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### Localization of Disease Osteoporosis in X-ray Images

Aashi Singh Bhadouria<sup>1</sup>, Ishan Singh Bhadouria<sup>2</sup>, Vanshika Patel<sup>3</sup>, Akshat Upasani<sup>4</sup>

<sup>1</sup>Assistant Professor, <sup>2, 3, 4</sup>EE-IOT, Madhav Institute of Technology and Science Gwalior, India

Abstract: People with osteoporosis are more likely to break bones, particularly in the wrist, hip, and spine. Determining the existence of osteoporosis requires measurements of bone quantity and quality, especially bone mineral density (BMD). Science may use many techniques in order to ascertain the BMD. Dual Energy X-ray Absorptiometry (DEXA) is one of the procedures that has gained the most widespread acceptance. The T-score is a method that uses bone mineral density to quantify the degree to which osteoporosis has progressed (BMD). The BMD assessment may be seen on X-ray or DEXA images. Bone mineral density (also known as BMD) is tested in order to make a diagnosis of osteoporosis. This article offers an overview of many popular image-processing methods used in BMD assessment. These methods include image augmentation, segmentation, and texture analysis. Due to its many advantages, DEXA is finding a wide variety of new applications in medicine and science. At the end of the piece, we take a quick look at the first techniques for determining BMD. Similarities between DEXA and X-ray images are also highlighted in the article. The methods of image processing that may be used to detect osteoporosis are detailed in the article. Methods for preparing X-ray and DEXA pictures for analysis, extracting features from those images, and segmenting them are described.

Keywords: BMD; DEXA; Feature extraction; Image processing; Osteoporosis; Segmentation X-ray

#### I. INTRODUCTION

Low bone mass is the hallmark of osteoporosis, which in turn causes bones to thin and increases the likelihood of fractures everywhere but mainly the hip, spine, and wrist. At magnifications of 12 and 13, under a microscope, the structure of the bone takes on the appearance of a honeycomb. Healthy bone resembles a honeycomb structure because of its spongy texture and large holes, whereas osteoporotic bone gives the appearance of brittle, crumbling shards. It is a significant public health issue in both wealthy and undeveloped nations across the world. Bone fragility affects both sexes equally. After the age of 50, both sexes are at equal risk for developing osteoporosis and suffering from osteoporotic fractures. Younger people may have osteoporosis if they have a genetic predisposition, a specific medical condition, or an allergy to a medicine. This disease has now affected over 200 million people globally. There may be a 50% rise in the worldwide fracture rate by the year 2025, according to projections. The vertebrae, the proximal femur, and the wrist are the most frequent locations for osteoporotic fractures, although they may happen anywhere (distal forearm). The density and makeup of bone tissue change throughout time, which impacts bone strength. An aging population means more cases of osteoporosis in postmenopausal women. Fractures of the hip (16%), lower arm (16%), and vertebrae (32% more common in women over 50 than men), respectively (15 percent). Hip and spine fractures are more severe and more common, and have been used in several studies to assess the worldwide burden of osteoporosis [1-3].

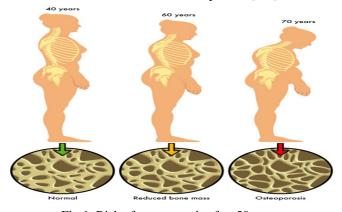


Fig 1. Risk of osteoporosis after 50 years



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- 1) Osteoporosis: Osteoporosis is diagnosed when the T-score is lower than -2.5 standard deviations. A T-score that is more than 2.5 standard deviations below normal AND the presence of a fragility fracture both indicate that a patient has severe osteoporosis (T-score d"-2.5 PLUS fracture).
- 2) Osteopenia: T-score > -2.5 -1.
- 3) Normal: T-score greater than -1.

Table 1. bone mineral density for Indian women

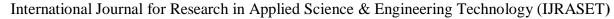
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Term	Definition		
Normal	MD T-score -1.0 indicates that a		
	woman's PBM is within 1 SD of the		
	average for her age group.		
Osteopenia	A T-score below -1.0 for young adult		
	women represents a BMD that is		
	between 1.5 and 3.5 standard deviations		
	below the PBM mean value.		
Osteoporosis	Bone mineral density (BMD) in women		
	in their twenties with a T-score of 2.5 is		
	more than 2.5 standard deviations (SDs)		
	below the population mean (PBM).		

Causes of low bone mineral density:

- a) Female gender.
- b) Anorexia nervosa with a body mass index below 19.
- c) Nicotine and tobacco use.
- d) Drinking four or more units of alcohol each day.
- e) Inadequate nutrition (especially if calcium-deficient) or malabsorption diseases like celiac disease.
- f) Sustained inability to move.
- g) ethnically either Caucasian or Asian.
- *h*) Inheritance of a family history of hip fracture.
- i) Cushing's syndrome or corticosteroid treatment.
- j) The degenerative spine condition known as ankylosing spondylitis.
- k) Arthritis Rheumatica.
- *l*) Condition of Crohn's.
- m) An early menopause (before 45) or a protracted case of secondary amenorrhea.
- *n*) Hypogonadism of the primary hypothalamus (men and women)
- o) Hyperparathyroidism that is primary
- p) Hyperthyroidism.
- q) Osteogenesisimperfecta.
- r) Post transplantation.
- s) Deterioration of the kidneys, chronic

The incidence of osteoporosis varies greatly across different racial and ethnic groups, according to data from the National Osteoporosis Foundation. A bone density scan is often used in osteoporosis diagnostics. The use of DEXA to assess bone density and thickness has become the norm. When doing a scan, DEXA employs a sophisticated kind of X-ray technology to create a picture. DEXA imaging involves sending two X-ray beams, each with a different energy peak, through the body to create a picture of the bone and soft tissue layers. When the entire volume of bone tissue is divided by its surface area, the result is the density of the tissue (BMD).

DEXA has certain advantages over other imaging modalities, such as its low radiation exposure and lack of invasiveness, but it also has some downsides, such as its high cost, extended scanning time, limited availability, and need for trained personnel. If the BMD could be calculated from digital X-rays, it would save a lot of time and money. Pictures of DEXA and X-rays taken of the same person are shown in Fig 3. Studies that analyze digital X-rays and directly estimate bone density are few.





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It has been suggested that X-ray texture analysis may be used to diagnose a variety of medical conditions effectively and cheaply. In order to determine the BMD, fractal dimension is used. Included in this article is a summary of studies examining the use of image processing techniques for segmentation, fracture detection, and pre-processing processes using X-ray and DEXA pictures in the study of osteoporosis.

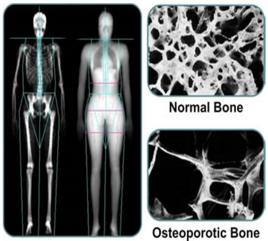


Fig 2. The Difference Between Healthy(up) and Osteoporotic Bone Tissue(down)

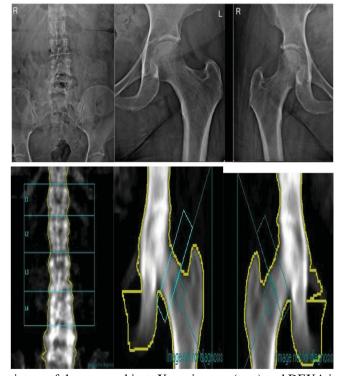


Fig 3. Sample picture of the same subject: X-ray images (top ) and DEXA images (bottom)

#### II. LITERATURE REVIEW

In order to give information that may be utilized to assist clinical decision-making, the Computerized Medical Picture Diagnostic System analyses an X-ray image of a patient's body as its input. Several studies have shown promise in utilizing X-ray images of humans as a means of diagnosing osteoporosis. The next paragraphs will discuss the efforts of several cutting-edge techniques and algorithms for identifying osteoporosis in human X-ray pictures.

Venkatesh, et.al. [2] have created a test that may detect hip osteoporosis in patients. The shoulders, elbows, wrists, and other parts of the human body have been ignored.



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Dr. Pravin, et.al. [3] have devised a technique for detecting osteoporosis in X-ray images using textural characteristics of the first order. The percentage of correct answers is just 66.66 percent.

Dr. Shubangi, et.al. [4] Several approaches for detecting osteoporosis have been discussed, including the KNN classifier, Fuzzy Expert System, Bone Mineral Density computation, and the Mathematical Morphological Approach.

Pravin, et.al. [5] textural analysis to create a technique for identifying osteoporosis in radiographic pictures. Only 87 x-rays of skeletal structures have been analyzed thus far.

Shubangi, et.al. [6] integrates time-lapse and panoramic photography to help find osteoporosis earlier. The algorithm is 73.33 percent accurate, with a sensitivity of 72.23 percent and a specificity of 72.23 percent on test data.

Bartosz, et.al. [7] suggests trying out some virtual bone density measuring devices. This method has the potential to detect osteoporosis, however, it is quite time-consuming.

Arment, et.al. [8] using a dual-frequency ultra-sonometer, have developed a method for detecting osteoporosis. They're already up to 76% sensitive and 70% specific.

Ramkumar, et.al. [9] Exhibit a computerized method of analyzing hand radiographs for the detection of erosions and osteophytes. The level of specificity is 70%. This technique is very accurate, with a sensitivity and specificity that are both close to 70%.

Kavya, et.al. [10] introduces a method for describing bone structure using morphological data obtained from radiological images of the calcaneus. For diagnostic purposes in dentistry, it is highly suggested.

Enny, I.S. and Rini [12] have revealed a method to predict future cases of osteoarthritis in the hands and knees. They have not considered any metrics or criteria for evaluation.

Yijie Fang, et.al. [18] The disease of osteoporosis was identified using multidetector CT scans based on CNN. The vertebral body was successfully segmented using the fully-linked NN. The results are derived from a CT scan analysis of the reference standards after processing (QCT). There's a chance that the model will prevent the vertebral bodies from calcifying on their own. The diagnosis was significantly altered due to discrepancies between expected and observed vertebral bodies. However, overfitting was evident in the built model due to external validations against the target population.

Tang, et.al. [28] developed a two-module convolutional neural network model for BMD detection in osteoporosis screening. The first part of this system finds the problem and divides it apart, while the second part utilizes the features of the problem area to identify the kind of BMD. The proposed method was effective for segmentation on form preservation with various lumbar vertebrae. The accuracy of the BMD detection was improved using the newly developed CNN. The resulting model successfully replicated real-world connections full of unpredictable interactions while also achieving the highest possible degree of precision for very intricate data. However, training each data sample individually took longer and used fewer data using the newly developed CNN technique.

Gwidon, [35] proposed a method based on fuzzy inference for identifying osteoporosis. They evaluated 20 X-rays from people of varying ages and found that their average bone density was 78.90%.

Ramkumar, [13] has written a men's osteoporosis consensus document.

Tomlison, et.al. [14] have detailed the several challenges that need to be conquered in order to develop a computerized system that can reliably diagnose osteoporosis from X-ray photographs.

Riandini, et.al. [15] It is possible to categorize osteoporosis radiography using the methods of K-Nearest Neighbor and Gray Level Co-occurrence Matrix (GLCM), both of which are feature extraction techniques. Even yet, they have only looked at 46 X-rays of the throat thus far.

Giuseppe, et.al. [21] possess Active Appearance Models with 81.2% accuracy for early diagnosis of osteoporosis.

Humbert et al. [31] developed a strategy for reconstructing 3D BMD distribution and femoral shape from DXA pictures. Single- and multiple-view DEXA devices' reconstruction accuracies were compared.

Tristan Whitmarsh et al. [28] Presented a BMD distribution as a statistical model for the building's characteristics. Through iteratively shifting the reference form and volume, we were able to improve the precision of each individual registration.

Reshmalakshmi [22] With the purpose of medical imaging detection of osteoporosis, a fuzzy inference framework was devised. Over the course of their study, twenty patients have given their time and input. Based on the comprehensive literature review shown above, there is no one best method or algorithm for identifying osteoporosis in X-ray images of humans. Results from different methods might vary in terms of exactness, precision, specificity, or sensitivity. We provide a method for analyzing X-ray images for osteoporosis using a Gaussian filter and fractal analysis, which improves upon previous methods. When used to x-rays of the skeleton, the fractal approach improves the precision of clinical diagnosis.

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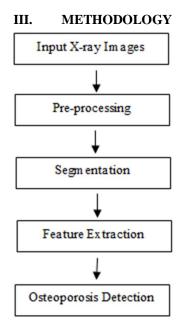
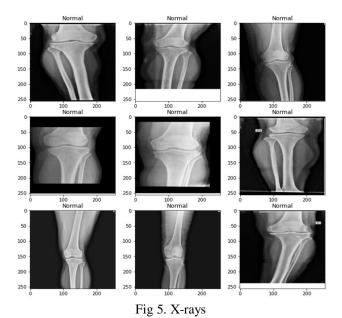


Fig 4. Flow Chart of osteoporosis detection in X-ray picture



A. X-ray
The user provides an X-ray of their forearm.

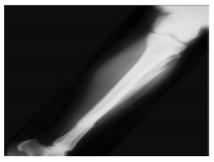


Fig 6. X-rays

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#### B. Pre-Processing

When an image is preprocessed, the noise that is present in it is decreased in order to improve its performance in any later image analysis that may be performed. It was the impetus behind the development of a number of image processing techniques that could remove noise from X-ray pictures.



Fig 7. Result of discrete step algorithm.

#### C. Segmentation

Using this procedure, the bone may be effectively separated from the tissue that surrounds it. First, an entropy image is created from the raw X-ray picture by using it as a source, and then the bone structure is isolated using thresholding.

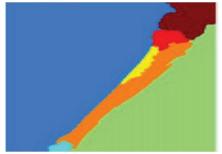


Fig 8. Result of watershed segmentation.

#### D. Feature Extraction

X-rays and other imaging modalities enable for the evaluation of bone density and internal structure. The bone disease may be accurately diagnosed with the use of texture analysis. The densities determined by DEXA measurements agreed well with those expected by the textural properties. X-ray images' textural qualities are linked to the BMD learned from DEXA. In particular, we found that picture brightness strongly correlates with BMD (r = 0.79, p 0.005).

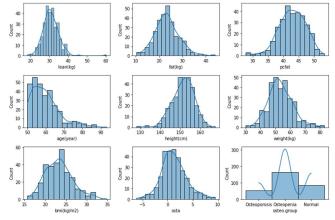


Fig 9. Feature Extraction





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#### E. Osteoporosis Detection

Several factors extracted from trabecular patterns were utilized to calculate the energy, which is in turn used to assess bone health and diagnose osteoporosis. The quality of the recorded picture is enhanced once photo noise has been reduced. X-ray images obtained before and after the diagnosis of osteoporosis are compared in Fig. 8, illustrating the efficacy of the proposed techniques. We obtained sample images from Google Images, the National Health Service, and imageprocessingplace.com, as well as physically collected images from the hospital for testing purposes.



Fig 10. Osteoporosis detection

Evaluation Metrics: Metrics are quantitative measures of an algorithm's or method's effectiveness. The effectiveness of the proposed approach was measured using many binary classification measures. Different osteoporosis detection methods/algorithms are shown in Table 1. with their starting settings, and in Table 2. with their performance metrics.

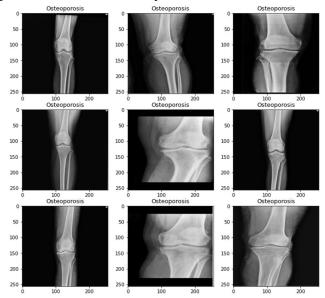


Fig 11. Result of Osteoporosis detection

#### IV. RESULTS AND ANALYSIS

When there aren't enough minerals in the bone, a metabolic condition known as osteoporosis may set up. Disc deterioration, low back pain, and a higher chance of vertebral body fracture all result from insufficient muscle strength. This means that the gradual weakening of bones associated with osteoporosis is diagnosed at the same time as the disease is progressing. Therefore, early detection of illness is essential. Methods for identifying osteoporosis disease have been established in the past, but they all had trouble localizing and segmenting the x-ray images.

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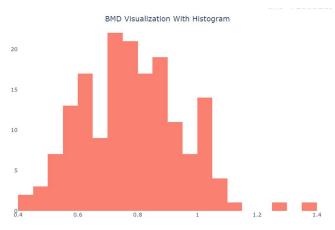


Fig 12. BMD Visualization with histogram

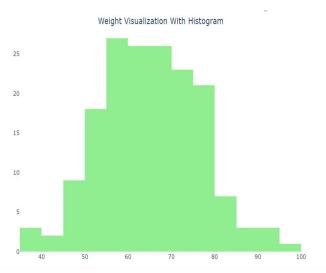


Fig 13. Weight Visualization with Histogram

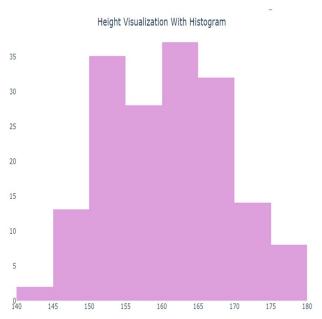


Fig 14. Height Visualization with Histogram



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#### Table 2. Initial Measures

No.	Measure	Description	
1	Positive (P)	Pixel belongs to an interesting class.	
2	Negative (N)	Pixel does not belong to a relevant class.	
3	True Positive (TP)	The pixel is considered positive by both the ground truth and the method.	
		For Example; TP stands for the pixels that the tested technique accurately identifies as osteoporosis as compared to the actual data.	
4	True Negative (TN)	The approach scores the pixel as negative even when the ground truth pixel is negative.  For Example; The pixels that the tested technique successfully identifies as healthy tissue are referred to as TN.	
5	False Positive (FP)	The approach scores higher than the ground truth pixel, which is negative.  For Example; FP stands for the pixels that the tested technique incorrectly identified as osteoporosis.	
6	False Negative (FN)	The pixel is rated positively in the ground truth but negatively by the method.  For Example; The pixels that the tested method incorrectly identified as healthy tissue are referred to as FN.	

Table 2. Metrics used for performance evaluation

No.	Measure	Description	
1	Accuracy	Relationship between the overall number of hits and the	
		overall number of mistakes and hits. The formula for	
		determining this number is $(TP + TN)/(TP + FN + FP +$	
		TN).	
2	Specificity	Percentage of all negative samples that were successfully	
		recognized. Calculation of this value: TN/(FP + TN)	
3	Sensitivity	A test's sensitivity is how well it can identify the patien	
		instances. Calculation of this value: TP/(TP + FN)	

#### Evaluation of several techniques for detecting osteoporosis



Fig 15. Comparison of osteoporosis detection





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Multiple techniques for detecting osteoporosis are compared above in Table 3 for their precision, specificity, and sensitivity. Our proposed algorithms achieved a better rate of accuracy (96.27%) than the Texture Based Technique (95.24%), the Shape Based Features (73.33%), and the Special DIP method (86.70%). In terms of accuracy, the recommended techniques yields gain of 1.03 percent, 22.94 percent, and 9.57 percent when compared to the Texture Based Method, the Shape Based Features method, and the Special DIP method, respectively.

The algorithm is said to be 12.38% more specific than the Texture Based Approach, 25.62% more specific than the Shape-Based Features, and 0.59% more specific than the Special DIP technique. The sensitivity of the recommended algorithm are improved by 14.82 percent when compared to the Shape Based Features technique and by 18.95 percent when compared to the Special DIP approach. When compared to the recommended approach, the sensitivity of the Texture Based Method is higher, at 95.20 percent. The algorithms used are describes as follows:

- 1) XGBRegressor: The XGBRegressor normally assigns an importance ranking to each predictor feature. An benefit of gradient boosting is that after the boosted trees have been constructed, getting relevance ratings for each attribute is not too difficult.
- 2) Random Forest Regression: A kind of ensemble learning, Random Forest Regression is used in supervised learning. The ensemble learning method improves upon the accuracy of predictions made by individual models by pooling the results of many machine learning algorithms.
- 3) Decision tree regression: By analysing an item's characteristics, decision tree regression trains a model to make accurate predictions and provide valuable, continuous output. When there is no discrete output, often known as a fixed set of numbers or values, the output is said to be continuous.
- 4) Lasso regression: Using lasso regression is one way to regularise data. It is favoured over regression methods because it produces more reliable forecasts. This model incorporates a shrinking element. Shrinkage occurs when individual data points become smaller until they finally reach the average. The lasso technique favours simple, sparse models (i.e. models with fewer parameters). This kind of regression shines when a model displays substantial multicollinearity or when you want to automate aspects of the model selection process like variable selection and parameter removal.
- 5) Linear regression: Linear regression is a technique for analysing data that involves using a second, related, and known data value to estimate the value of the unknown data. This method use a linear equation to mathematically depict the connection between the independent and dependent variables.
- 6) Ridge regression: Ridge regression is a method for estimating the coefficients of multiple-regression models in which the independent variables are highly linked. As an alternative to the inaccuracy of least square estimators, ridge regression was developed for use in linear regression models with specific multicollinear (highly correlated) independent variables (RR).

Dual X-ray Energy Absorptiometry (DEXA) is the gold standard for detecting fracture risk. DEXA, which was initially used routinely in the clinic in 1987, is the gold standard for measuring BMD in living organisms. It is a low-radiation, high-precision technology that has been standardized for ease of use and has an acceptable accuracy error of just 2% to 2.5%. 1-50 mSv, if done in conjunction with a test for vertebral fracture. Areal bone mineral density (BMD) may be measured by DEXA in the lumbar spine, proximal femur, and distal radius using two x-ray beams of different peak kilovoltages (30–50 keV and 70 keV), often without checking soft tissue.

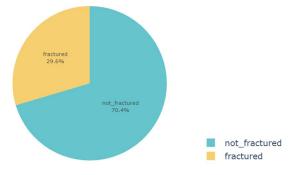
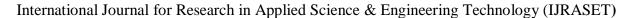


Fig 16. Patient fracture overall distribution

After utilizing computerized segmentation to gain accurate measures, the operator will next manually check and modify the lumbosacral spine in addition to the intertrochanteric and trochanteric areas and the femoral neck.





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The whole femur includes the intertrochanteric, trochanteric, and femoral neck regions. In addition to T scores and Z scores, DEXA also offers real density readings in grams per square centimeter. While the standard deviation of a Z-score is compared to a group of people of the same age, the standard deviation of a T-score is compared to a group of young adults. Bone mineral density measured by DEXA correlates well with biomechanically evaluating bone strength and accounts for around 70% of the variance in bone strength, making it a useful tool in the diagnosis of osteoporosis and osteopenia (1,17).

Although the World Health Organization's definition only applies to postmenopausal women, the International Society for Celiac Disease (ISCD) allows the use of these criteria in men aged 50 and above (18–20). The International Society for Clinical Densitometry has developed guidelines for the use of DXA in premenopausal women, males under the age of 50, and children (18 to 20). When comparing the BMD measurement of an individual to that of a group's reference population, a Z score of less than 22 is considered to be "below the predicted range for age." This is determined by contrasting the BMD measurement of an individual to that of the group's reference population. It is essential to keep in mind that the DEXA BMD test on its own is unable to diagnose osteoporosis in these groups. In Fig 11. and Fig 12., we see a sample DEXA scan image of the right femur and spine, respectively, along with their corresponding bone mineral density (BMD).

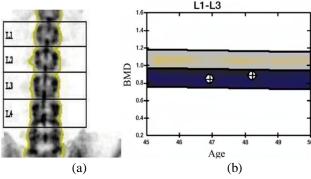


Fig 17. DEXA scan picture (a) a numbered spinal column(b) BMD of spine

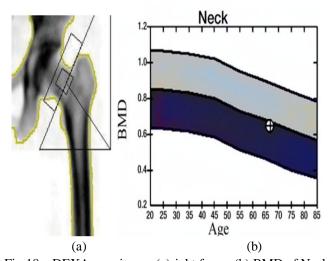


Fig 18. DEXA scan image (a)right femur (b) BMD of Neck

The bone size and mineral density may both be evaluated with DEXA. The amount of bone mineral density is expressed in grammes (BMC). After that, the bone mineral density (BMD) is converted into a value that is represented as a weight in grams per square centimeter (g/cm²) by dividing this number by the size of the bone that was scanned. The patient's bone density is converted to an age-adjusted or gender-specific peak bone mass equivalent. The T-score is produced from a comparison of the person's measured BMD to the median BMD of the young and healthy population, stratified by gender and race. This comparison is done in order to determine whether or not the individual has osteoporosis. This disparity is then scaled by the youth population's mean bone mineral density standard deviation. The Z-score is also determined by comparing an individual to a normative sample of people of the same age.

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Table 3. T-score and Z-score of various regions

Regio	Area(c	BMC(	BMD(g/c	T-	Z-
n	$m^2$ )	g)	$m^2$ )	score	score
Neck	4.35	2.81	0.64	-1.8	-0.2
roch	12.91	6.58	0.51	-1.9	-0.8
Inter	19.28	18.29	0.94	-1.0	-0.1
Total	36.54	27.69	0.75	-1.5	-0.2

$$T - score = \frac{\lambda - \mu}{\sigma}$$
 (1)

$$Z - score = \frac{\lambda - \beta}{\alpha}$$
 (2)

where  $\lambda$  is the patient's measured bone mineral density (BMD),  $\mu$  is the mean bone mineral density (BMD) of a young normal population,  $\sigma$  is the standard deviation of a young normal population's bone mineral density (BMD),  $\beta$  is the mean bone mineral density (BMD) of a group of people of the same age, and  $\alpha$  is the standard deviation of a group of people of the same age.

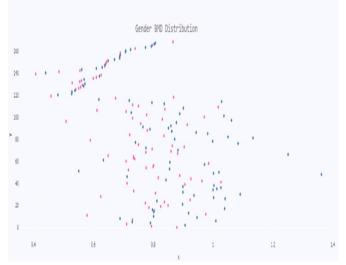


Fig 19. Gender BMD Distribution

Equations (1) and (2) may be used to provide numerical expressions for the T-score and Z-score, respectively. The T-score and age may be used to predict the likelihood of future fractures or the total number of potential fractures during the remaining years of a person's life. According to their T-score, patients are placed into one of three categories: healthy, osteopenia, or osteoporosis. A report by the WHO (World Health Organization) claims that T-score system, a bone mineral density (BMD) T-score of 1 SD is considered normal, 2.5 SD is osteoporotic, and 1.0 SD is osteopenia. If a patient's T-score is less than 2.5, they would be in the worst two percent of the normative sample. The T-score and Z-score for the spine are both included in the data shown in Table 4. Table 5 displays the values for the T-score and Z-score of the neck region.

Table 4. T-score and Z-score of the spine

Region	Area(cm <sup>2</sup> )	BMC(g)	BMD(g/cm <sup>2</sup> )	T-	Z-
				score	score
L1	12.10	9.51	0.78	-1.3	-0.7
L2	14.16	12.44	0.87	-1.4	-0.7
L3	15.77	15.27	0.96	-1.1	-0.4
Total	42.03	37.22	0.88	-1.2	-0.6

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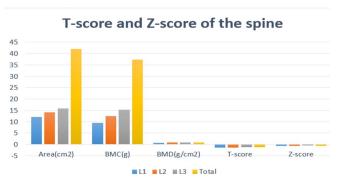


Fig 20. Bar graph representation of Table 4

Table 5. T-score and Z-score of the neck

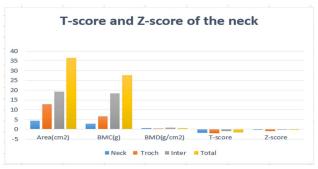


Fig 21. Bar graph representation of Table 5.

A Z-score [53] may also be used to represent how much an individual's BMD is beyond the norm for their age and gender. Clinical decision making and fracture risk assessment rely on these numbers. Long-term therapeutic follow-up may be monitored using Z-score. Regardless of the age of the patient, the Z-score is an effective tool for determining the root cause of osteoporosis. In postmenopausal women, a considerable increase in the risk of fracture is connected to every decline in bone density that is equal to or more than one standard deviation (SD), as shown by prospective studies.

Table 5. Indian Reference Data

	Reference Data				
No.	Term	Frequency	Percent%		
1.	Normal	149	68.7		
2.	Osteopenia	52	23.5		
3	Osteoporosis	16	7.8		
	Total	217	100.0		

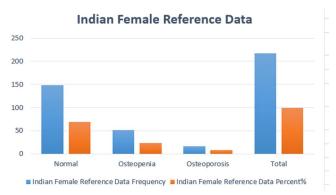


Fig 22. Bar graph representation of Table 6.



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#### V. CONCLUSION

Osteoporosis is a very lethal disease. In most countries, osteoporosis diagnosis is still mostly unknown due to issues such as the absence of a reference database and the high cost of scan equipment. DEXA is a respectable technique; however, it has its own limitations. Interpretation of the results of an evaluation performed using dual-energy X-ray absorptiometry may at times be challenging. Scanning the spine of someone with osteoarthritis might be difficult because of the condition's subtlety. Because of this, anomalies or prior spine fractures may produce false positives. You will not learn the root of poor bone density with a DEXA scan. After a brief recap, new studies on determining BMD, T-score, and Z-score from DEXA images using image processing techniques may be conducted [4,5,80]. Using image processing methods on digital X-ray pictures, bone density may be measured and the T-score determined. A new technique based on the concepts of deep learning may be offered to quantitatively assess BMD values in X-ray pictures as a potential way to contribute further to the process of diagnosing osteoporosis. In order to advise the people of developing countries on accessible, low-cost, and reliable BMD measurement equipment. An increase in knowledge about the illness, the implementation of prevention measures, and the broad use of accessible, efficient technologies are likely to lead to future advances in the treatment of this ailment.

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