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IMAGE & SIGNAL PROCESSING

A computer aided diagnosis system for measurement of mandibular cortical thickness on dental panoramic radiographs in prediction of women with low bone mineral density

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Abstract
Osteoporosis detection at earlier stages can enhance the life span of an elderly individual. The aim of the study is to perform semi-automated measurement of mandibular cortical thickness (MCT) on a dental panoramic radiograph (DPR) and thereby to predict the risk of low BMD among the studied population. The study involved 76 women (mean age: 57.2 ± 12.6 years). The DPR was obtained using KODAK 8000C system. The BMD of right total hip (T-BMD) was obtained using DPX Prodigy Dual-energy X-ray absorptiometry (DXA) Scanner. The DPR obtained were subjected to image processing techniques to perform MCT measurement. The region of interest was manually selected around the mental foramen and enhanced using a median filter. The Ostu segmentation was performed and connected component labelling operation was performed to determine the lower boundary by finding the contour with maximum area. Subsequently, the haar wavelet operation was carried out to find the magnitude and thereby select the upper delineating cortical boundary. The Pearson test results revealed ($r = 0.96$, $p < 0.01$) for the standard (manual) MCT measurement against the MCT measured using the proposed semi-automated scheme. ROC analysis revealed that MCT = 2.5 mm could be an optimal threshold in spotting individuals at risk of low BMD. The results of the study revealed that the MCT measured on a DPR using the proposed approach could be helpful for identifying individuals at risk of low BMD.

Keywords DPR · Low BMD · MCT · Osteoporosis · Ostu Segmentation · DXA

Introduction

The early diagnosis and screening of any diseases at an appropriate time could enhance the livelihood of an individual to a greater extent. The quality of life of an elderly can be highly affected by making them bedridden on ageing. Osteoporosis, a musculoskeletal disorder, if diagnosed at an appropriate time could significantly extend the life span of the concerned.

Osteoporosis is a skeletal disease resulting in an unnoticeable reduction in bone mass causing deterioration of bone micro-architecture. The disease results in increased risk of fractures at femur and spine even if subjected to a minimal fall. Osteoporosis have not been recognized a major health disorder in India and actually represents a huge public health burden [1]. Estimates reveal that about 80% of the urban Indian population are vitamin D deficient and incur fractures well earlier than their western counterparts [2, 3]. In developing nations like India, costs of fracture treatment are very high and which might be ill-affordable for even higher socioeconomic groups in the near future [4]. For the diagnosis of osteoporosis, dual energy X-ray absorptiometry (DXA) is often used. In India, the limited availability of DXA machines (0.26 DXA machines per one million of the general population) and its limited number at government hospitals restricts its access to a common man, thereby making diagnosis difficult [1]. A huge number of dental panoramic radiographs, offering greater opportunities for studying bones, are taken every year [3].

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The features of osteoporosis can often be observed in the films of affected individuals, and there are significant relationships between the mandibular cortical bone quality, quantity and bone mineral density (BMD) [4, 5]. Earlier studies on DPR have proved that these radiographs could provide invaluable information associated with the bones of an individual revealing that there exists a strong connection between oral health and bone health. The extent of osteoporosis can be observed in the DPR of a diseased, and there are significant relationships between the mandibular cortical bone quality, quantity and bone mineral density (BMD). Studies on various population across the globe has found that the various mandible radio-morphometric indices such as mandibular cortical thickness (MCT), panoramic mandibular index (PMI), trabecular bone mass and morphology of endosteal margin could be used to spot subjects at the risk of low BMD [5–13]. Postmenopausal women may visit their dentists for treatment of dental caries and periodontal diseases, therefore dentists are in a unique position to recommend them to visit medical professionals for diagnosis of osteoporosis. Studies by Klemetti et al. demonstrated that endosteal margin of mandible cortical bone could be a reliable tool to discriminate normal subjects from those with low BMD [14, 15]. Similarly, the usage of PMI proposed by Benson et al. as a prediction tool for low bone mass also has the potent to spot subjects with low BMD [8, 9].

Several studies have proved that a correlation exists between the mandibular cortical thickness (MCT) on dental panoramic radiographs and BMD at the hip, lumbar spine and forearm, the most common sites of osteoporosis fracture in postmenopausal women [5–7]. However, it is not easy to perform manual measurement of MCT on DPR for identifying postmenopausal women who are at risk of low BMD. Therefore an automated system for measurement of MCT on DPR may enable us to spot subjects with low skeletal BMD.

In the recent years, computer-aided diagnosis (CAD) system has been developed to minimize the human intervention and have increased the accuracy in osteoporosis diagnosis to a greater extent [16]. Earlier studies have demonstrated the use of a CAD system for osteoporosis screening with minimal manual assistance in the measurement of MCT [17, 18]. In our earlier attempt, we demonstrated that MCT along with trabecular bone area and chronological information (age) could improve the accuracy in osteoporosis diagnosis to a greater extent [19].

So, the aim of the present study is to develop a CAD system to automatically determine the MCT at the lower border of mandible on a DPR in order to identify subjects at risk of low BMD.

Materials and Methods

Study Population

The study is a sincere attempt to develop a semi-automated tool to determine MCT and to predict the risk of low BMD from a DPR. The data was collected from SRM Hospital and Research Centre with the approval of institutional ethics committee. The participants involved in the study provided a written voluntary consent. The study involved 76 women residing in a south Indian neighbourhood (mean age: 57.2 ± 12.6 years). The exclusion criteria included women undergoing hormone replacement therapy and calcium supplement therapy, who underwent a hysterectomy or oophorectomy, those with fractures, deformities or who were suffering from bone related disorders.

Imaging Techniques

The BMD measurement was performed at the right femur by means of a standard narrow fan beam scanner with multiple-view image reconstruction (DPX Prodigy DXA Scanner, GE Lunar Corporation, Madison, WI, USA). The WHO standard for diagnosing osteoporosis was followed to categorise the subjects according to their BMD.

The DPR scan was obtained by the use of a digital Orthopantomogram scanner (KODAK 8000C) at 70KV adopting the standard procedure. The DPR were evaluated individually by the authors to locate the region of interest (ROI), i.e., the mental foramen on the either sides of the mandible as well as the upper and lower boundaries of the mandibular cortical bone.

DPR Image Processing

Determination of MCT: Semi-Automated Method

The mental foramen is one of two small holes located on the lower jaw, which permits the passage of the mental nerve and other vessels that supplies the tissues of the mouth. The region around the mental foramen is affected by low contrast and hence the DPR was stretched to the appropriate range of intensity levels that corresponds to the ROI. The ROI measuring 128×128 pixels was manually placed and cropped in the region below the mental foramen of the mandibular cortical bone on the DPR. The block diagram of the proposed system is outlined in Fig. 1.

Lower Boundary Detection

The boundary of the objects was not sharp, therefore the portions that were considered as the background were eliminated and the enhancement was applied to the remaining objects. Thresholding, an operation that converts a gray-scale image into a binary image by assigning pixels into two classes that is above or below the threshold value. The segmentation was performed based on Otsu segmentation by a fixing a threshold based on the observed distribution of pixel values belonging to the foreground and background [17]. Subsequently, the

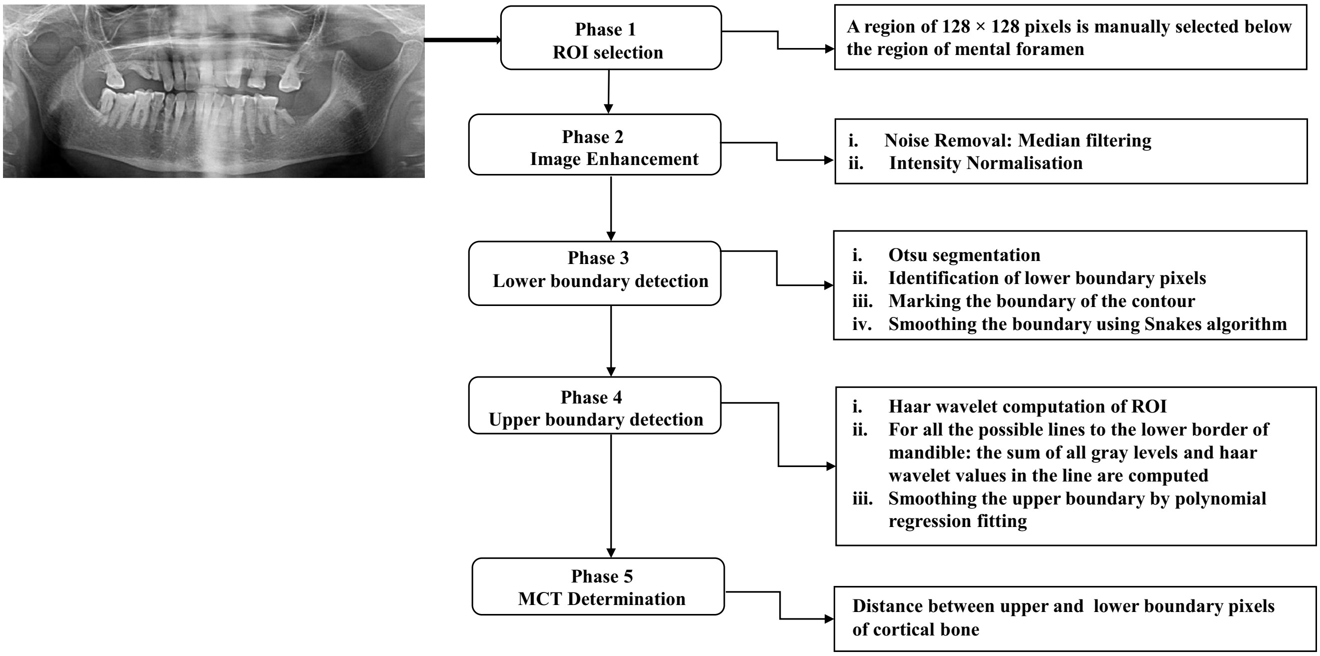

Fig. 1 Block diagram of the proposed semi-automated approach to measure MCT

resultant segmented image had pixels corresponding to two classes: objects and background. In-order to determine the lower boundary of mandibular cortical bone, the connected components labelling operation was performed by assigning a unique label to each maximal connected region of foreground pixels. A set of pixels among which each pixel is connected to all other pixels is called a connected component. A pixel P ∈ S is said to be connected to Q ∈ S if there is a path of pixels from P to Q consisting entirely of pixels of S. A component labelling aims in finding all the connected components in an image and assigns a unique label to all points in the same component [20]. The maximum connected component area was selected and its boundary was detected. Subsequently, the lower boundary of the mandible was determined by smoothing the contour using the traditional active contour algorithm [21].

Upper Boundary Detection

Once the lower boundary is determined, a line is fit to approximate the lower boundary. The haar wavelet is computed at the ROI [22]. For all the possible lines to the lower border of mandible: the sum of all gray levels and haar wavelet values in the line are computed. It was empirically determined that the line which has the maximum value for equation could be a good upper boundary delineator. The search for an optimum point is performed moving in the perpendicular direction. Finally, the smoothing of final contour was performed by polynomial regression fitting. Once the upper and lower boundaries of the mandible are determined, the width between them is determined and designated as MCT.

Determination of MCT: Manual Method

The MCT was measured bilaterally at the site of mental foramen. A line was drawn passing through the centre of mental foramen which is perpendicular to the tangent drawn to the lower border of mandibular cortex on the DPR. The measurement of MCT was performed along the line based on the protocol detailed by Taguchi.et al. The mean values of the MCT measured on the left and right hand side were considered.

Statistical Analysis

The data collected for the study were analysed using the SPSS software (package Version 17.0, SPSS Inc., USA).

The subjects were categorised according to their total femur BMD (T-BMD) based on the WHO classification of Osteoporosis. The study population were divided into two groups as follows: (a) normal ($n = 43$, age = 50.9 ± 11.5 years); for T - score ≥ −1; and (b) with low BMD ($n = 33$, age = 65.4 ± 8.6 years); for T - score ≤ − 1 SD.

The Analysis of variance (ANOVA) was performed for comparison and calculation of mean MCT determined using the manual and semi-automated approach for the entire groups. The t-test was performed to compare the assessed features (Age, MCT and BMD) between the normal and low BMD groups. The Pearson correlation test was performed to assess the connection between the DPR features and the BMD measures. The Kappa coefficient, a statistical measure of inter-rater reliability or agreement which is used to determine agreement between the authors for manual measurement on MCT. An inter-rater agreement with a kappa coefficient of 0.9

was found between the measurements carried out by the authors. Reliability measures using intra-class correlation coefficients also demonstrated better outcomes as follows: single measures (intra-class correlation: 0.98, confidence interval (CI): 92.2%–99.5%) and average measures (intra-class correlation: 0.99, CI: 95.9%–99.7%).

The Bland-Altman plot is a graphical plot to compare the MCT measurements made using semi-automated and manual methods. The differences in MCT measured using semi-automated and manual method are plotted against the mean MCT.

A receiver operating characteristic (ROC) analysis was performed to evaluate the performance of the proposed method in identifying individuals at risk of possible low BMD. The results of the statistical tests that demonstrated significance at the level of $p < 0.05$ were alone considered as significant.

Performance Assessment

It is essential to assess the performance of all the diagnostic tests based on their sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and accuracy.

True Positive (TP)

A true positive denotes a positive test result for an individual with low BMD.

False Positive (FP)

A false positive denotes a positive test result for an individual, but who actually is of normal BMD.

True Negative (TN)

A true negative denotes a negative test result for an individual with normal BMD.

False Negative (FN)

A false negative denotes a negative test result for an individual, but who actually is of low BMD.

Sensitivity: Measure of true prediction of low BMD

$$\text{Sensitivity} = \frac{\text{TP}}{\text{TP} + \text{FN}} \%$$

Specificity: Measure of true prediction of Normal BMD

$$\text{Specificity} = \frac{\text{TN}}{\text{FP} + \text{TN}} \%$$

Accuracy (Efficiency): Measure of true prediction of the proposed method

$$\text{Accuracy} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{FP} + \text{FN} + \text{TN}} \%$$

Positive Predictive Value (PPV)

$$\text{PPV} = \frac{\text{TP}}{\text{TP} + \text{FP}} \%$$

Negative Predictive Value (NPV)

$$\text{NPV} = \frac{\text{TN}}{\text{TN} + \text{FN}} \%$$

Results

The measurement of MCT on the DPR was performed as per the technique detailed in section 'Materials and methods'. The resultant images for the MCT measurement performed on the DPR is presented in the Fig. 2.

It was found that there exists a negative correlation for age ($r = -0.6$, $p < 0.01$) against T-BMD suggesting that BMD decreases on ageing. The manual measure MCT ($r = 0.74$, $p < 0.01$) and MCT measured using the proposed method ($r = 0.67$, $p < 0.01$) against T-BMD. The results of the Bland-Altman plot to examine the agreement between the MCT measurements made using the manual and semi-automated approaches are presented in the fig. 3. The semi-automated MCT measure demonstrated correlation at the level ($r = 0.96$, $p < 0.01$) against manual MCT measurement.

The mean MCT measured using the manual and semi-automated scheme for the low BMD group was 1.6 ± 0.5 mm and 1.7 ± 0.6 respectively, whereas for the normal group it was 2.8 ± 0.6 mm and 2.7 ± 0.6 mm respectively. The t test revealed a statistical significant difference at the level ($p < 0.01$) for MCT between the two groups suggesting that cortical bone thinning is evident with decrease of BMD (Table 1).

Table 2 shows the sensitivity and specificity pairs at different threshold levels of MCT to spot individuals at risk of low BMD at the right femur. When the threshold was fixed at MCT $\leq$ 2.3 mm, the sensitivity, specificity and accuracy values were 91%, 70% and 79% respectively for identifying individuals with low BMD at the right femur. The results based on the sensitivity and specificity measures infers that at about MCT = 2.3 mm, individuals are at higher possible risk of osteoporosis.

Discussion

The availability of DXA scan and its associated cost per scan has made Indian population ill affordable to undergo BMD assessment. This scenario is almost prevalent in most of the developing nations of the world [1]. Earlier studies across the

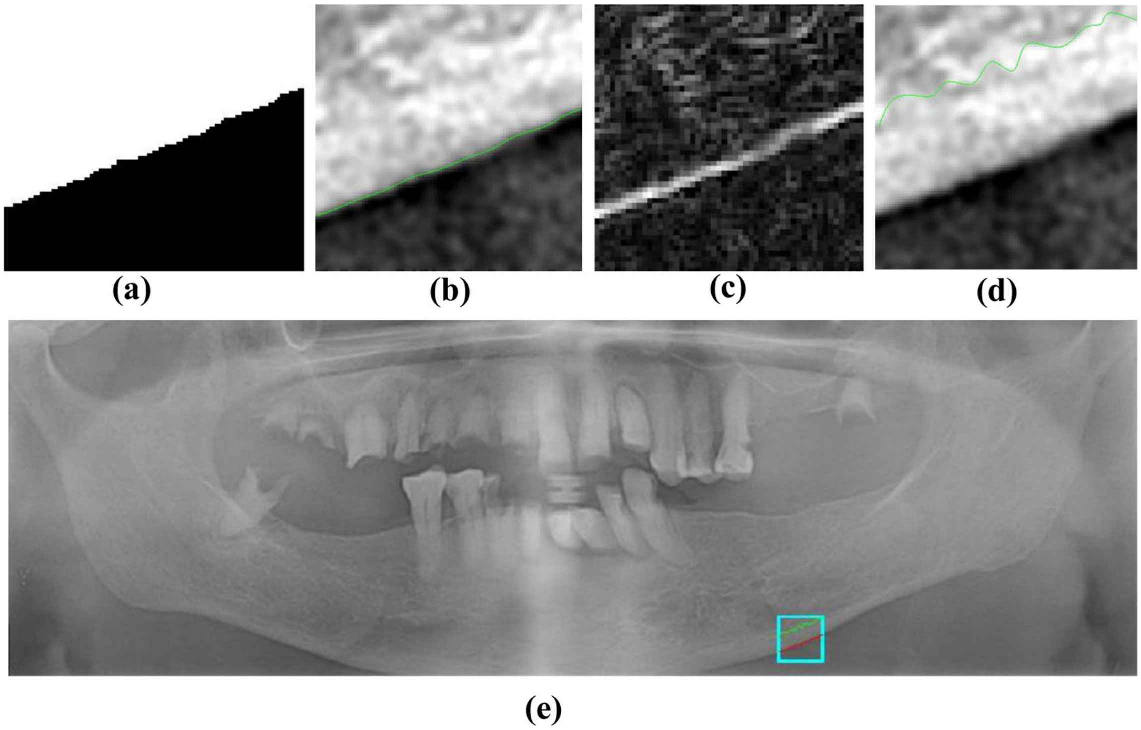

Fig. 2 Results: (**a**) Segmented foreground, (**b**) Detected lower boundary, (**c**) Haar wavelet magnitude, (**d**) Detected upper boundary, (**e**) DPR with detected upper and lower boundaries

globe have reported that measurements made on a DPR could be effectively considered as means of predicting low BMD [5–13]. The unavailability and scarcity of advanced imaging modalities in underdeveloped and developing nations of the world has created an urgency to develop alternative cost effective means in the prediction of low BMD. In our earlier attempt, we evidenced that the use of MCT along with age and the extent of trabecular bone could be a valid indicator in spotting individuals with low BMD among the south Indian population. The results of the study affirmed that the DPR could significantly contribute to osteoporosis diagnosis

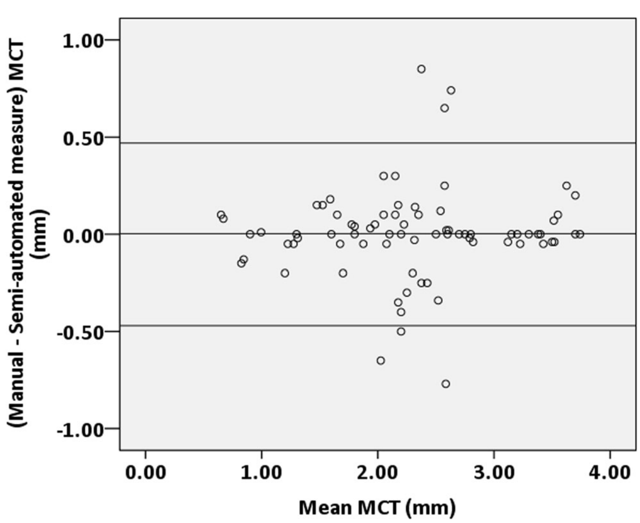

Fig. 3 Bland-Altman Plot

among the understudied south Indian community [19]. Similar studies by Kavitha et al. also found that a strong connection exists between the MCT and BMD measured at various skeletal sites for Japanese population [17]. On contrary, an earlier attempt by Mohajery and Brooks observed that MCT measured at various mandible sites did not exhibit statistical significant differences between the normal and diseased groups and suggested that the MCT could not be considered for prediction of osteoporosis [21]. Even though, the use of MCT for low BMD prediction has been justified in several earlier attempts, however to the best of our knowledge there seems to be no established standard threshold value of MCT for Indian community for osteoporosis risk assessment and thereby to recommend them for further examination. The suggested experimented threshold levels for MCT seems to vary for various populations across the globe, taking in account of the measurement scheme and imaging system specifications. The earlier clinical trials on the usage of MCT for the assessment low BMD employed threshold levels ranging from 2.9 mm to 4.7 mm to distinguish individuals at risk of possible osteoporosis [5–7] . In the current study, the mean MCT for the normal and low BMD groups were 2.77 ± 0.6 mm and 1.7 ± 0.5 mm respectively, which suggests that the most probable threshold for MCT should be less than 3 mm to recommend subjects for low BMD assessment. However, the larger differences in MCT values could be as questionable in terms of imaging modality and measurement techniques. An earlier attempt by Sapthagirivasan et.al on bone quality among

Table 1 Characteristics of the studied population

Characteristic	Normal	Low BMD	t- value	*p* value
Age (years)	50.9 ± 11.5	65.4 ± 8.6	−6.03	< 0.001
Manual measure MCT (mm)	2.8 ± 0.6	1.6 ± 0.5	8.65	< 0.001
Semi-automated measure MCT (mm)	2.7 ± 0.6	1.7 ± 0.6	7.11	< 0.001
DXA BMD (g/cm^2)	0.9 ± 0.09	0.7 ± 0.07	11.67	< 0.001

MCT: Mandibular cortical thickness, DXA: Dual Energy X-ray Absorptiometry, BMD: Bone mineral density

Indian population revealed that Indian women attain lower bone mass compared to their corresponding African counterparts. The results of earlier studies concurs that the mean MCT was lesser among the studied population compared with western counterparts [22] . However, a threshold for MCT could only be established on assessing a very large database and taking into account of various factors like socio-economic conditions. An earlier attempt by Muramatsu et al. on Japanese population found that the mean MCT for the osteoporosis and normal cases were 2.5 and 4.3 mm, respectively [18]. The mean MCT of Indians was much lower than Japanese population suggesting that Indian lack in bone strength compared to their Japanese counterparts. When the threshold was fixed at MCT = 2.5 mm, the sensitivity, specificity and accuracy values were 93%, 63% and 76% respectively for identifying individuals with low BMD at the right femur. The results of the study infers that the MCT threshold could most likely be fixed at about 2.5 mm to recommend further low BMD assessment, however it could be affirmed on validation with a larger sample size.

A computer aided system developed by Afrin et al. to measure MCT to spot individuals with low BMD demonstrated that the area under ROC curve was 0.78 for the computer-aided system and 0.83 for manual measurement for identifying women with low spine BMD. Similarly, Area under ROC curve for identifying women with low femoral BMD was 0.831 for manual measurement and 0.803 for the computer-aided system [23]. Similarly our study also demonstrated satisfactory results as the proposed semi-automated technique to measure MCT could spot individuals with low BMD. It was evident in the present study that there exists a small difference in the manual measure MCT and semi-automated measure MCT, as the location of mental foramen is user defined. It seems reasonable that the slight differences in the measurements are due to human perception in locating the lower and upper boundaries of the cortical bone. The proposed algorithm can be implemented as a computer aided system integrated with a DPR machine due to the wide availability of DPR machine, easy protocol, low capital investment and affordable scan cost.

The limitations of the present study are that the numbers of subjects are relatively less, and the study has to be validated on a larger population. The optimum thresholds for MCT to identify subjects with low BMD were associated with limited sensitivity and specificity.

Table 2 Performance characteristics at various threshold lengths of MCT to predict subjects at risk of low T-BMD

Threshold	Sensitivity	Specificity	PPV	NPV	Accuracy
≤ 2.8 mm	100% (CI: 89.42% to 100%)	41.86% (CI: 27.01% to 57.87%)	56.90% (CI: 50.60% to 62.98%)	100%	67.11% (CI: 55.37% to 77.46%)
≤ 2.7 mm	100% (CI: 89.42% to 100%)	53.49% (CI: 37.65% to 68.82%)	62.26% (CI: 54.49% to 69.45%)	100%	73.68% (CI: 62.32% to 83.13%)
≤ 2.6 mm	96.97% (CI: 84.24% to 99.92%)	96.97% (CI: 84.24% to 99.92%)	64.00% (CI: 55.43% to 71.76%)	96.15% (CI: 78.11% to 99.43%)	75.00% (CI: 63.74% to 84.23%)
≤ 2.5 mm	93.94% (CI:79.77% to 99.26%)	62.79% (CI:46.73% to 77.02%)	65.96% (CI: 56.55% to 74.25%)	93.10% (CI: 77.55% to 98.14%)	76.32% (CI: 65.18% to 85.32%)
≤2.4 mm	93.94% (CI:79.77% to 99.26%)	65.12% (CI: 49.07% to 78.99%)	67.39% (CI: 57.65% to 75.83%)	93.33% (CI: 78.21% to 98.20%)	77.63% (CI: 66.62% to 86.40%)
≤ 2.3 mm	90.91% (CI: 75.67% to 98.08%)	69.77% (CI: 53.87% to 82.82%)	69.77% (CI: 59.13% to 78.63%)	90.91% (CI: 76.96% to 96.77%)	78.95% (CI: 68.08% to 87.46%)
≤ 2.2 mm	84.85% (CI: 68.10% to 94.89%)	79.07% (CI: 63.96% to 89.96%)	75.68% (CI: 63.10% to 84.99%)	87.18% (CI: 74.93% to 93.93%)	81.58% (CI:71.03% to 89.55%)
≤ 2.1 mm	81.82% (CI: 64.54% to 93.02%)	88.37% (CI: 74.92% to 96.11%)	84.38% (CI: 69.99% to 92.59%)	86.36% (CI: 75.29% to 92.94%)	85.53% (CI: 75.58% to 92.55%)
≤ 2.0 mm	75.76% (CI: 57.74% to 88.91%)	93.02% (CI: 80.94% to 98.54%)	89.29% (CI:73.34% to 96.19%)	83.33% (CI: 73.12% to 90.19%)	85.53% (CI: 75.58% to 92.55%)

CI: 95% Confidence Interval, PPV: Positive Predictive Value, NPV: Negative Predictive Value

Conclusion

The MCT measured using the semi-automated scheme demonstrated correlation ($r = 0.96$, $p < 0.01$) against the manual approach suggesting that the proposed approach could be effectively used in identifying people at risk of low BMD. The results also recommends the secondary use of DPR which were primarily radiographed for dental diagnosis for low BMD prediction.

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Compliance with Ethical Standards

The study was conducted with the consent of institutional ethical committee (SRMIST- Institutional Ethical Committee).

This article is original and has not been published by any other journal.

Conflict of Interest The authors declare that they have no conflict of interest.

Informed Consent An informed consent was obtained from all participants in their native language.

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