MAGNETIC RESONANCE IMAGING PATTERNS OF BRAIN METASTASES AMONG PATIENTS WITH INTRACRANIAL NEOPLASMS AT MUHIMBILI NATIONAL HOSPITAL AND MUHIMBILI ORTHOPEDIC INSTITUTE

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By

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A Dissertation Submitted in (Partial) Fulfilment of the Requirements for the Degree of Master of Medicine (Radiology) at

Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation entitled ***"Magnetic Resonance Imaging Patterns of Brain Metastases Among Patients with Intracranial Neoplasms at Muhimbili National Hospital and Muhimbili Orthopedic Institute",*** in (partial) fulfilment of the requirements for the degree of Master of Medicine (Radiology) of Muhimbili University of Health and Allied Sciences.

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DECLARATION AND COPYRIGHT

I, **Dennis Charles Mkony**, declare that this dissertation is my original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

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DEDICATION

To my dearest love,

"Don't let anyone look down on you because you are young, but set an example for the believers in speech, in conduct, in love, in faith, and purity."

1Timothy 4:12

This work is dedicated to Neema Dennis, my beloved wife, whose constant support and love have been a constant source of inspiration throughout this journey.

"Omnia Vincit Amor."

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ABBREVIATIONS

ADC	Apparent Diffusion Coefficient
BM	Brain Metastases
CT	Computed Tomography
DWI	Diffusion-Weighted Imaging
FLAIR	Fluid Attenuation Inversion Recovery
GTD	Gross Tumor Diameter
MNH	Muhimbili National Hospital
MOI	Muhimbili Orthopaedic Institute
MRI	Magnetic Resonance Imaging
MUHAS	Muhimbili University of Health and Allied Sciences
PED	Perilesional Edema Diameter
SPSS	Statistical Package for Social Sciences
T1WI	T1 Weighted Imaging
T2WI	T2 Weighted Imaging

DEFINITIONS OF KEYWORDS

Brain Metastases:	Intracranial lesions with radiological features on MRI sequences in keeping with metastasis in patients with a known primary malignancy or histologically confirmed intracranial metastasis (1).
Intracranial neoplasm	Contrast enhancing space occupying lesion within the brain measuring at least 10mm in longest dimension and visible in 2 or more slices 5mm apart on T1WI post Gadolinium contrast administration(2).
Gross Tumor Diameter	Maximum diameter of the lesion on T1 post-contrast(3).
MRI pattern	Characteristic appearance of signals that indicates innate properties of a lesion(s) such as number, tissue's structure, composition, pathology and the peri-lesion tissues characteristics on MRI of the brain(4)
Perilesional Edema Diameter	Maximum diameter of the perilesional T2WI/FLAIR hyperintensity(5).
Perilesional fluid restriction:	Area with higher signal intensity on DWI and low ADC signal immediately surrounding the enhancing lesion(5).

ABSTRACT

Background: Metastatic brain lesions, have exhibited an increasing incidence paralleling advancement in cancer therapeutics. Diagnosis of brain metastases often involves MRI findings and clinical history. Despite advancements in diagnostic modalities, brain metastases continue to pose a challenge in differentiating it from other primary intracranial malignancies. This necessitates increasing precision of diagnostic tools. This study aimed to investigate the MRI patterns of brain metastases among patients with intracranial neoplasms in a regional context.

Objective: To determine MRI patterns of brain metastases among patients with intracranial neoplasms at Muhimbili National Hospital (MNH) and Muhimbili Orthopaedic Institute (MOI) from October 2023 to March 2024.

Material and Methods: A prospective cross-sectional study was conducted at the Department of Radiology and Medical Imaging at MNH and MOI. The study included 124 consecutive patients with intracranial neoplasms from October 2023 to March 2024. Statistical analysis was conducted using SPSS version 27. Continuous data were summarized with measures of central tendency and dispersion, while categorical data were presented as frequencies and percentages. Independent student t-tests were applied to compare means of continuous variables between two groups. Fisher's exact tests and bivariate and multivariate logistic regression analysis were employed to assess the associations, with a significance threshold of $p < 0.05$.

Results: The study comprised 124 consecutive patients diagnosed with intracranial neoplasms by MRI, with a mean age of 45.11 ± 19.434 years, and females accounting for 56.5%. Brain metastases constituted 21.0% of all intracranial neoplasms, with breast cancer as the leading primary malignancy, followed by lung cancer. Patients with brain metastases exhibited a significantly higher mean age compared to those with primary intracranial neoplasms (52.5 years vs. 43.15 years, $p = 0.029$) and a higher frequency among females (24.3% vs. 16.7%, $p = 0.301$). Brain metastases were significantly more likely to present as multiple lesions compared to primary intracranial neoplasms (76.9% vs. 9.2%, $p < 0.001$), with 32.46 higher odds ($p < 0.001$), and were more likely to occupy the grey-white matter junction (76.9% vs. 5.1%, $p < 0.001$), with 81.1 higher odds ($p < 0.001$). Additionally, brain metastases were more likely to

exhibit ring enhancements (53.8% vs. 11.2%, $p < 0.001$), with 9.08 higher odds ($p < 0.001$), and to have perilesional edema (92.3% vs. 60.2%, $p = 0.002$), with 7.67 higher odds ($p = 0.009$), along with more than 0.5 cm shift of midline structures (57.7% vs. 17.3%, $p = 0.000$), with 9.56 higher odds ($p < 0.001$), and higher mean PED/GTD ratio (2.2914 vs. 1.5783, $p < 0.001$). Conversely, brain metastases were less likely to present with poorly defined margins (3.8% vs. 30.6%, $p < 0.001$), with 0.09 lower odds ($p < 0.019$), irregular shapes (3.8% vs. 56.1%, $p < 0.001$), with 0.03 lower odds ($p < 0.001$), and to exhibit peri-enhancement fluid restrictions (7.7% vs. 31.6%, $p < 0.013$), with 0.19 lower odds ($p < 0.032$), when compared to primary intracranial neoplasms.

Conclusion: The likelihood of cerebral lesions as seen on MRI of patients with a known primary malignancy being due to metastasis is high on older patients, 50 years and above with multiple, round, ring-enhancing lesions with clearly defined margins at the grey-white matter junction. The likelihood is further enhanced by massive perilesional edema without areas of low ADC signal, sparing the cortex. Notably, not all solitary lesions are primary neoplasms.

Recommendation: Patients over 50 years with the imaging patterns demonstrating high likelihood for metastases and a known systemic malignancy may proceed with treatment options without biopsy from intracranial lesion(s) for histopathology.

Keywords: Brain metastases, Intracranial tumors, Brain MRI patterns, Primary Extracranial malignancies.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Metastatic brain lesions have manifested an increased incidence in conjunction with advancement in cancer therapeutics (1,6). Despite the diagnostic utility of magnetic resonance imaging (MRI) and spectroscopy, the prognosis remains uniformly poor, necessitating a deeper exploration of further diagnostic and therapeutic possibilities (1,6). Demographically, males and individuals within the 5th to 7th decades of life are notably more susceptible to brain metastasis, possibly indicative of sex-specific biological imbalance influencing metastatic dissemination rates (7). The complex combination of various factors, including epithelial-mesenchymal transition dynamics, immune evasion mechanisms, and the intricate process of breaching the blood-brain barrier, emphasizes the multifaceted nature of metastatic dissemination (7).

The anatomical distribution of brain metastases is hypothesized to exhibit subtype-specific variations, underpinned by the "seed and soil" hypothesis, whereby tumor cells thrive in microenvironments conducive to their growth (8). Primary cancer types predisposed to brain metastasis include lung, breast, and melanoma, with small-cell lung cancer demonstrating particularly aggressive behavior (9–11). MRI is the most sensitive method for multiple and solitary brain metastases detection(12), including T1WI, T1 + C, T2WI, FLAIR, and SWI sequences, other MRI techniques such as spectroscopy, perfusion imaging, or fractional anisotropy contribute to diagnosis precision(12). The radiological characterization of brain metastases through MRI typically delineates distinct features such as well-circumscribed lesions, preferential localization at the grey-white junction, and associated vasogenic edema, facilitating precise diagnosis and subsequent treatment (9–11).

The detailed MRI patterns of brain metastases assume a pivotal role in diagnosis guiding appropriate therapeutic decisions, acknowledging potential regional disparities in practice patterns and individual patient characteristics (1). Surgery is recommended for a small select group of patients with either solitary lesions or two accessible lesions that can be resected in a single surgical session. This approach also applies to patients with an extracranial systemic malignancy concurrently with an intracranial lesion that exhibits imaging features that favor

primary glial tumors warranting tissue for biopsy(13)(14). For this reason, diagnosis relies heavily on MRI findings due to its high sensitivity and specificity(15) combined with patient medical history. Despite advancements in diagnostic and therapeutic modalities, brain metastases continue to pose a substantial challenge in the field of oncology (11), prompting ongoing research endeavors aimed at diagnostic precision, prognostic outlook and therapeutic interventions to improve overall patient outcomes. This study aimed to investigate the MRI patterns of brain metastases among patients with intracranial neoplasms referred for brain MRI at Muhimbili National Hospital (MNH) and Muhimbili Orthopaedic Institute (MOI).

1.2 Problem Statement

Despite advancements in cancer therapeutics, the poor prognosis outlook of patients with brain metastases may partly suggests possible challenges is diagnostic precision necessary for guiding therapeutic decisions (1,6,11). The lack of comprehensive data concerning the proportion and imaging characteristics of metastatic brain lesions within Tanzania indicates a critical gap in knowledge. Determining the burden at health care facility level and understanding the imaging patterns justifies the need for studies so as to improve diagnostic precision and subsequent treatment plans for brain metastases.

1.3 Conceptual Framework

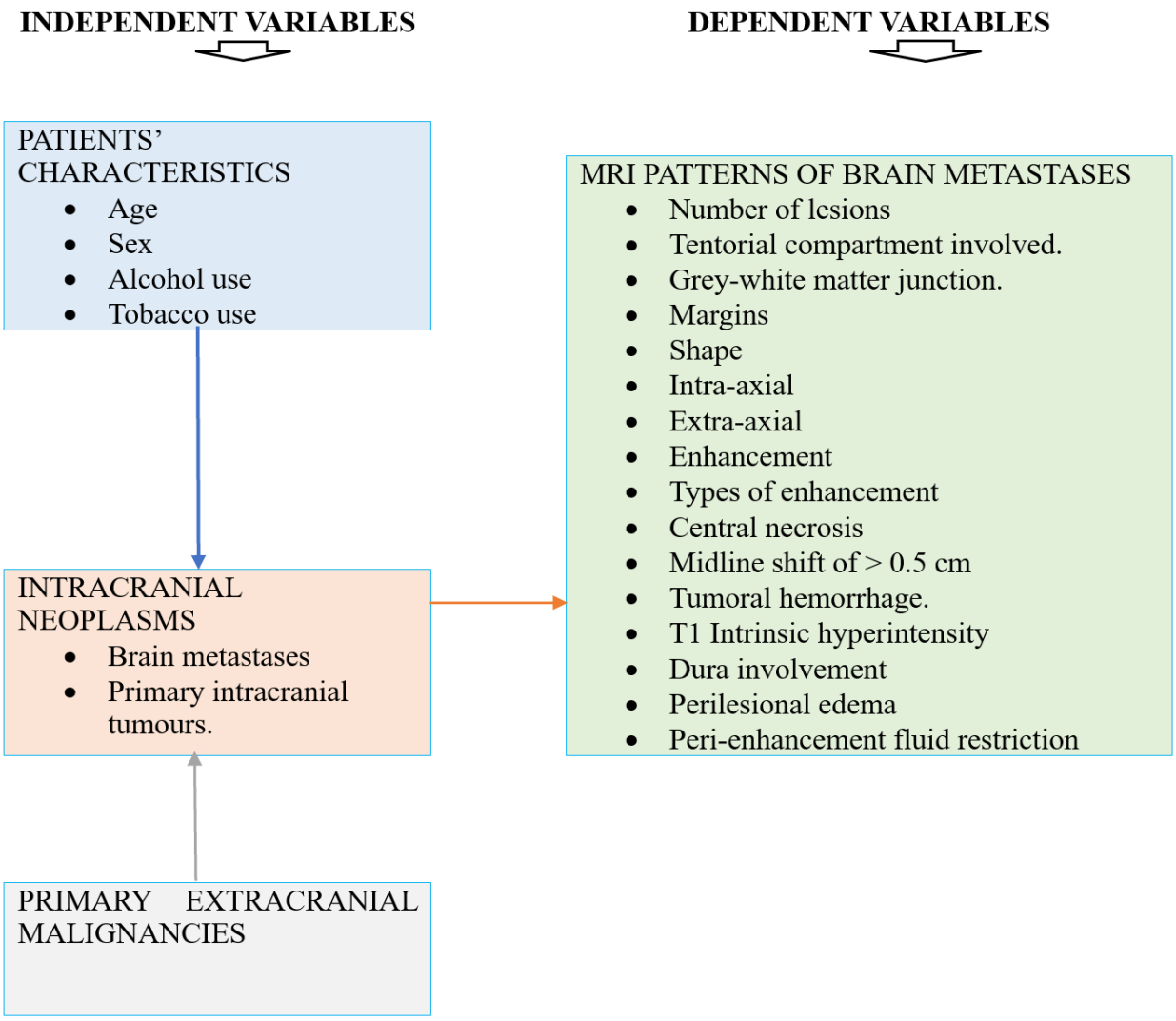


Figure 1 Conceptual Framework

Source: Principal investigator 2023

CONCEPTUAL FRAMEWORK CLARIFICATIONS

The conceptual framework guiding this study comprises four primary components: three major independent variables (patient characteristics, intracranial neoplasms, and primary extracranial malignancies), along with the dependent variables being the MRI patterns of brain metastases.

1.4 Rationale

This study aimed to determine the proportion of brain metastases among other intracranial neoplasms and deepen the understanding of their MRI patterns among patients referred for brain MRI at MNH and MOI. This understanding is crucial for an accurate diagnosis that determines prognostic outlook and ultimately the treatment plan. Additionally, accurate identification of these lesions through MRI can help improve diagnosis workflows, reduce unnecessary procedures and minimize healthcare costs associated with misdiagnosis and inappropriate treatment. Furthermore, conducting this research at MNH and MOI addresses the specific healthcare needs and challenges faced by patients within a unique regional, cultural, and health infrastructure context, as compared to the more researched Western societies.

1.5. Research Question

What is the proportion of brain metastases and their MRI patterns among patients with intracranial neoplasms at MNH and MOI?

1.6. Broad Objective

To determine the proportion of brain metastases and their MRI patterns among patients with intracranial neoplasms at MNH and MOI from October 2023 to March 2024.

1.7. Specific Objectives

1. To determine proportion of brain metastases and frequency of the primary malignancies among patients with intracranial neoplasms referred for brain MRI at MNH and MOI from October 2023 to March 2024.

2. To determine factors associated with brain metastases in patients referred for brain MRI at MNH and MOI from October 2023 to March 2024.
3. To determine association between MRI patterns and intracranial neoplasms (primary vs metastases) among patients attending MNH and MOI from October 2023 to March 2024.

1.8. Literature Review

1.8.1 Proportion of brain metastases among intracranial neoplasms and frequencies of primary extracranial malignancies.

A single-centered retrospective study in Cameroon done by Motah et al in 2021 included 200 patients with brain tumors, and reported that brain metastases accounted for 8%(16), whereas meningioma was the leading tumor (26.6%) followed by glioma (24.7%)(16). Another single centered study was conducted in Brazil by Bzuneck et al in 2022 included 96 patients diagnoses and treated for intracranial neoplasm. It was found brain metastases constituted of 21 patients (21.9%)(17). The leading primary was breast cancer (33.3%), followed by lung cancer (23.8%) and Melanoma (19.0%)(17). A study done in India by Saha et al in 2012 highlighted that the majority of cases presented with a known primary extracranial malignancy, indicating a metachronous presentation (18). Notably, lung cancer emerged as the predominant primary malignancy, comprising 45.0% of cases, followed by breast cancer (25.0%), melanoma (20.0%), and renal cancer (10.0%) (18). A similar pattern of primary malignancies was observed in a study conducted in Tunisia by Benna M et al in 2018, where lung malignancies also led at 45.0%, followed closely by breast cancer at 36.0% (19). Colorectal cancer represented only 5.0% of cases, with melanoma being the least prevalent at 1.0% (19).

1.8.2 Factors associated with brain metastases among patients referred for MRI in MNH and MOI

A study done in Nigeria by Jibrin et al in 2018 demonstrated a mean age of 35±17.1 years at diagnosis of intracranial tumor (20). However, a study done in South Africa by Fox et al in 2011 and another in Tunisia by Benna M et al, reported a higher mean age at diagnosis of brain metastases of 50.7 and 54 years respectively(21) (19). Males are reportedly more affected than females, comprising 55.4% of the cases (19). This finding contrasts with studies conducted in France by Tabouret et al 2012 and India by Saha et al in 2013, where it was observed that more female (52.8%) patients had brain metastases compared to male patients (47.2%) (18,22). While a study in Tunisia revealed a male predominance among patients with brain metastases, this finding was deemed statistically insignificant (19). In contrast, research conducted in the United

States highlighted a significant male predominance in such cases (23). In a study conducted in Korea by Jung et al in 2021, patients with brain metastases had a slightly higher mean age of 64 years compared to those with primary neoplasms, who had a mean age of 60 years, although this difference was not statistically significant (3). A study by Wu et al conducted in the United States among patients with lung cancer revealed a significant association between tobacco use and the development of brain metastases (24). Specifically, it was noted that among patients who had never smoked, 22.0% exhibited brain metastases, compared to 25.0% among former smokers and a notably higher prevalence of 45.0% among current smokers (24).

1.8.3 Association between MRI patterns and intracranial tumors (Primary vs Metastases).

Brain metastases typically present as spherical, hypointense lesions on T1-weighted images, suggestive of necrosis or hemorrhage, and hyperintense on T2-weighted images (4). Metastases primarily localize at grey/white matter junctions and arterial watershed areas. Perilesional vasogenic edema primarily involves white matter, sparing the cortex (4). Leptomeningeal metastases, mimicking meningiomas, pose diagnostic challenges, particularly in breast, prostate, and thyroid cancers (9,10,25). In a study done in India, it was reported that most metastatic lesions were supratentorial (97.2%), with a majority being multiple (77.8%) (18). Conversely, in a Korea based study by Jung et al in 2021, brain metastases commonly displayed a regular round shape (58.8%), well-defined margins (76.5%), homogeneous enhancement (58.8%), and hemorrhage (66.7%) (3).

Jung et al also reported, brain metastases were associated with a round or ovoid shape (58.8% vs. 14.3%, $p = 0.006$), well-defined margins (76.5% vs. 23.8%, $p = 0.003$), homogeneous enhancement (58.8% vs. 23.8%, $p = 0.046$), and absence of peritumoral neoplastic cell infiltration on T2-weighted imaging (64.7% vs. 14.3%, $p = 0.001$), apparent diffusion coefficient (ADC) maps (52.9% vs. 0.0%, $p = 0.000$), and exponential diffusion-weighted imaging (DWI) (70.6% vs. 0.0%, $p = 0.000$) (3). Another study conducted in Taiwan reported higher mean ADC values at the contrast-enhancing component and adjacent non-enhancing peritumoral edema of metastases to be significantly higher than those in high-grade glioma(26). A rather large

vasogenic perilesional edema sparing the cortex is reported in majority of cases of brain metastases contrary to high grade primary glial neoplasms(27). The vasogenic edema and related mass effect is reported to be responsible for the midline shift often observed and the neurological symptoms(27)

CHAPTER TWO

2.0 MATERIALS AND METHODS

2.1.Study Design

A cross-sectional study was conducted at the Department of Radiology and Medical Imaging at MNH and MOI. This study involved a structured review of patients' MRI images for intracranial neoplasm. Available medical records were also reviewed from the hospital database including histopathological results post- surgical resection of intracranial neoplasms. The gathered patients' images were accessed from the secure databases and picture archiving and communication systems of each respective institution. All patients with brain metastases were required to have primary cancer histology.

2.2 Study population and study area.

The study involved clinical, histopathological, and MRI findings of 124 consecutive patients with intracranial neoplasm referred for MRI at MNH and MOI between October 2023 and March 2024.

MNH and MOI are located in Ilala municipality in Dar es Salaam. MOI is equipped with two scanners: MAGNETOM Avanto 1.5 Tesla and MAGNETOM Sempra 1.5 Tesla. MNH is equipped with MAGNETOM Spectra 3 Tesla and MAGNETOM Sempra 1.5 Tesla. Both facilities use a head coil with 16 channels allowing better signal reception and image enhancing image quality. Approximately 25 patients with intracranial neoplasms are referred to the radiology departments of the two hospitals for MR imaging per month. The two hospitals collectively have 25 general radiologists with experience in neuroimaging, alongside 3 specialized neuroradiologists.

2.3 Sampling and Sample Size

2.3.1 Sampling strategy

Given that the population size is known and manageable, the study included a consecutive series of eligible patients diagnosed with intracranial neoplasm who had undergone brain MRI at MNH or MOI from October 2023 to March 2024.

2.3.2 Sample size estimation

Sample size estimation was based on a modified version of the Taro Yamane formula, based on the attendance number of patients with intracranial neoplasms who were referred for brain MRI. A pilot study which was conducted by the principal investigator in October 2023 demonstrated an average attendance of 21 patients with intracranial neoplasms per month, hence a total of 126 patients in 6 months.

Therefore;

$n = N / (1 + N (\mathscr{e})^2)$

$n = N / (1 + N (p\ e / t)^2)$

Where:

n = Sample size,

N = Population size = 126,

$\mathscr{e}$ = Adjusted margin of error = (p e / t),

e = Margin of error = 0.03,

p = Number of standard deviations that would include all possible = 2,

t = t-value for the selected alpha level of confidence level (95% confidence level) = 1.96,

Then;

$n = 126 / (1 + 126 (2x0.03/1.96)^2)$

n = 112.2

The additional 10% of those eligible for recruitment were included to cover the non-responses.

n = 123

Ultimately, the study comprised 124 individuals who satisfied the research criteria.

2.4 Inclusion criteria AND Exclusion criteria

2.4.1 Inclusion criteria

The inclusion criteria encompassed patients diagnosed with intracranial neoplasms who were referred for brain MRI examinations from October 2023 to March 2024.

2.4.2 Exclusion criteria

All patients who did not provide consent and those having intracranial tumors without MRI were excluded from the study.

2.5 Variables

The study examined three major independent variables (patient characteristics, intracranial neoplasms, and primary extracranial malignancies), along with the independent variable being the MRI patterns of brain metastases. The characteristics examined included age, sex, alcohol consumption, and tobacco use. Intracranial neoplasms were classified into two categories: brain metastases and primary intracranial neoplasms. The MRI pattern analyses encompassed the following parameters: number of lesions, involvement of the tentorial compartment, grey-white matter junction, margins, shape, intra-axial location, extra-axial location, enhancement characteristics, types of enhancement, presence of central necrosis, midline shift exceeding 0.5 cm, tumoral hemorrhage, intrinsic hyperintensity on T1-weighted images, dura involvement, perilesional edema, and peri-lesion fluid restriction.

2.6 Data Collection Methods

Data from patients with intracranial neoplasms were collected using a structured data collection form. The information was retrieved daily from the registries and the Picture Archiving and Communication System (PACS) for all patients from October 2023 to April 2024. The brain MRI findings were evaluated and compared in line with the study's objectives. The principal investigator interpreted all images, the images were then reviewed by registered radiologists with a minimum of 2 years of experience in neuroradiology. Collected data were also entered into the SPSS software daily for cleaning and analysis.

2.7 Investigation Tools and Validity and Reliability Issues

2.7.1 Imaging platform

Brain MRI scans at MNH and MOI were performed utilizing either 1.5T or 3T MRI scanner models, which are outfitted with the Telecommunications Information Mapping (TIM) and

Digital Office Technology (DOT) system by Siemens, headquartered in Munich, Germany. Skilled radiographers were tasked with supervising the operation of the equipment.

The minimum standard protocol for evaluating brain metastases includes the following imaging sequences:

- Pre- and post-contrast inversion recovery T1-weighted gradient echo (IR-GRE) scans in axial, sagittal, and coronal planes.
- Axial, sagittal & coronal 2D T2-weighted turbo spin echo imaging.
- Axial 2D or 3D T2-weighted fluid-attenuated inversion recovery (FLAIR) imaging.
- Axial 2D diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) with three directional sequences.

2.7.2 Validity and reliability

In order to uphold the study's reliability, the data collection instruments underwent comprehensive pretesting and subsequent adjustments as needed, ensuring the implementation of stringent data collection methods. Only comprehensive medical records were included in this study to ensure consistency and reliability. The principal investigator evaluated all brain MRI images aligning with study objectives, consulting with an independent neuroradiologist when uncertainties arose, to ensure the recording of the most precise reports.

2.7.3 Pretesting and pilot data tools

The principal investigator conducted a one-month preliminary study at MNH and MOI to assess and refine the data collection instruments used in this research. The pilot study involved examining twelve patients, representing 10% of the required medical records. Following an evaluation of data integrity findings from the pilot study, the checklist underwent a thorough review and necessary modifications. Insights gleaned from the pilot study were integrated into the main study to enhance the effectiveness and precision of the data collection tools.

2.8 Data Analysis

The statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 27. Continuous data were summarized using measures of central tendency along with

their corresponding measures of dispersion. Categorical data were summarized using frequencies and percentages. Independent t-tests were utilized to compare the mean age of the patients with primary intracranial neoplasm vs brain metastases. Fisher's exact tests were employed to evaluate the level of association between intracranial neoplasm type (brain metastases vs primary) and the dependent categorical variable being the imaging patterns. Additionally, binary regression analysis was conducted to calculate both unadjusted and adjusted odds ratios fore-mentioned variables that showed association on Fisher's exact test. A significance level of less than 0.05 was considered statistically significant.

2.9 Ethical Issues

The research proposal underwent thorough scrutiny and received ethical approval from the MUHAS Institutional Review Board. Additionally, permission to collect data was granted by the Executive Directors of MNH and MOI. Informed consent was obtained from each study participant, while consent from next of kin was secured for minors and critically ill patients. Stringent measures were implemented to safeguard the confidentiality of all information and data throughout the study. No patient identities were collected or utilized, and no identifying information was included in the data analysis. Moreover, access to the data was limited solely to the investigators.

2.10 Dissemination Plan

The dissertation will be submitted to MUHAS as a requirement for a Master of Medicine in Radiology, serving as a foundational contribution to the medical field in medical imaging. Findings will be disseminated to key stakeholders in clinical practice, including MNH and MOI, fostering collaboration. Ownership of the research outcomes will be jointly held by the university and the principal investigator, ensuring accountability and promoting transparency. Moreover, significant discoveries will be disseminated through publication in reputable journals, facilitating widespread access and catalyzing scientific advancement in the field of radiology and neuro-oncology.

CHAPTER THREE

3.0 RESULTS

3.1 Proportion of brain metastases among other intracranial neoplasms and frequencies of primary extracranial metastasized malignancies among patients referred for brain MRI at MNH and MOI.

Brain metastases constituted 21.0% of all cases among patients diagnosed with intracranial neoplasms (Figure 1). Glioma accounted for the majority of neoplasms 25.0% closely followed by meningiomas 24.2% and pituitary macroadenoma 12.2%. Among the cases of brain metastases, the primary extracranial malignancies were predominantly breast carcinoma, accounting for 30.8%, followed by lung carcinoma at 26.9% (Figure 2).

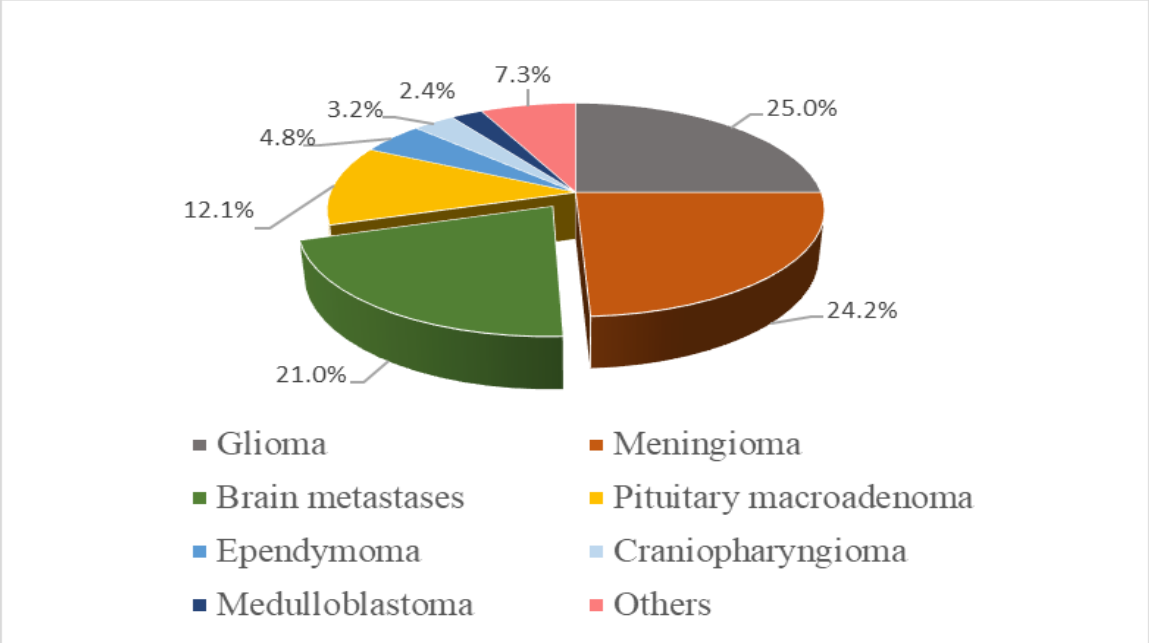


Figure 2: Proportion of BM among other intracranial neoplasms referred for brain MRI at MNH and MOI (n = 124).

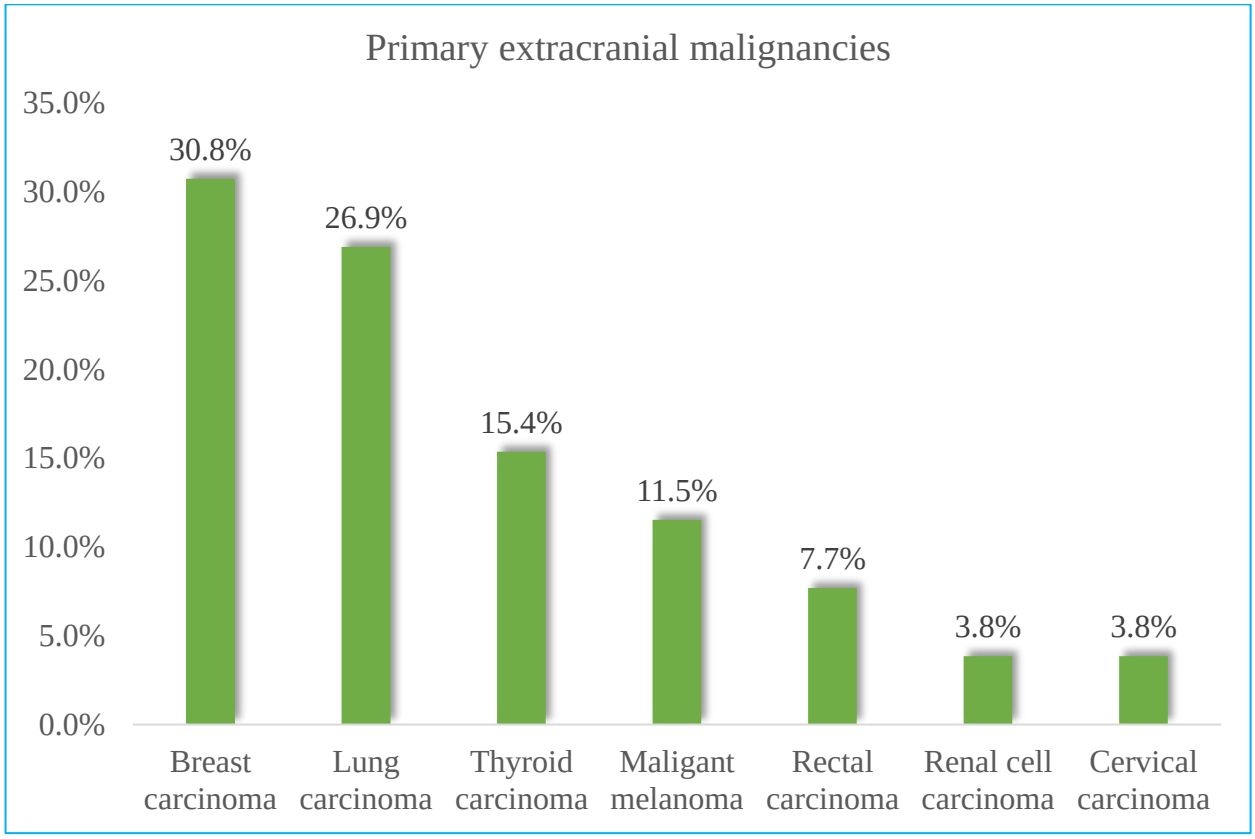


Figure 3: Frequencies of primary extracranial malignancies among patients with brain metastases referred for brain MRI at MNH and MOI (n = 26).

3.2 Factors associated with brain metastases in patients referred for brain MRI at MNH and MOI.

The study included 124 patients diagnosed with intracranial neoplasms, with a mean age of 45.1±19.4 years and an age range from 1 to 92 years. Among the participants, 56.5% were female, while males accounted for 43.5% of the cohort. The majority of patients, 58.1%, had no history of alcohol consumption, and 87.9%, reported no history of tobacco use. Patients with brain metastases exhibited a higher mean age compared to those with primary intracranial neoplasms (52.5 years vs. 43.2 years, p = 0.029). Brain metastases showed statistically insignificant higher frequency among females (24.3% vs. 16.7%, p = 0.301). Brain metastases was not found to be associated with alcohol consumption (23.1% vs. 19.4%, p = 0.624). Additionally, brain metastases appeared to be more common among individuals without a history of tobacco use (22.9% vs. 6.7%, p = 0.191). However, this association was also not statistically significant (Table 2).

Table 1: Factors associated with brain metastases in patients referred for brain MRI at MNH and MOI (n = 124).

		Intracranial neoplasms		
Variable		**Metastases (%)**	**Primary neoplasms (%)**	**P-value**
Age (years)	Mean	52.5	43.15	0.029*
Sex	Male	9 (16.7)	45 (83.3)	0.301
	Female	17 (24.3)	53 (75.7)	
Alcohol use	Yes	12 (23.1)	40 (76.9)	0.624
	No	14 (19.4)	58 (80.6)	
Tobacco Use	Yes	1 (6.7)	14 (93.3)	0.191
	No	25 (22.9)	84 (77.1)	

*Statistically significant

3.3 Association between MRI patterns and intracranial neoplasms (primary vs metastases) among patients attending MNH and MOI.

Brain metastases were more likely to present as multiple lesions compared to primary intracranial neoplasms (76.9% vs. 9.2%, $p < 0.001$), with 32.46 higher odds ($p < 0.001$). Additionally, brain metastatic lesions were 81.1 times ($p<0.001$) more likely to occupy the grey-white matter junction than the primary intracranial lesions (76.9% vs. 5.1%, $p < 0.001$). Moreover, brain metastatic lesions had 9.08 higher odds ($p<0.001$) to exhibit ring enhancements compared to primary intracranial neoplasms (53.8% vs. 11.2%, $p < 0.001$). Furthermore, brain metastases were more likely to have perilesional edema than the primary intracranial neoplasms (92.3% vs. 60.2%, $p = 0.002$), with 7.67 higher odds ($p = 0.009$). Brain metastases were also significantly associated with more than 0.5 cm shift of midline structures compared to primary intracranial neoplasms (57.7% vs. 17.3%, $p = 0.000$), with 9.56 higher odds ($p < 0.001$). Brain metastatic lesions also exhibited a significantly higher mean PED/GTD ratio compared to those with primary intracranial neoplasms (2.2914 vs. 1.5783, $p < 0.001$). (Table 4 and Table 5).

Brain metastases were significantly less likely to present with poorly defined margins compared to primary intracranial neoplasms (3.8% vs. 30.6%, $p < 0.001$), with 0.09 lower odds ($p < 0.019$). Additionally, brain metastatic lesions were less likely to present with irregular shapes than the primary intracranial lesions (3.8% vs. 56.1%, $p < 0.001$), with 0.03 lower odds ($p < 0.001$). Moreover, brain metastatic lesions were less likely to exhibit peri-enhancement fluid restrictions compared to primary intracranial neoplasms (7.7% vs. 31.6%, $p < 0.013$), with 0.19 lower odds ($p < 0.032$) (Table 4 and Table 5).

Table 2: Association between Intracranial neoplasms type and brain MRI patterns among patients referred for brain MRI at MNH and MOI (n = 124).

Variable		Intracranial neoplasms		P-value
		Metastases (%)	Primary neoplasms (%)	
Supratentorial	Yes	25 (96.2)	84 (85.7)	0.191
	No	1 (3.8)	14 (14.3)	
Number of lesions	Multiple	20 (76.9)	9(9.2)	<0.001*
	Solitary	6 (23.1)	89 (90.8)	
PED/GTD ratio	Mean	2.2914	1.5783	<0.001*
Infratentorial	Yes	12 (46.2)	16 (16.3)	0.001*
	No	14 (53.8)	82 (83.7)	
Both tentorial	Yes	11 (42.3)	2 (2.0)	< 0.001*
	No	15 (57.7)	96 (98.0)	
Grey/white matter junction	Yes	20 (76.9)	5 (5.1)	< 0.001*
	No	6 (23.1)	93 (94.9)	
Dura involvement	Yes	1 (3.8)	29 (29.6)	0.004*
	No	25 (96.2)	69 (70.4)	
Margin	Poorly-defined	1 (3.8)	30 (30.6)	0.004*
	Well-defined	25 (96.2)	68 (69.4)	
Shape	Regular	25 (96.2)	43 (43.9)	< 0.001*
	Irregular	1 (3.8)	55 (56.1)	
Intra-axial	Yes	21 (80.8)	42 (42.9)	< 0.001*
	No	5 (19.2)	56 (57.1)	
Extra-axial	Yes	3 (11.5)	56 (57.1)	<0.001*
	No	23 (88.5)	42 (42.9)	

Ring enhancement	Yes	14 (53.8)	11 (11.2)	< 0.001*
	No	12 (46.2)	87 (88.8)	
Uniform enhancement	Yes	1 (3.8)	43 (43.9)	< 0.001*
	No	25 (96.2)	55 (56.1)	
Heterogeneous enhancement	Yes	6 (23.1)	41 (41.0)	0.115
	No	20 (76.9)	59 (59.0)	
Nodular enhancement	Yes	5 (19.2)	3 (3.1)	0.010*
	No	21 (80.8)	95 (96.9)	
Central necrosis	Yes	13 (50.0)	29 (29.6)	0.051
	No	13 (50.0)	69 (70.4)	
Midline shift (>0.5 cm)	Yes	15 (57.7)	17 (17.3)	0.000*
	No	11 (42.3)	81 (82.7)	
Tumoral hemorrhage	Yes	13 (50.0)	26 (26.5)	0.022*
	No	13 (50.0)	72 (73.5)	
T1 Intrinsic Hyperintensity	Yes	7 (26.9)	1 (1.0)	0.000*
	No	19 (73.1)	97 (99.0)	
Perilesional edema	Yes	24 (92.3)	59 (60.2)	0.002*
	No	2 (7.7)	39 (39.8)	
Peri-enhancement fluid restriction	Yes	2 (7.7)	31 (31.6)	0.013*
	No	24 (92.3)	67 (68.4)	

*Statistically significant

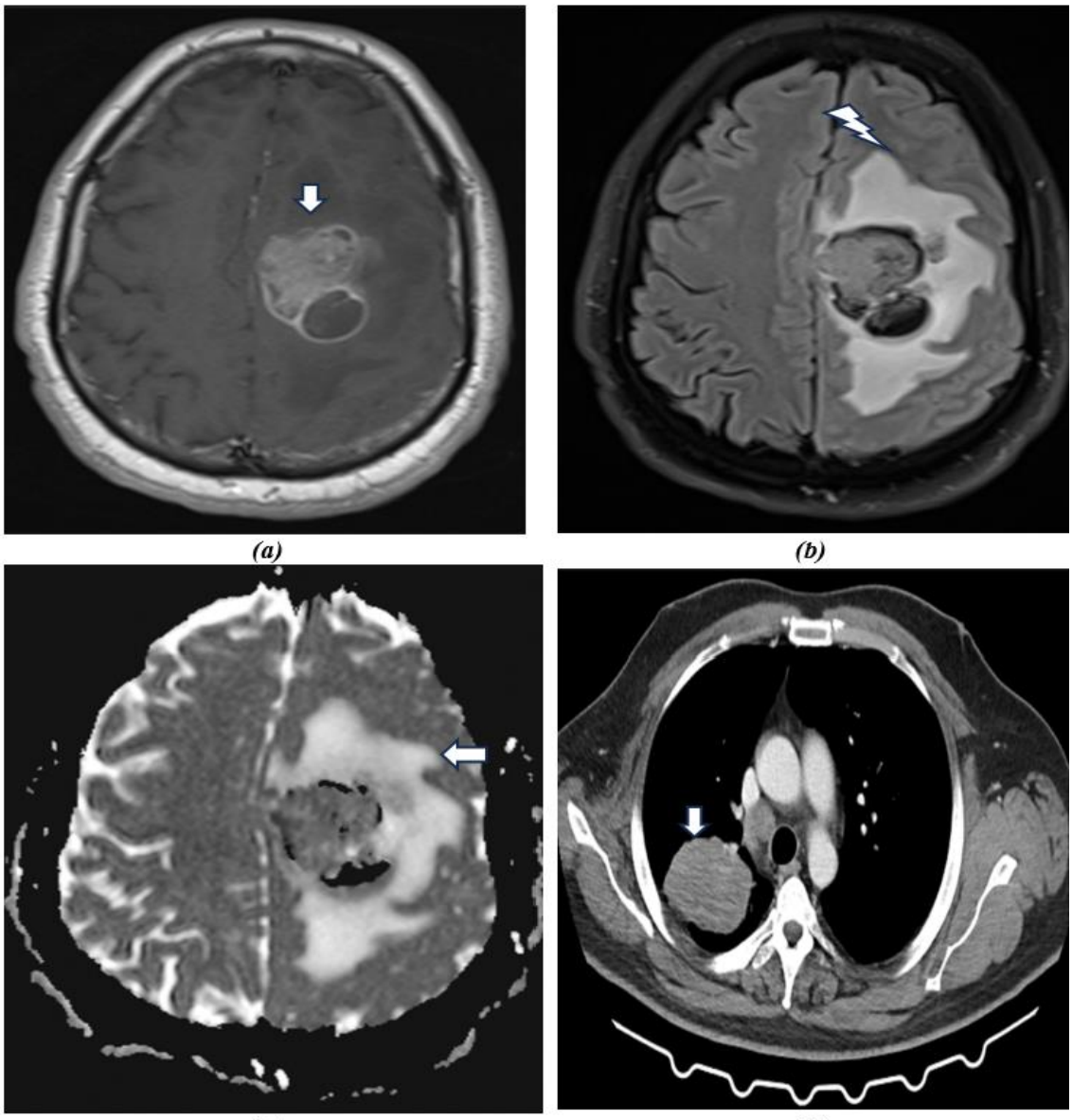
Table 3: Logistic regression analysis of Brain metastasis by brain MRI patterns among patients referred for brain MRI at MNH and MOI (n = 124).

	Crude					Adjusted				
	B	OR	95% CI		p-value	B	OR	95% CI		p-value
			LL	UL				LL	UL	
Primary neoplasms: Reference (All variables)										
Infratentorial compartment										
BM	1.48	4.39	1.718	11.233	0.002*	1.452	4.27	1.588	11.48	0.004*
Both tentorial compartments										
BM	3.561	35.2	7.093	174.68	<0.001*	3.325	27.8	5.45	141.8	<0.001*
Number of lesions (Multiple)										
BM	3.495	32.96	10.53	103.19	<0.001*	3.48	32.46	9.335	112.9	<0.001*
Grey/white matter junction										
BM	4.127	62.0	17.22	223.3	<0.001*	4.396	81.1	18.18	361.7	<0.001*
Dura involvement										
BM	2.352	0.1	0.012	0.736	0.024*	2.69	0.07	0.008	0.55	0.012*
Poorly-defined Margins										
BM	2.401	0.91	0.012	0.7	0.021*	2.466	0.09	0.011	0.672	0.019*
Irregular shape										
BM	3.465	0.03	0.004	0.24	<0.001*	3.541	0.03	0.004	0.228	<0.001*
Intra-axial										
BM	1.723	5.6	1.95	16.07	0.001*	1.856	6.4	2.147	19.07	<0.001*
Extra-axial										
BM	2.325	0.1	0.028	0.348	<0.001*	2.442	0.09	0.024	0.319	<0.001
Ring Enhancement										
BM	2.222	9.23	3.415	24.93	<0.001*	2.205	9.08	3.158	26.08	<0.001*
Uniform Enhancement										

BM	2.973	0.05	0.007	0.393	0.004*	3.51	0.03	0.004	0.246	0.001*
Nodular Enhancement										
BM	2.02	7.54	1.67	34.04	0.009*	2.065	7.89	1.541	40.37	0.013*
Central necrosis										
BM	0.867	2.38	0.984	5.752	0.054	0.963	2.62	1.034	6.633	0.042*
Midline Shift >0.5cm										
BM	1.871	6.5	2.545	16.59	<0.001*	2.257	9.56	3.32	27.51	<0.001*
Tumor Hemorrhage										
BM	1.019	2.77	1.137	6.743	0.025*	1.368	3.93	1.432	10.77	0.008*
T1 Intrinsic Hyperintensity										
BM	3.576	35.74	4.154	307.48	0.001*	3.447	31.42	3.463	285.1	0.002*
Perilesional edema										
BM	2.071	7.93	1.773	35.483	0.007*	2.037	7.67	1.661	35.38	0.009*
Peri-enhancement fluid restriction										
BM	1.714	0.18	0.04	0.81	0.025*	1.681	0.19	0.04	0.867	0.032*

BM: Brain Metastases, B = Coefficient, LL = Lower limit, UL = Upper limit, OR = Odd ratio.

*Statistically significant



(a) *(b)*

(c) *(d)*

(a) T1+C image demonstrating mixed heterogeneous and ring enhancement pattern (arrow: down).
(b) FLAIR image demonstrating a large vasogenic perilesional oedema (lightning bolt).
(c) ADC map demonstrating absent peri-enhancement fluid restriction (arrow: left).
(d) Contrasted Chest CT scan, axial view demonstrating enhancing lung tumour (adenocarcinoma).

Figure 4: Representative brain MRI and contrast-enhanced chest CT scan images obtained from a patient with solitary brain metastasis from lung adenocarcinoma.

CHAPTER FOUR

4.0 DISCUSSION

The present study observed a fifth of the patients with intracranial neoplasm had brain metastasis (21%). These findings are higher as compared to a study done in Cameroon (8%) but similar to that found in a study done in Brazil (21.9%). Among patients with brain metastases, the primary extracranial malignancies were predominantly breast carcinoma (30.8%), followed by lung carcinoma (26.9%). This was also similar to the single-centered study done in Brazil where breast cancer accounted for the primary malignancy in 33.3% of cases followed by lung cancer (23.8%)(17). These finding contrasts with studies conducted in India and Tunisia, where lung cancer was the leading primary extracranial malignancy, accounting for 45.0%, followed by breast cancer ranging between 25.0% to 36.0% (11,13). These findings emphasize on the importance of continuous surveillance to monitor changing epidemiological trends necessary for timely interventions in management of cancer.

The study population was predominantly female, comprising 56.5% of the total. The overall mean age was 45.1 ± 19.4 years. The mean age observed in this study exceeded that reported in a Nigeria based study, where the mean age at diagnosis of intracranial neoplasms was 35 ± 17.1 years. This disparity could be attributed to the larger sample size and extended study duration in the previous study (20). Patients with brain metastases demonstrated a significantly higher mean age (52.5) compared to those with primary intracranial neoplasms, in keeping with findings from a study conducted in South Africa and Tunisia where individuals with brain metastases were diagnosed at a mean age of 50.7 and 54 years respectively(28) (19). This consistent trend underscores the clinical relevance of age as a significant factor in the manifestation of brain metastases.

Brain metastases exhibited a higher frequency among females, although this difference did not reach statistical significance. This observation aligns with similar findings reported in studies conducted in India and France, where approximately 52.8% of brain metastases cases were also observed among females (18,22). While not statistically significant, this trend highlights the potential influence of gender on the development or detection of brain metastases.

Understanding such patterns is crucial for tailoring screening and diagnostic strategies, as well as optimizing treatment approaches, to address the specific needs of both male and female patients with brain metastases. In our study, brain metastases were observed more frequently among individuals with a history of alcohol consumption, although this association did not reach statistical significance. Similar findings were reported in a study from China (29).

Brain metastases exhibited various brain MRI patterns, with significantly elevated odds of displaying multiple lesions, involvement of both tentorial compartments, grey-white matter junction involvement, intra-axial location, ring enhancement, nodular enhancement, midline shift exceeding 0.5 cm, and perilesional edema with higher PED/GTD ratio. Conversely, brain metastases showed significantly lower odds of dura involvement, poorly defined margins, irregular shape, extra-axial location, uniform enhancement, and peri-enhancement fluid restrictions. Similar brain MRI patterns were demonstrated in a Korea based study by Jung M et al in 2021(3). These findings demonstrate diverse imaging characteristics of brain metastases, providing valuable insights for an objective approach for interpreting images enhancing accuracy in diagnosis.

4.1 Study Limitation(S)

This cross-sectional study provides a snapshot of data at a single time point. This limits the ability to monitor changes and outcomes over time. This constraint is crucial to acknowledge, increasing the need for longitudinal studies such as cohort study to observe variables over longer periods of time to capture disease progression, treatment response, and patient outcomes.

The inability to perform craniotomy on the majority of patients with brain metastatic lesions on MR imaging, limits the possibilities of obtaining tissue for histopathological correlation.

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

The study investigated brain MRI images of 124 consecutive patients with intracranial neoplasm at MOI and MNH. The likelihood of cerebral lesions as seen on MRI being due to metastasis rather than a primary neoplasm is high if the lesions are multiple, round, ring-enhancing with clearly defined margins at the grey-white matter junction. The likelihood is further enhanced by perilesional edema that spares the cortex, as well as having a maximum diameter greater than twice that of the enhancing tumor component, exerting mid-line shift and being without diffusion restriction within the perilesional edema in a patient older than 50 years. These MRI patterns were also observed in the occasional patients with solitary intracranial lesion that revealed histology results for metastases even without a known extracranial primary initially making the differential diagnosis of primary glial tumor viable.

5.2. Recommendations

Patients over 50 years with the imaging patterns demonstrating high likelihood for metastases and a known systemic malignancy may proceed with treatment options without undergoing cranial surgery to obtain biopsy for histopathology. When similar MRI characteristics are noted in an older patient with a solitary intracranial lesion, even without a known systemic malignancy, a primary malignancy workout prior to surgical consideration may benefit the patient by minimizing chances of unnecessary cranial surgical procedures and possible related complications.

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APPENDICES

Appendix 1: Investigation Tools

1. Patient particulars:

   Identification number

   Age:

   Gender:

   Contact Information (Optional):

2. MRI Scan Details:

   Date of MRI Scan:

   MRI Scan Reports Available: Yes / No

   Number of MRI Scans Conducted:

3. Imaging findings:

   Number of lesion(s); i) Solitary ii) Multiple iii) Innumerable

   If Multiple/ innumerable; Is there a site of predilection? Yes/ No

   If yes, Mention: ……..

   Neoplasm: Intraxial: Yes/No

   Extraxial: Yes/No

   Intracranial Neoplasm: Primary: Yes / No ; Metastasis: Yes / No

   If intracranial primary; Mention the tumor …….

   If intracranial metastasis: Mention primary tumor: …….

   Intracranial compartment with neoplasm: Supratentorial Yes/ No; Infratentorail Yes/ No

   Intracranial tissue the tumor arises from

   - i) Brain Parenchyma Yes/ No ii) Dura Yes/ No, iii) Skull Yes/ No

   The size of the neoplasm mass (If multiple/innumerable measure the largest)……

   Location of the lesion(s) i) Grey/White matter junction: Yes/ No

   Morphology of metastatic lesion(s) i) Mass forming ii) Cystic iii) Mixed

   Enhancement pattern

- i) Ring Yes/ No ii) Homogenous Yes/ No iii) Heterogenous Yes/No iv) Nodular Yes/ No

Perilesional edema Yes/No

PED/GTD ratio: …….

Does the perilesional edema spare grey matter? Yes/ No

Does the lesion (s) restrict diffusion? Yes/No

Is there restriction in diffusion in the regions surrounding the enhancing tumor? Yes/ No

Does the lesion demonstrate hemorrhage on SWI? Yes/ No

Is there T1 inherent high signal within the lesion prior to contrast? Yes/ No

Appendix 2: Consent Forms

INFORMED CONSENT FORM

(English version)

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES (MUHAS)

DIRECTORATE OF RESEARCH AND PUBLICATION

IDENTITY NUMBER: _____

Introduction

Salutations!

My name is Dennis Charles Mkony, Muhimbili University of Health and Allied Sciences (MUHAS) student with registration number HD/MUH/T.240/2021 doing a Master of Medicine in Radiology and Imaging. I am conducting research titled; **MAGNETIC RESONANCE IMAGING PATTERNS OF BRAIN METASTASES AMONG PATIENTS WITH INTRACRANIAL NEOPLASM AT MUHIMBILI NATIONAL HOSPITAL AND MUHIMBILI ORTHOPEDIC INSTITUTE**. You are kindly invited to take part in this research. I ask that you to read and understand well the information below before you accept or refuse to participate in this study.

PURPOSE OF THE STUDY:

The purpose of this study is to study the MRI patterns of metastatic brain lesions in patients at MNH and MOI with primary tumors elsewhere in the body. In addition to studying the imaging pattern, this study aims also to establish any associations of the imaging pattern with demographics and immune status related to HIV infection.

The result of this study will increase awareness and will help to maximize the diagnosis and treatment of metastatic brain disease.

This is also a requirement for the fulfilment of my Master of Medicine program.

STUDY PROCEDURE.

Only some information will be taken from you including your social demographic data and brief information about your primary malignancy, some information will be taken from your hospital

records including your MRI images from the picture and archive communication system (PACS) at MOI and MNH. There are no monetary charges for participating in this study.

RISKS AND BENEFITS TO THE PARTICIPANTS.

No, direct risk or harm is expected to the participant. By participating to this study will help future generations for better diagnosis and management for patients battling cancer who have developed brain metastasis. Be informed that your refusal to participate in this study will not affect your treatment plan.

CONFIDENTIALITY.

Information obtained from you will be strictly confidential and even your name will not appear on the questionnaire form.

PARTICIPATION WORD.

To participate in this study is completely voluntary and refusal will not affect your treatment by any means. You will be allowed to withdraw from the study as you wish.

CONTACTS AND QUESTIONS.

In case you have any question or doubt, please contact me through;

Dr. Dennis C. Mkony

Mobile: 0768 041934

Email: mkony361@gmail.com

For further questions concerning your rights as a participant, you may contact Dr. Nahya Salim, chairperson of the Research and Publication Committee, MUHAS. P.O Box 65001, Dar es Salaam-Tanzania. Tel +2552150302-6

PART B:

PARTICIPANT CONSENT FORM.

I have understood well what has been said to me by the investigator about the research plan and I have accepted to participate in this study. I VOLUNTARILY CONSENT TO PARTICIPATE.

Signature……

Mobile……. Date: ……

Appendix 3: Fomu Ya Idhini

(Toleo la Kiswahili)

CHUO KIKUU CHA TIBA NA SAYANSI SHIRIKISHI MUHIMBILI (MUHAS)

KURUGENZI YA UTAFITI NA UCHAPISHAJI

NAMBA YA UTAMBUZI: _____

Utangulizi

Heshima yako!

Jina langu ni Dennis C. Mkony, mwanafunzi wa udaktari kitengo cha Radiologia na mionzi chuo kikuu cha afya na sayansi shirikishi Muhimbili. Namba yangu ya usajili ni HD/MUH/T.240/2021. Ninafanya tafiti yenye kichwa; **MUONEKANO WA SARATANI ILIOSAMBAA KWENDA KWENYE UBONGO MIONGONI MWA MAGONJWA YOTE YA UVIMBE WA UBONGO KATIKA WAGONJWA WANAOHUDHURIA MNH NA MOI**. Ninaomba ushiriki wako katika utafiti huu. Aidha, kabla ya kukubali kushiriki au kukataa kushiriki naomba usome kwanza kwa umakini maelezo yanayofuata hapo chini.

LENGO LA UTAFITI HUU.

Lengo langu ni kutaka kujua namna mbalimbali ambazo uvimbe katika ubongo unaotokana na kusambaa kwa saratani kutoka sehemu nyingine ya mwili huonekana katika kipimo cha MRI. Sambamba na hili ninalenga kuangalia sababu za kibaiolojia zinazoweza kuhusishwa na kusambaa kwa saratani kwenda kwenye ubongo. Matokeo ya utafiti huu yatatumika kuongeza ujuzi zaidi kwa madaktari juu ya ugonjwa kusambaa kwa saratani kwenda kwenye ubongo. Pia tafiti hii ni hitaji la kitaaluma ili kuweza kuhitimu mafunzo yangu ya udaktari bingwa.

MCHAKATO / TARATIBU ZA UTAFITI.

Utafiti huu utahusisha maswali ambayo utaulizwa na mtafiti kuhusu taarifa zako binafsi na maelezo juu ya saratani iliyopelekea kusambaa kwenda kwenye ubongo endapo inajulikana, na taarifa juu ya kinga ya mwili hususani hali ya maambukizi ya VVU. Pia kuna baadhi ya taarifa zitachukuliwa kutoka kwenye mifumo ya kuhifadhi taarifa ikiwepo picha yako ya MRI ya ubongo. Hakuna gharama ama tozo yoyote utakayodaiwa kwa kushiriki utafiti huu.

FAIDA NA HASARA KWA MSHIRIKI.

Kwa kukubali kushiriki kwenye tafiti hii utasaidia ujuzi kuongezeka kwenye eneo hili la matibabu na hili litasaidia watu wengine siku za mbele. Hakuna hasara yoyote utakayopata kwa kukubali kushiriki. Vilevile kama hutakubali kushiriki haitaleta madhara yoyote kwako wala haitaathiri matibabu yako hospitalini hapa.

USIRI.

Taarifa zako binafsi katika tafiti hii ni siri na hata jina lako halitaonekana kwenye matokeo ya tafiti hii hivyo usiwe na shaka.

MAELEZO KWA MSHIRIKI.

Kushiriki katika utafiti huu ni jambo la hiari. Matibabu yako hayataathiriwa na kukubali ama kukataa kushiriki tafiti hii.

MAWASILIANO.

Kama utakuwa na swali lolote au shaka juu ya utafiti huu tafadhali wasiliana name kwa mawasiliano haya,

Dkt. Dennis C. Mkony

Simu: 0768041934

Baruapepe: mkony361@gmail.com.

Kama unayo maswali yoyote kuhusu haki zako kama mshiriki wa tafiti hii, unaweza kuwasiliana na Dkt. Nahya Salim, mwenyekiti wa kamati Utafiti na Machapisho, MUHAS. S.L.P 65001, Dar es Salaam-Tanzania. Simu +2552150302-6

SEHEMU B: FOMU YA KUKUBALI KUSHIRIKI.

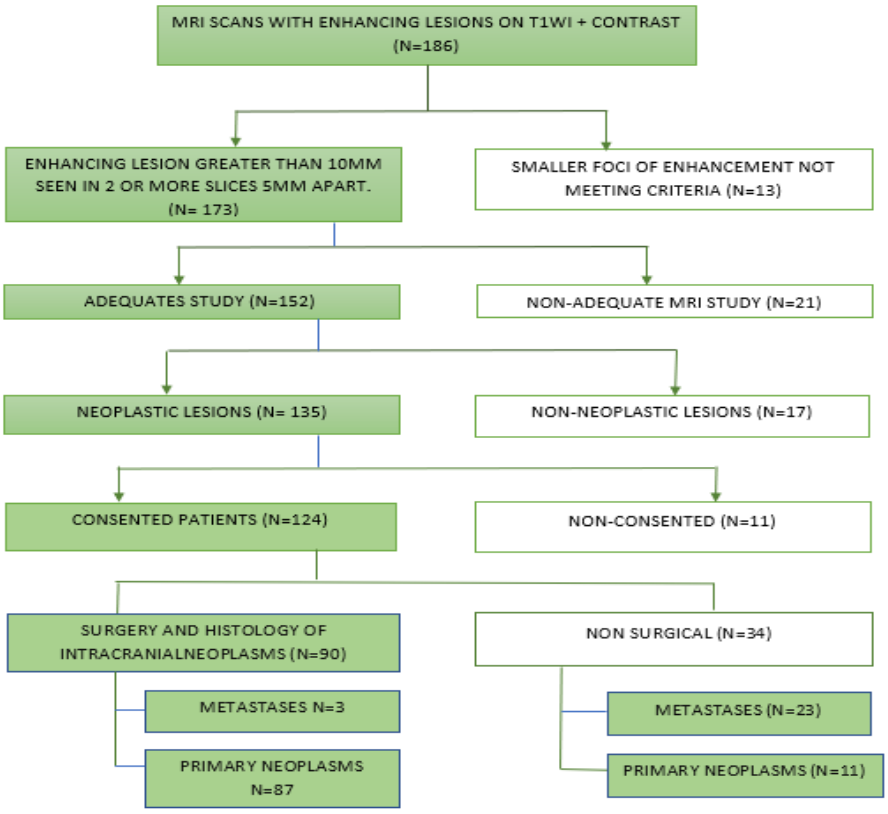
Nimesoma na kuelewa na nimesikiliza nakuelewa nilichoambiwa na mtafiti na nimekubali kushiriki utafiti huu bila kulazimishwa.

SAHIHI:

NAMBA YA SIMU:

TAREHE:

PATIENT FLOW CHART :



PATIENT FLOW CHART CLARRIFICATIONS :

A total of 186 contrasted brain MRIs of patients with intracranial enhancing lesions on T1WI were assessed. Of the 186 MRI scans, 173 had sizeable enhancing lesions greater than 10mm seen in atleast 2 slices that were 5mm apart. A total of 152 out of 173 patients had adequate study for image analysis with 135 being neoplastic lesions and 17 comprising of other non-neoplastic lesions. Of the patients with enhancing neoplastic intracranial lesions greater than 10mm, seen in atleast 2 slices spaced 5mm apart, 124 consented to be enrolled in the study. 90 participants out of 124 ultimately underwent surgery and had histology whereby 3 were diagnosed with metastases and 87 had other primary intracranial neoplasms. Of the 34 patients who were not operated, 23 were identified as patients with brain metastases based on imaging features, in conjunction with at least one other site of metastasis and a histologically proven primary cancer. Of the remaining 11 patients without current histology, 3 were identified with recurrent glioma based on radiological and clinical findings, previously underwent surgery for

tumor excision and biopsy. One with diffuse brainstem glioma by two neuroradiologists. One patient also had a non-accessible clival tumor, which was consensus-diagnosed as a clival chordoma by 2 radiologists. The remaining 6 patients had extra-axial tumors with pathognomonic features of meningiomas.

Appendix 3 : Ethical Clearances

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – RESEARCH, PUBLICATIONS

AND INNOVATION

Ref. No.DA.282/298/01.C/1924 Date: 03/10/2023

MUHAS-REC-10-2023-1924
DENNIS CHARLES MKONY
SCHOOL OF MEDICINE
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: MRI PATTERN OF METASTATIC BRAIN LESIONS AMONG PATIENTS WITH BRAIN TUMORS AT MUHIMBILI NATIONAL HOSPITAL AND MUHIMBILI ORTHOPEDIC INSTITUTE.

Reference is made to the above heading.

I am pleased to inform you that the Chairperson has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 03/10/2023
EXPIRATION DATE OF APPROVAL. 03/10/2024

STUDY DESCRIPTION:
Purpose:
The purpose of this cross-sectional prospective study is to observe the patterns of metastatic brain lesions and establish if any relation of the pattern to the primary tumors, demographics and HIV infection status

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2014801.pdf and in the MUHAS archives

The PI is required to:

1. *Submit bi-annual progress* reports and final report upon completion of the study.
2. *Report to the IRB any unanticipated* problem involving risks to subjects or *others including* adverse events where applicable.
3. *Apply for renewal* of approval of ethical clearance one (1) month prior its *expiration* if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain data transfer agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain material transfer agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country.
8. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
9. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
10. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/

Dr. Nahya Salim Masoud,
Chairman, MUHAS Research and Ethics Committee

Muhimbili University of Health and Allied Sciences
DIRECTOR
Research & Publications
Box 65001

Appendix 4 : Introduction Letter

UNITED REPUBLIC OF TANZANIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR – POSTGRADUATE STUDIES

In reply quote;
Ref. No. HD/MUH/T.240/2021 10th October, 2023

The Executive Director,
Muhimbili Orthopaedics Institute,
P.O. Box 65474,
DAR ES SALAAM

Re: INTRODUCTION LETTER

We would like to inform you that the bearer of this letter is Dennis Charles Mkony with Reg. No. HD/MUH/T.240/2021 is a student at Muhimbili University of Health and Allied Sciences (MUHAS) "pursuing MMed. Radiology.

As part of his studies, he will be doing an elective research titled: "**MRI Pattern of Metastatic Brain Lesions Among Patients with Brain Tumors at Muhimbili National Hospital and Muhimbili Orthopaedic Institute.**" he is being supervised by Dr. Merchis Mango from MOI and Dr. Christina Malichewa from MUHAS.

The research has been approved by the Chairman of University Senate.

Kindly provide him the necessary assistance to facilitate the conduct of his research.

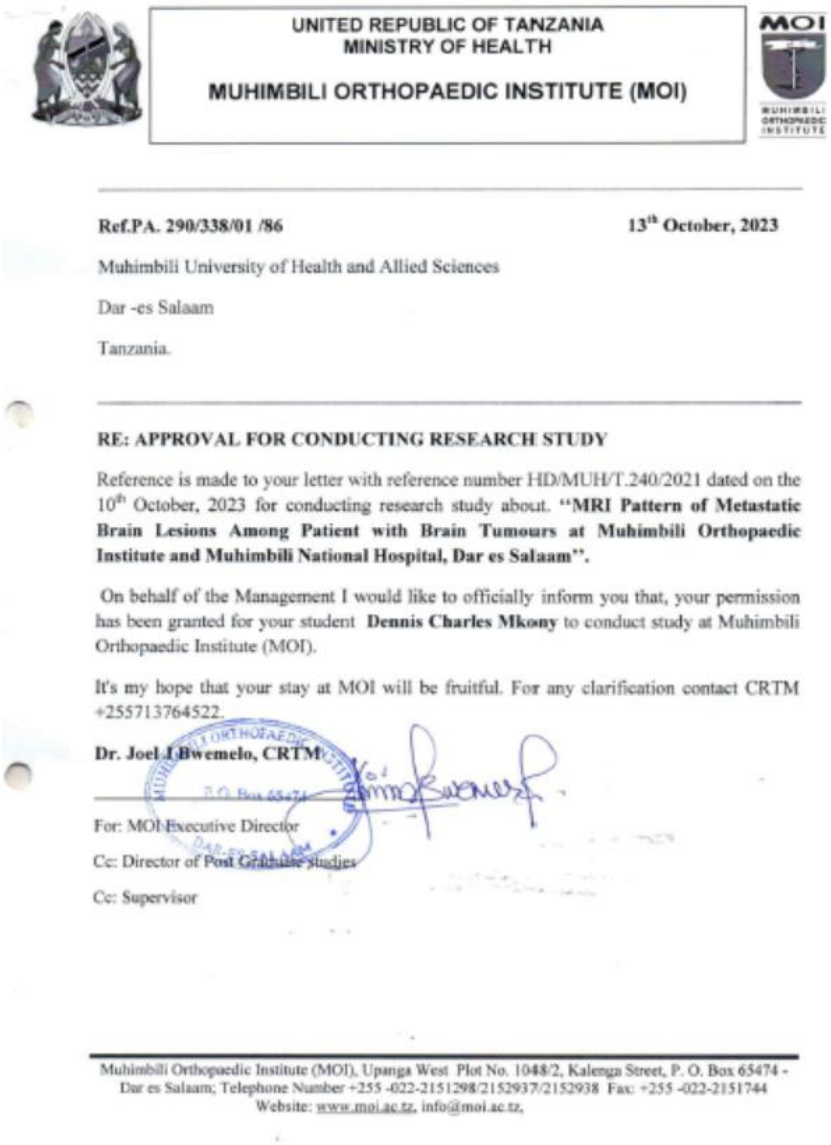
We thank you for your cooperation.

Victoria Mwaniwa
FOR: DIRECTOR, POSTGRADUATE STUDIES

c.c Dennis Charles Mkony

9 United Nations Road; Upanga West; P.O. Box 65001, Dar Es Salaam: Tel. G/Line +255-22-2150302/6; Ext. 1015; Direct Line:+255-22-2151378;Telefax:+255-22-2150465;E-mail:dpgs@muhas.ac.tz,Web https://www.muhas.ac.tz

Appendix 4 : Permission Letter



UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

MUHIMBILI ORTHOPAEDIC INSTITUTE (MOI)

Ref.PA. 290/338/01 /86 **13th October, 2023**

Muhimbili University of Health and Allied Sciences

Dar -es Salaam

Tanzania.

RE: APPROVAL FOR CONDUCTING RESEARCH STUDY

Reference is made to your letter with reference number HD/MUH/T.240/2021 dated on the 10th October, 2023 for conducting research study about. **"MRI Pattern of Metastatic Brain Lesions Among Patient with Brain Tumours at Muhimbili Orthopaedic Institute and Muhimbili National Hospital, Dar es Salaam".**

On behalf of the Management I would like to officially inform you that, your permission has been granted for your student **Dennis Charles Mkony** to conduct study at Muhimbili Orthopaedic Institute (MOI).

It's my hope that your stay at MOI will be fruitful. For any clarification contact CRTM +255713764522.

Dr. Joel J Bwemelo, CRTM

For: MOI Executive Director

Cc: Director of Post Graduate Studies

Cc: Supervisor

Muhimbili Orthopaedic Institute (MOI), Upanga West Plot No. 1048/2, Kalenga Street, P. O. Box 65474 - Dar es Salaam; Telephone Number +255 -022-2151298/2152937/2152938 Fax: +255 -022-2151744
Website: www.moi.ac.tz, info@moi.ac.tz,

THE UNITED REPUBLIC OF TANZANI

MINISTRY OF HEALTH

MUHIMBILI NATIONAL HOSPITAL

In reply please quote;

Ref. No.: MNH/CRTCU/Perm/2023/565 Date: 29th November, 2023

Head of Department
- Radiology
- Outpatient

Muhimbili National Hospital

RE: PERMISSION TO COLLECT DATA AT MNH

Name of Student	**Dennis C. Mkony**
Title	**- MRI pattern of Metastatic Brain Lesions among Patient with Brain Tumours at Muhimbili National Hospital and Muhimbili Orthopaedic Institute**
Institution	Muhimbili University of Health and Allied Sciences
Supervisor	Dr. Christina malichewa (MUHAS)
Co-supervisor	Dr. Sylvia Nsato (MNH)
Period	29th November, 2023 to 01st August, 2024

Approval has been granted to the above principal investigators to collect data at MNH. Dissemination of study findings at MNH shall be overseen by **Dr. Sylvia Nsato (MNH)** supervisor.

Kindly ensure the named principal investigator abide to the ethical principles and other conditions of the research approval.

Upanga West, Kalenga Street, Plot No. 10480/3, P.O. BOX 65000, Dar es Salaam, Tanzania.
Telephone: +255-22-2151367-9, Telephone: +255-22-2151351-2
Email: info@mnh.or.tz, Website: www.mnh.or.tz