups. The aim is to classify the ill-defined group of cortical measure into one of the defined groups by evaluating its membership value to the ordinary groups. Assigning a membership value should answer how fuzzy is the groups with respect to the available known groups. This fuzziness corresponds to the membership value of the rightly classified members compensated by the membership value of the wrongly classified members.

Let X_L and X_N be the set of cortical measures that have been classified to *osteoporosis* and *normal* skeletal BMD, with generic elements denoted by x_{Li} and x_{Ni}, respectively. Then the index of fuzziness $\gamma_L(t)$ for fuzzy set L and $\gamma_N(t)$ for fuzzy set N should be measured according to the defined group of each data.

Such functions are defined as

$$\gamma_L(t) = \left(\frac{\sum_{x \in X_L} (1-\mu_L(x,t))}{|X_L|} + \frac{\sum_{x \in X_N} \mu_L(x,t)}{|X_N|} \right) / 2,$$
$$\gamma_N(\mathrm{t}) = \left(\frac{\sum_{x \in X_N} (1-\mu_N(x,t))}{|X_N|} + \frac{\sum_{x \in X_L} \mu_N(x,t)}{|X_L|} \right) / 2, \quad (5)$$

where $|X_L|$ and $|X_N|$ respectively denote the number of X_L and X_N members in the training set. Note that $\gamma_N(t)$ tends to decrease, while $\gamma_L(t)$ tends to increase, with the incremental of t.

One of the indexes of fuzziness needs to be normalized to compare and find the intersection point at which both indexes of fuzziness achieve the most similar value. Normalization is done by finding out the normalization factor α which is computed as

$$\alpha = \frac{\gamma_N(x_{\max})}{\gamma_L(x_{\min})} \quad (6)$$

and by modifying all values in the index of fuzziness $\gamma_L(t)$.

4.2.3 Criterion Function

The optimal cut off threshold T can be determined by searching for the value so that the criterion function $J(t)$ is minimum, that is

$$T = \arg\min_{t \in X} J(t), \text{ where}$$
$$J(t) = \left|\gamma_N(t) - \alpha.\gamma_L(t)\right|. \quad (7)$$

The final result of these steps is T which will be used for defining fuzzy membership function of fuzzy sets L and N as defined in the above equation, where parameter t is assigned with T.

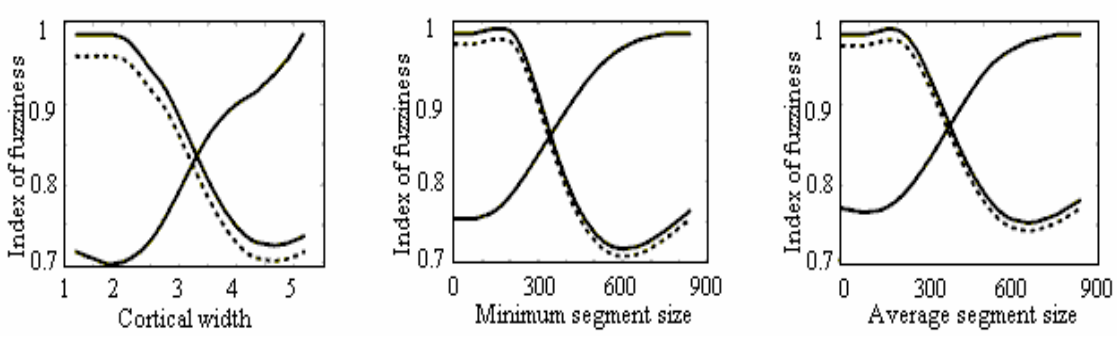

Figure 3. Index of fuzziness measured based on membership values

Since three variables composing the cortical measures are available, such a thresholding method is applied to each variable to obtain T_{cw}, T_{min}, and T_{avg}. These cut off thresholds correspond to the optimal cut off threshold of cortical width, minimum segment size, and average segment size as shown in Figure 3. This figure illustrates how the index of fuzziness measured based on membership values of the rightly classified members compensated by the membership value of the wrongly classified members for cortical width (a), minimum segment size (b), and average segment size(c). The decreasing and increasing lines correspond to osteoporosis and normal, respectively, where the decreasing lines have been normalized from the original ones (dashed line). The criterion function achieved least value at the intersection point at which the optimum cut off threshold is selected.

Note that the original index of fuzziness for fuzzy set L which is plotted as dashed line has been normalized with α and the normalized lines are shown above the original ones. The fuzzy membership functions then can be defined as the previous defined function by replacing t with the corresponding T as

$$\mu_{CL}=Z(x; c_{min}, T_{cw}),$$
$$\mu_{CN}=S(x; T_{cw}, c_{max}),$$
$$\mu_{ML}=Z(x; m_{min},T_{min}),$$
$$\mu_{MN}=S(x; T_{min}, m_{max}),$$
$$\mu_{AL}=Z(x; a_{min}, T_{avg}),$$
$$\mu_{AN}=S(x; T_{avg}, a_{max}), \quad (8)$$

where fuzzy membership functions μ_{CL} and μ_{CN} for cortical width, μ_{ML} and μ_{MN} for minimum size of segments, and μ_{AL} and μ_{AN} for average size of segment, respectively, correspond to *Low* and *Normal* linguistic variables. Parameter values of c_{min} and c_{max} for cortical width, m_{min} and m_{max} for average size of segments, a_{min} and a_{max} for average size of segments, respectively, are obtained from minimum and maximum values of the corresponding variables.

3.2. Fuzzy Neural Network

Given a set of input-output consists of N individuals
$(x^{(p)} ; y^{(p)})$, $p = 1, 2, \ldots, N$,
where $x^{(p)} \in R^{(3)}$ corresponds to measured cortical parameters and $y^{(p)} \in \{0, 1\}$ corresponds to normal BMD and osteoporosis groups, respectively. This system will extract rules that describe how osteoporosis can be identified by the three input variables.

The thresholding algorithm is motivated by minimizing the index of fuzziness between osteoporosis and normal skeletal BMD. As a result, we obtain two fuzzy sets corresponding to low and high variables denoted by L and H, respectively.

Fuzzy set H, however, still includes some individuals identified as low BMD. Classifying those individuals into L will decrease the specificity of the system. Therefore, for more accuracy, we define a new fuzzy set *medium* (M) between L and H into medium (M) and H by finding out the least value T_l among misclassified individuals in fuzzy set L and the largest value T_h among misclassified individuals in fuzzy set H. Thus, now each variable involves fuzzy sets L, M, and H, as in Figure 4.

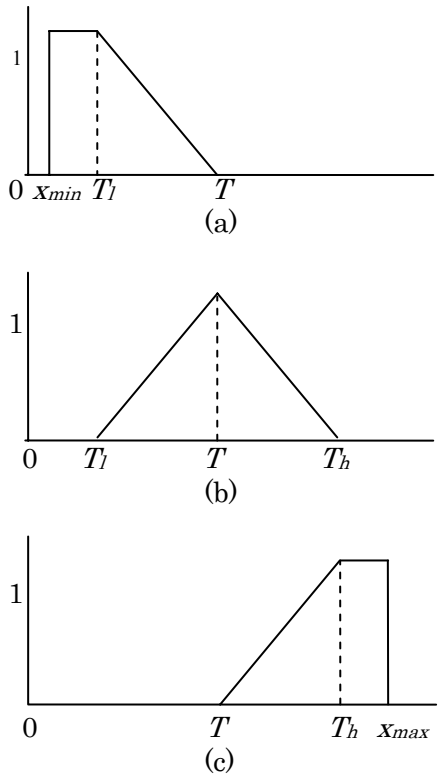

Figure 4. The fuzzy membership functions for L (a), M (b), and H (c).

Since we have three input variables and three subspaces for each variable, there exist 27 bins denoted by combinations of the variable values as shown in Figure 5. For fuzzy if-then rules of simple bins in which input variable i achieves high degree of membership of fuzzy sets Li or Hi, we may simply utilize rules such as

If x_1 is L_1 and x_2 is L_2 and x_3 is L_3 then y is osteoporosis.
If x_1 is H_1 and x_2 is H_2 and x_3 is H_3 then y is Normal BMD.

Variable x_1, x_2, x_3, and y correspond to cortical width, minimum and average segment sizes, and skeletal BMD, respectively, while L_i and H_i are fuzzy sets selected from $\{L_1, M_1, H_1\}$, $\{L_2, M_2, H_2\}$, and $\{L_3, M_3, H_3\}$.

Since some bins involve mixtures of normal BMD and osteoporosis individuals, the output label of some rules is difficult to define. In this case we assume that the output label of a rule corresponding to a bin is assigned as osteoporosis, if there exist one or more individuals identified as osteoporosis. Otherwise, the output label of the rule is assigned as normal BMD.

To this end, actually we have a set of rules which able to identify our aim. However, for achieving more accuracy, we incorporate multi layer perceptron (MLP) neural network. The structure of the neural network is determined by the rules defined before. It is noticed that each neuron in the input layer receives the weight of the corresponding rule. Therefore, the first layer is the input layer consisting 27 neurons corresponding to the number of fuzzy rules previously defined. The hidden layer consists of two neurons which are connected to 27 neurons in the first layer. We determine this number after some preliminary experiments in which adding more hidden neurons seems not so significant for improving the performance. The initial weights of interconnection links between input layer and hidden layer are assigned according to the output label of the rules.

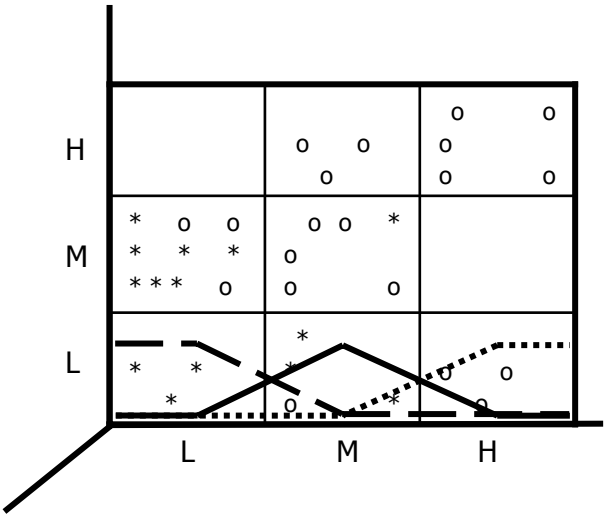

Figure 5. Combining 3 variables generates 27 subspaces.

Output from the hidden layer is used as input values for the output layer which content one neuron. This output neuron will indicate whether the individual is identified as having normal BMD or osteoporosis.

In the training phase, the weight of the fuzzy rules is fed to the input node of the neural network. The new neural network is trained using the gradient-decent-based Back-propagation (BP) algorithm to optimize the weighting coefficients. The learning rate parameter is set to 0.01, while the stopping criterion is determined by the maximum number of epoch as 1000. After optimization, this FNN system is applied to discriminate two sets of cortical bone images taken from dental panoramic radiographs, namely normal BMD and osteoporosis cases.

4. Experiment

We have extracted three input variables from dental panoramic radiographs taken from 100 postmenopausal women and one output variable (normal or osteoporosis) according to the

result of skeletal BMD assessment. We proposed a novel thresholding algorithm to find out optimum cut off thresholds for establishing the fuzzy membership functions. The fuzzy inference system is then incorporated with neural network as shown in Figure 6.

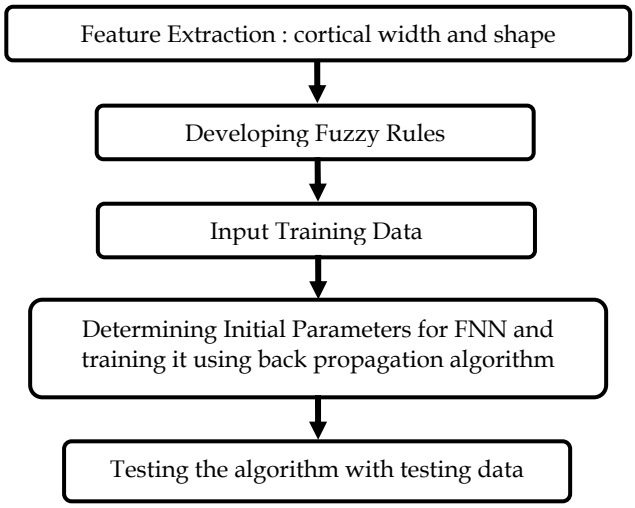

Figure 6. Flow chart of the Fuzzy Neural Network system

Half of 100 sets of measurements were randomly selected to construct the parameters of thresholding algorithm, fuzzy inference system, and weight of neural network links. Another 50 sets of measurements were applied to evaluate the validity of the system. For the reason of reliability to use for other groups in Japan or other groups over the world, we considered the ratio of samples between normal and osteoporosis which maintained to be similar with that of the total available samples.

We evaluated the performance of the proposed method in terms of sensitivity and specificity. Sensitivity (true positive fraction) is the probability that a diagnostic test is positive, given that the individual has been identified as having osteoporosis. Specificity (true negative fraction) is the probability that a diagnostic test is negative, given that the individual has been identified as having normal skeletal BMD. Positive predictive value, negative predictive value, accuracy and likelihood ratio for a positive risk result were also evaluated. The same procedure of such experiment, in selecting 50 new training data, setting the system parameters, and evaluate its diagnostic efficacy was repeated twice to ensure consistency of the system. The training data used in each experiment was differentiated by interchanging its composition, so as to evaluate the performance of the system when examining a different data set.

4.1. Results

The number of subjects identified as osteoporosis at the lumbar spine and the femoral neck were shown in Table 1 and Table 2, respectively. Sensitivity and specificity for identifying women with osteoporosis at the lumbar spine and the femoral neck for three experiments were shown in Table 3. Note that each experiment was conducted separately by using a set of training data which has different composition with those of the other experiment.

Mean sensitivity and specificity for identifying postmenopausal women with spine osteoporosis by new system were 94.5 % and 64.0 %, respectively. Those for identifying postmenopausal women with femur osteoporosis by this system were 90.9 % and 64.7 %, respectively.

Table 1. Number of subjects identified as having spine osteoporosis

	Experiment I		Experiment II		Experiment III	
	Normal	Osteoporosis	Normal	Osteoporosis	Normal	Osteoporosis
Measurement results:						
Osteoporosis	14	11	13	12	14	11
Normal	24	1	25	0	24	1

Table 2. Number of subjects identified as having femur osteoporosis

	Experiment I		Experiment II		Experiment III	
	Normal	Osteoporosis	Normal	Osteoporosis	Normal	Osteoporosis
Measurement results:						
Osteoporosis	13	9	11	11	12	10
Normal	21	2	23	0	22	1

Table 3. Diagnostic efficacy of the fuzzy neural network system in identifying women with osteoporosis

	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Accuracy (95% CI)	Likelihood ratio (+) (95% CI)
Lumbar spine						
Experiment I	91.7 (76.0 – 100.0)	63.2 (47.8 – 78.5)	44.0 (24.5 – 63.5)	96.0 (88.3 – 100.0)	70.0 (57.3 – 82.7)	2.5 (1.6 – 3.9)
Experiment II	100.0 (100.0 – 100.0)	65.8 (50.7 – 80.9)	48.0 (28.4 – 67.6)	100.0 (100.0 – 100.0)	74.0 (61.8 – 86.2)	2.9 (1.9 – 4.5)
Experiment III	91.7 (76.0 – 100.0)	63.2 (47.8 – 78.5)	44.0 (24.5 – 63.5)	96.0 (88.3 – 100.0)	70.0 (57.3 – 82.7)	2.5 (1.6 – 3.9)
Femoral neck						
Experiment I	81.8 (59.0 – 100.0)	61.8 (45.4 – 78.1)	40.9 (20.4 – 61.5)	91.3 (79.8 – 100.0)	66.7 (52.9 – 80.4)	2.1 (1.3 – 3.6)
Experiment II	100.0 (100.0 – 100.0)	67.6 (51.9 – 83.4)	50.0 (29.1 – 70.9)	100.0 (100.0 – 100.0)	75.6 (63.0 – 88.1)	3.1 (1.9 – 5.0)
Experiment III	90.9 (73.9 – 100.0)	64.7 (48.6 – 80.8)	45.5 (24.6 – 66.3)	95.7 (87.3 – 100.0)	71.1 (57.9 – 84.4)	2.6 (1.6 – 4.2)

CI: confidence interval

4.2. Discussion

This is the first computer-aided diagnosis system regarding the combination of the cortical width and shape detected on dental panoramic radiographs. In our recent system that used cortical width alone, the sensitivity and specificity were 88.0% and 58.7% for identifying women with spine osteoporosis and 87.5% and 56.3% for identifying women with femur osteoporosis, respectively (18). In our current study, mean sensitivity and specificity in three experiments were 94.5% and 63.2% for identifying women with spine osteoporosis and 90.9% and 64.7% for identifying women with femur osteoporosis, respectively. This indicates that the combination with two cortical measures may somewhat increase the diagnostic efficacy in identifying women

with osteoporosis.

Several screening tools based on simple questionnaire have been developed to identify postmenopausal women with low skeletal BMD or osteoporosis and the validation of these tools have been also evaluated in many countries. Koh et al. reported in 797 Asian women aged 45 years to 88 years that the sensitivity and specificity for identifying women with osteoporosis (14% of women) were 90.9% and 44.8%, respectively, when using Osteoporosis Self-Assessment Tool (OST) index consisting of 2 items (age and weight) (26). Richy et al. reported in 4,035 Caucasian women aged 45 years to 96 years that the sensitivity and specificity for identifying women with osteoporosis (19% of women) were 92% and 37%, respectively, when using OST index (27). Cook et al. reported in 208 Caucasian postmenopausal women aged 29 to 87 years that when the risk index range corresponding to a sensitivity of approximately 90% was chosen to define the low-risk group, the specificity of 6 questionnaire-based screening tools including OST index ranged from 14% to 38% (28). The diagnostic efficacy of the system in our study was better than that of several questionnaire-based screening tools in the previous studies, although the background of subjects was different between our study and theirs.

Our system has some limitations. The dental panoramic radiographs were digitized with the resolution of 300 dpi. Since we did not try to digitize with different resolutions, different parameter values that by default assigned in the system may need to be updated. Second, some inconsistent measurements caused by superimposition of the hyroid bone on dental panoramic radiographs may emerge some outliers in the feature space which may lead to less accuracy for identification. The robustness of this system in ignoring those outliers would be necessary to overcome such limitations. Third, only 50 dental panoramic radiographs were used for the development of the system and another 50 were used to evaluate the validation of the system. The ratio of normal to osteoporotic women in each set was controlled to be similar with that of normal to osteoporotic women in Japan. The experiment has repeated three times with changing the members of the training and test sets and preserving the ratio. However, a large number of dental panoramic radiographs would be necessary to develop more accurate computer-aided diagnosis system for the identification of postmenopausal women with osteoporosis in dental clinic.

5. CONCLUSIONS

In conclusion, mean sensitivity and specificity for identifying postmenopausal women with spine osteoporosis by the new system were 94.4 % and 64.0 %, respectively. Those for identifying postmenopausal women with femur osteoporosis were 90.9 % and 64.7 %, respectively. In comparison with the previous two computer-aided diagnosis systems applied individually, the new system achieved better sensitivity and specificity for identifying postmenopausal women with osteoporosis. Our results show that the dentists may identify postmenopausal women with osteoporosis more accurately by using FNN based computer-aided diagnosis system combining cortical width and shape on dental panoramic radiographs and refer them to medical professional for BMD testing.

REFERENCES

1. Cooper C. Epidemiology of osteoporosis 1999 Osteoporos Int **9**:S2–8.
2. Iki M, Kagamimori S, Kagawa Y, Matsuzaki T, Yoneshima H, Marumo F for JPOS study group 2001 Bone Mineral Density of the Spine, Hip and Distal Forearm in Representative Samples of the Japanese Female Population: Japanese Population-Based Osteoporosis (JPOS) Study. Osteoporos Int **12**:529-537.
3. Cadarette SM, Jaglal SB, Kreiger N, McIsaac WJ, Darlington GA, Tu JV 2000 Development

and validation of the Osteoporosis Risk Assessment Instrument to facilitate selection of women for bone densitometry. CMAJ **162**:1289-1294
4. Shimano T, Suzuki Y, Sasaki T 2002 Long-term trend of dental radiographic examination in Japan: analysis on health insurance data. Dent Radiol **42**:9-21 (in Japanese).
5. Klemetti E, Kolmakov S, Kroger H 1994 Pantomography in assessment of the osteoporosis risk group. Scand J Dent Res **102**:68-72.
6. Taguchi A, Suei Y, Ohtsuka M, Otani K, Tanimoto K, Ohtaki M 1996 Usefulness of panoramic radiography in the diagnosis of postmenopausal osteoporosis in women. Width and morphology of inferior cortex of the mandible. Dentomaxillofac Radiol **25**:263-267.
7. Bollen AM, Taguchi A, Hujoel PP, Hollender LG 2000 Case–control study on self-reported osteoporotic fractures and mandibular cortical bone. Oral Surg Oral Med Oral Pathol Oral Radiol Endod **90**:518-524.
8. Devlin H, Horner K 2002 Mandibular radiomorphometric indices in the diagnosis of reduced skeletal bone mineral density. Osteoporos Int **13**:373-378.
9. Horner K, Devlin H, Harvey L 2002 Detecting patients with low skeletal bone mass. J Dent **30**:171-175.
10. Drozdzowska B, Pluskiewicz W, Tarnawska B 2002 Panoramic-based mandibular indices in relation to mandibular bone mineral density and skeletal status assessed by dual energy Xray absorptiometry and quantitative ultrasound. Dentomaxillofac Radiol **31**:361-367.
11. Persson RE, Hollender LG, Powell LV, MacEntee MI, Wyatt CC, Kiyak HA, Persson GR 2002 Assessment of periodontal conditions and systemic disease in older subjects. I. Focus on osteoporosis. J Clin Periodontol **29**:796-802.
12. Nakamoto T, Taguchi A, Ohtsuka M, Suei Y, Fujita M, Tanimoto K, Tsuda M, Sanada M, Ohama K, Takahashi J, Rohlin M 2003 Dental panoramic radiograph as a tool to detect postmenopausal women with low bone mineral density: untrained general dental practitioners' diagnostic performance. Osteoporos Int **14**:659-64.
13. Taguchi A, Sanada M, Krall E, Nakamoto T, Ohtsuka M, Suei Y, Tanimoto K, Kodama I, Tsuda M, Ohama K 2003 Relationship between dental panoramic radiographic findings and biochemical markers of bone turnover. J Bone Miner Res **18**:1689-94.
14. Taguchi A, Suei Y, Sanada M, Ohtsuka M, Nakamoto T, Sumida H, Ohama K, Tanimoto K 2004 Validation of dental panoramic radiography measures for identifying postmenopausal women with spinal osteoporosis. AJR Am J Roentogenol **183**:1755-60.
15. Halling A, Persson GR, Berglund J, Johansson O, Renvert S 2005 Comparison between the Klemetti index and heel DXA BMD measurements in the diagnosis of reduced skeletal bone mineral density in the elderly. Osteoporos Int **16**:999-1003.
16. Taguchi A, Tsuda M, Ohtsuka M, Kodama I, Sanada M, Nakamoto T, Inagaki K, Noguchi T, Kudo Y, Suei Y, Tanimoto K, Bollen AM 2006 Use of dental panoramic radiographs in identifying younger postmenopausal women with osteoporosis. Osteoporos Int **17**:387-94.
17. Nakamoto T, Taguchi A, Asano A, Ohtsuka M, Suei Y, Fujita M, Sanada M, Ohama K, Tanimoto K 2004 Computer-aided diagnosis of low skeletal bone mass on panoramic radiographs. J Dent Res **83**, Special issue A, 1953
18. Arifin AZ, Asano A, Taguchi A, Nakamoto T, Ohtsuka M, Tsuda M, Kudo Y, Tanimoto K 2006 Computer-aided system for measuring the mandibular cortical width on dental panoramic radiographs in identifying postmenopausal women with low bone mineral density. Osteoporos Int **17**:753-9.
19. Farman AG, Farman TT 2000 Extraoral and panoramic systems. Dent Clin North Am **44**:257-72.

20. Orimo H, Hayashi Y, Fukunaga M, Sone T, Fujiwara S, Shiraki M, Kushida K, Miyamoto S, Soen S, Nishimura J, Oh-Hashi Y, Hosoi T, Gorai I, Tanaka H, Igai T, Kishimoto H; Osteoporosis Diagnostic Criteria Review Committee: Japanese Society for Bone and Mineral Research 2001 Diagnostic criteria for primary osteoporosis: year 2000 revision. J Bone Miner Metab **19**:331-7.
21. Fujiwara S, Masunari N, Suzuki G, Ross PD 2001 Performance of osteoporosis risk indices in a Japanese population. Curr Ther Res Clin Exp **62**:586–593.
22. Arifin AZ, Asano A, Taguchi A, Nakamoto T, Ohtsuka M, Tsuda M, Kudo Y, Tanimoto K 2006 Identification of low bone mineral density based on the mandibular cortex by fuzzy neural network. Proc. Joint 3rd International Conference on Soft Computing and Intelligent Systems and 7th International Symposium on advanced Intelligent Systems, 1860-1865.
23. Sezgin M, Sankur B 2004 Survey over image thresholding techniques and quantitative performance evaluation. Journal of Electronic Imaging **13**: 146-165.
24. Huang LK, Wang MJJ 1995 Image thresholding by minimizing the measures of fuzziness. Patter Recognition **28**: 41-51.
25. Arifin AZ, Asano A 2006 Image segmentation by histogram thresholding using hierarchical cluster analysis. Pattern Recognition Letters **27**:1515-1521.
26. Koh LK, Sedrine WB, Torralba TP, Kung A, Fujiwara S, Chan SP, Huang QR, Rajatanavin R, Tsai KS, Park HM, Reginster JY; Osteoporosis Self-Assessment Tool for Asians (OSTA) Research Group 2001 A simple tool to identify Asian women at increased risk of osteoporosis. Osteoporos Int **12**:699-705.
27. Richy F, Gourlay M, Ross PD, Sen SS, Radican L, De Ceulaer F, Ben Sedrine W, Ethgen O, Bruyere O, Reginster JY 2004 Validation and comparative evaluation of the osteoporosis self-assessment tool (OST) in a Caucasian population from Belgium. QJM **97**:39-46.
28. Cook RB, Collins D, Tucker J, Zioupos P 2005 Comparison of questionnaire and quantitative ultrasound techniques as screening tools for DXA. Osteoporos Int **16**:1565-75.