CHAPTER 2

LITERATURE REVIEW

2.1 BONE STRENGTH ANALYSIS

Bone is heterogeneous, biomechanically complex and serves multiple functions (Wehrli et al 2003). Bone strength is a central predictor of fracture risk, and a better understanding of the factors influencing strength will lead to an improved diagnosis of osteoporosis and the ability to assess the efficacy of treatments of the disease. It is altered by changing the tissue material properties of the bone or the structural properties of the bone. Small increases in porosity lead to disproportionate large losses in bone strength (Kleerekoper 1985). Bone strength is determined by a large number of interrelated factors. The most common method of assessing bone strength is to estimate loss of bone mass by bone mineral density (Keaveny 2001).

BMD reflects the bone mineral content averaged across a specific region of interest. Bone mineral density increases in all regions during childhood and results in enlargement of bone (Marija 2012). Reduction in BMD is considered one of the major risk factors for a femoral fracture (Fardellone 2008, Marshall 1996). BMD is the most widely used and accepted means of diagnosing osteopenia and osteoporosis (Hernandez 2006). Furthermore, risk factors of a proximal femoral fracture may be associated with femoral geometry and BMD values (Dincel 2008). Several studies have shown that variations in femoral geometric measurements such as hip axis length (Faulkner 1993), neck shaft angle (Boonen 1998), and femoral neck width are also associated with increased risk of proximal femoral fractures (Gnudi 2004, Gnudi 2002). Also, BMD measurements across the femoral-neck region are analysed for healthy and patients with a femoral-neck fracture. The results showed that the femoral-neck angle was significantly smaller in all examined are as around femoral neck, especially in the ward's triangle. Under a same loading condition, the stress level may easily reach its intensity limit and therefore cause a fracture.

Dual-energy x-ray absorptiometry is the common approach to provide an effective measure of bone mineral density (Dalle & Giannini 2004). It has been proved that DEXA is a quick, accurate, low-cost imaging method for the diagnosis of osteoporosis. BMD measurements can be obtained from any site in the body, but the standard sites are the lumbar spine, the proximal femur, and the distal forearm (Brunader & Shelton 2002, Unnanuntana 2010). These values are used for measuring bone density and estimating osteoporotic fracture risk, monitoring osteoporosis progression and therapeutic interventions. According to world health organization criteria, the diagnosis of osteoporosis in postmenopausal Caucasian women is based on the BMD alone, measured with DEXA of the proximal femur or spine. A T-score (standard deviation compared with a healthy, young reference population) of less than −2.5 is defined as osteoporotic, whereas a T-score between −1 and −2.5 is defined as osteopenic.

Kurabayashi et al (2009) have examined the effectiveness of BMD measurement in puerperal women for identification of persistent osteopenia and osteoporosis using DEXA and it is concluded that puerperal BMD remains static over the subsequent 5–10 years. If the women have a low BMD at this stage of their reproductive life, it tends not to improve during this time. BMD measurement at the puerperium is very useful for identifying women at risk of poor bone health before menopause. Perhaps identification of this at-risk group may lead to effective interventions to reduce fracture risk in later life.

A study was designed by Miazgowskiet et al (2007) to characterize associations between BMD, DEXA based hip strength indices, metabolic control and type one diabetic men chronic complication. The results of this study indicate that in middle-aged type one diabetic men, lumbar spine BMD is decreased and femur BMD is normal, when compared with healthy men, matched for age, weight, and height. Blake and Fogelman (2007) have reviewed the role of DEXA in the diagnosis and treatment of Osteoporosis. They analysed the advantages of central DEXA scans compared with alternative types of bone densitometry measurement such as QCT and quantitative ultra sound. The precision of high-resolution DEXA measurements of bone mineral status and body composition in small animal models are analysed by Lochmüller et al (2001). They proved that the reproducibility of the high-resolution dual energy X-ray absorptiometry is good.

The uniformity of BMD reduction with aging in trabecular bones is demonstrated by Morimoto et al (2000). The authors investigated age-related changes of BMD in the calcaneus, talus, and scaphoid bone using DEXA measurements. The study has shown that there were significant relationships between age and BMD in men and women. The distal radius BMD is estimated by Lee (2006) using the filling factor of trabecular bone in the X-ray image and correlated with BMD. The results proved that the estimated BMD shows a high linear correlation with the DEXA absorptiometry measurements. However, BMD alone is not a good predictor for fracture risk.

The strength of a bone is not only dependent on the degree of mineralization, but owes some of its mechanical behavior to the very properties of the minerals within bone (Paschalis 1996, Freeman 2001, Mendelsohn 1999, Fazzalari et al 1992, Yvonne 2012). Biomechanical aspect of bone engineering is a central issue in management of fracture and bone loss in osteoporosis (Pioletti 2010, Luo et al 1999). The relationships between bone strength and bone quality are analysed by Wakabayashi et al (2004). The composition of bone matrix, bone mass and architecture are altered, when the bone is influenced by pathologies. Statistical relationships between quantities describing bone architecture, its Fractal Dimension (FD) and mechanical properties have been analyzed in the study done by Cichanski (2010).

Microarchitecture defines patterns of bone alterations with aging and pathology (Roque 2013). The microarchitecture of the trabecular network has a substantial impact on bone strength. Also, characterization of the bone structural properties appears to be an important adjunct to the measurement of bone mass in determining fracture risk with greater accuracy. The behaviour changes in the function of bone affecting its internal architecture depend on the direction of the load application (Bankoff 2012). Recent observations indicate that bone strength is only partially explained by bone density. Bone volume alone accounted for only 76% of the variability in strength, whereas a combination of bone volume and several architectural features explained up to 90% of the strength variability (Dempster 2003). An investigation by Parkinson & Fazzalari (1994), reported that the strength of the trabecular bone structure was dependent on bone volume in a nonlinear manner.

Microarchitecture seems to be a determinant of bone fragility independent of bone density to prevent osteoporotic fractures (Dalle 2004). Osteoporosis is characterized by low BMD, and microarchitectural deterioration of bone tissue with an increased fracture risk. Risk factor of the osteoporotic fractures would lead to a better diagnosis of osteoporotic fractures when estimation of bone strength could probably be achieved if both bone structure and mass could be measured together (Benhamou 2001, Pramudito et al 2007).

Trabecular bone has a complex architecture. Its strength is related to trabecular connectivity and orientation (Goulet 1994). Anisotropy is the trait of an object that possesses different values for a given parameter, such as strength, when measured in different directions. Anisotropic structure of trabecular bone demonstrates mechanical integrity attributes dependent on the direction of loading. Author reports that with aging there is a preferential loss of trabeculae in vertebral bodies (Mosekilde 2000). This loss of trabeculae decreases the strength of the trabecular network due to a loss in connectivity and an increase in the length of unsupported trabeculae (Frost 1999, Parfitt 1983).

Sode et al (2010) have analyzed the regional variations of gender-specific and age-related differences in trabecular bone structure of the distal radius and tibia. The objective of this study is to characterize spatial variability in trabecular structure within a cross-section at the distal radius, tibia, gender and age effects using in vivo high-resolution peripheral quantitative CT. This study demonstrated that the conventional global analysis can obtain regional differences, but assuming bone status from that of smaller sub-region may introduce a confounding sampling error. Therefore the authors concluded that, a combined approach of investigating the entire region, each sub-region of the trabecular architecture and the cortical compartment may offer more complete information about the bone architecture.

A complete volumetric decomposition technique has been developed by Liu et al (2010) to segment trabecular bone microstructure into individual plates and rods. In this study, the trabecular type associated morphological parameters to the anisotropic elastic moduli of trabecular bone.

The results concluded that the morphological analyses provide a better characterization of the morphology and trabecular orientation of trabecular bone. The axial loading of trabecular bone is mainly sustained by the axially aligned bone volume. Results suggest that trabecular plates dominate the overall elastic properties of trabecular bone.

The relationship between elastic modulus and density of trabecular bone at various anatomical sites are analyzed by Morgan et al (2003). The results of this study established that there is no single, universal modulus–density relationship across anatomic site for on-axis loading. The age-related changes in volumetric bone mineral density and geometry in the trochanter in the femoral neck of Caucasian young and elderly women are assessed using volumetric QCT. The parameters bone mass, volumetric BMD, bone size and indices of structural strength are estimated. The use of volumetric QCT allowed separate analysis in cortical and trabecular bone sub-regions. The results described that the trochanter and the femoral neck present different patterns of age-related change in the cortical and trabecular compartments. Also authors suggested that, further study is required to better understand the importance of site dependence on the age-related pattern variation in the cortical and trabecular compartments for estimation of overall bone strength, and its ultimate clinical relevance.

A method to measure new structural features of trabecular bone on an elemental at rod and plate level has been proposed by Stauber & Muller (2006). This study shows that bone density or mass is not required to predict bone stiffness when structural properties are incorporated. It is proved that separate analysis of individual rods and plates may help in better prediction of age and disease-related fractures. In addition, the effects of pharmaceutical intervention in prevention of such fractures beyond BMD have also been analysed.

A venture to evaluate the variation of trabecular architecture in proximal femur of postmenopausal women in various sub regions such as neck, greater trochanter, intermediate region and Ward's triangle has been attempted by Phillips et al (2012). Mean trabecular width and percent bone area are calculated at such sites. The findings indicate that each of mean trabecular width and percent bone area vary within each proximal femur independently from each other, with dependence on site. The trabecular parameters showed significant differences among the sites.

It has been demonstrated that the mechanical performance of each sub-region of trabecular bone is highly dependent on the corresponding microstructure (Freeman 2001). BMD measured by DEXA at standard regions of interest cannot resolve the variations in trabecular density and microstructure that govern the mechanical behaviour of the proximal femur. Also it has been suggested that a quantitative Singh index can be used to monitor the trabecular microstructure at specific sub-regions of the proximal femur. It allows better predictions of hip fracture risk in individual patients and improved assessment of changing bone structure in response to pharmacological interventions.

The relation between bone tissue stiffness, degree of mineralization distribution and the possible changes during prenatal development are analyzed by Mulder (2007). The intra trabecular variations in bone tissue stiffness and degree of mineralization showed a similar pattern with lower variation at trabecular surfaces and higher in the cores. A strong correlation is found between these two variables, which remained unchanged during development. It has been concluded that bone tissue in fetal and newborn trabecular cores resembles adult trabecular bone tissue properties and is distributed in a regular radial pattern in trabeculae. It has been shown that the intratrabecular tissue stiffness develops along the same path as the degree of mineralization. Knowledge regarding intra trabecular tissue stiffness and mineralization results in better understanding of mechanical behaviour of trabecular bone on structural and tissue level.

Cortical and trabecular bone distribution in the femoral neck in osteoporosis and Osteoarthritis (OA) subjects are analysed by Podsiadlo et al (2008). Cancellous bone mass may increase toward the femoral neck and possible variation along the femoral neck at which the biopsies are taken. Results suggest that in addition to the cortical thinning, the loss of the trabecular bone mass and connectivity plays a role in the skeletal fragility associated with hip fracture. Furthermore, the spatial distribution of the trabeculae differs between osteoporosis and OA whereas cortical thinning is homogenous.

In another attempt by Zaino et al (2010), the regional variations of bone quantity, quality and its impact on femoral head collapse are analysed. The results proved bone quantity and quality are reduced in the fracture group as a whole; bone quantity is uniform in each femoral head, but the quality is reduced in the anterior portion. The quality is further reduced in the superior region of arthritic bone and in the lateral-inferior regions of the fractured bones. Tabor and Rokita (2007) have described a gray-level image-based approach to quantify structural anisotropy. Fabric tensor is derived directly from the gray-level 3D CT images of vertebral bodies, for which BMD and elastic modulus are measured. Multiple variable regression models, combining BMD and measures of structural anisotropy are then examined. The results have shown that the measures of structural anisotropy derived from gray-level images, significantly improve prediction of the elastic modulus, compared to BMD alone.

Bauer (2006) has investigated the difference in the trabecular microstructural parameters determined in male and female donors. This experimental study showed that textural parameters calculated from multi-slice spiral CT images of the femoral head may be used to predict biomechanically determined bone strength. In addition, this study also demonstrates that differences in BMD and trabecular structure between men and women are most pronounced at the trochanter and femora and are significantly larger in men than in women. The development of a useful microarchitecture indicator provides an appropriate strength of the bone. Hence, evaluation of micro architectural alterations of the trabecular bone is considered necessary for the estimation of mechanical strength of bone and analysis of osteoporosis (Fritscher et al 2009).

2.2 IMAGING OF TRABECULAR BONE

Recent advances in bone imaging have provided significant insight into the understanding of the prevalence, disease progression, and pathophysiology of metabolic bone disease, particularly osteoporosis. The development of imaging techniques allows a more direct assessment of microdamage and will enhance the ability to determine the degree to which this is relevant to bone quality. Ito (2011) & Donnelly (2011) have reviewed the recent progress in bone imaging and methods for assessing bone quality in osteoporosis research. The review show that the progress in bone imaging technology is promising to bring new aspects of bone structure in relation to bone strength to light, and to establish a means for analyzing bone structural properties in the everyday clinical setting. Advances in bone imaging techniques have provided tools for analyzing bone structure at the macro, micro and nano level. Currently available imaging modalities and image processing tools, like segmentation and surface meshing software, enable the accurate and realistic reconstruction of organ models (Ebbesen 1997). They allow the estimation of clinical parameters essential for surgical planning, navigation, and follow-up evaluation.

Quantitative assessment of macrostructure can be achieved using DEXA and QCT, particularly volumetric quantitative CT, high-resolution CT and high-resolution MR imaging. Compared with MR imaging, CT-based techniques have the advantage of directly visualizing the bone in the axial skeleton, with high spatial resolution. Micro CT (μCT), which provides a higher resolution of the microstructure and is principally applicable in vitro, has undergone technological advances such that it is now able to elucidate the physiological skeletal change mechanisms associated with aging and determine the effects of therapeutic intervention on the bone microstructure. In particular, synchrotron CT provides a more detailed view of trabecular structure at the nano-level. For the assessment of hip geometry, DEXA-based HSA and CT-based have been developed. DEXA-based HSA is a convenient tool for analyzing biomechanical properties and for assuming cross-sectional hip geometry based on two-dimensional 2D data, whereas CT based HSA provides these parameters three-dimensionally in robust relationship with biomechanical properties (Ito et al 2011).

Currently, trabecular structure is most frequently analyzed using 3D analysis methods based on computed microtomography. Non-metric indices of topological features of trabecular bone structure, such as Structure Model Index (SMI), connectivity density and degree of anisotropy, provide unique information relevant to bone quality (Sode 2008). It has been found that these indices were affected by spatial resolution of CT images. The results provide an upper bound for the accuracy of the non-metric indices under limited resolution scenarios. With recent technological advancement, in vivo assessment of these indices may be possible from images acquired using high-resolution imaging techniques such as CT, HR-pQCT and MRI. However, more detailed investigation of the dependence of non-metric indices on spatial resolution is needed to determine their applicability.

Manske et al (2010) have analysed the advantages and disadvantages of the clinical tools such as QCT, high-resolution peripheral QCT, Magnetic resonance imaging and finite element modelling which are used to evaluate bone strength. Finally it has been concluded that there is a desperate need for longer term prospective studies for the bone strength analysis. Also there has been an important evolution in imaging technology that has moved bone imaging research beyond DEXA. Thus, the field is poised to better understand the complex hierarchical structure of bone and the interconnectedness of the many factors that contribute to bone strength. The future is promising and the field continues to evolve toward the increased utility of medical imaging in clinical practice.

Majumdar (1998) has analyzed the trabecular bone architecture of the distal radius with femur fractures using MRI. This study shows that the structural measures determined by MRI of the distal radius and calcaneus may be used to differentiate postmenopausal patients with and without osteoporotic hip fractures. In addition, the results proved that the combination of high resolution MRI structural measures and BMD improves the diagnostic performance, which indicates the complementary information of these parameters is necessary in the assessment of osteoporosis.

Micro-CT and histomorphometry appears to be complementary techniques in the study of bone microarchitecture. The correlation between the micro-CT features estimated by inference technique and histomorphometry are derived. The results proved that the parameters of the micro-CT are well correlated with the bone histomorphometric features. Lammentausta (2006) has correlated the reference measurements of volumetric BMD and bone area fraction determined using a clinical peripheral QCT with MRI variables. The correlation coefficients between peripheral QCT variables and the mechanical properties and between MRI variables and the mechanical properties of trabecular bone are of similar magnitude and showed no statistical differences. This suggests the feasibility of MRI-derived variables in the assessment of mechanical and structural properties of human trabecular bone.

The assessment of trabecular bone structure of the calcaneus is evaluated by Diederichs et al (2009) using multi-detector CT. Further, correlation results are obtained with micro CT and biomechanical testing. This study showed the feasibility of trabecular microarchitecture assessment using multi-detector row CT in an experimental setup simulating the clinical situation. Also, the results proved that the multivariate models of BMD or structural parameters combined with texture indices improved prediction of bone strength significantly.

A method for the analysis of bone quality in the proximal femur based on model-based analysis of CT and X-ray images of femur trabecular bone has been proposed by Fritscher et al (2009). A combined representation of shape and spatial intensity distribution are used to create a statistical appearance model in order to assess the local bone quality in CT and X-ray images. The developed algorithms are tested and evaluated on femur specimen. It is shown that the tools and algorithms presented herein are highly adequate to automatically and objectively predict BMD values as well as a biomechanical parameter of the bone that can be measured intraoperatively.

An attempt based on sampling sphere orientation distribution method using mobile sampling spheres has been developed by Varga & Zysset (2009) for describing microstructural anisotropy of trabecular bone in gray scale images. This implementation on segmented and unsegmented 3D micro CT images of human trabecular bone samples of different anatomical locations is demonstrated. The results concluded that this is a reliable and efficient method to quantify anisotropy of human trabecular bone from 3D gray scale micro CT images.

2.3 ARCHITECTURE OF TRABECULAR BONE IN RADIOGRAPHS

Radiographic projection of trabecular bone produces a gray level textured image, which can be examined by structural and statistical analysis. Conventional radiographs have a resolution of up to 40 µm which has the potential to reflect bone microarchitecture. Recently, a new high-resolution X-ray device with direct digitization has been developed to provide a better precision of texture parameters than previously obtained on digitized films (Corroller et al 2012, Lespessailles et al 2006). Despite this technical limitation, radiographic texture analysis can describe properties of the trabecular bone and is correlated with 3D architecture parameters provided by conventional micro CT, synchrotron micro CT, and MRI (Pothuaud et al 2008).

Two dimensional methods are also used in the assessment of bone structure and mechanical properties of bones (Magland 2012). Bone X-ray radiographs have been suggested as a means of quantifying trabecular changes. X-ray imaging remains a very cost-effective technique, with many applications in both the medical and material science fields. An X-ray radiograph is a two-dimensional (2D) projection of a three-dimensional structure. This process transforms 3 dimensional (3D) objects into a 2D grey-level plain-projection image. In medical X-ray imaging, bone tissue constitutes the major natural contrast, due to its high content of calcium and other X-ray absorbing minerals. The morphology of cortical bone, vertebra and hip geometry can be evaluated from X-ray images directly (Ebbesen 1999). Furthermore, several X-ray-based techniques have been developed to evaluate bone mineral density, based upon the relationship between the grey level on 2D projection images and the attenuation of an X-ray beam at a single point.

Few methods of evaluating the trabecular structure using radiographs have been developed. Caldwell et al (Caldwell 1995) developed a method characterizing trabecular bone structure on vertebral digitized radiographs. Conventional radiographs offer a quick, non-invasive, available, and inexpensive method to assess skeletal tissue, but they are generally considered insensitive for alveolar bone lesions, since a 30–50% mineral loss is required for their delineation (Landis 1995). Singh et al (1970) developed a semi-quantitative index applied to femoral neck radiographs. This index is based on the existence of several arches of trabeculae in the femoral neck. To solve the variability problem of Singh index grading system, many authors proposed the various texture analysis methods for osteoporosis assessment by observing trabecular change in proximal femur. In order to be clinically useful, a texture metric should be robust to changes in image acquisition and digitization. It should be a multi-scale technique and be scale invariant (Dougherty 2001).

An attempt has been made by Apostol et al (2006) to determine the relevance of 2D radiographic texture analysis for the assessment of 3D bone micro-architecture. The results proved that 2D texture features are able to predict 3D micro-architecture parameters. Also the methodology proposed for evaluating the relationships between 3D micro-architecture and 2D texture parameters may also be used for optimizing the conditions for radiographic imaging. Texture analysis of direct magnification radiographs have shown that texture measures have relevance in predicting biomechanical properties (Link et al 1997, Veenlandet al 1997, Caligiuri et al 1994). Texture analysis of X-ray images tends to be an interesting tool in the study of arthritis and osteoporosis. Geraets et al (1993) studied trabecular patterns of hand-wrist radiographs and used seven features to describe the trabecular patterns. These features were highly intercorrelated and provided redundant information on the trabecular texture property.

Lespessailles et al (2007) proved that the radiological texture analysis can be readily used in vast populations. Also, the results proved that the combination of BMD and bone texture analysis on the calcaneus has in particular been shown to improve the fracture risk evaluation by adding information related to microarchitecture. It has been suggested that the features derived from the radiographic images are reproducible and have correlation with biomechanical properties and strength of the bone. Apostol et al (2006) have applied texture analysis to 2D radiographs and the correlations between 2D texture and 3D morphometric architectural parameters are derived. The results identified that radiographic image has relevant 3D information. The significant parts of the information that are available in 3D images are also available in the conventional radiograph (Delmas 2004).

A fractal method, for quantifying differences in the trabecular structure in the tibial bone between the subjects with and without knee has been suggested by Podsiadlo et al (2008). A newly developed augmented Hurst Orientation Transform (HOT) method is used in this study to calculate texture parameters for regions selected in X-ray images of non-OA and OA tibial bones. The HOT method provides a more detailed description of OA changes in bone anisotropy. It appears that the augmented HOT method applied to radiographic images is well suited to quantify OA changes in the tibial bone structure.

Benhamou et al (2001) have used fractal analysis to validate trabecular bone texture analysis from radiographic images. The objective is to determine whether fractal analysis of texture could distinguish osteoporotic fracture groups from control groups, either in vertebrae, hip, or wrist. This study suggests that the fractal analysis of texture applied to trabecular bone radiographs of calcaneus can improve the fracture risk evaluation by adding information related to microarchitecture, derived from analysis of conventional radiographic images. This information has proven to be independent of BMD but at the same time complementary to it, improving the fracture risk determination.

It has been suggested that mean gray level in 2D radiographs and ratio of bone volume to trabecular volume in 3D images could be used as the bone mass parameters. The study determined correlations between 3D and 2D parameters individually. In conclusion, it has been proved that the architectural parameters in 2D and 3D independently affect trabecular strength and the combination of the two can be used to improve bone strength predictability. It is recommended to obtain both 2D and 3D parameters whenever possible in further studies to improve the predictability of the study model. The level of correlation between the 3D characteristics of trabecular bone microarchitecture evaluated using micro CT reconstruction, and trabecular bone score evaluated using 2D projection images derived directly from 3D micro CT reconstruction has been determined by Pothuaud et al (2008). The results concluded that, applying trabecular bone score measurements to clinical X-ray images could be an effective and efficient solution to the routine clinical evaluation of trabecular bone microarchitecture analysis.

An attempt has been made by Defossez et al (2003) to analyze trabecular bone direction using radiographs. The results show that the trabecular pattern can however appear linear, fan shaped, curved or simply random at various bone locations. However, this trabecular arrangement is always optimised to make the bone suitable to sustain the applied stresses. In the femur bone, the neck region is extensively studied, since this location include longitudinal trabecular that follow a clear linear direction. The clarity of the trabeculae present in this linear pattern region can be visually appreciated, and is an indicator of bone quality. The BMD studies focusing on the femoral neck are indeed used to assess risk fracture in the hip.

Agarwal (2004) has analysed the trabecular bone architecture variation using radiographic images in a British medieval skeletal to examine age and sex-related changes. The significant age-related changes in trabecular bone structure, trabecular bone volume, trabecular number, trabecular separation, and anisotropic ratio have been observed. The results explain that the patterns of trabecular bone loss and fragility are generally found in modern populations that typically report continuing loss of bone structure and connectivity between middle and old age, and suggest greater loss in females.

Langton (2009) has generated the 3D proximal femur shape from a single projection 2D radiographic image. Results proved that this technique has the potential to derive volumetric density from BMD. Also, this method facilitates the 3D finite element analysis for the prediction of mechanical integrity of proximal femur. The multilevel features extracted from the radiographic images have been used by Mueen et al (2007) for image classification in content based image retrieval system.

2.4 FEMUR TRABECULAR BONE ANISOTROPY ANALYSIS

Bones are materials characterized by mechanical and structural anisotropic properties. The main directions of anisotropy of such materials are related to mechanical loads to which they are subjected in physiological conditions. The patterns of bone are oriented along the lines of mechanical forces applied to bone (Lespessailles 2006). The trabecular bone shows directional anisotropy due to this orientation. In most biological fractals, there is a definite preferred orientation and hence anisotropy is employed to assess the architectural directionality of the trabecular bone (Jin Y W 2007). The mechanical quality of trabecular bone depends on both its stiffness and its strength characteristics. Knowledge of these properties is important for the diagnosis of bone quality and fracture risk in bone. An indirect method of assessing the mechanical properties of trabecular bone by morphological parameters, derived from the bone architecture, has been developed. This method can accurately predict the mechanical stiffness characteristics of bone specimens by considering the combination of bone volume fraction and architectural anisotropy measurements.

Bone strength is not only depending on bone mass but also on the internal trabecular bone structure. During ageing, the bone mass is always reduced due to osteoporosis like disorders. In this case, the trabecular architecture is strongly modified which reduces the biomechanical competence. The resulting X-ray image of trabecular bone shows a non stationary and anisotropic texture. Humans have a greater overall degree of trabecular anisotropy than non-human hominoids and the regional pattern of anisotropy across the talus differs among species. Among the structural properties of trabecular bone, the degree of anisotropy is most often found to separate taxa with different habitual locomotors modes (Su et al 2013). An oriented fractal analysis can characterize both the roughness of the texture and its anisotropy.

A quantitative method based on the fast Fourier transform has been proposed by Imbault et al (2005) to obtain new anisotropy index known as degree of anisotropy from bone radiographs of the calcaneus. The intra and inter-observer reproducibility and a pilot clinical study comparing osteoporotic fracture cases to control cases are presented. The results demonstrate that the degree of anisotropy on radiographs is related to bone structure. The highest degree of anisotropy values in fracture cases suggests that the structure is more anisotropic in osteoporosis due to preferential deletion of trabeculae in some directions.

To quantify structural anisotropy, Cowin (1985) introduced the term fabric tensor and proposed equations relating fabric tensor and density to the elastic constants. It has been shown that variations of structural anisotropy and bone volume fraction, derived from ultra high-resolution μCT images, explain at least 90% of the variation of the apparent elastic constants. However, measures of structural anisotropy derived from low-resolution images that can be achieved in vivo have not correlated well with measures derived from μCT images and have not been shown to be as highly predictive of mechanical properties (Tabor 2007). Gomberg et al presented quantitative 3D assessment of trabecular bone anisotropy analysis of regional trabecular orientation based on MRI in vivo. The results revealed that the present method allows for analysis of small volumes containing only few individual trabeculae.

Ketcham & Ryan (2004) examined trabecular bone anisotropy using mean-intercept length (MIL), star volume distribution (SVD) and star length distribution (SLD) methods for three-dimensional data for computed tomography, and relate their results to each other. The results presented here corroborate previous investigations in which MIL, SVD and SLD analyses gave results that were qualitatively similar. Imbault et al (2005) derived new anisotropy index called DA on trabecular bone radiographic images using the fast Fourier transform. The highest DA values in fracture cases suggest that the structure is more anisotropic in osteoporosis due to preferential deletion of trabeculae in some directions.

2.5 SPECTRAL ANALYSIS

Two-dimensional transforms have been used extensively in image processing to tackle problems such as image description and enhancement. Fourier transform is one of the most widely used methods. Gregory et al (2004) have presented an analysis of trabecular bone structure in standard radiographs using Fourier transforms to identify contributions to hip fracture risk. The Fourier transform expresses the information in the image in terms of spatial frequencies rather than distances. It is found that Fourier transform can be used to describe structural information in images which may be related to fracture, independently of BMD. The results proved that there were no significant differences between the age, height, and weight or BMI of the fracture and control groups. Also the femoral neck-BMD is significantly lower in the fracture group in comparison to the control group.

Chappard et al (2005) have analysed the anisotropy changes in post-menopausal osteoporosis using the BMD and fractal parameters derived from Fast Fourier Transform. The results suggest that it is possible to improve the fracture risk evaluation by adding information related to the directional organization of trabecular bone derived from the FFT spectrum on conventional radiographic images. Also, the anisotropy indicators derived from Fourier transform analysis applied to trabecular bone radiographic images can distinguish vertebral fracture cases from control cases. The anisotropy indicators applied to calcaneus radiographs can provide a reliable characterization with a method derived from the Fourier transform of the gray levels. It is suggested that, these features when added to BMD and fractal analysis for anisotropy evaluation help to improve the detection of osteoporosis fracture risk. Prospective studies are needed to better understand the changes of anisotropy in osteoporosis and their ability to help the fracture risk prediction.

The quantitative method based on the FFT has been proposed by Imbault et al (2005) to obtain anisotropy indices on bone radiographs of the calcaneus and a validation on synthetic images is attempted. The intra and inter-observer reproducibility and a pilot clinical study comparing osteoporotic fracture cases to control cases are also presented. This study has shown that the degree of anisotropy can be determined on plain radiographs using spectral analysis. Degree of anisotropy evaluation could improve the osteoporotic fracture risk determination when combined with BMD and other textural parameters such as fractal analysis.

A wavelet is a waveform of sufficiently limited duration that has an average value of zero and tends to be irregular and asymmetrical (Mallat 1989). Wavelet analysis is a windowing technique with variable sized regions that allows long time intervals in regions where more precise low frequency information is required and short time intervals in regions where precise high-frequency information is required. Applications of wavelets in the analysis of medical images have been based on the decomposition of a signal in multi resolution theory (Strickland RN and Hahn H 1996).

Wavelets are shown to be good at catching zero-dimensional or point singularities, but two-dimensional piecewise smooth signals resembling images have one-dimensional singularities. Wavelets in two dimensions are obtained by a tensor-product of one dimensional wavelet and they are thus good at isolating the discontinuity across an edge, but will not see the smoothness along the edge. Recent analysis by Krug (2006) reveals that wavelets are a power tool to characterize and quantify trabecular texture in an image and the author concludes that wavelet based method is less sensitive to image noise at higher resolution. In the last decade, wavelet theory has been widely used for texture classification purposes. Discrete wavelet transform

(Mallat 1989) consists of decomposing the discrete signal into a hierarchy set of orthogonal approximation and detail functions, respectively.

Images are decomposed using Wavelet Transform (WT) and statistics such as mean, standard deviation, median and mode are derived from the decomposed sub-bands and are used as features for classification. Apart from these statistical features, co-occurrence features are extracted from the wavelet decomposed sub-bands in order to increase the correct classification rate (Arivazhagan & Ganesan 2003). In order to explore the middle-band characteristics, tree structured wavelet transform, pyramid structured wavelet transform, dual-tree complex wavelet transform, and wavelet packets were used for texture classification (Chang & Jay Kuo 1993).

A comparative study by Randen & Husoy (1999) shown that various filtering approaches yield different results for different images. The success of wavelets is mainly due to the good performance for piecewise smooth functions in one dimension. Wavelet-based method eliminates the structures in mammograms produced by normal glandular tissue of varying density, based on local average subtraction, and used probabilistic neural network for classification. A wavelet method is used to detect the presence of microcalcifications in mammograms (Mini et al 2004, Strickland & Hahn 1996).

Gabor filters have gained much attention for different aspects of computer vision and pattern recognition. Some successful applications include texture segmentation and texture feature extraction, fingerprints identification, face and iris recognition, edge detection, directional image enhancement, image compression, hierarchical image representation and recognition. Texture features derived using Gabor filters are used for content based image retrieval applications. Images are retrieved based on the similarities of the features. Xiang et al (2003) extracted textural features of trabecular bone from stained bone images using Gabor wavelets. Results indicated that Gabor wavelet analysis provides the insight of the frequency composition that can be localized to the pixel level.

Bone mass can be discriminated by the averaged texture energy across all orientations. Dominant bone lattice orientation can be determined by the orientations. This methodology has the potential to provide a tool for quantifying both bone mass and bone structural anisotropy. Gabor wavelet to extract features of magnetic resonance tumor images to differentiate between primary central nervous system lymphoma and glioblastomamultiforme. The experimental results show that this method used can distinguish different categories of tumour images

Gai et al (2013) proposed a study of the Reduced Quaternion Wavelet Transform (RQWT) which has one shift invariant magnitude and three angle phases at each scale from digital image analysis application. The features extracted from the sub-bands of the RQWT decomposition is proposed in the transform domain. The experimental results demonstrated that proposed method achieved higher texture classification accuracy rate than a famous wavelet transform based classifier.

The quaternionic wavelet transform is a recent improvement of standard wavelets that aims to yield coefficients with a shift-invariant magnitude and a phase containing geometric information. This transform makes use of a 2D generalization of the analytic signal which is a classical powerful tool for signal analysis. Soulard & Carre (2011) used quaternionic wavelet transform for image classification and comparison was made with complex wavelets. The results proved that the complex wavelet has good directionality; which was confirmed in practice by better recognition for some highly oriented textures. But its complex phase fails to provide such geometric information as of QWT. As a result, QWT outperforms complex wavelets.

The quaternion wavelet can overcome the drawbacks of Discrete Wavelet Transform (DWT) which are shift invariant and no phase. Meanwhile, it can also make up the defects of Continuous Wavelet Transform (CWT) with one phase which is not enough to capture the texture feature of banknote images. Gai et al (2013) proposed new bank note image feature extraction method based on QWT and generalized Gaussian density (GGD). The parameter sets of GGD for each sub-band are used as features and the BP neural network is applied as classifier in the classification system.

Quaternion Hilbert transform based space spatial frequency tool is improved version of Hilbert transform, and applied to the texture analysis. The experiments of texture analysis show that the new approach is efficient for the application in texture analysis. The local properties extracted are amplitudes, instantaneous frequencies and phases of the IMFs (Guanlei et al 2009). The texture image is decomposed to several 2D-IMFs by bidimensional empirical mode decomopsition. Then quaternion transform is used to get the quaternionic analytic signals, which is compatible with the associated harmonic transform. Finally, each 2D-IMF's local properties are analyzed using a new quaternionic representation. As an advanced method for describing the local properties of a 2D-signal, this algorithm could extract various parameters from each of 2D-IMF including instantaneous frequency (Qiao et al 2009).

2.6 SPATIAL ANALYSIS

Scale is the spatial resolution in determining the perception of structures. The scale provides a unified and parametric representation of orientation and anisotropy of local structures. Anisotropy quantifies the spatial localization and directional characterization of trabecular arrangement. Different methods are available to characterize the structural anisotropy on trabecular bone radiographs namely, mean intercept length (Keaveny et al 2001), fabric tensor methods (Javad et al 2012), Fourier transformation techniques and 2D fractal dimension methods (Jiang et al 1998, Lespessailles et al 1996). Although, several approaches have been reported, the major limitations of these approaches include the requirement of binary segmentation into bone and introducing significant errors at in vivo resolution where most bone voxels are only partially occupied. Recently tensor analysis are used which allows a space-variant process control to adapt with structures (Saha 2001).

Structure tensor analysis has been useful in visualization and quantification of tissue microstructure of digital microscopic images and MRI brain images. It has been found that ST analysis facilitated the identification and characterization of crossing fibers. And it builds upon the available tools to investigate the microstructure of the brain and validate diffusion MRI measures of anisotropy and fiber orientation. The method to visualize and quantify the microstructure of rat brain sections, and directly compared anisotropy from ST analysis and Diffusion Tensor Imaging (DTI). Moreover, it is demonstrated that ST analysis facilitated the identification and characterization of crossing fibers. This analysis has been useful in visualization and quantification of tissue microstructure of digital microscopic images and MRI brain images (Matthew & Joseph 2012). It is also used to quantify waviness properties of collagen fibers and their orientation in carotid arteries (Rezakhaniha et al 2012).

Fractional anisotropy derived using tensor analysis is found to useful in evaluation of cancellous bone quality of the femoral neck in postmenopausal women (Manenti 2013). Also, FA along with apparent diffusion coefficient is analyzed to assess the state of structure in cancellous tissue of vertebral bone marrow (Ueda 2010). Tschumprele & Deriche (2002) introduced nonlinear structure tensor based on isotropic nonlinear diffusion process for matrix-valued data. Anisotropic analysis was introduced by Brox & Weickert (2002). They showed the preservation of positive semi definiteness in a nonlinear structure tensor.

Structure tensor has proven its usefulness in many application fields such as corner detection texture analysis (Lindeberg 1994) diffusion filtering (Weickert 1998), and optic flow estimation. It has even been successfully employed in numerical mathematics for grid optimisation when solving hyperbolic differential equations. Structure tensor is introduced for optic flow estimation using local information in order to adapt the Gaussian kernel to the data. While nonlinear diffusion filtering and adaptive Gaussian smoothing are similar for small amounts of smoothing, significant differences arise when more substantial smoothing is performed. In this case, nonlinear diffusion based on the iterative application of very small averaging kernels can realize highly complex adaptive kernel structures (Granlund & Knutsson (1995), Nagel & Gehrke 1998).

Diffusion-weighted Magnetic Resonance (MR) imaging is used to measure the self diffusion of water in tissue, which is affected by the presence and orientation of physical barriers (Hagmann et al 2006). The orientation dependency of the diffusion barriers can be characterized by measuring the Diffusion Tensor (DT). Although diffusion-weighted MR imaging and DT imaging have been used to study the dynamics of water content and the fiber architecture in healthy muscles, diffusion MR imaging has been applied to also assess myopathies. DTI has provided unparalleled insight into the microstructure and connectivity of the nervous system. Intricate maps of connectivity are being used to interrogate the structural organization of the normal brain (Mori & Zhang 2006) and the disruption of such connections as a consequence of injury or disease. However, despite the widespread availability and abundance of DTI studies, accurate validation has been notoriously lacking. DTI is unique in its ability to derive microstructural tissue properties at a macroscopic scale.

Lacunarity is a multi-scale measure of texture describing the complex intermingling of the shape and distribution of gaps within an image. It quantifies the deviation of a geometric shape from translational invariance. It is not predicated on self-similarity and has been used most successfully with binarized images images (Weishampel 1998). A plot of a lacunarity against window size contains significant information about the spatial structure of an image at different scales. Lacunarity is related to the distribution of gap sizes. Low lacunarity geometric objects are homogeneous because all gap sizes are the same, whereas high lacunarity objects are heterogeneous (Henebry 1995).

Lacunarity can distinguish varying degrees of heterogeneity within an image, and in the case of a homogeneous image it can identify the size of a characteristic substructure. Lacunarity has been used previously to characterize landscape texture in binarized optical (Weishampel 1998) and Synthetic Aperture Radar (SAR) images (Henebry 1995). Lacunarity is used effectively in the analysis of the temporal distribution of earthquakes, rock unit mapping, simulation and quantification of forest canopy structure, texture classification of urban and in analysis of porosity in naturally fractured media (Mejia et al 2005). In medical applications, it has been applied in mammographic images to quantify the degree of heterogeneity of the parenchymal pattern for effective prediction of cancer risk (Manousaki 2005). Similarly this analysis is useful in differentiating the benign lesion and malignant lesion from digital mammograms and in automated assessment of melanocytic naevi and melanoma from microscopic images (Dong 2000). Also lacunarity has been used to differentiate three types of trabecular bone structure like healthy young, healthy perimenopausal, and osteoporotic patients from lumbar vertebra MR images (Zaia 2006).

Lacunarity measures the deviation of a geometric structure from translational invariance, or gappiness of geometric structure (Gefen et al 1983). It is important to note that objects that are homogeneous at a small scale can be heterogeneous at a larger scale (scale here refers to both measurement or window size and areal extent). Therefore, lacunarity is a scale-dependent measure of spatial complexity or texture of a landscape (Plotnick et al 1993). Unlike most other landscapes indices and measures (Gustafson 1998, Young & Chopping, 1996), the computed values of lacunarity are not sensitive to map boundaries but are sensitive to scale.

Keller et al (1989) used fractal dimension and lacunarity to describe and segment natural texture images. Mejia et al (2005) applied the lacunarity measure to breast cancer risk study and concluded that breast cancer risk is affected not only by the amount of mammographic density but also by the degree of heterogeneity of the parenchymal pattern. In the preliminary studies by Melo et al (2007), lacunarity was used as a texture measure to differentiate the benign lesion and malignant lesion.

Succolarity is a very useful method that integrates structural characteristics of real images. Succolarity is used to characterize the relative vulnerability of the Earth's surface to tectonic deformation using the geometrical characteristics of drainage systems (Shahzad et al 2010). This approach is also used to characterize satellite images of cities through its social aspects and to characterize the relative vulnerability of the earth's surface to tectonic deformation using the geometrical characteristics of drainage systems. It is also used in characterizing social aspects of cities by differentiating the formal and informal areas. Another application of succolarity method is to study the reservoir induced earthquakes (Melo & Conci2011). Succolarity is used in various medical applications such as diagnosis of vasculature obstructions in ultrasound images and in differentiating occlusions in carotid (Melo & Conci 2011). Fractal geometry has been used to characterize and quantify the response for cancer treatment. It is also used in studying blood flow in the lungs, to correlate the morphometric data from the intrapulmonary arteries with functional measurements of blood flow.

2.7 PRINCIPAL COMPONENT ANALYSIS

Principal components analysis transforms the dataset and offers a method to identify and rank the attributes according to the amount of variation within the data explained by each attribute (Gallo et al 2013). Principal Component analysis is used to generate scores from the profiles and is able to discriminate fracture and control groups better than fractal dimension (Gregory 2004). The PCA method extends previously developed method for analysis of histological sections of bone. The use of oriented profiles improved the performance of the analysis by selecting directions in which there was the most information about bone structure perpendicular to the preferred orientation of the trabeculae. In addition, the property of orthogonality between these components ensures that the variables generated are linearly independent. Benefits can also be found by the use of a model built on the mathematical distributions present in the data, rather than expecting the data to meet a given mathematical property, such as fitting a fractal distribution (Matthew 2012).

PCA has been employed in assessing the chest wall movement in pathologies like chronic obstructive pulmonary disease, emphysema, cystic fibrosis and muscular dystrophy. PCA has been widely used in respiratory measurements for identifying the most representative features (Ferrigno et al 1998). PCA was also used to explore overall rank orders for treatment, and relationships between outcomes with classes of asthma medication (Jenkins et al 2005).

2.8 EXTREME LEARNING MACHINE

Extreme learning machine resolves bioinformatic and biomedical classification problems. The results confirm that the ELM classifier is a promising candidate for improving accuracy and minimum sensitivity. (Monedero et al 2010). It is proposed that ELM algorithm can be easily implemented, which tends to reach the smallest training error, and obtains the smallest norm of weights and the good generalization performance, and runs extremely fast, in order to differentiate it from the other popular SLFN learning algorithms Huang et al (2006). The ELM with sigmoidal activation function and Gaussian Radial Basis Function (RBF) kernel function for protein sequence analysis is investigated; classification accuracy was very high, when compared with Back propagation base neural networks (Dianhui & Bin 2005). Kim et al (2007) evaluated a ELM algorithm for classifying arrhythmia using in the aspects of accuracy, sensitivity, specificity, and learning time.

Kwak & Kwon (2008) proposed cardiac disorder classification based on ELM. The method shows better performance than multi-layer perceptron, support vector machine, and hidden Markov model. Rong et al 2008 studied the performances of ELM for multi-categories classification applications. ELM classifier is used to classify the abnormal masses of digitized mammograms into benign and malignant tumours. Performance study shows that the ELM classifier is better than other classifiers in classifying the malignant and benign masses of the digitized mammograms. An approach to automate the detection and classification of tuberculosis bacilli in tissue section is carried out using image processing technique and feedforward neural network trained by ELM. This study indicates that the single hidden layer feed forward neural network using ELM is able to achieve acceptable classification performance compared to the back propagation training algorithms. Further, ELM also does classification in lesser computational time (Vani et al 2010).

The ELM with sigmoidal activation function and Gaussian RBF kernel function have been employed for protein sequence analysis (Huang et al 2006, Dianhui & Bin 2005). The results show that classification accuracy was very high, when compared with Back propagation based neural networks. Kim et al (2007) have evaluated ELM algorithm for classifying arrhythmia using the aspects of accuracy, sensitivity, specificity and learning time. Multicategory classification using ELM has been implemented for microarray gene expression in cancer diagnosis (Zhang et al 2007).

The performances of ELM for multi-categories classification applications have been studied (Rong et al 2008). ELM method to classify the abnormal masses of digitized mammograms into benign and malignant tumors has been proposed by Vani et al (2010). Performance study shows that the ELM classifier is better than other classifiers in classifying the malignant and benign masses of the digitized mammograms. Further, ELM also does this classification in lesser computational time.