SCHOOL OF MEDICINE

THE CORRELATION BETWEEN RADIOLOGICAL FEATURES AND HISTOPATHOLOGICAL FINDINGS AMONG PATIENTS WITH INTRACRANIAL MENINGIOMAS IN ELDORET, KENYA

BY

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The correlation between radiological features and histopathological findings among patients with intracranial meningiomas in Eldoret, Kenya

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DECLARATION

Student's Declaration:

I declare that this thesis is my original work, that it has never been presented elsewhere for academic purposes or otherwise to the best of my knowledge. The research work was carried out while pursuing my Master in Medicine in Radiology and Imaging course at the Moi University, School of Medicine. No part of this work may be reproduced without permission of the author and or Moi University.

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DEDICATION

I dedicate this thesis to my husband Dr. Abuodha O. Joseph for his support and encouragement in writing this thesis and to my children Charles and Christopher Abuodha, all of whom are a constant and daily inspiration in my life.

ABSTRACT

Background: Meningiomas are amongst the commonest primary brain tumours accounting for about 33% of all brain tumours. World Health Organization classifies meningiomas into three grades based on histopathology; the subtype of which affects the prognosis. Imaging plays a key role in the diagnosis of meningiomas and is often the first investigation aiding in its diagnosis. This study aims to establish if there is a correlation between histopathology and the radiological features of meningiomas.

Setting: The study was done at the Moi Teaching and Referral Hospital, Mediheal and Eldoret hospitals in Eldoret, Kenya.

Objective: To assess the radiological features of intracranial meningiomas in correlation to their histopathological findings among patients in Eldoret, Kenya.

Design: A cross-sectional study design was used.

Methods: Radiopathological correlation was done using CT scan and MRI images which had a confirmatory histopathology report. 55 patients were studied from May 2008 to December 2012.Consequctive data sampling technique was done. An inclusion criterion was presence of both histopathology and CT or MRI images while exclusion was where either lacked. Data was collected by using a data collection form and analysis was done by STATA version 12.

Results: The female to male ratio was 3:1. The mean age was 47 years. The age group most affected was 45-55 years. The common CT scan features encountered were extra-axial, hyperdense (87%), mass lesions (98%) with mild (36%) to moderate oedema (45%) that avidly enhanced with contrast either homogenously (47%) or heterogeneously (53%). Common MRI features encountered were extra-axial mass lesions (97%) which were isointense (61%) on T1 weighted sequences, hyperintense (65 %) on T2 weighted images, hyperintense (65%) on FLAIR images and enhanced (100%) when gadolinium contrast was injected. The common meningiomas encountered were grade I (95%) with the meningothelial (53%), fibroblastic (22%) and transitional (20%) subtypes seen. 3 grade II atypical meningiomas were found but no malignant meningioma was encountered in the study population. Correlation between the various radiological features and histopathology was only seen with the CSF variable and this was likely a chance finding.

Conclusion and Recommendations: Though imaging can reliably diagnose meningiomas, histopathological subtypes of meningiomas cannot be differentiated from each other based on radiological features. Further studies should be done on non-benign meningiomas which were few in this study and why secondary changes common in benign meningiomas. Histopathology should be improved by doing immunohistochemistry.

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LIST OF ABBREVIATIONS

CPA	Cerebellopontine Angle
CSF	Cerebrospinal fluid
CT Scan	Computer Tomography Scan
CVA	Cerebrovascular Accident
FLAIR	Fluid Attenuation Inversion Recovery
IQR	Interquartile Range
KNH	Kenyatta National Hospital
MRI	Magnetic Resonance Imaging
MRS	Magnetic Resonance Spectroscopy
MTRH	Moi Teaching and Referral Hospital
PET	Positron Emission Tomography
RT	Radiation Therapy
SOL	Space Occupying Lesion
Std	Standard deviation
WHO	World Health Organization

OPERATIONAL DEFINITION OF TERMS

Benign tumour	Tumours that do not infiltrate into the surrounding tissues
Leptomeninges	The inner two membranes that protect the brain; the pia and arachnoid
Malignant tumour	Tumours that are cancerous and invade surrounding tissues
Meninges	Three layered connective tissue membranes that protect the brain and spinal cord. They consist of the Leptomeninges (pia and arachnoid) and dura mater
Meningioma	A meningioma is a brain tumour of the meninges.
Primary brain tumor	Neoplasms that originate in the brain itself
Tumour/ Neoplasm	An abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of normal tissues and persists in the same excessive manner after cessation of the stimuli which evoked the change

CHAPTER ONE: INTRODUCTION

This chapter introduces one to the background of the research topic, the problem statement, the research questions, objectives and the justification for this study.

Background

Meningiomas are brain tumours of the meninges that arise from the arachnoid cap cells and are primary central nervous tumours with 10% being found in the spine. Despite being generally benign (some are malignant), their location within the central nervous system can cause serious morbidity and mortality. They account for about a third of all brain tumours, the incidence progressively increasing with age, with most cases occurring in older individuals (1).

Overall, meningiomas are more common in women, with a female to male ratio of about two or three to one (2) (3) (4) (5). This female predominance is less pronounced or absent in those with atypical or anaplastic meningiomas, in children, and with radiation-induced meningiomas. For spinal meningiomas, the female to male ratio is approximately nine to one with a large proportion of them occurring in the thoracic spine.

The clinical presentation of meningiomas depends on the type, location and size of the tumour. Tumours less than two centimetres have been found incidentally at autopsy as they never caused symptoms. Risk factors that have been identified for meningiomas include advancing age, prior radiation therapy, chromosomal abnormalities on chromosome 22 and female hormones. There is an association of meningiomas with neurofibromatosis type 2.

These individuals are at increased risk of developing multiple meningiomas. Head trauma has also been investigated as a possible risk factor for meningiomas (6) .

WHO grades meningiomas into three grades based on morphological criteria. The grades are benign meningiomas as grade I (>90%), atypical meningiomas as grade II (5%) and malignant/ anaplastic meningiomas as grade III (1-3%). (7) Within the various grades are different histopathological subtypes of meningiomas.

Treatment of meningiomas is by surgery, (8) (9) (10) radiation therapy (11) (12) (13)**,** or watching and waiting (active surveillance) (14)**.** Embolization may be useful to increase resectability in some patients with skull base meningiomas (15) (16) (17). The mainstay of treatment of symptomatic meningiomas is surgery. When not fully resected, surgery may be followed by radiotherapy to the remaining tumour cells. Radiotherapy may be used alone in cases where the tumour is in an inaccessible site. The role of chemotherapy in the management of meningiomas is still under research.

Diagnosis of meningiomas is initially by MRI and CT scan which is later confirmed by histopathology. MRI is the preferred imaging modality because it can show the dural origin of the tumour in most cases and better outlines tumour extent and vascularity. Histology assists in diagnosis by differentiating the various meningioma grades and subtypes. This is important in terms of recurrence and prognosis. The lower the grade, the lower the risk of recurrence and aggressive growth and therefore the better the prognosis. Prognostic factors include histology subtype, age at diagnosis, tumour size and treatment modality.

This study sought to establish if there is correlation between the radiological features and histopathological findings among patients with various meningioma grades and subtypes and

by so doing, outline the differences if any and come up with recommendations in order to effect timely and appropriate management of these patients.

Research Questions

This study aimed to answer the following questions: Amongst the patients seen at MTRH, Mediheal and Eldoret Hospitals in Eldoret, Kenya:

1. What are the radiological features of meningiomas seen on CT scan and MRI?
2. What are the meningioma histopathological grades and subtypes seen?
3. Is there any correlation between the radiological features seen on CT scan or MRI and the histopathology of the meningiomas?

Justification

Meningiomas account for a significant proportion of brain tumours (33%) and thus there is need to know more about meningiomas in regards to the association of histopathology and radiological features so as to better manage the patients who present to us. Though histopathology is the definitive diagnosis, it is often done much later after radiological studies, and thus if association is found, timely patient management can often be instituted early. There is limited information available in this region on radiopathological features of meningiomas. Despite the large body of knowledge on meningiomas, there is contradicting information on the association between the histopathology and the radiological patterns. In an English study by *Vassilouthis, J and Ambrose, J.* it was found that each of the meningioma variants exhibited common CT features that could be helpful in predicting the probable histology (18), while in another study in Australia by *Kizana, E. et al* the findings were

suggestive that the histology and imaging features had no correlation (19). Another study by *Demarael, P. et al* in Belgium found that "Different histologic subtypes may have a different MR appearance, but this does not suffice to reach a histologic diagnosis by MR imaging" (20). This study therefore helped verify whether or not different meningioma grades and subtypes had different radiological features and if there are differences, it aimed to outline them.

Both CT scan and MRI were used for the study so as to capture all patients with meningiomas. Despite CT scan being the modality initially used for imaging especially due to the high cost of MRI, a significant number of patients had initially done an MRI or done it as a complementary study where necessary. Both modalities were therefore used so as not to discriminate any patients. However, of note is that CT scanning is as efficacious as MRI in defining meningiomas, their size and surrounding oedema as evidenced by a review of radiological features of intracranial meningiomas by *Kizana E et al* at the Westmead hospital in Australia (19).

Problem Statement

Meningiomas are amongst the commonest brain tumours accounting for about 33% of all brain tumours. Despite a majority of them being benign, they can cause serious morbidity and mortality. Appropriate and timely management of patients is at times delayed awaiting histopathology results, since management varies with tumour location and grade despite surgery being the mainstay of treatment**.** Availability and affordability of the key imaging modalities is an issue yet imaging plays a key role in diagnosis and planning of management of these tumours, though the definitive diagnosis is normally by histopathology.

Objectives

Main Objective:

To determine the radiological features of meningiomas in relation to histopathology among patients in MTRH, Mediheal and Eldoret hospitals in Eldoret, Kenya.

Specific Objectives:

1. To determine the radiological features of meningiomas on CT scan and MRI seen amongst patients in Eldoret, Kenya.
2. To determine the meningioma histopathological grades and subtypes seen among patients in Eldoret, Kenya.
3. To assess the correlation of radiological features seen on CT scan or MRI to the histopathology of the meningiomas in patients in Eldoret, Kenya.

CHAPTER TWO: LITERATURE REVIEW

This chapter aims to give a detailed review of literature on radiological and imaging findings of intracranial meningiomas, the various meningioma grades and subtypes and the correlation of the imaging features to histopathological findings.

Medical writings from as early as the 18th century refer to tumours arising from the meninges but it was not until 1922 that the American neurosurgeon Harvey Cushing first introduced the term "meningioma" coining this term due to tumour origin from the leptomeninges (6).

Meningiomas account for a significant proportion of brain tumours (1). Like other brain tumours, they are diagnosed on the basis of clinical presentation, imaging and histopathological confirmation. Imaging and histology are especially important as they enable differentiation of the various brain lesions.

Meningiomas arise from the arachnoid cells, particularly those packing the arachnoid villi, which protrude as finger-like projections into the walls of the dural veins and sinuses. Most meningiomas grow inward toward the brain as discrete, well-defined, dural-based masses and are spherical or lobulated. Flat tumours termed *en plaque* infiltrate the dura and grow as a thin carpet or sheet of tumour along the convexity, dura, falx or tentorium. They often cause adjacent bone hyperostosis as reported by *Zimmerman et al* in a study on magnetic resonance imaging of meningiomas (21).

The dural attachment of meningiomas can be pedunculated or broad-based (sessile). Since the pia and arachnoid form a membranous barrier between brain and tumour, some meningiomas grow into the subarachnoid space, but invasion of the brain is infrequent. Meningiomas can arise anywhere from the dura, most commonly within the skull and at sites

of dural reflection such as the falx cerebri, tentorium cerebelli, and dura of the adjacent venous sinuses. Other less common sites include the optic nerve sheath and choroid plexus. A South African study found that the common meningioma sites included the convexity and parasagittal regions (22). Other common sites are the sphenoid and falcine regions as shown by an Australian study (19).

Symptoms from a meningioma are determined by the location of the mass and by the time course over which the tumour develops. Symptoms produced by a meningioma may be general or focal. General symptoms include headaches, nausea and seizures while focal symptoms depend on the affected area and may include hearing loss and visual loss. The commonest symptoms are headaches, mental status changes, and paresis, and the most common signs are paresis, normal examinations, and memory impairment as shown by a Canadian study (23). Meningiomas are frequently slow growing and often are asymptomatic or minimally symptomatic and are discovered during a neuroimaging study or at autopsy**.**

Although results from positron emission tomography (PET) and magnetic resonance spectroscopy (MRS) may predict the aggressiveness of a meningioma and the potential for recurrence, they are not routinely used since maximal surgical resection is the goal for all grades of meningioma. Prior to the arrival of the newer imaging modalities, meningiomas were diagnosed by radiography and angiography. Angiography was used to suggest the diagnosis of meningioma by demonstrating arterial supply from meningeal vessels and the delayed vascular blush that is characteristic of these lesions. The meningeal supply typically gives rise to a ‘spoke-wheel’ appearance and a characteristic ‘mother-in-law’ phenomenon, in which the contrast shows up early and stays late into the venous phase. (24) However, the

use of angiography is now limited to tumour embolization as a component of therapy prior to surgery. Imaging currently is by CT scan and MRI.

2.1 Radiological features of meningiomas on CT scan and MRI

The purposes of imaging as assessed by Moseley are to confirm an intracranial lesion, determine its probable nature, attempt to predict degree of aggressiveness, assess its location with respect to adjacent (vital) structures and attempt to predict response to treatment (25). Imaging therefore plays a key role in the management of meningioma patients.

On CT, the typical meningioma is a well-defined extra-axial mass that displaces the normal brain, is hyperdense on pre-contrast scans with underlying oedema and enhances homogenously with contrast. Meningiomas are smooth in contour, adjacent to dural structures, and sometimes calcified or multilobulated. Calcification of meningiomas, when present, occurs in a speckled, rim like, or nodular pattern. It occurs in 20-30% of patients (26).

The typical meningioma is isointense or hypointense to grey matter on T1 and isointense or hyperintense on proton density and T2 weighted images. Isointensity on MRI with normal surrounding brain may make diagnosis difficult on a non-contrasted scan, but intravenous contrast administration results in uniformly bright enhancement (24) (27). There is usually minimal perilesional oedema.

In about 15 per cent of cases, there is an atypical pattern with necrosis, cyst formation, or haemorrhage. Cyst formation may be as a result of trapped CSF. Indistinct margins, marked oedema, mushroom-like projections from tumour, deep brain parenchymal infiltration, and

heterogeneous enhancement all suggest, but do not prove, aggressive behaviour as described by *Shapir, J, et al.* (28).

CT scanning well depicts bony hyperostosis (29), which may be difficult to appreciate on MRI. CT scanning may, however, fail to demonstrate *en plaque* and posterior fossa meningiomas. CT scanning also has limitations in performing direct imaging in any other planes than axial. CT scanning is less helpful than MRI in differentiating types of soft tissue.

A study by *Inskip, et al* on the laterality of brain tumours found that meningiomas nonsignificantly occurred more on the left side (30).

Imaging enables the detection of multiple lesions. Multiple meningiomas were previously described as uncommon but with the advent of the newer imaging modalities, the frequency of detection has increased. *Sheehy and Crockard* described a rise in detection from 1.1% of cases to 8% with modern CT scanning (31). An Israel study done at Rambam medical centre found the incidence of multiple meningiomas to be 20% and on reassessment the incidence increased to 40% (32).

2.2 Histology of meningiomas

Histopathology enables distinguishing of the various meningioma grades and subtypes. (Refer to appendix IV) This is important as the various subtypes have different prognoses and different levels of recurrence. In a single series of 1799 meningiomas from 1582 patients followed for an average of 13 years after resection in Vienna, Austria, the nonrecurrence rate was 93% of WHO I tumours, 65% of WHO II, and 27.3% of WHO III (33).

Histopathology is the basis on which WHO has classified meningiomas. WHO grades meningioma subtypes into one of three categories based primarily upon histopathology

which affects the likelihood of recurrence and the rate of growth exhibited by each. The overall classifications are benign (Grade I), atypical (Grade II) and malignant (Grade III). (7) Generally, the higher the grade the higher the rate of growth and the more likely it is to recur.

A study by *Mahmood, A. et al.* in Henry Ford Hospital, Detroit Michigan found that 92% of the meningiomas were benign, 6.26% atypical, and 1.7% malignant (34). A local study done by *Chumba K.D*. in KNH (MMed thesis) found that the commonest histopathological subtypes were meningothelial and transitional representing 35% and 30% respectively. His study found that Grade II and III subtypes accounted for 15.9% and 4% respectively (35). A more recent study in KNH by *Wanjeri J.* (MMed thesis) found that grade I meningiomas were the commonest at 94.7% and Grade II and grade III represented 4% and 1.3% respectively with fibroblastic, transitional and meningothelial accounting for 25.4%, 25.4% and 22.5% respectively (36)**.**

2.3 Correlation between meningioma radiological features and histopathology

Many trials have been done to find out whether radiologic features can predict the subtype and prognosis of meningioma (18) (37) (38). Despite this, no consensus has been arrived at with different studies drawing varied conclusions. A Belgium study by *Demarael, P. et al* found that "Different histologic subtypes may have a different MR appearance, but this did not suffice to reach a histologic diagnosis by MR imaging." This was because on T1 appearances were similar but differed on T2 which gave more information than T1 (20).

The correlation between the radiological features and histopathology may be in terms of location, number of lesions, and presence of secondary changes amongst other features. The

aim is to establish if certain features seen on imaging can give a conclusive diagnosis on the expected histopathology.

A number of imaging features have been associated with aggressiveness, such as bone destruction, central areas of necrosis, indistinct tumour margins at the brain surface, irregular inward projections of tumour and mushrooming as described in a study by N*ew P. F et al.* (37). However, the findings are far from specific and have limitations for prognosis prediction. These characteristics do not seem to be useful in distinguishing between the high-grade meningiomas or even benign meningiomas with any degree of certainty.

An English study by *Vassilouthis, J and Ambrose, J*. found that the presence of marked oedema, absence of visible calcium aggregates, non-homogeneous contrast enhancement with non-enhancing "cystic" components and poorly defined irregular borders point to aggressive or invasive characteristics more commonly found in the angioblastic and syncytial variants (18).

Malignant meningiomas tend to have irregular, indistinct margins on CT scan with various authors reporting that calcification is often absent or scanty in them as also described by *Perry, A. et al* in their study (39). *Yuguang, L. et al* found similar findings while *Alvarez, F. et al* (38) described hypodense areas within meningiomas and presence of tumour fringes as signs of malignancy.

Marked perifocal oedema with a prominent pannus or tumour, extending well away from the globoid mass, termed "mushrooming" is not usually seen in benign meningiomas (37). Tumour interdigitation with brain substance may also occur with malignant meningiomas. Before contrast enhancement, malignant meningiomas appear moderately hyperdense but enhance well after contrast administration.

A study done by *Kim, E.Y. et al* in Korea concluded that rhabdoid meningiomas tend to have prominent peritumoral oedema, cystic components, and bone involvement (40). These findings support that malignant tumours are likely to cause this since rhabdoid meningiomas are categorized as WHO grade III meningiomas.

Various investigators have related the degree of peritumoral oedema to the tumour location (41) (42), size (43) (44), histopathological subtype (44) (45) and necrosis (46) while others refute this (47) (48). Secretory meningioma variants have marked peritumoral oedema which is probably due to the secretions (47) (43). A Tokyo study concluded that there was no correlation between the presence of oedema and location of the tumour or histological feature though meningothelimatous tumours were reported to have more peritumoral oedema (49). Peritumoral oedema is often disproportionate to the size of the meningioma which implies that the degree of oedema may not necessarily worsen with increasing grade of meningioma. However a study by *Tobias, A. M. et al* concluded that: "The degree of oedema as revealed by computer tomography and magnetic resonance imaging can be an important clinical predictive factor for the histopathological grade of the meningioma" (50).

Non-skull base location has been thought to be a risk factor for grade II and III meningioma. This shows that tumour location may actually be a predictor for histopathological grade. A study on intraventricular meningiomas by *Eun Y.K. et al* (40) found that about 58% were either atypical or malignant and that they had irregular lobulation. Another finding was that intratumoral necrosis was frequently seen in the atypical and malignant types of intraventricular meningioma. These findings support that location may affect the meningioma grade which in turn affects the presence or absence of secondary changes.

Tumour size is affected by the grading of the tumour and the period for which the patient has had symptoms. Tumour size contributes to symptomatology with many small meningiomas being found incidentally during imaging for other reasons or at autopsy (51) (52).

Secondary changes such as haemorrhage, necrosis and cystic change are uncommon and when present they give a heterogeneous pattern after contrast administration as opposed to the homogenous pattern of benign meningiomas.

A study by *Oguz, K.K. and Cila, A.* in Ankara, Turkey (53), found that all meningioma types had a similar peripheral type of enhancement while meningioma size was found to determine the type of enhancement seen whether capsular or peripheral**.** This was supported by *Maiuri, F.* who also refuted a correlation between contrast enhancement and histopathology (54)**.**

Cystic change may be intratumoral or peritumoral. High levels of intratumoral cystic and necrotic change are associated with the malignant variants of meningiomas. Cystic change may be due to trapped CSF.

Benign tumours are highly unlikely to have extracranial base of skull extension so when this feature is picked on imaging it is highly suggestive of atypical/ malignant meningiomas (55). Vascular features depend on the variant of the meningioma while mass effect is as a result of tumour size. Tumour size also plays a role in midline shift and herniation when present.

CHAPTER THREE: METHODOLOGY

This chapter outlines the methods that were used in conducting the study in terms of study design, study site, study population, sampling technique, eligibility criteria, sample size and data management and analysis.

3.1 Design

A cross-sectional descriptive study design was used. The CT and MRI images and reports of patients with meningioma on imaging were matched with their histopathological diagnosis.

3.2 Study site

The study was carried out in MTRH, Mediheal and Eldoret hospitals which are in Eldoret, Kenya. Eldoret is a town in Western Kenya. It is the county headquarters for Uasin-Gishu County. It lies 0° 31´N 35° 17´E. It is about 313 kilometres from Nairobi. It is the home of the Kalenjin community with its main socioeconomic activity being

agriculture.

MTRH is the second national hospital in the country. It is a parastatal. MTRH serves the entire population of Western Kenya and some parts of Eastern Uganda and South Sudan. It has a radiology department which offers CT scanning. Eldoret hospital and Mediheal are private hospitals in Eldoret with a catchment similar to MTRH. They offer both MRI and CT diagnostic services. All these hospitals diagnose and manage patients with meningomas. On average about 25 patients with meningiomas are operated on annually in the three hospitals.

3.3 Study population

The study population were patients presenting with meningioma at MTRH, Mediheal and Eldoret hospitals**.**

3.4 Sampling Technique

Consecutive sampling technique was used in recruitment of patients. Patients with meningomas referred to these hospitals who met the study's inclusion criteria were sampled as they presented themselves. However, 26 patients were studied by reviewing records and matching their radiological features and histopathological findings. 55 patients met the inclusion criteria and since our sample size was 42, sampling 42(76%) from 55 was as good as studying the whole number of patients. We therefore chose to study all the patients because the study would not subject the extra patients to unnecessary harm nor would it increase the cost of research by any significant amount. Those with CT scan or MRI images and reports were matched against the histopathology of the meningiomas.

3.5 Eligibility Criteria

3.5.1 Inclusion criteria

1. Must have been diagnosed with meningioma using either CT or MRI
2. Meningioma must have been confirmed with a histopathological diagnosis.

3.5.2 Exclusion criteria

1. CT or MRI images of patients who had synchronous brain tumours e.g. a pituitary adenoma and a meningioma or other brain pathology such as CVA

2. Patients who did not provide informed consent were not studied

3. Patients who lacked either imaging or histological diagnosis.

3.6 Sample size

The sample size was calculated using the following formula (Cochran, 1963). (71)

$$n = \left(\frac{Z_{1-\alpha/2}}{\delta} \right)^2 P(1-P)$$

Where

P= 0.8 (population proportion of those who have at least one of the three main subtypes of meningioma (fibroblastic, meningothelial and transitional**)**. The population proportion of 80% was obtained from the results of a study conducted in KNH (Chumba K.D., 2006).

δ =0.1 (the margin of error equal to the 10% used in this case and $Z_{1-\alpha/2}$ is the $(1-\alpha/2)\times 100\%$ quantile of the standard normal distribution).

n= 1.96^2x 0.8 x 0.2

0.1^2

= 62 which was then adjusted for finite population correction

n= $n/(1+n/N) = 62/(1+62/125) = 42$

n=42 patients with meningioma

Correction for the finite population size of 25 per year for 5 years of the study period was determined prior to data collection and led to ($n/(1+n/N) = 62/(1+62/125) = 42$)

3.7 Data Management and Analysis

3.7.1 Activities

The researcher assisted in image taking with the technicians and reporting by the radiologists.

The researcher filled the data collection tool after seeking consent from the patients and liaised with the pathologists in the reviewing of slides and writing of the histopathology reports.

3.7.2 Quality control

Quality control of the radiological image reports was achieved by seeking the opinion of two radiologists who independently reported on them after I had reported them.

The histopathological diagnosis was done by two pathologists who also independently reported on the slides.

3.7.3 Data collection

Data was collected on a data collection form based on a protocol outlined by *Bradac et al* (56) which gave a protocol for analysis of CT and MRI images of meningiomas. The forms were filled by the investigator and later transferred to a computer database. Collected data was only available to the investigator and the supervisors.

3.7.4 Data analysis

Data entry was done in a computerized database designed in Microsoft Access. Data analysis was performed using STATA version 12 Special Edition (SE) (College station, Texas USA). Categorical variables were summarized as frequencies and the corresponding percentages.

Continuous variables were summarized as mean and standard deviation (std) if they were normally distributed or median and their corresponding inter quartile range (IQR) if they had skewed distribution. Association between the categorical variables was assessed using the Fisher's exact test if the expected value (cell count) in at least one of the cells was less than 5 otherwise Pearson's Chi square test would be used. Participants' age was determined by subtracting the year of birth from the year of imaging. Age was categorized at ten years interval just to help investigate the relationship between the histopathological patterns and the age at an interval of a decade. The patients aged above 55 years were few thus we put them into one group to ensure balance in numbers in each age group**.**

3.8 Ethical considerations

Approval to carry out the study was sought from the Institutional Research and Ethics Committee (IREC). Permission to access patient records in MTRH, Mediheal and Eldoret hospitals was sought from the administration. All patient reports were kept confidential and the data obtained was password coded. Informed consent was sought from the patients and they were assured of their confidentiality. No coercion, inducement of patients was done and they were made to understand that they were free to withdraw at any time without it affecting their management. Collected data was only available to the investigator and the supervisors.

3.9 Limitations

1. The high cost of the imaging modalities used to study meningiomas.

2. Different imaging equipment due to large catchment area of the hospitals and therefore different quality of images with lack of standardization of images.

3.9 Study recruitment Schema

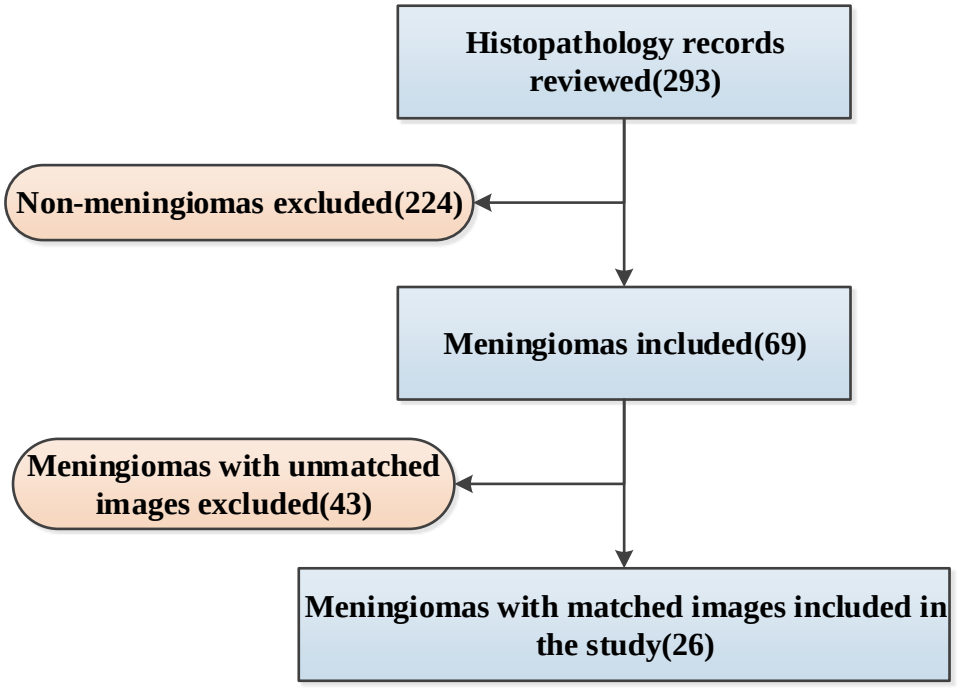


Figure 1: Schema for recruitment of subjects acquired by reviewing records

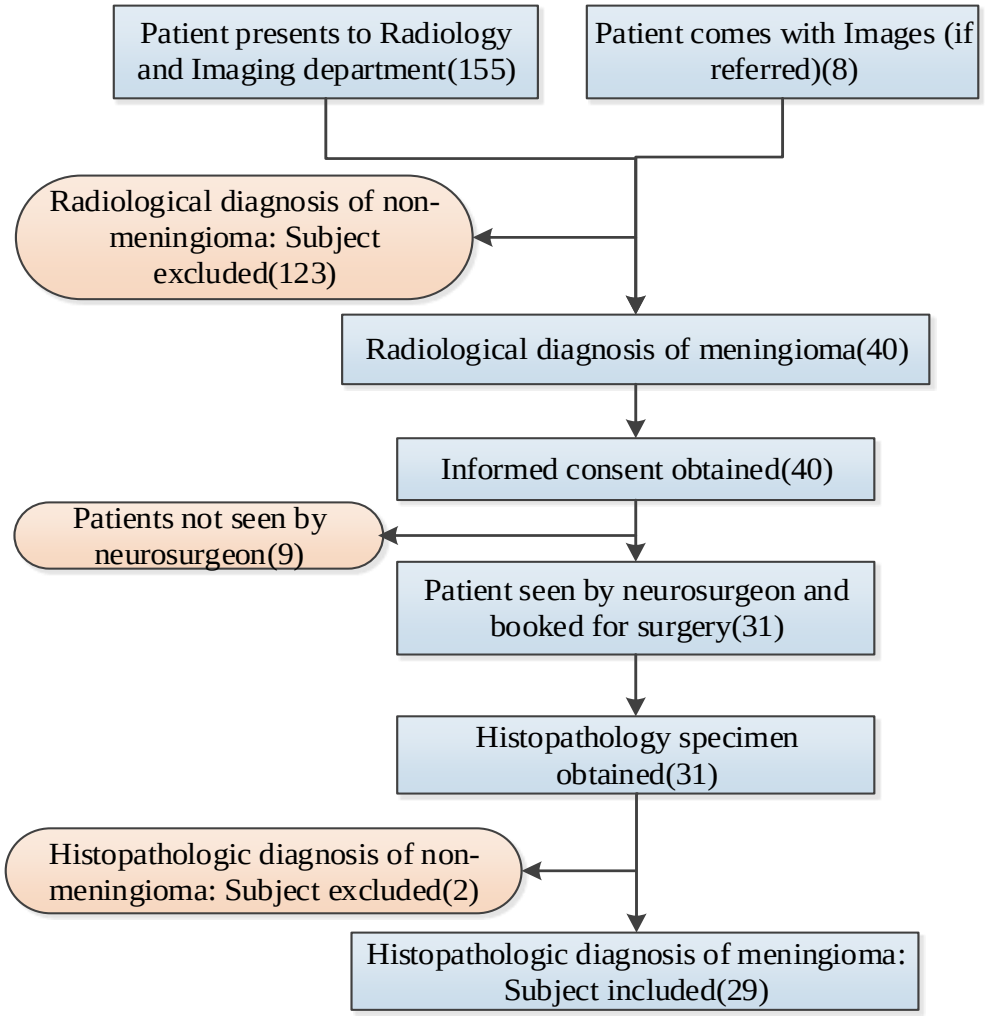


Figure 2: Schema for recruitment of subjects collected by principal investigator prospectively

CHAPTER FOUR: RESULTS

This chapter covers the results that were found from carrying out the study. It includes the patients' demographics, imaging features, histopathological findings and the correlation of imaging findings to histopathology.

4.1 Demographics of the participants

There were 55 participants who met the inclusion criteria in the study and whose data was finally analysed. There were 40 (73%) females in this study representing a ratio of 2.7:1 of female to male participants suffering from meningiomas. These results, though not equivalent, matches those in literature. Of the 55 participants included in the study, 26 (47%) were studied by reviewing records. There were 40 (73%) patients sampled from the Moi Teaching and Referral Hospital (MTRH), 9 (16%) from Mediheal and 6 (11%) from Eldoret Hospital. (Figure 3)

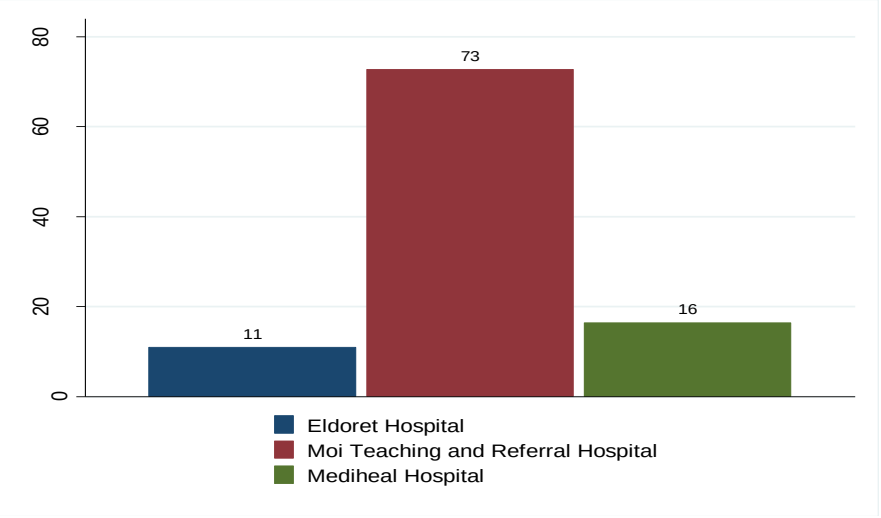


Figure 3: Distribution of patients by hospital

The patients' ages ranged from 25-77 years with an average age of 47 (std: 12.86) years and a median age of 47 (IQR: 36-55) years. Patients aged between 25-35 years were 24% (13), between 35-45 years were 22% (12), between 45-55 years were 31% (17) and 13 (24%) aged above 55 years. (Figure 4)

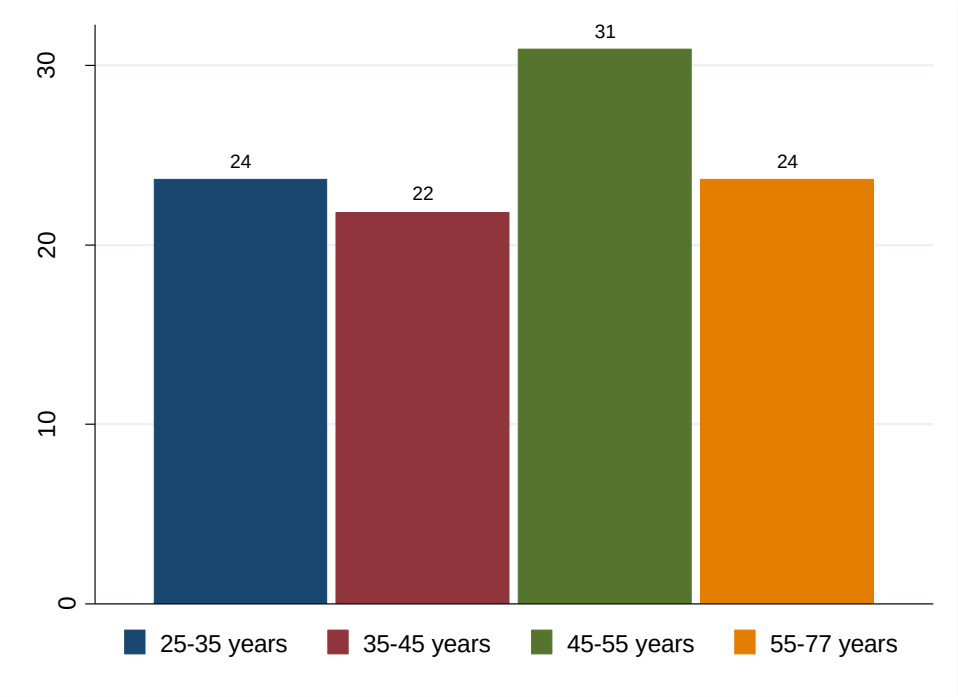


Figure 4: Distribution of patients by age groups

4.2 Radiological features of Meningiomas

Most of the lesions 16 (28%) were located at the convexity. Some 5(9%) were located at the falx and another 5(9%) in the posterior cranial fossa, 6 (10%) were located at the parasagittal and another 6(10%) were located at the sphenoidal ridge, 6(10%) were located in the olfactory groove, and 7(12%) were located at suprasellar region. The other locations included clival, petroclival, frontobasal, and petrous, and represented 11%. The side that was mostly

affected by the meningioma was the left representing 24(57%). The right accounted for 17(40%). One patient had both the right and the left side affected. There were 13 patients with midline lesions who were not included in computing the preceding proportions.

Almost all of the patients 52 (95%) had one lesion and most patients 53(96%) had a lesion size >3.0 cm. Of those that had one lesion, 50(96%) had the lesion size >3.0 cm while all those who had two lesions had their lesions >3.0cm. This gives a total of 53(96%) patients with lesion size greater than 3 cm. Fisher's exact test of association between the number of lesions and the size was not statistically significant. The average length of the lesions was 5.30 (std: 1.72) cm. The median length was 5.35 (IQR: 4-6.6) cm with a minimum of 1.7 cm and a maximum of 9.3 cm

Of the 55 participants, 2(4%) developed bone erosion while 7(13%) had hyperostosis. Forty six (84%) did not develop any bone affection. Oedema was extensive in one patient but mild and moderate in 21(38%) and 18(3%) respectively. Fifteen (27%) did not have oedema. None of the patients had brain invasion.

There was one patient who had coarse calcification and another one with fine calcification. Four (7%) of them had moderate calcification. Forty nine (89%) did not develop any form of calcification. Other secondary changes were not seen in 29 (53%) patients but necrosis was seen in 21(38%) patients and cyst formation was seen in 5(9%). Mass effect was absent in 9(16%) patients but mild in 20(36%), moderate in 25(45%) and severe in one of the patients. The tumor margins were distinct in all the patients.

The CSF pathway was also investigated in these patients and it was found that 12(22%) had a compressed CSF pathway, 20(36%) had displaced CSF pathway and 7(13%) had

obstruction of the CSF pathway. One person had both compressed and obstructed CSF pathway and another one with displaced as well as an obstructed CSF pathway. Fourteen (25%) patients did not have their CSF pathway affected. The shape was a mass in 54(98%) of the patients. One patient with atypical histopathology had an en plaque meningioma.

Of the 38 patients with density data available, there were 33(87%) of them with hyperdense density. Mixed density, isodense and hypodense densities were present in 2(5%), 2(5%) and 1(3%) patients, respectively. Irregular enhancement was present in 29(53%) of the patients while uniform enhancement was present in the remaining. There was no herniation in 45(82%) of the patients. Three (5%), 6(11%) and 1(2%) had subfalcine, tonsillar and transtentorial herniation respectively.

Vascular features seen included arterial encasement 4(7%), displacement of adjacent vessels 7(13%), displacement of adjacent vessels and increased vascularity of tumor 1(2%), identifiable tumor vessels 39(71%) and increased vascularity of tumor was present in 4(7%).

4.3 Histopathology of meningiomas among participants

Grade I meningiomas were seen in 52(95%) of the patients. This included 12(22%) fibroblastic meningiomas, 29(53%) meningothelial and 11(20%) transitional meningiomas. There were 3 (5%) grade II atypical meningiomas. Details are as shown in Figure 5.

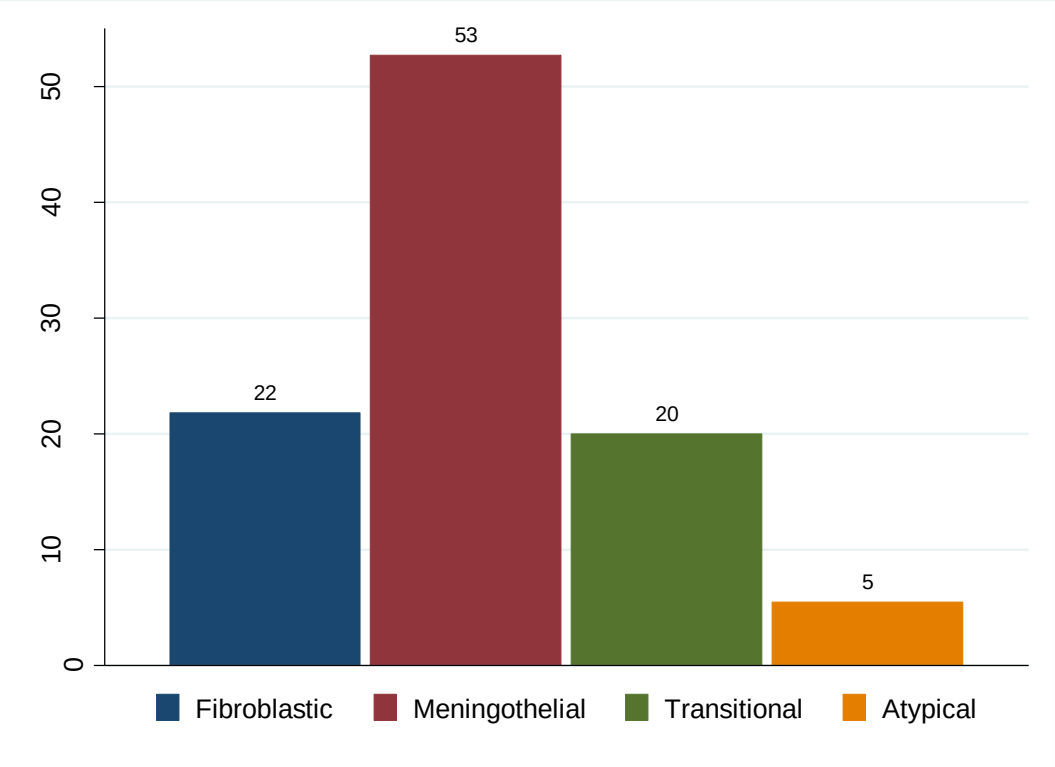


Figure 5: Distribution of the histopathological subtypes

4.4 Correlation of Radiological features and Histopathology

The test for association between the histopathological subtypes and the radiological features was not statistically significant except for association between the CSF pathway and the histopathological patterns (p-value=0.005). This association suggests that the patients suffering from Grade I histopathological types are more likely to have compression or displacement of the CSF pathways.

Table 1: Meningioma location by histopathological patterns

	Histopathological patterns					
Variable	**Grade I**			**Grade II**		**Fishers' exact test**
Location of the lesions	**Fibroblastic**	**Meningothelial**	**Transitional**	**Atypical**	**Total**	
Clival	0	1(100%)	0	0	**1(100%)**	**0.78**
Petroclival	0	1(100%)	0	0	**1(100%)**	
Convexity	2(13%)	9(56%)	3(19%)	2(13%)	**16(100%)**	
Falx	0	3(60%)	1(20%)	1(20%)	**5(100%)**	
Frontobasal	1(25%)	3(75%)	0	0	**4(100%)**	
Olfactory Groove	1(17%)	4(67%)	1(17%)	0	**6(100%)**	
Others (Suprasellar)	3(42%)	2(29%)	2(29%)	0	**7(100%)**	
Parasagittal	2(33%)	2(33%)	2(33%)	0	**6(100%)**	
Petrous ridge	0	1(100%)	0	0	**1(100%)**	
Posterior Cranial Fossa	3(60%)	2(40%)	0	0	**5(100%)**	
Sphenoidal Ridge	1(17%)	3(50%)	2(33%)	0	**6(100%)**	
Total	**13(22%)**	**31(53%)**	**11(20%)**	**3(5%)**	**58(100%)**	

Table 1 shows that among all the patients with convexity, 2(13%), 9(56%), 3(19%) and 2(13%) had fibroblastic, meningothelial, transitional and atypical meningioma, respectively while among those with falx, 3(60%) 1(20%) and 1(20%) had meningothelial, transitional and atypical meningioma. There were 4(67%) with olfactory groove who had meningothelial meningioma. Among all the patients who had sphenoidal ridge, 1(17%), 3(50%) and 2(33%) had fibroblastic, meningothelial and transitional meningioma respectively. The test of association between the location of the meningioma and the histopathological patterns showed no significant association.

Table 2: Side, number and size of the lesion by the histopathological pattern

	Histopathological patterns					
	Grade I			Grade II		
Variable	Fibroblastic	Meningothelial	Transitional	Atypical	Total	Fishers' exact test
Side of the lesions						
Left	6(25%)	12(50%)	6(25%)	0	**24(100%)**	**0.576**
Left; right	0	1(100%)	0	0	**1(100%)**	
Right	3(18%)	9(53%)	2(12%)	3(18%)	**17(100%)**	
Midline	3	7	3	0	**13**	
Total	**9(21%)**	**22(53%)**	**8(19%)**	**3(7%)**	**42(100%)**	
Number of lesions						
One	11(21%)	27(52%)	11(21%)	3(6%)	**52(100%)**	**1**
Two	1(33%)	2(67%)	0	0	**3(100%)**	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	
Size of the lesion						
1.5-3.0 cm	0	1(50%)	1(50%)	0	**2(100%)**	**0.492**
>3.0 cm	12(23%)	28(53%)	10(19%)	3(7%)	**53(100%)**	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	

Table 2 shows the distribution of the histopathological patterns by the side, number and size of the lesion. The results show that 6(25%), 12(50%) and 6(25%) of the patients with the lesion situated to the left had fibroblastic, meningothelial and transitional meningiomas, respectively. All three atypical meningiomas were right-sided and accounted for (18%) of the right-sided meningiomas. The others were fibroblastic 3(18%), meningothelial 9(53%) and transitional meningiomas 2(12%). One of the patients with a meningothelial meningioma had lesions situated on the left and right. The Fisher's exact test of association shows that there was no significant relationship between the side of the lesion and the histopathological pattern (p-value=0.576).

Among the three patients who had two lesions, one had fibroblastic meningiomas while the other two had meningothelial meningiomas (Table 2)

Among the patients who had one lesion, 11(21%), 27(52%) and 11(21%) were suffering from fibroblastic, meningothelial and transitional meningioma, respectively. The three patients who had atypical meningiomas all had one lesion. The test of association between the number of lesions and the histopathological patterns was not statistically significant (p-value=1.000).

All the patients who had a fibroblastic meningioma had the lesion size >3.0 cm. Similarly, all of the patients with atypical meningiomas had lesion size >3.0 cm. Among the patients with lesion size >3.0 cm, 28(53%) and 10(19%) had meningothelial and transitional meningiomas respectively. The test of association between lesion size and the histopathological patterns showed no significant relationship (p-value=0.492).

Table 3: Bone involvement by histopathological patterns

	Histopathological patterns					
	Grade I			**Grade II**		
Variable	**Fibroblastic**	**Meningothelial**	**Transitional**	**Atypical**	**Total**	**Fishers' exact test**
Bone involvement						
Bone erosion	0	2(100%)	0	0	**2(100%)**	**0.278**
Hyperostosis	0	3(43%)	3(43%)	1(14%)	**7(100%)**	
Nil	12(26%)	24(52%)	8(17%)	2(4%)	**46(100%)**	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	

Table 3 shows that there were 46(84%) of all the patients without any bone involvement of whom 12(26%) had fibroblastic meningioma, 24(52%) with meningothelial meningioma, 8(17%) with transitional meningioma and 2(4%) with atypical meningioma. All the patients with bone erosion had meningothelial meningioma. Among the patients with hyperostosis were 3(43%) with meningothelial meningioma, 3(43%) with transitional meningioma and

1(14%) with atypical meningioma. The test of association did not show any significant association between the bone involvement and the histopathological patterns.

Table 4: Severity of oedema by the histopathological patterns

	Histopathological patterns					
	Grade I			Grade II		Fishers' exact test
Variable	Fibroblastic	Meningothelial	Transitional	Atypical	Total	
Oedema						
Extensive	0	1(100%)	0	0	**1(100%)**	0.582
Mild	4(19%)	13(62%)	3(14%)	1(5%)	**21(100%)**	
Moderate	3(17%)	10(56%)	3(17%)	2(11%)	**18(100%)**	
Nil	5(33%)	5(33%)	5(33%)	0	**15(100%)**	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	

Among the patients with mild oedema, there were 4(19%), 13(62%), 3(14%) and 1(5%) with fibroblastic, meningothelial, transitional and atypical meningiomas, respectively. Of those with moderate oedema, 3(17%), 10(56%), 3(17%) and 2(11%) had fibroblastic, meningothelial, transitional and atypical meningiomas. Among the patients without any form of oedema, 5(33%) were fibroblastic, 5(33%) meningothelial and 5(33%) transitional meningiomas.

Table 5: Calcification, secondary changes and mass effect by histopathological patterns

	Histopathological patterns					
	Grade I			Grade II		Fishers' exact test
Variable	**Fibroblastic**	**Meningothelial**	**Transitional**	**Atypical**	**Total**	
Calcification						
Course	0	1(100%)	0	0	1(100%)	0.872
Fine	0	1(100%)	0	0	1(100%)	
Moderate	2(50%)	1(25%)	1(25%)	0	4(100%)	
Nil	10(20%)	26(53%)	10(20%)	3(6%)	49(100%)	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	
Other secondary changes						
Cyst form	1(20%)	4(80%)	0	0	5(100%)	0.766
Necrosis	3(14%)	11(52%)	5(24%)	2(10%)	21(100%)	
Nil	8(28%)	14(48%)	6(21%)	1(3%)	29(100%)	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	
Mass effect						
Mild	4(20%)	11(55%)	4(20%)	1(5%)	20(100%)	0.28
Moderate	7(28%)	14(56%)	2(8%)	2(8%)	25(100%)	
Severe	0	1(100%)	0	0	1(100%)	
Nil	1(11%)	3(33%)	5(56%)	0	9(100%)	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	
Brain invasion						
None	12(22%)	29(53%)	11(20%)	3(5%)	55(100%)	

Only two of the patients who had coarse or fine calcification had meningothelial meningiomas while among the 4(7%) patients who had moderate calcification, 2(50%) had fibroblastic meningioma, 1(25%) had meningothelial and another one had transitional meningioma as is apparent from Table 5. The rest of the patients did not have any form of calcification. The test of association between the existence of calcification and histopathological patterns was not significant.

Table 6: CSF pathway by histopathological patterns

	Histopathological patterns					
Variable	**Grade I Fibroblastic**			**Grade II Atypical**	**Total**	**Fishers' exact test**
		Meningothelial	**Transitional**			
CSF pathway						
Compression	1(8%)	6(50%)	2(17%)	3(25%)	**12(100%)**	**0.005**
Compression & obstruction	1(100%)	0	0	0	**1(100%)**	
Displacement	1(5%)	15(75%)	4(20%)	0	**20(100%)**	
Displacement & obstruction	1(100%)	0	0	0	**1(100%)**	
Obstruction	4(57%)	3(43%)	0	0	**7(100%)**	
Nil	4(29%)	5(36%)	5(36%)	0	**14(100%)**	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	
Tumour margins						
Distinct	12(22%)	29(53%)	11(20%)	3(5%)	**55(100%)**	

Table 6 shows that there were a substantial number of 6(50%) of the patients with compressed CSF pathway with meningothelial meningiomas. Among those who had displaced CSF pathway was a large proportion 15(75%) with meningothelial meningiomas. There were 4(29%), 5(36%) and 5(36%) without any CSF pathway affection who had fibroblastic, meningothelial and transitional meningioma, respectively. Table 6 shows a significant relationship between the histopathological patterns and the CSF pathway (p-value=0.005). Though there is an apparently significant association, this may be attributed just to chance because there is no inherent direction in which the data appear to follow. That is, the CSF pathway presentations are not predictive of the histopathological patterns.

Table 7: Density, enhancement and herniation by histopathological types

	Histopathological patterns					
	Grade I			Grade II		Fishers' exact test
Variable	Fibroblastic	Meningothelial	Transitional	Atypical	Total	
Density						
Hyperdense	7(21%)	18(55%)	8(24%)	0	**33(100%)**	0.203
Hypodense	0	1(100%)	0	0	**1(100%)**	
Isodense	0	1(50%)	1(50%)	0	**2(100%)**	
Mixed density	0	1(50%)	1(50%)	0	**2(100%)**	
Total	**7(18%)**	**21(55%)**	**10(27%)**	**0(0%)**	**38(100%)**	
Enhancement						
Irregular	5(17%)	16(55%)	6(21%)	2(7%)	**29(100%)**	0.852
Uniform	7(27%)	13(50%)	5(19%)	1(4%)	**26(100%)**	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	
Herniation						
Nil	10(22%)	22(49%)	11(24%)	2(4%)	**45(100%)**	0.587
Subfalcine	0	3(100%)	0	0	**3(100%)**	
Tonsillar	2(33%)	3(50%)	0	1(17%)	**6(100%)**	
Transtentorial	0	1(100%)	0	0	**1(100%)**	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	
Shape						
En-plaque	0	0	0	1(100%)	**1(100%)**	0.055
Mass	12(22%)	29(54%)	11(21%)	2(4%)	**54(100%)**	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	

From Table 7 we found that 33(63%) of the patients who had hyperdense lesions had either a fibroblastic 7(21%), meningothelial 18(55%) or transitional 8(24%) meningioma. 17(31%) of patients had an MRI only so density was not assessed for them. There was no significant relationship between the density of the lesion and the histopathological pattern. Herniation was not present in almost all of the patients across all the histopathological patterns. Enhancement was well balanced between irregular and uniform (Table 7).

Table 8: Vascular features by histopathological patterns

	Histopathological patterns					
	Grade I			Grade II		Fishers' exact test
Variable	Fibroblastic	Meningothelial	Transitional	Atypical	Total	
Vascular features						
Arterial encasement	1(25%)	2(50%)	1(25%)	0	**4(100%)**	**0.704**
Displacement of adjacent vessels	2(29%)	3(43%)	1(14%)	1(14%)	**7(100%)**	
Displacement of adjacent vessels; Increased vascularity of tumour	0	1(100%)	0	0	**1(100%)**	
Identifiable tumour vessels	8(21%)	22(56%)	8(21%)	1(3%)	**39(100%)**	
Increased vascularity of tumour	1(25%)	1(25%)	1(25%)	1(25%)	**4(100%)**	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	

Table 8 shows the distribution of the vascular features by the histopathological patterns. The data is sparse in the cells of this table. Of the patients with identifiable tumour vessels there were 22(56%) with meningothelial meningiomas, 8(21%) with fibroblastic meningiomas and 8(21%) with transitional meningiomas. There was no significant association between the histopathological patterns and the vascular features (p-value=0.704).

Table 9: Histopathological patterns by age groups

	Histopathological patterns					
	Grade I			Grade II		Fishers' exact test
Variable	Fibroblastic	Meningothelial	Transitional	Atypical	Total	
Age group						
25-35 years	3(23%)	8(62%)	1(8%)	1(8%)	**13(100%)**	**0.693**
35-45 years	1(8%)	7(58%)	4(33%)	0	**12(100%)**	
45-55 years	6(35%)	7(41%)	3(18%)	1(6%)	**17(100%)**	
55-77 years	2(15%)	7(54%)	3(23%)	1(8%)	**13(100%)**	
Total	**12(22%)**	**29(53%)**	**11(20%)**	**3(5%)**	**55(100%)**	

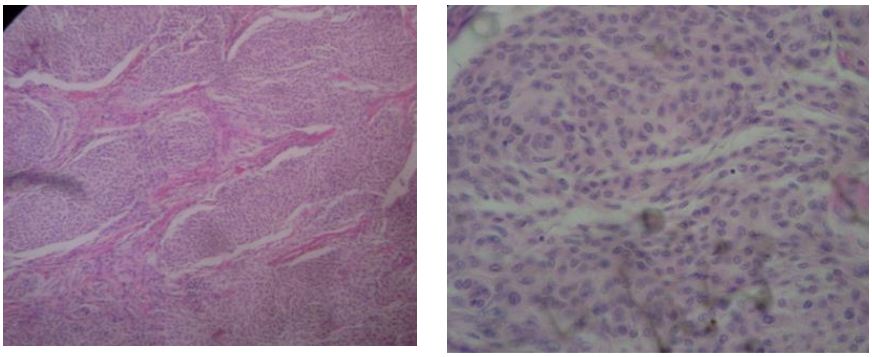
The histopathological subtypes are well distributed across the age groups. The test of association between the age groups and the histopathological types was not statistically significant (p-value=0.693) indicating that there was no particular age group that was associated with a certain type of meningioma. That is, all meningiomas were well distributed across all the age groups (Table 9).

Table 10: MRI Intensity by Histopathological patterns

	Histopathological patterns					
	Grade I			Grade II		Fishers' exact test
Variable	Fibroblastic	Meningothelial	Transitional	Atypical	Total	
T(1) Intensity						
Hypointense	0	4(80%; 31%)	1(20%; 17%)	0	**5(100%; 16%)**	**0.636**
Isointense	7(37%; 78%)	6(32%; 46%)	4(21%; 67%)	2(11%; 67%)	**19(100%; 61%)**	
Mixed Intensity	2(29%; 22%)	3(43%; 23%)	1(14%; 17%)	1(14%; 33%)	**7(100%; 23%)**	
T(2) Intensity						
Hyperintense	7(35%; 78%)	6(30%; 46%)	5(25%; 83%)	2(10%; 67%)	**20(100%; 65%)**	**0.867**
Hypointense	0	1(100%; 8%)	0	0	**1(100%; 3%)**	
Isointense	0	2(100%; 15%)	0	0	**2(100%; 6%)**	
Mixed Intensity	2(25%; 22%)	4(50%; 31%)	1(13%; 17%)	1(13%; 33%)	**8(100%; 26%)**	
Flair Intensity						
Hyperintense	7(35%; 78%)	6(30%; 46%)	5(25%; 83%)	2(10%; 67%)	**20(100%; 65%)**	**0.867**
Hypointense	0	1(100%; 8%)	0	0	**1(100%; 3%)**	
Isointense	0	2(100%; 15%)	0	0	**2(100%; 6%)**	
Mixed Intensity	2(25%; 22%)	4(50%; 31%)	1(13%; 17%)	1(13%; 33%)	**8(100%; 26%)**	

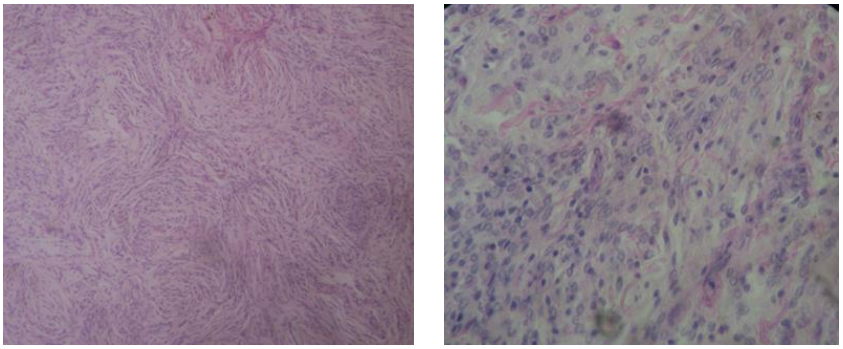
Majority of the meningiomas (61%) were isointense on T1 imaging with hypointense and mixed intensity accounting for 16% and 23% respectively. Of those that were isointense the majority were fibroblastic (37%) followed by meningothelial (32%). 80% of those that were hypointense were meningothelial. On T2 imaging, 65% of tumours were hyperintense followed by those with mixed intensity at 26%. The findings on flair were similar to those on T2 imaging. No association was found between tumour intensity and histopathology (Table 10).

4.5 Histopathological images



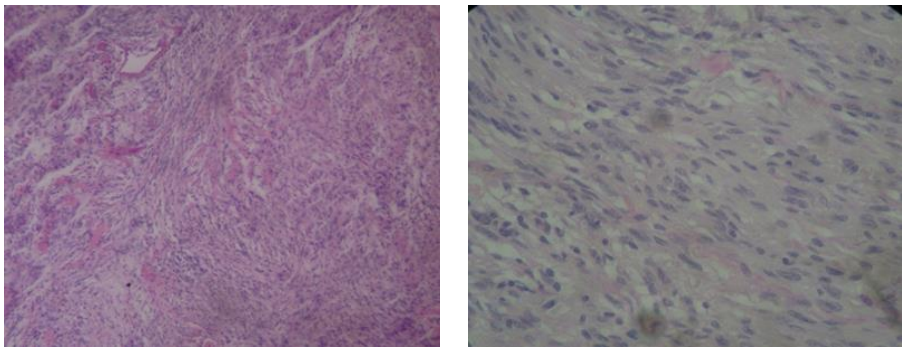
(A) (B)

Figure 6: Meningothelial meningioma (A) Low power (B) High power



(A) (B)

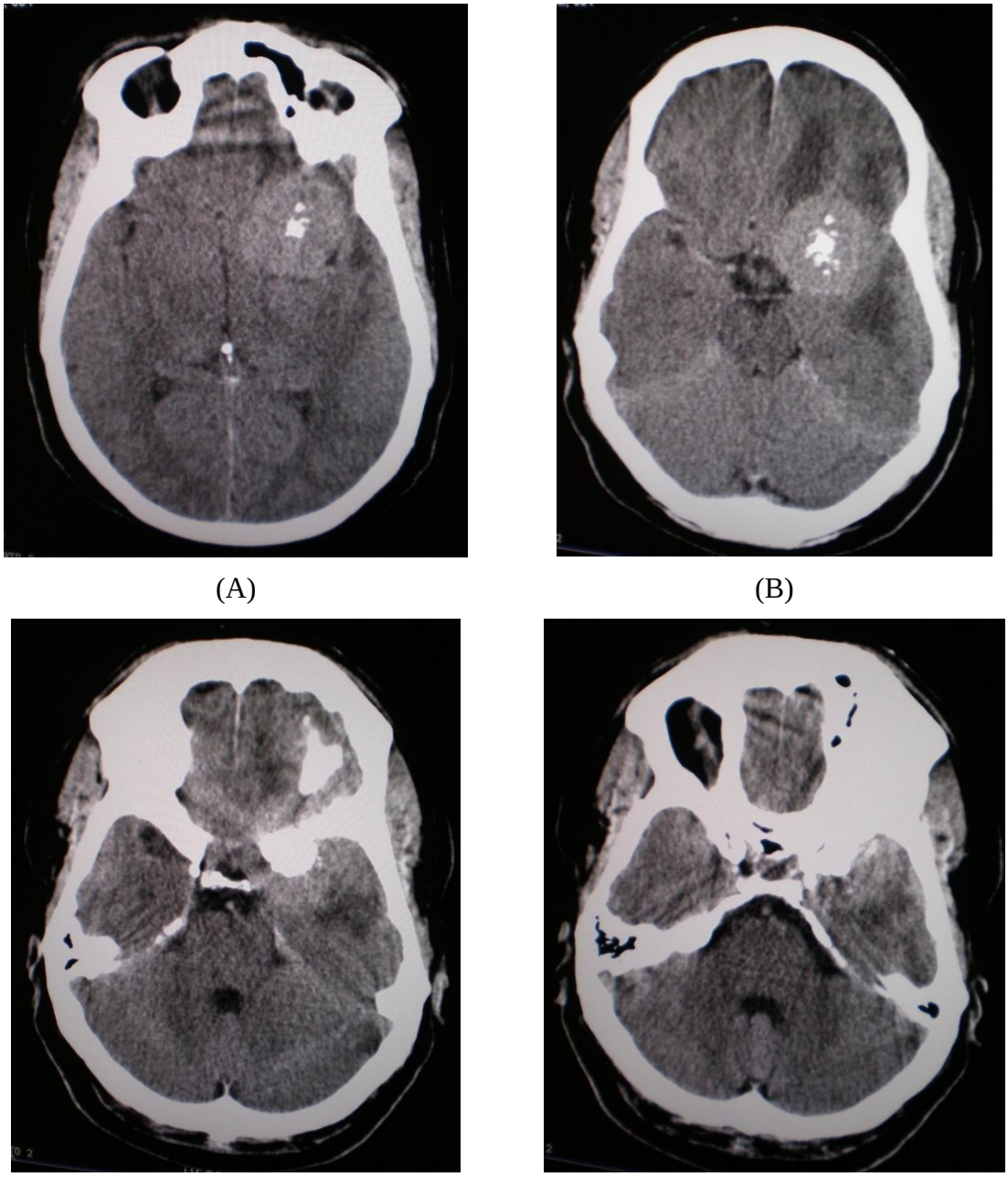
Figure 7: Transitional meningioma (A) Low power (B) High power



(A) (B)

Figure 8: Fibroblastic meningioma (A) Low power (B) High power

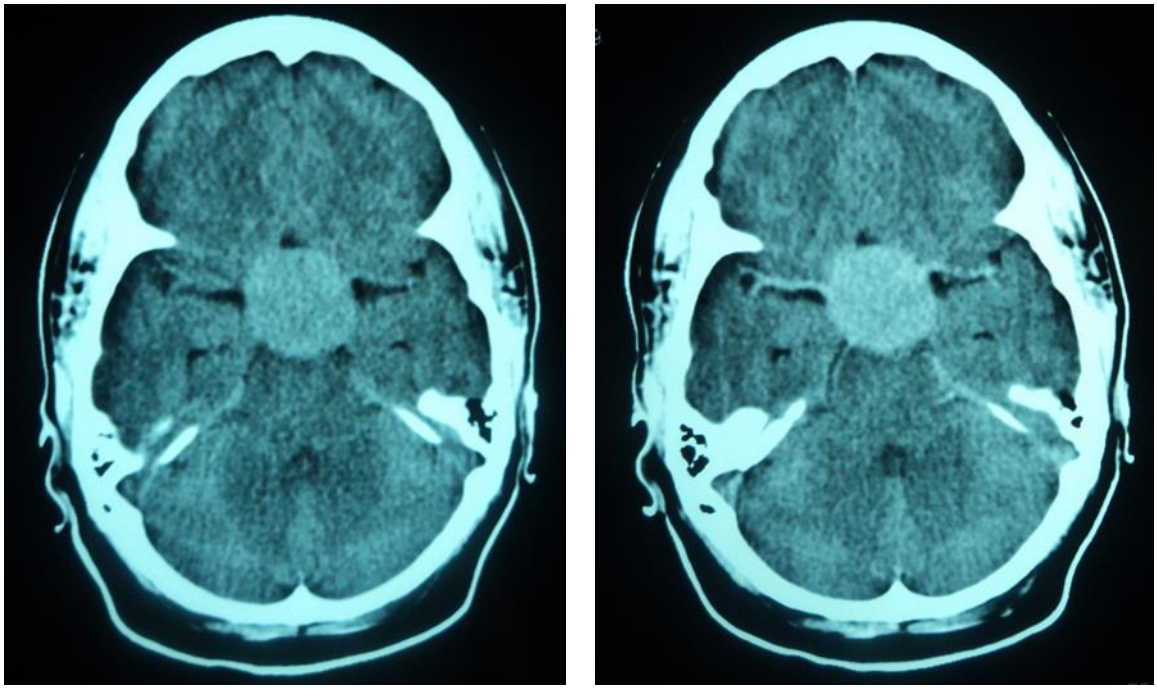
4.6 Radiological images



(A) (B)

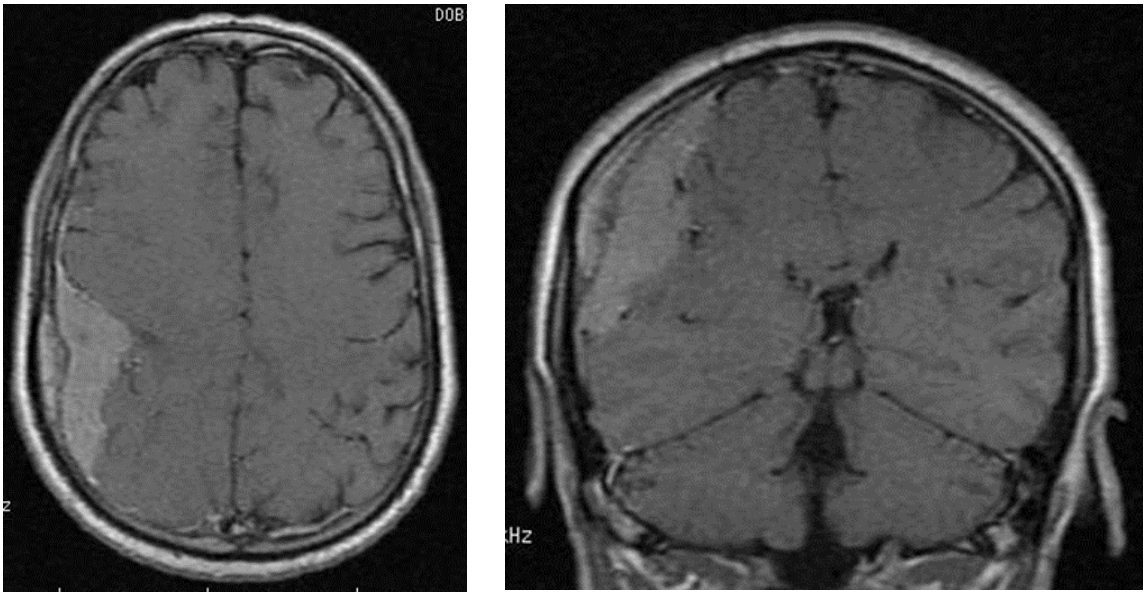
(C) (D)

Figure 9: Left Sphenoid wing CT scan of meningioma with calcification and bone hyperostosis (A) Non-contrast (B), (C), (D) Contrast enhanced. Minimal enhancement seen post contrast. It was found to be a transitional meningioma on histology



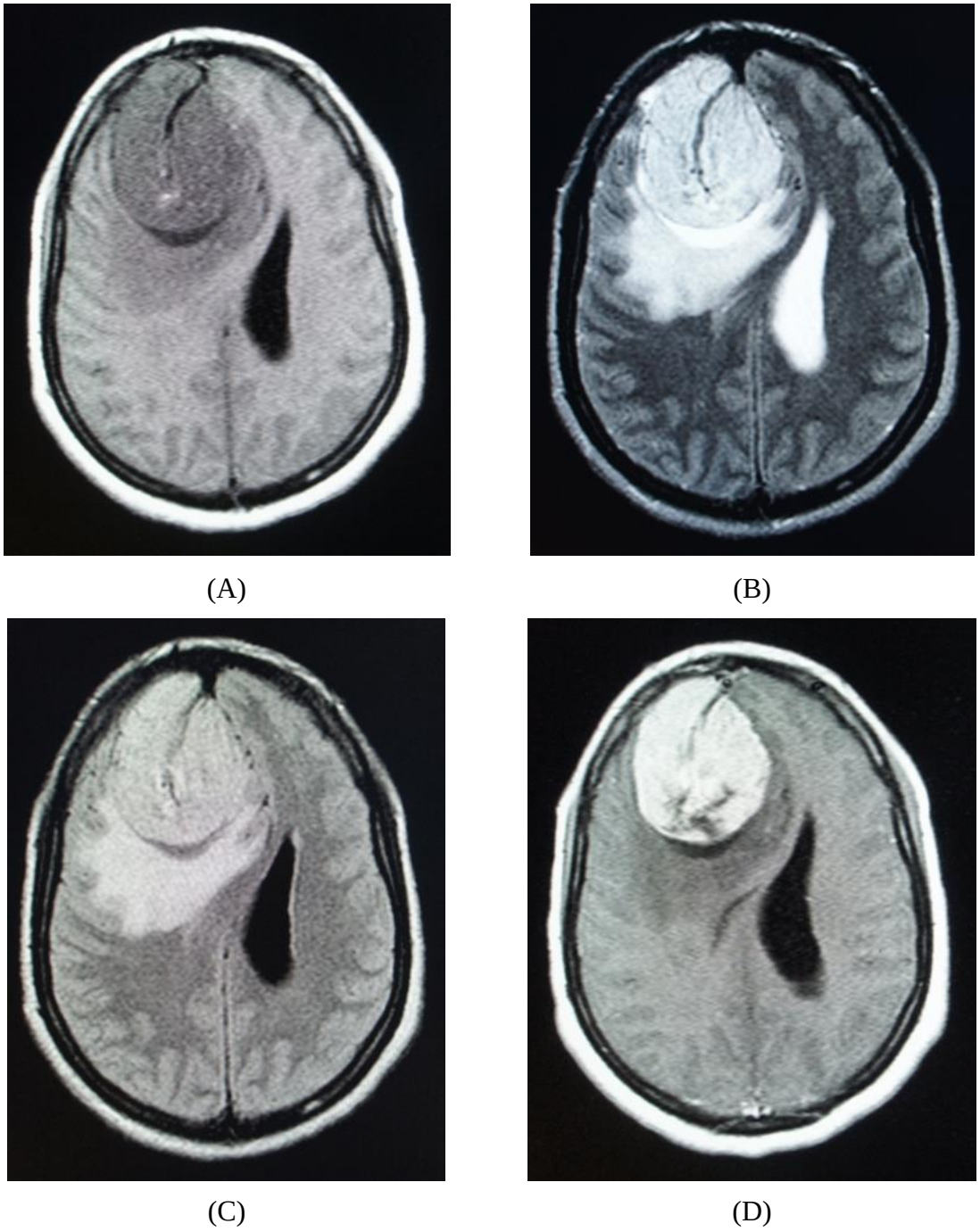
(A) (B)

Figure 10: CT scan of suprasellar meningioma found to be of meningothelial subtype on histology in 31 year old female patient. (A) Non-contrast enhanced (B) Contrast enhanced



(A) (B)

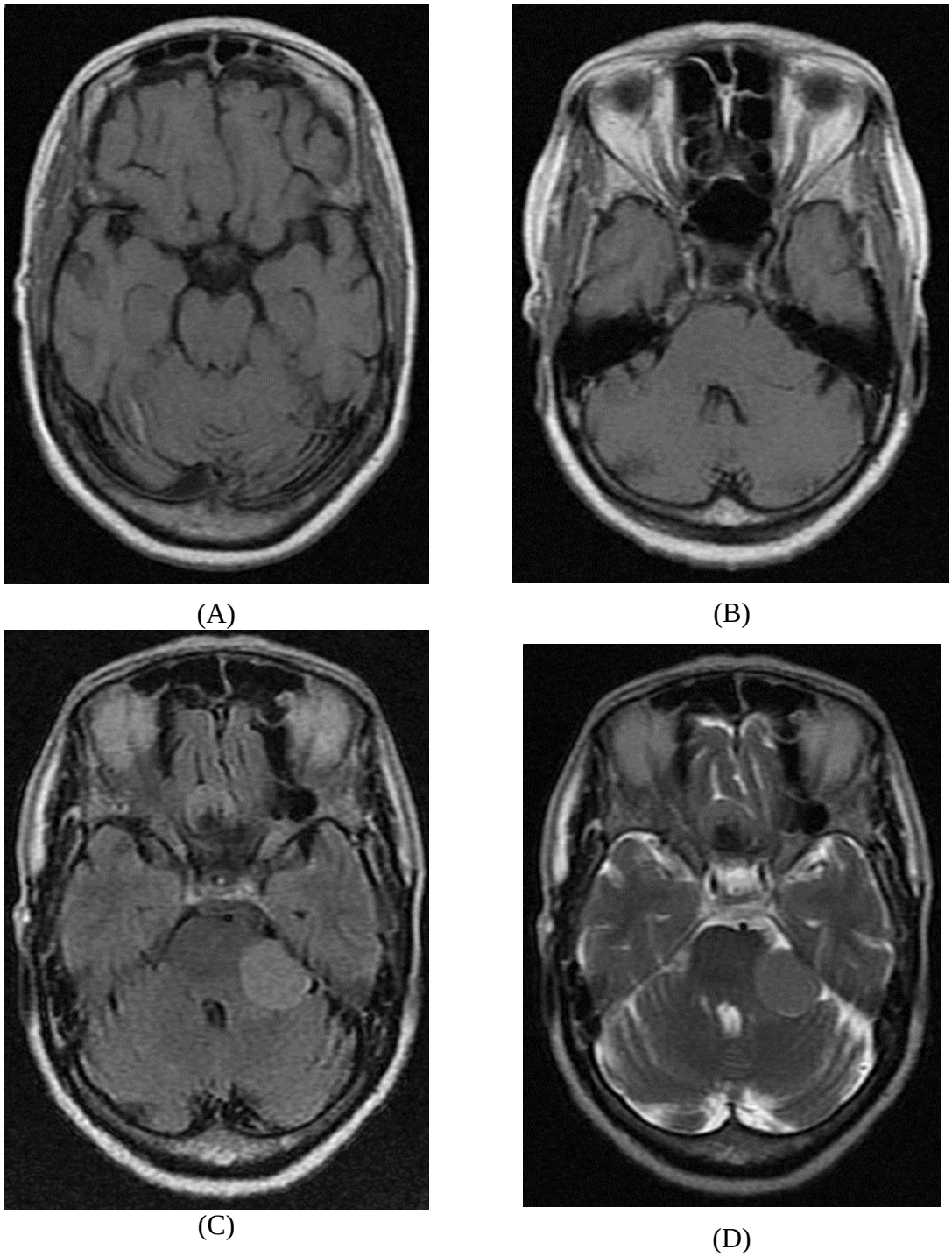
Figure 11: MRI of convexity en plaque meningioma in 49 year old male patient found to be of atypical subtype: Gadolinium enhanced. (A) Axial view (B) Parasagittal view



(A) (B)

(C) (D)

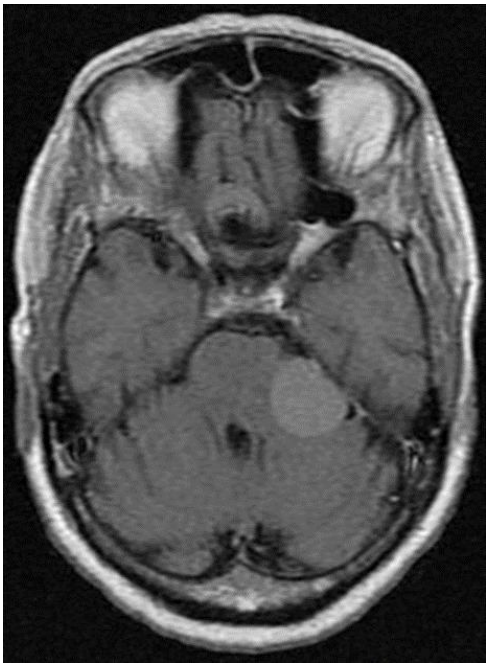
Figure 12: MRI of large parasagittal meningioma found to be of meningothelial subtype on histology in a 38 year old female patient. (A) T1 (B) T2 (C) FLAIR (D) Gadolinium enhanced



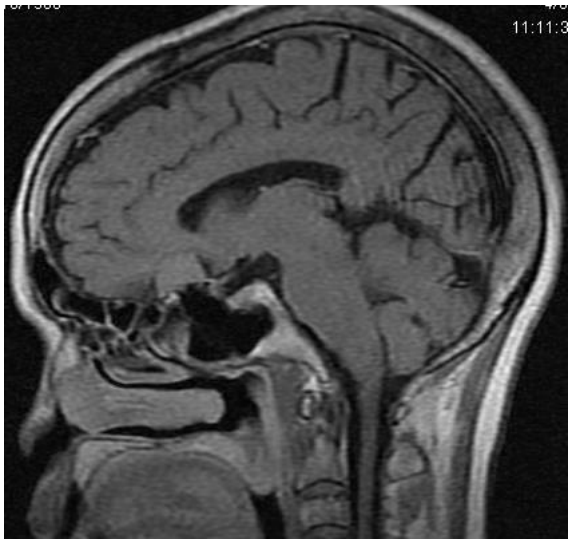
(A) (B)

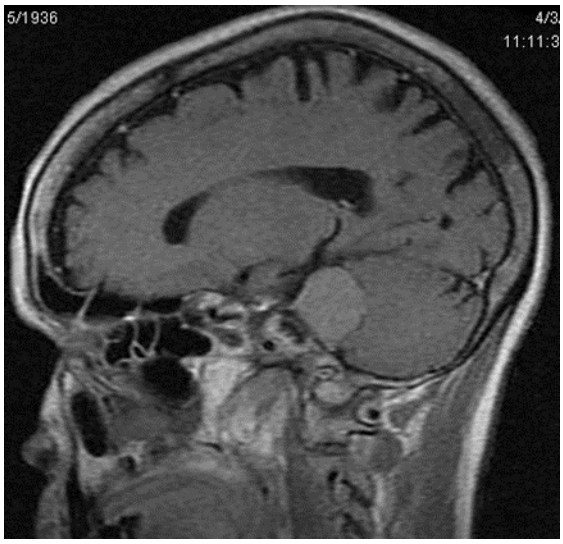
(C) (D)

Figure 13: MRI Images of a patient with multiple meningiomas which were of fibroblastic subtype on histology in a 77 year old female patient. (A) T1 image (olfactory groove) (B) T2 image (CPA) (C) FLAIR image (Olfactory groove and CPA) (D) T2 image (Olfactory groove)



(A)





(B) (C)

Figure 14: MRI gadolinium enhanced images of a patient with multiple meningiomas that were of fibroblastic subtype on histology in a 77 year old female patient. (A): Axial-Olfactory Grove and CPA (B) Sagittal-Olfactory groove (C) Sagittal-CPA

CHAPTER FIVE: DISCUSSION

This chapter is a discussion of the results found by this study and presented in the previous chapter.

5.1 Demographics of participants

In this study, 47% of the patients were studied by reviewing records while the rest were from data collected by the principal investigator with the largest number of patients accounting for 73% of the studied patients being from MTRH.

The female to male ratio in our study was 2.7:1. This is almost equivalent to a study by *Thomas B-G, et al* who reported a ratio of 3.1 (5). Benign meningiomas have been reported more in women with a male predominance seen in the atypical and malignant meningiomas. This may be attributed to hormonal factors being a risk factor for meningioma development.

The incidence of meningiomas generally increases with age though in this study there was a slight decrease in the age groups 35-45 and >55 years. This was probably due to reduced surgical intervention in older patients who present with co-existing comorbidities and associated general poor health in our setup.

5.2 Radiological features of meningiomas

The common radiological features of the meningiomas seen in Eldoret on CT were hyperdense (87%), mass lesions(100%) with mild (36%) to moderate edema (45%) that avidly enhanced with contrast either homogenously(47%) or heterogeneously (53%) while the common MRI features seen were mass lesions (97%) which were isointense (61%) on T1 weighted sequences, hyperintense (65%) on T2 weighted images,

hyperintense (65%) on FLAIR images and enhanced (100%) when gadolinium contrast was injected.. Studies with findings similar to or different from this are discussed under the specific variables.

5.3 Patterns of Meningioma grades and subtypes

The common meningioma subtypes in Eldoret were meningothelial, transitional and fibroblastic. These are all grade I meningiomas and accounted for 95% of all meningiomas. The remaining 5% were grade II atypical meningiomas with no malignant (grade III) meningiomas being encountered in the study population. A study by *Chumba, D.K.* in 2005 in KNH found that grade I tumours were the commonest accounting for 80.1% of the meningiomas. Grade II and III tumours accounted for 15.9% and 4% respectively (35). A more recent study in KNH by *Wanjeri, J.* in 2011 found that like in our study, grade I meningiomas were the commonest at 94.7% and Grade II and grade III represented 4% and 1.3% respectively (36). A study by *Mahmood, A. et al.* in Henry Ford Hospital, Detroit Michigan had similar findings to this study with 92% of the meningiomas being benign, 6.26% atypical, and 1.7% malignant (34).

The commonest subtypes in KNH were meningothelial and transitional accounting for 35% and 30% respectively as per *Chumba D. K* while *Wanjeri, J.* found that fibroblastic, transitional and meningothelial accounted for 25.4%, 25.4% and 22.5% respectively. In Eldoret, however, meningothelial meningiomas were accounting for 53% followed by fibroblastic at 22% then transitional at 20%.

Of the encountered grade II meningiomas, 67% were in men. This is similar to findings in other parts of the world in which grade II and III meningiomas are found to be more common

in men than women as described by a study done by *Alvarez, F. et al*.2005 in which male predominance was seen in the non-benign group of meningiomas (38). This may be due to hormonal factors which play a role for benign meningioma development not playing a role in atypical and malignant meningiomas.

5.4 Correlation between radiological features and histology findings

The commonest location of meningiomas was found to be in the convexity accounting for 28%. Of these 56% were of the meningothelial subtype. This convexity location finding is similar to a study done in South Africa by *Vivier, J. et al.* in which convexity meningiomas were the greatest and accounted for 25% (22). In the South African study the next commonest location was the parasagittal region which accounted for 21% unlike this study in which suprasellar was the next commonest location accounting for 12%. The meningothelial subtype was the commonest in all locations apart from the posterior cranial fossa and suprasellar region where fibroblastic was the commonest. No association between location and histopathological pattern was established.

98% of the patients had globular (mass) tumours. Only one patient had an *en plaque* tumour and it was associated with adjacent bone hyperostosis. En plaque tumours are reported to be uncommon with no clear prevalence or incidence information being quoted. This study found this to be the case as only one e*n plaque* tumour was encountered.

When the midline lesions were not considered, the left represented 57 % as compared to 40% on the right. Non-significant left side affection is similar to a study done by *Inskip et al.* on the laterality of brain tumours in which meningiomas were found to nonsignificantly occur

more on the left than on the right (30). No association was found to histopathology as regards to the side affected.

95% of all patients seen had only one lesion with all the atypical meningiomas having one lesion only. Of those with two lesions, 67% were meningothelial and 33% were fibroblastic. This study's figure of 5% for multiple lesions is in keeping with *Sheehy and Crockard* who described a rise in detection from 1.1% of cases to 8% with modern CT scanning (31). This however is much lower than a study by *Borovich, B. et al* done at Rambam medical centre in Israel which reported 20% multiple meningiomas at first assessment that increased to 40% on reassessment (32). This difference could be due to failure to detect very small meningiomas initially on imaging. Statistically no association was found between the number of lesions and histopathology.

Large lesions, that is lesions greater than 3 centimetres represented 96% in the study population with the average length of encountered lesions being 5.30 centimetres. Of these, meningothelial accounted for 53%. The remaining 4% was due to medium sized lesions with no small lesions being encountered. These findings differ from those of a study done in Westmead Hospital, Australia by *Kizana, E. et al* in which 8% of the lesions were small, 46% medium and 46% large (19). These differences could be as a result of delayed diagnosis in our setup due to a low index of suspicion as time is lost managing the wrong disease and meanwhile the tumours are increasing in size. It may also be due to a smaller percentage of calcified meningiomas (11%) than the 20 to 30% described by *Greenberg et al* (26). Calcified meningiomas are thought to grow at a slower rate. There was no association found between the size of the tumour and histopathology in either study.

Bone involvement, which is best appreciated on CT but can be detected on MRI was absent in 84% of the study patients. 13 % of the study patients had hyperostosis. Of those with hyperostosis, the commonest location affected was the sphenoidal ridge accounting for 43% followed by the convexity at 29%. In Westmead hospital, Australia, 27% of the patients had hyperostosis with 48% being in the convexity region and 24% in the sphenoidal region (19). The findings are similar in regards to which two locations are most affected but differ in that while sphenoidal ridge was most affected in this study, the convexity was most affected in Westmead hospital.

Bone erosion was encountered in 4% of the study patients comparable with a study at Westmead hospital which had 3% (19). It was only seen in patients with meningothelial meningiomas. No significant association was found between bone involvement and histopathological patterns.

Oedema was extensive in one patient but mild and moderate in 38% and 33% respectively while 27% of patients did not have oedema in this study. In the Westmead study 28% did not have edema, while it was mild, moderate and extensive in 33%, 25% and 14% respectively. Similarity was seen in the patients without edema and those with mild edema. Extensive edema has been thought to be due to atypical or malignant meningiomas or patients with larger lesions. However, in this study, extensive edema was seen with a meningothelial meningioma whose size was smaller than the average tumor length in the study of 5.3 cm. Histopathological subtype has been thought to affect extent of edema but does not always correlate with the extensiveness as described by *Jagadha, V. and Deck, J.H.* All the atypical meningiomas had edema associated with them with 67% having moderate edema. No association was found between edema and histopathological pattern in this study or the one

at Westmead Hospital, Australia unlike the study in Brazil by *Tobias, A. M. et al* that reported an association with histopathological grade (50).

None of the patients had brain invasion and tumor margins appeared distinct in all patients comparable with the Westmead study in which 85% had distinct margins on CT and 90% on MRI. This could be due to majority of the meningiomas being benign and not invading surrounding brain tissue.

Calcification was seen in only 11% of the study patients which is much lower than the 20-30% described by *Greenberg, H. et al.* All calcified meningiomas were grade one with 50% being meningothelial. No association was found between histopathology and calcification.

53% of the patients did not have any secondary changes. Of those with secondary changes necrosis was seen more frequently than cyst formation. Secondary changes were encountered more frequently than is described for meningiomas. An English study found that secondary changes pointed towards non-benignity of meningiomas. This finding may be as a result of the large tumor sizes seen in this study. Larger tumors may outgrow their supply and undergo necrotic change. No association was found between histology and presence of secondary changes.

Mass effect was absent in 16% of patients encountered. Of those with mass effect, moderate effect was the most encountered seen in 45% of patients. One patient had severe mass effect and his meningioma subtype was meningothelial. This patient also had the largest tumor encountered and it also caused bone erosion. Mass effect has been associated with tumor size rather than histopathological grade or subtype. No association was found between histopathology and mass effect.

75% of the patients had their CSF pathway affected. Of those in whom it was affected, compression was the commonest finding followed by displacement. All the patients with atypical meningiomas developed compression. A significant relationship between histopathology and CSF pathway affection was found though this is likely to have been a chance finding as no specific pattern was appreciated in the data.

The density was hyperdense in 87% of the patients who had CT scans. This is in keeping with literature as the typical appearance of a meningioma is a hyperdense lesion on CT scanning pre-contrast that avidly enhances homogeneously post contrast. The hyperdense appearance was the most frequently encountered in all the grade one meningiomas. None of the patients with an atypical meningioma had a CT scan done. No significant association existed with histopathological patterns.

In this study, on T1 isointense meningiomas were the commonest (61%) unlike Westmead hospital, Australia where hypointense (53%) were the commonest. (19) On T2 imaging, most meningiomas (65%) were hyperintense. In Westmead majority (45%) were also hyperintense on T2. Our study used FLAIR sequence while the Westmead one used Proton Density sequence. No association was found between the MRI intensities and histopathology in either study. This differed from a study done at University Hospital, Belgium concluded that different histologic subtypes may have a different MR appearance, but that did not suffice to reach a histologic diagnosis by MR imaging (20).

Irregular enhancement occurred in 53% of the meningiomas encountered. This irregular enhancement was as a result of secondary changes such as necrosis. This heterogeneous pattern was observed in 67% of the atypical meningiomas. Except for the fibroblastic variant,

irregular enhancement was more frequent than uniform enhancement. No association was found between enhancement and histopathology. This is similar to a study in Ankara, Turkey that found that different meningioma variants have similar enhancement pattern (53). Meningiomas generally enhance homogenously but the heterogeneous enhancement in this study could have been due to most of the lesions (96%) being large as tumor size has been associated with secondary changes especially necrosis which in turn causes heterogeneous enhancement.

83% of the studied patients had no herniation. Herniation was seen in 70%, 20% and 10% of meningothelial, fibroblastic and atypical meningiomas respectively. In those in whom there was herniation, tonsillar herniation was the commonest. This finding is differs from that seen in Weastmead hospital in which herniation was mostly subfalcine (19). No radiopathological association was seen. Herniation is more likely to be affected by tumor size and location as opposed to tumor subtype.

Of the vascular features, identifiable tumor vessels were most encountered both in our study and the one at Westmead hospital. No association to histopathology was seen.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

This chapter covers the conclusions drawn from the study and the recommendations thought appropriate as a result.

6.1 Conclusions

1. A) The common CT scan features encountered were extra-axial, hyperdense, mass lesions with mild to moderate edema that avidly enhanced with contrast either homogenously or heterogeneously.

   B) The common MRI features encountered were extra-axial mass lesions which were isointense on T1 weighted sequences, hyperintense on T2 weighted images, hyperintense on FLAIR images and enhanced when gadolinium contrast was injected.

2. The common meningiomas were grade I with meningothelial, fibroblastic and transitional subtypes seen.

3. Though imaging can reliably diagnose meningiomas, histopathological subtypes of meningiomas cannot be differentiated from each other based on radiological features.

6.2 Recommendations

1. Histopathological diagnosis of meningiomas in terms of grade and subtype should be continued and improved in terms of immunohistochemistry

2. Further studies should be conducted on why secondary changes occur in a significant number of grade I meningiomas yet they have been found in other studies to be common in non-benign meningiomas and also a study of non-benign meningiomas which were very few in this study.

REFERENCES

1. CBTRUS. CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2004-2006. Hinsdale, Illinois www.cbtrus.org:; 2010.
2. Marosi C, Hassler M, Roessler K, Reni M, Sant M, Mazza E, et al. Meningioma. Critical Reviews in Oncology/Hematology. 2008 August; 67(2): p. 153-171.
3. Umansky F, Shoshan Y, Rosenthal G, Fraitfeld S, Spektor S. Radiation-induced meningioma. Neurosurgical Focus. 2008; 24(5): p. E7.
4. Claus EB, Bondy ML, Schildkraut JM, Wiemels JL, Wrensch M, Black PM. Epidemiology of intracranial meningioma. Neurosurgery. 2005; 57(6): p. 1088-1095.
5. Backer-Grøndahl T, Moen BH, Torp SH. The histopathological spectrum of human meningiomas. International journal of clinical and experimental pathology. 2012; 5(3): p. 231-242.
6. Cushing H. Meningiomas: their classification, regional behaviour, life history and surgical end results. reprint ed.: Hafner Publishing Company 1962; 1938.
7. Kleihues P, joe s, joe r, joe t. Tumors of the Nervous System: Meningeal tumours. In Louis DN, Cavenee WK, Otmar OH, Wiestler D, editors. WHO Classification of Tumors of the Central Nervous System. Lyon: International Agency for Research on Cancer; 2007. p. 176-184.
8. Kallio M, Sankila R, Hakulinen T, Jääskeläinen J. Factors affecting operative and excess long-term mortality in 935 patients with intracranial meningioma. Neurosurgery. 1992 July; 31(1): p. 2-12.
9. Simpson D. The recurrence of intracranial meningiomas after surgical treatment. Journal of Neurology, Neurosurgery and Psychiatry with practical neurology. 1957 February; 20(1): p. 22-39.
10. Stafford SL, Perry A, Suman VJ, Meyer FB, Scheithauer BW, Lohse CM, et al. Primarily resected meningiomas: outcome and prognostic factors in 581 Mayo Clinic patients, 1978 through 1988. Mayo Clinic Proceedings. 1998 October; 73(10): p. 936-942.
11. Kondziolka D, Flickinger JC, Perez B. Judicious resection and/or radiosurgery for parasagittal meningiomas: outcomes from a multicenter review. Gamma Knife Meningioma Study Group. Neurosurgery. 1998 September; 43(3): p. 405-413; Discussion 413-414.

12. Lee JY, Niranjan A, Mclnerney J, Kondziolka D, Flickinger JC, Lunsford LD. Stereotactic radiosurgery providing long-term tumor control of cavernous sinus meningiomas. Journal of Neurosurgery. 2002 July; 97(1): p. 65-72.

13. Pollock BE, Stafford SL, Utter A, Giannini C, Schreiner SA. Stereotactic radiosurgery provides equivalent tumor control to Simpson Grade 1 resection for patients with small- to medium-size meningiomas. International Journal of Radiation Oncology, Biology and Physics. 2003 March 15; 55(4): p. 1000-1005.

14. Yano S, Kuratsu J, Kumamoto Brain Tumour Research Group. Indications for surgery in patients with asymptomatic meningiomas based on an extensive experience. Journal of Neurosurgery. 2006 October; 105(4): p. 538-543.

15. Carli DF, Sluzewski M, Beute GN, van Rooij WJ. Complications of particle embolization of meningiomas: frequency, risk factors, and outcome. American Journal of Neuroradiology. 2010 January; 31(1): p. 152-154.

16. Oka H, Kurata A, Kawano N, Saequsa H, Kobayashi I, Ohmomo T, et al. Preoperative superselective embolization of skull-base meningiomas: indications and limitations. Journal of neuro-oncology. 1998 October; 40(1): p. 67-71.

17. Rosen CL, Ammerman JM, Sekhar LN, Bank WO. Outcome analysis of preoperative embolization in cranial base surgery. Acta Neurochirurgica. 2002 November; 144(11): p. 1157-1164.

18. Vassilouthis J, Ambrose J. Computerized tomography scanning appearances of intracranial meningiomas. An attempt to predict the histological features. Journal of Neurosurgery. 1979 March; 50(3): p. 320-327.

19. Kizana E, Lee R, Young N, Dorsch NW, Soo YS. A review of the radiological features of intracranial meningiomas. Australasian Radiology. 1996 November; 40(4): p. 454-462.

20. Demaerel P, Wilms G, Lammens M, Marchal G, Plets C, Goffin J, et al. Intracranial meningiomas: correlation between MR imaging and histology in fifty patients. Journal of Computer Assisted Tomography. 1991 January-Febuary; 15(1): p. 45-51.

21. Zimmerman RD, Fleming CA, Saint-Louis LA, Lee BC, Manning JJ, Deck MD. Magnetic resonance imaging of meningiomas. American Journal of Neuroradiology. 1985 March-April; 6(2): p. 149-157.

22. Vivier J, Bardien S, Van der Merwe L, Brusnicky J, Zaharie D, Keyser R, et al. A study of meningiomas in South Africa: investigating a correlation between clinical

presentation, histopathology and genetic markers. British Journal of Neurosurgery. 2009 February; 23(1): p. 63-70.

23. Rohringer M, Sutherland GR, Louw DF, Sima AA. Incidence and clinicopathological features of meningioma. Journal of Neurosurgery. 1989 November; 71(5 part 1): p. 665-672.

24. Granger A, Sainsbury R, Wilkinson T, MacFarlane M. Multiple meningiomas: case report and review of the literature. Journal of Clinical Neuroscience. 2000 March; 7(2): p. 149-152.

25. Moseley I. Imaging Techniques in the Investigation of Cerebral Tumours. In Bleehen NM, editor. Tumours of the brain. Illustrated ed. Berlin: Springer-Verlag; 1986. p. 35-45.

26. Greenberg HS, Chandler WF, Sandler HM. Brain Tumors New York: Oxford University Press; 1999.

27. Gruber T, Dare AO, Balos LL, Lele S, Fenstermaker RA. Multiple meningiomas arising during long-term therapy with the progesterone agonist megestrol acetate. Case report. Journal of Neurosurgery. 2004 February; 100(2): p. 328-331.

28. Shapir J, Coblentz C, Malanson D, Ethier R, Robitaille Y. New CT finding in aggressive meningioma. American Journal of Neuroradiology. 1985 January-February; 6(1): p. 101-102.

29. Stein SC, Hurst RW, Sonnad SS. Meta-analysis of cranial CT scans in children. A mathematical model to predict radiation-induced tumors. Pediatric Neurosurgery. 2008; 44(6): p. 448-457.

30. Inskip PD, Tarone RE, Hatch EE, Wilcosky TC, Selker RG, Fine HA, et al. Laterality of brain tumors. Neuroepidemiology. 2003 March-April; 22(2): p. 130-138.

31. Sheehy JP, Crockard HA. Multiple meningiomas: a long-term review. Journal of Neurosurgery. 1983; 59(1): p. 1-5.

32. Borovich B, Doron Y, Braum J, Feinsod M, Goldsher D, Gruszkiewicz J, et al. The incidence of multiple meningiomas--do solitary meningiomas exist? Acta Neurochirugica. 1988; 90(1-2): p. 15-22.

33. Maier H, Ofner D, Hittmair A, Kitz K, Budka H. Classic, atypical, and anaplastic meningioma: three histopathological subtypes of clinical relevance. Journal of Neurosurgery. 1992 October; 77(4): p. 616-623.

34. Mahmood A, Caccamo DV, Tomecek FJ, Malik GM. Atypical and malignant meningiomas: a clinicopathological review. Neurosurgery. 1993 December; 33(6): p. 955-963.

35. Chumba KD. Histological spectrum of meningiomas seen in KNH: A retrospective and prospective study. University of Nairobi digital repository. 2006.

36. Wanjeri J. Histology And Clinical Pattern Of Meningiomas At The Kenyatta National Hospital, Nairobi, Kenya. University of Nairobi, Digital Repository. 2011.

37. New PF, Hesselink JR, O'Carroll CP, Kleinman GM. Malignant meningiomas: CT and histologic criteria, including a new CT sign. American Journal of Neuroradiology. 1982 May-June; 3(3): p. 267-276.

38. Alvarez F, Roda JM, Pérez Romero M, Morales C, Sarmiento MA, Blázquez MG. Malignant and atypical meningiomas: a reappraisal of clinical, histological, and computed tomographic features. Neurosurgery. 1987 May; 20(5): p. 688-694.

39. Perry A, Stafford SL, Scheithauer BW, Suman VJ, Lohse CM. Meningioma grading: an analysis of histologic parameters. The American Journal of Surgical Pathology. 1997 December; 21(12): p. 1455-65.

40. Kim EY, Kim ST, Kim HJ, Jeon P, Kim KH, Byun HS. Intraventricular meningiomas: radiological findings and clinical features in 12 patients. Clinical Imaging. 2009 May-Jun; 33(3): p. 175-180.

41. Fine M, Brazis P, Palacios E, Neri G. Computed tomography of sphenoid wing meningiomas: tumor location related to distal edema. Surgical Neurology. 1980 May; 13(5): p. 385-390.

42. Gilbert JJ, Paulseth JE, Coates RK, Malott D. Cerebral edema associated with meningiomas. Neurosurgery. 1983 June; 12(6): p. 599-605.

43. Go KG, Wilmink JT, Molenaar WM. Peritumoral brain edema associated with meningiomas. Neurosurgery. 1988 August; 23(2): p. 175-179.

44. Trittmacher S, Traupe H, Schmid A. Pre- and postoperative changes in brain tissue surrounding a meningioma. Neurosurgery. 1988 May; 22(5): p. 882-885.

45. Benzel EC, Gelder FB. Correlation between sex hormone binding and peritumoral edema in intracranial meningiomas. Neurosurgery. 1988 August; 23(2): p. 169-174.

46. Jagadha V, Deck JH. Massive cerebral edema associated with meningioma. Canadian Journal of Neurological Sciences. 1987 February; 14(1): p. 55-58.

47. Alquacil-Garcia A, Pettigrew NM, Sima AA. Secretory meningioma: A distinct subtype of meningioma. The American Journal of Surgical Pathology. 1986 February; 10(2): p. 102-111.

48. Chen TC, Zee CS, Miller CA, Weiss CA, Tang G, Chin L, et al. Magnetic resonance imaging and pathological correlates of meningiomas. Neurosurgery. 1992 December; 31(6): p. 1015-1021; Discussion 1021-1022.

49. Ide M, Jimbo M, Kubo O, Yamamoto M, Imanaga H. Peritumoral Brain Edema Associated with Meningioma: Histological Study of the Tumor Margin and Sorrounding Brain. Neurol Med Chir. 1992; 32: p. 65-71.

50. Mattei TA, Mattei JA, Ramina R, Aguiar PH, Plese JP, Marino Jr. R. Edema and malignancy in meningiomas. Clinics. 2005 June; 60(3): p. 201-206.

51. Nakasu S, Hirano A, Shimura T, Llena JF. Incidental meningiomas in autopsy study. Surgical Neurology. 1987 April; 27(4): p. 319-322.

52. Vernooij MW, Ikram MA, Tanghe HL, Vincent AJ, Hofman A, Krestin GP, et al. Incidental findings on brain MRI in the general population. The New England Journal of Medicine. 2007 November 1; 357(18): p. 1821-1828.

53. Oguz KK, Cila A. Rim enhancement of meningiomas on fast FLAIR imaging. Neuroradiology. 2003 February; 45(2): p. 78-81.

54. Maiuri F, Laconetta G, de Divitiis O, Cirillo S, Di Salle F, De Caro ML. Intracranial meningiomas: correlations between MR imaging and histology. European Journal of Radiology. 1999 July; 31(1): p. 69-75.

55. Hsu CC, Pai CY, Kao HW, Ksueh CJ, Hsu WL, Lo CP. Do aggressive imaging features correlate with advanced histopathological grade in meningiomas. Journal of Clinical Neuroscience. 2010 May; 17(5): p. 584-587.

56. Bradac GB, Ferszt R, Kendall BE. Cranial meningiomas: diagnosis, biology, therapy Germany: Springer-Verlag; 1990.

57. Pramesh CS, Saklani AP, Pantavaidya GH, Heroor AA, Naresh KN, Sharma S, et al. Benign metastasizing meningioma. Japanese Journal of Clinical Oncology. 2003 February; 33(2): p. 86-88.

58. Hasselblatt M, Nolte KW, Paulus W. Angiomatous meningioma: a clinicopathologic study of 38 cases. The American Journal of Surgical Pathology. 2004 March; 28(3): p. 390-393.

59. Ng HK, Tse CC, Lo ST. Microcystic meningiomas-an unusual morphological variant of meningiomas. Histopathology. 1989 January; 14(1): p. 1-9.

60. Louis DN, Hamilton AJ, Sobel RA, Ojemann RG. Pseudopsammomatous meningioma with elevated serum carcinoembryonic antigen: a true secretory meningioma. Case report. Journal of Neurosurgery. 1991 January; 74(1): p. 129-132.

61. Kepes JJ, Chen WY, Connors MH, Vogel FS. "Chordoid" meningeal tumors in young individuals with peritumoral lymphoplasmacellular infiltrates causing systemic manifestations of the Castleman syndrome. A report of seven cases. Cancer. 1988 July 15; 62(2): p. 391-406.

62. Zorludemir S, Scheithauer BW, Hirose T, Van Houten C, Miller G, Meyer FB. Clear cell meningioma. A clinicopathologic study of a potentially aggressive variant of meningioma. The American Journal of Surgical Pathology. 1995 May; 19(5): p. 493-505.

63. Joseph E, Sandhyamani S, Rao MB, Nair S, Radhakrishnan W. Atypical meningioma: a clinicopathological analysis. Neurology India. 2000 December; 48(4): p. 338-342.

64. Perry A, Scheithauer BW, Stafford SL, Lohse CM, Wollan PC.., "Malignancy" in meningiomas: a clinicopathologic study of 116 patients, with grading implications. Cancer. 1999 May 1; 85(9): p. 2046-2056.

65. Ludwin SK, Rubinstein LJ, Russell DS. Papillary meningioma: a malignant variant of meningioma. Cancer. 1975 October; 36(4): p. 1363-1373.

66. Pasquier B, Gasnier F, Pasquier D, Keddari E, Morens A, Couderc P. Papillary meningioma. Clinicopathologic study of seven cases and review of the literature. Cancer. 1986 July 15; 58(2): p. 299-305.

67. Lantos PL, Vandenberg SR, Kleihues P. Tumours of the nervous system. In Graham DI, Lantos PL, editors. Greenfield's Neuropathology. London: Arnold; 2002. p. 909-926.

68. Thomas HG, Dolman CL, Berry K. Malignant meningioma: clinical and pathological features. Journal of Neurosurgery. 1981 December; 55(6): p. 929-934.

69. Fabiani A, Trebini F, Favero M, Peres B, Palmucci L. The significance of atypical mitoses in malignant meningiomas. Acta Neuropathologica. 1977 June 15; 38(3): p. 229-231.

70. McLendon R, Bigner DD, Rosenblum M. Russel & Rubinstein's Pathology of Tumors of the Nervous System. 7th ed.: CRC Press; 2006.

71. Dubois PJ. Brain Tumours. In Rosenberg RN, editor. The Clinical Neurosciences: Neuropathology. Illustrated ed. California: Churchill Livingstone 1983; 1983. p. 1-455.

72. Ahyai A, Spaar FW. DNA and prognosis of meningiomas: a comparative cytological and fluorescence-cytophotometrical study of 71 tumours. Acta Neurochirurgica. 1987; 87(3-4): p. 119-128.

73. Kleihus P, Burger PC, Schithauer BW. Histological typing of tumours of the central nervous system. In Kleihues P, Cavenee WK, editors. Pathology and Genetics of Tumours of the Nervous System, WHO Classification of Tumours. 2nd ed. Berlin: Springer-Verlag; 1993.

74. Louis DN, Scheithauer BW, Budka H, von Deimling A, Kepes JJ. Meningiomas. In Kleihues P, Cavenee WK, editors. Pathology and Genetics. Tumours of the Nervous System, WHO Classification of Tumors. Lyon: IARC Press; 2000. p. 176-184.

75. Kleihues P, Burger PC, Schithauer BW. Histological Typing of Tumours of the Central Nervous System (International Histological Classification of Tumours); 2000.

76. van Tilborg AA, Al Allak B, Velthuizen SC, de Vries A, Kros JM, Avezaat CJ, et al. Chromosomal instability in meningiomas. Journal of Neuropathology and experimental Neurology. 2005 April; 64(4): p. 312-322.

77. Kros JM, Wolbers JG. [Meningiomas: prognostic relevance of histopathologic and genetic markers]. Nederlands Tijdschrift voor Geneeskunder. 2001 November 10; 145(45): p. 2160-2165.

78. Wada K, Maruno M, Suzuki T, Kagawa N, Hashiba T, Fujimoto Y, et al. Chromosomal and genetic abnormalities in benign and malignant meningiomas using DNA microarray. Neurological Research. 2005 October; 27(7): p. 747-754.

79. Weber RG, Boström J, Wolter M, Baudis M, Collins VP, Reifenberger G, et al. Analysis of genomic alterations in benign, atypical, and anaplastic meningiomas: toward a genetic model of meningioma progression. Proceedings of the National Academy of Sciences of the United States of America. 1997 December 23; 94(26): p. 14719-14724.

80. Espinosa AB, Tabernero MD, Maîlo A, Sayaqués JM, Ciudad J, Merino M, et al. The cytogenetic relationship between primary and recurrent meningiomas points to the need for new treatment strategies in cases at high risk of relapse. Clinical Cancer Research. 2006 February 1; 12(3 part 1): p. 772-780.

81. Maillo A, Orfao A, Sayaques JM, Diaz P, Gómez-Moreta JA, Caballero M, et al. New classification scheme for the prognostic stratification of meningioma on the basis of

chromosome 14 abnormalities, patient age, and tumor histopathology. Journal of Clinical Oncology. 2003 September 1; 21(17): p. 3285-3295.

82. Tabernero MD, Espinosa AB, Maîlo A, Sayaqués JM, Alquero Mdel C, Lumbreras E, et al. Characterization of chromosome 14 abnormalities by interphase in situ hybridization and comparative genomic hybridization in 124 meningiomas: correlation with clinical, histopathologic, and prognostic features. American Journal of Clinical Pathology. 2005 May; 123(5): p. 744-751.

APPENDICES

APPENDIX I: IREC APPROVAL

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
Tel: 33471/2/3

Reference: IREC/2011/41
Approval Number: 000618

26th April, 2011

Dr. Mary Kerubo Onyinkwa
P. O. Box 2052
ELDORET- KENYA

Dear Dr. Onyinkwa

RE: FORMAL APPROVAL

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

"Radiological features of intracrnial meningiomas in correlation with histopathology in Eldoret, Kenya".

Your proposal has been granted a Formal Approval Number: **FAN: IREC 000618** on 26th April, 2011. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 25th April, 2012. 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.

Yours Sincerely,

28/04/2011
DR. W. ARUASA
AG. CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
APPROVED
26 APR 2011
P.O. Box 4606 ELDORET

cc: Director - MTRH
Dean - SOM
Dean - SPH
Dean - SOD

APPENDIX II: DATA COLLECTION FORM

RADIOLOGICAL AND HISTOLOGICAL FEATURES OF INTRACRANIAL MENINGIOMAS: STUDY QUESTIONNAIRE

SECTION A: STUDY ALLOCATION

1. **Subject allocation ID:** _____
   (To be generated in serial for each participant depending on hospital)

SECTION B: DEMOGRAPHIC DETAILS

Gender: □ Male □ Female

A) Date of Birth: _____

B) Age (If date of birth unavailable) _____ Years

SECTION C: IMAGING (RADIOLOGICAL FEATURES)

1. **Location**
   - □ Convexity
   - □ Falx
   - □ Sphenoidal ridge
   - □ Parasagittal
   - □ Frontobasal
   - □ Posterior cranial fossa
   - □ Middle cranial fossa
   - □ Petrous ridge
   - □ Tentorial
   - □ Foramen magnum
   - □ Parasellar
   - □ Clival
   - □ Others

2. **Number of lesions**
   - □ One
   - □ Two
   - □ More than two *(Specify Number)*

3. **Size**
   - □ <1.5cm
   - □ 1.5-3.0cm
   - □ >3.0cm

4. **Bone involvement**
   - □ Nil
   - □ Bone erosion
   - □ Hyperostosis
   - □ Both

5. **Oedema**
   - □ Nil
   - □ Moderate
   - □ Mild
   - □ Extensive

6. **Brain invasion** □ Yes □ No

7. Calcification
   - □ Nil
   - □ Moderate
   - □ Fine
   - □ Coarse

8. Other secondary changes
   - □ Nil
   - □ Cyst formation
   - □ Hemorrhage

9. Mass effect □ Nil □ Moderate □ Mild □ Severe

10. Tumor margins □ Distinct □ Indistinct □ Cleaved

11. CSF Pathway □ Nil □ Displacement □ Obstruction

12. Shape □ Mass □ *En plaque*

13. Density □ Hyperdense □ Isodense □ Hypodense □ Mixed density

14. Enhancement □ Nil □ Irregular □ Uniform

15. Herniation □ Nil □ Transtentorial □ Subfalcine □ Tonsillar

16. **Vascular features**
- □ Identifiable tumor vessels
- □ Arterial encasement
- □ Infiltration of venous sinuses
- □ Displacement of adjacent vessels
- □ Increased vascularity of tumor

SECTION D: HISTOPATHOLOGY

GRADE I	**GRADE II**	**GRADE III**
□ Meningothelial □ Fibrous (Fibroblastic) □ Transitional □ Psammomatous □ Angiomatous (vascular) □ Microcystic □ Secretory □ Lymphoplasmacyte-Rich □ Metaplastic	□ Atypical □ Clear cell □ Chordoid	□ Anaplastic (malignant) □ Papillary □ Rhabdoid

APPENDIX III: CONSENT FORMS

ENGLISH CONSENT FORM:

My name is Dr Mary K. Onyinkwa. I am a qualified doctor, registered by the Kenya Medical Practitioners and Dentists Board (Registration number A6646). I am currently pursuing a Masters degree in Radiology at Moi University. I would like to recruit you into my research which involves studying of radiological features of meningiomas in correlation to the histopathological subtype.

INFORMATION ABOUT MENINGIOMAS

A meningioma is a brain tumor arising from the meninges, which are the coverings of the brain. It is one of the commonest tumors of the brain. It is more common in women and tends to affect older persons. It is uncommon in children but they can also get it. Common presenting complaints of patients include, headache, nausea and vomiting, seizures, visual, and auditory disturbances. Factors that have been thought to cause meningiomas are ionizing radiation, hormones, genetic factors and head trauma. About 90% of meningiomas are benign which means they do not spread into surrounding tissues but a small percentage are malignant which means they can invade surrounding tissues. Benign tumors are less aggressive than malignant ones. There are three grades of tumors. Grade I (benign), II (atypical) and III (malignant). The higher the grade, the worse the prognosis of the meningioma but generally meningiomas have a good prognosis. Diagnosis of meningiomas is achieved by imaging mainly by CT scanning and MR imaging. After surgery the subtype is diagnosed by histopathology.

Your test results will be kept confidential and you will be informed of the results and what they mean. Treatment does not depend on your participation in this study. Appropriate treatment will be offered to you depending on what your results reveal.

This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

If you need further clarifications please contact IREC using the address below.

The Chairman IREC,

Moi Teaching and Referral Hospital,

PO Box 3,

Eldoret.

Tel: 33471/2/3

YOUR consent:

Adults above 18 years of age

I have been adequately informed that I am being recruited into a study on radiological features of meningiomas in correlation with the histology subtype. The investigator has also informed me that my participation in this study is voluntary and will not exclude me from treatment even if I were to opt out and that my confidentiality will be respected.

Sign: …….

Name: …….

Date: …….

YOUR consent:

Patients below 18 years of age

I have been adequately informed that my son/daughter is being recruited into a study on radiological features of meningiomas in correlation with the histology subtype. The investigator has also informed me that his/her participation in this study is voluntary and will not exclude him/her from treatment even if he/she were to opt out and his/ her confidentiality will be respected.

Patient's PARENT/GUARDIAN:

Sign: …….

Name: …….

Date: …….

KISWAHILI CONSENT FORM:

Jina langu ni Daktari Mary K. Onyinkwa. Mimi ni daktari aliyefuzu nakusajiliwa na bodi ya madaktari wa Kenya (Kenya Medical Practitioners and Dentists Board) Nambari yangu ya bodi ni A 6646. Mimi ni msomi wa shahada ya juu (Masters) ya udaktari (Radiology) katika chuo kikuu cha Moi University. Ningependa ujiunge na uchunguzi ninaofanya kujua kama picha za ubongo zinazofanywa za ugonjwa wa saratani wa meningioma zinaambatana na aina ya hisologia.

TAARIFA JUU YA MENINGIOMA

Meningioma ni aina ya saratani ya ubongo inayoathiri tando zinazofunika ubongo. Meningioma ni mojawapo ya saratani ya ubongo inayoathiri watu wengi Kushinda saratani zingine za ubongo. Inaaathiri wanawake sana kushinda wanaume na inaathiri watu ambao wana miaka mingi. Haiathiri watoto sana lakini pia wao wanaweza kuipata. Mara mingi wagonjwa huja hospitalini wakiwa na shida ya kichwa kuuma, kusikia kutapika au kutapika, kufanya kama mtu mwenye kifafa, shida ya macho na ya masikio. Vitu vinavyofikiriwa kuleta saratani ya meningioma ni kama vile mionzi, homoni, maumbile na kiwewe kichwani. Saratani ya meningioma inaweza kuwa ile ambayo haiathiri tishu zinazoizunguka au inayoathiri tishu zinazoizunguka. Kuna gredi tatu za meningioma. Gredi I, II, III. Gredi inavyozidi kuenda juu ndivyo madhara yake yanakuwa mabaya zaidi lakini mara nyingi ikitibiwa watu wengi hupata kuendelea vizuri. Utambuzi wa meningioma ni kwa kufanya CT scan au MRI ya ubongo. Baada ya kupasuliwa, utambulizi hufanywa na histologia.

Matokeo yako yatawekwa kwa njia ya kuheshimu haki yako ya kutojulisha yeyote. Utajulishwa kuhusu matokeo yako na maana kwa afya yako. Hautakatazwa matibabu iwapo

utachagua ama usichague kushiriki katika uchunguzi huu. Matibabu yafaayo yatapewa kulingana na matokeo yako.

Uwe huru kuuliza maswali yoyote.Uchunguzi huu umehidhinishwa na kamati ya kusimamia machunguzi ya wasomi na haki ya wanaochunguzwa (Institutional Research and Ethics Committee-IREC) katika chuo kikuu cha Moi University na hospitali kuu ya Moi Teaching and Referral.

Iwapo unahitaji maelezo zaidi tafadhali wasiliana na IREC kwa kutumia anwani ifuatayo.

Mwenyekiti IREC,

Moi Teaching and Referral Hospital,

S. L. P. 3,

Eldoret.

Simu: 33471/2/3

HIDHINI yako:

Walio na miaka 18 na zaidi

Nimeelezwa ipasavyo ya kwamba ninashiriki katika uchunguzi wa usomi utakayo chunguza iwapo picha za ubongo zinazofanywa za ugonjwa wa saratani wa meningioma zinaambatana na aina ya hisologia.Mchunguzi pia amenieleza kuwa sitakosa matibabu nikikataa kushiriki katika uchunguzi huu

Sahihi: …….…….

Jina: ….……..……

Tarehe: …….…….

HIDHINI yako:

Walio na miaka chini ya 18

Nimeelezwa ipasavyo ya kwamba mwana wangu anashiriki katika uchunguzi wa usomi utakayo chunguza iwapo picha za ubongo zinazofanywa za ugonjwa wa saratani wa meningioma zinaambatana na aina ya hisologia Mchunguzi pia amenieleza kuwa mwanangu hatakosa matibabu akikataa kushiriki katika uchunguzi huu na na kwamba matokeo yake yatawekwa kwa njia ya kuheshimu haki yake ya kutojulisha yeyote.

MZAZI ama MLINZI:

Sahihi: …….…….

Jina: ….……..……

Tarehe: …….…….

APPENDIX IV: COMPUTED TOMOGRAPHY (CT) RESONANCE IMAGING (MRI) ANALYSIS PROTOCOL (Bradac et al)

Location of lesion

Size: small 0-1.5 cm, medium 1.5-3 cm, large >3 cm

Shape: mass, en plaque

Margin: distinct, distinct with rim, indistinct

Bone changes: nil, hyperostosis, destruction

Mass effect: nil, mild, moderate, severe

Oedema: nil, mild, moderate, severe

Alteration of cerebrospinal fluid pathway: obstruction, displacement

Herniation: nil, subfalcine, transtentorial, tonsillar

Cystic changes: central and single, multiple, peripheral and single/multiple

Calcification: nil, fine, moderate, coarse

Haemorrhage: presence, absence

Enhancement (CT only): nil, uniform, irregular

Density (CT): hyperdense, hypodense, isodense, mixed density

Signal intensity (MRI) relative to cerebral cortex, TI-, T2-, multiple proton-density weighted sequences: hyperintense, hypointense, isointense, mixed density

Vascular features: identifiable tumour vessels, arterial encasement, infiltration of venous sinuses, displacement of adjacent vessels, increased vascularity of tumour

APPENDIX V: TABLE SHOWING HISTOPATHOLOGICAL FEATURES OF THE MENINGIOMA GRADES AND SUB TYPES

Table 11: Histopathological features of the meningioma grades and sub-types

Grade I (Benign) : >90%. Expression of vimentin is common: expression of glial fibrillary acidic protein and anti-leu-7 uncommon. Fatty degeneration, haemorrhage, calcification and cyst formation can also occur. Treatment approach is the same for all subtypes.	
Meningothelial Meningioma	Common; Cells arranged in lobules surrounded by thin collagenous septae in a syncytium (delicate intricately interwoven tumour cell processes not visible on light microscopy), resemble normal arachnoid cells, uniform, oval nuclei, delicate even chromatin pattern, occasionally central clearing (secondary to glycogenation), low/absent mitotic activity, nuclear polymorphism with a few bizarre giant cells, well-formed whorls and psammoma bodies.
Fibrous (Fibroblastic)	Common. Cells predominantly spindle shaped, resemble fibroblasts, arranged in wide, parallel and interlacing bundles on a matrix abundant in collagen and reticulin. Spindle shaped nuclei retain features of meningothelial cells. Cells with features of meningothelial meningioma also seen. Well-formed whorls and psammoma bodies present focally.
Transitional	Features transitional between meningothelial and fibroblastic. Meningothelial cells arranged in lobules alternating with spindle shaped cells in fascicles. Conspicuous whorls with psammoma bodies in the centre are frequent.
Psammomatous	Abundant psammoma bodies that may become confluent forming irregular calcified masses. Have a transitional appearance with whorl formation. Stroma may contain amyloid (57).
Angiomatous	Have numerous blood vessels on the background of a typical meningioma. The vascular channels may be small, medium sized, thin walled or with hyalinised thickened walls. Moderate nuclear pleomorphism may be noted (58).

Microcystic	Stellate cells with elongated processes and a loose, mucinous background giving appearance of many small cysts. Many pleomorphic cells may be seen (59). Differentiated from clear cell meningioma by presence of pale fluid in between the tumour cells in microcystic variant compared to glycogen in the cytoplasm of the clear cell.
Secretory	Focal epithelial differentiation characterized by intracellular lumina containing eosinophilic hyaline material, known as pseudo-psammoma bodies, surrounded by cell membranes with microvilli. Remaining tumour shows features of a meningothelial or transitional meningioma. Marked vascular pericyte proliferation may be noted. Marked peritumoral oedema usually seen (47) (60).
Lymphoplasmacyte-rich	Show extensive chronic inflammatory cell infiltrate consisting of lymphocytes and plasma cells often obscuring the tumour cells in the background. The original architectural pattern may be of a meningothelial, fibrous or a transitional variant.
Metaplastic	Show striking focal mesenchymal differentiation. Meningothelial, transitional or fibrous variants may show osseous, cartilaginous, lipomatous, myxoid or xanthomatous changes. Groups of cells or larger areas showing any of these changes may alternate with the usual pattern. The degree of changes to categorise this variant is not clearly defined (33).
Grade II (Atypical): Have increased mitotic activity (≥4 mitoses per high powered field) and three or more of: increased cellularity, small cells with a high nuclear: cytoplasmic ratio, prominent nucleoli, uninterrupted pattern-less or sheet-like growth, or foci of spontaneous or geographical necrosis. 5% (2)	
Chordoid	Histopathologically similar to a chordoma with trabeculae of eosinophilic, vacuolated cells in a myxoid background, interspersed with typical areas of meningioma. Chronic inflammatory cells may be prominent. Psammoma bodies are uncommon. The patients may have haematological conditions (61).

Clear Cell	Pattern-less and composed of sheets of polygonal cells with clear glycogen rich cytoplasm. Classic features of a meningioma may be few. Extensive hyalinization may be seen. Whorl formation and psammoma bodies are rare. Associated with a more aggressive behaviour (62).
Atypical	Increased mitotic activity or three or more of the following: increased cellularity, small cells with high nucleus: cytoplasm ratio, prominent nucleoli, uninterrupted pattern-less or sheet-like growth and foci of spontaneous or geographic necrosis (33) (63). Increased number of macrophages and lymphocytes has been associated with atypical variants. Studies suggest the inclusion of brain invasion as a feature for diagnosis of atypical meningiomas (39) (64).
Grade III (Malignant): 3-5%. Supportive features include: loss of usual meningioma growth patterns, infiltration of underlying brain, ≥20 mitoses with atypical forms and multifocal microscopic foci of necrosis.	
Papillary	Rare group usually in younger patients, characterized by presence of a perivascular papillary or pseudopapillary pattern in at least part of the tumour. The cells are uniform with nuclear features of meningothelial cells and have long, broad or tapering processes that radiate towards blood vessels. A rich peripapillary reticulin network is present. The rest of the areas show the usual meningiothelial pattern. Mitotic activity is usually high and areas of necrosis are common. These tumours have a high chance of local and brain invasion, recurrence and metastasis (65) (66).
Rhabdoid	Patches or sheets of rhabdoid cells, which are rounded with eccentrically placed nuclei, prominent nucleoli and eosinophilic cytoplasm. Cells have paranuclear hyaline inclusions, which ultrastructurally consist of whorls of intermediate filaments entrapping lysosomes and other organelles.

Anaplastic (malignant)	Exhibit features of frank malignancy more than that described for atypical meningiomas. Other features include obvious malignant cytology, lack of typical arrangement, features resembling sarcoma, carcinoma or melanoma and a high mitotic index – 20 or more mitotic figures per 10 high power fields. (7) (67) Invasion into brain parenchyma alone is not enough to make a diagnosis of anaplastic meningioma. Some studies have shown that presence of atypical mitoses is an important feature of malignancy (68) (69).