THE DIAGNOSTIC VALUE OF CONTRAST ADMINISTRATION FOLLOWING NORMAL NON-CONTRAST BRAIN COMPUTED TOMOGRAPHY IN MANKWENG HOSPITAL

by

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[redacted]

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DEDICATION

To God be the glory. This study is dedicated to the following people:

In memory of my beloved parents, Mr. Famanda Peter Sibiya and Mrs. Kwatisa Sibiya, on whose shoulders I stood, I cannot thank you enough for the lifelong lessons and unconditional love you provided. While you rest in eternal peace, one of my biggest dreams was achieved. I am comforted by the knowledge that you contributed immensely to my growth. I know you would have been so proud of me.

To my cherished children, Refilwe, Tiko, Nyiko, and Xihlovo, you are the wind that propels me forward. Thank you for your understanding, for enduring the challenges, and for trusting the process. This journey is meant to inspire you.

To my siblings, Mrs. Rose Hlungwani, Mrs. Johannah Mthombeni, and Mr. Royal Sibiya, thank you for your unwavering support and protection. Your midnight prayers bear fruit in the light of day. My niece, Miss Patience Hlungwani, I will always remember your love and support throughout my studies. I love you dearly.

This special dedication goes to my dear friend, Dr. Nkhensani Charmaine Mashaba. In you, I have found a selfless sister and an incredible human being. I am in awe of your wisdom and faith—prayer item 21 is now off the list.

To Miss Pinkie Bembe and Miss Tlangelani Maluleke, this is for you! I am truly grateful for the lessons and inspiration you've provided. I have witnessed you move mountains for me. May the heavens bless and keep you, my friends.

Lastly, to Mrs. Tsakani Mamafa, thank you for being an amazing mother to my children. Your heart is golden, and I will forever cherish our friendship.

DECLARATION

I, Rivalani Queen Sibiya declare that "**THE DIAGNOSTIC VALUE OF CONTRAST ADMINISTRATION FOLLOWING NORMAL NON-CONTRAST BRAIN COMPUTED TOMOGRAPHY IN MANKWENG HOSPITAL",** (mini-dissertation) hereby submitted to the University of Limpopo, for the degree of Master of Medicine in Diagnostic Radiology, has not previously been submitted by me or anyone I know for a degree at this or any other university, that it is my work in design and execution, and that all material contained herein has been acknowledged.

Sibiya R.Q. (Dr)

Surname, Initials (title)

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DEFINITION OF KEY CONCEPTS

Computed tomography (CT): is a non-invasive imaging technique that utilizes a rotating x-ray tube and multiple detectors. In this process, a beam of X-rays is directed at a patient lying on a scan table, and the detectors capture the X-rays as they exit the body (Ginat & Gupta, 2014). For the purposes of this study, computed tomography will be defined in this manner.

Contrast Medium: A dye designed for intravascular, intrathecal, and intraluminal administration, aimed at achieving a localized increase in X-ray attenuation by altering the tissue's response to applied X-ray energy (Reiser, Hricak & Knauth, 2014; Dispenza & Ditto, 2018). In this study, the term "contrast" refers specifically to contrast medium administered intravenously.

Contrast-Enhanced Computed Tomography: A computed tomography (CT) scan conducted after the intravenous administration of contrast. In this study, the same meaning applies.

Diagnostic Value: The effectiveness of a test in improving clinical outcomes (Mallett, Halligan, Thompson, Collins & Altman, 2012). In this study, diagnostic value pertains to the usefulness of contrast administration in confirming or revising a diagnosis made using non-contrast-enhanced computed tomography of the brain.

Ionizing Radiation: Particles with energy sufficient to penetrate and move through biological material, breaking atomic bonds, releasing ions and free radicals, which may lead to chemical changes (Borek, 1993). In this context, ionizing radiation refers specifically to X-rays used in diagnostic imaging.

Meningitis: Inflammation of the meninges, which include the dura mater, arachnoid mater, and pia mater. These membranes surround the brain and spinal cord, and inflammation can result from either infectious or non-infectious processes (Taxirovich, 2023).

Neurocysticercosis: A helminthic infection of the brain caused by the ingestion of undercooked or raw pork that contains viable larvae (cysticerci). The infection can lead to various neurological symptoms, most commonly seizures (Carabin., Ndimubanzi., Budke., Nguyen., Qian., Cowan., Stoner., Rainwater & Dickey, 2011).

Radiodensity: The degree to which tissues absorb or attenuate radiation, such as X-rays, with water serving as the reference point (0 units). Radiodensity ranges from approximately -1000 units (air) to over +1000 units (cortical bone) and is measured in Hounsfield units (Bushberg & Seibert, 2020).

ABSTRACT

BACKGROUND: The use of intravenous contrast during computed tomography (CT) scans enhances the detection and characterization of pathologies. However, its high cost, along with the potential adverse effects of the contrast agents and radiation, presents significant challenges for the resource-limited public health sector in South Africa. It is the responsibility of radiologists to justify the use of intravenous contrast and the exposure of patients to ionizing radiation.

AIM: This study aims to determine whether the administration of contrast significantly alters the diagnosis of normal non-contrast CT brain scans.

METHODS: A descriptive retrospective cross-sectional study was conducted at Mankweng Hospital, analysing 181 brain CT images acquired between January 1, 2021, and January 31, 2022. All patients underwent consecutive non-contrast CT (NCCT) and contrast-enhanced CT (CECT) scans, with CECT performed immediately following NCCT. A simple random sampling approach was employed. Senior registrars reported the scans, a consultant radiologist verified the reports, followed by a discussion of a subset of equivocal scans in a consensus meeting. Results were recorded and statistically analysed using SPSS. The kappa coefficient was utilized to measure the agreement between the NCCT and CECT scans, with all statistical analyses conducted at a 5% level of significance.

RESULTS: Among the 181 sampled scans, 88 (48.6%) were initially reported as normal on NCCT. Of these, 84 (95.5%) remained normal after contrast administration, while 4 (4.5%) exhibited significant diagnostic changes after receiving the contrast. The kappa coefficient of 0.945 indicated almost perfect agreement between the NCCT and CECT scans ($p < 0.005$). The administration of contrast provided additional diagnostic value primarily in immunocompromised patients or those with fever, seizures, or decreased levels of consciousness.

CONCLUSION: This study demonstrates that administering contrast following a normal NCCT brain scan may not be necessary. Omitting this step could reduce healthcare costs, scan time, and radiation exposure. Radiologists should justify the use of contrast and repeat scans based on clinical information. We recommend adopting a “scan, review, and justify” approach to optimize resource utilization and

minimize harm. Future studies should investigate the cost-effectiveness of this approach.

Keywords: Appropriateness, Brain computed tomography, non-contrast brain CT, contrast–enhanced brain CT, brain neuroimaging and contrast.

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LIST OF ABBREVIATIONS

ACR	**:**	American college of radiation
ALARA	**:**	As low a s reasonably achieved
BBB	**:**	Blood-brain barrier
CECT	**:**	Contrast-enhanced computed tomography
CT	**:**	Computed tomography
LP	**:**	Lumbar puncture
PACS	**:**	Picture archiving and communication system
NCCT	**:**	Non-contrast computed tomography
MRI	**:**	Magnetic resonance imaging.
RVD	**:**	Retroviral disease

CHAPTER ONE: INTRODUCTION AND BACKGROUND TO THE STUDY

1.1 Introduction

Computer tomography (CT) of the brain is a fundamental neuro-imaging modality in assessing intracranial pathology, assisting clinicians in diagnosing and rapidly managing patients (Broder, 2011). According to Nishtar, Ahmad, Noor & Muhammad (2019), brain CT makes up a significant proportion of all ordered CT scans. This is consistent with findings from an Australian study (Maxwell., Ha., Bulsara., Doust., Mcrobbie., O'Leary., Slavotinek & Moorin, 2021) which showed that non-contrast computed tomography (NCCT) brain scans were the most commonly requested type of CT scan in the emergency department between 2003 and 2015, accounting for 68% of all scans. Furthermore, the study demonstrated a marked increase in brain CT utilisation with a doubling of scans per 1000 visits from 40 in 2011, to nearly 80 in 2015 indicating a significant upward trend in usage over time.

Factors such as increasing availability and improved technological advancement of CT scanners have been mentioned as the cause of the increasing number of scans performed. Medico-legal pressures and discrepancy in level of clinician experience are also contributing factors towards the high number of performed imaging. The increasing demand for imaging examinations has unintended consequences that outweigh the potential benefits. The surge in imaging volumes contribute to radiologist's workload, fatigue, and burnout, potentially compromising accurate image interpretation. Increased diagnostic time and costs impact healthcare resources and patient care (Rosol, Ciesielka, Matlakiewicz, Grześków, Cebula, Gruszczyńska & Winder, 2022; Fouche, Jekins & Vermeulen 2021; Nishtar, Ahmad, Noor & Muhammad, 2019; Kanzaria, Hoffman, Probst, Caloyeras, Berry & Brook, 2015). It is crucial to implement responsible scanning practices, optimize protocols, and ensure careful patient selection to maximize the benefits of brain scanning while minimizing risks.

Indications for brain CT scan include seizures, psychosis, headache, decreased level of consciousness, focal neurological deficit, movement disorders, and follow-up of known intracranial pathology (Bent - Lee, Shen, Bang & Bobinski, 2015; Berkowitz,

2017; Fouche *et al*., 2021; Taesdale & Aitken, 2009). A Brain CT scan has been shown to be effective in detecting calcified lesions, such as those found in tumours like oligodendroglioma and neurocuteneous disorders such as tuberous sclerosis. However, it is less sensitive when it comes to detecting small cortical lesions and low-grade tumours (Cendes, Theodore, Brinkmann, Sulc & Cascino, 2016). At Mankweng Hospital, Brain CT scans can be performed in one of two ways: as a single-step process, which involves either a non-contrast computed tomography (NCCT) scan or a contrast-enhanced scan, or as a two-step process, where an initial NCCT scan is followed by a contrast-enhanced CT (CECT) scan.

The pathology being investigated can often be visualized or suspected through a non-contrast-enhanced scan (Tamangani, 2016). A non-contrast brain CT scan provides satisfactory results as a primary method for detecting ischaemic infarcts, intracranial hemorrhage, congenital malformations, hydrocephalus, and tumours (Likeman, 2013). In contrast, contrast-enhanced CT scans are recommended when brain tumours or infections are suspected (Tamangani, 2016; Cendes *et al*., 2016).

Contrast agents increase x-ray attenuation within organ tissues, resulting in greater density differences among body tissues (Bae, 2010). The quality of tissue enhancement is directly proportional to iodine concentration, which ranges from 25 to 30 Hounsfield units per milligram of iodine per millilitre at tube voltages between 100 and 120 kVp (Bae, 2010). The Hounsfield unit, originally known as the CT number, measures tissue attenuation in CT scans, quantifying tissue radiodensity relative to water, which has a Hounsfield unit of zero (Hounsfield, 1973).

Unlike other body tissues, neural tissues (such as the brain, spinal cord, and nerves) have a selectively permeable membrane known as the blood-brain barrier. This barrier protects against contrast agents, plasma proteins, and inflammatory cells (Smirniotopoulos *et al.,* 2007). An intact blood-brain barrier can prevent contrast from reaching neuronal tissues. However, conditions such as tumours, infections, and inflammatory processes can compromise the blood-brain barrier, leading to contrast leakage into the extravascular space. This can result in specific imaging characteristics that may favor particular diagnoses over others (Miles, 2009).

Contrast-enhanced computed tomography (CECT) is beneficial for characterizing intracranial pathology that alters the blood-brain barrier, as it reveals affected areas

through enhancement (Chishti, Al Saeed, Al-Khawari, & Shaikh, 2003). Additionally, contrast aids in the identification of abnormal vascular structures, including aneurysms and arteriovenous malformations, by highlighting regions with increased regional blood flow (Broder, 2011). Some vascular lesions and lesions that resemble brain parenchyma may only be detectable during the brain CECT phase (Minne', Kisansa, Ebrahim, Suleman & Makhanya, 2014).

Though contrast is valuable in medical imaging, its administration carries risks of adverse effects, which can range from mild, self-limiting reactions to severe and life-threatening complications (Mehta, 2011). Additionally, intravenous contrast administration can increase scanning time and costs for healthcare facilities (Minne' *et al*., 2014; Shuaib, Tiwani, Chokshi, Johnson & Khosa, 2015). It has also been found that contrast administration can lead to increased radiation doses; for equivalent CT exposures, contrast-enhanced tissues can receive significantly higher radiation doses than non-enhanced tissues, with increases exceeding 100% in tissues that absorb high levels of iodine (Perisinakis., Pouli,Tzedakis., Spanakis., Hatzidakis., Raissaki & Damilakis, 2018; Sahbaee *et al*., 2017). Hence, this factor must be considered when designing CT protocols.

The practice of performing CECT of the brain following non-contrast CT (NCCT) in patients presenting with neurological symptoms, especially when the NCCT scan appears normal, has been questioned by researchers in both developing and developed countries. Studies in Europe conducted by Branson, Doria, Moineddin and Shroff (2007) and in the United States by Shuaib *et al*. (2015) have explored this issue. Additionally, a study in Ghana by Jimah, Sarkodie, Offei, Idun, Anim, Brakohiapa and Botwe (2022), along with two studies from South Africa by Minne' *et al*. (2014) and Stipp, Holl, and Scholtz (2004), also questioned the necessity of using contrast in patients with normal NCCT brain scans. They concluded that the use of intravenous contrast is only justified in specific clinical situations, such as when meningitis, cerebral tuberculosis, or brain tumours are suspected.

1.2 Research problem

Contrast-enhanced brain computed tomography is typically performed following a non-contrast brain CT(Broder,2011). However, previous research has shown that routine administration of contrast following a normal brain NCCT scan does not frequently play a significant role in revealing occult pathology not depicted on an NCCT scan. Intravenous contrast administration and re-scanning following the acquisition of a non-contrast brain scan is a practice dating back to the times of early-generation scanners. This practice is still upheld to date even with improved scanner capabilities (Shuaib *et al*., 2015). Despite the work done on this topic and as observed by the researcher at her institution (Mankweng Hospital), intravenous contrast is still routinely administered in patients who present with neurological symptoms and signs, even in instances where a non-contrast brain CT scan is normal. Radiologists have a duty to prioritize patient safety, adhere to the principle of “do no harm’ and provide efficient imaging services (European Society of Radiology, 2022). However, this mandate is compromised when a blanket approach is adopted in brain CT imaging, leading to indiscriminate use of contrast, which can result in unnecessary risk and potential harm to patients.

1.3 Purpose of the study

1.3.1 Research aim

This study seeks to find out if contrast administration significantly changes the diagnosis of a normal NCCT brain scan in Mankweng Hospital radiology department.

1.3.2 Research objectives

- To determine the total number of brain CT scans done for non-traumatic indications at Mankweng Hospital.

- To evaluate the number of normal and the number of abnormal NCCT brain scans at Mankweng Hospital.
- To determine the number of normal NCCT brain scans that show pathology after contrast administration and those that remained normal.
- To calculate the prevalence of abnormalities which are only apparent after contrast administration.

1.3.3 Study Hypothesis

The diagnosis of normal brain scan on NCCT remains the same after contrast administration (CECT).

1.4 Research methodology

1.4.1 Research design

This single-centre study employed a descriptive cross-sectional retrospective design on randomly selected brain CT scans acquired over 13 months (from 01 January 2021 to 31 January 2022).

1.4.2 Sampling frame and sample size

A sampling frame is a comprehensive list of all units or individuals selected from a target population that meet specific research criteria. From this frame, a representative sample is subsequently selected through a randomized procedure (Rukmana, 2024). In this study, the target population included all brain CT scans performed during the designated study period. Out of this population, only 358 brain CT scans met the inclusion criteria, as they all contained both non-contrast CT (NCCT) and subsequent contrast-enhanced CT (CECT) scans. These 358 brain CT scans constitute the sampling frame. The minimum required sample size calculated for this study was 170, and a random sampling method utilizing a random number table was employed.

1.4.3 Data collection

This study involved an audit of existing non-contrast and contrast-enhanced brain CT scans. The audit was conducted by radiology registrars and an attending general radiologist using a sequential reading design. The observers analysed the brain CT scans in a specific order, starting with the non-contrast CT scan (NCCT) and then immediately evaluating the corresponding contrast-enhanced CT scan (CECT) for each patient. This process generated two reports for each patient before the observer proceeded to the next brain CT scan (Schalekamp, van Ginneken, Schaefer-Prokop & Karssemeijer, 2014).

The observers i.e., radiologist and radiology registrars accessed CT images blinded to patient's clinical histories. Observers were instructed to generate their reports independently, without consulting the initial report. All results were documented in an Excel spreadsheet and later transferred to the Statistical Package for the Social Sciences (SPSS) version 25 for statistical data analysis.

1.4.4 Data analysis

The Statistical Package for the Social Sciences (SPSS) was used to analyse the data. A descriptive statistical analysis was performed for each variable. For categorical variables such as gender, scan outcomes, and age categories, the number and percentage were calculated. For numerical variables, such as age in years, the mean and standard deviation were computed. To assess inter-rater agreement between the NCCT and CECT scan reports, the kappa statistic was employed. All statistical analyses were conducted at a 5% significance level.

1.4.5 Reliability and Validity

Reliability in quantitative research refers to the consistency and precision of the measures, instruments, and procedures used to collect data (Sürücü & Maslakçı, 2020). The data collection form used in this study was adopted from Minne *et al*. (2014), who investigated the prevalence of undiagnosed abnormalities in non-

contrast-enhanced computed tomography compared to contrast-enhanced computed tomography of the brain. Their study demonstrated the reliability of measuring the diagnostic value of intravenous contrast following normal brain CT scans. In this research, reliability was further enhanced through a secondary review process in which a consulting radiologist evaluated all scans, thereby verifying the accuracy of the initial reports prepared by the observing registrars.

Validity in imaging research refers to the extent to which an imaging modality or protocol accurately reflects the true characteristics or features of the phenomenon being studied, such as the presence of disease or the distortion of anatomical structures (Bogduk, 2022). Internal validity specifically focuses on the careful planning and implementation of strategies to ensure that the study's results accurately reflect the phenomenon being studied, without being influenced by methodological errors and biases (Patino & Ferreira, 2018).

To enhance internal validity in this study, several strategies were adopted: sampling was randomized, scans were reconstructed to 0.5 mm and adjusted for symmetry before review, and observers were blinded to existing brain CT scan reports to minimize bias in anticipating certain findings. The scans were assessed on reporting station monitors used by radiologists during their working hours at Mankweng Hospital. A brain CT scan was deemed abnormal if one or more of the following criteria were identified: asymmetry between the cerebral and cerebellar hemispheres in terms of volume, sulcation, or density; loss of grey-white matter differentiation; abnormal density of the grey or white matter; space-occupying lesions; non-physiological calcifications or mineral deposits within the brain parenchyma; vascular lesions, including ischemia, hemorrhage, aneurysms, or malformations; dural venous thrombosis; surface collections; dural-based lesions; or meningeal enhancement.

External validity refers to how well the findings of a study can be replicated in similar subjects in different settings (Partino & Ferreira, 2018). The retrospective design of this study was based on existing clinical data generated using standardized CT protocols on a Toshiba Aquilion ONE CT scanner. Quality assurance procedures consistent with clinical standards were applied to ensure data integrity and accuracy.

1.4.6 Bias

Bias in research refers to systematic errors made by the researcher, whether intentionally or unintentionally, that compromise the accuracy, reliability, and validity of study results (Polit & Berk, 2017). Bias can occur at any stage of the research process, including study setting, sampling, data collection, and data analysis.

Sampling bias occurs when a sample is collected in a way that gives some members of the intended population a lower or higher probability of being selected than others (Blumenthal-Barby, 2016). In this study, potential sources of systematic error include patient selection and instrumentation (CT scanner) bias.

To minimize unintended bias in sampling, patients referred from all medical disciplines were considered for the study, regardless of the referring doctor's position within the medical hierarchy. Additionally, bias was minimized by ensuring that all subjects (brain CT scans) included in the sample frame met the established inclusion criteria. The sample was selected using a simple random method.

To further enhance the study's integrity, additional techniques were implemented, as described earlier. These measures complement the reliability and validity strengthening methods discussed previously, providing a robust framework for ensuring the accuracy and generalizability of the findings.

1.5 Ethical considerations

Research ethics is a crucial principle in any study, as it ensures respect for participants and upholds integrity (Jacobs, 2008). This study followed ethical guidelines to protect patient privacy and confidentiality. Key considerations included obtaining approval from the University of Limpopo Turfloop Research Ethics Committee (TREC) and relevant authorities. Due to the impracticality of obtaining consent, the study was granted a waiver. Additionally, measures were put in place to ensure anonymity, confidentiality, and data protection, all while complying with the World Medical Association's Declaration of Helsinki, (2013).

1.6 Significance of the study

This study aimed to evaluate the diagnostic value of administering contrast after a normal non-contrast computed tomography (NCCT) scan of the brain at Mankweng Hospital. The findings from this research have the potential to guide changes and improve brain imaging protocols, ultimately enhancing patient safety and financial efficiency at Mankweng Hospital and potentially many other hospitals across South Africa.

1.7 Outline of the study

This mini-dissertation consists of five chapters. Chapter One provides a narrative aimed at clarifying the purpose of the study. It outlines the background and motivations that prompted the researcher to undertake this study. The research problem, research questions, aims, objectives, and significance of the study are detailed. Additionally, the chapter discusses the reliability and validity of the study as well as ethical considerations.

Chapter Two focuses on relevant literature that highlights the significance and implications of contrast usage in brain CT imaging. This chapter presents publications that challenge the necessity of acquiring contrast-enhanced CT scans of the brain when the non-contrast scan appears normal.

Chapter Three outlines and justifies the research methodology applied in this study, detailing the research setting, study design, sampling methods, data collection techniques, and analysis procedures.

Chapter Four presents the results of the study, aligning them with the study objectives. Finally, Chapter Five analyses the results, comparing them with existing literature. This chapter also includes the study's conclusion and the recommendations made by the researcher based on the study results.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This literature review examines the use of contrast in brain CT imaging, specifically following a normal non-contrast scan. It synthesizes existing research, evaluates guidelines, and explores the practice of administering contrast. Key topics covered include the enhancement of normal brain structures and surrounding tissues on CT, the current guidelines for administering contrast after a normal non-contrast CT brain scan, and the rationale behind this practice. This review aims to establish a foundation for determining the prevalence of brain abnormalities that are only visible after contrast administration. The main keywords include appropriateness, brain computed tomography, non-contrast brain CT, contrast-enhanced brain CT, brain neuroimaging, and contrast.

2.2 Enhancement of normal brain and surrounding tissues on computed tomography

Understanding tissue radiodensity is essential in CT imaging. The administration of contrast enhances tissue resolution, allowing for the differentiation between normal and abnormal tissues (Miles, 2009; Smirniotopoulos., Murphy., Rushing., Rees & Schroeder, 2007). This improved visualization enables radiologists to evaluate tissue response to normative benchmarks, facilitating accurate diagnosis and characterization of various pathologies (Rodgers & Tadi, 2023).

Intracranial blood vessels exhibit a significant increase in radiodensity following contrast enhancement due to intravascular enhancement. In contrast, the normal brain shows minimal change in radiodensity after contrast administration, primarily due to the blood-brain barrier (BBB) affecting interstitial enhancement (Smirniotopoulos *et al*., 2007). Although the dural reflections show increased radiodensity after contrast administration because they lack a BBB, this effect is often masked in areas of the dura adjacent to the inner table of the skull, owing to the naturally high density of the bone.

Non-contrast brain CT scans have demonstrated high sensitivity in detecting calcifications, space-occupying lesions, strokes, and intracranial hemorrhage (Qader *et al*., 2023; Likeman, 2013). The use of contrast can enhance sensitivity in characterizing abnormalities found on non-contrast CT scans, such as the presence of vasogenic edema alongside occult lesions in certain cases.

Rizk., Platon., Tasu., Becker., Pereira., Perneger., Shanmuganathan., Lövblad & Poletti, (2013) point out that certain brain pathologies can only be detected on CT after the administration of contrast, including arterial dissection, venous thrombosis, and post-operative complications. Similarly, Minnie *et al*. (2014) concluded that non-contrast CT has a low diagnostic yield in detecting vascular pathologies like dural venous thrombosis and arteriovenous malformations. However, a retrospective study by Tayyebi and colleagues found that non-contrast CT can be accurately used with high specificity and sensitivity to diagnose acute dural venous thrombosis (Tayyebi., Akhavan., Shams., Salehi., Farrokh., Yousefi & Abbasi, 2020)

2.3 Brain computed tomography imaging guidelines

2.3.1. The American college of radiologists (ACR) appropriateness criteria

The American College of Radiology (ACR) has made significant contributions to addressing the overutilization of diagnostic tests in neuroimaging. Through a rigorous process involving multidisciplinary expert consensus, thorough literature reviews, and evidence-based research, the ACR has developed comprehensive guidelines known as the Appropriateness Criteria. These guidelines are continuously updated to reflect the latest scientific evidence and clinical practices. They serve as a framework to assist clinicians in making informed decisions about neuroimaging, thereby promoting clinical effectiveness, patient safety, resource optimization, and quality improvement (Buethe, Nazarian, Kalisz & Wintermark, 2016).

The ACR Appropriateness Criteria rate neuroimaging modalities for specific clinical scenarios on a scale of 1 to 9: a score of 1 to 3 indicates that a test is usually not appropriate, scores of 4 to 5 suggest that a test may be appropriate, and scores of 7 to 9 indicate that a test is usually appropriate. This scoring range reflects the variability

of opinions among panel members, accommodating both minority and majority perspectives and illustrating the complexity of decision-making in this field.

Table 3. 1: Appropriate category names and definitions of assigned ratings.

Appropriateness category name	**Rating**	**Appropriateness category definition**
Usually appropriate	7, 8, or 9	The imaging procedure is indicated in the specified clinical scenario at a favourable risk-benefit ratio for the patients.
May be appropriate	4, 5, or 6	The imaging procedure may be indicated in the specified clinical scenario as an alternative to an imaging procedure with a more favourable risk-benefit ratio or the risk-benefit ratio for patients is equivocal.
May be appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendations. "may be appropriate" is a rating category, and a rating of 5 is assigned.
Usually not appropriate	1, 2, or 3	The imaging procedure is unlikely to be indicated in the specified clinical scenario or a risk-benefit ratio for the patients is likely to be unfavourable

(*ACR Appropriateness Criteria® headache: 2022)*

The appropriateness of brain CT scans performed as a single step (NCCT) and two-step procedures (NCCT and CECT) is clearly outlined in the ACR appropriateness criteria. This discussion will focus on the appropriateness ratings assigned to single-step (NCCT) and two-step brain CT scans for each condition and variants relevant to this study, as informed by the latest ACR appropriateness criteria.

2.3.1.1 Headache

According to the ACR guidelines, the single-step brain CT scan is rated as the only "usually appropriate "modality in initial imaging of thunderclap headache variant whilst rated as 7-9 "usually appropriate" for the diagnosis of acute hemorrhage, mass effect, and hydrocephalus in four variants. In contrast, the current literature does not provide sufficient evidence to justify the routine use of two-step CT for the initial evaluation of all variants. It is important to note that in three other variants: Migraine or tension-type headache, trigeminal neuralgia, and headache with features of hypotension both single-step and the two-step scans are rated as 1-3, "usually not appropriate" (Utukuri,

Shih, Ajam, Callahan, Chen, Dunkle, Hunt, Ivanidze, Ledbetter, Lee, Malu, Pannell, Pollock, Potrebic, Setzen, Shih, Soares, Staudt, Wang & Burns, 2023). **Table 2.2** represents a summary of how single-step (NCCT only) and two-step (without and with contrast) brain CT scans were rated by ACR appropriateness criteria, for imaging patients with headache.

Table 3. 2: Single-step versus two-step CT imaging rating according to ACR appropriateness criteria

Headache variants	**Single step NCCT ACR appropriateness rating**	**Two-step CECT ACR appropriateness rating**
Migraine or tension type headache	Usually not appropriate	Usually not appropriate
Trigerninal cephalagia	Usually not appropriate	Usually not appropriate
Sudden onset headache, reaching maximum intensity in one hour	Usually appropriate	Usually not appropriate
Headache with features of intracranial hypertension	Usually appropriate	Usually not appropriate
Headache with features of intracranial hypotension	Usually not appropriate	Usually not appropriate
New onset headache in pregnancy or peripartum period	Usually appropriate	Usually not appropriate
Headache with red flags (increased severity, frequency, fever, neurological fallout, old of onset>50years, history of trauma or cancer, post-traumatic).	Usually appropriate	Usually not appropriate
Headache without red flags	Usually not appropriate	Usually not appropriate

2.3.1.2 Cerebrovascular diseases (stroke and stroke like conditions)

The American College of Radiology (ACR) rated the non-contrast computed tomography (NCCT) scan a 9, indicating that it is usually appropriate. They described it as the gold standard test for diagnosing clinically suspected parenchymal hemorrhage. Additionally, NCCT was deemed usually appropriate for cases of clinically suspected subarachnoid hemorrhage, suspected dural venous sinus thrombosis, focal neurological deficits, and for follow-up after proven parenchymal hemorrhage.

In contrast, two-step CT imaging was rated as “usually not appropriate” for evaluating all cerebrovascular disease variants relevant to this study. The current literature does not provide sufficient evidence to support the routine use of either CT imaging method for monitoring asymptomatic patients with carotid bruit or known carotid stenosis (Pannell., Corey., Shih., Austin., Chu., Davis., Ducruet., Hunt., Ivanidze., Kalnins & Lacy,2024).

2.3.1.3 Seizures and Epilepsy

In the imaging of patients with seizures and epilepsy, the American College of Radiology (ACR) recommends a single-step brain scan for patients experiencing acute seizures without a history of trauma, as well as for those who present with changes in seizure semiology. A non-contrast computed tomography (NCCT) scan can quickly identify conditions such as intracranial hemorrhage, ischemic infarcts, tumours, vascular malformations, and hydrocephalus. The two-step scanning method (NCCT followed by contrast-enhanced computed tomography, or CECT) is generally not considered appropriate for any of the six seizure variants discussed in the literature (Lee., Burns., Ajam., Broder., Chakraborty., Chong., Kendi., Ledbetter., Liebeskind., Pannell & Pollock, 2020).

There are specific ACR appropriateness criteria for children with seizures. Generally, brain CT scans are not recommended for children, particularly those between 1 month and 5 years old, especially when seizures are associated with fever. However, a single-step NCCT may be suitable for imaging focal and generalized seizures in children aged 1 month to 18 years and in the neonatal period. The two-step approach is not typically recommended for these types of seizures (Trofimova, Milla., Ryan., Pruthi., Blount., Desai., Glenn., Islam., Kadom., Mirsky & Myseros, 2021).

2.3.1.4 Altered mental state, coma, delirium and psychosis

In the four altered mental state variants, NCCT is usually recommended for 3, while the two-step approach is not usually recommended for any variant (Luttrull., Boulter., Kirsch., Aulino., Broder., Chakraborty., Choudhri., Ducruet., Kendi., Lee & Liebeskind, 2019).

2.3.1.5 Dementia

The single-step non-contrast computed tomography (NCCT) scan is generally considered appropriate for all variants. In contrast, the two-step brain CT scan is typically not recommended for all variants (Moonis, Subramaniam, Trofimova, Burns, Bykowski, Chakraborty, Holloway, Ledbetter, Lee, Pannell, Pollock, Powers, Roca, Rosenow, Shih, Utukuri & Corey, 2020).

2.3.1.6 Orbits, vision and visual loss

CT brain imaging is generally not recommended for most variants in this category (ARC rating 1-3). However, non-contrast CT (NCCT) rated 4-5 ,may be appropriate for patients with pre- and post-chiasmatic symptoms, and a two-step imaging approach rated 4-5 may be suitable for those with post-chiasmatic symptoms (Kennedy., Corey., Policeni., Agarwal., Burns., Harvey., Hoang., Hunt., Juliano., Mack & Moonis, 2018.).

2.3.1.7 Dizziness and ataxia

CT scans are generally not preferred for dizziness and ataxia, except in cases of chronic recurrent vertigo with brainstem deficits, where they may be considered appropriate (rated 4-6) by experts (Wang., Thompson., Shih., Ajam., Bulsara., Burns., Davis., Ivanidze., Kalnins., Kuo & Ledbetter, 2024).

2.3.2. Asian guidelines

Asian guidelines published by Chishti *et al*., (2003) developed after evaluating the role of contrast-enhanced CT in the MRI era utility are as follows:

- Withholding contrast injection when the NCCT clearly defines the pathology (e.g., vascular events like hemorrhage and ischaemic infarcts)
- Contrast injection at the radiologist's discretion when NCCT is abnormal, but not diagnostic.

Several studies have supported the Asian guidelines regarding the use of contrast-enhanced CT (CECT). For instance, Shuaib *et al*. (2014) reported that CECT does not significantly improve the diagnosis and management of patients with neurological symptoms, except when it is used to characterize abnormalities detected on non-contrast CT (NCCT). Similarly, Bennimahadeo and Maharajh (2016) concluded that the use of intravenous contrast in brain CT imaging should be guided by clinical

presentation, specifically recommending that indicators such as seizures, lateralizing signs, and worsening headaches should be considered. These studies reinforce the Asian guidelines for the judicious use of contrast, emphasizing the significance of NCCT and clinical context in making decisions about contrast administration.

Additionally, a review of major radiology and medical databases (such as PubMed, Sabinet, Elsevier, and Google Scholar) did not reveal any African or South African guidelines that directly compare the appropriateness of single-step versus two-step approaches in CT imaging of the brain. The absence of accessible local guidelines underscores the importance of taking local contexts into account when developing imaging protocols.

2.4 Use of intravenous contrast after obtaining normal non-contrast brain

In patients exhibiting clinical neurological abnormalities, a normal non-contrast computed tomography (NCCT) brain scan does not always rule out the presence of pathology. While NCCT is known for its high sensitivity, specificity, and positive and negative predictive values (Qader *et al*., 2023), the use of contrast enhancement can enhance the detection of subtle lesions that are isodense to brain tissue, as well as small lesions that lack secondary effects such as vasogenic edema or hydrocephalus. This section reviews the existing literature on the value of contrast enhancement following a normal NCCT brain scan, focusing on the frequency and characteristics of abnormalities that may be missed on NCCT but revealed through contrast-enhanced CT (CECT).

A study conducted by Stipp and colleagues at Steve Biko Academic Hospital in South Africa examined the necessity of intravenous (IV) contrast in normal CT brain scans performed for the evaluation of adult-onset seizures. The study involved 205 patients referred by the neurology department, and all scans (100%) were normal following the administration of contrast. The normal post-contrast CT findings included 186 normal pre-contrast scans, 11 age-related changes, and 8 normal variants. Both age-related changes and normal variants were classified as non-causative findings (Stipp *et al*.,

2004). This research focused specifically on outpatients with adult-onset seizures referred from the neurology department.

In another study conducted in South Africa by Minne and colleagues, a total of 701 NCCT brain scans were reviewed, revealing that only 10 (1.42%) were genuinely abnormal (Minne *et al*., 2014). The brain CT scans included patients with a broad range of neurological symptoms.

A multi-centre study conducted in Ghana by Jimah *et al*. (2022) examined the use of contrast medium in computed tomography (CT) for patients presenting with headaches. The study included a total of 477 brain scans, of which 382 were from patients who underwent both Non-Contrast Computed Tomography (NCCT) and Contrast-Enhanced Computed Tomography (CECT), while 95 scans were from patients who only had NCCT performed.

In comparing the two groups, the researchers found that the rate of abnormal scans was 43.7% (166 out of 382) in the CECT group, which was higher than the 37.9% (36 out of 95) observed in the NCCT group. Notably, contrast administration was necessary in only 11.3% (43 out of 382) of the CECT cases. The authors reported that for the majority of the studies analysed, radiologists were able to reach the same diagnosis using either NCCT or CECT, indicating that contrast administration was not essential to determine if the brain CT scan was normal.

Additionally, a study conducted by Shuaib *et al*. (2015) in Ireland aimed to assess the value of contrast and non-contrast brain CT in an acute setting. This research took place in two teaching hospitals' emergency departments over a two-year period and involved a sample of 379 patients presenting with various symptoms: headache (48%), dizziness (19%), altered mental state (13%), and seizures (10%). Among the 261 NCCT scans, 68% were normal, while 32% were abnormal. Remarkably, only one of the normal NCCT scans revealed an abnormality (an arteriovenous malformation) after contrast administration. The study concluded that CECT of the brain increased financial expenditure without providing any significant value.

Branson and his colleagues (2007) investigated whether contrast enhancement is necessary after obtaining a normal non-contrast brain CT in a paediatric population. Their findings indicated that inter-reader agreement for different anatomical regions ranged from good (κ coefficient of 0.63) to very good (κ coefficient of 0.88) for non-contrast and contrast-enhanced scans. The sensitivity, specificity, positive predictive value, and negative predictive value for non-contrast scans were 97%, 89%, 87%, and 97%, respectively. The use of contrast material changed the original normal or equivocal diagnosis to an abnormal diagnosis in only five patients (2.7%) of the 183 normal non-contrast scans. They concluded that non-contrast CT of developing brains has high sensitivity and specificity for diagnosing pathological findings. The use of intravenous contrast material after non-contrast CT scans in children rarely altered the diagnosis.

Rizk *et al*. (2013) conducted a retrospective study to determine whether unenhanced brain CT was sufficient for diagnosing patients presenting with headaches. They analysed a sample of 74 patients, categorizing their non-contrast CT scans into three groups: 1. normal (59 patients), 2. non-contrast CT diagnostic with no need for further imaging (4 patients), and 3. those with intracranial pathology requiring further imaging (11 patients). A review of the contrast-enhanced CT scans showed that no new pathology was detected in groups 1 and 2. The contrast-enhanced scans confirmed the presence of previously diagnosed pathology in group 3. They concluded that non-contrast CT might be sufficient for diagnosing secondary headaches.

Wood, Parisi & Finch (1990) aimed to assess the value of performing contrast-enhanced brain CT in conjunction with non-contrast CT for evaluating acute central nervous system disorders. They reviewed a sample of 322 cases originating from the emergency room. The most common reasons for scanning included seizure activity (34%), headache (30%), focal neurological deficit (10%), and altered mental status (8%). The results showed that 75% of the non-contrast scans were normal. The contrast-enhanced scans revealed abnormalities not evident on the non-contrast scans in three cases, although this information did not affect patient management.

Wood *et al* (1990) concluded that, in acute settings, if a non-contrast CT is normal, a contrast study is usually unnecessary. Therefore, "given the additional risks of contrast infusion, the contrast study, if needed, is generally best obtained at a later date, after a more careful evaluation of the patient's history and medical records." If the non-contrast CT scan is abnormal, a contrast-enhanced CT scan may be beneficial, but it is often not needed to direct acute patient management (Wood, Parisi, & Finch, 1990).

Contrary to the studies mentioned earlier, a study conducted in India by De Souza, Nalini & Srikanth (2013) found that non-contrast computed tomography (NCCT) of the brain had lower sensitivity in detecting solitary cerebral neurocysticercosis. In thieir study, 86 patients who presented with new-onset seizures underwent imaging using NCCT, followed by contrast-enhanced computed tomography (CECT) and non-contrast magnetic resonance imaging (MRI), with a subsequent contrasted MRI. Of the patients who had a single cysticercus lesion identified on CECT, 30 (34.8%) showed no detectable abnormalities on the prior NCCT scans. The results indicated that CECT was more sensitive than NCCT in diagnosing cerebral neurocysticercosis.

2.5 Conclusion

The literature review indicates that the diagnosis of a normal brain on non-contrast computed tomography (NCCT) scans is unlikely to change with the administration of contrast material (CECT). This conclusion is based on the principles of tissue radiodensity and the physiology of nervous system tissue enhancement, which limit the enhancement of normal brain parenchyma due to the blood-brain barrier (BBB). By understanding these fundamental principles, along with the clinical context and specific indications, radiologists can make informed decisions about whether to proceed with a CECT scan or to rely solely on the NCCT. This approach ultimately helps optimize imaging protocols and improve patient care.

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Introduction

This chapter details the methodology of the study, including the study setting, population, sampling, data collection, and analysis processes. It also describes how bioethical principles were integrated into the research.

3.2 Study setting

This study was conducted at Mankweng Hospital, a tertiary healthcare institution located in the Limpopo province of South Africa. As one of two tertiary referral centers in the province, Mankweng Hospital offers advanced medical care and specialized services to a diverse patient population, primarily consisting of referrals from regional and district hospitals in the Mopani district.

During the study period, patients from various departments including emergency (casualty), internal medicine, paediatrics, psychiatry, and ophthalmology were referred for brain CT scans. The Radiology Department, equipped with a multidetector Toshiba Aquilion ONE 620 slices scanner, served as the primary site for data collection.

The hospital's Picture Archiving and Communication System (PACS) was launched in the last quarter of 2020, so any scans performed before this period are not available for review. At the time the brain scans were acquired, the department was staffed by two consultant radiologists and a rotating team of medical officers and registrars.

Brain CT scans were acquired in the axial plane with a slice thickness of 5 mm and were multiplanar reformatted into axial, sagittal, and coronal images with a thickness of 0.5 mm. The administration of intravenous Iohexol (Omnipaque) was weight dependent, with hand-injected dosages ranging from 1 ml to 2 ml/kg for patients and from 40 ml to 100 ml for adults during brain CT imaging.

3.3 Research design

Research design is a strategic plan that outlines the approach, methods, and procedures for collecting, analysing, and interpreting data. This framework enables researchers to address specific research questions, achieve study objectives, and manage bias in a reasonable manner (Mitchell & Jolley, 1988). Importantly, aligning with this framework helps prevent the publication of false or misleading results, which can have serious consequences for future research and patient outcomes (McKeever, 2021).

The present study employed a descriptive cross-sectional retrospective design to examine the diagnostic value of contrast enhancement following normal non-contrast computed tomography (NCCT) brain scans. This design offers several advantages, including efficient data collection, cost and time savings, and a comprehensive overview of current practices at the study site. However, it also has limitations, such as selection bias, concerns about data quality, and restricted generalizability. These limitations will be addressed in the relevant subsequent sections.

3.3.1. Sampling method

3.3.1.1 Population

Understanding sampling methods and designing effective research studies requires a comprehensive grasp of population concepts. When conducting research, it is crucial to differentiate between the three population concepts that exist within a hierarchy (Casteel & Bridier, 2021).

Population of Interest: The study begins with a broad group of individuals, organizations, or entities relevant to the investigation.

Target Population: From the population of interest, a more specific and manageable group emerges, characterized by shared attributes and accessibility. This refined group, known as the target population, serves as the foundation for the study (Salkind, 2010).

Study Population (Sample Frame): Finally, a precise listing of potential participants or data sources is derived from the target population. This list provides the basis for sample selection and represents a subset of the target population from which the sample is chosen (Hu, 2014; Salkind, 2010).

This study focuses on evaluating the diagnostic value of contrast after normal non-contrast CT (NCCT) brain scans. The population of interest encompasses all 1,732 CT scans of patients imaged at Mankweng Hospital between January 2021 and January 2022 as recorded in the CT patient record books. The target population consists of all 637 brain CT scans. Specifically, the study population or sample frame includes 358 brain scans that were acquired using a two-step approach: non-contrast CT followed immediately by contrast-enhanced CT (CECT), which meet the study's inclusion criteria.

3.3.1.2 Sampling method

A sample is a subset of individuals or items chosen from a larger study population, with the intention that the analytical findings observed in this smaller group can be generalized to the entire population (Rubin & Babbie, 2016). Sampling refers to the process of selecting the specific group from which the researcher will collect data (Etikan & Bala, 2017). While it would be ideal to audit the entire target population that meets the inclusion criteria, this was not feasible in this case due to limited resources. Therefore, to reduce bias and increase validity, a simple random sampling method was employed to select the minimum required sample size. Simple random sampling is a probability sampling technique in which every member of the target population has an equal chance of being selected for the study (Bhardwaj, 2019). A random number table (see Annexure 1) was utilized to select 181 scans from the 358-member target population.

3.3.1.3 Inclusion criteria

- Brain CT scans acquired in a two-step manner, that is non-contrast brain CT and subsequent post-contrast CT scans.

3.3.1.4 Exclusion criteria

- Brain CT scans with features of head trauma and previous cranial surgery.
- Scans Brain showing extra-cranial pathology.
- Single-step NCCT or CECT brain scans.

3.3.1.5 Sample size calculation

Sample size calculation is essential in research and must be conducted properly to ensure that researchers reach accurate conclusions. Incorrect calculations can lead to flawed results, which may invalidate the study (Pourhoseingholi, Vahedi & Rahimzadeh, 2013). Khan, Qashqari, & Al-Ali (2013) estimate that the sensitivity of brain CT scans is at least 95%. Previous studies have indicated that the prevalence of abnormal non-contrast computed tomography (NCCT) findings in the brain is about 30%. According to Alashaari & Alshamari (2021), a binomial distribution refers to a repeated experiment or trial with only two possible outcomes, such as success or failure, functional or defective, male or female, etc. This study aims to either support or challenge the value added by contrast administration following a normal NCCT scan, and therefore, it follows a binomial distribution. The minimum required sample size for this study was calculated using the prevalence study formula outlined by Daniel (1999);

where n is the sample size, Z is the statistic corresponding to confidence level, P is expected prevalence (obtained from similar studies), and d is precision (corresponding to effect size).

A researcher needs to know the assumed prevalence (P) to use in the sample size calculation formula. This value can be estimated based on previous studies within the field or from a pilot study with a small sample size. The choice of assumed P is crucial, as the precision (d) should be selected based on the value of P. However, there are insufficient guidelines for choosing an appropriate level of precision.

Some authors recommend selecting a precision level when the prevalence of the disease is expected to be between 10% and 90%. On the other hand, if the assumed prevalence is very low (below 10%), a precision level of 5% may not be suitable. For instance, if the assumed prevalence is 1%, a precision of 5% would be overly crude and could lead to an inappropriate sample size. A more conservative approach would be to set the precision to one-fourth or one-fifth of the prevalence in cases of low P.

In this study, the researcher presents a sample size calculation using an assumed prevalence of P = 0.3, a precision of 5%, and a desired confidence level of 95%.

$$n = \frac{(1.96x1.96x0.3x0.7)}{(0.05x0.05)}$$

=322.7

Therefore, incorporating the finite population of 358, the minimum sample size(small) required in this study was calculated as follows:

$$n = \frac{(322.7)}{1} + \frac{(322.7 - 1)}{358}$$

=170

3.3.2. Data collection

3.3.2.1 Approach and method

A review of archived brain CT images was chosen as the method for data collection. The total number of scans assigned to each registrar varied based on their availability, with each registrar reading a minimum of 20 scans and a maximum of 45 scans. To limit the workload and reduce fatigue, the number of cases reviewed was restricted to 10 per week.

This study employed a sequential reading design, where a non-contrast CT (NCCT) scan was assessed immediately followed by an assessment of the contrast-enhanced CT (CECT) scan. The sequential reading design has been shown to be superior to an independent reading design, which allows for a time gap between the reviews of the two modalities (NCCT and CECT in this case). This approach minimizes interobserver variability by enhancing the correlation between NCCT and CECT, leading to improved diagnostic outcomes (Schalekamp, van Ginneken, Schaefer-Prokop & Karssemeijer, 2014). Observers evaluated the brain scans without being privy to the clinical information or existing reports.

3.3.2.2 Characteristics of the data collection instrument

A data collection form (Annexure 2) modelled after the data collection instrument employed by Minne' *et al* (2014) was utilized to record information gathered from each brain scan. The standardized tool ensured consistency in data collection, incorporating similar variables as follows: The form contains a demographic section (A) that includes the assigned study number, the patient's age (A1), gender (A2), and their clinical background (A3) as documented in the patient's clinical records. Section B focuses on the radiological findings as noted by the radiology doctor. Both NCCT and CECT brain scans were evaluated, and the findings were categorized as normal, abnormal, or equivocal in section B1. The final diagnosis was documented in section B2.

3.3.2.3 Data collection process

Data collection unfolded in three phases:

Phase 1

A total of one hundred eighty-one (181) sampled scans were distributed among five senior radiology registrars for independent assessment. To simulate routine practice at Mankweng Hospital, the observers utilized the Beacon G23SP+ 2MPS PACS grayscale medical display monitors, which are commonly used for daily image interpretation. To enhance the diagnostic value of the brain CT scans, the observers were instructed to adjust all CT images for symmetry before assessment, allowing for

simultaneous visualization of the bilateral internal auditory canals in the same axial slices. The findings from the sequentially reported non-contrast CT (NCCT) and contrast-enhanced CT (CECT) scans were recorded on a data collection form as normal, equivocal, or abnormal.

Phase 2

In this study, each senior registrar independently reviewed the studies assigned to them. The Non-Contrast Computed Tomography (NCCT) scans were evaluated first, followed immediately by the Contrast-Enhanced Computed Tomography (CECT) reporting, with no delay between them. Observers were encouraged to label any findings as equivocal if they had even the slightest doubt, allowing for the opinions of other observers to be sought during a consensus meeting.

Scans reported by the senior registrars as abnormal (Group A) or normal (Group B) were then reviewed by a consultant radiologist with over 10 years of experience in the field. Any scans with equivocal findings were reviewed by a panel consisting of five observers: four senior registrars and the consultant radiologist. The panel discussed ten out of the 181 cases that were marked as equivocal during two consensus meetings, with a maximum of five scans being discussed in each meeting. The final diagnosis was recorded based on the majority view shared by at least three panel members. All equivocal scans and their final diagnoses, determined by consensus, are presented in Annexure 3. Ultimately, all 181 reviewed scans were categorized into three groups based on their final diagnoses.

Group A: abnormal NCCT and CECT results, with a final diagnosis of abnormal

Group B: Normal NCCT and CECT results, with a final diagnosis of normal

Group C: normal NCCT, and abnormal CECT results, with a final diagnosis of abnormal

Phase 3

The researcher examined the available medical records and existing brain CT reports of the sampled patients. Clinical information was recorded in section A3 of the respective data collection forms. The final diagnoses noted on these forms were then compared to the corresponding formal CT reports. This phase was important for two reasons: first, to identify patients with pathologies that were missed, and second, to recognize patients who were diagnosed with abnormalities that could not be detected during the audit.

3.3.3. Data analysis

The researcher organized the information collected from the data collection forms into an Excel spreadsheet. The data was then entered into the Statistical Package for Social Sciences (SPSS) version 26 for Windows. Data analysis involved both descriptive and inferential statistical methods. Descriptive statistics were used to present frequencies and percentages for all categorical variables, such as gender and radiological findings (including NCCT brain and CECT scan results). Continuous variables, such as age, clinical presentation, comorbidities, and co-existing pathologies, were summarized with their corresponding means and standard deviations.

Inferential statistics utilized the Chi-square test of independence to assess associations among various categorical variables. Additionally, Cohen's kappa coefficient (κ) was calculated to evaluate the level of agreement between NCCT and CECT outcomes. The interpretation of kappa statistics is provided below (Viera & Garrett, 2005).

Table 3. 3: Interpretation of Kappa

Poor slight fair Moderate Substantial Almost perfect

0.0 .20 .40 .60 .80 1.0

Kappa	**Agreement**
<0	Less than a chance agreement
0.01-0.20	Slight agreement
0.21- 0.40	Fair agreement
0.41-0.60	Moderate agreement
0.61-0.80	Substantial agreement
0.81- 0.99	Almost perfect agreement

(Viera & Garrett, 2005).

3.4 Ethical consideration

This section outlines the ethical measures taken to ensure the integrity of the study. The relevance of the study to diagnostic radiology was validated by the acting head of the Pietersburg-Mankweng Complex, who granted permission to conduct the research. Subsequent approvals were obtained from the School Senior Degrees Committee (SSDC), the Faculty of Higher Degrees Committee, the University of Limpopo TREC (Ethical Clearance Certificate Number TREC/548/2022, Annexure 7), the Limpopo Department of Health (Annexure 8), and the Chief Executive Officer of Mankweng Hospital (Annexure 9). These approvals ensure compliance with regulatory requirements prior to data collection.

Because accessing patients' clinical data was necessary for this study, great care was taken to protect privacy and maintain patient confidentiality when accessing, using, and recording relevant clinical information.

Participant Vulnerability: The study did not involve human participants, which minimized participant vulnerability. However, patient medical records were utilized, and all ethical considerations regarding this are discussed in the relevant section.

Anonymity and Confidentiality: The researcher upheld the fundamental principles of medical research as outlined in the Helsinki Declaration: “the privacy and dignity of human subjects will be preserved” (World Medical Declaration, 2013). Patient names, hospital names, and CT numbers were excluded from this research paper. To maintain confidentiality, a unique study number was assigned in place of the patients’ legal identities on the data collection sheets. Study findings are generalized without disclosing information about specific individuals whose brain CT scans were sampled.

Data Protection: Access to the compiled sample frame list was restricted to the researcher and designated observers. The PACS and Radiology Information Systems (RIS) at Mankweng Hospital's radiology department ensure secure data storage, requiring personalized login credentials for access. Hard-copy medical records are stored in a limited-access area, accessible only to authorized personnel.

Consent: Consent was waived by TREC as per the National Health Research Ethics Council (NHREC) guideline of 2015, as obtaining consent from all patients whose scans were sampled would have been impractical and challenging.

Potential Harm: Although this study did not reveal any harm or adverse effects, the researcher acknowledged potential risks. Discrepancies between the reports generated during the study and the existing CT scan reports could have led to the identification of previously overlooked pathologies or the nullification of significant diagnoses, potentially impacting patient care. However, the study’s focus on accurate diagnosis and reporting aimed to mitigate these risks and ensure optimal patient care.

Conflict of Interest: The researcher declares no conflict of interest; no financial or personal relationships influenced the conduct or outcome of this study. The results and conclusions presented are unbiased and objective.

3.5 Conclusion

This chapter discusses the research methodology, which includes research design, sampling, data collection methods, data analysis, reliability and validity, and ethical considerations. The results of the data analysis will be presented in the following chapter.

CHAPTER 4: PRESENTATION AND INTEPRETATION OF THE FINDINGS

4.1 Introduction

This study aimed to evaluate the impact of contrast material on the diagnostic outcomes of normal Non-Contrast Computed Tomography (NCCT) brain scans conducted at a rural academic hospital. The objective was to determine whether the use of contrast enhances diagnostic accuracy compared to what is achieved through standard NCCT imaging. The objectives of the study were as follows:

- to determine the total number of brain CT scans performed for non-traumatic indications at Mankweng Hospital.
- to identify the number of normal and abnormal NCCT brain scans,
- to ascertain the number of normal NCCT brain scans that revealed pathology after contrast administration.
- to calculate the prevalence of abnormalities that are only detectable on Contrast-Enhanced Computed Tomography (CECT) following a normal NCCT

This chapter details and interprets the findings of the study. It is organized into several subsections as follows:

1) Demographic characteristics of the participants
2) The number of normal and abnormal NCCT brain scans
3) Ascertain the number of normal brain scans that revealed pathology after contrast administration versus those that remained normal
4) Prevalence of abnormalities that are only detectable on CECT.

4.2 Number of brain CT scans performed for non-traumatic indications

During the study period, a total of 1,732 scans were conducted, of which 637 were brain scans (see Figure 4.1). These 637 brain scans included patients with head trauma (88), those who had undergone cranial surgical intervention (12), patients with facial or orbital tumours (22), and those with medical indications (515). Among the 515 medical patients with no history of trauma or cranial surgery, 358 (69.5%) underwent both NCCT and subsequent CECT, 149 (28.9%) had NCCT only, and 8 (1.5%) had CECT only.

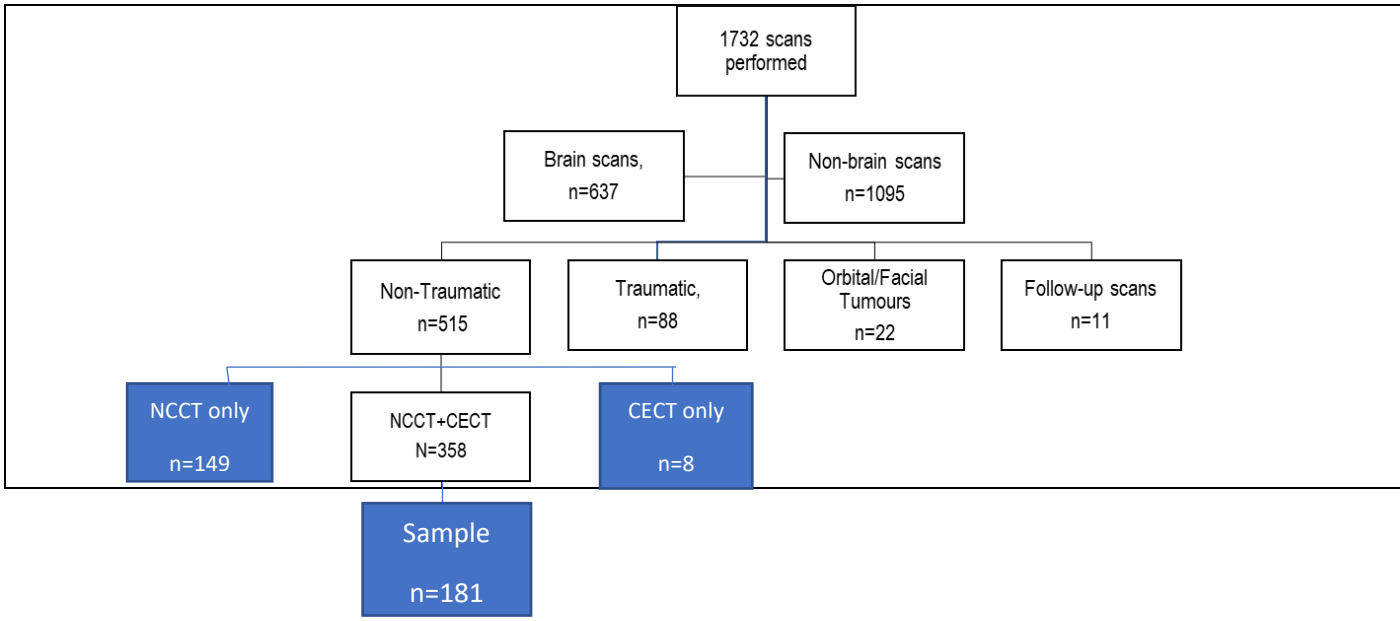

Figure 4. 1: Flowchart of CT scans performed during the study period

Table 4.1 presents the indications for brain CT imaging in a total of 181 patients, as gathered from medical records and existing brain CT scan reports. The most common indications for these scans included seizures (34 cases), unilateral motor deficits (31 cases), headaches (25 cases), and visual impairments (22 cases). Less frequent indications were neonatal encephalopathy (1 case) and cognitive decline (2 cases), among others. It is important to note that the clinical records for 26 of the scans could not be retrieved, leaving the indications for these scans unknown.

Table 4. 1: Indications for brain CT imaging retrieved from records prior evaluation

Indicators	**Count**	**%**
Seizure	34	18.8
Unilateral motor deficit	31	17.1
Headache	25	13.8
Visual impairment	22	12.2
Psychosis	9	5.0
Confusion	7	3.9
Meningitis	7	3.9
Cranial nerve palsy	6	3.3
Neurodevelopmental delay	4	2.2
Cognitive decline	2	1.1
Ataxia	2	1.1
Organophosphate poisoning	1	0.6
paraparesis	1	0.6
Allergic conjunctivitis	1	0.6
Macrocephaly	1	0.6
Neonatal encephalopathy	1	0.6
Unknown (no retrievable data)	26	14.4
Total	**181**	**100.0**

4.3 Number of normal and abnormal NCCT brain scans

Figure 4.3 shows the scan results for both non-contrasts computed tomography (NCCT) and contrast-enhanced computed tomography (CECT). It indicates that NCCT scans had a higher incidence of abnormalities, with 51.4% classified as abnormal compared to 48.6% classified as normal. Similarly, CECT scans also showed a trend toward abnormalities, with 54.1% being abnormal and 45.9% normal. However, there was no significant difference in the proportion of abnormalities reported in NCCT and CECT scans ($p = 0.5986$).

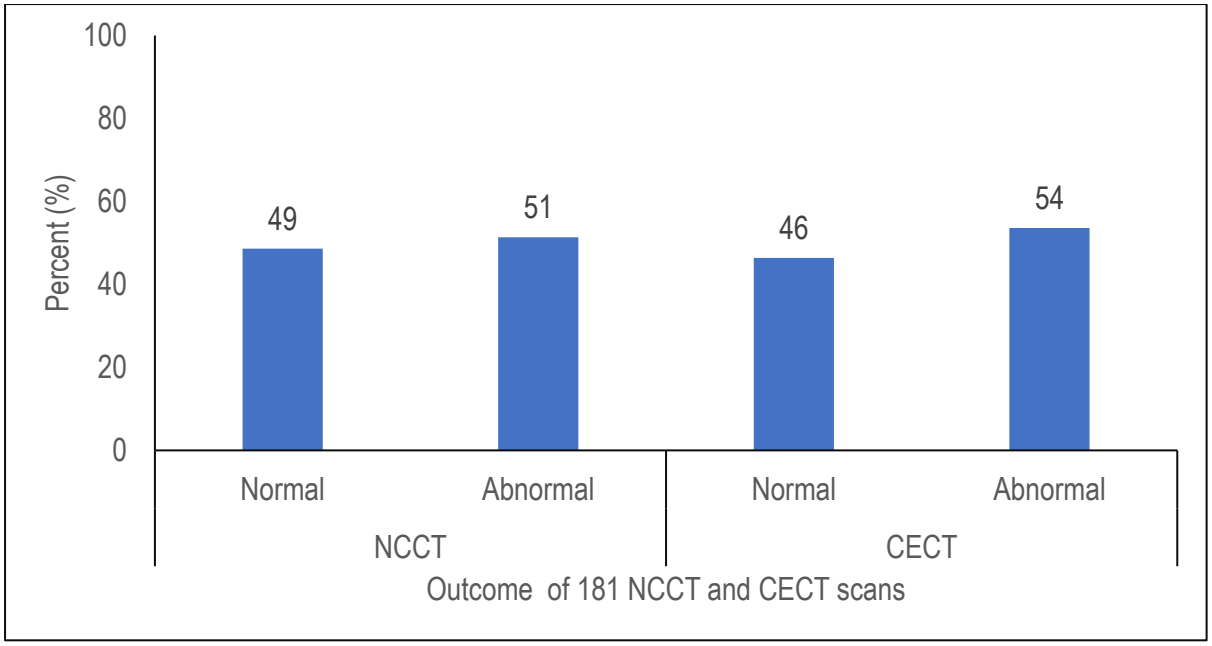

Figure 4. 2: Scan Results

Table 4. 2: Distribution of indications for normal and abnormal NCCT scan

	TOTAL	Normal NCCT		Abnormal NCCT	
		No	%	No	%
Seizure	34	23	67.6	11	32.4
Unilateral motor deficit	31	4	12.9	27	87.1
Headache	25	19	76.0	6	24.0
Visual impairment	22	15	68.2	9	40.9
Psychosis	9	4	44.4	5	55.6
Confusion	7	3	42.9	4	57.1
Meningitis	7	4	57.1	3	42.9
Cranial nerve palsy	6	5	83.3	1	16.7
Neurodevelopmental delay	4	2	50.0	2	50.0
Cognitive decline	2	1	50.0	1	50.0
Ataxia	1			1	100.0
Organophosphate poisoning	1	1	100.0		
paraparesis	1	1	100.0		
Allergic conjunctivitis	1	1	100.0		
Macrocephaly	1			1	100.0
Neonatal encephalopathy	1			1	100.0
Unknown (no retrievable data)	26	5	19.2	21	80.8

In Table 4.2, out of the 34 cases identified as seizures, the majority (67.6%) displayed normal findings on the non-contrasted computed tomography (NCCT) scans, while a minority (32.4%) showed abnormal results. Furthermore, the data revealed that most cases of headaches (76.0%) and visual impairments (68.2%) also presented with normal NCCT results. In contrast, a significant majority of cases with unilateral motor deficits (87.1%) exhibited abnormal findings on the NCCT scans.

4.4 Prevalence of abnormalities that are only detectable on Contrast-Enhanced Computed Tomography (CECT)

The study focused on the incidence of missed pathology in non-contrast computed tomography (NCCT) within a cohort of 181 cases, despite the lack of documented clinical indications in 26 of those cases (see Table 4.3). Out of the 181 NCCT scans, 88 were initially classified as normal. However, contrast-enhanced computed tomography (CECT) scans later identified 4 of these as abnormal. Additionally, 93 cases that were deemed abnormal by NCCT scans were confirmed as such by CECT scans, resulting in a total of 97 true positive cases.

Table 4. 3: NCCT and CECT outcome cross tabulation

		CECT		**Total**
		Normal	**Abnormal**	
NCCT	Normal	84	4	88
	Abnormal	0	93	93
	Total	84	97	181

Pearson Chi-Square: 165,7; p<0.001
Kappa statistics: 0.945; p<0.001

The Chi-square test of independence was utilized to assess the association between various NCCT and CECT, revealing a p-value of less than 0.05. This indicates a statistically significant relationship between the two modalities. The sensitivity was 100% (84/84) and specificity was 95.9% (93/97).

The Kappa statistic, which is frequently used in statistics to measure inter-rater reliability or the consistency of two clinical diagnostic methods, was used to evaluate the agreement between the two methods. A score that represents the degree of agreement above and beyond what would be predicted by chance is produced by this statistic. The Kappa agreement between the two methods of 0.945 was discovered in this investigation, indicating nearly perfect concordance between the methodologies.

4.5 Demographic characteristics of the participants

Brains scans of 181 patients who underwent computed tomographic imaging of the brain during the period of the study were sampled. Their mean age was 41.2 years with a standard deviation of 23.0 ranging from 14 weeks to 121 years. The majority (65.7%) of the study participants were 50 years and younger (**Figure 4.3**).

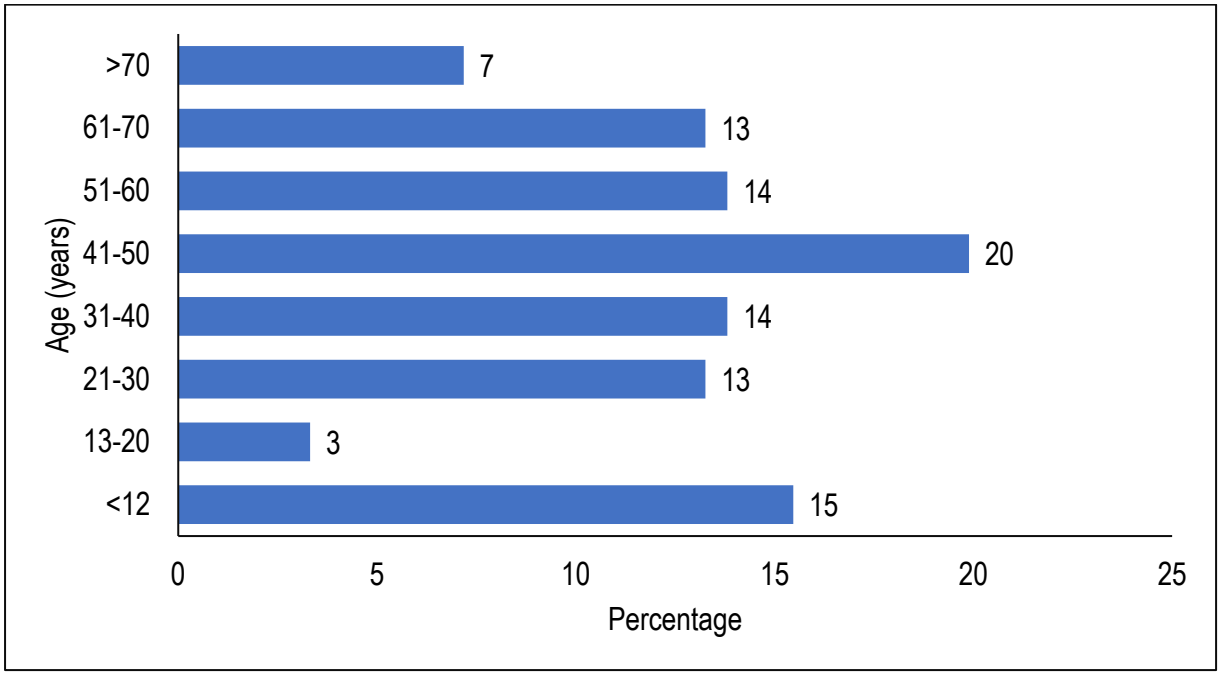

Figure 4. 3: Age distribution of the participants

The participant group comprised slightly more males than females, with males at 51.4% and females at 48.6% (Figure 4.3).

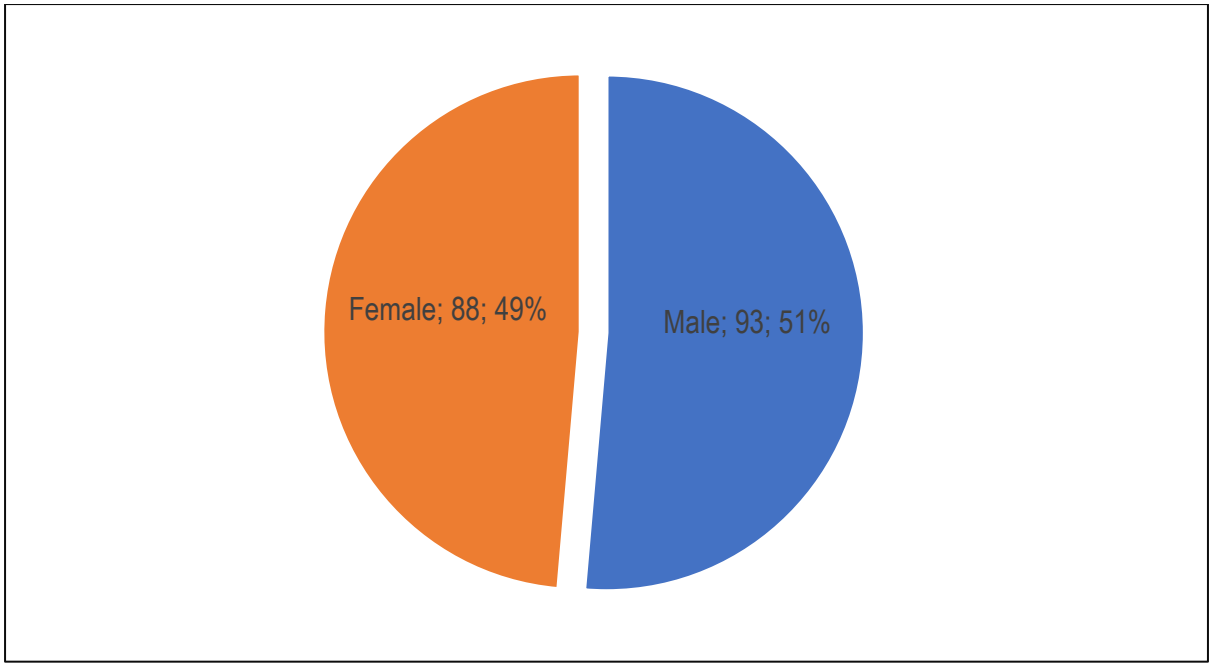

Figure 4. 4: Sex distribution of the participants

The comparison of ages between males and females shows that females were slightly older than males; however, this difference was not statistically significant (41.7±24.0 compared to 40.1±22.8, p=0.646).

4.6 Number of normal NCCT brain scans that revealed pathology after contrast administration(CECT).

The table below displays the age, sex, and indications for the four scans initially classified as normal by Non-Contrast Computed Tomography (NCCT) but later reclassified as abnormal by Contrast-Enhanced Computed Tomography (CECT).

Table 4. 4: Patients whose scans have been reclassified

PI	Age	Sex	Indications
1	0-month	F	• Congenital blindness
2	6 yrs	F	• Seizures (status epilepticus) • Fever with GCS of 8/15
3	30 yrs	F	• Known with Bipolar mood disorder and Retroviral Disease • Presented with fever and confusion (GCS 14/15)
4	40 yrs	F	• Known with Retroviral Disease, • Presented with fever, vomiting and signs of meningeal irritation.

4.7 Conclusion

This chapter presents the findings of the study, which will be discussed and compared with relevant literature in the following chapter. In summary, out of 181 scans, 88 (48.6%) showed no abnormalities before contrast injection (NCCT), while 93 (51.4%) exhibited pathological findings. Following contrast injection (CECT), an additional 4 scans (2.2%) revealed pathologies that were not detected on the NCCT, underscoring the significance of contrast in reducing false negatives. The most common reason for conducting a brain CT scan in patients with an initially normal non-contrast CT (NCCT) was seizures.

Importantly, all NCCT scans that identified pathology remained positive after the contrast was administered, resulting in no false positives. The rate of missed pathology on NCCT was 2.21% (4 out of 181). The study indicates that the use of contrast typically did not change the diagnosis from a normal NCCT brain scan. Given the low prevalence of missed pathology on NCCT (2.21%), it suggests that contrast enhancement may not be necessary for most patients with an initially normal NCCT result and therefore we fail to reject the null hypothesis.

CHAPTER 5: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1. Introduction

Chapter 5 discusses the research findings from Chapter 4, integrating them with the existing body of knowledge in the field. This chapter explores the study's contributions to the development of brain CT imaging protocols, revealing key implications for future research and clinical practice.

Furthermore, it provides evidence-based recommendations for enhancing current practices at Mankweng Hospital, while also acknowledging and addressing the study's limitations, thus offering a comprehensive, multifaceted perspective.

5.2 Brain CT scans performed for non-traumatic indications

Brain CT scans represent a significant portion of all CT imaging performed in various medical institutions. Their importance in clinical settings is highlighted by their utility in diagnosing a wide range of conditions, from head injuries to incidental psychiatric findings. This investigation aimed to determine the overall number of brain CT scans conducted for non-traumatic reasons.

During the study period at this rural hospital, brain scans accounted for 38.9% (637 out of 1,732) of all imaging procedures. The majority of these scans (80.8%) were performed for non-traumatic purposes, while 13.8% were for trauma-related issues, 3.5% were for orbital or facial tumours, and 1.7% were follow-up scans after cranial surgery. Among the total number of brain scans (n=515), 358 (69.5%) included both non-contrast CT (NCCT) and subsequent contrast-enhanced CT (CECT). Additionally, 149 (28.9%) scans were performed using only NCCT, and 8 (1.5%) scans were done using only CECT.

The brain scan rate observed in this study is slightly lower than the 49.5% reported at Groote Schuur Hospital in Cape Town, South Africa (Jacobs, 2017). These findings also contrast with the rates of 68% in Ghana (Jimah *et al*., 2022) and 83% in Australia (Maxwell *et al*., 2021). The absence of dedicated neurology and neurosurgery

departments at this institution likely contributes to the lower demand for brain imaging, explaining the notably smaller proportion of brain scans conducted in this study.

5.3 Demographic Characteristics

Gender: The demographic analysis reveals a nearly equal distribution of cases by sex, with 51.4% of cases being male and 48.6% female. Similar studies have indicated that gender trends are comparable, with men often being more prevalent (Jimah *et al*., 2022). However, some research has shown the opposite, reporting a higher number of females than males (Shuaib *et al*., 2015; Maxwell *et al*., 2021).

Age: The current study finds that the average age of participants is 41.2 years (±23), which is younger than the average age of 47 years (±29) reported in a study conducted in an emergency department in the USA between January 2008 and December 2010 (Shuaib *et al*., 2015). The age differences might be attributed to various factors that warrant further investigation.

5.4 Number of normal and abnormal NCCT brain scans

5.4.1 Proportion of normal and abnormal NCCT brain scans

Previous studies on brain CT imaging have often found that normal non-contrast computed tomography (NCCT) scans are common, even when clinical indications suggest otherwise (Ugwuanyi *et al*., 2020; Jacobs, 2017). For example, Shuaib *et al*. (2015) reported that 68% of NCCT scans were normal in a sample of 379 patients, while 32% showed abnormalities. In contrast, this study reveals a higher incidence of abnormalities at 51.4%, compared to 48.6% of normal NCCT scans. This difference may be due to several factors, such as variations in patient demographics, the timing of the scan in relation to symptom onset, or advancements in imaging technology that improve the detection of subtle abnormalities.

5.4.2 Indications associated with normal NCCT

Previous studies have identified common indications associated with normal non-contrast computed tomography (NCCT) findings. Wood *et al*. (1990) found that seizures, headaches, and focal neurological deficits were frequently associated with normal NCCT results. According to Branson *et al*. (2007), the needs and circumstances related to neuroimaging in children are specific. The indications for brain CT scans in the population differ from those in adults and include seizures, congenital malformations, suspected space-occupying lesions, and stroke. This study focuses on four primary indications: seizure, unilateral motor deficit, headache, and visual impairment.

In this study, we investigated the relationship between the primary presenting symptom and the NCCT outcome. The results showed that, except for cases involving patients with a unilateral motor deficit presenting with a headache, seizures and visual impairment frequently resulted in normal NCCT outcomes, with headaches showing the highest rate of normal findings. The following sections will provide an in-depth discussion of these indications.

Seizures: Seizures are a common reason for performing brain imaging in both urgent and planned situations. Out of 181 analysed scans in the current study, 34 (18.8%) had seizures as the primary reason for undergoing a brain CT scan. Among these cases, 23 (67.6%) were reported as having normal NCCT results. Notably, one patient had a shift in diagnosis from normal to abnormal on contrast-enhanced CT (CECT), indicating a false negative.

In their 1990 study, Wood *et al*. conducted a single-center investigation to assess the utility of CECT in detecting non-traumatic central nervous system diseases in an emergency department. They found that out of 322 scans analysed, seizures accounted for 109 (34%) of the images. Among these, 78 (71.6%) showed normal findings on NCCT.

A study conducted in South Africa (Stipp *et al*., 2004) explored the necessity of using contrast in normal NCCT scans for adult-onset seizures. The results revealed that all

scans were normal in NCCT, including those categorized as normal, non-causative age-related changes, and normal variants. Importantly, the study noted that the diagnosis did not change after contrast administration. Although conducted on scanners with more limited capabilities than current technology, these findings remain relevant, emphasizing the importance of careful patient selection and focused imaging approaches in neuroimaging. This is particularly significant as technological advancements continue to improve diagnostic accuracy.

Unilateral Motor Deficit: The American Heart Association recommends non-contrast computed tomography (NCCT) brain scans as the primary imaging method for evaluating patients suspected of having acute ischemic stroke (Powers *et al*., 2019). This recommendation is based on the accessibility and rapid acquisition of CT scans compared to MRI scans. Timely imaging is crucial for the prognosis and acute treatment of stroke patients. Strokes and other brain conditions may present as localized neurological impairments.

In a study by Ferro *et al*. (2022), it was found that 16% of the participants exhibited focal neurological deficits, with 25.9% showing normal NCCT results. A multi-center study conducted in Uganda investigated the relationship between clinical stroke diagnoses and brain CT findings in patients with unilateral neurological deficits. The most common finding in this study was ischemic stroke, identified in 45.9% of cases, while approximately one-third of the scans revealed either normal findings or other pathologies. Notably, normal CT results were reported in 33.3% of the cases (Vincent *et al*., 2023).

In contrast, the majority of cases with unilateral motor deficits (87.1%) in this study displayed abnormal findings on NCCT scans, while only a small percentage (12.9%) showed normal results. Importantly, the administration of contrast did not change any normal results to abnormal ones in this group. While both studies took place in developing countries, our study is limited to a single site, and it is important to note that this rural hospital lacks specialized neurology services.

***Headache*:** Headaches accounted for 25 cases (13.8%) of the sampled scans. Among these patients, 76% had normal outcomes, while 24% exhibited abnormal findings.

Notably, the use of contrast in these cases did not alter the diagnosis from normal to abnormal. Jimah *et al*. (2022) reported similar findings, with 62.1% of the NCCT group showing normal results among individuals experiencing headaches. Furthermore, a study by Rizk *et al*. (2013) found that 79.7% of 74 brain scans from individuals with headaches were normal. A review of these scans after contrast administration did not change the diagnosis. These results suggest that a normal NCCT may negate the need for a contrast-enhanced CT (CECT) brain scan in patients presenting with headaches.

Visual Impairment: Visual impairment had a relatively minor impact in other studies, accounting for only 2.4% of patients in research conducted by Wood *et al*. in 1990. In this study, visual impairment was responsible for 22 cases, constituting 12.2% of the overall sample. Among these cases, 68% exhibited normal results on NCCT scans, and none of the regular scans in this group were classified as abnormal after subsequent CECT. The higher proportion of visual impairment cases in our study may be attributed to the inclusion of scans ordered by the ophthalmology department and the limited availability of MRI, which is the preferred imaging method for patients with visual abnormalities (Kennedy *et al*., 2018).

5.5 Prevalence of abnormalities that are only detectable on CECT

Multiple studies indicate a low prevalence of missed pathology in Contrast-Enhanced Computed Tomography (CECT). In a study by Shuaib *et al*. (2013), it was reported that out of 261 normal Non-Contrast Computed Tomography (NCCT) scans, only one displayed abnormal findings on CECT, resulting in a false-negative rate of 0.26%. Similarly, Chishti *et al*. (2003) found that the prevalence of missed pathology in NCCT was 0.2%, with only one abnormality detected in 496 CECT scans among patients who exhibited no clinical focal signs and had normal NCCT results.

Branson *et al*. (2007) indicated that the prevalence of missed pathology in paediatric patients is modest, at approximately 2.7%. The current study found that the prevalence of missed pathology on NCCT stands at 2.2%. These findings suggest that CECT may

be unnecessary in many cases. Considering the potential risks associated with contrast administration, such as allergic reactions and nephrotoxicity, along with increased institutional costs and added pressure on radiologists, the evidence implies that NCCT may be sufficient for diagnostic purposes, reserving CECT for specific scenarios where the benefits outweigh the risks.

In this study, CECT scan identified meningitis as the undetected condition in four cases that presented normal findings on NCCT. Previous research has indicated that certain conditions, including meningitis, dural venous thrombus, vascular malformations, dural lesions, pituitary lesions, neurocysticercosis, and enhancing nodules, may not be detected on NCCT scans (Minnie *et al*., 2014; Shuaib *et al*., 2014; Wood *et al*., 1990). The study by Minne' and colleagues in 2014 recorded the highest number of disease categories, showcasing varying levels of variability, which could be attributed to the use of larger cohorts and multi-centre settings.

In this investigation, it was found that if the CECT phase had been omitted, four scans (Group C) showing simple meningitis would have remained undetected. In cases of meningitis, cranial imaging, particularly cranial CT scan, is essential for identifying contraindications for lumbar puncture (LP). This is critically important in patients at risk of complications, such as brain herniation. Complications suspected often include space-occupying lesions (e.g., brain abscess, empyema), brain edema, or hydrocephalus, especially in individuals experiencing neurological deficits, seizures, or altered states of consciousness (Nagra., Wee., Short., and Banerjee., 2011).

Upon reviewing medical records, it was noted that three patients in Group C displayed symptoms indicative of meningitis. Notably, one of these cases had confirmed LP results of meningitis prior to undergoing a brain CT scan, which was performed to evaluate potential complications. The other two patients exhibited concerning clinical symptoms experiencing convulsions and a decreased state of consciousness strongly suggesting possible contraindications for lumbar puncture.

The fourth case in Group C involved a newborn who was diagnosed with congenital blindness, which was the reason for the scan. There was no documented evidence of clinical suspicion of meningitis or any history of sexually transmitted illnesses during

the mother's prenatal period that could have raised concerns. This case highlights how Contrast-Enhanced Computed Tomography (CECT) can uncover unexpected pathologies that may not be identified through clinical examination alone.

While certain complications of meningitis can be seen on Non-Contrast Computed Tomography (NCCT), CECT is typically not necessary for diagnosis. Instead, CECT is used to analyze and specify anomalies, as well as to narrow down potential causes. In this instance, the diagnosis of meningitis was confirmed using CECT. However, it is essential to recognize that a lumbar puncture (LP), rather than CECT, is the definitive method for detecting meningitis (Nagra *et al*, 2011).

Conversely, a recent study conducted in India (De Sauza *et al*., 2013) found that NCCT is not as effective as CECT at identifying individual Neurocysticercosis lesions in patients aged 6 to 52 who are experiencing new-onset seizures. This study revealed that out of 86 individuals with a single lesion identified on CECT, 30 had no abnormalities when their NCCT scans were retrospectively analysed. The investigation noted an undetected Neurocysticercosis occurrence of 4.16% among a total sample size of over 701 individuals. In Group C of the current study, there were no missed diagnoses of Neurocysticercosis. This likely results from differences in study settings, populations, and sample sizes, as well as a low incidence of Neurocysticercosis in the Limpopo province. Therefore, the results of the present investigation cannot be generalized to regions with a high prevalence of Neurocysticercosis, emphasizing the importance of local disease prevalence and diagnostic techniques.

Additionally, senior registrars and an attending general radiologist conducted an analysis of a randomly selected set of pre-existing brain CT scans that included both NCCT and CECT components, as described in Chapter 3. Each registrar assessed the NCCT and CECT scans of patients in sequence. The training approach at Mankweng Hospital typically involves radiologists verifying scans read by registrars.

An expert radiologist reviewed the scans in Groups A, B, and C and reclassified a patient with a meningioma from Group C to Group A. Initially, a registrar had reported that the NCCT scan appeared normal, while the CECT revealed an actively enhancing

meningioma. This finding indicated that the lesion had a density similar to that of brain tissue on NCCT and lacked calcifications. However, the radiologist's careful observation identified hyperostosis of the adjacent bone, a distinctive feature of meningiomas that can be seen in bone window settings. This case illustrates the potential for errors in diagnostic imaging resulting from various factors, including human and technical limitations such as interruptions, fatigue, insufficient clinical data, and the phenomenon known as "satisfaction of search," where findings lead to premature conclusions that overlook other potential findings. This underscores the critical importance of expertise in image interpretation to minimize these errors.

5.6 Conclusion

In conclusion, brain scans accounted for 38.9% of all the cases scanned during the study period, with 51.4% of those being male and middle-aged. Abnormalities were detected on non-contrast computed tomography (NCCT) in 51.4% of patients and on contrast-enhanced computed tomography (CECT) in 54.1% of cases. The typical symptoms observed prior to classification using NCCT and CECT included seizures, hemiplegia, headaches, and visual abnormalities. Except for patients with hemiplegia, individuals experiencing headaches, seizures, and visual impairments often showed normal results on NCCT scans. The incidence of undetected abnormalities on NCCT was 4 cases (2.2%), affecting two female children and two female adults.

Brain CT imaging is a crucial diagnostic tool for evaluating brain and intracranial abnormalities in cases of central nervous system illnesses. Regardless of age and gender, it is common to find normal CT results, irrespective of the specific reasons for the examination. The study establishes that NCCT is a reliable method for identifying a range of conditions, including infarcts, hemorrhage, tumours, congenital abnormalities, midline displacement, and hydrocephalus.

Among the 88 patients with normal NCCT scans, follow-up CECT scans detected meningeal enhancement in four cases. However, this did not lead to significant changes in patient management. This finding supports existing research and confirms that CECT rarely yields substantial results when a prior NCCT scan is normal. Additionally, it promotes the judicious use of contrast-enhanced imaging, evidence-

based service delivery, and patient care, thereby aiding in cost reduction and time savings. These objectives can be achieved when radiologists are diligent and committed to carefully evaluating risks and benefits while adhering to the ALARA (As Low As Reasonably Achievable) principle.

5.7. Recommendations

This study's findings lead to the following recommendations:

Radiologists should conduct a thorough analysis of all non-contrast computed tomography (NCCT) images to accurately identify those that fall within the normal range. This comprehensive examination ensures precise problem detection and effective management.

Once normal scans are identified, the use of contrast should be reserved for specific cases based on the patient's individual circumstances and clinical indications. This approach is intended to justify the administration of contrast and minimize repeated radiation exposure. A previous study by Novoa, Santos, Silva, Jurado & Del (2020) supports this recommendation.

For patients who are clinically suspected of having complicated meningitis, a contrast-enhanced computed tomography (CECT) scan may not be necessary if the NCCT appears normal.

Future research should investigate the correlation between abnormal NCCT and abnormal CECT results, as well as evaluate the effects of contrast administration on diagnosis and management plans. These studies could provide valuable insights for improving CT imaging protocols and enhancing patient outcomes.

5.8. Contribution of the Study

The findings of this investigation align with the conclusions of previous studies, indicating that administering contrast after a normal non-contrast computed tomography (NCCT) scan is usually not beneficial. Therefore, in most cases, the use of contrast may be unnecessary after obtaining a normal NCCT scan. This approach can reduce costs related to consumables and the time needed for scanning and interpreting the results.

Delivering intravenous (IV) contrast requires various consumables, such as IV needles, alcohol wipes, and strapping materials, all of which significantly increase costs. Additionally, using contrast may lead to extra expenses related to managing adverse reactions, which in critical situations could necessitate resuscitation, hospitalization, or even dialysis. These factors collectively add to the overall financial burden of administering contrast.

Time is another important variable, that can be easily overlooked. Saving time through efficient contrast administration can boost productivity, leading to quicker reporting and a greater capacity for patients in CT scanning schedules. This optimization enhances resource allocation and workflow.

Minimizing the harmful effects of radiation is crucial, particularly by reducing the radiation dosage through the elimination of repeated patient exposure during contrast-enhanced CT (CECT) imaging. This practice aligns with the internationally accepted ALARA (as low as reasonably achievable) principle, which aims to optimize radiation protection by minimizing exposure to ionizing radiation to the lowest feasible level.

5.9. Limitation of the study

This study has several limitations. It was conducted at a single healthcare facility, which means that the findings may not be applicable to other facilities in South Africa. Since the study was retrospective, standardization of various variables was not possible. In particular, the concentration, rate of injection, and doses of the intravenous contrast varied among individuals.

Additionally, the time between contrast injection and the acquisition of the CECT scan was not standardized because hand injection was used. However, there is no significant impact on the pattern of enhancement if images are acquired immediately after the healthcare professional administering the contrast leaves the scan room.

In diagnostic radiology, interpretation errors cannot be completely eliminated. In this study, each reader only reviewed a subset of the scans assigned to them, which were later verified by a radiologist. Ideally, having all observers review all scans would have provided a more reliable estimation of inter-observer agreement metrics. However, this "fully crossed design" could have negatively affected daily workflow due to the heavy reading burden it would impose. As a result, an incomplete block design (with multiple observers, each reporting their own scans) was utilized due to the limited number and availability of experts.

At the time of data collection, the radiologist involved in the study was the only specialist employed at the study site. This could have introduced bias into the consensus diagnosis, as most observers were registrars, and the opinion of the sole senior radiologist may have dominated, potentially leading to an underestimation of disagreements.

In imaging studies, the gold standard typically involves a reference test an imaging modality with better diagnostic capabilities than the one under investigation or a histological diagnosis. However, these options are not always practical. Applying a reference test like MRI would have been challenging, if not impossible, in this retrospective study due to limited availability of MRI scans and prolonged waiting times. This could compromise diagnostic accuracy due to potential disease progression or improvement over time. Such constraints hindered the ability to use a reference test to validate the CT scan results, introducing a potential limitation to the study's diagnostic accuracy. Nevertheless, this limitation is somewhat mitigated because the primary aim of the study was to investigate the diagnostic value of contrast administration after a normal brain NCCT scan using CT scan data, rather than evaluating the CT scan's overall performance.

Out of the 181 evaluated scans, clinical records could not be retrieved for 26 of them, which represents 14.7% of the total. This significantly impacts the ability to capture the complete range of scan indications. However, this missing data does not influence the statistical outcomes (i.e., Kappa statistics for agreement) of the results, as the observers were blinded to clinical information and prior reports

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SECTION 8: LIST OF ANNEXURES

ANNEXURE 1: Kendall and Smith random number table

Sixty-first Thousand

	1–4	5–8	9–12	13–16	17–20	21–24	25–28	29–32	33–36	37–40
1	08 09	25 21	56 40	11 11	51 36	16 01	86 16	87 48	34 79	45 50
2	85 70	47 73	56 80	45 73	25 15	65 95	49 64	68 70	24 62	44 06
3	77 02	55 10	00 62	96 32	54 43	59 23	72 98	90 62	95 31	79 78
4	48 05	67 10	19 58	16 39	14 47	81 46	10 05	35 84	96 86	37 72
5	58 41	33 33	72 25	83 26	46 56	07 53	22 87	19 39	64 54	85 73
6	75 77	09 84	29 21	25 60	27 25	97 30	95 35	00 72	84 29	72 79
7	11 63	40 75	46 41	83 98	66 49	12 28	59 21	07 13	81 67	91 06
8	90 39	26 05	98 89	59 65	31 51	05 18	07 40	38 52	99 74	07 83
9	62 09	35 63	44 60	60 54	75 59	03 70	55 00	24 45	00 04	36 41
10	07 99	77 21	47 72	90 58	71 75	13 28	79 44	53 05	31 76	89 51
11	63 44	48 76	85 78	83 78	41 61	55 62	69 77	04 53	06 31	53 53
12	55 01	49 46	60 61	56 87	57 86	38 70	26 50	24 13	36 68	87 68
13	00 20	31 46	29 62	86 79	00 48	06 48	03 78	93 16	66 54	45 68
14	92 27	23 00	67 18	69 52	06 17	63 55	82 95	08 80	85 42	43 51
15	86 83	98 89	69 58	20 30	18 89	69 89	06 55	08 36	05 18	71 05
16	86 07	68 18	42 52	31 65	29 34	49 66	83 13	03 39	37 24	97 79
17	31 13	97 47	94 37	70 49	63 44	41 40	05 01	04 13	62 02	09 17
18	97 31	60 25	87 60	46 13	17 92	33 23	05 43	83 13	15 58	68 84
19	63 21	01 69	56 97	71 18	62 04	91 11	63 89	44 56	92 93	96 62
20	32 99	29 35	83 10	77 30	82 01	60 91	40 44	24 14	51 84	79 51
21	37 16	00 68	25 67	15 20	98 41	86 70	98 77	30 07	61 31	95 69
22	96 15	51 68	08 31	45 39	18 88	91 75	03 62	94 25	12 57	72 47
23	86 56	84 96	34 17	75 83	20 55	16 93	92 97	08 05	87 72	35 12
24	33 34	22 49	72 00	91 03	10 37	16 23	43 61	84 52	13 14	28 23
25	33 00	67 08	80 45	79 47	65 10	30 63	90 12	44 22	59 86	46 37

Sixty-second Thousand

	1–4	5–8	9–12	13–16	17–20	21–24	25–28	29–32	33–36	37–40
1	91 67	62 06	42 72	16 53	66 11	78 01	63 33	19 35	06 08	34 20
2	35 91	74 75	57 68	82 44	77 01	63 27	07 35	19 78	01 04	28 35
3	86 48	35 21	23 53	89 89	89 37	84 93	10 34	74 87	79 80	33 45
4	11 68	06 59	15 16	10 66	46 02	54 09	80 02	88 23	93 15	09 87
5	97 53	76 74	26 39	72 47	72 64	65 60	50 36	16 62	17 82	88 77
6	68 94	97 81	43 60	63 00	29 99	46 71	78 56	33 23	36 28	68 36
7	99 97	14 22	43 39	30 93	07 11	18 28	08 68	37 57	58 58	32 55
8	53 73	58 60	17 11	91 35	90 93	04 50	47 46	31 50	94 48	68 24
9	98 52	87 22	64 88	98 05	02 90	78 69	74 48	05 36	08 11	56 03
10	54 51	99 66	09 42	35 50	44 83	43 77	75 13	44 23	53 63	27 89
11	62 54	12 49	87 32	79 15	22 01	31 15	64 27	54 02	48 09	20 34
12	18 93	09 83	28 29	05 07	09 48	52 41	70 87	85 92	06 44	14 75
13	13 60	47 66	18 93	97 10	01 31	77 29	90 68	43 93	09 32	10 75
14	42 03	19 31	74 16	25 60	69 26	58 91	27 12	13 04	69 44	27 12
15	01 09	88 42	48 67	81 53	83 50	42 30	46 18	27 24	06 91	49 22
16	43 65	18 87	12 29	27 70	32 03	61 13	02 16	66 29	05 29	59 38
17	36 01	79 98	54 30	96 44	57 37	29 20	32 29	46 22	67 67	28 89
18	38 56	48 18	41 73	27 63	70 90	44 99	28 44	57 82	89 29	92 64
19	00 63	85 50	92 11	66 57	65 93	35 32	13 96	77 92	39 71	30 60
20	07 01	87 09	12 52	85 18	31 65	08 63	13 76	28 02	41 76	83 38
21	57 59	42 87	02 78	68 60	83 94	37 45	60 07	46 30	21 66	42 50
22	85 66	04 86	77 69	50 78	27 37	66 05	77 23	02 97	73 10	87 13
23	18 38	06 89	49 06	41 34	25 05	78 91	07 69	01 76	74 28	05 72
24	72 73	09 49	64 11	61 87	40 79	47 74	68 80	49 92	16 27	63 20
25	97 63	55 80	34 49	20 14	23 65	77 56	98 42	22 22	02 86	44 91

Source: Fagg and Smalley (2018), as adapted from Kendall and Barington (1971)

ANNEXURE 2: Data collection form

STUDY NUMBER:
Section A: Demographics
A1: Age

A2: Gender

M	F

A3: Clinical information

Clinical information

Section B: Radiological findings
B1

	NECT			CECT		
Pathology	**yes**	**No**	**equivocal**	**Yes**	**No**	**equivocal**

B2. Specify pathology (Final diagnosis)

Observer: registrar/radiologist *(circle)*

ANNEXURE 3: Results by consensus

STUDY NO	AGE	GENDER	Registrar NCCT	REGISTRAR CECT	CONSENSUS NCCT	CONSENSUS CECT	FINAL DIAGNOSIS
3	34	Male	Equivocal	Abnormal	Abnormal	Abnormal	PRES
17	65	Male	Equivocal	normal	Normal	Normal	Normal
34	49	Male	Equivocal	normal	Normal	Normal	Normal
52	31	Male	Equivocal	Normal	Normal	Normal	Normal
67	87	Female	Normal	Equivocal	Normal	Normal	Normal
84	71	Male	Equivocal	Equivocal	Normal	Normal	Normal(age related atrophy)
147	26	Female	Equivocal	Abnormal	Abnormal	Abnormal	Abnormal
163	23	Male	Equivocal	Normal	Normal	Normal	Normal
174	0	Male	Normal	Equivocal	Normal	Abnormal	Meningitis
179	42	Male	Normal	Equivocal	Normal	Normal	Normal

ANNEXURE 4: Diagnosis Outcome (Group A)

DIAGNOSIS	TOTAL number
brain atrophy(not age appropriate)	8: **1 also had intra-axial calcifications
Intraaxial calcifications	4
Infarcts	37
Extra-axial collections	7
Intraaxial hemorrhage	1
Extra-axial neoplasm	9: choroid plexus tumour(1) , pituitary macroadenoma(3), meningioma (4) and pineal gland tumour (1)
Intra-axial lesions	9: cystic (1), soft tissue (6), multiple rim-enhancing lesions (2) need MRI (infective versus neoplastic) ** 1 also had infarct
infection	10 (complicated meningitis(9), subdural empyema(1).
White matter disease	10
Congenital malformations	1
Brain oedema(vasogenic)	2

ANNEXURE 5: Ethics Clearance Certificate

University of Limpopo
Department of Research Administration and Development
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 3935, Fax: (015) 268 2306, Email: tukiso.sewapa@ul.ac.za

TURFLOOP RESEARCH ETHICS COMMITTEE

ETHICAL CLEARANCE CERTIFICATE

DATE: 18 June 2024

PROJECT NUMBER: TREC/548/2022: PG-Renewed

PROJECT:

Title: The diagnostic value of contrast administration following normal non-contrast brain computed tomography in Mankweng Hospital.
Researcher: RQ Sibiya
Supervisor: Dr N. Muambadzi
Co-Supervisor/s: Dr F. Ooko
Dr S.F Sithole
School: Medicine
Degree: Master of Medicine in Diagnostic Radiology

PROF D MAPOSA
CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE

The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council, Registration Number: **REC-0310111-031**

Note:
i) **This Ethics Clearance Certificate will be valid for one (1) year, as from the abovementioned date. Application for annual renewal (or annual review) need to be received by TREC one month before lapse of this period.**
ii) **Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee, together with the Application for Amendment form.**
iii) **PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.**

Finding solutions for Africa

ANNEXURE 6: Permission from Limpopo Department of health

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF
HEALTH

Ref : LP_2022-11-015
Enquires : Ms PF Mahlokwane
Tel : 015-293 6028
Email : Phoebe.Mahlokwane@dhsd.limpopo.gov.za

Rivalani Queen Sibiya

PERMISSION TO CONDUCT RESEARCH IN DEPARTMENTAL FACILITIES

Your Study Topic as indicated below;

THE DIAGNOSTIC VALUE OF CONTRAST ADMINISTRATION FOLLOWING NORMAL NON-CONTRAST BRAIN COMPUTED TOMOGRAPHY IN MANKWENG HOSPITAL

1. Permission to conduct research study as per your research proposal is hereby Granted.
2. Kindly note the following:
   a. Present this letter of permission to the Office Clinical Executive Director a week before the study is conducted.
   b. This permission is **ONLY** for **Mankweng Hospital**
   c. In the course of your study, there should be no action that disrupts the routine services, or incur any cost on the Department.
   d. After completion of study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
   e. The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
   f. **The approval is only valid for a 1-year period.**
   g. If the proposal has been amended, a new approval should be sought from the Department of Health
   h. Kindly note that, the Department can withdraw the approval at any time.

Your cooperation will be highly appreciated

12/12/2022

Head of Department **Date**

pp

Private Bag X9302, Polokwane
Fidel Castro Ruz House, 18 College Street, Polokwane 0700. Tel: 015-293 6000/12. Fax: 015 293 6211.
Website: http/www.limpopo.gov.za

The heartland of Southern Africa – Development is about people!

ANNEXURE 7: Permission from Mankweng Hospital CEO

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH
MANKWENG HOSPITAL

Ref: S5/3/1/2
Enq: Modula MC
Tel: 015 286 1042/1022
Email:Motlatso.Modula@dhsd.limpopo.gov.za
From: HR Training and Development

TO: Dr Sibiya RQ

REQUEST FOR PERMISSION TO CONDUCT RESEARCH AT MANKWENG HOSPITAL

1. The above matter has reference.
2. This is to confirm that the CEO has granted you permission to conduct research on **"THE DIAGNOSTIC VALUE OF CONTRAST ADMINISTRATION FOLLOWING NORMAL NON-CONTRAST BRAIN COMPUTED TOMOGRAPHY IN MANKWENG HOSPITAL"**
3. We wish you all the best with your research.

Yours in service delivery

pp _____ 01 / 03 / 2023
Director: Corporate Services Date
Mr. Sibuyi MV

_____ 01 / 03 / 2023
Acting Chief Executive Officer Date
Dr. Muila SL

Private Bag X1117, SOVENGA, 0727 Tel: 015 286 1000 Fax: 015 267 0206
Houtbos Road, Sovenga
The heartland of Southern Africa – development is about people!

ANNEXURE 8: Language editing confirmation letter of support

LETTER OF SUPPORT SERVICES

Date: 11 / 11 /2024

This letter is to confirm that the student, RIVALANI QUEEN SIBIYA, studying at the **UNIVERSITY OF LIMPOPO**, discussed the project with the title "**THE DIAGNOSTIC VALUE OF CONTRAST ADMINISTRATION FOLLOWING NORMAL NON-CONTRAST BRAIN COMPUTED TOMOGRAPHY IN MANKWENG HOSPITAL**" with me.

Lr Research & Data Analysis Consulting confirms that the following support services were provided for this study:

- Language editing of the research report.

We assure that the research report and all information contained within it will be treated with the utmost confidentiality. This information will not be used for any purpose other than to fulfill the services requested.

Name: Ms. Livhuwani Mphaphuli Nedzingahe
Designation: Research consultant & Statistician
Company details: Lr Research & Data Analysis Consulting (PTY) Ltd

Signature

Date 11/01/2024