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Research Report

Computer aided diagnosis for osteoporosis based on trabecular bone analysis using panoramic radiographs

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ABSTRACT

Background: *Mandibular bone on panoramic radiographs has been proven to be useful for identifying postmenopausal women with low skeletal bone mineral density (BMD). One of the important parts of mandibular bone is trabecular bone. Trabecular bone architecture is one of the factors that governs bone strength and may be categorized as a contributor to bone quality.* ***Purpose:*** *The purposes of this study were to develop a computer-aided system for measuring trabecular bone line strength on panoramic radiographs in identifying postmenopausal women with osteoporosis and to clarify the diagnostic efficacy of the system.* ***Methods:*** *Reduction and expansion of trabecular bone sample images using a two level gaussian pyramid for removing noises and small segments are first introduced. Then, line strength at each pixel was calculated based on its existence on the trabecular bone with emphasizes line segment which has similar orientation with the root of tooth. The density was measured with respect to line strength of segment structure which has similar orientation with the root of tooth, either on the left and the right in the mandibular bone. Number of pixels in the line segment area was compared with a threshold value to determine whether normal or osteoporosis.* ***Results:*** *From experiment on 100 data, we achieved accuracy of 88%, sensitivity of 92%, and specificity of 86.7%.* ***Conclusion:*** *The computer-aided system of trabecular bone analysis may be useful for detecting osteoporosis using panoramic radiographs.*

Key words: *Computer-aided, line strength, trabecular bone, osteoporosis, panoramic radiographs*

ABSTRAK

Latar belakang: *Tulang mandibula pada panoramik radiografi telah banyak diteliti dan terbukti mampu digunakan untuk mengidentifikasi wanita pasca menopause dengan BMD (Bone Mineral Density/Ketebalan Mineral Tulang) rendah. Salah satu bagian tulang mandibula yang penting adalah tulang trabekula. Arsitektur tulang trabekula merupakan salah satu dari faktor-faktor yang mempengaruhi kekuatan tulang dan dapat digolongkan sebagai kontributor bagi kualitas tulang.* ***Tujuan:*** *Penelitian ini bertujuan untuk membangun sebuah sistem dengan bantuan komputer untuk mengukur kekuatan garis pada tulang trabekula dan menggunakannya untuk mendeteksi osteoporosis pada wanita postmenopause.* ***Metode:*** *Pertama, dilakukan sampling pada sebagian tulang mandibular yang menghasilkan sebuah sampel citra. Sampel citra ini selanjutnya diperbaiki dari derau (noise) dengan menggunakan piramida gaussian dua level. Kekuatan garis pada tiap piksel dihitung berdasarkan orientasi segmen garis tulang trabekula yang sejajar dengan akar gigi. Setelah dilakukan binerisasi, luasan segmen yang dihasilkan dihitung dan dibandingkan dengan sebuah nilai ambang (threshold). Bila luasan melebihi nilai threshold maka dikategorikan sebagai normal. Sebaliknya bila luasan dibawah nilai threshold, dikategorikan sebagai osteoporosis.* ***Hasil:*** *Berdasarkan eksperimen terhadap 100 data, sistem mampu mencapai akurasi identifikasi sebesar 88%, sensitivitas 92%, dan spesifisitas 86,7%.* ***Kesimpulan:*** *Sistem analisa trabecular bone dengan bantuan komputer ini dapat digunakan oleh para dokter gigi untuk mendeteksi osteoporosis menggunakan panoramik radiografi.*

Kata kunci: *Sistem berbantukan komputer, kekuatan garis, tulang trabekula, osteoporosis, panoramik radiografi*

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INTRODUCTION

The number of hip fractures because of osteoporosis worldwide was rising from about 1.3 million in 1990. Moreover, it is estimated to be 4.5 million in 2050.[1] The U. S. Surgeon General reported that if there is no serious handling until 2020, half of Americans were predicted to have osteoporosis.[2] One parameter should be measured to determine whether someone has osteoporosis or not is called the bone mineral density (BMD), measured on lumbar spine and femoral neck.

The commonly used scanner for measuring bone is dual-energy x-ray absorptiometry (DXA). However, DXA is very expensive and not every hospital has DXA even in developed countries.[3] On the other hand, postmenopausal women rarely visit medical expert to diagnose osteoporosis. Postmenopausal women would realize that they had osteoporosis after any bone fractures caused by an accident.

Postmenopausal women may have greater opportunity to visit dentists for treatment of dental caries and periodontal disease than to visit medical professionals for diagnosis of osteoporosis. A large number of panoramic radiographs were taken for diagnosis of teeth and jaws in general dental practice.

Trabecular bone is one of important parts of panoramic radiographs. The trabecular bone pattern may be analyzed visually by experts or with computer-aided methods to estimate the probability of having osteoporosis and predict the risk of future fractures.[4] Degrees of inter-examiner and intra-examiner agreement of visual assessment of the trabecular pattern are also expected to be relatively low because the trabecular pattern of the jaws is more diverse than that of the general skeleton, such as the vertebrae and proximal femur.[5] However, other researchers analyzed trabecular bone pattern using customized image analysis software.[6-9] We proposed a method to analyze trabecular bone tissue using multiscale line operator on Gaussian pyramid.[10] The line strength of trabeculae that has similar orientation with the root of teeth is measured on both left and right sides of the mandible. High correlation between both experimental results and bone mineral density (BMD) assessed by DXA scanner proves the effectiveness of this method.[10]

The purposes of this study were to develop a computer-aided system for measuring trabecular bone line strength on panoramic radiographs in identifying postmenopausal women with osteoporosis and to clarify the diagnostic efficacy of the system. The density is measured with respect to line strength of segment structure which has similar orientation with the root of tooth. This study also determined the threshold value of line strength considered as the osteoporosis sign.

MATERIALS AND METHODS

There were 531 women visited our clinic for DXA measurement between 1996 and 2001, 100 postmenopausal women aged 50 years or older with no previous osteoporosis diagnosis (mean 59.6 years; range 50–84 years) were randomly recruited for this study. None of the subjects had metabolic bone disease (hyperparathyroidism, hypoparathyroidism, Paget's disease, osteomalacia, renal osteodystrophy, or osteogenesis imperfecta), cancers with bone metastasis, or significant renal impairment or were taking medication that affect bone metabolism, such as estrogen. None had a history of smoking, and none had bone-destructive lesions in the mandible. No subject had menstruated for at least 1 year.

Panoramic radiographsy was taken for all subjects with informed consent at the time of DXA measurements of the lumbar spine (L2–L4). All panoramic radiographs were obtained with a AZ-3000 (Asahi Co., Kyoto, Japan) at 12 mA and 15 s; kVp 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. Appearance of the mandibular inferior cortex was bilaterally clear in the radiographs. All radiographs were digitalized with the resolution of 300 dpi using a flat-bed scanner (ES-8000, Epson, Japan).

When using the definition of the Japanese Society for Bone and Mineral research[11], 54 of the 100 women presented 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. The rate of women with osteoporosis in the lumbar spine in our study was similar to that (26%) in 1,033 postmenopausal women aged 50 years or older in the Adult Health Study (AHS) cohort in Japan.[12]

Region of interest (RoI) was taken from four different areas of an image. Two RoIs are taken from the left hand side and the right hand side. The location of trabecular bone samples are between root of the tooth and cortical bone.

Area where sample is taken on panoramic radiographs is illustrated in Figure 1 (a). Figure 1 (b) and Figure 1 (c) show samples from left hand side, whereas Figure 2 (d) and Figure 2 (e) are samples from right hand side. In this experiment, each sample size which marked with white box is 128 × 128 pixels.

Multiscale line operator is one of line detection algorithm used for detecting linear structure on mammographic image together with other line detection methods.[13] Comparing with other methods, the line operator algorithm was proved to give good result from signal to noise aspect, line width accuracy, and localization. In the early implementation of multiscale line operator algorithm, the algorithm is used to detect asbestos fiber.[14] This algorithm is applied for detecting linear structure of iris blood vessel.[15]

Multiscale line operator requires parameters of angle (θ) and length (M).[16] Angle controls the number and size of analyzed rotation. Angle size per rotation is sum of the current and previous angle size until the limit 180 degree. Length parameter is needed to make moving window with length M. We used 12 rotations with angels of 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, and 165 degree. Moving

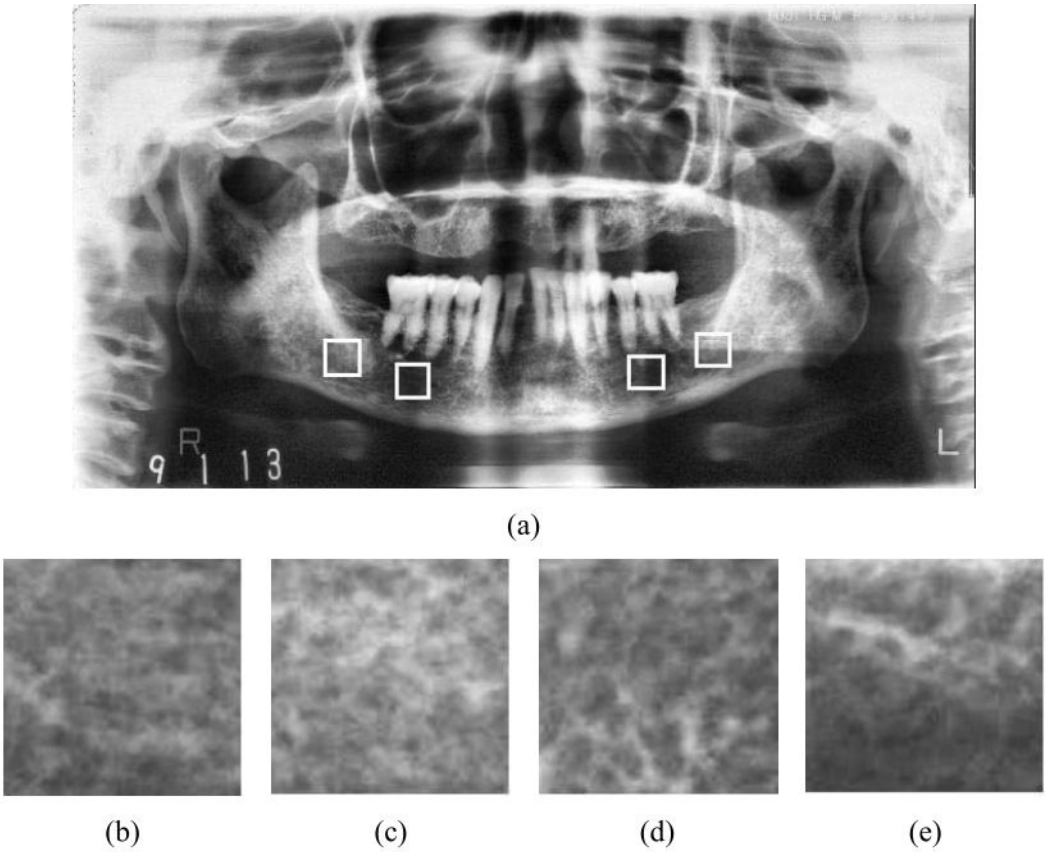

Figure 1. Input image. a) Four samples from a dental panoramic radiographs, b) and c) Two left hand side samples, d) and e) Two right hand side samples.

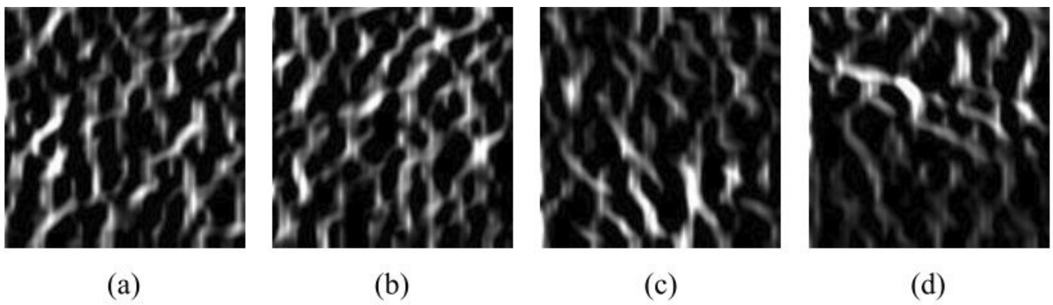

Figure 2. Output image. a) and b) Result of linear strength detection applied to images in Figure b) and c), respectively, c) and d) Result of linear strength detection applied to images in Figure d) and e), respectively.

window size of 5 × 5 is applied to each pixel for analyzing it with 24 neighbor pixels around.

Given a region of interest image, at each pixel (x, y), multiscale line operator algorithm measures the line strength S(x, y) by calculating the contribution of the foreground minus the contribution of the background. For each angle θ, the foreground mask has a line of length M and width one pixel, oriented at the angle θ. The foreground value, F(x, y, θ), is the sum of the pixel values multiplied by the corresponding foreground mask values. Similarly, the background mask is a rectangle of size M M, oriented at the angle θ. The background value, B(x, y, θ), is the sum of the image pixels multiplied by the corresponding background mask elements. The line-strength image value, S(x, y), is calculated by:

$$g_l(i,j) = \sum_m \sum_n w(m,n) g_{l-1}(2i + m, 2j + n) \quad (1)$$

Linear strength detection detects structure of trabecular bone line segment which has similar orientation with root of tooth. Detection of line strength in left hand side sample has orientation 0, 15, and 30 degrees. The right hand side one has orientation 330, 345, and 360 degrees. Angle size parameter, θ, used in multiscale line operator algorithm is appropriate with angle to be detected. It is 0, 15, and 30 for left side sample and 330, 345, and 360 for right one.

Local linear structures which have good contrast and also match the foreground mask will have high values in the line strength map. Bilinear interpolation is used to create the rotated image for non-zero angles to get better result.

Each segment of the line structure has different width. To estimate the problem, we require multiscale analysis method. In this paper, we use Gaussian pyramid to solve multiscale analysis problem. Gaussian pyramid is generated by first smoothing the image with an appropriate smoothing filter and then subsampling the smoothed image as many as desired levels. This produces a set of gradually more smoothed images. Nevertheless, the more smooth an image, the less sampling density. If we illustrate it graphically, this multiscale representation will look like a pyramid, from which the name has been obtained. Images produced at the lower levels of the pyramid have higher resolutions, whereas those produced at the higher levels have lower resolutions.

The levels of the pyramid obtained iteratively as follows. For $0 < l < N$:

$$g_l(i,j) = \sum_m \sum_n w(m,n) g_{l-1}(2i + m, 2j + n) \quad (2)$$

However it is convenient to refer to this process as a standard REDUCE operation and simply write:

$$g_l = REDUCE\,(g_{l+1}) \quad (3)$$

where w(m, n) is "generating kernel". The structure of generating kernel is [0.25 - a/2, 0.25, a, 0.25, 0.25 - a/2] and a = 0.4. The equivalent weighting functions are particularly Gaussian-like when a = 0.4, when a = 0.5 the shape is triangular, when a = 0.3 it is flatter and broader than a Gaussian. With a = 0.6 the central positive mode is sharply peaked and is flanked by small negative loobs.

After the line strength structure of the trabecular bone is detected, those images are transformed into binary images. This method changes the background into black with zero value and changes the image object (foreground) into white with one value.

Measurement of line strength in trabecular bone is applied to the binary image at each pixel based on its existence on the trabecular bone with prioritizes line segment which has similar orientation with the root of tooth. The total value of line strength is the mean of line strength in four samples on every panoramic radiographs. The number of the bone segment is used to decide whether the patient is affected osteoporosis or normal.

RESULTS

Sample image from panoramic radiographs is processed using multiscale line operator algorithm and Gaussian pyramid. Figure 2(a), 2(b), 2(c), 2(d) show result images from detection of trabecular bone linear strength structure applied to images in Figure 1 (b), 1 (c), 1 (d), and 1 (e), respectively. Output for image in Figure 1 (b) and 1 (c) from line strength structure detection using orientation 0, 15, and 30 degrees is shown in Figure 2 (a) and 2 (b). Figure 2 (c) and 2 (d) show images from line strength detection using orientations 330, 345, and 360 degrees for image shown in Figure 1 (d) and 1 (e), respectively.

After processing with multiscale line operator algorithm and Gaussian pyramid, sample trabecular bone image is converted to binary image. The total value of line strength from four black and white samples on every panoramic radiographs is added. After that, mean value of line strength on one panoramic radiographs is calculated. From 100 panoramic radiographs used in this experiment, line strengths are compared with threshold.

The cutoff threshold of trabecular bone line strength was selected as 3450 by which sensitivity achieved approximately 92%. The result of line strength and its correlation with osteoporosis status is shown in table 1. The average pixel number of black and white image is used to diagnosis osteoporosis by comparing the number with threshold. This number is preferably 3400–3500, and more preferably 3425–3475, and 3450 is the best threshold value for the RoI size of 128 x 128. The number of subjects identified by mandibular trabecular density that less than and equal to the threshold are 10 and 23 for normal and osteoporotic subjects, respectively. While for trabecular density > the threshold, there are 65 and 2 subjects for normal and osteoporotic, respectively.

Image that has a wide average of line strength of segment structure of trabecular bone means that the image was not affected by osteoporosis. Image that has a small average of line strength of segment structure of trabecular bone means that the image is potentially affected by osteoporosis. Diagnostic efficacy of manual and computer-aided automatic measurements is presented in Table 2. This method achieved of accuracy of 88%, sensitivity of 92%, and specificity of 86%. The correlation between BMD and trabecular bone line strength is 52%.

DISCUSSION

Various diagnosis and treatment for osteoporosis has been discussed and some of them has been implemented.[17] Even though there have been several studies regarding osteoporosis on postmenopausal women in Indonesia,[18] however this study is the first demonstration comparing correlations between skeletal BMD and trabecular bone line strength measured by a computer-aided system on digitized panoramic radiographs for postmenopausal women. Line strength measurement has been used for robust classification of anatomical types (vessels, spicules, ducts, etc) in a mammogram.[13]

In other study about trabecular bone for osteoporosis detection, it shows 92% sensitivity and 96% specificity.[8] We have the same sensitivity but lower specificity. In our previous study,[19] sensitivity and specificity for computer-aided system were about 88.0% and about

Table 1. Mean of line strength and its BMD assessment result

No.	Mean of line strength structure	BMD assessment result	No.	Mean of line strength structure	BMD assessment result
1.	3549.00	Normal	51.	3031.00	Osteoporosis
2.	2653.50	Osteoporosis	52.	3734.00	Normal
3.	3753.00	Normal	53.	3947.25	Normal
4.	3239.50	Osteoporosis	54.	4005.50	Normal
5.	3565.25	Normal	55.	3522.25	Osteoporosis
6.	3619.50	Normal	56.	3717.50	Normal
7.	3997.00	Normal	57.	3688.50	Normal
8.	3266.75	Osteoporosis	58.	3328.50	Osteoporosis
9.	2840.50	Osteoporosis	59.	3820.75	Normal
10.	3849.75	Normal	60.	3595.00	Normal
11.	4178.00	Normal	61.	3039.75	Osteoporosis
12.	3302.50	Osteoporosis	62.	4249.50	Normal
13.	3760.50	Normal	63.	2754.25	Normal
14.	4025.50	Normal	64.	3797.25	Normal
15.	2610.50	Osteoporosis	65.	3527.75	Normal
16.	4086.00	Normal	66.	3887.25	Normal
17.	3876.00	Normal	67.	3967.50	Normal
18.	3913.00	Normal	68.	2870.00	Normal
19.	3439.25	Osteoporosis	69.	2995.50	Osteoporosis
20.	4145.25	Normal	70.	3643.25	Normal
21.	3420.00	Osteoporosis	71.	3863.50	Normal
22.	3150.75	Normal	72.	3050.75	Osteoporosis
23.	3996.25	Normal	73.	2977.50	Osteoporosis
24.	4306.25	Normal	74.	3564.75	Normal
25.	3309.00	Osteoporosis	75.	2885.00	Osteoporosis
26.	4022.25	Normal	76.	3528.75	Normal
27.	3624.00	Normal	77.	3287.50	Osteoporosis
28.	4002.50	Normal	78.	3427.75	Osteoporosis
29.	4572.75	Normal	79.	3524.75	Osteoporosis
30.	3364.00	Normal	80.	3877.00	Normal
31.	3755.00	Normal	81.	3121.75	Osteoporosis
32.	3565.00	Normal	82.	3662.75	Normal
33.	4048.25	Normal	83.	3185.50	Normal
34.	3793.75	Normal	84.	3448.00	Osteoporosis
35.	3629.75	Normal	85.	3050.00	Normal
36.	3515.75	Normal	86.	4328.00	Normal
37.	3191.00	Osteoporosis	87.	3662.25	Normal
38.	3623.00	Normal	88.	3839.00	Normal
39.	3891.75	Normal	89.	3195.00	Normal
40.	4077.50	Normal	90.	4021.50	Normal
41.	4563.00	Normal	91.	3040.75	Osteoporosis
42.	3673.75	Normal	92.	3510.75	Normal
43.	4318.25	Normal	93.	3691.75	Normal
44.	3599.00	Normal	94.	3521.00	Normal
45.	3736.50	Normal	95.	3665.25	Normal
46.	3891.25	Normal	96.	3085.00	Osteoporosis
47.	3875.25	Normal	97.	3153.75	Normal
48.	4557.25	Normal	98.	3499.50	Normal
49.	2981.75	Normal	99.	3267.50	Normal
50.	3493.75	Normal	100.	3655.50	Normal

58.7%, respectively. Although it was used cortical bone on mandible as subject, we get similar result by using trabecular bone. With our image analysis system, we measure line strength of trabecular bone and compare it with threshold value. If it is lower than threshold, the dentist could consider the advisability of further treatment

Table 2. Diagnostic efficacy of manual and computer-aided automatic measurements of mandibular cortical width in identifying women with low skeletal bone mineral densities

Computer-aided system	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Accuracy (95% CI)	Likelihood ratio (+) (95% CI)
Automatic measurement	92.0 (81.4–100.0)	86.7 (79.0–94.4)	69.7 (54.0–85.4)	97.0 (92.9–100.0)	88.0 (81.6–94.4)	6.9 (3.8–12.4)

CI : Confidence Interval

for dual energy X-ray absorptiometry. It is also possible that general dental practitioners can identify women with low skeletal BMD by using digital panoramic radiographs with our computer-aided system.

Another advantage is due to low cost assessment. We need only a file which scanned from panoramic radiographs as the input file for our system. Using conventional DEXA scanner it needs about Rp 900.000,- for assessment on lumbar spine and femoral neck. Using this system we only need to have a panoramic radiograph and the assessment system which cost about Rp 100.000,- and Rp 50.000,- respectively for each assessment. Panoramic radiograph can be easily taken in clinic and then scanned. Considering these advantages, it is very possible to implement our proposed system to examine Indonesia woman.

This computer-aided system, however, has some limitations. Dentists were asked to determine manually regions of interest (RoIs) along trabecular bone area. Error tends to occur with this determination due to the existence of root. Automatic determination of the RoIs would be necessary to maintain good reproducibility around the world. The robustness of this system would be also necessary to overcome this system limitation.

In conclusion, our approach of analyzing trabecular bone using panoramic radiographs has sensitivity and specificity of 92% and 86.7%, respectively. Thus, we suggest that the computer aided diagnosis system may be useful for detecting osteoporosis.

REFERENCES

1. Gullberg B, Johnell O, Kanis JA. World-wide projections for hip fracture. Osteoporos Int 1997; 7(5): 407–13.
2. U.S. Department of Health and Human Services. Bone health and osteoporosis: a report of the Surgeon General. U.S. Department of Health and Human Services, Public Health Service, Office of the Surgeon General, Rockville, MD. 2004. pp. 4.
3. Kanis JA, Johnell O. Requirement for DXA for the management of osteoporosis in Europe. Osteoporos Int. 2005; 16(3): 229–38.
4. Majumdar S. Current technologies in the evaluation of bone architecture. Curr Osteoporos Rep 2003; 1(3): 105–9.
5. Lindh C, Horner K, Jonasson G, Olsson P, Rohlin M, Jacobs R, Karayianni K, van der Stelt P, Adams J, Marjanovic E, Pavitt S, Devlin H. The use of visual assessment of dental radiographs for identifying women at risk of having osteoporosis: the OSTEODENT project. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008; 106(2): 285–93.
6. Ruttimann UE, Webber RL, Hazelrig JB. Fractal dimension from radiographs of peridental alveolar bone: A possible diagnostic indicator of osteoporosis. Oral Surg Oral Med Oral Pathol 1992; 74(1): 98–110.
7. Law AN, Bollen AM, Chen SK. Detecting osteoporosis using dental radiographs: a comparison of four methods. J Am Dent Assoc 1996; 127(12): 1734–42.
8. Faber TD, Yoon DC, Service SK, White SC. Fourier and wavelet analyses of dental radiographs detect trabecular changes in osteoporosis. Bone 2004; 35(2): 403–11.
9. White SC, Atchison KA, Gornbein JA, Nattiv A, Paganini-Hill A, Service SK, Yoon DC. Change in mandibular trabecular pattern and hip fracture rate in elderly women. Dentomaxillofac Radiol 2005; 34(3): 168–74.
10. Arifin AZ, Asano A, Taguchi A, Nakamoto T, Yuniarti A, Dewi LR, Studiawan H. Line strength measurement for trabecular bone analysis of mandible on panoramic radiographs. Proceeding of The International Workshop on Advanced Image Technology 2010, Kuala Lumpur, Malaysia, 2010 January 11-12. p. 1–5.
11. 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. Diagnostic criteria for primary osteoporosis: year 2000 revision. J Bone Miner Metab 2001; 19(6): 331–7.
12. Fujiwara S, Masunari N, Suzuki G, Ross PD. Performance of osteoporosis risk indices in a Japanese population. Curr Ther Res Clin Exp. 2001; 62: 586–93.
13. Zwiggelaar R, Astley SM, Boggis CRM, Taylor CJ. Linear structure in mammographic images: detection and classification. IEEE Trans on Medical Imaging. 2004; 23(9): 1077–86.
14. Dixon RN, Taylor CJ. Automated asbestos fiber counting. Proc Inst Phys Conf Series 1979; 44: 178–85.
15. Farnel DJJ, Hatfield FN, Knox P, Reakes M, Spencer S, Parry D, Harding SP. Enhancement of blood vessels in digital fundus photographs via the application of multiscale line operators. Journal of Franklin Institute 2008; 345: 748–65.
16. R. Marti, R. Zwiggelaar and C. Rubin Tracking mammographic structures over time 12th British Machine Vision Conference. Proceedings of the 12th British Machine Vision Conference. 2001: 143–52.
17. Kawiyana, IKS. Osteoporosis patogenesis diagnosis dan penanganan terkini. J Peny Dalam 2009; 10(2): 157–70.
18. Kawiyana, IKS. Interleukin-6 yang Tinggi sebagai Faktor Risiko terhadap Kejadian Osteoporosis pada Wanita Pascamenopause Defisiensi Estrogen. J Peny Dalam 2009; 10(1): 18–24.
19. Arifin AZ, Asano A, Taguchi A, Nakamoto T, Ohtsuka M, Tsuda M, Kudo Y, Tanimoto K. Computer-aided system for measuring the mandibular cortical width on panoramic radiographs in identifying postmenopausal women with low bone mineral density. Osteoporos Int 2006; 17(5): 753–9.