CHAPTER 1

INTRODUCTION

1.1 BONE BIOMECHANICS

The goal of biomechanics is to determine the alterations of the structural level of bone due to disease or a conscious intervention. The most devastating complication of bone disease is the structural collapse of the bone. It is also essential to appreciate that bone is extremely sensitive to its mechanical environment, and to a large extent, it is the functional milieu that defines its morphology and ultrastructural organization.

Evaluation of relations between biomechanical performance and bone mass depend on the nature of the specific measures which indicate bone fragility, stiffness, toughness and strength. In addition, these assays can be performed under a number of different loading conditions such as compression, tension, shear or bending alone or in combination and can be applied either cyclically or monotonically, short- or long-term, and at different loading rates (Jacqueline 2011).

An understanding of biomechanics help determine the pathogenesis of bone disease and mechanisms of treatment and the biomechanical strategies can retard, prevent or even reverse the structural demise of the bone. Therefore bone biomechanics research remains complex and contemporary (Rubin & Rubin 2006, Pioletti 2010).

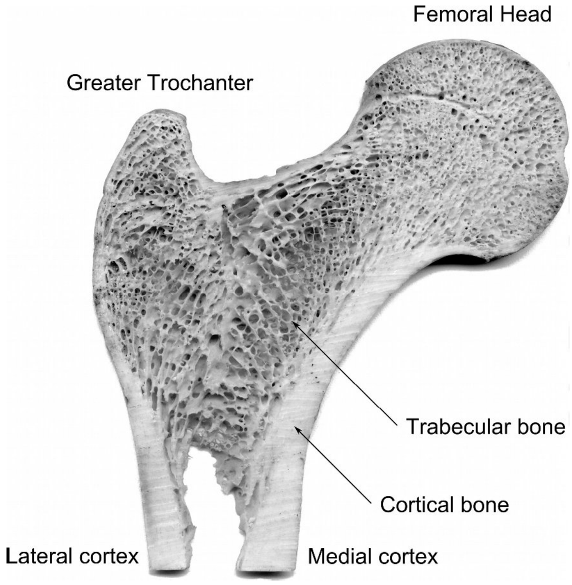

Figure 1.1 Anatomy of the human proximal femur (Phillips et al 2012)

1.2 FEMUR BONE

In humans, the femur is the largest, longest, and strongest bone of the human skeleton and has the ability to support upto 30 times the weight of an adult. It is extending from the hip to the knee and is the most proximal bone of the leg in vertebrates capable of walking or jumping. It is strong under compression (Huang et al 2012). Figure 1.1 shows the anatomy of femur bone.

The rounded, smooth head of the femur fits into a socket in the pelvis called the acetabulum to form the hip joint. The head of the femur is joined to the bone shaft by a narrow piece of bone known as the neck of the femur. The neck is a point of structural weakness and a common fracture site. The lower end of the femur hinges with the tibia to form the knee joint. A typical femur structure includes medullary cavity, yellow marrow, periosteum and articular cartilage. In every part of the femur there is a remarkable adaptation of the inner structure of the bone to the mechanical requirements due to the load on the femur-head. Many studies have focused on geometry, biomechanical properties, and fractural type of a human femur (Huang et al 2012).

There are the two kinds of bone that comprise femur namely cortical and cancellous or trabecular bone. These two types are classified on the basis of porosity and the unit microstructure. Cortical bone appears very dense and is formed from a layer of low porosity ranging between 5% and 10%. It is found primarily in the shaft of long bones and forms the outer shell around trabecular bone at the end of joints and the vertebrae.

Femur trabecular bone is porous type of bone with porosity ranging from 50% to 90% (Phillips 2012). Trabecular bone is formed from a series of struts, giving rise to a structure in which there is a spatial variation of continuum level porosity and directionally dependent stiffness throughout the femur (Andrew 2012, Keaveny et al 2001). The trabecular bone forms a pattern of net-like strands varying in thickness and number (Smyth et al 1997). The orientation and density of these patterns in proximal femur are heterogenous.

Five distinct strength regions which demonstrate the quality of femur bone are identified using Singh delineation method (Singh et al 1970). The principal compressive group carries load from the hip joint, through the femoral head towards the medial cortex, the primary tensile group arches from the lateral cortex through to the femoral head; the secondary compressive group spans in a diffuse manner from the medial cortex across the femoral shaft; the secondary tensile group spans in a diffuse manner from the lateral cortex across the medial shaft; the greater trochanter group is considered to be a tensile group running within the greater trochanter. Also is the presence of Ward's triangle, an area of low trabecular density, as well as the femoral canal running between the medial and lateral cortex of the femoral shaft (Phillips 2012).

The compressive group which is the thickest and most closely packed trabeculae in the upper end of the femur and the tensile group, which curves upward and inward across the neck of the femur, are considered as the most important strength regions (Singh et al 1970, Smyth et al 1997). Trabeculae show considerable variation in structure in these sub-anatomic strength regions of femur.

1.3 TRABECULAR ARCHITECTURE

The structure of trabecular bone has been hypothesized as trajectories of compressive and tensile stress, resulting in an optimized structure. These strength patterns are evaluated by bone quality factors which include Bone Mineral Density (BMD), architecture and geometric properties of femur (Faulkner et al 2006, Cheung et al 2009, Laskey et al 2011, Donnelly 2011).

Non-invasive assessment of mechanical strength of bone remains an important issue. The most common approach to assess bone strength is to estimate its mineral content using BMD (Karlsson et al 2006). The distribution of tissue level mineral is altered during osteoporosis like bone disorders which may alter tissue-level mechanics. These changes are anatomically distinct and do not occur throughout the proximal femur (Linden et al 2001). As BMD reflects both bone volume and the degree of mineralization, it has been regarded as an alternate measure for bone strength. Dual Energy X-ray Absorptiometry (DEXA), an X-ray based technique with low radiation dose that is used to measure BMD, is the basis of clinical osteoporosis assessment and monitoring. The biomechanical properties of trabecular bone depend not only on BMD but also on trabecular microarchitecture (Lespessailles et al 2006, Martin 1991, Landis 1995). The prediction of bone strength can be improved when BMD is combined with measures of trabecular microarchitecture (Diederichs et al 2009).

Bone microarchitecture is the architectural arrangement of bone tissue around the bone axis along, or about which it is loaded (Faulkner et al 2006, Donnelly 2011). The femur trabecular microstructure is typically oriented, such that it is organized along the lines of mechanical forces applied to bone. This microstructural directionality contributes to trabecular bone anisotropy (Keaveny et al 2001). The architectural deterioration caused by pathology results in alterations of structural anisotropy. An understanding of anisotropy of bone is important for diagnosis of osteoporosis like bone disorders. So, it is important to measure the alterations of anisotropy that could reveal the pathological conditions.

The evolution of the orientations allows quantifying the degree of deterioration of the bone. In normal subject both compressive and tensile types of trabeculae are uniformly distributed, where as in an osteoporotic subject, the number of tensile trabecular patterns decrease gradually and disappear completely for a patient with severe osteoporosis. Also, compressive trabeculae become thinner and their number decreases much less quickly during the disease. As a result, a radiograph of an osteoporotic subject will be more anisotropic than that of a normal subject (Lemineur et al 2004).

1.4 MEDICAL IMAGING METHODS

Advances in imaging techniques have provided tools that allow characterization of bone quality and quantity at the macro, micro and nano-level (Ito et al 2011). Methods such as Computed Tomography (CT), Quantitative Computed Tomography (QCT) and high-resolution Magnetic Resonance Imaging (MRI) are employed for characterizing bone geometry and microarchitecture. QCT is based on the differential absorption of ionizing radiation by calcified tissue. The attenuation measurements are compared with a standard reference to calculate bone mineral equivalents. QCT permits in vivo Three Dimensional (3D) quantification of bone density separately in the trabecular and cortical bone compartments. It is also used to perform macroscopic assessment of 3D bone geometry in vivo. An important drawback of QCT is its delivery of ionizing radiation to patients which is higher than for DEXA.

The high-resolution peripheral QCT scanners have facilitated in vivo imaging of 3D trabecular morphology at peripheral site like the distal radius. The primary advantage of this technique is that trabecular bone can be resolved, and morphologic parameters such as bone volume fraction, trabecular thickness, trabecular separation, and trabecular number can be calculated. Though this technique has the benefit of reduced radiation doses relative to those from whole-body QCT scans, it is largely restricted to peripheral sites.

MRI allows imaging of the trabecular network at peripheral sites. During scanning, a strong magnetic field and a series of radio frequency pulses are applied to the specimen to generate 3D images of the hydrogen in the water within skeletal tissues. A critical advantage of this technique is its ability to generate 3D images of bone geometry and microarchitecture without ionizing radiation, but the disadvantage is the long scan time required for high resolution images. Also, higher spatial resolution is the trade-off with signal-to-noise ratio.

All these techniques produce 3D images of trabecular bone but their applicability to large populations may be limited by their cost, greater radiation exposure, lengthy time required for the analytical procedure and availability (Lespessailles et al 2007). Also, noise is significant in MRI and

CT. On the other hand, X-ray imaging remains a very cost-effective technique, with many applications in both the medical and material science fields. X-ray equipment is capable of an excellent spatial resolution of 50 µm when compared with the 30 µm spatial resolution of CT equipment and 300 µm spatial resolution of MRI equipment. The digital radiograph saves the image that is formed by X-rays which are more or less absorbed when passing through various tissues or materials, depending upon the substance's composition, thickness, and density (Lee et al 2006). **S**everal X-ray based techniques have been developed based upon the relationship between the gray level on two dimension (2D) projection images and the attenuation of an X-ray beam at a single point (Podsiadlo et al 2008).

Digital radiography has the potential to reflect bone microarchitecture (Pothuaud 2008 et al). Standard X-ray examination allows detection of changes not only in the outer cortical part of the bone, but also changes in the inner trabecular bone microarchitecture (Defossez et al 2003, Gregory et al 2004). Radiographs are commonly obtained at the hip, spine, and calcaneus for the purpose of analysing trabecular bone (Corroller et al 2012). The 3D microarchitecture of trabecular bone is indirectly visualized in a two-dimensional X-ray projection as a pattern that can be quantified and analysed.

The observation of trabecular pattern change, for diagnosis of osteoporosis was first proposed in the 1960s using radiographs of proximal femur. The diagnosis was known as Singh index grading system (Pramudito et al 2007). The relationship between plain radiographic patterns and 3D trabecular architecture shows that the plain radiograph contains architectural information directly related to the underlying 3D structures such as porosity and connectivity (Pothuaud et al 2008). However, two-dimensional projection-based images do not directly portray a material's microarchitecture. Hence texture based analysis has been proposed as an indirect measurement to assess the architecture of the bone (Lespessailles et al 2007, Podsiadlo et al 2008, Corroller et al 2012).

Texture plays an important role in the human visual system for pattern recognition and interpretation. In image interpretation, pattern is defined as the overall spatial form of related features. The repetition of certain forms results in a characteristic pattern which is found in many natural objects. Textural analysis is well suited to characterization of spatial arrangement as smooth or rough, coarse or fine, homogeneous or random texture (Avery et al 1992). It is able to yield localized texture information on a pixel level, and provide more insight into structure (Yingling et al 2006). Texture analysis of trabecular bone X-ray images appears to be a promising approach in the understanding of the pathophysiological mechanisms in bone disease. The texture features can be derived using two different approaches which include spectral and spatial methods.

1.4.1 Spectral Analysis

Transforms have been used extensively in image processing for enhancement and feature extraction. Methods based on multiresolution or multichannel analysis such as wavelet transform has been introduced for characterizing the image textures (Gonzalez & Woods 2001). They perform better than traditional single resolution techniques in characterizing textures such as coarseness, periodicity and directionality. Wavelets provide unified framework for spatial scale analysis and balanced frequency response that reflects all high frequency changes. They offer a simultaneous localization in time and frequency domain. Wavelets have the great advantage of being able to separate the fine details in an image. Very small wavelets can be used to isolate very fine details in an image, while very large wavelets can identify coarse details. A wavelet transform can be used to decompose an image into component wavelets (Sifuzzaman et al 2009).

A number of wavelet families like Symlet, Coiflet, Daubechies and biorthogonal wavelets are in use. They vary in various basic properties of wavelets like compactness. Among them, Haar wavelets belonging to Daubechies wavelet family are most commonly used wavelets as they are easy to comprehend and fast to compute. Haar transform can be viewed as a series of averaging and differentiating operations on a discrete function. It can be easily examined that both the lowpass and highpass filters of Haar wavelet are quadratic in nature (Subramani et al 2006). Wavelet analysis is used for solving difficult problems in mathematics, physics, and engineering, with modern applications as diverse as wave propagation, data compression, signal processing, image processing, pattern recognition and computer graphics. They are successfully used in functional medical imaging. Wavelet-based texture analysis has been also reported for several biological structures (Lee et al 2003).

Gabor wavelets are 2D spatial filters that are both frequency and orientation tunable. Gabor's theory leads to the idea that a visual system should analyse visual information most economically by using pairs of perceptive fields of symmetrical and asymmetrical response profiles in order to achieve minimum uncertainty in both spatial localization and spatial frequency. Thus they have the ability to perform multi-resolution decomposition due to its localization both in spatial and frequency domain. Gabor filters can be either convolved with the whole image or applied to a limited range of positions. In such a case, a region around a pixel is described by the responses of a set of Gabor filters of different frequencies and orientations, all centred at that pixel position. Gabor filters have gained much attention for different aspects of computer vision and pattern recognition.

Gabor filters are efficient in reducing image redundancy and robust to noise. Some successful applications include texture segmentation and texture feature extraction, finger prints identification, face and iris recognition, edge detection, directional image enhancement, image compression, hierarchical image representation and recognition.

Complex-valued samples are obtained using a quaternion-valued equivalent of the analytic signal obtained from a one-sided quaternion Fourier transform which refer to as the hypercomplex representation of the complex signal. This representation may be interpreted as an ordered pair of complex signals or as a quaternion signal. Orthonormal complex modulation can be represented mathematically by a polar representation of quaternions. Quaternion Wavelet Transform (QWT) is a local Quaternion Fourier Transform (QFT) which consists of a real part and three imaginary parts that are organized in quaternion algebra. The first two QWT phases describe the shifts of the image features in the vertical and horizontal directions and the third QWT phase describe the texture information of the image. The QWT has been applied to many fields such as image segmentation, edge detection and texture image classification (Gai et al 2013).

Hilbert-Huang Transform (HHT) consists of Empirical Mode Decomposition (EMD) and Hilbert spectral analysis (Huang et al 1998). HHT offers much better temporal and frequency resolutions when compared to wavelet and Fourier transform analyses. This method permits analysing 1D nonlinear and non-stationary data. EMD reflects the decomposition for the multi-texture images and Hilbert spectrum computes the local frequencies. Hilbert Transform (HT) of the Intrinsic Mode Functions (IMFs) led to meaningful representations for the instantaneous frequency of the data. HT is applied to the decomposed IMFs and the energy, frequency, time distribution, designated as the Hilbert spectrum are constructed from which the time localities of events are preserved. HHT have found many successful applications in analysing a very diverse range of data sets in biological and medical sciences, geology, astronomy, engineering, and others. Quaternion Hilbert Transform (QHT) is an important tool to analyse the frequency, amplitude, phase, direction and intrinsic dimension for 2D signals (Xu et al 2012). QHT is the optimal selection because it can give more useful information than other HTs. Performing QHT on every IMF is beneficial for the textural analysis.

1.4.2 Spatial Analysis

Advances in image processing techniques have provided tools for analysing local spatial structure of bone at the macro and micro level. Classical methods for texture analysis are complemented by alternative structure descriptors that exploit local geometric behavior or topological properties for characterizing structure in pattern recognition problems. However these methods imply rotation invariant properties, making it desirable for structure descriptors to capture directional preferences in imaging datasets, which will be referred to as capturing “anisotropy”. In addition to identifying directional preferences of image features, it is often helpful to also define measures that objectively quantify the degree of rotation invariance provided by local feature extraction. Recently, Structure Tensor (ST) method has been used to quantify anisotropy indices.

Structure tensor is second-moment matrix derived from the gradient of a function. It provides more powerful description of local patterns better than a simple gradient (Nicolescu & Medioni 2003, Bigun et al 2005). Based on its Eigen values and the corresponding eigenvectors, the tensor summarizes the predominant directions of the gradient in a specified neighborhood of a point and the degree to which those directions are coherent. Eigen values, Eigen vectors and indices of anisotropic are deduced from the ST. All of these parameters provide information about the local microstructure and geometry of the tissue.

ST applies a linear technique such as Gaussian convolution for averaging information within a neighbourhood. The Gaussian convolution is equivalent to linear diffusion. The local neighbourhood for the integration is fixed in both size and shape and cannot adapt to the data. Therefore the limitation of Gaussian convolution is addressed by using nonlinear diffusion techniques which smooth the data while respecting discontinuities (Perona & Malik 1990, Weickert 1998). The local neighbourhood of the ST defined by the Gaussian kernel, is adapted to the data and avoids smoothing across discontinuities. Fractional Anisotropy (FA) derived using tensor analysis is found to be useful in evaluation of cancellous bone quality of the femoral neck in postmenopausal women. Also, FA along with apparent diffusion coefficient is analysed to assess the state of structure in cancellous tissue of vertebral bone marrow (Ueda et al 2010).

Textural patterns that are often complex and exhibit scale-dependent changes in structure are described using a textural feature called lacunarity (Gefen et al 1983, Lin & Yang 1986, Allain & Cloipre 1991). Lacunarity, which can also describe the spatial distribution of real data sets, is a measure of translational invariance of an object, and quantifies aspects of patterns that exhibit scale-dependent changes in structure. Translational invariance is highly scale-dependent, so lacunarity is considered a scale-dependent measure of heterogeneity (Plotnick et al 1996). The lacunarity morphometric uses multiscale windowing to measure the spatial heterogeneity and anisotropy, and is sensitive to local aggregation or clustering (Henebry & Kux 1995). Lacunarity has several practical advantages for the assessment of spatial heterogeneity, as its computation is simple to implement and it exhaustively samples the image to quantify scaling changes. Lacunarity is used successfully to characterize the trabeculation pattern in vertebral bone with sufficient sensitivity to distinguish different degrees of bone quality during aging and osteoporosis (Dougherty & Henebry 2002).

Recently it has been shown that succolarity analysis is a complementary approach to fractal analysis. This analysis is very useful, if the input texture has direction or flow information (Melo & Conci 2008). It helps to quantify the orientation of textural patterns and contribute to further characterization based on orderly arrangement of the patterns in the images. This method integrates structural characteristics of real images on pattern recognition process.

Succolarity on fractal sets is defined as evaluation of the degree of filaments that allow percolation. It measures the percolation capacity of an image. In chemistry and material science, percolation concerns the movement or filtering of fluids through porous materials. In engineering, it refers to the slow flow of fluids through porous media. In mathematics and physics, it is generally referred to simplified regular or random lattice models of random systems and the nature of connectivity on them. An important different model of percolation, in a diverse class altogether, is directed percolation, where connectively along a limit depends upon the direction of flow. It is used in various medical applications such as diagnosis of vasculature obstructions in ultrasound images and in differentiating occlusions in carotid.

1.4.3 Feature selection

Dimension reduction is a necessary step in the effective analysis of massive high-dimensional datasets. Dimensionality reduction strategies may be characterized by feature selection process. The feature selection approach attempts to reduce the number of variables by selecting the best subset of the original feature set, according to some criterion (Ferrigno et al 1998).

Principal Component Analysis (PCA) is a statistical method used to transform the input space into a new lower dimensional space and has been used to identify and summarize many inter-relationships that exist among individual variables. In this, inter-correlated variables are combined into a smaller number of new variables called principal components. The first principal component accounts for much of the variability in the data and each succeeding component accounts for the remaining variability. The uncorrelated variables are linear combinations of the original variables and the last of these variables can be removed with minimum loss of real data in order to identify new meaningful underlying variables. Statistically, the observed correlation matrix is used to make inferences about the identities of any latent variables. It is an automated and systematic examination of correlations among manifest variables, aimed at identifying underlying latent principal components (Samanwoy et al 2008, Hughes et al 2004). PCA technique has been investigated previously by researchers for signal and image processing applications (Salaffi et al 2000).

1.4.4 Classification

The primary goal of pattern classification is supervised or unsupervised learning. Among the various frameworks in which statistical pattern recognition has been traditionally formulated, the statistical approach has been most intensively studied and used in practice. Multilayer perceptron or feedforward neural network schemes and methods from statistical learning theory, such as, logistic regression, k-nearest neighbour, multiple linear regression, and support vector machine have been used already in classifying patterns. However, it is clear that gradient descent-based learning methods are generally very slow due to improper learning steps or may easily converge to local minima. And many iterative learning steps may be required by such learning algorithms in order to obtain better learning performance

(Huang et al 2006). Recently, Extreme Learning Machine (ELM) has been proposed, which significantly reduce the amount of time needed to train a neural network.

Extreme Learning Machine (ELM) is a new data mining scheme used as a decision making tool. The ELM modeling scheme is a new framework unlike the standard neural network, it is a Single Hidden Layer Feedforward Neural networks (SLFNs) which randomly chooses the input weights and analytically determines the output weights. It also tends to provide the best generalization performance at extremely fast learning speed.

ELM has several advantages such as ease of use, faster learning speed, higher generalization performance, suitable for many nonlinear activation function and kernel functions. ELM requires higher number of hidden neurons due to the random determination of the input weights and hidden biases (Liu & Wang 2010). ELM is used with many nonlinear activation function and kernel functions to provide less training time and high classification accuracy. It is extended to the case of radial basis function networks, which allows the centres and impact widths of RBF kernels to be randomly generated and the output weights be calculated.

In biomedical studies, diagnostic tools and techniques are used to determine the presence or absence of diseases. Validation of the tools and techniques is an evaluation method that is used to determine its robustness for a particular use. Validation involves calculating objective measures of test performance, such as, sensitivity, specificity, positive predictive value and negative predictive value. The ideal diagnostic test would correctly identify subjects with and without the disease with 100% accuracy (Fawcett 2006).

1.5 OBJECTIVES OF THE THESIS

The following are the objectives of the thesis:

- Extraction of sub anatomic regions in femur radiographic images,
- Quantitative analysis of anisotropy in the delineated sub anatomic regions using spectral and multiscale spatial methods, and
- Exploring the possibility of identifying abnormality using anisotropic indices and machine learning methods.

1.6 ORGANISATION OF THE THESIS

The work reported in the thesis is organized into 6 chapters. Chapter 2 gives a comprehensive review of the literature on assessment of trabecular architecture, using wavelets, Gabor, quaternions, structure tensor, lacunarity and succolarity. Spectral analysis using different wavelet transforms are also discussed. And also the features selection technique and classification scheme are included. Chapter 3 describes the methods and protocols; Chapter 4 focuses on the results of the above mentioned methods. Chapter 5 deals with the significant conclusions.