RADIOGRAPHIC ASSESSMENT OF THE ASSOCIATION OF UPPER FEMUR GEOMETRY AND TEXTURE FEATURES TO HIP OSTEOARTHRITIS AND FRACTURE

Yaw Adjei
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Master’s Program in Biomedical Engineering: Biomechanics and Imaging
Faculty of Medicine
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Abstract

Osteoarthritis (OA) is a common joint disease found mostly in the elderly that progressively leads to the loss of articular cartilage, along with subchondral bone changes (sclerosis) and joint space narrowing, eventually resulting in joint failure. Osteoporosis (OP), another bone disorder mostly of the elderly, is the gradual loss of bone tissue mass (bone mineral density (BMD)) resulting in reduction in bone strength and an increased risk of fracture. Bone geometry also plays a role in developing a fracture or not. OA causes increase in bone volume, but fracture is still prevalent in OA patients. The aim of this study was to investigate association of upper femur geometry and texture features to hip OA and hip fracture using radiography.

Supine anteroposterior radiographs of hip and BMD from 125 postmenopausal women were used for this research. Hip geometry parameters and texture related parameters were obtained from the radiographs. Participants’ weight, height, and body mass index (BMI) were also used in this research.

OA was found in women with higher weight, BMI, femur neck BMD, neck diameter (ND), and neck cortex thickness, and shorter joint space width (JSW). OA women also had higher homogeneity index of Laplacian images of femur neck and lower entropy of Laplacian images of femur neck. Fractures were more common among women with lower neck BMD, and higher femoral neck axis length, JSW, hip axis length (HAL) and acetabular width (w). For cervical fractures, JSW and w were higher. Women with trochanteric fractures had lower neck BMD and head diameter, and higher ND and HAL. Upper femur geometry may play a role in the initiation and progression of OA and OP, and trabecular microarchitectural changes in OA are relatively distinct. Higher weight, BMI and neck BMD are predisposing factors for OA. Lower neck BMD is a predisposing factor for trochanteric fracture.

Keywords: Osteoarthritis, osteoporosis, radiography, fracture, upper femur geometry, image texture analysis.
## List of Abbreviations and symbols

<table>
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<th>Term</th>
<th>Description</th>
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<tr>
<td>2D</td>
<td>Two Dimensional</td>
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<td>3D</td>
<td>Three Dimensional</td>
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<td>ADR</td>
<td>Acetabulum Depth Ratio</td>
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<td>BMD</td>
<td>Bone Mineral Density</td>
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<td>BMI</td>
<td>Body Mass Index</td>
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<td>CCD</td>
<td>Charge-Coupled Device</td>
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<td>CT</td>
<td>Computed Tomography</td>
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<td>d</td>
<td>Acetabulum depth</td>
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<td>ELV</td>
<td>Extra Low Voltage</td>
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<td>Ent_Lap_head</td>
<td>Entropy, obtained from Laplacian of femur head</td>
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<td>Ent_Lap_neck</td>
<td>Entropy, obtained from Laplacian of femur neck</td>
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<td>Ent_LBP_head</td>
<td>Entropy, obtained from Local Binary Pattern of femur head</td>
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<td>Ent_LBP_neck</td>
<td>Entropy, obtained from Local Binary Pattern of femur neck</td>
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<tr>
<td>FACIT</td>
<td>Fibril Associated Collagens with Interrupted Triple helices</td>
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<td>FNAL</td>
<td>Femoral Neck Axis Length</td>
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<td>FNC</td>
<td>Femoral Neck Cortex Thickness</td>
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<td>GLCM</td>
<td>Gray Level Co-occurrence Matrix</td>
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<td>HAL</td>
<td>Hip Axis Length</td>
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<td>HD</td>
<td>Femoral Head Diameter</td>
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<td>HI_Lap_head</td>
<td>Homogeneity Index, obtained from Laplacian of femur head</td>
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<td>HI_Lap_neck</td>
<td>Homogeneity Index, obtained from Laplacian of femur neck</td>
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<td>JSW</td>
<td>Hip Joint Space Width</td>
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<tr>
<td>LBP</td>
<td>Local Binary Pattern</td>
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<td>ND</td>
<td>Femoral Neck Diameter</td>
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<td>Acronym</td>
<td>Description</td>
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<tr>
<td>NICE</td>
<td>National Institute for Health and Care Exchange</td>
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<td>NSA</td>
<td>Neck Shaft Angle</td>
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<td>OF</td>
<td>Obturator Foramen</td>
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<td>SD</td>
<td>Standard Deviation</td>
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<td>SDM</td>
<td>Signature Dissimilarity Measure</td>
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<td>w</td>
<td>Acetabulum width</td>
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<td>$\mu$</td>
<td>Attenuation Coefficient</td>
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1. Introduction

Osteoarthritis (OA) and osteoporosis (OP) are two common medical conditions of the elderly that are often associated with disability (or reduced mobility) (Lane 2007) and fracture (Cosman et al. 2014, Hernlund et al. 2013, Kanis et al. 2013) respectively, coupled with their huge economic burden they place on patients and the national health care of many countries. At the advanced stages of the diseases most patients of OP or OA may need a form of (replacement) surgery, especially if it involves loading bearing joints like hips and knees.

OA probably results from the progressive degeneration of articular cartilage, along with changes (sclerosis) of the subchondral bone. Other usual macroscopic changes of the subchondral bone associated with OA are the formation of subchondral bone cysts and osteophytes. (Buckwalter et al. 2005, Lane 2007, Li et al. 2013). OA generally affects all tissues of the (synovial) joint; articular cartilage, subchondral and metaphyseal bone, synovium, ligaments, joint capsules, and the muscles that acts across the joint, leading to joint failure (Buckwalter et al. 2005). OA pathogenesis is not understood (Lane 2007, Buckwalter et al. 2005). OA has no cure, but when detected early, the progression of the disease can be impeded (Buckwalter et al. 2005, Egloff et al. 2012, Lane 2007).

Medical diagnosis of OA is usually confirmed with plain radiograph of the affected joint based on the Kellgren-Lawrence (KL) grading with the presence of other complementary symptoms of the disease. Radiographic diagnosis and grading of OA is based on joint space narrowing, subchondral bone density increase, deformity of the bone ends, and presence of osteophytes (Buckwalter and Martin 2006, Kellgren and Lawrence 1957). KL grading is subjective, semi quantitative, with reported moderate to substantial intra- and interrater reliability variation among assessors. (Damen 2014, Günther and Sun 1999, and Kellgren and Lawrence 1957). Thus an improved diagnostic criteria of OA where there will be higher specificity and reduced (or no) intra- and interrater differences, and user independent will be a highly appreciated model.

Prior studies on radiographic categorization of OA mainly focuses on joint space width measurement (Buckland-Wright 1999) and the presence of osteophytes. (Altman et al. 1991, Kellgren and Lawrence 1957) Kinds et al. (2011) demonstrated the use of bone density estimation in discriminating OA from control patients from plain radiographs,
which is usually affected by image acquisition parameters and post-processing algorithms (Kinds et al. 2011). Another potential method of extracting information related to bone structure from plain radiograph is texture analysis. Texture analysis is independent of imaging conditions. Hirvasniemi et al. (2014) showed the potential of Laplacian and Local Binary Patterns (LBP) in bone OA analysis of the knee, whose effectiveness has not been studied in hip OA as of now.

OP is a skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, thereby predisposing a bone to fracture. (Cosman et al. 2014, Hernlund et al. 2013, Kanis et al 2013, WHO 843 1994). OP is an asymptomatic disease, and is usually detected in the advanced stage when the disease is complicated by fracture(s)—spontaneous or by minimal trauma (Cosman et al. 2014).

Areal (or sometimes volumetric) bone mineral density (BMD) measurement, assessed with Dual energy X-ray Absorptiometry (DXA), is the usual diagnostic procedure used to confirm the existence of OP (Cummings et al. 1993, Johnell et al. 2005, Marshall et al. 1996, Schott et al. 1998). Notwithstanding the high specificity of BMD in predicting the existence of OP, studies have shown that individuals with BMD outside the osteoporotic range are also liable to fracture (Marshall et al. 1996, Schuit et al. 2004, Stone et al. 2003). Biomechanical analysis also show that the mechanical strength of bone is not determined by only BMD (bone mass), but also by other factors which are not captured in BMD analysis. Pulkkinen et al. (2010) showed that the commonly used T-score criterion classification of OP (T-score ≤ -2.5) better discriminates trochanteric fractures from controls, and that about half of cervical hip fractures occur in individuals with BMD outside the osteoporotic range. It has also been shown that individuals with trochanteric fractures usually have general and higher bone loss (Duboeuf e al. 1997, Mautalen et al. 1996, Pulkkinen et al. 2004, Schott et al. 2005), whereas cervical hip fractures are dictated by femur structural parameters (Duboeuf e al. 1997, Gnudi et al. 2002, Partanen et al. 2001, Pulkkinen et al. 2004, Pulkkinen et al. 2010, Pulkkinen et al. 2011). In order to capture all the risk factors associated with developing fracture, other imaging modalities like Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) (Bauer et al. 2006, Baum et al. 2010, Herlidou et al. 2004, Huber et al. 2008, Hudelmaier et al 2005, Lammentausta et al. 2006, Müller et al. 2006, Showalter et al. 2006), which are three-dimensional (3D), have been used to assess the risk of fracture. With plain radiography
being relatively cheap and widely available, it still suffice to improve the specificity of it. Skeletal trabecular texture (Benhamou et al. 2001, Boehm et al. 2009, Chappard C et al. 2005, Gregory et al. 2004, Vokes et al. 2006) and geometrical (Gnudi et al. 2002, Gnudi et al. 2012, Partanen et al. 2001, Pulkkinen et al. 2004, Pulkkinen et al. 2010, Pulkkinen et al. 2011) analyses of OP bones continue to be on the rise. In a recent study by Thevenot et al. (2014), it was demonstrated that trabecular bone texture analysis was a better predictor of femoral neck fracture than BMD using homogeneity index calculated from gray level co-occurrence matrix (GLCM) of Laplacian images from plain radiographs. In this study, the use of femur upper geometry and bone texture features in the prediction of hip OA and fracture was investigated. Supine anteroposterior hip radiographs from 125 postmenopausal women were used for this research. BMD of each participant was also taken. Hip geometry parameters and trabecular texture features were extracted from the radiographs to ascertain their correlation with hip OA and fractures. Participants’ weight, height, and body mass index (BMI) were also collected to assess their relevance in the development of OA and fracture.
2. Literature Review

2.1 Articular cartilage, bone, and subchondral bone

The hip joint, which is a synovial joint, is made up of the following tissues; hyaline articular cartilage, joint capsule, synovium, ligament, meniscus and subchondral bone. The bone in the human hip joint include the upper femur and the lateral inferior section of the pelvic (around the acetabulum). The hip transmits load from the trunk to the lower limbs.

2.1.1 Composition and Structure of Articular Cartilage

Articular cartilage is a hyaline cartilage, with a substantial volume which does not ossify. It consists of cells, water and macromolecule matrices. The matrices define the mechanical properties of the articular cartilage. Chondrocytes, the only cell in normal articular cartilage, contribute to about 1% of the total volume of mature human articular cartilage. The wet weight of the articular cartilage is about 80% water. Articular cartilage fluid also contains gases, cations (e.g. Sodium) and the macromolecules. Twenty to 40 per cent of the wet weight of the articular cartilage is structural macromolecules, i.e. collagens, proteoglycans, glycoproteins, and non-collagenous proteins. (Buckwalter et al. 2005).

Each chondrocyte is surrounded by an extracellular matrix, but remains metabolically active (anaerobic) (Buckwalter and Mankin 1997), and have the essential organelles required for matrix synthesis, including endoplasmic reticulum and Golgi membranes. Dry cartilage contains about 60% collagen, 25 to 35% proteoglycans, and 15 to 20% proteins and glycoproteins. Collagen type II is the most abundant collagen in the cartilage, making up 90 to 95% of the collagens. The structural arrangement of the various collagen fibers into a tight network throughout the articular cartilage defines the tensile stiffness and strength of the tissue, and also helps in holding together the large proteoglycans and the non-collagenous proteins. The principal proteoglycans found in articular cartilage are large aggregating proteoglycan monomers or aggrecans and small proteoglycans including decorin, biglycan, and fibromodulin (Buckwalter and Mankin 1997). The
proteoglycans are usually negatively charged, and are bonded to the cations in the cartilage fluid. Most of the interfibrillar space of the cartilage matrix are filled by aggrecans, making up about 90% of the total cartilage proteoglycan mass. There are a variety of non-collagenous proteins and glycoproteins found in normal articular cartilage, but their functions and behaviour are not well understood. (Buckwalter et al. 2005).

The depth from the surface of the articular cartilage determines its cellular morphology and probably function. The depth also determines the composition, organization, mechanical properties of the matrix. The articular cartilage can be divided into four zones; calcified, deep, transitional and superficial zones. Figure 1 shows the structure of articular cartilage and subchondral bone, with the appropriate zones. The boundaries of the various zones cannot be distinctively defined, as there is a smooth transition of cellular and matrix composition from one zone to the next zone. (Buckwalter et al. 2005).

The superficial zone is the thinnest zone of the articular cartilage, and it is made up of two layers. An acellular sheet of fine fibrils with little polysaccharide is the topmost layer of the superficial zone. Lying inferiorly to the acellular sheet is a flat ellipsoidal-shaped chondrocyte whose major axis are parallel to the articular surface. The matrix synthesized by these chondrocytes has a high concentration of collagen, but low concentration of proteoglycan relative to the other cartilage zones. The high concentration of collagen in this layer contribute to the relatively high tensile stiffness and strength, but low permeability of the superficial zone. This zone also contains the highest concentration of water and fibronectin. (Buckwalter et al. 2005).

The transitional zone is usually several times bigger, and its cell have higher concentration of synthetic organelles, endoplasmic reticulum and Golgi membranes compared to the superficial zone. Cells of the transitional zone appear spheroidal in shape and synthesize a matrix that has larger-diameter collagen fibrils, a higher concentration of proteoglycan, but lower water concentrations and collagen than superficial zone matrix. (Buckwalter et al. 2005). The transitional zone is very resistant to compression (kneejointsurgery.com 2015).

The deep zone has spheroidal shaped chondrocytes, which lie perpendicular to the joint surface. The largest-diameter collagen fibrils, and the highest concentration of proteoglycans are found in this zone, but has the least water concentration. (Buckwalter et al. 2005). The deep zone is also very resistant to compression. (kneejointsurgery.com
The calcified zone, which is relatively thin, separates the uncalcified deep zone from the subchondral bone. The calcified zone cells have a smaller volume relative to the deep zone, with only small amounts of endoplasmic reticulum and Golgi membranes. (Buckwalter et al. 2005). A thin basophilic line, known as tidemark, sectionalizes the calcified zone from the uncalcified zones (Buckwalter et al. 2005), and a sharp borderline called cement line also separates the calcified cartilage from the subchondral bone (Li et al. 2013).

**Figure 1.** The Structure of Articular Cartilage and Subchondral Bone.

### 2.1.2 Composition and Structure of Bone

The human bone is a metabolically active live tissue, undergoing a lifetime modelling and remodelling. Bone modelling is the process whereby bones change their overall shape and size in response to physiological influences and mechanical forces to help the skeleton to adapt to changing biomechanical forces so as to remove damage and maintain
bone strength (Clarke 2008, Kobayashi et al. 2003). Bone remodelling is the process in which old and micro-damaged bones are replaced with new mechanically stronger bones to help preserve bone strength (Burr 2002, Clarke 2008, Parfitt 2002, Raisz 1999). Bone modelling rarely occurs in adults than remodelling (Kobayashi et al. 2003), but may be altered by diseases or pharmacological agents (Lindsay 2006, Ubara et al. 2003, Ubara et al. 2005). A variety of human bones make-up the skeletal system, the classification of which may be based on macrostructure, or microstructure and content. At the macrostructure level, a bone may be classified as, long, short, flat or irregular. By content, a bone may be trabecular or cortical.

Long bones (Figure 2) are made-up of a hollow shaft or diaphysis; a flared, cone shaped metaphysis beneath the growth plates; and above the growth plate is rounded epiphysis. A dense and solid cortical bone make-up the diaphysis, while the metaphysis and epiphysis are composed of honeycomb-like network trabeculae bone surrounded by a relatively thin shell of a dense cortical bone. At joints, subchondral bone surrounds the trabecular bone, which are finally lined by articular cartilage. (Clarke 2008).

In human adults, 80% of the skeleton is cortical bone, with the remaining 20% being trabecular bone, and the ratio of cortical to trabecular is different for different bones and skeletal sites. The radial diaphysis has the highest amount of cortical bone, 95% to 5% trabecular. (Clarke 2008).

Osteons are the basic units of both cortical and trabecular bones. Cortical osteons are known as the Haversian system, which are in the shape of a cylinder, with approximate length of 400mm and 200mm base width, and forming a network of branches within the cortical bone. Haversian system walls are formed from concentric lamellae. Metabolically, cortical bones are less active relative to trabecular bone in humans. The higher the cortex undergo remodelling, the less dense it becomes, thus increased porosity. Normally, healthy aging adults have a thinning cortex and increased cortical porosity. (Clarke 2008).

Lining the inner and outer surfaces of cortical bones are the endosteum and periosteum respectively. The periosteal surface normally experience higher bone formation than resorption, which contributes to increase in bone diameter with age. However, endosteal bone formation is typically less than resorption, contributing to the expansion of marrow
with age. Osteons of the trabecular are called packets, which are made up of plates and rods averaging 50 to 400mm in thickness. (Clarke 2008).

Cortical and trabecular bones are normally formed in lamellar pattern, which involves the laying of collagen fibrils in alternating orientations (Eriksen et al. 1994, Seeley et al. 1998), which contribute to the strength of normal lamellae bones. Woven bones, which are made of collagen fibril laid in a disorganised manner, are weaker than lamellae. Woven or primary bone is the first type of developmental bone formed, and may also be seen in high bone turnover abnormal conditions such as osteitis fibrosa systica and Paget’s disease. (Clarke 2008).

Surrounding the outer cortical bone surface is the periosteum, a fibrous connective tissue containing blood vessels, nerve fibres, and osteoblasts and osteoclasts. At the outer cortical surfaces of the bone, the periosteum perforate into the underlying bone tissues, hence attaching tightly to the bone by thick collagenous fibers known as the Sharpey fibres (Clarke 2008, Seeley et al. 1998).

During childhood and adolescence, longitudinal and radial growth of the bones occurs. During bone remodelling, discrete packets of old bones are removed and replaced by newly synthesized proteinaceous matrix, which subsequently mineralized to form new bone, thus preventing bone microdamage. Bone remodelling starts during foetal development till death. (Clarke 2008).

Four types of cells are found in human bone; osteoprogenitor cells, osteoblasts, osteocytes, and osteoclasts. Osteoblasts form bone tissues, osteocytes maintain them, and are broken down by osteoclasts. Osteoprogenitor cells are precursors to osteoblasts, which become osteocytes after matrix mineralization. Osteoprogenitor cells, derived from mesenchyme, are unspecialised and divide through mitosis, and are found on all bone surfaces. (University of Glasgow 2015).

Terminally differentiated osteoblasts are known as osteocytes, and osteocytes function within syncytial networks to support bone structure through intercellular adhesion, and bone metabolism by regulating the exchange of mineral in the bone fluid within lacunae and canalicular network. During osteolysis (bone resorption), osteocytes may function as phagocytes due to their lysosome content. Osteocyte-osteoblast cell syncytium are primarily mechanosensors (Bonewald 2006) and that stress signals from bending and stretching of bone are transduced into biological activity by them. The average half-life
of osteocytes is 25 years (Knothe Tate et al. 2004). Oestrogen deficiency (Plotkin et al. 2005) and glucocorticoid treatment may trigger osteocyte apoptosis. Bone remodelling is carried out by bone remodelling units, composed of tightly coupled group of osteoclasts and osteoblasts that sequentially resorb old bones and form new ones. Osteoclasts secret acidifying H+ ions to dissolve bone matrix. Osteoblasts that are matured and active secrete collagen type I and other matrix proteins in a vectorial fashion to form bone. These matured active osteoblasts have large nuclei, enlarged Golgi structures, and extensive endoplasmic reticulum. Microarchitectural deterioration is caused by high bone turnover with greater bone resorption than formation. (Clarke 2008).

At the molecular level, composition of bone by percentage is; 50 to 70% mineral, 20 to 40% organic matrix (protein), 5 to 10% water, and less than 3% lipids. Hydroxyapatite \((\text{Ca}_{10} \text{(PO}_4)_6 \text{(OH)}_2)\) is the dominant mineral in bones, with small amounts of Carbonate, Magnesium and acid Phosphate. Collagenous proteins make up 85 to 95% of bone.

**Figure 2.** Structure of Normal Bone.
proteins, mostly collagen type I (Brodsky and Persikov 2005), with very small amounts of collagen types III and V, and Fibril Associated Collagens with Interrupted Triple helices (FACIT). Collagen types III, V, and FACIT are only found in bones at certain stages of bone formation, and may help determine the diameter of collagen fibril. The nonfibrillar collagens, FACIT, act as molecular bridges to facilitate the organisation and stability of bone extracellular matrices. The remaining 10 to 15% bone protein, which are non-collagenous, include proteoglycans, glycosylated proteins, and γ-Carbonated Proteins. On molar basis, equal amounts of collagenous and non-collagenous proteins are synthesized and secreted by osteoblasts. (Clarke 2008).

Bone’s mechanical rigidity and load-bearing strength is determined by its mineral content, while its elasticity and flexibility is dependent on the amount of organic matrix present (Seeley et al. 1998). Laying of bone mineral first begins at the hole zones between the ends of collagen fibrils. Vitamin D indirectly excites the mineralization on unmineralized bone matrix. Dentin matrix protein 1 and bone sialoprotein are the main promoters of bone mineralization. (Clarke 2008).

About 50 to 70% of bone strength is determined by bone mass. The larger a bone is, the stronger it is regardless its mineral density. Bone strength increases to the fourth power for every radial increase. The ratio of cortical to trabecular bone at a given skeletal site independently affect bone strength. (Clarke 2008).

The skeletal bones serve as a framework for the rest of the body, aid in movement and locomotion through the provision of levers for the muscles, maintain mineral homeostasis and acid-base balance, maintain a conducive environment for haematopoiesis within the marrow spaces (Parfitt 2002), store growth factors and cytokines for future use, and enclose and protect vital internal organs and structures. (Clarke 2008, Seeley et al. 1998).

### 2.1.3 Composition and Structure of the Subchondral Bone

The subchondral bone lies just underneath the deep calcified articular cartilage (Burr and Gallant 2012, Madry et al. 2010). The subchondral bone consist of two distinct anatomic entities: the subchondral bone plate and subchondral trabecular bone (Clark and Huber 1990), both of which are lamellae. (Goldring and Goldring 2010, Li et al. 2013). The subchondral bone plate, a thin cortical lamella, lies just beneath the calcified cartilage
(Clark and Huber 1990, Milz and Putz 1994). The subchondral bone (end) plate is porous structure with channels occupied by vessels and nerves. These vessels and nerves run from the subchondral trabecular to the calcified cartilage (Holmdahl and Ingelmark 1950, Madry et al. 2010). The channels are more at highly stressed areas of a joint. The channels are narrower and form a tree-like mesh in regions with thicker subchondral bone plate, while they are wider and ampulla like at thin regions (Milz and Putz 1994). Supporting the subchondral bone plate is the subchondral trabecular bone (Clark and Huber 1990, Madry et al. 2010). The subchondral bone trabecular functions as a shock-absorber (Kawcak et al. 2001) and also may play important role in cartilage nutrient supply and metabolism (Castañeda et al. 2012). The subchondral trabecular is more porous and metabolically active, with more blood vessels, sensory nerves, and bone marrow than the subchondral bone plate (Suri and Walsh 2012). Subchondral trabecular bone structure exhibit preferential spatial orientation and parallelism, that is, mechanically anisotropic (Holopainen et al. 2008). The subchondral bone is a dynamic structure that adapt to mechanical stress imposed across the joint, thereby adjusting trabecular orientation and scale parameters in according to the principal stress on the joint through bone modelling and remodelling (Goldring 2012, Holopainen et al. 2008, Kawcak et al. 2001, Milz and Putz 1994, Walker et al. 2013).

### 2.2 Osteoarthritis

OA is a joint disease characterize primarily by the progressive loss of normal articular cartilage structure and function due to cartilage degeneration, along with subchondral bone remodelling and sclerosis, and usually subchondral bone cysts and marginal osteophytes formation. OA causes all the joint structures to undergo pathological change simultaneously, but usually the first to be affected is the superficial zone of the articular cartilage. (Li et al. 2013). Other names for OA are degenerative arthritis and hypertrophic arthritis. OA is one of the leading causes of disability in the elderly (Lane 2007). OA is more common in people over 60 years, and in elderly women more than men (Li et al. 2013), and it usually leads to inflammation of the affected joint, (Lane 2007) hence the suffix –itis. OA usually affect the vertebrae, hip, knee, foot and hand joints. In OA, the progressive loss of articular cartilage occur together with the attempted repair of articular
cartilage, remodelling and sclerosis of the subchondral bone, and usually the formation of subchondral bone cysts and marginal osteophytes (Lane 2007, Li et al. 2013). Deeper trabecular texture analysis has also revealed microscopic changes in the trabecular as well (Papaloucas et al. 2005). In some other instances, especially following extreme mechanical damage, chondrocytes of the articular cartilage may die, making tissue repair almost impossible. OA may also cause pain, restriction of movement, (Lane 2007) crepitis with movement, effusion and deformity at the affected joint. Changes that occur in the subchondral bone include increased density or subchondral sclerosis, formation of cysts and fibrous or cartilaginous tissue, and osteophytes. (Lane 2007, Li et al. 2013). At the latter stages of the disease, when articular cartilage has been completely lost, thickened, dense subchondral bone will be articulating with a similar opposing denuded bony surface, which is usually the cause of crepitus. OA may lead to shortening of the limb (s) involved, deformity and instability due to the combined effect of bone remodelling and articular cartilage loss. Articular cartilage loss leads to secondary changes in the synovium, ligaments, capsules and the muscles that move the affected joint. The synovial membrane usually become inflamed in response to the change of its normal environment. (Buckwalter et al. 2005).

OA may develop of an unknown cause, for which it is called primary osteoarthritis or idiopathic osteoarthritis (Lane 2007), which happens to be the most common osteoarthritis. However, osteoarthritis caused by joint injury, infection, hereditary factor (s), or developmental, metabolic (Lane 2007) and neurologic disorders is known as secondary osteoarthritis. (Buckwalter et al. 2005).

Postulated risk factors for primary OA risk are advanced age, genetic predisposition for OA, (Lane 2007) hormonal and metabolic disorders, inflammation, and immunologic disorders. (Buckwalter et al. 2005).

2.2.1 Diagnosis of OA

OA diagnosis primarily includes symptoms identification, review of medical history, and physical examination. Plain radiography is usually used to ascertain the existence of OA. Magnetic Resonance Imaging (MRI), arthroscopy, and laboratory examination of synovial fluid are other complementary procedures in the diagnosis of OA.
Symptoms and signs of OA include, gradual onset of pain, morning stiffness and pain (Lane 2007), restriction of movement, crepitus with joint movement, joint effusions, joint deformities and subluxations (Buckwalter et al. 2005). OA diagnosis with plain radiographs is usually based on the Kellgren-Lawrence grading (Table 1) (Kellgren and Lawrence 1957).

**Table 1.** Classification criteria for different Kellgren-Lawrence (KL) grades in the hip.

<table>
<thead>
<tr>
<th>KL grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – Normal</td>
<td>No radiographic features of osteoarthritis (OA)</td>
</tr>
<tr>
<td>1 – Doubtful OA</td>
<td>Doubtful narrowing of joint space and possible osteophytes</td>
</tr>
<tr>
<td>2 – Minimal OA</td>
<td>Definite osteophytes and narrowing of the joint space</td>
</tr>
<tr>
<td>3 – Moderate OA</td>
<td>Moderate multiple osteophytes, definite narrowing of the joint space, some sclerosis, and possible deformity of bone contour</td>
</tr>
<tr>
<td>4 – Severe OA</td>
<td>Large osteophytes, marked narrowing of the joint space, severe sclerosis, and definite deformity of bone contour</td>
</tr>
</tbody>
</table>

MRI, a non-invasive imaging modality with no radiation exposure can be used to visualize joint morphology; volume, thickness, articular cartilage, curvature, and changes in subchondral bone (Burstein and Gray 2003, Lammentausta et al. 2006). A white blood cell count of less than 1000 per cubic millimetre is an indication of OA. Alternatively, erythrocyte sedimentation rate of less than 20mm/hr is also an indication of OA (Lane 2007).

According to the American College of Rheumatology hip OA is expected if hip pain exist with at least any 2 of the following;

- an erythrocyte sedimentation rate of less than 20mm/hr
- radiographic evidence of femoral or acetabular osteophytes
- radiographic evidence of joint space narrowing (superior, axial, or medial)

2.2.2 **Treatment of OA**

OA treatment therapy aim to relieve pain and preserve function (Buckwalter et al. 2005, Egloff et al. 2012, Lane 2007). Both Pharmacological and non-Pharmacological regimens are used in the treatment of OA (Lane 2007). Fransen et al. (2014) showed that exercise interventions is an effective treatment for OA of the hip. Randomised studies on the treatment of OA using aquatic therapy and acupuncture showed functional improvement (Hinman et al. 2007, Witt et al. 2006). Weight loss may also be a good step in managing OA (Lane 2007). Walking with cane to improve balance and the use of insoles have also been suggested to limit the progression of OA. Pharmacological interventions like analgesics, at least effective doses, may be prescribed to relief pain. Analgesics like Nonsteroidal Anti-inflammatory Drugs (NSAIDS) can cause gastrointestinal disturbance like peptic ulcer, hence it is usually taken with proton-pump inhibitors. (Lane 2007).

For OA patients experiencing chronic discomfort and substantial functional impairment, arthroplasty, osteotomy, or at worst total (hip) joint replacement surgery may be considered to reduce pain and disability (Egloff et al. 2012, Lane 2007).

2.3 **Osteoporosis**

Osteoporosis (OP), literally meaning ‘porous bone’ is a disease of the skeletal system characterised by low bone mass and microarchitectural deterioration of bone tissue, which predisposes a bone to fracture (Cosman et al. 2014, Hernlund et al. 2013, WHO 843 1994). Sites usually affected by OP are the spine, hip, distal forearm and proximal humerus. OP fractures may remain asymptomatic or cause pain, immobility (especially hip fractures), loss of function (especially vertebra fractures) and mortality as well. The human bone is in a state of continual remodelling, with older bone tissues being replaced by new ones. A disruption in the balance between the rates of bone replacement and degradation, specifically with higher degradation rate than replacement, leads to osteoporosis (Cosman et al. 2014). OP is diagnosed by measuring the BMD (Blake and Fogelman 2007, Davidsson 2010), which is the amount of bone (mineral) mass per unit volume (volumetric density) or per unit area (areal density) (Davidsson 2010), both of
which can be measured in vivo using densitometric techniques (Blake and Fogelman 2007, Davidsson 2010). DXA remains the most widely used densitometric technique for measuring BMD. Other common methods of measuring BMD are Quantitative Ultrasound (QUS) and Quantitative Computed Tomography (QCT) (Davidsson 2010). DXA scans can be used to assess the bone mineral content (BMC) and BMD of the whole skeleton as well as of specific sites, which may be sites most vulnerable to fracture (Davidsson 2010, Genant et al. 1996). With most conventional X-rays being two dimensional, areal density rather than true volumetric density is used. In vitro studies of isolated vertebra and proximal femur showed that areal BMD accounts for about two-thirds of the variance of bone strength. The vertebral column and the femur remains the most assessed areas for BMD measurements. (Kanis et al. 2013).

X-ray-based BMD measurements exposes the body to (small amounts of) radiation.

### 2.3.1 Diagnosis of Osteoporosis

The most often used parameter for the description of BMD is the T- or Z-score, both of which are measured in units of standard deviation (SD). A person’s T-score is the difference between his/her BMD and the mean BMD in a healthy young adult, of the same gender and ethnic group, with the difference expressed as a ratio of the young adult population standard deviation (Figure 3). In Z-scores, a person’s BMD is subtracted by the mean BMD of persons of similar age, gender and ethnic group, and expressing the difference relative to age-matched population standard deviation. (Blake and Fogelman 2007) Z-score is mostly used in the assessment of children and adolescents OP (Kanis et al. 2013). Operationally, OP is defined based on the T-score for BMD assessed at the femoral neck. A person is classified as being osteoporotic if his/her BMD is 2.5SD or more below the mean BMD of a young adult of the population in question (WHO 2004) (Figure 3). A low BMD with SD between -1 and -2.5 is referred to as osteopenia. This diagnostic criteria is used because for any age and BMD at the femoral neck and hip, major osteoporotic fracture risks are the same for men and women (Looker et al. 1998), thus the femoral neck has been adopted as the reference site for the diagnosis of osteoporosis (Kanis and Glüer 2000). OP fracture risk factor of at least 1.5-fold exist for each SD decrease in BMD from the mean (Carmona 2004, Marshall et al. 1996). Some
risk factors for developing OP are age, glucocorticoid exposure, rheumatoid arthritis and low calcium intake (Cosman et al. 2014). Factors that predisposes a person to OP include: lifestyle (e.g. smoking, alcohol abuse, frequent falling), genetically predispose disease (e.g. cystic fibrosis), endocrine disorders (e.g. diabetes), rheumatologic and autoimmune diseases (e.g. lupus and rheumatoid arthritis), and so on (Carmona 2004).

![Figure 3. BMD Classification using T-scores.](image)

### 2.3.2 Treatment of OP

A variety of lifestyle treatment options exist for persons suffering from OP. These include adequate intake of Calcium and Vitamin D, lifelong participation in regular weight-bearing and muscle strengthening exercise, cessation of tobacco use for smokers, identification and treatment of alcoholism for alcoholics, and treatment of risk factors for falling. (Cosman et al. 2014).

For persons at higher risk of fracture (very low BMD), pharmacological interventions, and usually in combination with lifestyle treatment options, may be considered. Treatment with pharmacological interventions should not be a lifelong option, as there are usually unpleasant side effects, of which some are life threatening. Some of the effects of pharmacological drugs are, oesophagus and stomach inflammation, renal function
disturbances, rhinitis, epistaxis, myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, deep vein emboli and osteosarcoma. (Cosman et al. 2014).

2.4 Fractures

Fracture is a break in the continuity of a bone, with or without displacement of fragment. Fracture is always accompanied by soft tissue damage—torn vessels, bruised muscles, lacerated periosteum, and contused nerves (Duckworth and Blundell 2010). Complete fractures have complete break through the bone radial cross-section at the point of fracture and complete separation of bone is involved. In incomplete fractures, break in bone continuity is not complete radially at the site of fracture, but bone is continuous at parts of the bone at the point of fracture, e.g. greenstick fracture. (Newton 2015).

Non-comminuted fractures results in only two segments of bone, whereas comminuted fractures results in more than two bone segments. Comminuted fractures are usually difficult to fix compared to non-comminuted fractures, especially gross comminuted fractures. (Duckworth and Blundell 2010, Newton 2015).

Fracture that remain within the skin and the musculature surroundings is known as closed fracture. On the other hand, a fracture that is exposed to outside environment is known as open fracture. (Newton 2015).

Fractures may also be classified according to the anatomical location of the fracture. Examples of such classification are, diaphyseal, metaphyseal, epiphyseal plate, epiphyseal, condular, and articular fractures. In addition, the exact bone involved helps in ease identification of the location of the fracture (Newton 2015).

Alternatively, fractures may be named according the magnitude and direction of the force causing it. The common classifications are; transverse, spiral or oblique, greenstick, crush, burst, avulsion, and subluxation. (Duckworth and Blundell 2010, Newton 2015).

2.4.1 Causes of Fractures

The underlying cause of a fracture may be pathological or non-pathological (trauma). Trauma remains the major cause of fractures, which may be e.g. as a result of automobile or sports injury. Traumatic fractures are rarely predictable, since the amount of force
causing it is rarely calibrated. Most traumatic fractures are comminuted (or multiple). Pathological fractures are caused by an underlying bony or systemic disease(s), that makes one, many, or all bones of the skeletal system abnormal, thus becoming more susceptible to fracture. When bone becomes susceptible to fracture, a low-energy trauma usually fractures such bones. Even the person’s own weight may necessitate a pathologic fracture, thus fracture occurs spontaneously without any major trauma. Common diseases causing pathological fracture are type 2 diabetes (Giangregorio et al. 2012, Schwartz et al. 2011), neoplasia, bone cysts, osteoporosis, nutritional hyperparathyroidism, and osteomyelitis. (Newton 2015).

FRAX©, a computer based tool developed by a WHO Scientific group is also used in many health centres to predict probability of a future fracture. According to FRAX©, factors that predispose a person to fracture are; age, gender, prior osteoporotic fracture, low femoral neck BMD, low body mass index (BMI), oral glucocorticoids intake, rheumatoid arthritis, parental history of hip fracture, smoking, excessive alcohol intake, and other secondary causes of osteoporosis. (Cosman et al. 2014, University of Sheffield 2015).

2.4.2 Diagnosis of Fractures

Fractures diagnosis is done through review of fracture history, physical signs and radiological examination. Knowledge about the trauma type and severity may reveal an underlying pathological condition or not. Common symptoms like pain (and the severity of it), and loss of function are important indications of the type, location, and cause of fracture. Loss of sensation or motor power is an indicative of nerve or vascular damage. Physical indicators like tenderness, deformity, swelling, local temperature increase, crepitus, and loss of function, which may be present or not, are also associated with fractures. (Duckworth and Blundell 2010, Newton 2015).

X-ray examination gives additional information to that obtained by clinical judgment described above. Plain radiographs, which is two-dimensional (2D) is usually used. (Newton 2015) CT may be used to obtain 3D image of the fractured bone. Radiography may complement physical monitoring and evaluation of fracture healing process.
Radiography also helps reduce incision/open area during surgery. (Duckworth and Blundell 2010).

2.4.3 Hip Fractures

Fractures occurring in the area between the edge of the femoral head and 5cm below the lesser trochanter are termed as hip fractures (NICE 2014). Hip fractures are generally classified into two main groups, based on their location with regard to the capsule—intracapsular, and extracapsular fracture (Frost et al. 2010, Jones et al. 2015). Subgroups also exist within these two main classifications, depending on fracture location, fracture level, displacement or not, and comminution (Jones et al. 2015).

Fracture of bones within the hip capsule are termed intracapsular, and the most general types of them are femoral head fracture and femoral neck (cervical) fracture. Cervical fractures are of great medical concern because of their tendency to damage the small intracapsular vessels that provide the majority of the blood supply to the femoral head, thereby leading to higher morbidity and mortality from cervical fractures (Jones et al. 2015).

Extracapsular fractures are fractures occurring outside the hip capsule, and are commonly referred to as trochanteric fractures (Jones et al. 2015, NICE 2014).

2.4.4 Treatment of Hip Fractures

Fracture treatment generally involve reduction, maintenance of reduction, and rehabilitation. Open fractures require emergent medical attention, and often debridement may be needed. (Duckworth and Blundell 2010).

Fracture reduction is the surgical restoration of a fractured dislocated bone to the normal bone alignment. Some (closed) fractures may be reduced by manipulation under anaesthesia. Where anaesthesia is inappropriate, traction (usually for trochanteric fractures), a weight attached to gently pull bones together, may be used (Hip Fracture 2015). Misalignment of bone (fragment) may lead to functional impairment, difficulty in mobility or immobility, difficulty in uniting bones, soft tissue (nerves and vessels) damage, and low aesthetic appearance. Sometimes open reduction is employed for
accurate bone fixation. Fractured bone may also be stabilized with a nail or fixator after traction. (Duckworth and Blundell 2010).

After reduction, stability is maintained intrinsically for fractures which do not require additional stabilization, otherwise external splintage or internal fixation is applied (Duckworth and Blundell 2010). Most hip fractures are kept stable using internal fixation devices like screws, pins, plates (fastened with screws) and nails. Some displaced hip fractures may require hip arthroplasty (hemiarthroplasty or total hip replacement) (Hip Fracture 2015, NICE 2014).

In rehabilitation, the affected limb is moved and used as much as possible, and it is done when there is cortical-to-cortical union. Rehabilitation usually helps to stimulate complete union and prevent joint stiffness. (Duckworth and Blundell 2010).

2.5 X-rays

2.5.1 Basic Physics of X-rays

X-rays are emitted when high speed electrons are stopped by a target metal. The most common means of producing electrons is by thermionic emission. In thermionic emission, a current is passed through a metal of high melting point, where the current (energy) gained by the metal (free) electrons is converted to electron vibrational energy, causing the metal to heat. The vibrational energy of the electrons causes some of the electrons to move to higher energy state, thus becoming loosely bound to the metal atoms (Tutorvista 2015). With a higher positive voltage (metal) nearby the heated metal, the loosely bound electrons escape their atoms toward the higher positive voltage metal. The higher voltage metal is referred to as anode (target), and the heated metal is the cathode. (A level Medical Physics 2013, Beiser 2003a).

The accelerated electrons, upon reaching the anode with sufficient energy is usually able to knock-out electrons from the anode metal atoms, and give it sufficient kinetic energy to escape the metal atom (A level Medical Physics 2013). The minimum amount of energy required to liberate an electron from the surface of a metal is known as the work function of the metal (Beiser 2003a). The knocking out of electrons from the anode leads to the creation of holes, thereby ionizing the metal anode. If the accelerated electron from the
cathode has much energy, inner electron is liberated from the target anode atom. With inner electron liberation, the next higher orbital electron drops to fill the hole created in the lower orbital. The de-excitation of the higher orbital electron to lower orbital leads to release of photon whose energy is equal to the difference in energy level between the higher and lower orbital.

The photon released by the de-excitation of atom electrons is known as X-ray, for its frequency is in the x-ray range of the electromagnetic spectrum, with frequencies just above the Ultraviolet and below Gamma rays. Estimated frequencies of x-rays are $10^{17}$ - $10^{20}$ Hz.

The faster the accelerated electron (high kinetic energy), the more penetrating the resulting X-rays, and the greater the number of accelerated electrons, the greater the intensity of the resulting X-ray photon. For heavier atoms like tungsten, upon knocking out of an inner electron, e.g. a K-shell electron, a series of electron de-excitation happen, due to the subsequent filling of the lower orbital by higher orbital (s) till the hole moves to the last (outermost) orbital, all of which produces radiation of different wavelengths due to the difference in energy between the higher and the lower orbitals involved. This explains why X-ray spectra of metals are continuous in nature, with the highest intensity corresponding to the energy difference between L- to K-shell orbitals electron transition. (Beiser 2003a).

Two main types of X-ray radiation are produced using thermionic emission; bremsstrahlung (braking radiation) and characteristic radiation. Bremsstrahlung is caused by the decrease in kinetic energy of the accelerated cathode electrons by the target anode atoms’ electric field as the electrons get closer to the anode, and also causing a change in trajectory of the accelerated electrons. This change in kinetic energy is converted to X-ray photon radiation. The greater the kinetic energy of the accelerated electron and the heavier the anode metal, the more energetic the bremsstrahlung. Characteristic radiation is emitted when K-shell electron is knock-out by the accelerated electron and subsequent filling by higher orbital electron (s). For multi electron (heavier) metals like Molybdenum, there could be more than one characteristic radiation, since not only L-K electron transitions occur after knocking out K-shell electrons. (Beiser 2003a, Nave 2015).
Another phenomenon that contribute to the continuum of x-ray spectra in the Auger phenomenon. In the Auger phenomenon, higher energy x-ray photons emitted due to electron transition eject other higher orbital electrons of the same atom of the anode metal, leading to a decrease in the original x-ray photon energy that ejected the electron. (Beiser 2003b).

2.5.2 X-ray tube

The X-ray tube (figure 4) is an evacuated (vacuum) glass tube with a heating cathode and target anode some distance apart, and maintained at several kilovolts potential difference. Electrons are generated from the cathode through thermionic emission. The tube is evacuated to allow the flow of electrons from the cathode to the anode unimpeded. The anode is tilted to direct the generated x-ray through a relatively thin section of the glass envelope. The tilt of the target results in glancing collision by the electrons, with most of their energy (about 99%) going into heat. Thus effective cooling mechanism of the anode of an x-ray tube is required. This is achieved by rotating the anode, with the end immersed in a flowing water or oil. (Beiser 2003a).

Figure 4. X-ray Tube.
2.5.3 X-ray Detectors

A variety of x-ray detectors are available, they can be broadly be classified, according to the use, as for; imaging and dose measurement (Hendee and Ritenour 2002b and 2002c). For imaging, image contrast results from the difference in attenuation coefficients of the various body tissues (Hendee and Ritenour 2002a). Dense tissues like bones have high attenuation coefficients and as such appear brighter due to low energy X-ray hitting the detector, whereas loose or low dense tissues like fat and lipids have low attenuation coefficients and as such appear darker due to high energy x-rays hitting the detector (Hendee and Ritenour 2002c). Most imaging detectors use scintillator, e.g. Thallium-doped Caesium Iodide ((CsI) Tl) and Sodium Iodide (NaI (Tl)), which convert X-ray photons to light photons at an amplification, thus reducing the radiation exposure to the patient (Hendee and Ritenour 2002b). The needed image is then produced, on a film (e.g. silver bromide and silver iodide crystals in gelation matrix), using computed radiography technology (image first captured on storage phosphor, and later released upon exposure to light through a photomultiplier, and a computer is used to combine the received signals into image), or using semiconductor technology to convert the light photons to electric signals (photodiode/charge-coupled device (CCD)) which may then be processed with a computer to produce the needed image in digital format (Hendee and Ritenour 2002c). Most DXA systems use digital imaging technology because of their high spatial resolution (Davidsson 2010).

2.5.4 X-ray Absorptiometry

X-ray used in diagnostic radiology interaction with matter (body tissue) results in one of these three processes: coherent (elastic or Rayleigh) scattering, photoelectric absorption, and Compton (inelastic) scattering.

Rayleigh or Coherent scattering occurs when (low energy) X-rays incident on an atom, thus the atom receives energy only sufficient to cause bound electrons to vibrate at a frequency similar to that of the incident X-ray photon. The electron re-radiates a photon of similar energy (frequency), but with small change in direction (angle) without absorption. (Bailey et al. 2014). This elastic scattering is a source unwanted radiation to
diagnostic radiology personnel, but does not exceed 10% of the total interaction processes in diagnostic radiology. (Davidsson 2010).

Photoelectric absorption occurs when an x-ray photon with sufficient energy (greater than the binding energy of an orbital electron) incidents on a material, leading to the ionisation of the material. Ionisation is usually accompanied by the emission of a lower energy fluorescence, especially when the incident photon has sufficient energy to liberate electrons closer to the atomic nucleus, as higher orbital electrons drops to fill the holes created leading to the emission of photons. The probability of photoelectric absorption increases quite sharply with photon energy just slightly above an electron’s binding energy due to the following reasons: the increase in the number of electrons available for interaction, and the occurrence of resonance phenomenon when photon energy just exceeds the binding energy of a given shell. This phenomenon is known as absorption edge. (Bailey et al. 2014, Davidsson 2010).

Compton scattering occurs when an incoming photon ejects an atom’s electron (usually outer electron) and still have sufficient energy to continue, but in a new direction due to the loss of energy. (Bailey et al. 2014). Two main unwanted effects of Compton scattering are: image contrast reduction (which should be removed by collimation before detector), and major radiation source for radiology personnel. (Davidsson 2010).

When an X-ray photon $I_0$, incident on a matter, the above absorption processes contribute to the total attenuation of the X-ray flux passing through the matter to produce a new photon $I$, which is related by the equation 1 below (Davidsson 2010):

$$I = I_0 e^{-\mu t}$$

(1)

where, $I_0$ is the incident photon, $I$ is the attenuated photon, $t$ (cm) is the material thickness, and $\mu$ (cm$^{-1}$) is the linear attenuation coefficient.

The linear attenuation coefficient $\mu$ decreases with increasing incident photon energy in the diagnostic energy range, increases with matter (tissue) density due to the relative increase in number of atoms per unit volume, increases with atomic number due to the increase in nuclear forces for higher proton atoms, and increases sharply for energies just above the absorption edge energy.
Linear attenuation coefficient may be expressed as mass attenuation coefficient by representing the thickness as mass per unit area by multiplying the thickness by density.

2.6 Hip Geometry


In OA studies, upper femur geometrical parameters found to increase the risk of hip OA are, wider femoral neck diameter (ND) (Arokoski et al. 2002, Bendaya et al. 2015, Castaño-Betancourt et al. 2013, Javaid et al. 2009), a more medial centroid femur position (Javaid et al. 2009), greater cross-sectional moment of inertia of femur (Javaid et al. 2009), greater section modulus (Javaid et al. 2009), higher sacral slope (Bendaya et al. 2015), higher acetabular angle of Idelberger and Frank (Bendaya et al. 2015), higher femoral mechanical angle (Bendaya et al. 2015), pistol grip deformity (higher femoral head eccentricity) (Bendaya et al. 2015, Doherty et al. 2008), right–left asymmetries in centre-edge acetabular angle (Bendaya et al. 2015), longer hip axis length (HAL) (Castaño-Betancourt et al. 2013), higher pelvic width (Castaño-Betancourt et al. 2013), higher triangular index (femur head asphericity) (Castaño-Betancourt et al. 2013), acetabular dysplasia (lower Wiberg angle or lower acetabular depth (d)) (Castaño-Betancourt et al. 2013, Murphy et al. 1995, Reijman et al. 2005), and abnormal neck shaft angle (NSA) (extremely higher or lower) (Doherty et al. 2008).

For OP fractures, apart from the generally accepted predisposing factor—lower BMD—and other complementary factors outlined in the FRAX assessment tool, longer (HAL) (Duboeuf et al. 1997(cervical), Faulkner et al. 1993 (all), Gnudi et al. 2002 (cervical), Peacock et al. 1995 (general)), shorter ND (Duboeuf et al. 1997 (trochanteric)), lower medial calcar femoral cortex width (Partanen et al. 2001 (general), Pulkkinen et al. 2004 (all)), lower femoral shaft cortex width (FSC) (Glüer et al. 1994 (general), Partanen et al. 2001 (general and cervical), Pulkkinen et al. 2004 (all), Pulkkinen et al. 2010 (all)), lower femoral neck cortex width (FNC) (Glüer et al. 1994 (general), Partanen et al. 2001 (general and cervical), Pulkkinen et al. 2004 (all), Pulkkinen et al. 2010 (all)).
(general and cervical), Pulkkinen et al. 2004 (all), Pulkkinen et al. 2010 (all), lower femoral shaft diameter (FSD) (Partanen et al. 2001 (general and cervical), Pulkkinen et al. 2004 (general and cervical)), lower trochanteric width (Partanen et al. 2001 (general)), higher NSA (Alonso et al. 2000 (general), Gnudi et al. 2002 (cervical), Partanen et al. 2001 (general and trochanteric), Pulkkinen et al. 2004 (general and cervical), Pulkkinen et al. 2010 (general and cervical)), lower outer pelvic diameter (general and trochanteric) (Partanen et al. 2001), lower inner pelvic diameter (Partanen et al. 2001 (general)), and higher acetabular width (w) (Partanen et al. 2001 (cervical), Pulkkinen et al. 2004 (cervical)) may also contribute to upper femur fractures.

In this study, the relevance of the following upper femur geometries: NSA, femoral neck axis length (FNAL), HAL, HD, ND, FNC, hip joint space width (JSW), w, d, acetabular depth-to-width ratio (ADR), and obturator foramen width (OF), in relation to the development of hip OA and fracture were analysed.

2.7 Trabecular Texture Analysis

With observed trabecular microarchitectural changes in OA (Buckwalter et al. 2005, Lane 2007, Li et al. 2013) and OP (Cosman et al. 2014, Hernlund et al. 2013, Kanis et al. 2013, WHO 843 1994) conditions, bone trabecular texture analysis has also become a new research area for improved diagnosis of OA and OP. In OA, subchondral bone sclerosis has been reported to shield the deeper trabecular from loading stress, leading to localized osteoporosis. The net effect of this stress shielding is to cause fine to medium vertical trabeculae to thin and may be lost, whereas principal load bearing vertical trabecular thickens. Thickening of the vertical trabecular results in the recording of higher BMD of trabecular of OA patients. (Papaloucas et al. 2005). The main microarchitectural change that occur in OP is the aggravated loss of trabecular plates, thus thinning of trabecular rods. This lead to disordered and fragile skeletal microarchitecture (Cosman et al. 2014).

Hirvasniemi et al. (2014) the use of Laplacian and LBP was used to distinguish OA patients from controls. Majority of the texture analysis methods for OA have been applied on plain knee radiographs. A variety of texture operators have been used to discriminate OP fractures from controls. Both in vivo (Benhamou et al. 2001, Rachidi et al. 2008) and in vitro (Chappard et al. 2010, Le Corroller et al. 2012, Huber et al. 2009, Vokes et al. 2006) studies have shown the potential of radiographic texture analysis to discriminate OP fractures from controls. Other radiographic texture analysis is effective in the discrimination of OP fractures from controls when combined with BMD (Kolta et al. 2012 (in vitro), Lespessailles et al. 2008 (in vivo)). Studies by Wilkie et al. (2008) demonstrated the ability of radiographic texture analysis to monitor osteolysis over time. Chappard D et al. (2005) and Guggenbuhl et al. (2006) showed that bone texture analysis reflects the true volumetric structure of bones. The use of gradient (or Laplacian) based texture operators was used to discriminate hip OP fractures from controls by Pulkkinen et al. (2011) and Thevenot et al. (2014).

In this study, we focus on the use of entropy of LBP and Laplacian based, and Homogeneity Index of Laplacian based radiographic images of upper femur head and neck trabeculae for the analyses of the dependence hip OA and hip fracture on trabecular texture.
3. **Aims of the Study**

The main aims of this study were to investigate:

1. The association of different geometrical features in upper femur measured from pelvic radiographs to the hip OA and future hip fracture,
2. The relationship between the occurrence of hip OA and hip fractures, and
3. The association of upper femur bone texture parameters to the occurrence of OA and future hip fracture.
4. **Materials and Methods**

4.1 **Study Subjects**

The study sample consisted of 125 postmenopausal women, born between 1924 and 1927, inclusively, who were originally recruited from a larger population-based cohort study started in 1997 (Korpelainen et al. 2003). The selection was made from 618 postmenopausal who attended a follow-up study in 2006, during which their pelvic radiograph and BMD measurement of the femoral neck were taken. Participants’ weight, height, and body mass index (BMI) were also taken. Overexposed radiographs were excluded from the research. Detailed exclusion criteria can be found from Thevenot et al. 2014.

The fracture history of these selected women between December 1997 and June 2012 was obtained from hospital discharge registers. By June 2012, 23 of these women had experienced hip fracture.

The procedures of the study were in accordance with the Helsinki Declaration, and was approved by the formal ethics committee. Informed and written consent were obtained from all participants.

4.2 **Imaging, OA grading, and measurement of geometrical parameters**

Digital anteroposterior radiographic images of participants were acquired using an X-ray system (DR 9000; Eastman Kodak Company, Rochester, NY) at 70 kV; automatic exposure; resolution, 2560 x 3072 (pixel size; 0.139 x 0.139 mm²); and 14 bits. Images were taken with patients in standard supine position and the beam focused on the femoral head. Radiographs were acquired from the participants right hip (n = 123), except for patients (n = 2) in which it was not possible to image the right hip, mostly due to the presence of prosthesis in the right femur.

Public domain software developed by the National Institutes of Health (Image J, version 1.48v; [http://rsb.info.nih.gov/ij/](http://rsb.info.nih.gov/ij/)) was used to assess geometric parameters: NSA, FNAL, HD, ND, FNC, HAL, JSW, d, w, ADR, and OF (Figures 6 and 7). The dimensions were
determined by using a calibration scale, which consisted of a block of known distance, included in the radiographs.

**Figure 6.** Hip geometrical parameters measured from radiographs. A-B, femoral neck axis length (FNAL); A-F, hip axis length (HAL); B-E, joint space width (JSW); D-DD, head diameter (HD); C-CC, neck diameter (ND); femoral neck shaft angle (NSA); and femoral neck cortex thickness (FNC).
Figure 7. Hip geometrical parameters measured from radiographs. Acetabulum width (w) and depth (d); and ‘a’, obturator foramen width (OF).

To evaluate the reproducibility of the geometrical measurements, both intra- and interoperator of geometrical measurements were done. Two intraoperator measurements were made at an interval of 4 months for all the geometric parameters. A one-time measurement of the following geometric parameters: NSA, FNAL, HD, ND and FNC, for 93 of the images selected randomly by another operator was used to evaluate the interoperator reproducibility. Both intraoperator measurements were compared with that of the interoperator values, thus 2 interoperator reproducibility parameters were obtained. In all measurements, operators were blinded to the fracture, and KL grading of subjects. BMD measurements were made by using a DXA device (Delphi QDR series; Hologic, Bedford, Mass) from a standard supine anteroposterior position. The BMD was assessed at the femoral neck by using the standard protocol of the manufacturer’s software. OA classification was based on the KL grading (Table 1) (Kellgren and Lawrence 1957).
Processing of acquired radiographic images were performed with a custom-made algorithm (MATLAB version R2014b, The MathWorks, Inc., Natick, MA, USA) with a graphical interface that allows the user to rotate the image and select the region of interest (ROI) on the radiograph.

The ROI (size: 100 x 100 pixels) for the femur neck was at the femur inferomedial side (neck-to-head transition area) containing the principal compressive fibre group. Fibres orientation were parallel to the side of the rectangle used in selecting the ROI (Figure 8). The head ROI (100 x 100 pixels) was at the meeting area of the principal compressive fibre and principal tensile fibre groups (Figure 8).

The reproducibility of the texture parameters has already been ascertained (Hirvasniemi et al. 2014, Thevenot et al 2014), with values less than 1.6%.

From the ROIs, Local Binary Pattern (LBP) (Ojala et al. 1996) and second order partial derivatives (Laplacian (Lap)) were calculated to obtain LBP- and Laplacian-based images. The Laplacian method has been described thoroughly previously (Thevenot et al. 2014). Briefly, the image was pre-processed first with median filtering (3 x 3) to reduce image noise and subsequently, disk-shaped morphologic top- and bottom-hat operations were performed. A Laplacian-based matrix was derived from the ROI and was then calculated perpendicular to the trabecular main orientation. The values were converted to a scale between 0 and 1. The original ROI was then multiplied by the square root of the Laplacian matrix. To obtain the final image, the grey scale values were expanded to the full dynamic range. In the LBP method, the eight neighbour pixels for each pixel in the ROI were examined and an 8-bit LBP-value was calculated (Hirvasniemi et al. 2014).

Image entropy (Ent), which is a statistical textural measure of randomness was calculated for both LBP (Ent_LBP) (Hirvasniemi et al. 2014) and Laplacian (Ent_Lap) (Thevenot et al. 2014) results from each ROI (neck and head). The entropy for both LBP and Laplacian results was calculated using the equation (2):

\[
Ent = - \sum P_i \log_2 P_i
\]

where \(P_i\) is the number of occurrence of the gray-level value \(i\) in the image.
Figure 8. Regions of interest (ROIs) for the femoral neck and head.

Entropy describes the distribution of the local patterns in the LBP method and the distribution of the grayscale values in the Laplacian method. If Ent\_LBP = 0, there is only single pattern occurring in the original image, whereas Ent\_Lap = 0 means that all pixel values in the Laplacian-based image are the same.

Another texture measure called Homogeneity Index (HI), was calculated from the Laplacian based images from each ROI. HI was derived from the gray-level co-occurrence matrix (GLCM) (Haralick et al. 1973) that was calculated in horizontal direction (0 degrees) with a distance of one pixel. If all adjacent pixel values in an image are the same, HI is one.
4.4 Statistical Analysis

Statistical analyses were performed using the statistical software SPSS (SPSS version 20.0; SPSS Inc., Chicago, USA). Independent samples t-test was used for the assessment of differences between groups. The intra- and interoperator reproducibility of the geometric measurements were performed using the root-mean-square coefficient of variation according to the following equation (3):

\[
CV_{RMS} = \sqrt{\frac{\sum_{j=1}^{n} (CV_j)^2}{n}}
\]

where, \(CV_j\) is the individual coefficient of variation for the subject j and n is the number of images analysed for each (geometric) parameter.
5. Results

Table 2 shows the results of the intra- and interoperator reproducibility for the geometrical parameters evaluated using CV_{RMS} (equation 3). Interoperator HD measurements produced the best reproducibility results (CV_{RMS} of 0.91%), while intraoperator JSW was the worst to reproduce (CV_{RMS} of 13.96%).

Table 2. Intraoperator and Interoperator Root Mean Squared Coefficient of Variation (CV_{RMS}).

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Intraoperator CV_{RMS} [%]</th>
<th>Interoperator CV_{RMS1} [%]</th>
<th>Interoperator CV_{RMS2} [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSA</td>
<td>1.95</td>
<td>0.95</td>
<td>2.29</td>
</tr>
<tr>
<td>FNAL</td>
<td>1.30</td>
<td>1.15</td>
<td>2.10</td>
</tr>
<tr>
<td>HD</td>
<td>1.14</td>
<td>0.91</td>
<td>1.31</td>
</tr>
<tr>
<td>ND</td>
<td>2.29</td>
<td>4.08</td>
<td>2.84</td>
</tr>
<tr>
<td>FNC</td>
<td>5.42</td>
<td>11.63</td>
<td>12.13</td>
</tr>
<tr>
<td>HAL</td>
<td>1.73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JSW</td>
<td>13.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OF</td>
<td>1.84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>w</td>
<td>2.64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d</td>
<td>4.98</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

From Table 3, it can be seen that the distribution of KL grading in the women with and without hip fracture was rather similar.

Table 3. Fracture Distribution for the various KL grades.

<table>
<thead>
<tr>
<th>Fracture Type</th>
<th>KL0 (Controls)</th>
<th>KL1</th>
<th>KL2</th>
<th>KL3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Fracture</td>
<td>56 (54.9 %)</td>
<td>20 (19.61 %)</td>
<td>21 (20.59 %)</td>
<td>5 (4.9 %)</td>
<td>102</td>
</tr>
<tr>
<td>Fracture (all)</td>
<td>13 (56.52%)</td>
<td>3 (13.04%)</td>
<td>5 (21.74%)</td>
<td>2 (8.7%)</td>
<td>23</td>
</tr>
<tr>
<td>Cervical</td>
<td>10 (66.67 %)</td>
<td>2 (13.33 %)</td>
<td>2 (13.33 %)</td>
<td>1 (6.67 %)</td>
<td>15</td>
</tr>
<tr>
<td>Trochanteric</td>
<td>3 (37.5 %)</td>
<td>1 (12.5 %)</td>
<td>3 (37.5 %)</td>
<td>1 (12.5%)</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>23</td>
<td>26</td>
<td>7</td>
<td>125</td>
</tr>
</tbody>
</table>
The differences between OA and control groups by the various geometrical parameters, weight, height, BMI, and neck BMD are presented in Table 4. KL1 grade group was eliminated from the analyses to boost the confidence of the OA and control groupings. The ND and JSW had the most significant difference between controls and OA. The differences in weight, BMI, neckBMD and FNC between OA and controls were also statistically significant (p < 0.05).

Table 4. Means of OA and Controls for the various geometrical parameters, weight, height, BMI, and neck BMD.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n = 69)</th>
<th>OA (n = 33)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>64.95</td>
<td>70.09</td>
<td>0.041</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156.36</td>
<td>156.2</td>
<td>0.927</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.51</td>
<td>28.635</td>
<td>0.017</td>
</tr>
<tr>
<td>neckBMD (g/cm²)</td>
<td>0.61</td>
<td>0.676</td>
<td>0.005</td>
</tr>
<tr>
<td>NSA (Deg)</td>
<td>127.2</td>
<td>126.7</td>
<td>0.615</td>
</tr>
<tr>
<td>FNAL (mm)</td>
<td>99.06</td>
<td>99.44</td>
<td>0.767</td>
</tr>
<tr>
<td>HD (mm)</td>
<td>46.94</td>
<td>47.73</td>
<td>0.146</td>
</tr>
<tr>
<td>ND (mm)</td>
<td>34.14</td>
<td>36.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FNC (mm)</td>
<td>4.97</td>
<td>5.391</td>
<td>0.038</td>
</tr>
<tr>
<td>JSW (mm)</td>
<td>5.84</td>
<td>4.166</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAL (mm)</td>
<td>114.9</td>
<td>115.9</td>
<td>0.535</td>
</tr>
<tr>
<td>ADR</td>
<td>0.330</td>
<td>0.324</td>
<td>0.500</td>
</tr>
<tr>
<td>OF (mm)</td>
<td>31.73</td>
<td>32.30</td>
<td>0.781</td>
</tr>
<tr>
<td>w (mm)</td>
<td>55.53</td>
<td>55.92</td>
<td>0.607</td>
</tr>
<tr>
<td>d (mm)</td>
<td>18.31</td>
<td>18.03</td>
<td>0.603</td>
</tr>
</tbody>
</table>

Table 5 shows the values for various texture parameters for OA and control groups, without KL1 grades. Only clear images were considered for this analysis. Neck HI_Lap
produced the highest relative difference between the means of OA and controls (p = 0.001). All other texture parameters, except neck Ent_Lap, differed significantly between the groups (p < 0.05).

**Table 5.** Means of OA and Controls for the various texture parameters (clear images only).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n = 68)</th>
<th>OA (n = 30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ent_LBP_neck</td>
<td>6.845</td>
<td>6.829</td>
<td>0.477</td>
</tr>
<tr>
<td>Ent_Lap_neck</td>
<td>6.558</td>
<td>6.211</td>
<td>0.003</td>
</tr>
<tr>
<td>HI_Lap_neck</td>
<td>0.781</td>
<td>0.813</td>
<td>0.001</td>
</tr>
<tr>
<td>Ent_LBP_head</td>
<td>6.809</td>
<td>6.743</td>
<td>0.030</td>
</tr>
<tr>
<td>Ent_Lap_head</td>
<td>5.873</td>
<td>5.542</td>
<td>0.002</td>
</tr>
<tr>
<td>HI_Lap_head</td>
<td>0.836</td>
<td>0.863</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Means of the various geometrical features, BMI, neckBMD, weight and height for fracture (n = 23) and control (non-fracture) subjects are presented in Table 6. Acetabulum width (w) of patients recorded the relative highest difference between fracture and control subjects (p = 0.011). Femur neck BMD, FNAL, JSW, and HAL also showed a significant difference between fracture and controls subjects (p < 0.05). When only cervical fractures were considered (Table 7), only the differences in JSW and w were statistically significant (p < 0.05). Similarly, with only trochanteric fractures, the differences in neckBMD, HD, ND and HAL were statistically significant (p < 0.05) (Table 8).
**Table 6.** Geometrical parameters, weight, BMI and neckBMD for fracture and control subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n = 102)</th>
<th>Fracture (n = 23)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>66.63</td>
<td>68.72</td>
<td>0.468</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>155.6</td>
<td>157.9</td>
<td>0.090</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.50</td>
<td>27.38</td>
<td>0.910</td>
</tr>
<tr>
<td>neckBMD (g/cm²)</td>
<td>0.65</td>
<td>0.594</td>
<td>0.037</td>
</tr>
<tr>
<td>NSA (Deg)</td>
<td>127.0</td>
<td>127.5</td>
<td>0.678</td>
</tr>
<tr>
<td>FNAL (mm)</td>
<td>98.44</td>
<td>101.1</td>
<td>0.046</td>
</tr>
<tr>
<td>HD (mm)</td>
<td>46.95</td>
<td>48.04</td>
<td>0.060</td>
</tr>
<tr>
<td>ND (mm)</td>
<td>34.58</td>
<td>35.65</td>
<td>0.104</td>
</tr>
<tr>
<td>FNC (mm)</td>
<td>5.086</td>
<td>4.89</td>
<td>0.401</td>
</tr>
<tr>
<td>JSW (mm)</td>
<td>5.15</td>
<td>6.15</td>
<td>0.017</td>
</tr>
<tr>
<td>HAL (mm)</td>
<td>114.2</td>
<td>117.7</td>
<td>0.046</td>
</tr>
<tr>
<td>ADR</td>
<td>0.327</td>
<td>0.321</td>
<td>0.582</td>
</tr>
<tr>
<td>OF (mm)</td>
<td>31.93</td>
<td>29.16</td>
<td>0.196</td>
</tr>
<tr>
<td>w (mm)</td>
<td>55.21</td>
<td>57.24</td>
<td>0.011</td>
</tr>
<tr>
<td>d (mm)</td>
<td>18.02</td>
<td>18.39</td>
<td>0.540</td>
</tr>
</tbody>
</table>
Table 7. Geometrical parameters, weight, BMI and neckBMD for cervical fracture and control subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n = 102)</th>
<th>Cervical Fracture (n = 15)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>66.63</td>
<td>69.81</td>
<td>0.363</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>155.6</td>
<td>159.4</td>
<td>0.070</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.50</td>
<td>27.31</td>
<td>0.884</td>
</tr>
<tr>
<td>neckBMD (g/cm²)</td>
<td>0.648</td>
<td>0.620</td>
<td>0.370</td>
</tr>
<tr>
<td>NSA (Deg)</td>
<td>127.0</td>
<td>127.9</td>
<td>0.533</td>
</tr>
<tr>
<td>FNAL (mm)</td>
<td>98.44</td>
<td>100.6</td>
<td>0.167</td>
</tr>
<tr>
<td>HD (mm)</td>
<td>46.95</td>
<td>47.63</td>
<td>0.326</td>
</tr>
<tr>
<td>ND (mm)</td>
<td>34.58</td>
<td>34.81</td>
<td>0.766</td>
</tr>
<tr>
<td>FNC (mm)</td>
<td>5.086</td>
<td>4.958</td>
<td>0.649</td>
</tr>
<tr>
<td>JSW (mm)</td>
<td>5.147</td>
<td>6.247</td>
<td>0.029</td>
</tr>
<tr>
<td>HAL (mm)</td>
<td>114.2</td>
<td>116.4</td>
<td>0.271</td>
</tr>
<tr>
<td>ADR</td>
<td>0.327</td>
<td>0.327</td>
<td>0.992</td>
</tr>
<tr>
<td>OF (mm)</td>
<td>31.93</td>
<td>28.81</td>
<td>0.236</td>
</tr>
<tr>
<td>w (mm)</td>
<td>55.21</td>
<td>57.40</td>
<td>0.024</td>
</tr>
<tr>
<td>d (mm)</td>
<td>18.02</td>
<td>18.78</td>
<td>0.307</td>
</tr>
</tbody>
</table>
Table 8. Geometrical parameters, weight, BMI and neckBMD for trochanteric fracture and control subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n =102)</th>
<th>Trochanteric Fracture (n = 8)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>66.63</td>
<td>66.68</td>
<td>0.992</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>155.6</td>
<td>155.2</td>
<td>0.852</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.50</td>
<td>27.51</td>
<td>0.994</td>
</tr>
<tr>
<td>neckBMD (g/cm²)</td>
<td>0.648</td>
<td>0.544</td>
<td>0.011</td>
</tr>
<tr>
<td>NSA (Deg)</td>
<td>127.0</td>
<td>126.8</td>
<td>0.891</td>
</tr>
<tr>
<td>FNAL (mm)</td>
<td>98.44</td>
<td>102.1</td>
<td>0.082</td>
</tr>
<tr>
<td>HD (mm)</td>
<td>46.95</td>
<td>48.80</td>
<td>0.036</td>
</tr>
<tr>
<td>ND (mm)</td>
<td>34.58</td>
<td>37.23</td>
<td>0.012</td>
</tr>
<tr>
<td>FNC (mm)</td>
<td>5.086</td>
<td>4.763</td>
<td>0.380</td>
</tr>
<tr>
<td>JSW (mm)</td>
<td>5.147</td>
<td>5.956</td>
<td>0.225</td>
</tr>
<tr>
<td>HAL (mm)</td>
<td>114.2</td>
<td>120.0</td>
<td>0.031</td>
</tr>
<tr>
<td>ADR</td>
<td>0.327</td>
<td>0.311</td>
<td>0.333</td>
</tr>
<tr>
<td>OF (mm)</td>
<td>31.93</td>
<td>29.81</td>
<td>0.556</td>
</tr>
<tr>
<td>w (mm)</td>
<td>55.21</td>
<td>56.93</td>
<td>0.174</td>
</tr>
<tr>
<td>d (mm)</td>
<td>18.02</td>
<td>17.67</td>
<td>0.706</td>
</tr>
</tbody>
</table>

The means of the various texture parameters for cervical fractures and controls (without trochanteric) fractures is presented in Table 9, along with their p-values. The statistically most significant differences in texture parameters were in Ent_LBP_head and HI_Lap_head with p-values of 0.001 and 0.029 respectively.
Table 9. Texture parameters for cervical fractures and controls (without trochanteric fractures) (clear images only).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (n = 99)</th>
<th>Cervical Fracture (n = 13)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ent_LBP_neck</td>
<td>6.838</td>
<td>6.793</td>
<td>0.162</td>
</tr>
<tr>
<td>Ent_Lap_neck</td>
<td>6.445</td>
<td>6.279</td>
<td>0.301</td>
</tr>
<tr>
<td>HI_Lap_neck</td>
<td>0.789</td>
<td>0.808</td>
<td>0.155</td>
</tr>
<tr>
<td>Ent_LBP_head</td>
<td>6.804</td>
<td>6.667</td>
<td>0.001</td>
</tr>
<tr>
<td>Ent_Lap_head</td>
<td>5.805</td>
<td>5.527</td>
<td>0.059</td>
</tr>
<tr>
<td>HI_Lap_head</td>
<td>0.839</td>
<td>0.867</td>
<td>0.029</td>
</tr>
</tbody>
</table>

When comparing texture parameters between trochanteric fractures and controls, no significant differences were found.
6. Discussion

In this study, we investigated the association of different geometrical features in upper femur measured from pelvic radiographs to the hip OA and future hip fracture. Also, we investigated the relationship between the occurrence of hip OA and hip fractures, and association of upper femur bone texture parameters to the occurrence of OA and future hip fracture. Based on previous studies on geometrical features in upper femur, it was hypothesized that lower NSA (Moore al. 1994) and longer HAL (Castaño-Betancourt et al. 2013) predisposes a person to OA, whereas higher NSA and lower cortical thickness (Partanen et al. 2001, Pulkkinen et al. 2004, Pulkkinen et al. 2010, Pulkkinen et al. 2011) predisposes a person to increased risk of cervical fracture. One main factor that encouraged bone texture analysis was the changes that occur in bone structure in osteoporotic (Cosman et al. 2014, Hernlund et al. 2013, Kanis et al. 2013) and osteoarthritic (Buckwalter et al 2005, Lane 2007, Egloff et al. 2012) conditions.

OA patients (KL ≥2) had less hip fractures, but due to the limited sample size in subgroup analyses, the current study does not give confirmation whether persons having OA have reduced risk to develop hip fractures. Blain et al. (2008) found a substantial increase in trabecular bone volume of postmenopausal OA (compared to OP) patients, and that OA patients generally have thicker cortical thickness, all of which decreases the tendency of a bone to fracture. This inverse relationship is in agreement with some previous studies (Cumming and Klineberg 1993, Franklin et al. 2010, Vestergaard et al. 2009), but contrary to those from other studies made (Arden et al. 1999 and Jones et al. 1995).

The current results indicate that weightier women are at a higher risk of developing OA compared to women of low weight. Blain et al. (2008) and Lohmander et al. (2009) also found higher prevalence of hip OA among overweight people. OA data on other body parts like wrist and knee also found persons with higher weight to be at risk of developing OA (Carman et al. 1994, Felson et al. 1997, Spector et al. 1994), and that obesity even accelerates the progression of OA (Cooper et al. 2000, Schouten et al. 1992).

Biomechanically, the reason for this increase in OA among overweight persons is due to the high force exercised on the joint, making the articular cartilage and subchondral bone more susceptible to damage. Rising glucose and insulin levels due to excess body fat are
also attributed to joint inflammation, thereby increasing the progression of OA (Arthritis Research Campaign).

Height of participants did not show any dependence on OA. Liu et al. (2007) found the probability of having a hip replacement, which OA is a considered a major precursor to it, to increase among taller women. According to Hunter et al. (2005) (and Blain et al. 2008 in comparison with OP patients) tall people are at risk of developing knee OA. Biomechanically, this independence relation is expected, as tall people usually have larger bones and thick cartilage, which experience high impact forces. Short people have small bones and thin cartilage, which experience low impact forces. Conversely, extremely tall and short people may be at risk of developing OA.

From our study elderly women with higher BMI were found to be at higher risk of having OA. A study by Jiang et al. (2011) and Oliveria et al. (1999) also produced similar results. Results for OA dependence on BMI is relatively tied to obesity as obese persons have higher BMI.

In our study, participants with higher femoral neck BMD were found to be at higher risk of developing OA. Arden and Nevitt (2006), Blain et al. (2008), and Nevitt et al. (1995) found the same trend. Even though in our study OA subjects were found to have higher FNC too, which may contribute to higher BMD value with areal BMD measurement, observed thickening of larger weight bearing trabeculae could also result to higher BMD among OA subjects (Papaloucas et al. 2005).

In our research, NSA of controls was larger, but was not significantly different compared to OA subjects, which was in agreement with that obtained by Reikerås and Høiseth (1982) and Bendaya et al. (2015). The HD of OA patients in our group were slightly higher than controls (p = 0.146), similar to results obtained by Bendaya et al. (2015) and Jonhson et al. (2012). ND of OA patients were significantly higher than in control group (p < 0.005). Arokoski et al. (2002) and Johnson et al. (2012) also found higher femur ND among OA patients. Thus ND could be a diagnostic factor in predicting OA among patients. The reason for this has not been scientifically ascertained, but biomechanically one may speculate that since OA patients are generally weightier, bone remodelling contribute to the increase in ND to accommodate the higher impact force from the body’s upper parts.
There was a significant positive correlation between FNC and OA. Blain et al. (2008) and Turmezei et al. (2013) found a similar trend, but Preidler et al. (1997) found no correlation between cortical thickness and OA. The higher FNC among OA subjects could be the result of the higher weight and BMI among OA patients, thus triggering more osteoblast activity, leading to higher periosteal appositional deposition. Joint sites of higher cortical content can exert higher force on joint articulating structures, which may eventually lead to damage of articular cartilage, thus accelerating the progression of OA.

JSW for OA subjects were significantly lower than controls. This result was expected since in the KL grading JSW is one of the measures that affect the KL grade. Joint space narrowing remains one of the main predictors of OA. HAL of OA subjects was similar to controls, which was contrary to the findings by Castaño-Betancourt et al. (2013).

In this study, Ent_Lap_Neck was significantly higher for controls than for OA subjects. The cause of this higher value is that, the normal bone texture is intuitively more random than OA bones as bone fibrils are laid in alternate fashion (Eriksen et al. 1994, Seelay et al. 1998). Higher values of Ent_LBP_head and Ent_Lap_head could be caused by the same randomness among normal bone trabecular texture, but the veracity of femur head entropy values need further verification from separate femur head studies with no acetabulum influence.

The higher homogeneity index HI_Lap_neck could be attributed to increase in load bearing (vertical) trabeculae thickness and cross-connectivity among OA patients, especially in advanced OA (Papaloucas et al. 2005, Buckland-Wright et al. 1996). For higher HI_Lap_head among OA, fractal signature analysis, which measures horizontal and vertical trabeculae separately (Messent et al. 2005a), of the same ROI by Papaloucas et al. 2005 showed increase in vertical trabeculae thickness and cross-connectivity, thus higher homogeneity among OA femur head. The increased homogeneity index of OA subjects may also be further aggravated by subchondral bone sclerosis which contribute to increase in BMD of OA patients, thus the bone texture becomes more homogenous. But due to the overlap of the acetabulum for the femoral head ROI, further studies may be needed to ascertain the higher value of HI_Lap_head.

In general, subjects with lower femoral neck BMD were more prone to fracture. Also, FNAL, JSW, HAL, and w were higher among subjects with fractures. Lower BMD (osteoporosis) is regarded as one of the high risk factors of a fracture, supported by
numerous studies (Cosman et al. (2014), Kanis et al. (2013), Marshall et al. (1996)) due to the effect it has on bone structure, by making it porous and fragile. Fracture grouping elucidated that femoral neck BMD is a predictor of trochanteric fractures compared to cervical fractures. This shows one of the limitations of (projectional) DXA, by overestimating the neck BMD due to the cortical thickness of the femur cervix (for there were more cervical fractures even with least difference in average BMD) and also site specific BMD as the best indicator of fracture (Pulkkinen et al. 2004). FNAL of general hip fractured cases were significantly higher than non-fractured cases.

NSA was not a general predictor of fracture in our study. Compared with other studies where NSA was a predictor of hip fractures (Alonso et al. 2000, Gnudi et al. 2002, Partanen et al. 2001, Pulkkinen et al. 2004, Pulkkinen et al. 2010, Thevenot et al. 2014), our study population generally had lower NSA than in the other studies.

FNAL was a significant predictor of hip fractures in general, with longer length being at those at higher risk. However, when cervical and trochanteric fractures were considered separately, the significance disappeared. In studies by Pulkkinen et al. (2004) and Pulkkinen et al (2010) no statistical significance was found FNAL in relation to fractures, but controls had slightly higher FNAL.

HD in trochanteric fracture cases was higher than in the non-fractured hips. Partanen et al. (2001), and Pulkkinen et al. (2004) found no difference between HD of controls and fractured cases. In a comparison of HD of cervical and trochanteric fractures, Patton et al (2006) found no significant difference between the HDs of cervical and trochanteric fractured patients. Calis et al. (2004) found no difference between the HDs of controls and fractured subjects.

ND was statistically significantly higher only when trochanteric fractures were considered. Pulkkinen et al. (2004) also obtained similar results, with higher ND for trochanteric fractures, but was not statistically significant. Calis et al. (2004) found ND of fractured patients to be significantly higher than controls.

JSW was higher and statistically significant for all fractures and for cervical fractured subjects than for controls, but not on trochanteric fractures.

HAL was longer for all fractures and for trochanteric fractures as well, but not for cervical fractures. Gnudi et al. (2002) found a positive correlation between longer HAL and incidence of cervical fractures. Pulkkinen et al. (2004), Pulkkinen et al. (2010), and
Pulkkinen et al. (2011) found no significant correlation between HAL and fractures, but HAL of cervical fractured patients were generally longer. Longer HAL and higher ND in trochanteric fracture group may due to the moment exerted on the femur shaft at the trochanteric side, since the higher ND (even with lower BMD) is able to shield the femur neck from the forces from the upper extremity, thus making the trochanteric more susceptible to fractures in such cases.

Our study did not find ADR, d, or OF to be a predictor of a hip fracture. The parameter w for fractured subjects were higher than for controls, and was statistically significant for fractures in general and for cervical fractures, but not for trochanteric fractures when compared with controls. Partanen et al. 2001, and Pulkkinen et al. 2004 also found higher w to be a predictor cervical fractures. Thus more studies may be done to ascertain the validity of our findings.

The Ent_LBP_head and HI_Lap_head were significant predictors for cervical fractures, with lower and higher values for cervical fractures, respectively. This inverse relationship may not be considered as a research finding, due to the overlapping of the acetabulum and the femur head at the site of texture analysis.

With the aging population on the increase, accurate diagnosis of the diseases of the aged are also needed, and with this method in which in vivo samples were used, it could be a welcoming research results of the health care system of many countries. Incorporating it into diagnostic radiographic machines will be the optimum choice to relief the cost of obtaining and analysing of samples.

Our study has number of limitations. Since all images were taken in 2D, geometrical parameters were dependent on hip positioning. More detailed analysis on the relation of these geometrical parameters to OA and OP should be studied in 3D environment in future. Texture analysis from the femoral head is problematic from projectional images. This is because the acetabulum is summed in the image and the femur bone structure is not distinct there. Therefore the texture measures from the head are prone to errors. Also, the soft (fat) tissue might have produced errors in the image. Furthermore, the manual selection of ROIs and the inability to monitor the progress of OA are other limitations of this research. The results cannot be generalized into whole population since relatively elderly women were studied, and the number of OA and fracture cases were low.
population used this study might have been biased since all fracture cases were selected and were presented in OA analyses.
7. Summary

In this in vivo study we found higher ND and FNC, and lower JSW among OA subjects. Higher weight, BMI, and femur neck BMD were also associated with OA. Subjects with general hip fractures had lower neck BMD, and higher FNAL, JSW, HAL, and w. For subjects with cervical fractures, higher JSW and w were found among them. Lower neck BMD and HD, and higher ND and HAL were found among subjects with trochanteric fractures.

Our study did not ascertain whether OA is predisposing factor for hip fractures or not, mainly due to the limited sample population used.

Lower Ent_Lap_Neck and higher HI_Lap_neck were found among OA subjects. Lower Ent_LBP_head and Ent_Lap_head, and higher HI_Lap_head found among OA subjects, may have been due to the overlap of the acetabulum in the ROI for the head. Similarly, for subjects with cervical fractures, Ent_LBP_head was lower, and HI_Lap_head was higher, but this inverse relationship may also have been due to the overlap of the acetabulum in the ROI of the femur head.

Our research shows that upper femur geometry may play a role in the initiation and progression of OA and OP. The results support the use of bone fibers of the main compressive system in the prediction of OA. The high discrimination of the method, coupled with its high reproducibility make it a robust and cheap method that might be utilised in clinical diagnosis. Another good feature of the bone texture analysis method is that it is less affected by variation in imaging parameters (like X-ray tube current, image exposure time, grid parameters) than direct evaluation of grayscale values.

Further studies with a larger study group is needed to ascertain the clinical validity of the method. Other strong indicators of OA might be combined with it to improve the specificity of the method.
References


