COMPARISON BETWEEN RADIOGRAPHIC AND HISTOPATHOLOGICAL DIAGNOSIS OF PRIMARY BONE TUMOURS AT MOI TEACHING AND REFERRAL HOSPITAL

BY

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A RESEARCH THESIS SUBMITTED TO MOI UNIVERSITY, SCHOOL OF MEDICINE IN PARTIAL FULFILLMENT FOR THE AWARD OF A MASTER OF MEDICINE IN DIAGNOSTIC RADIOLOGY AND IMAGING

COMPARISON BETWEEN RADIOGRAPHIC AND HISTOPATHOLOGICAL DIAGNOSIS OF PRIMARY BONE TUMOURS AT MOI TEACHING AND REFERRAL HOSPITAL

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DECLARATION

I declare that this thesis is my original work written in partial fulfillment for the award of a Master of Medicine in Diagnostic Radiology and Imaging and has not been submitted to any other university or organization.

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DEDICATION

I would like to dedicate this study to my loving husband Charles for his unending support and encouragement, my daughter Samara for her constant love and smiles. To my parents and my siblings for their unlimited support and love, and above all the almighty God who has seen me through my entire life.

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ABBREVIATIONS

AAOS American Academy of Orthopedic Surgeons

CI Conventional imaging

CT Computed Tomography

FDG fluorodeoxyglucose

IREC Institutional Research and Ethics Committee

MRI Magnetic Resonance Imaging

MTRH Moi Teaching and Referral Hospital

PET Positron emission Tomography

WHO World Health Organization

OPERATION DEFINITION OF TERMS

Bone tumours:	This is neoplastic or abnormal growth of tissue in bone
Primary bone tumour:	Bone tumour originating from bone derived cells and tissue
Secondary bone tumour:	Bone tumour which originate in other body sites and spread (metastasize) to the bone.
Benign:	This is a tumour that lack the ability to invade neighbouring tissues.
Malignant:	This is a tumour characterized by rapid abnormal cell growth, invasiveness and metastasis.
Sensitivity	Ability of a test to identify disease among those who have it
Specificity	Ability of a test to exclude disease among those who do not have it

ABSTRACT

Background: A primary bone tumor is an abnormal tissue growth arising from bone. Primary bone tumors are uncommon, but they are important causes of morbidity and mortality. Management outcome depend on early diagnosis. Plain radiography is the primary imaging modality of these primary bone tumours. It is cheap and readily available compared to the scarce histopathology services in our region.

Objective: To determine the plain radiographic features of primary bone tumours and assess the percentage agreement between plain radiographic and histopathological diagnosis of primary bone tumours at MTRH.Also to assess the sensitivity and specificity of plain radiography in diagnosing primary bone tumours.

Methods: This was a cross sectional, descriptive study conducted from 1st October, 2016 to 30th September, 2017, at MTRH, Eldoret-Kenya. A total of forty seven patients who had both the radiological and histological results of primary bone tumours were enrolled into the study. Data was collected using questionnaires where the radiographic diagnosis of the correspondents were filled in to the questionnaire. Histopathological diagnoses were followed up and recorded. Data was analyzed using STATA/MP version 13E. The radiological and histopathological diagnoses were then categorized separately using WHO classification of bone tumors.Percentage agreement between plain radiographic and histopathological diagnoses of primary bone tumours at MTRH as well as sensitivity and specificity of plain radiography in diagnosing primary bone tumours established.

Results: The age of participants ranged from 10 to 74 years with a mean age of 26 years. The commonest presenting symptom was painless bony swelling, that is 29(61%) of cases. Plain radiography diagnosed 19(40.4%) of the cases as benign, majority being ameloblastoma and 28 (59.6 %) as malignant bone tumours with majority being osteogenic sarcoma. Lesion margin had a strong association with final histological diagnosis ($p<0.001$, Fisher Exact test,) while soft tissue involvement had a weak association with the histological diagnosis ($p=0.176$, Fisher Exact test). Percentage agreement of radiology and histopathology was higher for malignant bone tumours at 82.14% in comparison to their benign counterpart at 68.42%. The observed percentage agreement between the two diagnostic tests was 87%.plain radiography sensitivity was 88.2% and specificity was 86.7%.

Conclusion: There was excellent percentage agreement between radiological and histopathological diagnoses in diagnosis of primary bone tumours with a good plain radiography sensitivity and specificity.

Recommendation: Plain radiography can be used to diagnose primary bone tumours when histopathology services are unavailable, that is in resource poor set-ups.

CHAPTER ONE

INTRODUCTION

1.1 Background Information

Bone tumors develop when cells within a bone divide uncontrollably, forming a lump or mass of abnormal tissue. Bone tumors can affect any bone in the body and develop in any part of the bone i.e. from the surface to the center of the bone, called the bone marrow. It could be benign or malignant but most commonly the term is used for primary tumors; it is less exactly applied to secondary or metastatic tumors found in bone. Most bone tumors are not cancerous (benign) i.e. are usually not life-threatening and, in most cases, will not spread to other parts of the body.

Depending upon the type of tumor, treatment options are wide-ranging i.e. from simple observation to surgical removal of the tumor. Some bone tumors are cancerous (malignant) i.e. they can metastasize or spread of cancer cells throughout the body). In almost all cases, treatment for malignant tumors involves a combination of chemotherapy, radiation, and surgery.

When a bone tumor is cancerous, it is either a primary bone cancer or a secondary bone cancer. A primary bone cancer actually begins in bone while a secondary bone cancer begins somewhere else in the body and then metastasizes or spreads to bone. Secondary bone cancer is also called metastatic bone disease. Types of cancer that begin elsewhere and commonly spread to bone include breast, lung, thyroid, renal and prostate cancer. Although the incidence of benign bone tumors is higher than the incidence of primary malignant tumors, it is likely that benign lesions are underestimated because they often are asymptomatic and not clinically recognized.

Bone tumours account for 0.5% of all malignancies in the world(Yeole & Jussawalla, 1998), and of this primary bone tumor accounts for 0.2% , whereas involvement of skeletal tissue by metastatic disease is much more common. Primary bone tumours account for 5% of all paediatric tumours.(Jain, Sunila, Mruthyunjaya, Gadiyar, & Manjunath, 2011)

In African countries such as Uganda and Zimbabwe ,the incidence is low with a rate between 0.5 and 1.6 per 100,000 population(Omololu et al., 2002). More precisely, Uganda has a prevalence of 1%(Dodge, 1964) .This is per a study carried out in Uganda between 1964 and 1968 inclusive, whose findings showed osteosarcoma to be the commonest primary malignant bone tumour with a peak age of 10 - 19 years. This is similar to what has been reported elsewhere. Despite the low prevalence, it is still a major cause of morbidity and mortality in the world. Very few studies have been conducted on bone tumours in Africa.

According to data at Eldoret cancer registry at MTRH, a study conducted on burden and pattern of cancer in western Kenya between 1999 to 2006, the incidence of bone cancer was found to be 1.1%(Tenge, Kuremu, Buziba, Patel, & Were, 2009). World wide primary bone tumours tend to affect male more than females(del Carmen Baena-Ocampo, Ramirez-Perez, Linares-Gonzalez, & Delgado-Chavez, 2009; Mohammed & Isa, 2007).Among different types of primary bone cancer, Osteosarcoma constitutes the highest proportion (36%) of cases, followed by chondrosarcoma, osteoclastoma(Giant cell tumour) and Ewing's sarcoma.

Little is known about the etiology of bone tumours. It is likely that both genetic and environmental factors are involved.

Differing incidence between different ethnic groups and association of malignant bone tumours with certain genetic conditions suggest that there may be an underlying genetic basis for bone tumours at least in some patients. The finding of space-time clustering also suggests the involvement of environmental factors. Other epidemiological factors mentioned to be linked include mechanical trauma, ionizing radiation and chronic osteomyelitis. The risk of bone cancer increased substantially with increased cumulative dose of radiation to the bone and also increased linearly with increased cumulative dose of alkylating agents(Hawkins et al., 1996). The same study also showed that individuals who had cancer in childhood are at higher risk of developing bone cancer than any other type of second primary cancer .Although the risk of developing bone cancer within 20 years of 3-year survival did not exceed 0.9%.

Significant interest and effort in osteogenic sarcoma has led to the identification of numerous etiologic agents. Several chemical agents such as beryllium, viruses such as FBJ, subsequently found to contain the src-oncogene, and radiation were shown to be potent inducers of osteosarcoma. Paget's disease, electrical burn, or trauma all are thought to be other factors that may contribute to the pathogenesis(Fuchs & Pritchard, 2002). A genetic predisposition to osteosarcoma is found in patients with hereditary retinoblastoma, characterized by mutation of the retinoblastoma gene RB1 on chromosome 13q14(Ottaviani & Jaffe, 2009).

A study in the United states on age-period-cohort analysis of primary bone tumours incidence revealed that estrogen signaling pathway has been shown to stimulate proliferation of normal and malignant chondrocyte and therefore estrogen exposure may increase the risk for Chondrosarcoma (Anfinsen et al., 2011).

The clinicians and the pathologists handling management responsibility must have high index of suspicion as to the nature of bone lesion in order to establish the diagnosis of bone tumors. Radiographic evaluation, combined with the clinical history and histologic examination, is necessary for accurate diagnosis.

A systematic approach to the radiographic evaluation of skeletal lesions has been described by (Madewell, Ragsdale, & Sweet, 1981), who studied and correlated hundreds of radiographic and pathologic specimens. They considered the radiograph as the gross specimen from which a detailed histologic interpretation could be made and biologic activity accurately diagnosed.

Radiological diagnosis takes into account the site of lesion, borders of the lesion, type of matrix, type of bone destruction, type of periosteal reaction, nature and extent of soft tissue involvement and number of lesions. Patient age is also an important clinical factor in the diagnosis of bone tumors, because various lesions have predilections for specific age groups(Miller, 2008).

The radiographic parameters of benign and malignant tumors are quite different. Benign tumors have round, smooth, well-circumscribed borders. No cortical destruction and generally no periosteal reaction are found. Malignant lesions have irregular, poorly defined margins. Evidence of bone destruction and a wide area of transition with periosteal reaction are noted.

A study conducted at Kenyatta National Hospital, Nairobi, on comparison of roentgenography and histopathology in the diagnosis of bone tumours by (Kimari, 1995). This study recommended the need of cooperation between the clinician, the radiologist and pathologist in establishing correct diagnosis.

Bone scan, angiography, computed tomography (CT), and magnetic resonance imaging (MRI) are generally not helpful in determining a diagnosis of bone tumours

but are important in delineating the extent of local involvement. MR imaging is the examination of choice for staging bone tumors. CT is preferred to MR imaging only when the characteristics of the lesion are inadequately defined on plain radiographs, for example in flat bones(Sundaram & McLeod, 1990)

Plain radiographs form the basis for initial imaging of suspected bone tumors. It provides excellent resolution, allows for assessment of lesion characteristics, and is often more specific than MRI in generating a reasonable differential diagnosis. The plain radiograph is a necessary and cost-effective investigation for patients who present with a bony mass without pain, patients who have incidental radiographic abnormalities, patients with painful bone lesions, and patients with pathologic fractures. Analysis of the plain radiographic abnormalities, therefore, is a critical part of the work-up of the musculoskeletal oncology patient.

Although plain film radiograph is commonly the first objective evidence to suggest a bone tumor, a definitive diagnosis is rarely made with a plain radiograph alone, and must be correlated with clinical data and the results of pathologic examination of the specimen.

This study was done to determine what percentage of primary bone tumour diagnosis made from plain radiographs agreed with the histopathological diagnosis at Moi Teaching and Referral Hospital (MTRH).Also it was to establish the sensitivity and specificity of plain radiography in diagnosis of primary bone tumours.

1.2 Problem Statement

Bone tumours have been identified to be on the rise in Kenya and other parts of the world. It accounts for 0.5% of all malignancies in the world(Yeole & Jussawalla, 1998) and 1.1% in western Kenya (Tenge et al., 2009). It causes morbidity and mortality cutting across all age groups. The challenge is heightened in developing countries due to limited diagnostic and therapeutic facilities as well as due to ignorance. Management of bone tumours depend mainly on the radiological and histopathological diagnosis. Although plain radiographs are readily available, the histopathology services are scarce in our region. Bone tumours tend to be aggressive and progress faster. Therefore, these tumours like those in any other part of the body are better managed with early diagnosis and subsequent treatment. There are very few studies in Africa on the comparison between radiographic and histopathological diagnosis of primary bone tumours .The study is aimed at determining the percentage agreement between plain radiography in diagnosis of bone tumours in comparison with histopathology at MTRH, as well as plain radiography sensitivity and specificity.

1.3 Justification of the Study

The mortality rates from bone cancer has risen significantly among both males (from 0.47 to 0.80) and females (from 0.41 to 1.04) in Africa and Kenya included, indicating a 7% increase among males and an increment of more than 15% among females for a period of 10 years(Ghadirian, Fathie, & Emard, 2001). Their management is dependent on early and accurate diagnosis which is made primarily by clinical evaluation ,but differentials are drawn by use of basic imaging modality like plain radiography and confirmation made by histopathological report from bone biopsies taken. Plain radiography is readily available in our set up and cheaper as

compared to other imaging modalities like CT scan. Because management decisions are often based on plain radiograph as the initial imaging technique, there is a need to generate accurate information regarding its sensitivity and specificity ,and the percentage agreement between radiography and histopathology in diagnosing these primary bone tumours. This is to ascertain on how good plain radiography is in screening bone tumours in areas with limited resources i.e. absence of histopathology services. This will prompt early decision making on further management of these bone tumours. There is no documented information on the comparison of the two diagnostic methods of bone tumours in MTRH and there are few published studies on the same in Kenya. This data, when available, has the potential to guide the process of developing diagnostic protocols for MTRH and peripheral hospitals.

1.4 Research Question

1. What are the plain radiographic features of primary bone tumours in MTRH?
2. What is the percentage agreement between radiographic and histopathologic diagnosis of primary bone tumours at MTRH?
3. What is the sensitivity and specificity of plain radiography in diagnosis of primary bone tumours?

1.5 Research Objectives

1.5.1 Broad objectives

To determine the strength of agreement between radiological and histopathological diagnosis of primary bone tumours at Moi Teaching and Referral Hospital.

1.5.2 Specific Objective

1. To describe the radiographic features of primary bone tumours at MTRH.
2. To assess the percentage agreement between plain radiographic and histopathological diagnosis of primary bone tumours at MTRH.
3. To evaluate the sensitivity and specificity of plain radiography in diagnosis of primary bone tumours.

CHAPTER TWO

LITERATURE REVIEW

2.1 Epidemiology

In comparison to the myriad of other tumors, bone tumor is relatively uncommon, constituting only 0.5% of the all body malignancies (Ghadirian et al., 2001). The age-adjusted incidence rate of primary malignant bone tumors in the United States is 0.9 per 100 000 persons per year, accounting for approximately 0.2% of all malignancies. The three most common primary bone malignancies (osteosarcoma, chondrosarcoma, and Ewing's sarcoma) account for only 0.2% of all malignancies in the UK and USA; however, in children (< 15 years) malignant bone tumors account for approximately 5% of all malignancies (Unni, Inwards, Bridge, Kindblom, & Wold, 2005).

Majority of primary bone tumors are benign and since many are non-symptomatic they remain undetected or are detected only incidentally at radiographic examinations for other reasons thus poorly documented. The principal malignant tumors of bone are: a) osteosarcomas that occur mostly in the leg bones of children and young adults; this form is more frequent among girls under 15 and boys over 15; its incidence is higher among nonwhites than whites; b) chondrosarcomas that usually afflict people over 40 years of age; this is a slow-growing tumor that often starts in the pelvic bones; and c) Ewing's sarcoma, a cancer that impacts mainly children and teenagers; this form infiltrates large bones such as those of the thigh, upper arm, shin or pelvis; two times as many males are affected as females; a fast-growing tumor, its incidence is almost 9-fold higher among whites than blacks.

According to the U.S. Surveillance, Epidemiology and End Results Program, osteosarcomas contribute 36% of all types of bone cancer, followed by chondrosarcomas and Ewing's sarcomas with around 30% and 16% respectively(Ghadirian et al., 2001).

In a study conducted in Mexico between 2000 to 2005, it revealed that benign bone tumors accounted for 71.6% of cases and malignant bone tumors for 28.4%. The tumors affected men in 53.7% of cases and women in 46.3% of cases, with an average age at presentation of 25 years. The femur was the most common location of the tumors (39.9%), followed by the tibia (17.7%) and humerus (11.8%)(del Carmen Baena-Ocampo et al., 2009).

Malignant bone tumours comprise 3–5% of cancers diagnosed in children aged 0–14 years and 7–8% of cancers in adolescents aged 15–19 years in resource-rich populations. In teens and children, osteosarcoma and Ewing sarcoma are the commonest.

In the Americas, Chinese males in Hawaii have the highest incidence rate of bone cancer (6.4 per 100,000). Actually, this is the highest rate in the world. Among females, Paraguay has the highest incidence rate in the region (1.6 per 100,000). The highest male-female ration (9.0) in the world is found among Japanese Americans in Los Angeles, California. In the United States, Filipino males and Japanese females have the lowest incidence rates for bone cancer (Ghadirian et al., 2001).

Only a few countries in Africa have reliable statistics on bone cancer. In Nigeria (Ode et al., 2014)found that the benign tumours consisted of osteochondroma17.9%, Giant cell tumour 17.9%, fibrous histiocytoma 16.4% and osteoid osteoma 12%,

while the malignant variety were osteosarcoma 50%, fibrosarcoma 29.4% and Chondrosarcoma 11%. Mali has the highest standardized rate among males (1.4 per 100,000), while Algeria exhibits the highest rate among females (1.2 per 100,000), with a male/female ratio ranging from 0.75 to 1.55.

Cohen's (1960) kappa statistic (*K*) has long been used to quantify the level of agreement between two raters in placing persons, items, or other elements into two or more categories. Hence this test –statistic can be used to measure the level/strength of agreement between different raters (Orthopedists, radiologists and pathologists) in placing/diagnosing bone tumors into the different WHO categories. Kappa values are easily calculated online. In a study on pattern of bone tumours carried out in Addis Ababa university, Ethiopia found out that the level of agreement between radiological and histopathology diagnosis of bone tumours was a corrected Cohen's kappa value of 0.82 which is an excellent level of agreement ($k > 0.75$) between radiological and histological diagnoses of all bone tumors(Wamisho, Admasie, Negash, & Tinsay, 2009) .On a study done on periosteal chondroid tumors on radiologic evaluation with pathologic correlation, moderate agreement was reached between the radiologic and the pathologic diagnosis (χ=0.55)(Group, 2007).

A Kenyan study carried out by (Kimari, 1995) on bone tumour diagnosis at Kenyatta National hospital, Nairobi on comparison of roentgenography and histopathology in the diagnosis of bone tumours where 78 cases were analysed in this study,42 cases were found to be malignant on both radiology and histology,10 cases were found to be benign on both radiology and histology and 23 of the lesions had the same specific diagnosis on both radiology and histology.

The mortality rates from bone cancer rose significantly among both males (from 0.47 to 0.80) and females (from 0.41 to 1.04) in Africa, indicating a 7% increase among males and an increment of more than 15% among females for a period of 10 years. In America, a 0.3% increase in male and a 0.4% rise in female mortality from bone cancer have been reported. This indicates delay in diagnosis and treatment of these bone cancers. The five-year survival rate of adults and children for all types of bone tumours combined is about 70%. For adults with chondrosarcoma, the five year survival rate is about 80% (Ghadirian et al., 2001).

2.2 Plain Radiograph Findings of Bone Malignancies

Plain radiographs form the basis for initial imaging of suspected bone tumors. Radiography has been the optimal modality in distinguishing nonaggressive from aggressive osseous disease (Sundaram & McLeod, 1990) and (Colleran, Madewell, Foran, Shelly, & O'Sullivan, 2011), but the determination of whether a lesion is benign or malignant is based on histopathology. The appropriateness criteria established by the American College of Radiology, dictate that for the initial evaluation of a bone lesion radiographs should be the first line of investigation. If the radiograph shows normal or indeterminate findings, additional imaging studies are frequently required(Berquist et al., 2000). Radiographic evaluation is based on the classification system described by Lodwick, which classifies lesions based on four main groups of characteristics (Lodwick, 1965), including;

i. Destruction of bone
ii. Proliferation of bone
iii. Mineralization of tumor matrix
iv. Location, size and shape of the tumor.

2.2.1 Patterns of bone destruction include;

a) **Geographic pattern** of bone destruction with a **sclerotic rim**. This refers to a well-defined area of lysis. The sclerotic rim is more commonly seen in the weight-bearing bones and represents bone reaction to the lesion. Its presence means that the bone has been given sufficient time to react. Some authors say that the sclerotic rim signifies benignancy to about 95%.

b) **Cortical expansion** is defined as visible widening of the affected portion of bone. In many cases, an interrupted periosteal rim will surround the expanded portion of bone. This pattern may be seen in locally aggressive tumors and in low grade malignancies.

c)**"Moth-eaten" pattern** is an ill-defined zone of multiple small radiolucencies that may coalesce. This is due to rapidly growing lesions, poorly defined with aggressive, infiltrative patterns of bone destruction(Madewell et al., 1981).

d) **Permeative pattern** is characterized by numerous tiny radiolucencies in between the residual bone trabeculae. Due to the minute size of radiolucencies the lesion may be difficult to see and to delineate on the plain film. They are indicative of destruction involving both medullary and cortical bone. They are seen in **high grade malignant neoplasms and in osteomyelitis.**

Moth-eaten and permeative patterns are associated with more aggressive lesions. However, some malignant lesions such as fibrosarcoma and chondrosarcoma can arise within a benign lesion, and as such radiologic-pathologic apparent discordance can arise with an aggressive histology in a benign appearing radiographic lesion. Of note, the fastest margin of tumor growth would be radiographically invisible permeative lesion, as this involves the widest of margins.

2.2.2 Pattern of bone proliferation

Proliferation of bone includes both encapsulated and unencapsulated patterns, with unencapsulated growth being more aggressive. This feature is particularly characterized by different patterns of periosteal reaction. Periostitis is often subtle and can mislead the radiologist attempting to classify a lesion as benign or aggressive. Classic, aggressive-appearing periostitis is described as having an "onion-skin," "sunburst", or "hair-on-end" appearance. A Codman triangle pattern is another aggressive configuration. Benign patterns are those that have had sufficient time to organize and, thus, show solid thick or wavy unilamellar periosteal changes.

Recognizing periosteal reaction of any type remains important, as this effectively excludes several lesions from the differential (Cronin & Hughes, 2012). If periostitis is present, fibrous dysplasia, solitary bone cyst, nonossifying fibromas, and enchondromas can be removed from consideration unless complicated by fracture. Therefore, solid or unilamellated periosteal reaction is a nonaggressive appearance, since it indicates that the underlying lesion is slow growing and is giving the bone a chance to wall the lesion off. A multilamellated or "onionskin" appearance suggests an intermediate aggressive process, such as one that waxes and wanes or one that the bone is continually trying to wall off but cannot (Kricun, 1983).

Broadly speaking, periosteal reaction can be classified as continuous, interrupted, or complex, depending on its morphology. Continuous forms include both nonaggressive and aggressive morphologies, with the terms smooth and continuous representing examples of nonaggressive periosteal reaction, and lamellated or ''onion-skin'' representing examples of an aggressive reaction. Interrupted patterns include the Codman's angle or triangle, which is a focal periosteal elevation, and interrupted, speculated patterns. Complex patterns include a mix of various types.

2.2.3 matrix mineralization patterns (calcification or ossification) are helpful in identification of bone producing and cartilage producing tumors.

a) **Osteoid-** Aggressive bone-forming tumors produce amorphous osteoid, which is often less dense than normal bone. Less aggressive bone-forming tumors produce better organized, denser bone (Lovell, Winter, Morrissy, & Weinstein, 2006). Malignant osteoid can be recognized radiologically as cloudlike or ill-defined amorphous densities with haphazard mineralization (Sweet, Madewell, & Ragsdale, 1981). This pattern is seen in osteosarcoma. Mature osteoid, or organized bone, shows more orderly, trabecular pattern of ossification. This is characteristic of the benign bone-forming lesions such as osteoblastoma.

b) Chondroid -Chondroid matrix is classically described as stippled, flocculent, or ‘‘ring and arc’’ configuration, and when aggressive can be seen in the setting of chondrosarcoma. The gradual increase in mineralization with time is termed “maturation” and can be seen in tumors such as fibrous dysplasia, nonossifying fibroma, fibrous cortical defect, osteoid osteoma, and Bone Island. (Yanagawa et al., 2001). Maturation is an indolent process and should not be confused with the rapid posttherapeutic response of aggressive lesions that have responded well to systemic or radiation therapy.

Radiologically, it is usually easier to recognize cartilage as opposed to osteoid by the presence of focal stippled or flocculent densities, or in lobulated areas as rings or arcs of calcifications. They are best demonstrated by CT. whatever the pattern; it only suggests the histologic nature of the tissue (cartilage) but does not reliably differentiate between benign and malignant processes.

c) Fibrous matrix, as seen in fibrous dysplasia, demonstrates a ‘‘ground glass’’ radiographic density as a result of small, abnormally arranged trabeculae of immature woven bone (Greenspan, 2011).

2.2.4 Location, size and shape of bone tumour

Location, size, and shape also play a role in the evaluation of a bone tumor as in it can be a clue to its diagnosis, since some entities have size criteria. For example, osteoid osteoma and osteoblastoma are histologically similar lesions, but they differ in size: The nidus of an osteoid osteoma is less than 1.5 cm in diameter, while the osteoblastoma is larger than 1.5 cm (White & Kandel, 2000). Traditionally, a well-defined lytic lesion in the cortex of a long bone with a sclerotic rim has been termed a fibrous cortical defect if it is less than 3 cm in length and a nonossifying fibroma if it is larger than 3cm (Resnick & Niwayama, 2002).Generally speaking, malignancies tend to be larger and more spherical. Differential diagnosis is aided also by location, as some tumors originate in the diaphyseal, metaphyseal, or epiphyseal location. Age of the patient also aids in formation of a differential diagnosis, as different tumors tend to favor different age groups.

Radiographic appearance of the metastatic tumors can be:

-Purely lytic (kidney, lung, colon, and melanoma)

-Purely blastic (prostate and breast carcinoma)

-Mixed lytic and blastic (most common appearance)

For patients presenting with metastatic disease, the radiographic appearance of the lesions may help in differentiating it from primary bone tumours and to guide the search for a primary of these metastatic lesion(Rosenthal, 1997). The radioisotope bone scan has been the preferred imaging screening modality for metastatic bone lesions.

Once the lesion has been assessed radiographically, if there are aggressive features, further imaging evaluation is warranted. This is particularly true in the setting of cortical destruction or suspected extension into the adjacent soft tissues. The degree of soft tissue involvement is more accurately characterized by contrast enhanced CT or MRI (Oudenhoven et al., 2006), which allow better discrimination of the extent of disease. This is often not possible at plain radiography, as both tumor and adjacent normal soft tissues are of the same density and attenuate the X-ray to the same degree.

2.3 General Histologic Assessment of the Lesion

Primary benign and malignant bone tumours vary widely in their clinical behaviour and pathological features. The nomenclature and classification of primary bone tumours is based mainly on the pathway of tumour cell differentiation; this is usually evidenced by the type of connective tissue matrix formed by tumour cells. The histogenesis of many primary bone tumours, however, is not known and a number of bone tumours are by convention classified by distinct morphological or clinicopathological features (e.g. giant cell tumour of bone) or by karyotypic and molecular genetic abnormalities (e.g. Ewing's sarcoma) (Mangham & Athanasou, 2011). Biopsy is the definitive diagnostic procedure.

The following are the most important histologic features to consider:

a. Pattern of growth (e.g., sheets of cells vs. lobular architecture)
b. Cytologic characteristics of the cells
c. Presence of necrosis and/or hemorrhage and/or cystic change
d. Matrix production
e. Relationship between the lesional tissue and the surrounding bone (e.g., sharp border vs. infiltrative growth)

In addition to correct classification and in some cases grading, the pathologist has to report on margins, relation of tumor to cortex, periosteum, surrounding soft tissues, joints, etc., and the presence of vascular invasion as well as give information of importance for staging (Dorfman & Czerniak, 1998)

Bone tumour diagnosis cannot be made without integrating clinical, radiological, and histologic appearances (Priolo & Cerase, 1998). Biologically different types of tumors may have overlapping histologic features thus it is always advisable to obtain a list of differential diagnoses from a radiologist.

2.4 Sensitivity and specificity of plain radiography in primary bone tumour diagnosis

Sensitivity and specificity of a test are virtually constant whatever the prevalence of the condition,unlike positive and negative predictive value which are affected by the prevalence of the condition under consideration**(Salkić, 2008).**sensitivity and specificity are also known as diagnostic accuracy. Conventional radiography demonstrates a sensitivity of 76.4% and a specificity of 55.0%, in diagnosis of aneurysmal bone cyst(Mahnken et al., 2003).This is a study of comparison between plain radiography and histopathology as the gold standard in diagnosis of aneurysmal bone cyst.The sensitivity and specificity of plain radiography in diagnosing osteomyelitis(a mimic of bone tuomours) are both 75%(Yuh et al., 1989). The current scientific data have shown that panoramic images i.e orthopantogram have 97% sensitivity and 45% specificity for identifying hyperplastic conditions in the temporomandibular joint(Shintaku, Venturin, Langlais, & Clark, 2010).The challenge in this study is that it was localized to the temporomandibular region only.

A comparison study of hybrid FDG positron emission tomography/computed tomography (PET/CT) with conventional imaging (CI) modalities in detecting

malignant lesions, in pediatric primary bone tumor,where PET/CT had higher sensitivity and specificity than CI (83%, 98% and 78%, 97%, respectively)(London et al., 2012).This was in comparison to histopathology as the gold standard.Conventional imaging includes plain radiography,computed tomography and magnetic resonance imaging.On a study on FDG–PET for detection of recurrences from malignant primary bone tumors: comparison with conventional imaging where histopathology was used as the gold standard too ,FDG–PET had a sensitivity of 0.96, a specificity of 0.81 and an accuracy of 0.90. Corresponding values for conventional imaging were 1.0, 0.56 and 0.82.conventional imaging had a higher sensitivity compared toFDG- PET scan.(Franzius et al., 2002)

CHAPTER THREE

RESEARCH DESIGN AND METHODOLOGY

3.1 Study Design

This was a cross sectional descriptive study carried out over a period of one year, starting from October 2016 to September 2017.Patients sent to radiology and imaging department for musculoskeletal radiography whose radiographs were suggestive of primary bone tumours took part in the study. Their histology results were followed up by the researcher .A comparison between their radiological features and histopathological findings were evaluated. Histopathology results acted as the gold standard in diagnosing the primary bone tumours.

3.2 Study Site

The study was conducted at the Radiology and Imaging and pathology departments of Moi Teaching and Referral Hospital, Eldoret. The hospital has over 800 bed capacity and is the only referral hospital in western part of Kenya with a catchment area of 16.24 million (as per 2010 Kenya population census survey report).The hospital is located along Nandi road in Eldoret town (310 km northwest of Nairobi the capital city of Kenya).

MTRH is a tertiary (level 6) health facility serving as a teaching hospital for Moi University School of Medicine, Public health and Dentistry. Others include Kenya Medical Training Center (KMTC) Eldoret and University of Eastern Africa Baraton, School of Nursing.

MTRH is also a training center for medical, clinical and nursing officer interns. The facility has several departments including Surgery, Pediatrics, Pathology and Radiology and Imaging among others. Radiology and imaging department

encompasses imaging modalities like plain radiography, ultrasound, CT scan, MRI, mammography, fluoroscopy and interventional radiology

3.3 Study Population

The study population consisted of all patients done plain radiography of the bones at the radiology and imaging department, MTRH whose radiographs were suggestive of primary bone tumor were eligible to participate in the study. The target population included both inpatients and outpatients in the period of 1st October 2016 to 30th September 2017.

3.4 Eligibility Criteria

3.4.1 Inclusion criteria

The following inclusion criteria was applied:

- Patients whose plain radiographs were suggestive of primary bone tumours.
- Patients who consented to the study.

3.4.2 Exclusion criteria

- Patient with known other non-bone primary tumours
- Patients lacking histopathology results.
- Patients who declined to consent to the study.

3.5 Sampling Techniques

3.5.1 Sampling and Recruitment

This was a census study executed via consecutive sampling over a period of one year (1st October 2016 to 30th September 2017). This method was chosen owing to the small number of patients who presented in the past two years with primary bone tumours in MTRH i.e. 51 in the year 2015 and 56 patients in 2014. Every patient whose plain radiograph was suggestive of primary bone tumour was recruited into the

study after consenting to it. Children were assented by the parents or guardians to participate in the study.

3.6 Study Procedures

Clinicians in the wards and outpatient clinics were sensitized to refer all patient with suspected bone tumour basing on the clinical presentation e.g. those with painful or painless bony swelling and pathological fractures. Once at the radiology and imaging department, patients were imaged in the x-ray room as per the MTRH protocol. The images were obtained in two perpendicular planes which were then reported by the principle researcher and at least two radiologist consultants. Patients whose plain radiographs were radiologically diagnosed to be primary bone tumours were recruited into the study after meeting the inclusion criteria. A questionnaire was filled guided by the researcher. As per the protocol, all the biopsy samples or resected tumours were send for histology for optimal diagnosis. The specimens received were fixed in 10% formalin, grossed, processed and sections taken from paraffin embedded tissues. The sections were stained with routine hematoxylin and eosin stains. Immunohistochemical stains were done if indicated. The final histological diagnosis was arrived at after an agreement on the diagnosis was reached by at least two pathologists. The histology diagnosis was then followed up by the researcher. Tumors were divided into benign and malignant according to WHO classification. The final histopathological diagnoses were correlated with the radiological diagnoses and their percentage agreement calculated. The plain radiography sensitivity and specificity in diagnosing primary bone tumours was then established.

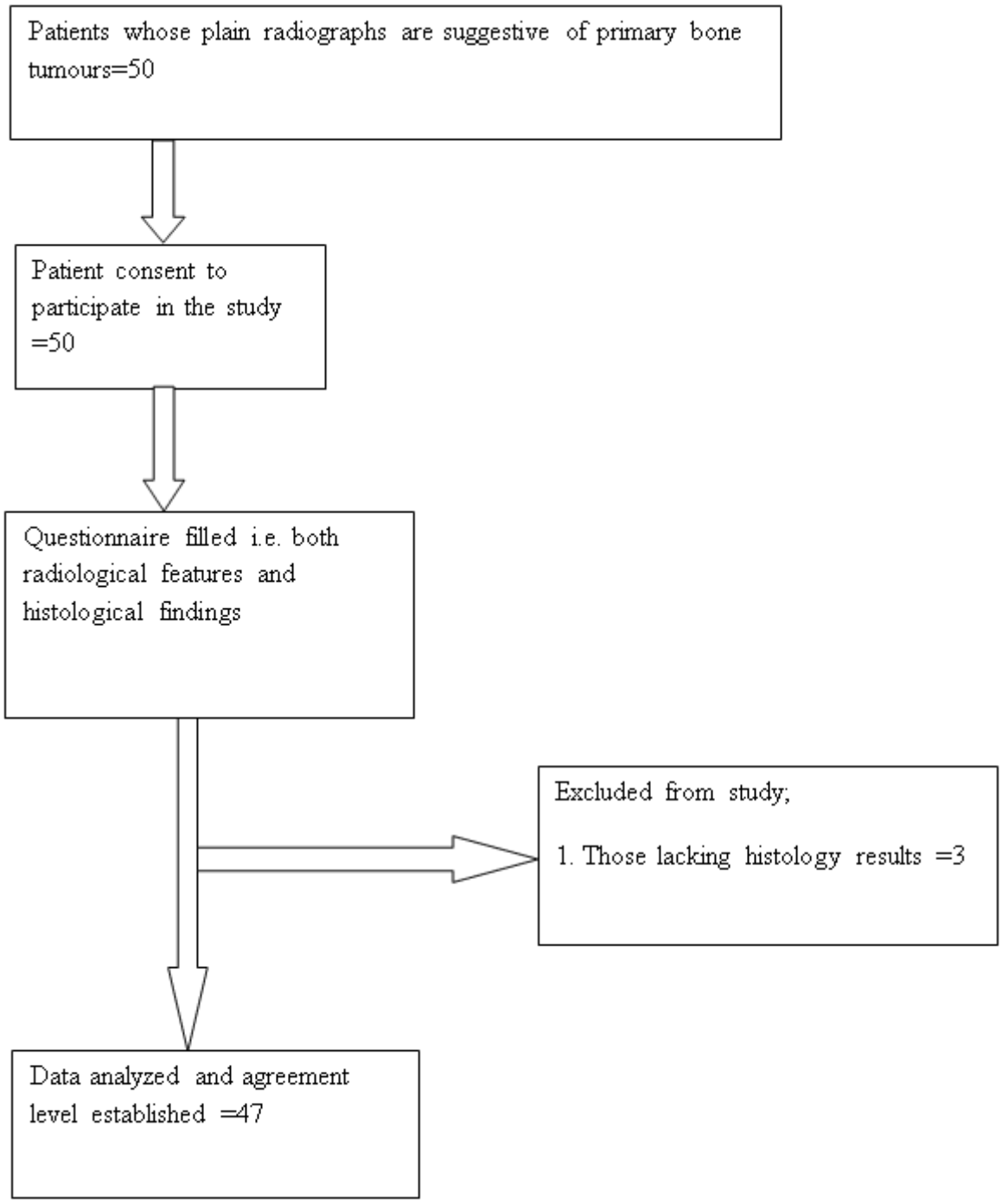

Figure 1: Recruitment schema

3.7 Data Collection and Management

3.7.1 Data collection tools

Data was collected between 1st October 2016 and 30th Sept 2017. Prior to data collection, informed consent and assent were obtained from prospective study participants (Appendix 1). Data was collected using a structured data collection tool divided into three sections (Appendix 2) .The first section was a closed ended questionnaire in which the patients' bio data was established. This was done during an interviews lasting 5-10 minutes with each study participant. The second part comprised filling in the patient's plain radiographic features as reported by the principal investigator and at least two radiology consultants. The third part of the questionnaire entailed filling in the histology diagnosis, agreed upon by at least two pathologists, of the corresponding study participant.

3.7.2 Data quality and security

Data was double entered into a computer for purposes of validation. The computer was password protected and access allowed only for authorized persons. Databases obtained were stored electronically, copies of filled questionnaire were stored in locked cabinets located in the principal investigators residence.

3.7.3 Data processing and analysis

Data was analyzed using STATA version 13E. Univariate analysis was used to calculate frequencies of socio-demographic characteristics, radiographic features and histological findings of primary bone tumours. Bivariate analysis was used to calculate the percentage agreement between the radiological and histological diagnosis of primary bone tumour .The results of this analysis were presented in tables and figures. Descriptive data was summarized and reported.

3.8 Ethical Considerations

Ethical clearance was sought from IREC before the commencement of data collection. A consent form explaining the rationale and benefits of the study to the public health system was used to seek informed consent from potential interviewees. Assent for participants below 18 years of age was sought from the primary guardian or parent. Participation in the study was on a voluntary basis, the participants were at liberty to withdraw from the study at any stage without being penalized. There were no incentives for participants. The interviews were conducted in a confidential manner; participant names were not recorded. No study participant was identified by name in any report or publication derived from information collected for the study. Data collected was stored in lockable cabinets, databases created were password protected to avoid unauthorized access.

The results of the research will be presented to the Hospital's management and the university's department of Radiology and Imaging for use as necessary. It will also be available for academic reference in the College of Health Sciences Resource Centre. The results of this research shall be availed for publication in a reputable journal of medicine for use by the wider population in the general improvement of patient management and as a reference for future studies.

CHAPTER FOUR
RESULTS

4.1 Introduction

There were 50 cases who were seen in radiology department with a diagnosis of primary bone tumours, however 3 cases were dropped from the analysis because their histology results were unavailable.

4.2 Demographic information

The median age of the patients was 18 (IQR 14, 35) years, minimum age was 10 and maximum age 74 years. Mean age was 26.2(SD 16) years. Peak age was between 10 to 18 years (49%). Males were 24(51%) while females were 23(49%)

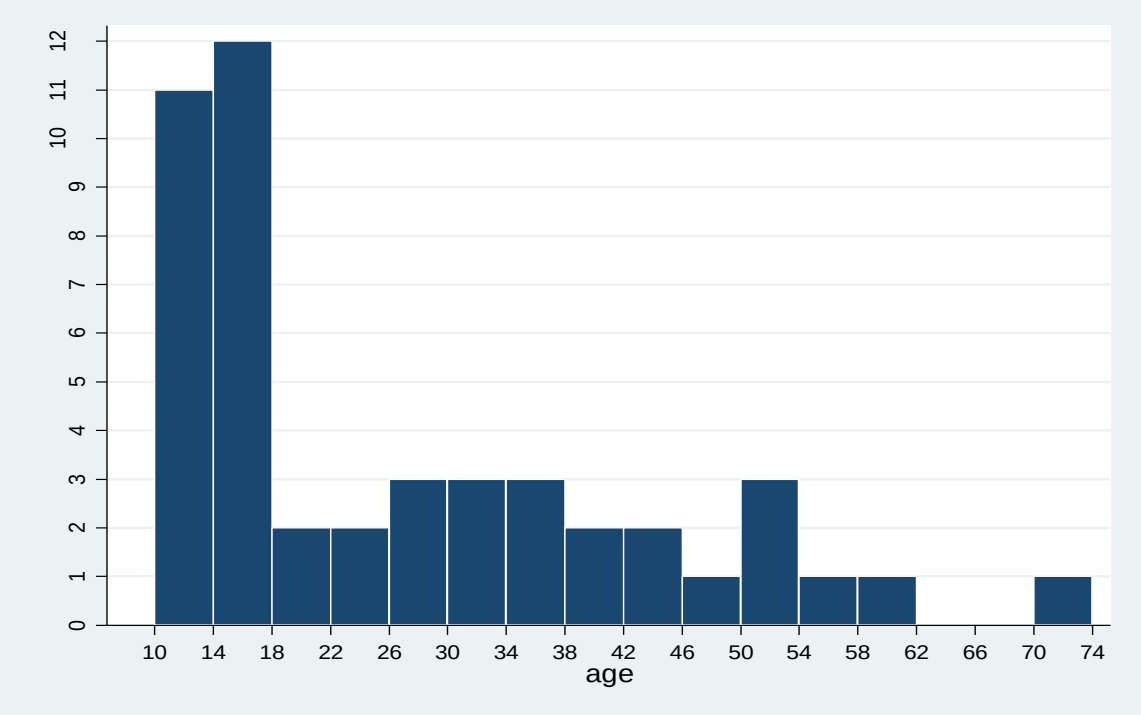

Figure 2: Age distribution

4.3 Clinical Presentation

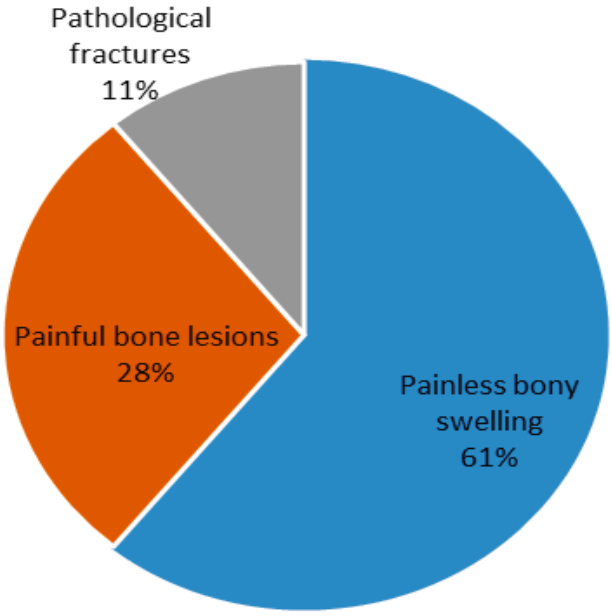

Figure 3: Signs and symptoms

4.4 Plain Radiographic Examination

Table 1: Location of the bone lesion

Variable	Categories	Frequency	Percent
Longitudinal	Diaphysis	4	8.5
	Mixed	7	14.9
	Epiphysis	8	17.0
	Metaphysis	8	17.0
	Others	20	42.6
Transverse	Cortex	2	4.3
	Medulla	4	8.5
	Mixed	41	87.2

NB: Other in the above table, on longitudinal location, implies bone tumour on the skull and axial skeleton.

Most 20(42.6%) of the cases were classified as others in regard to longitudinal location of bone lesion, those with bone lesion located on metaphysis and epiphysis were 8(17.0%) each. On transverse location majority 41(87.2%) had a mix of cortex and medulla.

Table 2: Radiological features of bone tumours

Variable	Categories	Frequency	Percent
Borders of lesion	Regular	23	48.9
	Irregular	24	51.1
Type of bone destruction	Geographic pattern	30	63.8
	Moth-eaten pattern	9	19.2
	Permeative pattern	5	10.6
	Mixed	3	6.4
	Cortical expansion	0	0
Type of matrix mineralization	Osteoid matrix	35	74.5
	Chondroid matrix	7	14.9
	Fibrous matrix	4	8.5
	Mixed	1	2.1
Type of periosteal reaction	Solid	21	44.7
	Interrupted	15	31.9
	Complex	6	12.8
	Continuous	5	10.6
Soft tissue involvement	Yes	34	72.3
	No	13	27.7

Borders of lesion were almost equally distributed for both regular (48.9%) and irregular (51.1%), while geographic pattern of bone destruction was classified in 30 (63.8%) of the patients. Type of matrix mineralization was mostly classified as osteoid matrix 35 (74.5%), while periosteal reaction were mostly solid 21 (44.7%) or interrupted 15 (31.9%). Only 13 (27.7%) of the patient didn't have soft tissue involvement.

4.5 Final Radiological Diagnosis

Table 3: Radiological diagnosis

Diagnosis	Categories	Frequency	Percent
Benign (40.4%)	Ameloblastoma	8	42.1
	Ossifying fibroma	3	15.8
	Odontogenic keratocyst	3	15.8
	Chordoma	2	10.5
	Fibrous dysplasia	1	5.3
	Osteochondroma	1	5.3
	Aneurysmal bone cyst	1	5.3
Malignant (59.6%)	Osteogenic sarcoma	19	67.9
	Chondrosarcoma	6	21.4
	Multiple myeloma	3	10.7

Radiology diagnosed 19 (40.4%) cases to be benign while 28 (59.6%) were classified as malignant. Malignant were classified in only three categories that is, osteogenic sarcoma 19 (67.9%), chondrosarcoma 6 (21.4%) and multiple myeloma 3 (10.7%). However benign were classified into 7 types, ameloblastoma being the majority 8 (42.1%), Ossifying fibroma and Odontogenic keratocyst were each 3 (15.8%) of the patients.

4.6 Histological Diagnosis

Table 4: Histological diagnosis

Diagnosis	Frequency	Percent
Osteogenic sarcoma	19	40.4
Ameloblastoma	7	14.9
Multiple myeloma	3	6.4
Chondrosarcoma	3	6.4
Metastatic carcinoma	2	4.3
Osteochondroma	2	4.3
Odontogenic keratocyst	2	4.3
Reactive bone formation	1	2.1
Ossifying fibroma	1	2.1
Desmoplastic fibroma	1	2.1
Giant cell tumour	1	2.1
Fibrous dysplasia	1	2.1
Synovial sarcoma	1	2.1
Squamous cell carcinoma	1	2.13
Nasolabial cyst	1	2.13
Malignant round blue cell tumour	1	2.13

4.7 Comparing Radiological and Histological Findings

Table 5: Comparison of radiological features with histological diagnosis

Variable	Categories	Benign n(%)	Malignant n(%)	p-value
Borders of lesion	Regular	14(60.9)	9(39.1)	0.001
	Irregular	3(12.5)	21(87.5)	
Soft tissue involvement	Yes	7(53.8)	6(46.2)	0.176*
	No	10(29.4)	24(70.6)	

* Fisher's Exact test

The margin of the lesion is a great predictor of the final histological diagnosis of the bone tumour whose p value is <0.001. Soft tissue involvement is not a predictor of any outcome i.e whether benign or malignant and is not significant statistically with a p value of 0.176.

Table 6: Percentage agreement for specific radiological and histology diagnosis

Radiology diagnosis	Total cases	Cases correctly diagnosed	Agreement %
Fibrous dysplasia	1	1	100.0
Osteochondroma	1	1	100.0
Multiple myeloma	3	3	100.0
Osteogenic sarcoma	19	17	89.5
Ameloblastoma	8	7	87.5
Ossifying fibroma	3	2	66.7
Odontogenic keratocyst	3	2	66.7
Chondrosarcoma	6	3	50.0
Chordoma	2	0	0.0
Aneurysmal bone cyst	1	0	0.0

Considering histology to be the gold standard test, then we can say that radiology was able to diagnose 100% for fibrous dysplasia, osteochondroma, and multiple myeloma.

Could not correctly diagnose chordoma and aneurysmal bone cyst (0%) while for chondrosarcoma radiology diagnosed half (50%) of the cases right.

Table 7: Overall percentage agreement for radiological and histology diagnoses

Type of tumour as per radiology	Total cases	Number with Agreement	Percentage with Agreement
Benign	19	13	68.42
Malignant	28	23	82.14
Total	47	36	76.6

The observed percentage agreement was 87%.Malignant tumours were more likely to be diagnosed correctly (82.1%) compared to benign tumours which had 68.4% agreement proportion. However there is no significant association between radiology diagnosis (Benign/Malignant) and the percentagel of agreement between radiography finding and histology results ($\chi^2 = 1.188, p = 0.312$).

Table 8: Disagreement between radiological and histology diagnosis

Radiological diagnosis	Pathological Diagnosis	Frequency
Osteogenic sarcoma	Reactive bone formation	1
Osteogenic sarcoma	Metastatic carcinoma	1
Ossifying fibroma	Odontogenic keratocyst	1
Ameloblastoma	Malignant round blue cell tumour	1
Odontogenic keratocyst	Squamous cell carcinoma	1
Chondrosarcoma	Osteogenic sarcoma	1
Chondrosarcoma	Osteochondroma	1
Chondrosarcoma	Synovial sarcoma	1
Chordoma	Osteogenic sarcoma	1
Chordoma	Metastatic carcinoma	1
Aneurysmal bone cyst	Giant cell tumour	1
Total		11

The above table shows the 11 cases where there was disagreement between radiological diagnosis and histological diagnosis.

Table 9:The overall plain radiographic Sensitivity and specificity in diagnosis of primary bone tumours

Radiology diagnosis	Histology diagnosis		Sensitivity	Specificity
	Benign	Malignant		
Benign	15	4	88.2%	86.7%
Malignant	2	26		
Total	**17**	**30**		

The plain radiographic sensitivity is 88.2% and specificity is 86.7% in diagnosis of primary bone tumour.

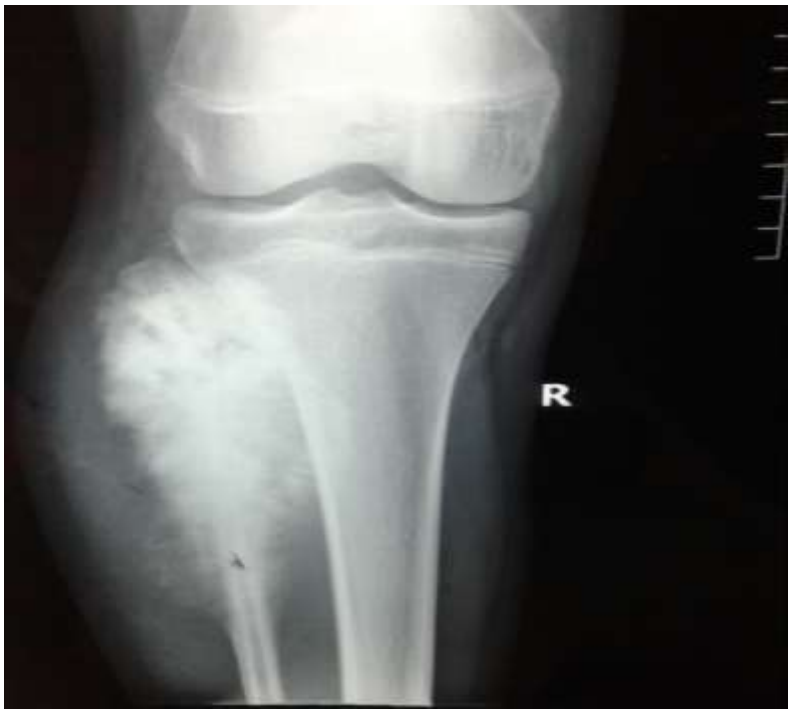

Figure 4: Radiograph of the right leg showing irregular sclerotic proximal fibula bony lesion with adjacent soft tissue involvement, diagnosed as osteogenic sarcoma

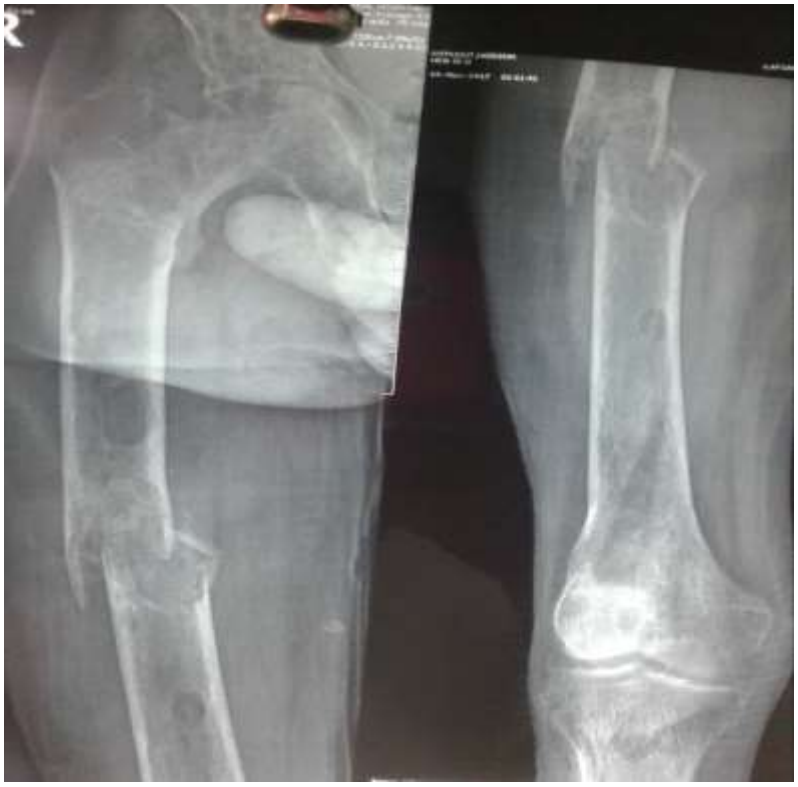

Figure 5: Radiograph of the right femur showing pathological fracture at mid shaft with multiple lytic lesions diagnosed as multiple myeloma

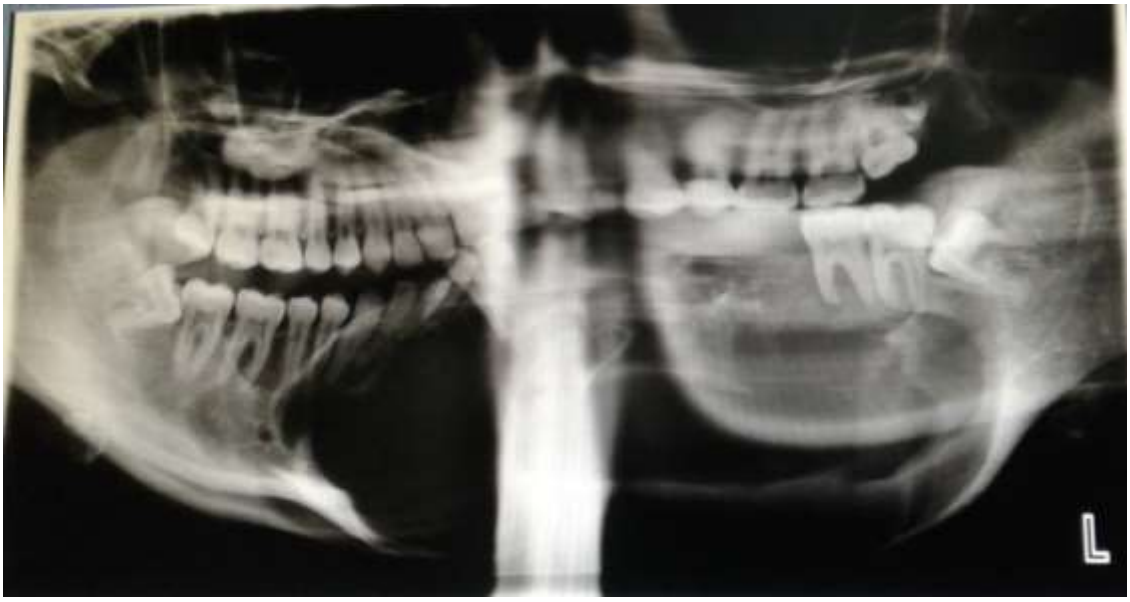

Figure 6: Orthopantogram showing large cystic bone lesion within the body of the mandible with adjacent absent and displaced, hanging roots of the remaining teeth diagnosed as ameloblastoma

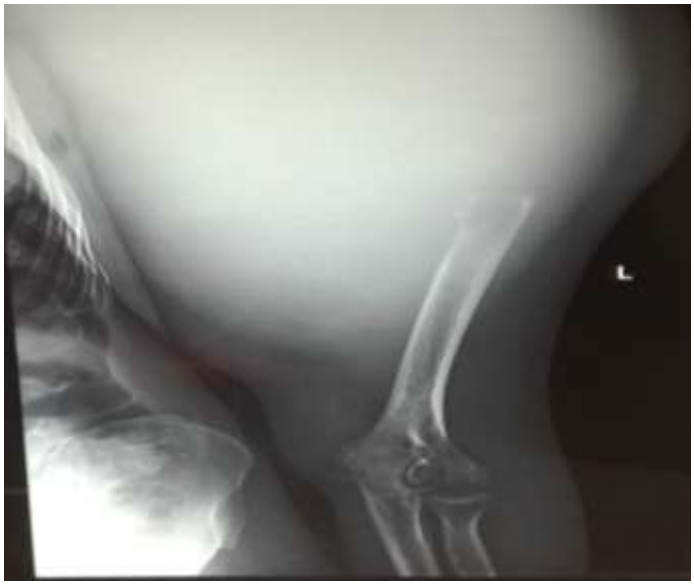

Figure 7: Radiograph of left humerus showing a large regular, sclerotic bone lesion with adjacent bone cortical thinning on the proximal shaft diagnosed as osteogenic sarcoma

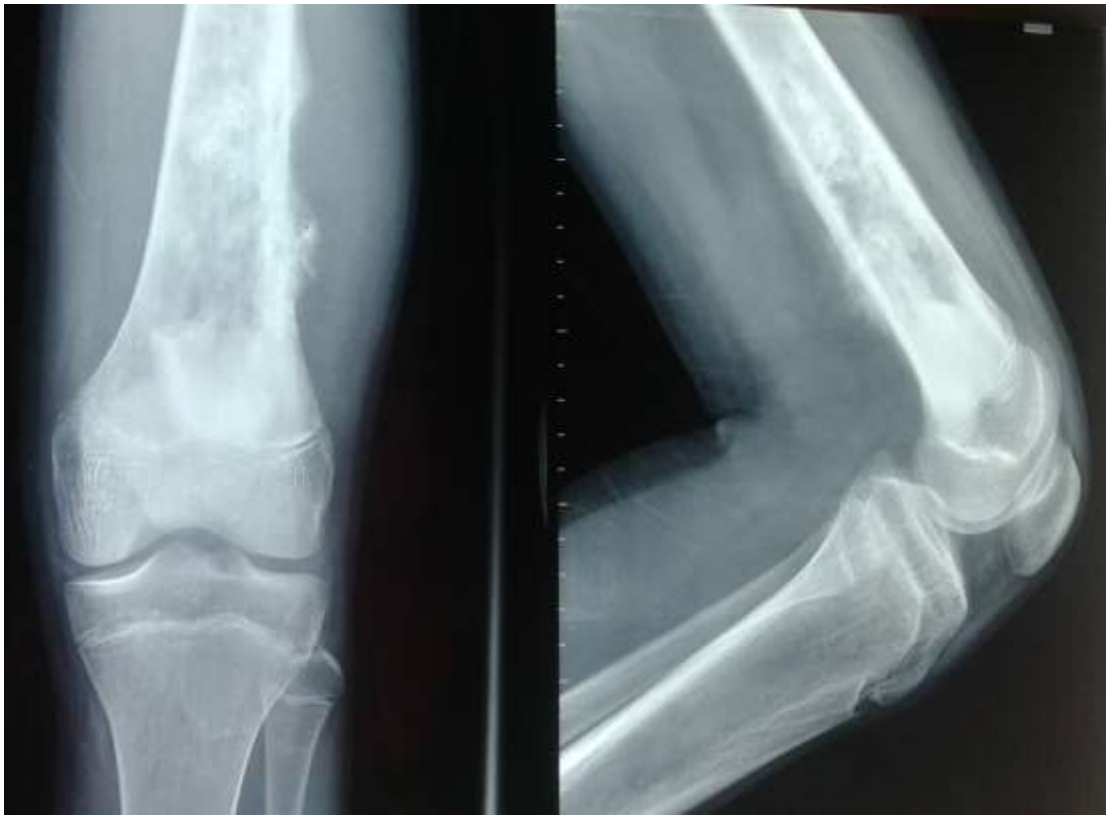

Figure 8: Radiograph of the left distal femur and proximal tibia and fibula, showing metadiaphysial femoral marrow sclerotic lesion with lamellated periosteal reaction, diagnosed as Ewing's sarcom

CHAPTER FIVE

DISCUSSION

5.1 Introduction

The purpose of this study was to determine the percentage agreement of between radiographic and histopathological diagnosis of primary bone tumours at MTRH.

Plain radiographs form the basis for initial imaging of suspected bone tumors. It provides excellent resolution, allows for assessment of lesion characteristics.

Although plain film radiograph is commonly the first objective evidence to suggest a bone tumor a definitive diagnosis is rarely made with a plain radiograph alone, and must be correlated with clinical data and the results of pathologic examination of the specimen.

5.2 Demographic characteristics

A total of 47 patients (aged 10 to 74 years)with median age of 18yrs (IQR 14, 35) and mean age of 26yrs were studied .The peak age was 10-18 years (49%). This finding is consistent with a similar study that found out that the peak age was in the second decade (Jain et al., 2011). Males were 24 (51%) while females were 23 (49%). This shows a male to female ratio of 1:1, similar to a study in Ethiopia (Negash, Admasie, Wamisho, & Tinsay, 2009).

5.3 Presenting symptom of primary bone tumours

The most common presenting symptom was painless bony swelling at 59.6%, followed by painful bony lesion at 27.7%. This differed with a similar study in India where pain with swelling was the commonest presenting complain (Patil, 2012). The painless bony lesions in our study explains why there is a delay in hospital

presentation by these cases. Symptoms are important in evaluation of primary bone tumours as they help in generating differential diagnoses.

5.4 Radiographic characteristics of primary bone tumours

Radiography is the optimal initial imaging modality for evaluating undiagnosed primary bone tumors. The advantage of radiographic technique is to collapse the density of all points in the imaging plane into a 2D image. The obtained image allows the efficient evaluation of characteristics that reflect the biologic activity or growth rate of primary bone tumors ,for example lesion margins, periosteal reaction, cortical expansion, thinning, and destruction (Costelloe & Madewell, 2013)

The specific radiographic appearance of primary bone tumours helps to narrow down the list of differential diagnoses and will often lead to a single correct diagnosis.

The location of the lesion in the bone, both transversely and longitudinally, can also be useful in narrowing the differential (Cronin & Hughes, 2012)

Majority of these primary bone tumours in terms of longitudinal location were classified as other (42.6%) because they were not tumours of the long bones .Most were maxillofacial and axial skeleton tumours .The long bone tumours, majority affected the epiphysis and metaphysis at 17% each. This was so because majority being osteogenic sarcoma whose their site of predilection is at the end of the long bones. On transverse location, majority were cutting across the cortex and the medulla of the bone affected.

Assessment of the margins is the greatest contributing factor to radiographic assessment of the biologic potential of the lesions (Costelloe & Madewell, 2013). The irregular borders of the bone tumours were slightly dorminant at 51.1%. This was so because malignant tomours were more in this study, and they are rapidly growing

tumours thus more bone formation/destruction resulting in irregularity. The imaging characteristic that is most reflective of whether the primary bone tumour is aggressive (typically malignant) or nonaggressive (typically benign) in nature is the appearance of the margin, which is an indicator of the growth rate of the lesion(Lodwick, Wilson, Farrell, Virtama, & Dittrich, 1980).

Geographical pattern of bone destruction was more common at 63.8%.This pattern is seen in less aggressive tumours e.g. benign, multiple myeloma and low grade chondrosarcoma which cumulatively represented a majority of this study's findings. This tumours have narrow zone of transitional zone and can have a sclerotic rim or not. This explains why both benign and low grade malignant bone tumours display this characteristic.

The commonest type of matrix mineralization was osteoid matrix at 74.4%. This type of matrix is found in both benign and malignant bone tumors and therefore does not closely correlate to malignant potential but it is useful in identifying the histologic type of the bone tumor (Madewell et al., 1981).In this study there was a high figure of osteogenic sarcoma and ossifying fibroma which both have osteoid matrix pattern. The solid type of periosteal reaction at 44.7% formed the majority.

Most of the primary bone tumours had soft tissue involvement (72.3%). This is mostly seen in malignant tumours which formed a majority of this study's findings. Tumour extension beyond the cortex to create a soft tissue mass generally indicates an aggressive lesion (Wyers, 2010)

Plain radiography diagnosed 40.4% of cases as benign majority being ameloblastoma and 59.6% as malignant. Osteogenic sarcoma formed a majority of malignant bone tumours at 67.9%

The high incidence of Ameloblastomas seen in this study is because MTRH being a regional referral hospital, more cases are referred to this facility for further treatment thus the high figure. It also tends to affect blacks more ,that is as per a south African study that found out that ameloblastoma is very much more common in Blacks than Whites in the population at risk (Shear & Singh, 1978). Ameloblastoma is also the commonest odontogenic tumour among blacks while odontomas is the commonest among whites(Lu et al., 1998). Ameloblastoma has also been noted to be the commonest odontogenic tumour in Africa and this was as per a study in Tanzania (Simon, Stoelinga, Vuhahula, & Ngassapa, 2002). This differ with a similar studies in India(Patil, 2012) and Addis Ababa (Negash et al., 2009) that found giant cell tumour and exostosis to be the commonest benign primary bone tumours respectively.

Osteogenic sarcoma is the most common primary malignant bone tumour, and this is a common observation in other African studies (Mohammed & Isa, 2007; Omololu et al., 2002) and in the world (Mirabello, Troisi, & Savage, 2009).

5.5 Histological diagnoses

A spectrum of 16 different types of histological bone tumours were diagnosed by the histopathology department. This indicates presence of a variety of primary bone tumours in MTRH as a referral hospital.

5.6 Comparison between radiological and histological findings

The bone lesion margins have a strong association with the final diagnosis i.e. whether it is a benign or malignant bone lesion. In this study,87.5% of those with irregular margins turned out to be malignant while 60.9% of the lesions with regular margins were found out to be benign with a p value of <0.001.This is a strong association and it implies that bone tumour margins is a predictor of whether it is

benign or malignant tumour .This is also demonstrated by a study in Netherlands on usefulness of radiography in differentiating enchondroma (benign) and grade 1 chondrosarcoma (malignant), which found out that lesion margin and lobulated contours were the only radiographic characteristics that allowed significant discrimination (p=0.004 and 0.009 respectively) (Geirnaerdt et al., 1997). There was weak association of soft tissue involvement and the ultimate diagnosis with a p value 0.176. This is because plain radiography is limited in evaluation of soft tissue involvement by bone tumours as it primarily involves the identification of fatty or calcified components(Morley & Omar, 2014).The other plain radiographic characteristics i.e. pattern of bone destruction, type of matrix mineralization and type of periosteal reaction have no association with the ultimate histological diagnosis of bone tumour. This was due to the small numbers in each sub-classification of these characteristic thus unable to generate any conclusion.

Considering histology to be the gold standard test, in this study radiology was able to diagnose more than 85% of multiple myeloma, osteogenic sarcoma and ameloblastoma. It could not correctly diagnose chordoma and aneurysmal bone cyst (0%) while for chondrosarcoma radiology diagnosed half (50%) of the cases correctly.

The disagreement of radiologically diagnosed cartilaginous bone tumours e.g. chondrosarcomas and chordomas was high at 55.6% cumulatively. Despite the fact that most cartilage tumors present with characteristic features on medical imaging, the differential diagnosis between the various types still pose a challenge. This is illustrated by the limited discriminating power of a set of plain film parameters, including margins, sclerotic rim, contour, thickening or thinning of the cortex, expansion, periosteal reaction, and soft tissue extension. For example, in a correlation

study between radiological and histological diagnosis ,only ill-defined margins and lobulated contours allow significant discrimination between enchondroma and grade-I chondrosarcoma (Wang, De Beuckeleer, De Schepper, & Van Marck, 2001).In our study, what was diagnosed radiologically as chondrosarcoma turned out histologically to be a osteochondroma, osteogenic sarcoma and synovial sarcoma. Also what was thought to be chordoma radiologically was diagnosed to be osteogenic sarcoma and metastatic carcinoma histologically.

The percentage agreement between radiology and histology departments in diagnosing primary bone tumours was higher for malignant bone tumours (82.14%) as compared to benign bone tumours (68.42%). This was similar to a study done in Kenyatta national hospital(Kimari, 1995) where 54.8% of the malignant lesions had the same specific diagnosis on radiology and histology higher than benign bone tumours at 30%.In our set up in reference to the findings of this study, primary malignant bone tumours are more common than benign thus the better the experience in diagnosing the same. Osteochondroma, multiple myeloma, osteogenic sarcoma and ameloblastoma, all demonstrated excellent agreement i.e. more than 85%. This mean you can comfortably rely on plain radiography in diagnosis of the primary bone tumours.

The overall percentage agreement between the two tests was 76.6%.This is excellent agreement. The 23.4% disagreement is due to the deficits of plain radiography which include anatomic overlap that can obscure abnormalities and a limited capacity to evaluate soft tissue. It is also limited for determining the degree of extraosseous tumor volume, relationship of extraosseous tumor to surrounding structures, and extent of disease in the intact marrow cavity. MRI is the modality of choice for simultaneously

evaluating these relationships (Aisen et al., 1986; Tehranzadeh, Mnaymneh, Ghavam, Morillo, & Murphy, 1989). MRI have a lower sensitivity for the detection of mineralized matrix when compared with CT.

Plain radiography sensitivity and specificity are 88.2% and 86.7% respectively were established from this study. The sensitivity was higher and specificity lower in this study compared to an Australian study on comparison of hybrid FDG positron emission tomography/computed tomography (PET/CT) with conventional imaging (CI) modalities in detecting malignant lesions, in pediatric primary bone tumor,where PET/CT had higher sensitivity and specificity than CI (83%, 98% and 78%, 97%, respectively)(London et al., 2012).This was in comparison to histopathology as the gold standard.On a study by European society of medical oncologist on FDG–PET for detection of recurrences from malignant primary bone tumors: comparison with conventional imaging where histopathology was used as the gold standard too .conventional imaging had a sensitivity of 1.0, a specificity of 0.56 and an accuracy of 0.82(Franzius et al., 2002).This demonstrated a higher sensitivity and lower specificity compared to our study.

Conventional radiography demonstrates a sensitivity of 76.4% and a specificity of 55.0%, in diagnosis of aneurysmal bone cyst(Mahnken et al., 2003).This is lower compared to our study ,meaning it has a lower diagnostic accuracy for aneurysmal bone cyst individually compared to overall diagnosis of primary bone tumours. The current scientific data have shown that panoramic images i.e orthopantogram have 97% sensitivity and 45% specificity for identifying hyperplastic conditions in the temporomandibular joint(Shintaku et al., 2010).The challenge in this study is that it was localized to the temporomandibular region only.

5.7 Study limitations

1. Small sample size

CHAPTER SIX
CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

1. The bone lesion margins have a strong association with the final diagnosis i.e. whether it is a benign or malignant bone lesion with a p of <0.001 where as soft tissue involvement have a weak association with the ultimate diagnosis with a p value 0.176. Commonest radiologically diagnosed primary benign bone tumour was ameloblastoma and malignant bone tumour was osteogenic sarcoma

2. The percentage agreement between radiology and histology was higher for primary malignant bone tumours (82.14%) than for primary benign bone tumours (68.42%).The observed percentage agreement between the two diagnoses was 87%.

3. The overall Plain radiography sensitivity and specificity are 88.2% and 86.7% respectively ,in diagnosis of primary bone tumours

6.2 Recommendation

Radiologists should note that bone lesion margin is a key feature to assess when characterizing primary bone tumour lesions into either benign or malignant.

Plain radiography should be used in diagnosis of primary bone tumours in absence of histopathological services i.e. in resource poor set up.

REFERENCES

Aisen, A. M., Martel, W., Braunstein, E. M., McMillin, K. I., Phillips, W. A., & Kling, T. (1986). MRI and CT evaluation of primary bone and soft-tissue tumors. *American Journal of Roentgenology, 146*(4), 749-756.

Anfinsen, K., Devesa, S. S., Bray, F., Troisi, R., Jonasdottir, T., Bruland, O., & Grotmol, T. (2011). Age-period-cohort analysis of primary bone cancer incidence rates in the United States (1976-2005). *Cancer Epidemiology and Prevention Biomarkers*, cebp. 0136.2011.

Berquist, T., Dalinka, M., Alazraki, N., Daffner, R., DeSmet, A., el-Khoury, G., . . . Newberg, A. (2000). Bone tumors. American College of Radiology. ACR Appropriateness Criteria. *Radiology, 215*, 261.

Colleran, G., Madewell, J., Foran, P., Shelly, M., & O'Sullivan, P. J. (2011). *Imaging of soft tissue and osseous sarcomas of the extremities.* Paper presented at the Seminars in Ultrasound, CT and MRI.

Costelloe, C. M., & Madewell, J. E. (2013). Radiography in the initial diagnosis of primary bone tumors. *American Journal of Roentgenology, 200*(1), 3-7.

Cronin, M. V., & Hughes, T. H. (2012). Bone tumors and tumor-like conditions of bone. *Appl Radiol, 41*(10), 6.

del Carmen Baena-Ocampo, L., Ramirez-Perez, E., Linares-Gonzalez, L. M., & Delgado-Chavez, R. (2009). Epidemiology of bone tumors in Mexico City: retrospective clinicopathologic study of 566 patients at a referral institution. *Annals of diagnostic pathology, 13*(1), 16-21.

Dodge, O. (1964). Bone tumours in Uganda Africans. *Br J Cancer, 18*(4), 627.

Dorfman, H., & Czerniak, B. (1998). Bone tumors. St. Louis, Missouri: Mosby: Inc.

Franzius, C., Daldrup-Link, H., Wagner-Bohn, A., Sciuk, J., Heindel, W., Jürgens, H., & Schober, O. (2002). FDG–PET for detection of recurrences from malignant primary bone tumors: comparison with conventional imaging. *Annals of oncology, 13*(1), 157-160.

Fuchs, B., & Pritchard, D. J. (2002). Etiology of osteosarcoma. *Clinical Orthopaedics and Related Research®, 397*, 40-52.

Geirnaerdt, M., Hermans, J., Bloem, J. L., Kroon, H. M., Pope, T., Taminiau, A., & Hogendoorn, P. (1997). Usefulness of radiography in differentiating enchondroma from central grade 1 chondrosarcoma. *AJR Am J Roentgenol, 169*(4), 1097-1104.

Ghadirian, P., Fathie, K., & Emard, J.-F. (2001). Epidemiology of bone cancer: An overview. *Journal of Neurological and Orthopaedic Medicine and Surgery, 21*, 8-16.

Greenspan, A. (2011). *Orthopedic imaging: a practical approach*: Lippincott Williams & Wilkins.

Group, S. L. I. C. a. E. D. S. (2007). Reliability of histopathologic and radiologic grading of cartilaginous neoplasms in long bones. *JBJS, 89*(10), 2113-2123.

Hawkins, M. M., Wilson, L. M. K., Burton, H. S., Potok, M. H., Winter, D. L., Marsden, H. B., & Stovall, M. A. (1996). Radiotherapy, alkylating agents, and risk of bone cancer after childhood cancer. *JNCI: Journal of the National Cancer Institute, 88*(5), 270-278.

Jain, K., Sunila, R. R., Mruthyunjaya, C., Gadiyar, H., & Manjunath, G. (2011). Bone tumors in a tertiary care hospital of south India: A review 117 cases. *Indian journal of medical and paediatric oncology: official journal of Indian Society of Medical & Paediatric Oncology, 32*(2), 82.

Kimari, P. K. (1995). *Bone tumour diagnosis; a comparison of roentgenography and histopathology in the diagnosis of bone tumours: a study at Kenyatta National Hospital, nairobi.* University of Nairobi.

Kricun, M. (1983). Radiographic evaluation of solitary bone lesions. *The Orthopedic clinics of North America, 14*(1), 39-64.

Lodwick, G. S. (1965). A probabilistic approach to the diagnosis of bone tumors. *Radiol Clin North Am, 3*(3), 487-497.

Lodwick, G. S., Wilson, A. J., Farrell, C., Virtama, P., & Dittrich, F. (1980). Determining growth rates of focal lesions of bone from radiographs. *Radiology, 134*(3), 577-583. doi: 10.1148/radiology.134.3.6928321

London, K., Stege, C., Cross, S., Onikul, E., Graf, N., Kaspers, G., . . . Howman-Giles, R. (2012). 18 F-FDG PET/CT compared to conventional imaging modalities in pediatric primary bone tumors. *Pediatric radiology, 42*(4), 418-430.

Lovell, W. W., Winter, R. B., Morrissy, R. T., & Weinstein, S. L. (2006). *Lovell and Winter's pediatric orthopaedics* (Vol. 1): Lippincott Williams & Wilkins.

Lu, Y., Xuan, M., Takata, T., Wang, C., He, Z., Zhou, Z., . . . Nikai, H. (1998). Odontogenic tumors: a demographic study of 759 cases in a Chinese population. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, 86*(6), 707-714.

Madewell, J. E., Ragsdale, B. D., & Sweet, D. E. (1981). Radiologic and pathologic analysis of solitary bone lesions. Part I: internal margins. *Radiol Clin North Am, 19*(4), 715-748.

Mahnken, A., Nolte-Ernsting, C., Wildberger, J., Heussen, N., Adam, G., Wirtz, D., . . . Haage, P. (2003). Aneurysmal bone cyst: value of MR imaging and conventional radiography. *Eur Radiol, 13*(5), 1118-1124.

Mangham, D. C., & Athanasou, N. A. (2011). Guidelines for histopathological specimen examination and diagnostic reporting of primary bone tumours. *Clinical sarcoma research, 1*(1), 1.

Miller, T. T. (2008). Bone tumors and tumorlike conditions: analysis with conventional radiography. *Radiology, 246*(3), 662-674.

Mirabello, L., Troisi, R. J., & Savage, S. A. (2009). Osteosarcoma incidence and survival rates from 1973 to 2004. *Cancer, 115*(7), 1531-1543.

Mohammed, A., & Isa, H. (2007). Pattern of primary tumours and tumour-like lesions of bone in Zaria, Northern Nigeria. *West Afr J Med, 26*(1), 37-41.

Morley, N., & Omar, I. (2014). Imaging evaluation of musculoskeletal tumors *Orthopaedic Oncology* (pp. 9-29): Springer.

Negash, B., Admasie, D., Wamisho, B., & Tinsay, M. (2009). Pattern of Bone Tumours Seen at Addis Ababa University, Ethiopia.

Ode, M., Misauno, M., Nwadiaro, H., Onche, I., Shitta, A., & Amupitan, I. (2014). Pattern and Distribution of Primary Bone Tumours in Jos Nigeria.

Omololu, A., Ogunbiyi, J., Ogunlade, S., Alonge, T., Adebisi, A., & Akang, E. (2002). Primary malignant bone tumour in a tropical African University teaching hospital. *West Afr J Med, 21*(4), 291-293.

Ottaviani, G., & Jaffe, N. (2009). The etiology of osteosarcoma *Pediatric and adolescent osteosarcoma* (pp. 15-32): Springer.

Oudenhoven, L. F., Dhondt, E., Kahn, S., Nieborg, A., Kroon, H. M., Hogendoorn, P. C., . . . De Schepper, A. (2006). Accuracy of radiography in grading and tissue-specific diagnosis--a study of 200 consecutive bone tumors of the hand. *Skeletal Radiol, 35*(2), 78-87. doi: 10.1007/s00256-005-0023-y

patil, p. (2012). *a study of agreement between histopathological and clinico-radiological diagnosis of bone tumours and tumour-like lesions.*

Priolo, F., & Cerase, A. (1998). The current role of radiography in the assessment of skeletal tumors and tumor-like lesions. *European journal of radiology, 27*, S77-S85.

Resnick, D., & Niwayama, G. (2002). Skeletal metastases. *Diagnosis of Bone and Joint Disorders. 4th ed. Philadelphia, PA: WB Saunders Co*, 4274-4351.

Rosenthal, D. I. (1997). Radiologic diagnosis of bone metastases. *Cancer, 80*(S8), 1595-1607.

Salkić, N. N. (2008). Objective assessment of diagnostic tests validity: a short review for clinicians and other mortals. Part II. *Acta Medica Academica, 38*(1), 39-42.

Shear, M., & Singh, S. (1978). Age-standardized incidence rates of ameloblastoma and dentigerous cyst on the Witwatersrand, South Africa. *Community dentistry and oral epidemiology, 6*(4), 195-199.

Shintaku, W. H., Venturin, J. S., Langlais, R. P., & Clark, G. T. (2010). Imaging modalities to access bony tumors and hyperplasic reactions of the temporomandibular joint. *Journal of Oral and Maxillofacial Surgery*, *68*(8), 1911-1921.

Simon, E., Stoelinga, P., Vuhahula, E., & Ngassapa, D. (2002). Odontogenic tumors and tumor—like lesions in Tanzania. *East Afr Med J, 79*(1), 3-7.

Sundaram, M., & McLeod, R. A. (1990). MR imaging of tumor and tumorlike lesions of bone and soft tissue. *AJR Am J Roentgenol, 155*(4), 817-824. doi: 10.2214/ajr.155.4.2119115

Sweet, D. E., Madewell, J. E., & Ragsdale, B. D. (1981). Radiologic and pathologic analysis of solitary bone lesions. Part III: matrix patterns. *Radiol Clin North Am, 19*(4), 785-814.

Tehranzadeh, J., Mnaymneh, W., Ghavam, C., Morillo, G., & Murphy, B. J. (1989). Comparison of CT and MR imaging in musculoskeletal neoplasms. *J Comput Assist Tomogr, 13*(3), 466-472.

Tenge, C. N., Kuremu, R. T., Buziba, N. G., Patel, K., & Were, P. A. (2009). Burden and pattern of cancer in Western Kenya. *East Afr Med J, 86*(1), 7-10.

Unni, K., Inwards, C., Bridge, J., Kindblom, L., & Wold, L. (2005). Tumors of the Bones and Joints (Atlas of Tumor Pathology series IV). *Washington, DC: American Registry of Pathology*, 324-330.

Wamisho, B. L., Admasie, D., Negash, B. E., & Tinsay, M. W. (2009). Osteosarcoma of limb bones: a clinical, radiological and histopathological diagnostic agreement at Black Lion Teaching Hospital, Ethiopia. *Malawi Med J, 21*(2), 62-65.

Wang, X., De Beuckeleer, L., De Schepper, A., & Van Marck, E. (2001). Low-grade chondrosarcoma vs enchondroma: challenges in diagnosis and management. *Eur Radiol, 11*(6), 1054-1057.

White, L. M., & Kandel, R. (2000). Osteoid-producing tumors of bone. *Semin Musculoskelet Radiol, 4*(1), 25-43.

Wyers, M. R. (2010). Evaluation of pediatric bone lesions. *Pediatric radiology, 40*(4), 468-473.

Yanagawa, T., Watanabe, H., Shinozaki, T., Ahmed, A. R., Shirakura, K., & Takagishi, K. (2001). The natural history of disappearing bone tumours and tumour-like conditions. *Clin Radiol, 56*(11), 877-886. doi: 10.1053/crad.2001.0795

Yeole, B. B., & Jussawalla, D. J. (1998). Descriptive epidemiology of bone cancer in greater Bombay. *Indian J Cancer, 35*(3), 101-106.

Yuh, W., Corson, J., Baraniewski, H., Rezai, K., Shamma, A., Kathol, M., . . . Platz, C. (1989). Osteomyelitis of the foot in diabetic patients: evaluation with plain film, 99mTc-MDP bone scintigraphy, and MR imaging. *American Journal of Roentgenology, 152*(4), 795-800.

APPENDICES

Appendix I: Consent Form

English Version

Investigator: My name is Dr. Kiplagat Nancy. I am a qualified doctor, registered by the Kenya Medical Practitioners and Dentists Board. I am currently pursuing a Masters degree in Radiology and Imaging at Moi University. I would like to recruit you into my research which is to study the comparison between radiographic and histopathologic diagnosis of primary bone tumours at Moi teaching and referral hospital.

Purpose: This study will seek to compare the radiographic and histopathological diagnosis of primary bone tumours seen at MTRH. The results will help in improving care of patients.

Procedure: All patients referred by clinicians to imaging department whose plain radiograph of the bone suggest primary bone tumor in the will be guided by the researcher to fill the questionnaire. Their histology results shall be followed up by the researcher .A comparison between their radiographic and histopathologic diagnosis will be determined. Their strength of agreement between the two diagnoses will be measured using Cohen's kappa test.

Benefits: There will be no direct benefits of participating in this study. Study subjects will be accorded same quality of management as non-study subjects

Risks: There are no anticipated risks to the participants attributable to this study.

Confidentiality: All information obtained in this study will be treated with utmost confidentiality and shall not be divulged to any unauthorized person

Rights to Refuse: Participation in this study is voluntary, there is freedom to refuse to take part or withdraw at any time. This study has been approved by the Institutional

Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

Sign or make a mark if you agree to take part in the study

Parent/Guardian: …… Investigator:…….. Date:…….

Kiswahili Version

Mpelelezi: jina langu ni Dr Kiplagat Nancy. Mimi ni daktari aliohitimu, kusajiliwa na bodi ya Kenya ya Madaktari na Madaktari wa meno. Mimi sasa natafuta shahada ya uzamili katika Radiology na Imaging katika Chuo Kikuu cha Moi. Ningependa kukusajili wewe katika utafiti wangu ambao ni wa kujifunza matokeo ya picha wa mifupa kwa walio na saratani ya mifupa ikilinganishwa na matokeo ya mahabara ya sehemu ndogo ya hiyo mifupa katika hospitali ya mafundisho na ya rufaa ya moi.

Kusudi: Utafiti huu watajaribu kueleza matokeo ya picha(x ray) wa mifupa kwa walio na saratani ya mifupa ikilinganishwa na matokeo ya mahabara ya sehemu ndogo ya mfupa

Utaratibu: Watu wote ambao wana dalili za saratani ya mfupa watasajilwa katika utafiti huu.Watapigwa picha ya X-ray na sehemu ndogo ya mfupa katika sehemu iliyo na dalili ya saratani kujukuliwa kwenye mahabara ili kufanyiwa uchunguzi.matokeo ya mahabara na yale ya picha yatalinganishwa. Data zitakusanywa kwenye fomu za ukusanyaji data. Hifadhi zitakazo tumika katika ukusanyaji wa data zitawekwa katika kabati iliyofungwa katika nyumba ya mpelelezi mkuu katika kipindi cha utafiti.

Faida: Hakuna faida moja kwa moja ya kushiriki katika utafiti huu. Wanaofanyiwa utafiti watakuwa nahaki nakupewa ubora sawa na wale ambao hawatofanyiwa utafiti huo.

Hatari: Hakuna hatari ya kutarajia kwa washiriki inatokana na utafiti huu.

Usiri: habari zote zilizopatikana katika utafiti huu wa kutibiwa zitawekwa kwa usiri mkubwa na wala haitatolewa kwa mtu yeyote asiye husika na utafiti.

Haki ya kukataa: Kushiriki katika utafiti huu ni hiari yako, kuna uhuru wa kukataa kuchukua sehemu au kutoka wakati wowote. Utafiti huu imekuwa kupitishwa na

Utafiti wa Taasisi na Kamati ya Maadili (IREC) ya Chuo Kikuu cha kufundishia Moi na Hospitali ya Rufaa.

Kusaini au kufanya alama kama unakubali kushiriki katika utafiti

Mgonjwa/ Mlezi: ..... Mpelelezi:.....

Tarehe: .....

Participant Statement

I Mr/Mrs/Miss,……..hereby give consent to Kiplagat Nancy to include in the proposed study entitled "**comparison between radiographic and histopathological diagnosis of primary bone tumours at Moi teaching and referral"**. I have read the information concerning this study, and I fully understand the aim of the study and what will be required of me if I accept to take part in the study. The risks and benefits have been explained to me. Any questions I have concerning the study have been adequately answered and I am satisfied.

I understand that I can withdraw from this study anytime if I wish so without giving any reason and this will not affect my access to normal health care and management.

Name of Participant or respondent.....

(Jina la mhojiwa)

Signature/*Sahihi*.....**Or/Ama**Thumb print *(Left)/ Alama ya kidole gumba (Kushoto)*

Date/*Tarehe*.....

Name of Witness.....

(*Jina la shahidi)*

Signature/*Sahihi*.....Date/Tarehe……

[The name and signature of the witness is ONLY necessary if the participant is illiterate.]

(For patients under 18 years)

Name of Guardian/ Parent giving

consent……

Signature/*Sahihi*…… Or/*Ama* Thumb print *(Left)/Alama ya kidole*

Gumba (kushoto)

Date/*Tarehe*……

Name of the person taking consent……

(Jina la anayetoa idhini

Signature/*Sahihi*….....Date/*Tarehe* ……

Sign or make a mark if you agree to take part in the study

Parent/Guardian: …… Investigator: …….. Date:

Appendix 2: Study Questionnaire

SOCIO-DEMOGRAPHICS

Date: ……. Medical Record Number: ……

Serial Number…….

Age…… Gender…….Male ☐ Female ☐

County of residence.....

Phone number……...

PRESENTATION

1.Bony swelling without pain Yes ☐ No ☐

2.Painful bone lesions Yes ☐ No ☐

3.Pathologic fractures Yes ☐ No ☐

PLAIN RADIOGRAPHY EXAMINATION

1. Number of bone lesions…….

2. Location of bone lesion a) longitudinal axis i.e. i) Diaphysis

ii)Epiphysis

iii) Metaphysis

iv) Mixed

b) Transverse axis i.e. i) cortex

ii) Medulla

3. Borders of the lesion; regular ☐ irregular ☐

4. Type of bone destruction (tick appropriately)

a) Geographic pattern

b)"Moth-eaten" pattern

c) Permeative pattern

d) Cortical expansion

e) Mixed pattern

5. Type of matrix mineralization (tick appropriately)

a) Chondroid matrix,

b) Osteoid matrix or

c) Fibrous matrix

d) Mixed matrix

6. Type of periosteal reaction (tick appropriately)

a)Continuous e.g. onion-skin

b) Interrupted e.g. codman's triangle

c) Complex pattern i.e a mix of various types

d) Solid type

7. Presence of soft tissue involvement, Yes ☐ No ☐

FINAL RADIOLOGIC DIAGNOSIS

1. Benign bone tumour Yes ☐ No ☐

If yes, specify…….

2. Malignant bone tumour Yes ☐ No ☐

If yes, specify……..

HISTOLOGIC DIAGNOSIS

What is the histopathological diagnosis……

Appendix 3: IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOITEACHINGANDREFERRALHOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOIUNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference IREC/2016/97
Approval Number: 0001695

23rd February, 2018

Dr. Kiplagat Nancy Jebor,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
23 FEB 2018
APPROVED
P. O. Box 4606 - 30100 ELDORET

Dear Dr. Kiplagat,

RE: APPROVAL OF AMENDMENT

The Institutional Research and Ethics Committee has reviewed the amendment made to your proposal titled:-

"Comparison between Radiographic and Histopathological Diagnosis of Primary Bone Tumors at Moi Teaching and Referral Hospital".

We note that you are seeking to make an amendment as follows:-

1. To change the title to above from "***Correlation of Radiographic Features and Histopathological Diagnosis of Primary Bone Tumours at Moi Teaching and Referral Hospital".***

The amendment has been approved on 23rd February, 2018 according to SOP's of IREC. You are therefore permitted to continue with your research.

You are required to submit progress(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change(s) or amendment(s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: CEO - MTRH Dean - SPH Dean - SOM
Principal - CHS Dean - SOD Dean - SON

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2016/97
Approval Number: 0001695

28th July, 2016

Dr. Kiplagat Nancy Jebor,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
28 JUL 2016
APPROVED
P. O. Box 4606-30100 ELDORET

Dear Dr. Kiplagat,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Correlation between Radiographic Features and Histopathological Findings of Primary Bone Tumours at Moi Teaching and Referral Hospital".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1695*** on 28th July, 2016. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 27th July, 2017. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc	CEO	-	MTRH	Dean	-	SOP	Dean	-	SOM
	Principal	-	CHS	Dean	-	SON	Dean	-	SOD