BONE MICROARCHITECTURE: AN ALTERNATE APPROACH FOR FRACTURE RISK ESTIMATION

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Abstract

The indication of Osteoporosis includes both, the reduction in bone mineral mass and the consequent change in bone microarchitecture. The weakness of bones due to degradation of trabecular microarchitecture is the major result of osteoporosis and vertebral fracture. Investigating microarchitecture of the bone is the key to predicting fracture risk in osteoporosis at an earlier stage. A significant amount of literature has been published indicating that the microarchitecture of bone is correlated to bone texture appearing in an X-ray. The understanding and classification of the bone texture should help to estimate bone fracture risk. This will also help to diagnose Osteoporosis at an earlier stage through plain X-rays, which is currently been done through expensive Dual-energy X-ray absorptiometry (DXA, previously DEXA) scans. This is especially helpful in developing countries like in the sub-continent, which are densely populated with relatively higher proportion of population being susceptible to Osteoporosis.

Introduction

Currently around 50% of worldwide elderly population is affected by osteoporosis (Wita, 1995). The disability due to Osteoporosis has become a major problem especially in developing countries. This epidemic (Kanis *et al*., 1994; Khuwaja *et al*., 2005) disease affected 8.9 million people per year worldwide. In Pakistan, there are 9.91 million people (7.19 females) suffering from osteoporosis (Shaikh *et al*., 2013) and this figure is projected to increase to 11.3 million by 2020 (Mithal, 2009). Osteoporosis is a pathological condition of the bone wherein the density of the bone minerals is decreased significantly. The condition is characterized by decrease in the strength and function of the bone. As a result the interior of a bone becomes abnormally porous, just like a sponge, and is liable to fracture under minor stress. The World Health Organization (WHO) defined Osteoporosis as "faulty and weakened bone structure due to the low bone mineral content per unit volume" (WHO, 2011). Low BMD in elderly people can be prevalent, as BMD is associated with age (primary Osteoporosis), but the socio-economic, race, ethnic factors and lack of awareness are among other causes of secondary osteoporosis worldwide. In Pakistan, 40 million people have osteopenia (Mithal, 2009), a precursor to Osteoporosis, in which the patient has a BMD lower than average BMD of the population. A large number of these young Osteopenic patient might become Osteoporotic in future (Fatima *et al*., 2009; Mamji *et al*., 2010) if preventive measures are not been taken.

The Dual-Energy X-ray Absorptiometry (DEXA) is declared gold standard (Kanis, 2002) to diagnose Osteoporosis. Bone mineral content is directly measured by DEXA, and represents in T-score and Z-score (The Joint Commission, 2008), at skeletal site such as the lumber spine, hip and/or 1/3 rd of the distal-radius (Kanis, 1994). Patient's BMD T-score and Z-Scores are based on comparison to the young population standard and to an age and gender matched healthy population (Yung *et al*., 2012) respectively. Hence, the patient is assessed on their BMD referenced to typical population values. The problem that exists in Pakistan is the expense of DEXA scans in tandem with their availability. As of 2010 only 16 DEXA scanners were available nationwide (Kalra, 2013). Osteoporosis is very common, and a large percentage of the population cannot afford the DEXA scan. In addition, the reference values are compared to age-matched population of the same kind, that is, Pakistani patient T-score and Z-score values must be compared to similar population (Pakistani/South Asian) reference values, to ensure the accurate diagnosis. Currently, in South Asia no local population based BMD reference values exist (Ho-Pham *et al*., 2011), the DEXA supplier uses BMD reference values which are not obtained from South Asian population. This could lead to an erroneous diagnosis and effect the subsequent prevention actions. Hence, there is a need to develop a reference population values for South Asia to obtain a like for like assessment, and subsequently the correct medication.

The criteria defined by WHO to categorize T-score for diagnosing Osteoporosis (Kanis, 1994) is based on American population (Table 1). Based on the above discussion the BMD values of South Asian population

cannot be compared to American population (Roy *et al*., 2005) due to factors like body composition, life style, nutrition, and race (Alekel *et al*., 2002; Carey *et al*., 2007). It has also proven by literature that the peak BMD of Asian, Black and White population are different (Cromer *et al*., 2004; Malhotra and Mithal, 2008; Raffat *et al*., 2015; Shakil *et al*., 2010). Researchers should focus to develop local population based reference values.

Table 1: T-score reference values defined by WHO.

Diagnosis	**T-score Relative to Bone Mineral Density**
Normal	BMD value with in 1 SD, (T-score ≥ -1)
Osteopenia	BMD value more than 1 SD below the mean & less than 2 SD below the mean, (-1 > T-score > -2.5)
Osteoporosis	BMD value 2.5 SD or more below the mean, (T-score ≤ -2.5)
Severe Osteoporosis	BMD value 2.5 SD or more below the mean with fragility fracture, (T-score ≤ -2.5)

The above discussion pertained to the use of BMD values as indicative of Osteoporosis. But this is only part of the story. The bone strength does not only depend on BMD (Benhamou *et al*., 2001; Cortet *et al*., 2002) but

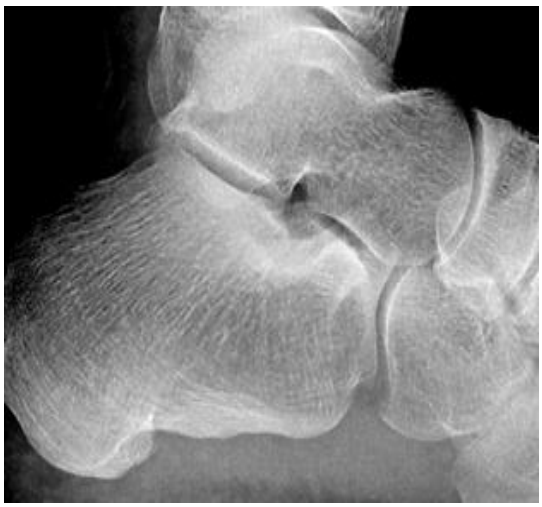

Fig. 1. Radiographic Appearance of Trabecular Bone.

also on microarchitecture of the bone that is trabeculae of bone. The gold standard DEXA scan provides no information of the quality of the microarchitecture structure. The trabeculae gives the texture appearing in X-ray images (Fig. 1), which can be useful to predict Osteoporosis (Lespessailles *et al*., 2007) at an earlier stage. The X-ray provides 2D projection of trabecular microarchitecture that can help to investigate the variation of actual microarchitecture of bone.

The texture features extracted from X-rays are reflective of trabecular bone structure. Common texture features can be used to correlate fracture risk along with BMD. Although, the relation between texture in X-ray image and trabecular architecture is significantly correlated, but this has been largely neglected until recently as researchers worldwide focus on BMD to diagnose Osteoporosis. Many Osteoporosis predicting tools do not require BMD value as an input (Adler *et al*., 2003; Cadarette *et al*., 2000; Lydick *et al*., 1998; Lynn *et al*., 2008; Sedrine *et al*., 2002; Shepherd *et al*., 2007), to the extent that even the renowned FRAX (Ettinger *et al*., 2010; Kanis *et al*., 2008) tool which is in use by doctors worldwide makes BMD an optional input. The correlation between fracture risk estimation and X-ray texture analysis of trabeculae are discussed in the following literature review.

Conventional X-ray Based Diagnosis: The state-of-the-art is the use of DEXA machines to determine bone mineral density to diagnose the extent of Osteoporosis. This is a routine activity in countries where DEXA machines are part of most hospitals. In the absence of DEXA machines, Osteoporosis is currently diagnosed with the help of X-Rays using the following techniques.

Singh index is one of the parameters in the X-ray measurement of Osteoporosis. Evaluation of Singh index is studied as a simple means for estimating bone mass on X-ray of the bones suspected of Osteoporosis. It has much to do with the trabeculae patterns seen in X-ray imaging of the bones.

According to orthopedics, no apparent change in the X-ray is visible until there is a loss of about 40% of bone. The femoral neck has most apparent trabecular pattern in X-ray, which is parallel along the compression and stress lines caused by weight bearing in a healthy person (Jhamaria et al., 1983). Osteoporosis causes these patterns of trabeculae in femur neck to change. A typical Singh index (Singh *et al*., 1970) describes the patterns of trabeculae in the bone at the top of the femur. The X-ray is graded into six steps according to visibility of the normal pattern of trabeculae (Fig. 2).

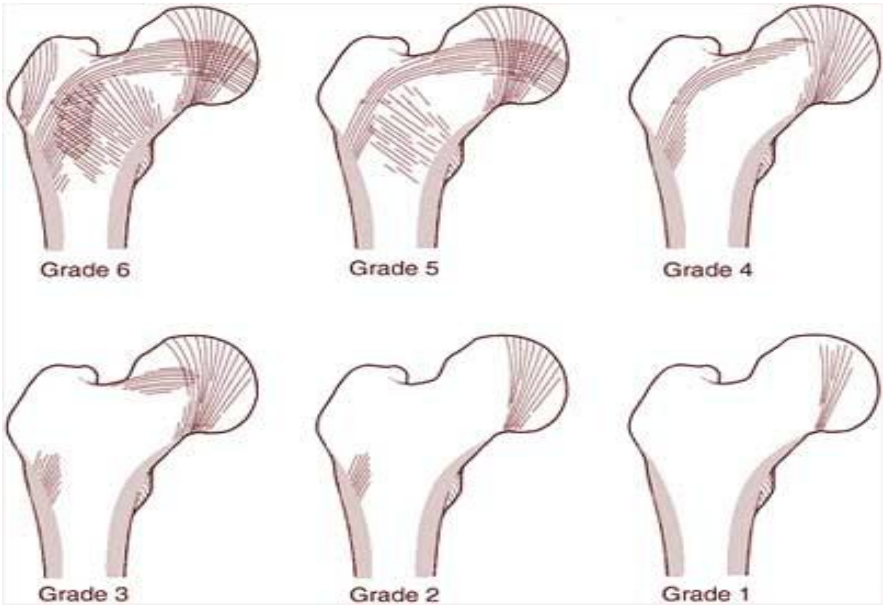

Fig. 2. Trabecular Pattern in Femur Neck Visible in X-ray (Singh *et al* ., 1970).

- Grade 1: The principal compressive trabeculae is reduced in number (severe Osteoporotic patient)
- Grade 2: The principal compressive trabeculae are seen prominently.
- Grade 3: Several things are observed. There is a break in the continuity of the bone tensile.
- Grade 4: The principal tensile trabeculae or trabeculae are visibly reduced but can be traceable between the lateral Cortex and the upper portion of the Femur Neck.
- Grade 5: The principal tensile trabeculae or trabeculae is accentuated.
- Grade 6: All trabecular pattern groups are visible on the x-ray image (healthy person).

The commonly used parameters of proximal Femur geometry as neck shaft angle (A), Femoral neck length (B), Femoral neck diameter (C), Femoral head diameter (D) and the width of cortical Femoral shaft (X-Y) can be seen (Fig. 3).

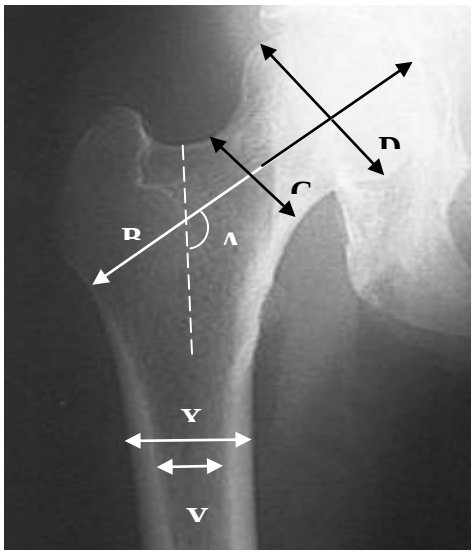

Fig. 3. Parameter of Femur Geometry.

According to orthopedics, fracture risk requires that, if (X-Y) ≤ Y/4, the bone is deemed to be heavily Osteoporotic (Fig. 3). However, by this stage, it is too late to prescribe any medication that will cure the disease, and the patient remains a high fracture risk candidate. Identification of Osteoporosis using this process can only be done when the disease is at its advanced stage, as the detection using the above formula is only visible after extensive Osteoporosis.

The BMD, trabeculae and X-rays are significantly correlated. Lee *et al*. (1994) has done a pioneering work which shows the existence of a correlation between BMD and X-rays texture. Study also statistically correlated BMD with Meunier index, Singh index and Calcaneal index. Veenland (1999) performed a comprehensive analysis of bone texture appearing in X-rays and established a strong correlation between bone texture and BMD. The finding also suggested that bone strength can be predicted with texture features, BMD, fracture stress and texture features as factors. Karunanithi *et al*. (2007) confirmed the findings of Veenland in his study, which based on right femoral neck BMD of 70 females (25 pre-menopause and 45 post menopause). They used power spectral density and Fourier transform to analyze X-rays of the subjects and found significant influence of age in BMD and trabecular appearance of bone in X-rays. Studies (Chappard *et al*., 2010; Rachidi *et al*., 2008) done recently also confirmed the correlation of texture features of bone with BMD independently of gender. According to Pitt *et al*. (2011) low BMD causes the presence of bone bars in X-rays, which shows the correlation of texture features and BMD (Kursunoglu *et al*., 1986). Maiti *et al*. (2011) used limited number of samples, about 10, but pursue the research of Pitt *et al*., and obtain similar correlations. Sapthagirivasan *et al*. (2011) proposed a model and diagnose Osteoporosis from texture features extracted from 50 X-ray samples using dual tree complex Wavelet transform. According to Benhamou *et al*. (2001), texture analysis can be used to assess bone microarchitecture, and in conjunction with BMD, can be used to predict Osteoporosis at an early stage. His study also showed that calcaneus X-ray texture analyzed by Fractal analysis can distinguish Osteoporotic fractured and control groups. Pramudito *et al*. (2007) used different texture features i.e. Gabor feature, Wavelet and Fractal dimension extracted from X-rays and correlated them with Singh index. Only 41 samples were used but the correlation was very high. Karabulut *et al*. (2010) also reported the significant correlation between Singh index and BMD on the basis of 47 females Osteoporotic subjects.

In the medical domain image analysis techniques have significant role, especially for diagnosing different diseases. The different images like X-rays, MRI, CT scan and others are used to diagnose diseases by extracting and analyzing different image features obtained through image processing techniques. Texture analysis algorithms are capable to give distinctive information from texture. It provides the exact location (pixels) where the information has changed. Since Benoit (1984) noticed the existence of Fractal nature of image textures, the Fractal analysis has been applied in different Field and played vital role in diseases diagnosis. The literature has shown significant results of texture analysis of X-rays by using different algorithms for diagnosing Osteoporosis. Significant results were obtained from X-rays by using Fractal analysis (Benhamou *et al*., 2001; Chappard *et al*., 2005; Fazzalari and Parkinson, 1998; Lespessailles *et al*., 2008; Lin *et al*., 1999; Mallard *et al*., 2013; Pothuaud *et al*., 1998; Pramudito *et al*., 2007), geometrical measurement of bone (Chappard *et al*., 2010; Glüer *et al*., 1995; Karabulut *et al*., 2010; Karlsson *et al*., 1996; Partanen *et al* ., 2001; Pulkkinen *et al* ., 2004, 2010, 2011) and Singh index (Karabulut *et al* ., 2010; Karlsson *et al* ., 1996; Pramudito *et al* ., 2007;). These studies show potential use of X-rays in diagnosing Osteoporosis at an earlier stage besides using DEXA scans which are expensive. Fracture risk of hip and proximal femoral geometry are significantly correlated. The commonly studied parameters of Femur are femoral neck length and diameter, neck shaft angle, Femur head diameter, cortical width and others (Figure-3).

Discussion

From the literature review above, use of texture analysis of bone microarchitecture as an additional factor, it would be expected that the fracture prediction would improve further. Incorporation of Artificial Intelligence techniques could also improve the fracture risk estimation by exploiting underlying non-linear relationship between texture features and fracture risk. The studies mentioned above emphatically suggest the presence of correlation between texture features, BMD and fracture risk. The review also indicates that whilst BMD is an indicator, it is not enough, as texture features provide an indication to the bone microarchitecture. Together, they would improve fracture risk estimation than each on its own.

Given that the gold standard still is BMD, none of the studies have attempted to provide a relationship between BMD and texture features, and how they relate to fracture risk, though they all allude to this. In a structural sense, there will be extensive bone mineral deterioration in which BMD alone will be sufficient. It is in this area, that texture features together with BMD values will be able to highlight increased fracture risk. This characterization can be modeled using Machine Learning techniques like Artificial Neural Networks (Shaikh *et al*., 2014), which are capable of understanding underlying relationships between variables.

Conclusion

The literature clearly shows that the texture and Fractal features extracted from X-Rays are reflective of the trabecular bone structure and correlate with fracture risk. It also suggests that texture and Fractal features can be used as part of a computational tool to assess the presence of Osteoporosis and fracture risk. It can be an economical, accurate and an alternate solution to diagnose Osteoporosis at an earlier stage.

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