

Bone Density versus Bone Quality as a Predictor of Bone Strength



Jindal M^{1*}, Lakhwani OP², Kaur Omkar³, Agarwal S² and Garg Keerty

¹Department of Orthopaedics, Kalpana Chawla Govt Medical College, India

²Department of Orthopaedics, ESI – PGIMSR, India

³Department of Pathology, ESI – PGIMSR, India

⁴Department of Anaesthesia, Guru Nanak Medical College, India

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***Corresponding author:** Mohit Jindal, Assistant Professor, Department of Orthopaedics, Kalpana Chawla Govt Medical College, Tel: +91 9891904545; Email: mohitjindal2006@gmail.com

Abstract

Introduction: Bone mineral density (BMD) is considered to be the standard method to evaluate bone strength and stratify risk of fracture Kanis et al. [1,2]. However, while easy to administer, the limitation of relying on BMD measurements is that they are uniplanar measurements in terms that the three-dimensional structure of bone is reduced to two dimensions and then the BMD values are computed. Also BMD measures only the mineral component of bone and does not give any information regarding its microstructure. Materials engineering has demonstrated that all the material properties including mechanical properties are a function of material microstructure understood as spatial properties and arrangement of constituent basic structural elements; in the case of bone these being the trabeculae. Thus the evaluation of bone microstructure plays important role in defining material properties of bone including the bone Strength.

Materials and Methods: In this study we have used cubical bone specimens obtained from patients undergoing hip replacement procedures and compared their BMD values with those obtained using static Histomorphometry (Trabecular No., Trabecular Separation, Trabecular Thickness and Bone Volume) to their axial compression strength (using Yield point at failure measured in Megapascals).

Results: We found a better correlation was found between microstructural parameters and Bone strength {Bone Volume (Spearman correlation 0.9652), Trabecular Number (Spearman correlation 0.7646), Trabecular Separation (Spearman correlation 0.7541) Trabecular Thickness (Spearman correlation 0.6726)} as compared to BMD and Bone strength (Spearman correlation 0.3746).

Discussion and Conclusion: While using Bone Mineral Density (BMD) as a sole predictor of bone strength, Bone Quality (microstructural indices) also needs to be considered. Bone Quality appears to be a better predictor of bone strength as compared to Bone density. However Histomorphometric Bone Quality parameters will require invasive procedures and no other in vivo imaging modality has been available to quantitatively measure Bone Microstructure. Bone Density measurement on the contrary is still a rather more available in vivo imaging modality to determine bone strength and still finds its place as a surrogate marker of Bone strength. There is a need of development of newer noninvasive in vivo imaging methods (microstructural computerized tomography) that assess bone strength independent of BMD and utilize measures for Bone Quality and these methods should improve the assessment of fracture risk and response to treatment.

Keywords: Histomorphometry; Bone Quality; Bone Density; BMD

Introduction

Bone mineral density (BMD) is considered to be the standard method to evaluate bone strength and stratify risk of fracture Kanis et al. [1,2]. However, while easy to administer, the limitation of relying on BMD measurements is that BMD measures only the mineral component of bone and does not give any information regarding its microstructure. Furthermore, studies have shown that higher BMD measurements do not directly translate to mechanical properties of bone and fracture risk. Schuit SC, van der Klift M, Weel AE, de Laet CE, Burger H et al. [3] evaluated the fracture incidence and association with bone mineral density in elderly men and women and found

that only 34% women and 21% men with non vertebral fracture had BMD in osteoporotic range.

Stacey A Wainwright [4] also in their study only half of elderly women with incidental hip fracture had Bone Mineral Density in osteoporotic range at base line. This single BMD value, while easy for means of comparison between individuals, may not provide sufficient evaluation of bone trabecular architecture. Hence additional data is needed for predicting bone strength. Our study aims at assessing BMD Versus Histomorphometry so as to assess a better predictor of Bone Strength and hence propensity to fracture.

Materials and Methods

The structural and mechanical characteristics of Bone have been extensively studied to understand the functional adaptations associated with the properties of biological material. It is known that morphology varies between bones and even within a bone Pugh et al. [5], Raux, et al. [6], Williams & Lewis [7], Whitehouse et al. [8] as do the mechanical properties Brown & Ferguson [9], Ciarelli et al. [10]. While measures of apparent density used as an estimate of mechanical properties does not

explain all the variance nor does it account for the structural organization of the trabecular bone, thus rendering this scalar measure inadequate for predicting the material properties Goldstein [11]. Materials engineering has demonstrated that all the material properties including mechanical properties are a function of material microstructure understood as spatial properties and arrangement of constituent basic structural elements, in the case of bone these being the trabeculae. Thus the evaluation of bone microstructure plays important role in defining material properties of bone including the bone Strength.



Figure 1: Deep freezers.



Figure 2: 40X image for calculation of Bone Volume in the same sample.

The relationship between trabecular micro-architectural pattern and bone strength has long been proposed. The importance of trabecular arrangement in bone and their significance in bone strength was first observed by Hermann Von Meyer an anatomist and Karl Culmann an engineer (1860). This arrangement of trabeculae ensures the maximum strength with the available bone material. Julius Wolff also based his theory on the similarity of trabecular pattern and maximum stress which formed the main idea in Wolff's law. Currently, micro-architecture of trabeculae can be measured by several histomorphological parameters like the number of trabeculae defined in a given volume (Tb.N), their mean thickness (Tb.Th), their average separation distance (Tb.Sp) and their three-dimensional volume (BV/TV). Histomorphometric evaluation of these microstructural indices has the potential of giving a better estimate of actual bone strength than BMD values Parfitt et al. [12]. Availability of the material to be used for simultaneously measuring the BMD and histomorphometric characteristics and its correlation with mechanical bone strength is a big challenge. Allogenic bone graft procured and processed from bone bank can serve as the substrate for this purpose. Hence this in vitro study is being undertaken using the retrieved femoral heads from living donors processed in bone bank (deep freezing and gamma irradiation) as a substrate to compare the bone mineral

density (measured by dual energy x ray absorptiometry) and bone quality indices (measured using histomorphometry) as a better indicator of bone strength (Figures 1 & 2)..

In this Experimental in vitro study carried in 2012 -2014, femoral heads retrieved during surgical hip replacement procedures were made devoid of all soft tissue and cartilage and cut into equal cubical pieces. Exclusion criteria included femoral Head involved in - infection, Paget's disease, Rheumatoid arthritis, osteoarthritis, neoplastic conditions, pathological fractures and other pathological conditions which were non representative of general population. Each piece was subjected to DEXA Scan, Compression tests and Histomorphometric analysis.

Bone Mineral Density

Areal Bone Mineral Density was measured using the dual energy x ray absorptiometry (DEXA) scan and analyzed.

Biomechanical Compression Testing

Each piece of the bone sample was tested for failure in Compression tests using (model 4482, Instron Corporation) at a constant unilateral deformation rate 0.5 mm/sec. The resultant deformation curve was analysed and yield point calculated (Figures 3-5).

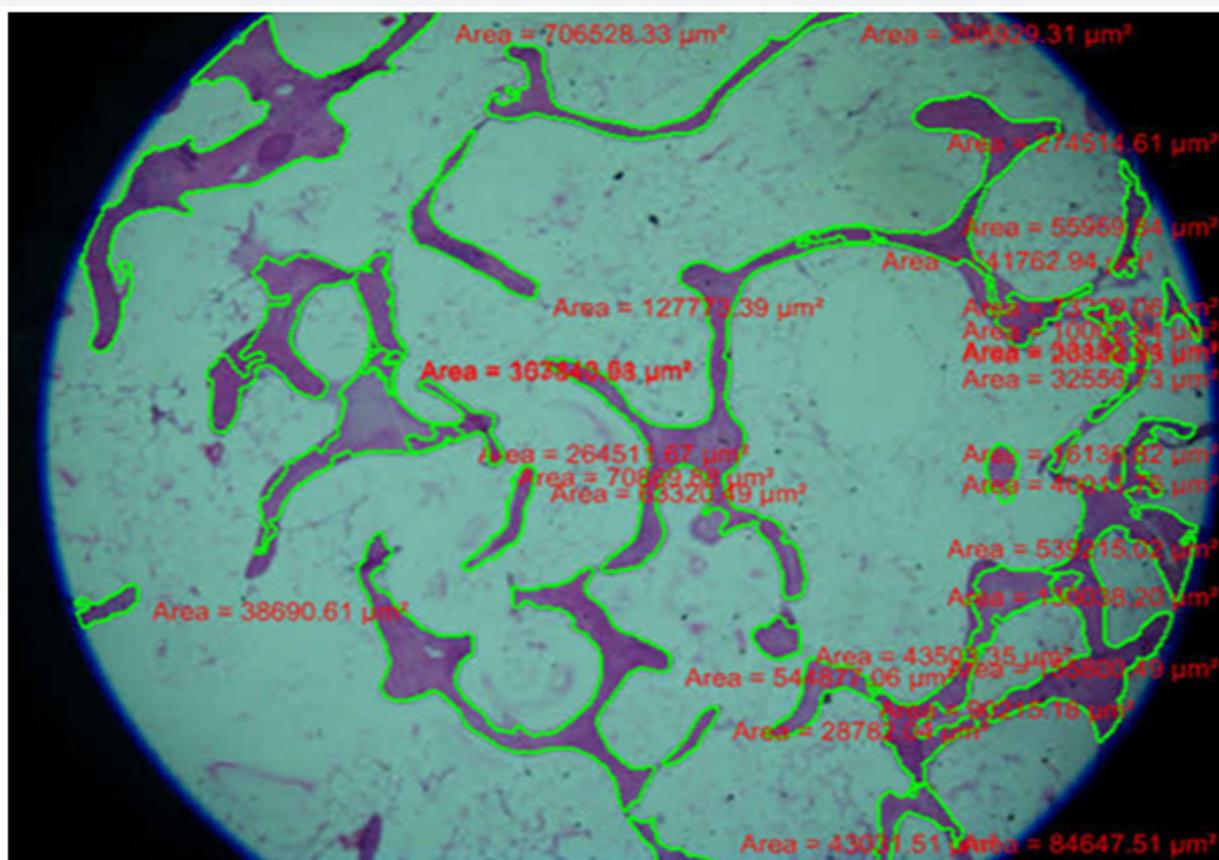


Figure 3: 40X microscopic image for calculation of Trabecular No. in the same sample Trabecular number was calculated and found to be 74 in number.

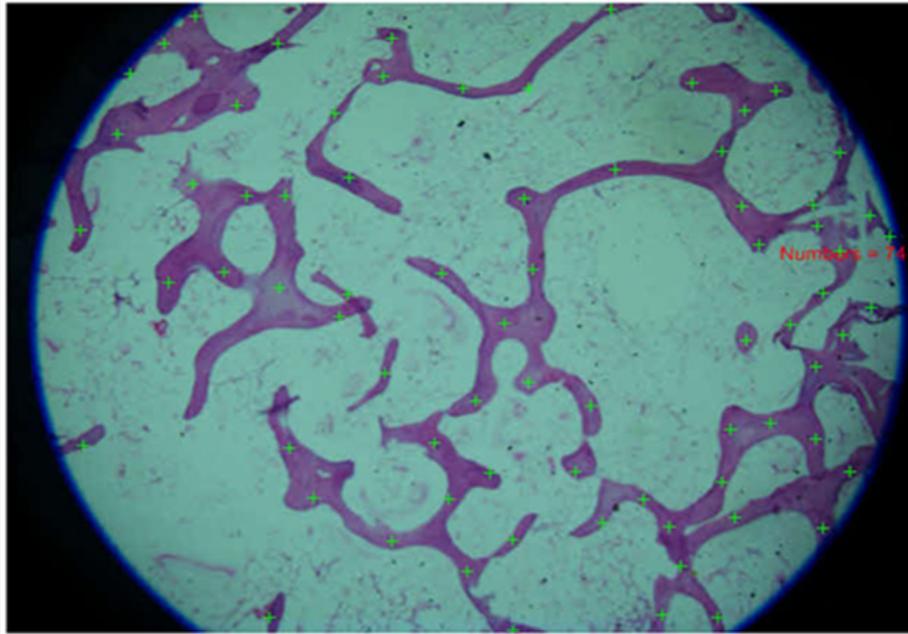


Figure 4: Picture shows 40X microscopic image for calculation of Trabecular Thickness in the same sample. Mean Trabecular Thickness was calculated and found to be 161.03µm.

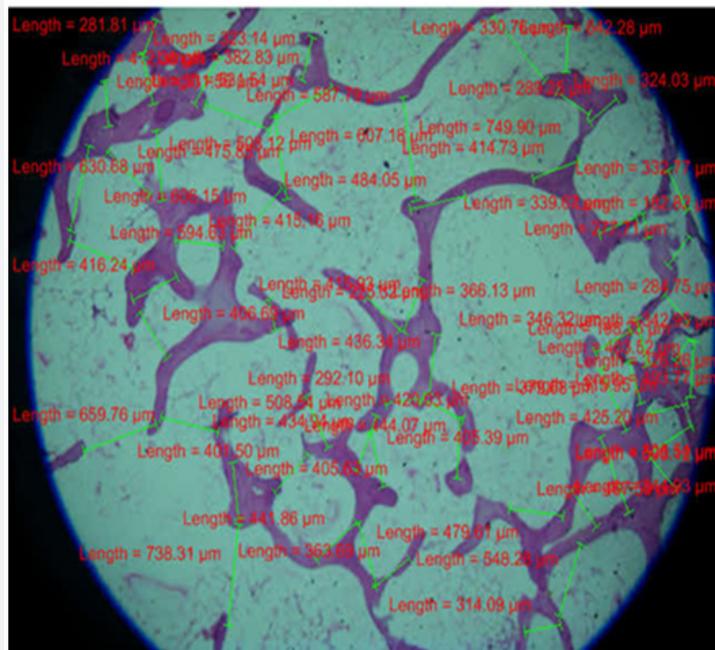


Figure 5: Picture shows 40X microscopic image for calculation of Trabecular Separation in the same sample. Mean Trabecular separation was calculated and found to be 423 µm.

Histomorphometric Analysis

Bone histomorphometry is a quantitative histological examination of bone to access micro structure and predict the biomechanical strength. Preparation The Cancellous bone graft material decalcified using 5% Nitric acid for a period of 10 days

(solution changed every 2 days) then dehydrated in ascending grades of alcohol, cleared in xylene and embedded in paraffin. Paraffin sections of 5 micrometre cut using microtome and stained with Hematoxylin & Eosin. The image was processed using NIKON based computerized softwares [40X Magnification] and histomorphometric parameters calculated (Figures 6 & 7).

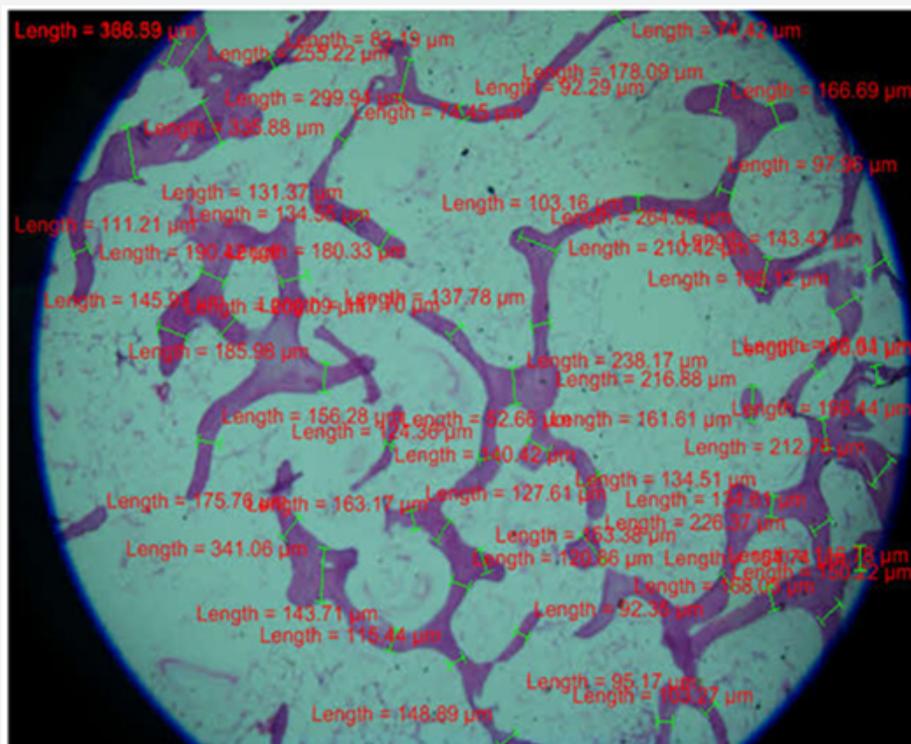


Figure 6: Picture shows the compression test being carried on the cubical bone specimen using instron 4482 at a compression rate of 0.5 mm/min.



Figure 7: Bone specimens on a computer screen for BMD assessment.

Parameter undertaken to analyze the structure include

- i. Bone volume (Trabecular bone volume/Tissue volume) - Represents the area occupied by the trabeculae Vs the total area of the field. Trabecular bone volume (volume of total cancellous bone) measured and expressed as percentage.
- ii. Trabecular number - number of trabeculae per unit

area. In this study single high power is taken as unit area.

- iii. Trabecular Thickness – mean trabecular thickness is measured and analysed.
- iv. Trabecular separation –mean of average distance between the two trabeculae is measured and analysed.

Results

Bmd as A Measure Of Bone Strength

BMD of all calculated bone samples are compared to their corresponding compression strength at Yield Point

On comparison the spearman first rank correlation coefficient was 0.3746 corresponding to a p value of 0.0172(<0.05) indicating that a significant positive correlation is present between BMD and compression strength of cancellous bone (Figure 8).

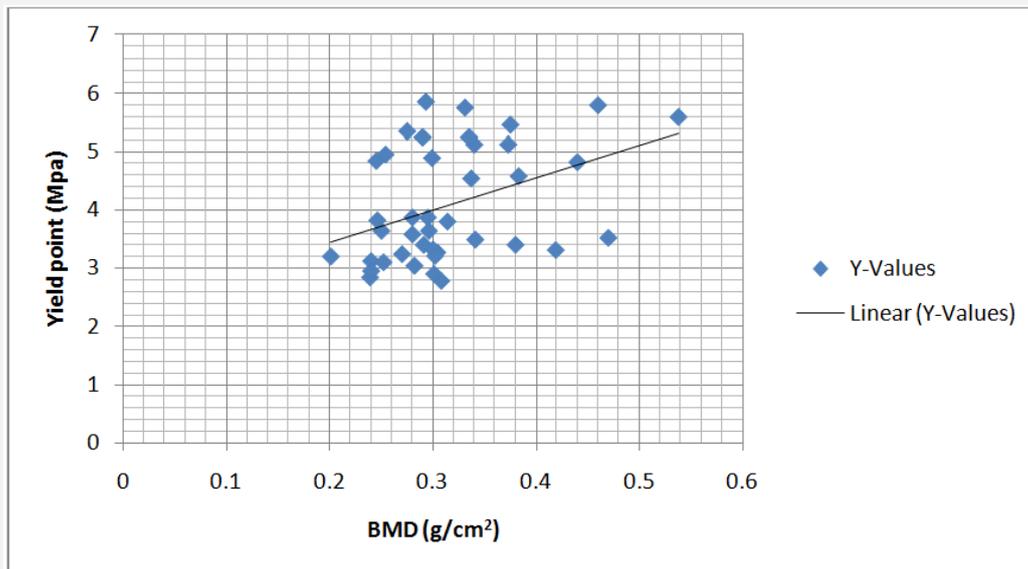


Figure 8: Scatter diagram showing correlation between BMD on y axis and Bone Strength as measured by compression strength at Yield Point on x axis.

Microstructural Parameters as a Measure of Bone Strength

Trabecular number(Tb.N) versus Compression strength

Analysis was done between all measured values of Trabecular Number and compared to their corresponding compression

strength measured through their corresponding yield point. On performing statistical tests, Spearman first rank correlation coefficient was 0.7646 which was found statistically significant. A scatter diagram depicting the correlation is hereby drawn (Figure 9).

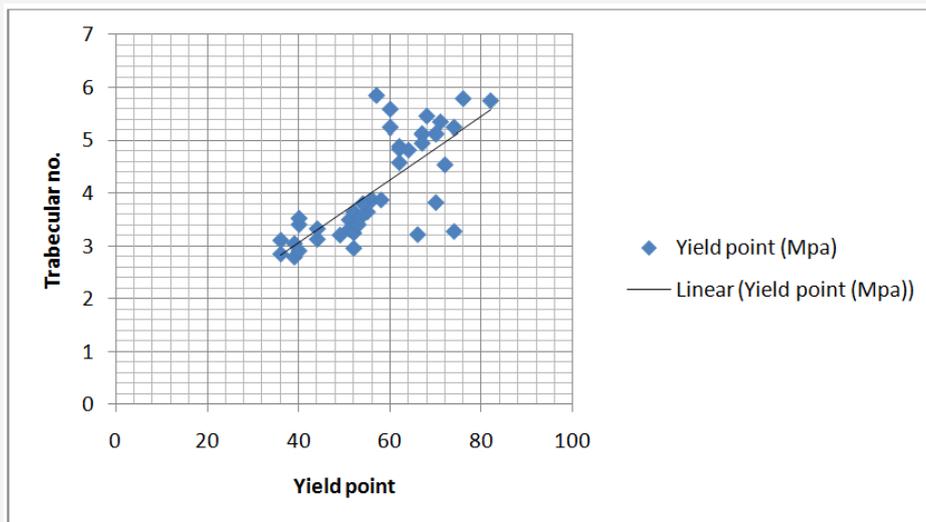


Figure 9: Scatter diagram depicting the positive correlation between the measured values of Trabecular Number on y axis versus compression strength measured through their corresponding yield Point on x axis. As seen from the diagram the values are roughly matching with the central line and so have been found statistically significant on correlation analysis implying the relevance using Trabecular no. as a marker of bone strength.

Trabecular Thickness versus Bone strength

Analysis was done between all measured values of Trabecular Thickness and compared to their corresponding measured through their corresponding yield point obtained.

On performing statistical tests, Spearman first rank correlation coefficient was 0.6726 which was found statistically significant. A scatter diagram depicting the correlation is hereby drawn (Figure 10).

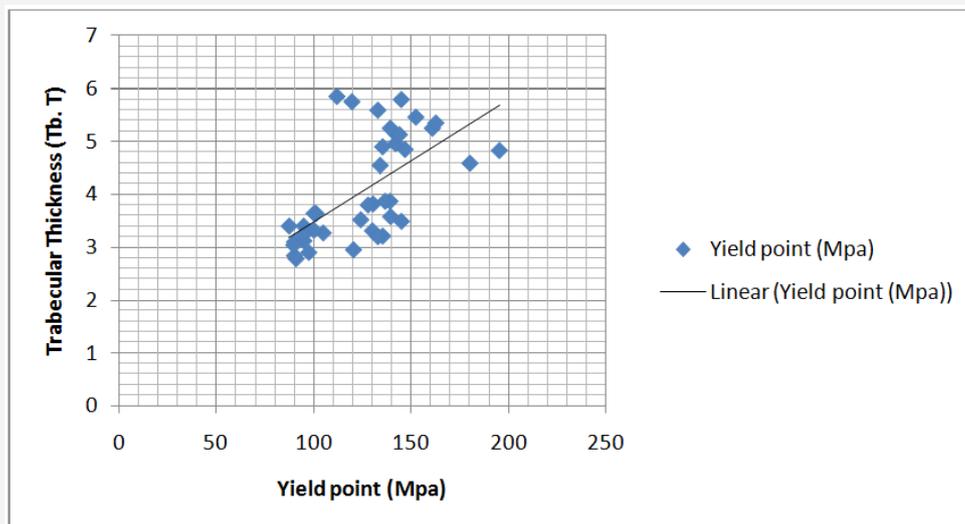


Figure 10: Scatter diagram depicting the positive correlation between the measured values of Trabecular Thickness on y axis versus compression strength measured through their corresponding yield point on x axis. As seen from the diagram the values are roughly matching with the central line and so have been found statistically significant on correlation analysis implying the relevance using Trabecular Thickness as a marker of bone strength.

Trabecular separation Vs Bone strength

Analysis was done between all measured values of Trabecular Separation and compared to their corresponding compression strength measured through their corresponding yield point

obtained. On performing statistical tests, Spearman first rank correlation coefficient was 0.7541 which was found statistically very significant. A scatter diagram depicting the correlation is hereby drawn (Figure 11).

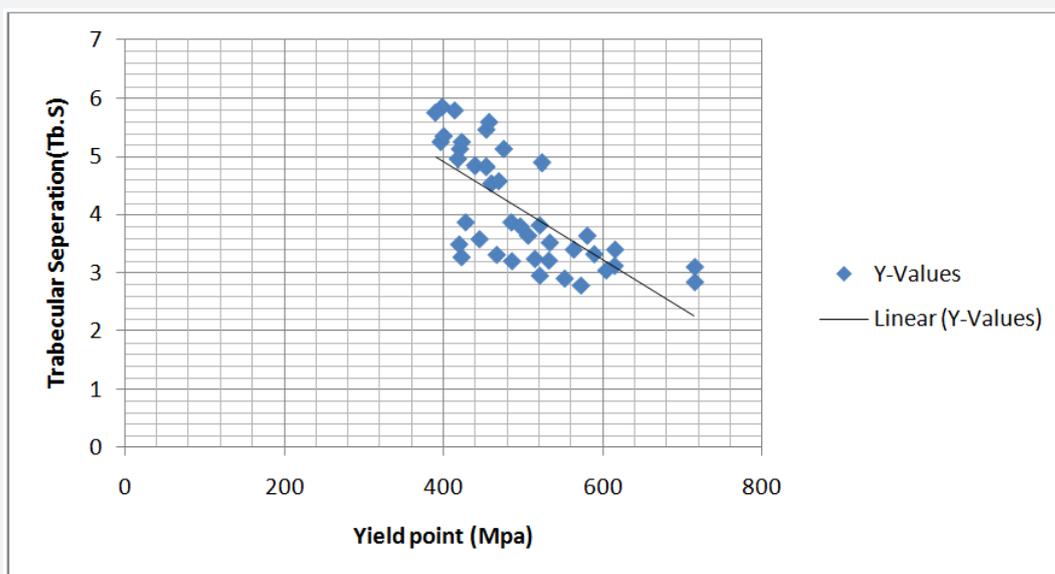


Figure 11: Scatter diagram depicting the negative correlation between the measured values of Trabecular Separation on y axis versus compression strength measured through their corresponding yield point on x axis. As seen from the diagram the values are roughly matching with the central line and so have been found statistically significant on correlation analysis implying the relevance using Trabecular Separation as a marker of bone strength.

Bone Volume versus Bone strength

Analysis was done between all measured values of Bone Volume and compared to their corresponding compression strength measured through their corresponding yield point

obtained. On performing statistical tests, Spearman first rank correlation coefficient was 0.9652 which was found statistically very significant. A scatter diagram depicting the correlation is hereby drawn (Figure 12).

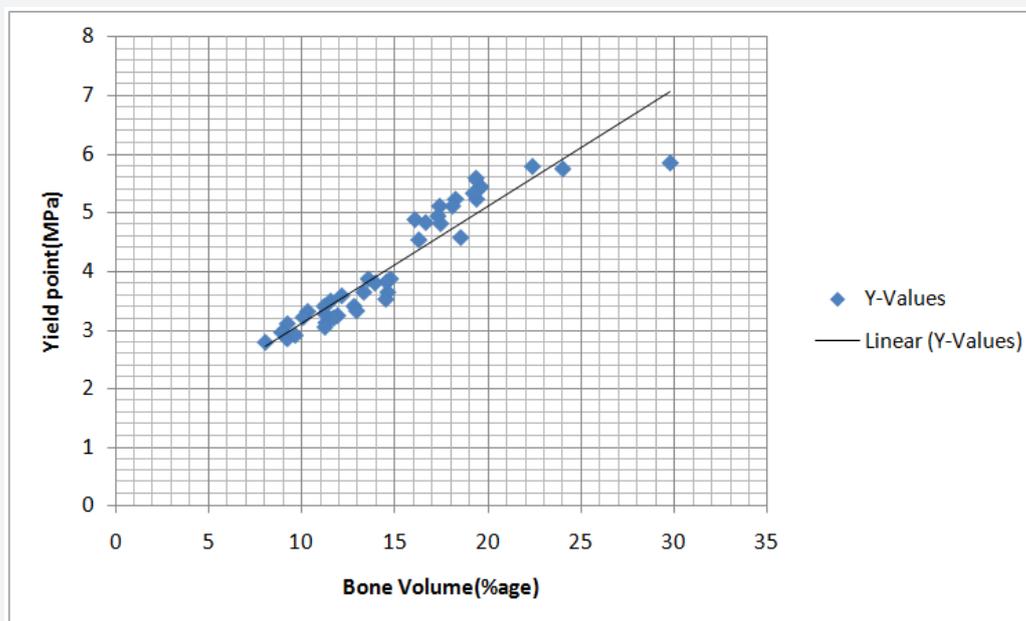


Figure 12: Scatter diagram 5 depicts the positive correlation between the measured values of Bone Volume on y axis versus compression strength measured through their corresponding yield point on x axis. As seen from the diagram the values are roughly matching with the central line and so have been found statistically significant on correlation analysis implying the relevance using Bone Volume as a marker of bone strength.

Discussion

Osteoporosis is characterized by increased skeletal fragility as a result of reduced bone strength. The most severe consequences include bone fractures from unexpected and sudden increased in load (e.g. in accidents) which the bone is not usually accustomed to. The condition in osteoporosis where bone strength is compromised results from the imbalance where bone formation rate is reduced compared to resorption. For every 10% loss of bone mass, the fracture risk doubles. Osteoporosis is becoming a major health concern with the rapidly graying population in many countries. Bone fractures from falls and accidents could result in major costs in hospitalizations and surgery, especially for the elderly where the chances of complete recovery is low and permanent disability is likely.

Measures of Bone Strength

Bone Mineral Density (BMD) measured by Dual Energy X-ray Absorptiometry (DXA), has been traditionally used for the diagnosis of osteoporosis and thereby Bone Strength. However, recent research is indicating that the DXA test is not as reliable a measure of bone strength as originally thought. In fact, several studies have shown that many fractures occur in people with only moderately decreased Bone Mineral Density Wainwright

et al. [4] Further, half of all postmenopausal fractures occur in women with Bone Mineral Density test results that indicate that their bone density levels are not low enough for them to be categorized as having osteoporosis Schuit et al. [13]. Quality of bone structure is more important than the density when determining the bone strength. The BMD measured by DXA does not provide information on the bone quality and it does not provide any insight into the architectural structure of bones.

Bone Quality

Bone quality is defined as the sum of the structural and material properties of the trabecular bone. The structural properties of bone refer to the trabecular microstructure. Trabecular or cancellous bone is made up of many interconnected trabeculae which may be composed of narrow rod like trabeculae or the flatter plate-like trabeculae. The more of the thicker plate-like trabeculae present in the structure as compared to the thinner, rod-like trabeculae, the better the quality and strength of the bone. Now, bone quality is measured by various microstructural indices i.e. Trabecular number, Trabecular Separation, Trabecular Thickness and Bone volume which are measurable by Histomorphometry Parfitt et al. [14], Mc Donnell et al. [15], Manal H Moussa et al. [16], Charles S Haworth [17].

In this study BMD and Microarchitectural indices of Bone quality were used as measures of bone strength (Table 1). A significant correlation was found between bone strength and microstructural indices of bone quality. Although BMD measurements were also found to be significantly associated with Bone strength, the measure of its significance was much less when compared to Bone Quality indices. Among the Bone Quality indices, Bone volume was the most significantly associated with Bone strength followed by Trabecular Number.

The order of significance was; Bone Volume (Spearman correlation 0.9652)>Trabecular Number(Spearman correlation 0.7646)> Trabecular Separation (Spearman correlation 0.7541)>Trabecular Thickness (Spearman correlation 0.6726)>>BMD(Spearman correlation 0.3746) As expected, microstructural parameters i.e. Bone Quality were found to be more correlated with Bone Strength as compared to Bone Density measurements.

Table 1: Observation Table.

S.No.	BMD Measurements	Histomorphometric Analysis				Compression Testing
	(g/cm ²)	Tb.N.	Tb.T (µm)	Tb.S (µm)	B.V. (%)	Yield points at failure (Mpa)
1	0.293	57	112	399.06	29.76	5.84
2	0.291	40	95	615.29	12.8	3.4
3	0.34	67	142.66	421.23	17.39	5.12
4	0.308	39	91.06	572.56	8.04	2.78
5	0.375	68	152.55	454.22	19.61	5.45
6	0.299	62	135.46	523.91	16.07	4.89
7	0.335	74	161.03	423.55	18.24	5.24
8	0.341	51	145.12	420.27	11.54	3.49
9	0.538	60	133.06	457.69	19.34	5.58
10	0.295	56	139.25	428.34	14.75	3.87
11	0.296	55	101.31	506.49	14.61	3.64
12	0.419	51	130.26	467.27	10.31	3.31
13	0.47	40	124.24	533.59	14.5	3.52
14	0.245	62	146.94	440	16.64	4.84
15	0.46	76	145.04	414.72	22.37	5.78
16	0.24	44	95	614.67	11.3	3.12
17	0.44	64	195.44	454	17.44	4.82
18	0.29	60	139.44	397.06	19.37	5.24
19	0.275	71	162.79	400.91	19.2	5.34
20	0.254	67	142.09	418.66	17.3	4.95
21	0.304	74	105	423.25	11.24	3.27
22	0.3	44	100.2	589.25	12.94	3.32
23	0.246	70	130.56	521.05	14.54	3.82
24	0.239	36	90.22	715	9.22	2.84
25	0.373	70	144.13	476	18.08	5.12
26	0.27	52	95.01	515.02	11.92	3.24
27	0.25	52	100.31	580.37	13.32	3.64
28	0.28	54	139.58	445.67	12.14	3.58
29	0.337	72	134.24	460.44	16.27	4.54

30	0.28	58	136.74	485.56	13.56	3.87
31	0.252	36	90.22	715	9.22	3.1
32	0.302	66	135.52	532.39	10.07	3.21
33	0.38	53	87.53	563.57	11.2	3.4
34	0.24	52	120.53	521.07	8.92	2.95
35	0.331	82	119.71	390.36	24	5.74
36	0.282	39	89.84	604.25	11.24	3.04
37	0.383	62	180.25	469.74	18.52	4.58
38	0.314	54	128	496.76	13.92	3.8
39	0.301	40	97.6	552.23	9.64	2.9
40	0.201	49	133.04	486.31	11.71	3.2

Conclusion

In our study while comparing the Bone Strength with Bone Mineral Density and Histomorphometric parameters, a better correlation was found between microstructural parameters and Bone strength {Bone Volume (Spearman correlation 0.9652), Trabecular Number (Spearman correlation 0.7646), Trabecular Separation (Spearman correlation 0.7541) Trabecular Thickness (Spearman correlation 0.6726)} as compared to BMD and Bone strength (Spearman correlation 0.3746). While using Bone Mineral Density (BMD) as a sole predictor of bone strength, Bone Quality (microstructural indices) also needs to be considered. Bone Quality appears to be a better predictor of bone strength as compared to Bone density. However Histomorphometric Bone Quality parameters will require invasive procedures and no other in vivo imaging modality has been available to quantitatively measure Bone Microstructure. Bone Density measurement on the contrary is still a rather more available in vivo imaging modality to determine bone strength and still finds its place as a surrogate marker of Bone strength. There is a need of development of newer noninvasive in vivo imaging methods (microstructural computerized tomography) that assess bone strength independent of BMD and utilize measures for Bone Quality and these methods should improve the assessment of fracture risk and response to treatment.

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