

**APPLICATION OF DIFFUSION WEIGHTED MAGNETIC
RESONANCE IMAGING (MRI) OF THE BRAIN AT THE
KENYATTA NATIONAL HOSPITAL**

DISSERTATION

**TO BE SUBMITTED IN PART
FULFILMENT FOR THE DEGREE OF MASTER OF MEDICINE IN
DIAGNOSTIC IMAGING AND RADIATION MEDICINE,
UNIVERSITY OF NAIROBI**

BY

DR MBURU ROBERT NJENGA

**DEPARTMENT OF DIAGNOSTIC IMAGING AND RADIATION
MEDICINE**

UNIVERSITY OF NAIROBI

University of NAIROBI Library



0467112 9

**UNIVERSITY OF NAIROBI
MEDICAL LIBRARY**

1.0 Acknowledgement


First and foremost I wish to express my sincere gratitude to my supervisors Dr. Alfred Odhiambo, Fellow in Neuroradiology, and a Senior lecturer at the University of Nairobi and Dr. Nyabanda Rose, MRI specialist at Kenyatta National Hospital whose encouragement and guidance made it possible for this dissertation to be written.

I am greatly indebted to my colleagues for their enthusiasm; constructive criticism especially with introduction of this new imaging modality. Understanding of this new imaging modality continues as days pass by.

I also extend deep gratitude to the radiographers at the Kenyatta National Hospital who have ensured performance of this imaging technique. This is in particular to the ones working in the MRI room.

2.0 Declaration

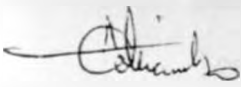
I Dr Mburu Robert Njenga declare that the work contained herein is my original idea and has not been presented at any other place to the best of my knowledge.

Signature..........Date.....7/8/2007.....

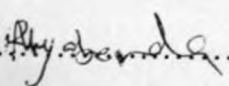
3.0 Approval by supervisors

This research dissertation has been submitted with our approval as university supervisors.

Dr. Alfred Odhiambo, MBChB, MMED (NBI), Fellow;
Neuroradiology, Senior lecturer, Department of Diagnostic Imaging
and Radiation Medicine University of Nairobi.

Signature..........Date.....11/8/2007.....

Dr. Nyabanda Rose
MBChB, MMED (NBI), MRI specialist,
Kenyatta National Hospital.

Signature..........Date.....6/8/07.....

4.0 ABBREVIATIONS

ADC	:	Apparent Diffusion Coefficient
CSF	:	Cerebral Spinal Fluid
CT	:	Computed Tomography
DTI	:	Diffusion Tensor Imaging
DW	:	Diffusion Weighted
DWI	:	Diffusion Weighted Imaging
FLAIR	:	Fluid Attenuation Inversion Recovery
KNH	:	Kenyatta National Hospital
Kshs	:	Kenya Shillings.
MRI	:	Magnetic Resonance Imaging
MS	:	Microsoft office
PROACT II	:	Phase II randomised trial of recombinant pro-urokinase by direct arterial delivery in acute middle cerebral artery stroke
SO	:	Signal without diffusion
SPSS	:	Statistical Package for Social Scientists
T	:	Tesla
T2WI	:	T2 weighted Imaging
T1WI	:	T1 Weighted Imaging
Turbo STEAM:		high speed stimulated echo pulse sequence
US	:	United states

1.0 Acknowledgement.....	ii
2.0 Declaration.....	iii
3.0 Approval by supervisor.....	iii
4.0 Abbreviations.....	iv
5.0 Table of contents.....	v
6.0 Abstract.....	vi
7.0 Literature review.....	1
7.1 Diffusion imaging.....	1
7.2 Studies on stroke imaging.....	3
7.3 Conventional imaging in ischaemic stroke.....	5
7.4 Acute stroke imaging using DWI.....	7
7.5 Other causes of positive DWI.....	9
7.6 Perfusion weighted imaging.....	10
7.7 Diffusion perfusion mismatch.....	11
7.8 Diffusion tensor imaging.....	11
7.9 Disadvantages of DWI.....	11
7.10 Conclusion.....	12
8.0 Objectives.....	12
8.1 Broad objectives.....	12
8.2 Specific objectives.....	12
9.0 Justification.....	12
10.0 Research question.....	13
11.0 Method and materials.....	13
11.1 Imaging techniques.....	13
11.2 Study design.....	13
11.3 Study area.....	14
11.4 Study population.....	14
11.5 Sample size justification.....	14
11.6 Sampling methods.....	15
11.7 Inclusion criteria.....	15
11.8 Exclusion criteria.....	15
12.0 Data management.....	15
12.1 Data collection.....	15
12.2 Data analysis.....	16

13.0 Ethical consideration.....	17
14.0 Results.....	18
15.0 DWI & ADC descriptions of the cases.....	25
16.0 Discussion.....	26
17.0 Conclusion.....	28
18.0 Recommendation.....	30
19.0 Figures.....	31
20.0 Appendix 1.....	43
21.0 Appendix 2.....	45
22.0 References	46

LIST OF TABLES

Table14.1 (clinically suspected disease).....	21
Table 14.2(MRI lesion description).....	22
Table 14.3(infarcts).....	23
Table 14.4(site of infarct).....	23
Table 14.5(analysis of all cases).....	24

FIGURES

Figure 14.1: Age distribution (n=165).....	18
Figure 14.2: Sex distribution (n=165).....	19
Figure 14.3 Presenting complaints of the patients (n=165).....	20
Figure 19.0 Images.....	30

6.0 Abstract

Aim: To demonstrate the spectrum of findings (intensities) at Diffusion Weighted Imaging (DWI) of different brain pathology using the 1.5T Phillips Intera MRI scanner.

Method: This was a Hospital based prospective study at Kenyatta National Hospital (KNH) at the Radiology Department using questionnaires, and MRI images. A random sampling was applied to get the patients who underwent brain scan and had a diagnosis as per the clinical and MRI findings.

The signal intensities of brain lesions on diffusion Weighted Imaging were documented. The intensity of the lesion was also described on other sequences e.g. T1W, T2W, FLAIR, e.t.c. The diagnosis was made from both the history and the MRI appearances of the lesions.

The data collected from the patients/MRI records was entered in a Microsoft access database and exported to a specialised statistical package for analysis with an assistance of a Bio-statistician.

Results:

The results are presented in summarised tables; graphs and form the platform for the conclusion and recommendations. Among the lesions described are infarcts, tumours, demyelinating disorders and infective processes. This is further described in the methodology.

7.0 Literature Review

7.1 Diffusion imaging.

This is an excellent non-invasive method of measuring the diffusion characteristics of biological tissue. Diffusion imaging makes use of the variability of the Brownian motion of water molecules in brain tissue.⁵⁸ Brownian motion refers to the random movement of molecules. In biological tissues, diffusion is not truly random because tissue has structure. Cell membranes, vascular structures, and axon cylinders, for example, limit or restrict the amount of diffusion. Also, chemical interactions of water and macro-molecules affect diffusion properties. Therefore, in the brain, water diffusion is referred to as an apparent diffusion.

In normal brain tissue, water motion in the extra cellular fluid is relatively unrestricted and randomly oriented. The MR diffusion sequence is designed in such a way that this random water motion produces signal loss on diffusion-weighted images; the result is a uniform gray appearance to normal brain tissue (*Fig 19.1*). In contrast, disease processes that restrict the motion of water molecules produce high signal-intensity instead of the uniform gray intensity of normal tissue.

To obtain diffusion-weighted images, pair of strong gradient pulses is added to the pulse sequence. The first pulse dephases the spins, and the second pulse rephases the spins if no net movement occurs. If net movement of spins occurs between the gradient pulses, signal attenuation occurs. The degree of attenuation depends on the magnitude of molecular translation and diffusion weighting. The amount of diffusion weighting is determined by the strength of the diffusion gradients, the duration of the gradients, and the time between the gradient pulses.

Diffusion imaging is performed optimally on a high-field (1.5 T) echo-planar system, but it can be accomplished with a turbo STEAM sequence on systems with conventional gradients.

The diffusion data can be presented as signal intensity or as an image map of the apparent diffusion coefficient (ADC). Calculation of the ADC requires 2 or more acquisitions with different diffusion weightings. A low ADC corresponds to high signal intensity (restricted diffusion), and a high ADC to low signal intensity on diffusion-weighted images.

In the setting of acute cerebral ischemia, if the cerebral blood flow is lowered to 10 ml/100gm/min, the cell membrane ion pump fails and excess sodium enters the cell, which is followed by a net movement of water from the extra cellular to intracellular compartment and cytotoxic edema. Diffusion of the intracellular water molecules is

restricted by the cell membranes. The restricted diffusion results in a decreased ADC and increased signal intensity on diffusion-weighted images. Severe ischemia can lower the ADC by as much as 56% of normal tissue at 6 hours.

In patients who present with symptoms of cerebral ischemia, diffusion-weighted images are very helpful to identify any area of acute ischemia and to separate the acute infarction from old strokes and other chronic changes in the brain. Only the acute infarcts appear hyperintense on the diffusion images. Sub acute and chronic infarcts, vasogenic edema, the punctate and confluent changes of deep white matter ischemia, are not bright.

7.2 Studies on stroke imaging

Peter E. Ricci, did a lot of research focusing on advanced MR imaging techniques as they relate to cerebral ischemic disease, brain tumours, and neurorehabilitation.

MR diffusion and perfusion imaging techniques, by virtue of their ability to identify and characterize acutely ischemic tissue, have the potential to significantly improve clinical decision making in and care of stroke patients. At the Colorado Neurological Institute, MR diffusion and perfusion imaging techniques have been integrated into the routine stroke imaging protocols. Although CT remains the initial imaging study in all patients that present with an acute neurologic

deficit, it is used primarily to exclude the presence of hemorrhage and other stroke mimickers. Diffusion-weighted MR imaging is now performed in all patients in whom ischemic stroke is a diagnostic consideration.

Background: - It is estimated that between 700 000 to 750 000 new or recurrent strokes occur each year in the US, making it the most common neurological problem encountered in the country.⁴⁶ It accounts for more than 50% of hospital admissions for neurological disease and is the most common cause of long-term disability in US.⁴⁷

Because stroke and its associated complications are so common, imaging tests, such as computed tomography (CT), magnetic resonance (MR) imaging, cerebral angiography, and a variety of nuclear medicine studies are frequently performed. While each of these imaging tests provides valuable diagnostic information, each also has well known limitations. One of the most significant limitations of these conventional imaging tests is the inability to reliably detect acute ischemic infarcts.

Recent advances in imaging, particularly in the field of MR imaging, have the potential to revolutionize both the imaging and care of acute stroke patients through the identification and characterization of acutely ischemic tissue. The recent acceptance of intravenous rt-PA as a viable therapy for infarcts within 3 hours of symptom onset ^{48,49} and promising results with intra-arterial rt-PA within the first 6 hours of an

ischemic stroke⁵⁰, have made reliable detection of hyperacute stroke within these time periods absolutely essential when use of this or other potentially dangerous thrombolytic agents are being considered. The goals of this article are to introduce readers to these new MR techniques and provide examples of how they can be used effectively for identification of very early ischemic strokes.

7.3 Conventional imaging in ischemic stroke

In contrast to the high sensitivity for detection of “stroke mimickers”, CT scanning is less reliable at detecting early ischemic stroke. Initial reports suggested CT detected only 58% of ischemic strokes within the first 24 hours after symptom onset.⁶ More recent data obtained as part of the PROACT II thrombolysis trial has suggested that CT may actually detect 75% of hyperacute infarcts (i.e. infarcts less than 6 hours old).⁵² In that study, the investigators found the most common abnormal CT findings to be edema in the insular ribbon (46%), cerebral cortex (43%), or lentiform nucleus (39%), or a hyperdense middle cerebral artery (34%). Despite this apparent improvement in the ability of CT to detect hyperacute infarcts, missing 25% of infarcts in the first 6 hours still raises questions about the reliability of CT.

Detection of very early infarcts is widely considered to be better with MR imaging than with CT because of its superior contrast resolution. This was confirmed in one early study that found an 82% detection rate of ischemic infarcts in the first 24 hours with MR versus 58% with CT.⁵³

In a series of 70 patients with 72 infarcts, Ricci et al, were able to detect 96% of the lesions with conventional MR scanning techniques in the first 24 hours.⁵³ However, detection rates in the first 6 hours with conventional MR techniques remain poor. Furthermore, 30% of infarcts detected with conventional MR imaging can increase in size on follow-up studies⁵¹, which suggests that the initial study either underestimates the size of the infarct or that it doesn't detect ischemic tissue that is at risk for subsequent infarction.

The poor sensitivity of conventional CT and MR for identifying hyperacute infarcts stems from their inability to detect the main pathologic changes occurring within that 6-hour time period: decreased cerebral blood flow and development of cytotoxic edema. The most common vascular change detected with CT scanning is the hyperdense vessel sign, which is the result in situ thrombus or an embolus (*Figure 19.2*). Most commonly seen in the middle cerebral artery, it is present in only one-third of cases. Even though MR imaging is more sensitive than CT to alterations in cerebral blood flow, it detected altered flow in only 50% of infarcts in the first 8 hours in one study.⁵⁴

At the cellular level, as described above, cytotoxic edema results, causing total water content of the brain to increase by less than 3%.⁵⁵ With CT and MR imaging, this small fluid shift can occasionally be seen as gyral swelling; in most instances however, the changes are too subtle to be reliably detected. Vasogenic edema, results in much larger

fluid shifts than those seen in cytotoxic edema. Because of the large fluid shifts involved, vasogenic edema is more readily detected with conventional CT and MR. Unfortunately, this type of edema typically takes between 4 to 6 hours to develop once blood flow decreases to critical ischemia levels⁵⁵. If blood flow is completely disrupted, vasogenic edema can take even longer to develop.

7.4 Acute stroke imaging using DWI

Two new imaging techniques, MR diffusion imaging and dynamic susceptibility-weighted MR imaging (also known as MR perfusion imaging), are gaining acceptance as the premier stroke imaging techniques because they permit accurate, reliable diagnosis and characterization of ischemic strokes within the critical first 6-hour time period needed to initiate thrombolytic therapy. These techniques, which use very different approaches to gather physiologic rather than anatomic information about ischemic or infarcted tissue, are generating considerable excitement in the medical community because of their potential to improve clinical decision-making in and the care of stroke patients.

What makes diffusion imaging so valuable in the stroke imaging armamentarium is its ability to reliably detect hyperacute ischemic infarcts when other imaging tests are still normal (*Figure 19. 3*), its ability to help determine infarct age, and, its ability to distinguish small lacunar infarcts from chronic microvascular ischemic changes.

Cytotoxic edema has been found to occur as early as one minute after vessel occlusion.⁵⁵

When viewed against the uniform gray signal of normal tissue, infarcted areas become much more conspicuous than infarcts seen with more conventional MR techniques.⁵³ (*Figure 19.4 and 19.5*)

In experimental models of cerebral infarction, abnormal signal within infarcted tissue has been detected on MR diffusion studies within 15 minutes of vascular occlusion.^{1,2,59} More importantly, diffusion imaging has proven to be greater than 95% sensitive and specific for detecting infarcts within the first 6 hours of symptom onset in humans, making it the most reliable method currently available for infarct identification.^{4,58}

As the infarct evolves, cell membranes break down, releasing the intracellular water back into the extracellular space. Water motion becomes relatively unrestricted once again causing the high signal in the infarct on diffusion images to fade back to gray. Typically, this return to normal signal-intensity on diffusion-weighted images occurs 10 to 14 days following the onset of the stroke.⁵⁹ This change in signal intensity can be useful when trying to determine the age of ischemic infarcts (*Figure 19.6*)

7.5 Other causes of positive DWI

- Bacterial abscess
- Epidermoid tumour
- Acute demyelination
- Tumors undergoing central necrosis
- Tumors with high nuclear: cytoplasmic ratios
- Acute encephalitis
- Jacob Creutzfeld disease
- Elevated protein or subacute blood
- T2 shine-through (High ADC).

Bacterial abscesses may exhibit restricted diffusion due to thick cellular debris within the central cavity. Other diseases of the brain, such as non-bacterial infections, neoplasia, contusions, and demyelinating diseases, are not associated with cytotoxic edema, and therefore as a rule, they are not hyperintense on the diffusion images. One exception is epidermoid tumors, which have restricted diffusion due to the waxy consistency of their contents. Also, the central portions of some primary and secondary brain tumors may exhibit restriction diffusion as they outgrow their blood supply and become ischemic. Occasionally, an acute multiple sclerosis plaque may be mildly hyperintense with diffusion weighting.

Lesions with prolonged T2 relaxation times are commonly mildly hyperintense on diffusion-weighted images. This phenomenon of T2

shine-through and can easily be distinguished from true restricted diffusion on the ADC map. Only true restricted diffusion is low signal on the ADC map.

Recently, its utility has been investigated in several other brain diseases, including epilepsy ⁵, Alzheimer disease ⁽⁶⁾, multiple sclerosis ^(7,8), and Parkinson disease ⁽⁹⁾.

7.6 Perfusion Weighted Imaging

In imaging of stroke, perfusion imaging is of great importance in establishing those with salvable brain.

With the development of ultra-fast scanning techniques, these studies are now possible with MR scanners where they have the added benefit of superior spatial resolution compared to the nuclear medicine techniques. The “bolus-tracking” MR technique, first described by Villringer, is the most commonly used type of MR perfusion study.⁶⁰

7.7 Diffusion Perfusion Mismatch

The difference between the diffusion and perfusion abnormalities provide a measure of the ischemic penumbra or the brain tissue at risk for infarction (*Figure 19.7*). Restricted diffusion generally indicates unsalvageable brain tissue that is destined for infarction. The perfusion abnormality encompasses all regions with reduced cerebral blood flow. If the diffusion abnormality matches the area

of decreased perfusion, no salvable ischemic brain tissue is present. If the perfusion abnormality is larger than the area of restricted diffusion, the difference identifies the region of reversible ischemia that can be saved if blood flow is re-established promptly.

7.8 Diffusion tensor imaging (DTI) ^{41, 42,43,44,45}

Diffusion may be restricted due to structural confinement such as the case in white matter fibers. In the white matter the hydrogen nuclei have certain directions of preferred travel, such as along the direction of the axonal fibers. Moving in this direction is easier since going perpendicular to the fiber would cause a collision and restrict movement. It is this anisotropic diffusion information that diffusion tensor imaging (DTI) is able to quantify and display.

Directional information can be used to create images of white matter tracks.

7.9 Disadvantages of DWI

Most important difficulty is motion sensitivity, which can cause ghosting artifacts or complete signal loss. This motion could be due to involuntary head motion or physiological blood pressure - related pulsation of the brain tissue.

7.10 Conclusion

DW MRI can be performed during a standard cranial MR examination and add useful clinical information in several brain disorders besides acute ischaemic stroke.

8.0 OBJECTIVES

8.1 Broad Objective

To determine the role of Diffusion Weighted Imaging (DWI) in the imaging of the brain pathology.

8.2 Specific Objectives

- 1) Role of DW MRI in the diagnosis and aging of cerebral infarcts.
- 2) To determine whether DWI and ADC can be used to distinguish brain abscesses from cystic or necrotic tumours which are difficult to distinguish by conventional MRI techniques.
- 3) Role of Diffusion imaging in demyelinating conditions.

9.0 Justification

With new and powerful MRI scanners being introduced in the country, there is a growing need to make full use of the equipments. The equipments come with multiple sequences of which if fully utilized, would be of great benefits in giving correct diagnosis.

MRI has a wide range of sequences and each examination has its protocol. Some of the new sequences include MR spectroscopy and the above discussed. MR spectroscopy requires specialized software.

Advent of computer has made all this possible. Running the sequences as per the agreed protocol per disease imaged will result in more accurate MRI diagnosis.

Early diagnosis of reversible stroke would lead to treatment hence less debilitation of patients.

10.0 Research Question

What is the role of DWI in improving the diagnosis of different brain pathology.

11.0 Method and materials

11.1 Imaging Techniques

The imaging was performed with a 1.5T Intera MRI. A standard head coil with standard restraints is used to fix the volunteer's head position. In addition to axial DW images, conventional T1-weighted, T2-weighted, fluid-attenuated inversion recovery, and proton density-weighted images were obtained where necessary. ADC maps were also done where necessary. The findings were discussed with the Radiologists working in the department. This were then fend into the data sheet awaiting analysis.

11.2 Study Design

This is a descriptive study. The signal intensities of the imaged pathology are described. This fell between hypointense, isointense and hyperintense. This basis of description is as used by other authors in different studies quoted in the literature review.

11.3 Study Area

The study was carried out at the X-ray department of Kenyatta National Hospital (KNH).

11.4 study Population

Patients referred from the wards, casualty department, clinics and from private facilities that underwent MR imaging of the Brain at KNH.

11.5 Sample Size Justification

Primary outcome variable = proportion of the brain pathology imaged with DWI.

Best value of expected percentage (proportion) = 10% (Approximately, 2 out of 7 patients undergo brain imaging).

Desired width of 95% confidence interval. (Fisher & Van Belle) formula for sample size calculation.

The formula for the estimation of a single proportion will be as follows at 80% power,

$$n = \frac{Z^2_{1-\beta/2} \times P(1-P)}{\partial^2}$$

n = required sample size, P = the expected proportion, ∂ = the required precision

Substituting in the above formula we get;

$$n = \frac{(1.96^2) * 10\% (1-10\%)}{0.05^2} = 139.8 \approx 140 \text{ patients.}$$

Therefore 140 patients will be required to obtain a 95% confidence interval at +/-5.

11.6 Sampling Method

Being a descriptive study and targeting to look at intensities of different brain pathology in the brain on DWI, the images with pathology were included during the specified period of time.

11.7 Inclusion Criteria

Patients who had and did not have notable changes on DWI were included in the study. The main aim was to describe the appearance of the pathology on DWI. If the final diagnosis cannot be made, the changes noted were described.

11.8 Exclusion Criteria

Images which showed normal brain were excluded from the study.

12.0 Data Management

12.1 Data Collection

The Principal Investigator was assisted by colleagues in X-ray department Kenyatta National hospital. Relevant data of eligible patients were collected. This included looking at all images on the computer as they are saved in the hard disc for some time. This was followed by comparing with the radiologist report. The intensities of the pathology in question was recorded into a data collection sheet. With the help of a bio-statistician these was entered into computer software ready for analysis. SPSS software was used.

12.2 Data Analysis

On feeding the data to the computer software, analysis was done. The analysis included grouping the pathology in form of a table. This was as per the disease and intensities portrayed on T1W, T2W, DWI and ADC.

Microsoft office was also used especially MS word in both the writing of the proposal and analysis.

MS PowerPoint was used when grouping images and the writings on them.

The data acquired is presented in form of tables, pie charts, and graphs. Images are also shown in the final report.

12.3 Testing the Positive Predictive Value of DWI

Ideally a test should be very accurate, that is, in the presence of disease it should be able to detect it all the time and in the absence, it should always be negative. Similarly, it should enable us to narrow the diagnosis. Such a test however is rare to come by, and the diagnostic tests most often used are less accurate than the ideal tests. The parameters used to gauge the performance of a test are its sensitivity and specificity. Sensitivity of a test is the proportion of people with the disease who have a positive test for the disease. Specificity of the test is the proportion of people without the disease who have a negative test.

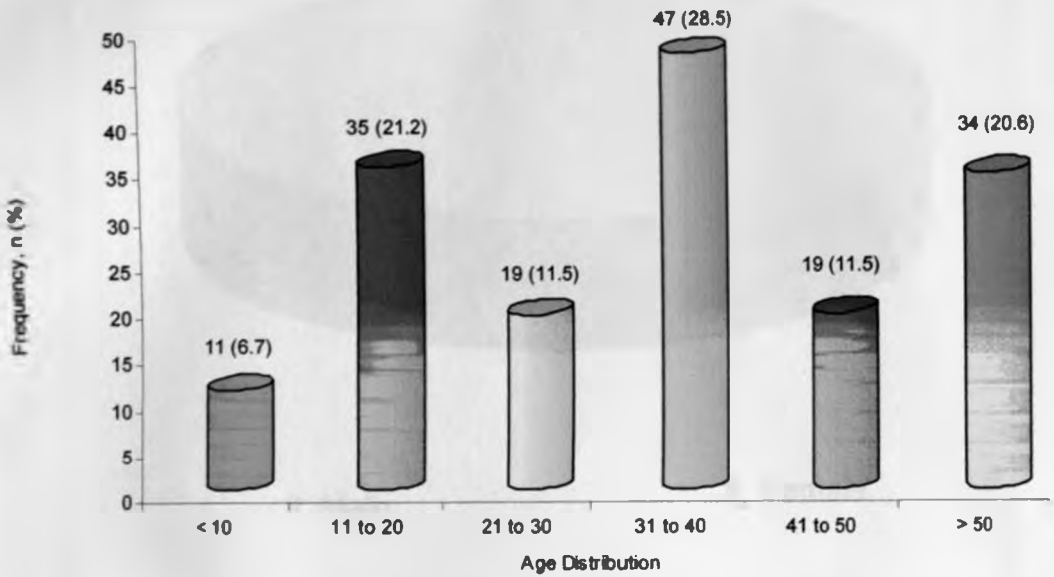
13.0 ETHICAL CONSIDERATION

Patient's identity and any information will be kept anonymous by the principal investigator and will not appear in any publications. The patient's records will neither be photocopied nor will the names of the referring clinicians be recorded. The information on the questionnaire will be accessible only to the investigator, radiologist, radiographer and the biostatistician.

The approval to conduct the study will be sought from Kenyatta National Hospital Ethics Committee.

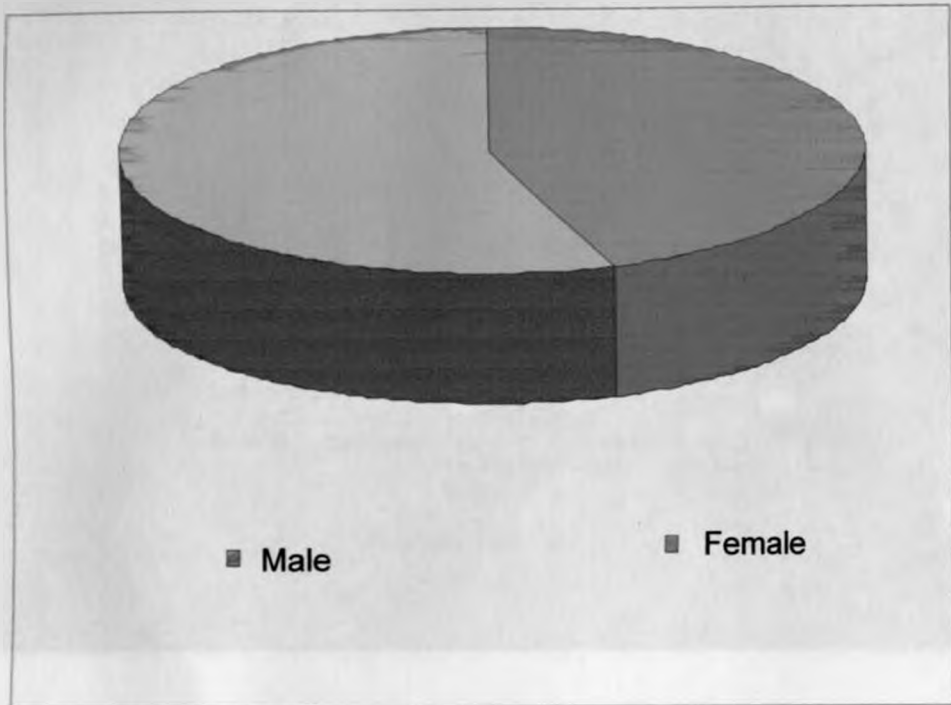
14.0 RESULTS

Figure 14.1: Age Distribution (n = 165)



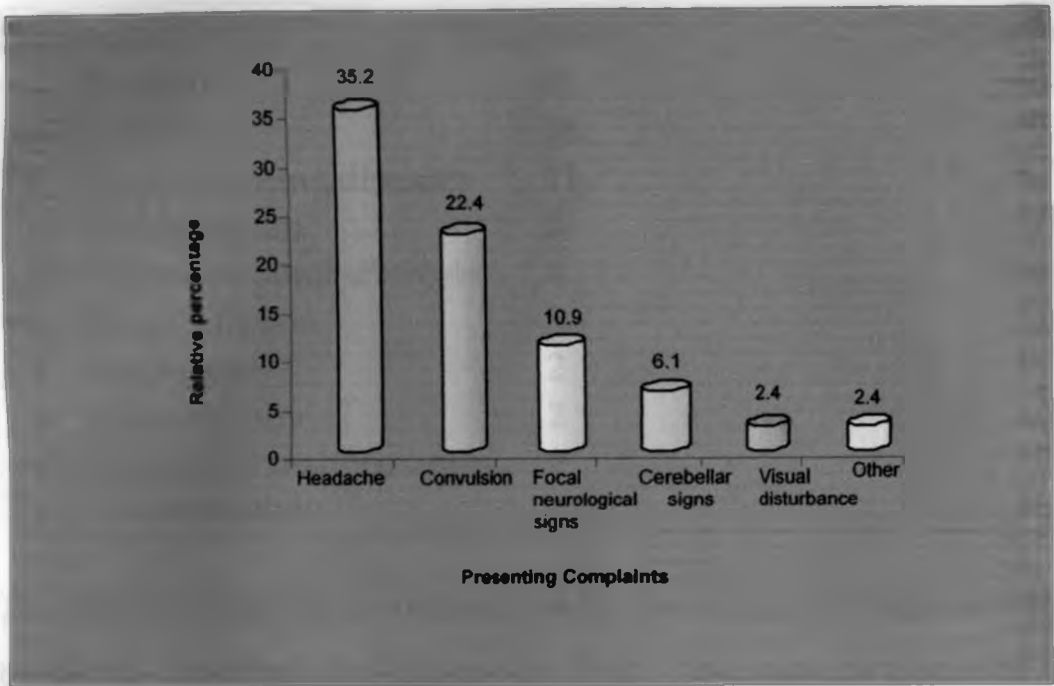
The mean age of the patients was 34.68 years (SE = 1.4) with the minimum age being 4 year while the oldest patients was 78 years (range = 74 years. Peak age of presentation was 4th decade. Least scanned were under 10 years.

Figure 14.2: Sex Distribution (n = 165)



91 (55.2%) MRI images belonged to male patients while female were 74 (44.8%). Male to female ratio was 1.2:1.

Figure 14.3: Presenting Complaints of the patients (n = 165)



Most of the patients as indicated in the request forms and demonstrated in figure 3 presented with headache. These were 58 (35.2%). Convulsions comprised 37(22.4%), focal neurological signs 18(10.9%), Cerebellar signs 18(6.1%), visual disturbances 4(2.4%), and 4(2.4%) of the forms were not clearly indicated.

Table 14.1: Clinically Suspected Diagnosis

Diagnosis	Frequency	Percentage
• Tumour	31	18.8
• Infarcts	18	10.9
• Demyelinating diseases	11	6.7
• Parkinsonism	5	3.0
• Mesialtemporal sclerosis	4	2.4
• Brain infection	3	1.8
• Metastasis	2	1.2
• Brain atrophy	2	1.2
• Congenital malformation	2	1.2
• Not indicated	87	52.7

The MRI findings were correlated with the clinical findings in order to make the most probable diagnosis. This is because the duration of the study could not allow for histological correlation. Table 1 shows the clinically suspected diagnosis before the MRI scan. This was as indicated in the request form. The commonest reason for MRI request were due to tumours followed by cerebral vascular accident comprising 31(18.8%) and 18(10.9%) patients respectively. However a large portion did not clinically state the suspected diagnosis. This added up to 87(52.7%) of the request forms.

Table 14.2 : Lesion Description on MRI

Site	Frequency	Percentage
• Cerebral	82	49.7
• Cerebellar	9	5.5
• Pituitary	8	4.8
• Sinonasal	2	1.2
• Brain Stem	1	0.6
• Meningial	1	0.6
• Pineal	1	0.6
• Normal	82	49.7

82(49.7%) of the MRI scans done had lesions found in the cerebral hemisphere. This was 49.7% of the patients studied. Following were cerebellar lesions comprising 5.5%. 82(49.7%) of the MRI scans studied were found normal. This is as indicated in table 2.

Table 14.3: Infarcts(n=23)

Stage of infarct	Number of cases
Acute	18
Subacute	5
Chronic	-

Out of the 23 cases of brain infarct 18(78.26%) were acute, 5(21.74%) were subacute as shown in table 3. No chronic infarct was noted among the studied cases.

Table 14.4: Site of infarct (n=23)

Site of the infarct	No of cases
Anterior cerebral circulation	2
Middle cerebral circulation	14
Posterior cerebral circulation	4
Lacunar	3

14(60.86%) of the infarcts involved the middle cerebral territory. They ranged from small to large infarcts. Only five were noted to have the roughly triangular shaped. All the others were irregular.

Anterior circulation, posterior circulation and lacunar infarcts comprised 2(8.69%), 4(17.3%) and 3(13%) respectively.

Table 14.5: DWI & ADC (n=165)

Diagnosis	DWI					ADC				
	Hypo	Hyper	ISO	Heterogeneous	No Change	Hypo	Hyper	ISO	Heterogeneous	No Change
Abscess	5	-	-	-	-	4	1	-	-	-
Schizencephaly	2	-	-	-	-	2	-	-	-	-
White matter hyperintensities	-	11	2	-	-	1	-	4	-	-
Craniopharyngioma	-	-	-	4	-	4	-	-	-	-
Mesialtemporal sclerosis	-	-	2	-	7	-	-	2	-	7
Metastasis	2	-	-	-	-	2	-	-	-	-
Infarcts	4	18	1	-	-	18	4	1	-	-
Chiari malformation	-	-	-	-	2	-	-	-	-	2
Sinonasal Tumour	2	-	-	-	2	-	-	-	-	-
Glioblastoma multiforme	2	-	-	-	-	-	2	-	-	-
Subarachnoid haemorrhage	1	-	-	-	-	1	-	-	-	-
Ventricular asymmetry	-	-	-	-	4	-	-	-	-	4
Atrophy	2	-	-	-	-	-	-	-	-	-
Pituitary Adenoma	-	-	-	-	-	-	-	-	-	-
Haemorrhage	2	1	-	-	-	2	1	-	-	-
PNET	4	-	-	-	-	-	4	-	-	-
Subependymoma	-	-	4	-	-	-	-	4	-	-
Medulloblastoma	-	4	-	-	-	2	2	-	-	-
Esthesioneuroblastoma	-	-	-	2	-	-	-	-	2	-
Hemangioblastoma	2	-	-	-	-	-	-	-	2	-
Pinealblastoma	-	-	-	1	-	-	-	-	1	-
Parkinsonism	-	-	1	-	-	-	-	-	-	-
Cerebritis	1	1	-	-	-	1	1	-	-	-
Demyelinating diseases including multiple sclerosis and progressive multifocal leucoencephalopathy.	-	7	1	-	-	-	-	1	-	-

15.0 DWI & ADC descriptions of the cases (table 14.5)

Images were interpreted in term of the intensities they portrayed on different sequences.

Out the 165 patient's MRI studied different pathology was diagnosed. This included infarcts, haemorrhage, congenital malformations, cystic masses, demyelinating diseases, tumours and infective processes.

The most diagnosed were infarcts that comprised 23(13.93%) of all cases.

Out of all the diagnosed infarcts 18(78%) were hyperintense on DWI and hypointense on ADC. 4(17.39%) were hypointense on DWI and hyperintense on ADC. 1(4.61%) was isointense on both DWI and ADC.

Other diagnosed were brain abscesses. All of the 5 cases were hypointense on DWI. 4 of them were hypointense on ADC while one was hyperintense as shown in table 14.5.

There were 13 cases of non-specific white matter hyperintensities especially on T2W comprising 7.8% of all studied MRI scans. 11(84.61%) of these were hyperintense on DWI.

Only five had ADC done. Out of these 4 were isointense and one hypointense.

There were nine cases of mesial temporal sclerosis. No intensity changes were noted in all on both DWI and ADC.

8(4.84%) cases of demyelinating disease showed high signal on DWI. This included multiple sclerosis and progressive multifocal leucoencephalopathy.

The congenital malformation with cerebrospinal fluid (csf) spaces maintained the intensity of the csf.

Primitive neuroectodermal tumours comprised 2.4% of the cases studied. They were hypointense on DWI and hyperintense on ADC.

16.0 DISCUSSION

The overall objective of the study was to determine the application of DWI of different brain pathology as seen at Kenyatta National Hospital.

In the study more emphasis was laid on diagnosis and aging of infarcts, determination of whether DWI and ADC can be used to distinguish brain abscesses from cystic or necrotic tumours which are difficult to distinguish by conventional MRI techniques and use of DWI in demyelinating conditions.

MRI having become a very crucial tool in brain imaging radiologist's nightmare in diagnosing different brain pathology has markedly been reduced.

DWI has become a routine in the brain protocol at Kenyatta National Hospital. It's not just confined to imaging of stroke. This has been due to a growing interest to learn how different pathology appears on DWI.

All these have in particularly happened in the past one year. Two years are not over since the installation of the MRI equipment.

Marked dedication was noted in putting this new imaging modality into use.

DWI was done using b value of 1000 s/mm². Dating the infarcts was described depending on the intensity they portrayed

Out of the 23 cases diagnosed as infarct, all were dated. 18(78.26%) were acute infarcts while 5(21.74%) were subacute. Acute infarct had high signal on DWI and low signal on ADC.

These findings especially in imaging of the infarcts were in keeping with other studies performed in other centers.

Burdette⁵⁹ reviewed cerebral infarction: time course of signal intensity changes on diffusion-weighted MR images and drew ADC intensity graphs over a time.

In this study only one study was possible; hence ADC intensity graphs over time could not be achieved.

The other objective was to determine the use of DWI in demyelinating diseases. Seven out of the eight cases imaged showed a high signal on DWI. Acute demyelinating disorder tends to give a high signal in DWI as per the literature review. However, with chronicity the intensity reduces. Patients could have come during the acute stage in this study.

The final objective was to determine whether DWI can differentiate abscesses and necrotic tumour. During the duration of study, five cases diagnosed as brain abscesses were hypointense on diffusion imaging. Abscesses tend to be of high signal due to thick cellular content as per

literature review. These could have had less cellular content. Two cases of abscesses had Glioblastoma multiforme as the differential diagnosis. Large portions of the lesions were also hypointense on DWI. This heterogeneity was attributed to necrotic changes.

As per the literature review abscesses are expected to give a high signal on DWI.

17.0 CONCLUSION

Based on the findings of this study and on objectives that were set, the following conclusions were made :

The use of DWI technique is growing very fast with marked improvement of understanding of its applications.

Despite the study having not covered all brain pathology, note of appearance of different brain pathology is being made on a daily basis.

Use of DWI in imaging of infarcts was re-emphasized in this study as per the findings. This is particularly acute infarcts.

Some cases of cerebral haemorrhage were noted to present the same way as infarcts especially on DWI. This was due to the spastic effect of haemorrhage on vessel causing brain infarct (image 19.9). However

most are heterogenous on T1WI due to haemorrhage and infarction.

DWI has a role in imaging of haemorrhagic infarcts. Chronic infarct were not noted in the duration of study. This could be because they are picked well on CT scanning hence not sent for MRI.

DWI has a role in imaging of demyelinating disease. High signal is expected in the patients coming early in the onset of the disease.

Abscesses can present same way as necrotic tumours. It seem they cannot be clearly differentiated from each other.

Most cystic masses imaged showed intensities just like cerebrospinal fluid(image 19.13,19.14). However DWI is good in differentiating epidermoid cyst from arachnoid cyst. Epidermoid cyst has restricted diffusion hence bright in DWI (Images19.16a and 19.16b)

No intensity changes were noted in patients who had mesial temporal sclerosis and had presented with epilepsy. These was in all sequences including DWI and ADC.

The only case of clinically diagnosed parkinsonism showed no intensity changes on all sequences including DWI.

Artifacts were noted especially in the frontal lobe(image 19.12)
This should not be confused with infarcts.

In the duration of study no case of alzheimer's disease was recorded.

18.0 RECOMMENDATION

1. Studies on application of DWI need not end here. A lot remain undone. Picking one pathology and studying it extensively would give more comprehensive findings and reduce the error index. This would even be more appropriate if done over a longer study period.
2. Tissue histological diagnosis was found to be very crucial in some cases in which the diagnosis was not definite. This would make it possible to clearly document the DWI findings. To do this more time of study would also be required. This would be a comparative study.
3. Follow up of patients with MRI was found necessary especially in assessing the intensity changes of different brain pathology over time. This is particularly infarcts as they evolve from acute to chronicity. It would be expensive for the patient.

19.0 Figures

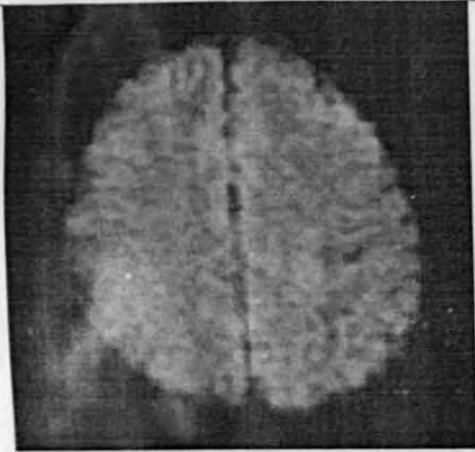


Fig 19.1: Normal diffusion weighted image.



Figure 19.2(A): Dense middle cerebral artery sign. The CT scan was obtained on a 51 year old male who presented to the emergency department with left sided weakness.

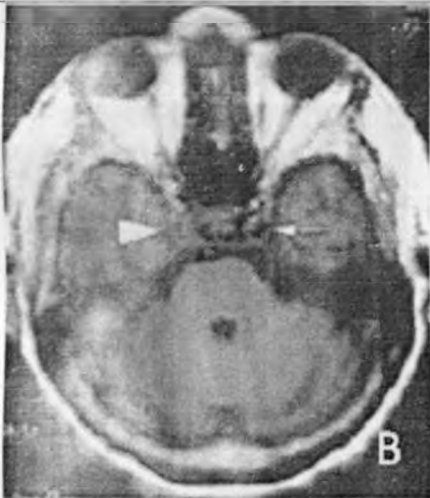


Figure 19.2(B): Absent carotid artery flow on MRI in another patient. There is a black signal in the left internal carotid artery (small white arrow)

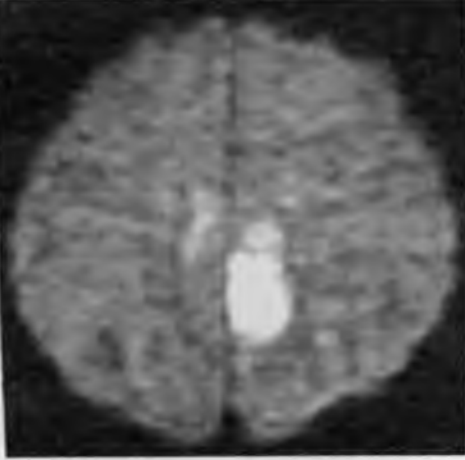


Figure 19.3: Diffusion weighted image in acute ischaemia show a hyperintense area in the centrum semiovale

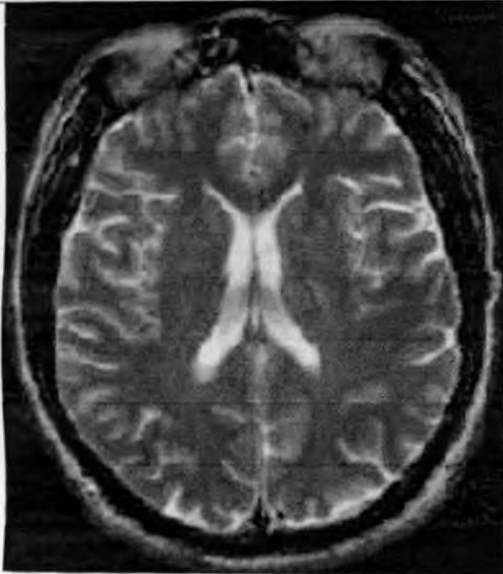


Figure 19.4(A): T2W image of hyperacute infarction. Vague signal change is present in the superior portion of the left basal ganglia. This being a common location for the small vessel ischemic changes that are seen in the normal aging brain, unequivocal diagnosis of acute infarction is not possible.



Figure 19.4(B): Diffusion imaging of the same patient (4A) showing the hyperacute infarct. This image, clearly demonstrates a high signal intensity infarction in the left basal ganglia.

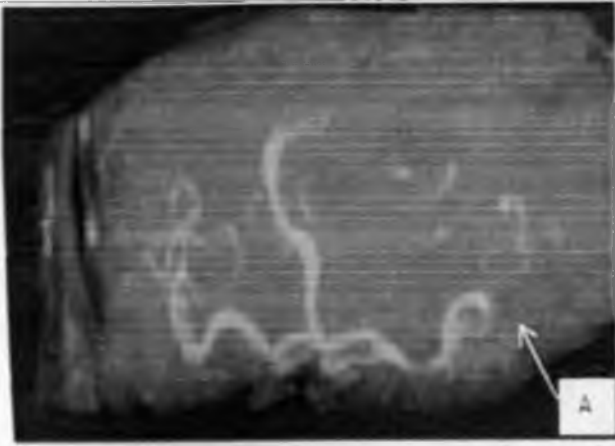


Figure 19.5(A) MRA - left middle cerebral branches are without flow. Branches of the middle cerebral artery are not visualized as compared to the opposite side. (Arrow).

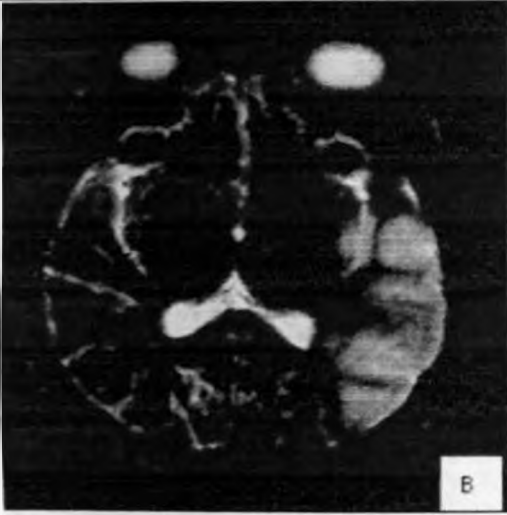


Figure 19.5(B): T2-weighted MR show 12 hour old left MCA infarct. There is a hyperintense region on the left in the territory of middle cerebral artery.



Figure 19.5(C) Diffusion weighted image show the infarct with greater conspicuity. This is in the same territory as shown in A and B.

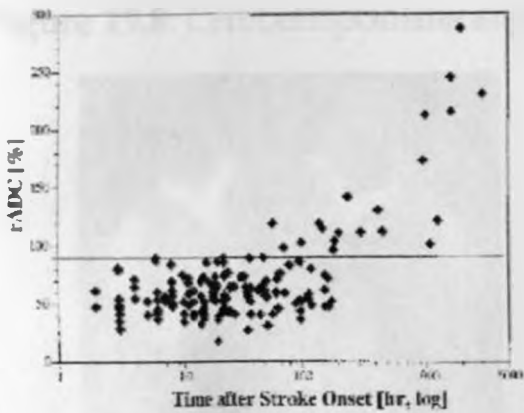


Figure 19.6:- The graph shows that with time, the ADC will rise. This is at about 7 days. This is important in aging the infarct.

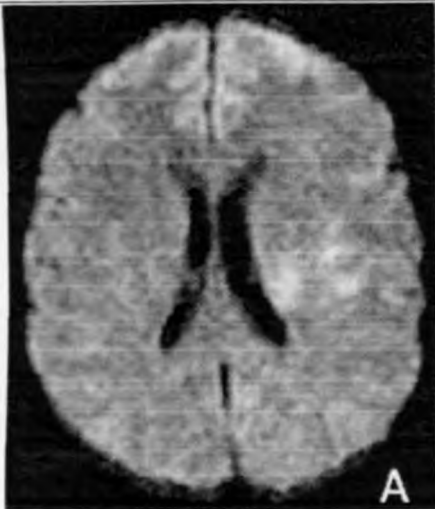


Figure 19.7(A). Diffusion-weighted image obtained from a patient with right-sided weakness reveals a small infarct in the left corona radiata. Although diffusion imaging is very sensitive for infarct detection, it typically underestimates final infarct size.

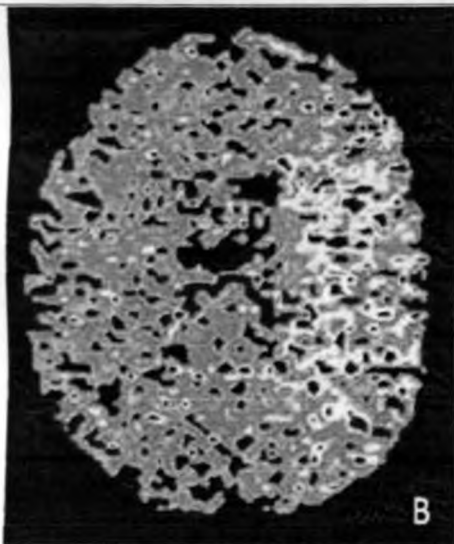
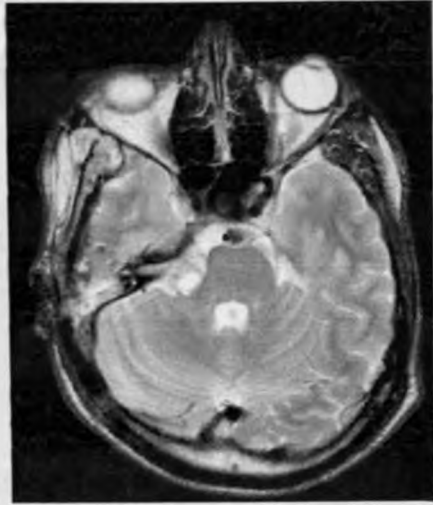


Figure 19.7(B): Mean transit time map obtained at the same level reveals a much larger area of hypoperfusion (the area of increased signal intensity). The difference in volume between the diffusion and perfusion images is felt to represent the ischemic penumbra, the territory at risk for subsequent infarction.

Figure 19.8: Cerebellopontine angle tumour- acoustic schwannoma



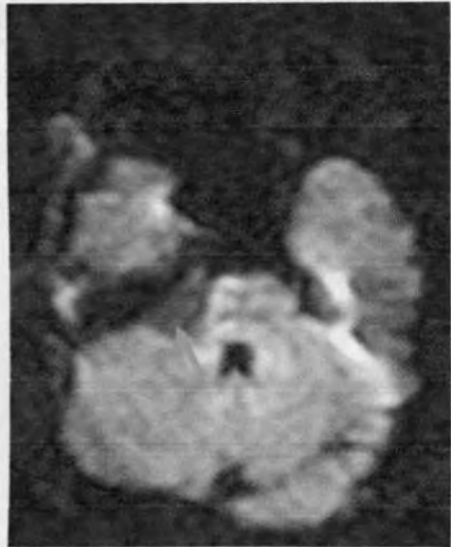
a) T1W image



b) T2W image



c) Gadolinium
enhanced



d) DWI

UNIVERSITY OF NAIROBI
MEDICAL LIBRARY

Figure 19.9: Haemorrhagic infarct in parietal region and acute infarct in occipital region (same patient)

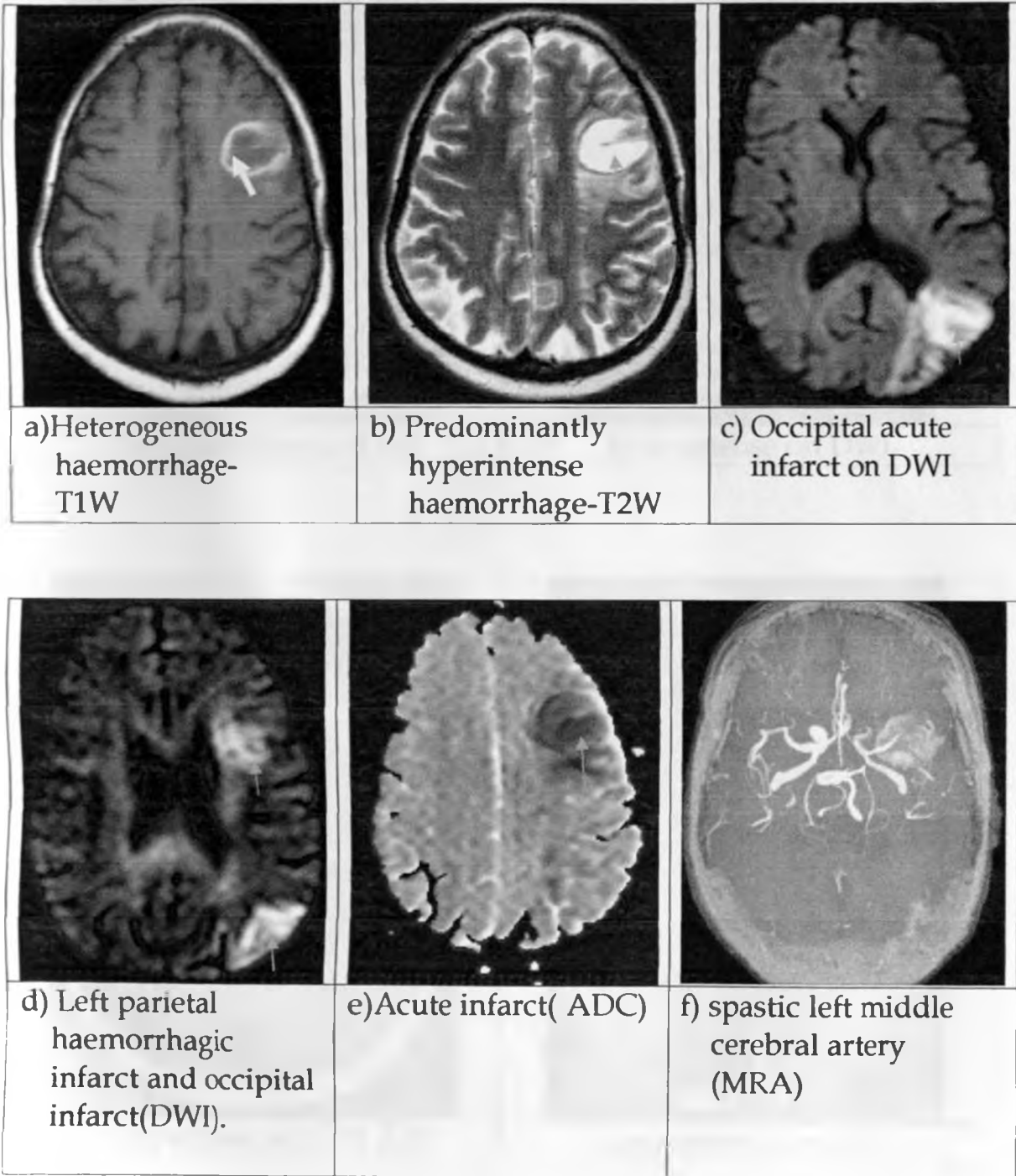


Figure 19.10: sub acute infarct

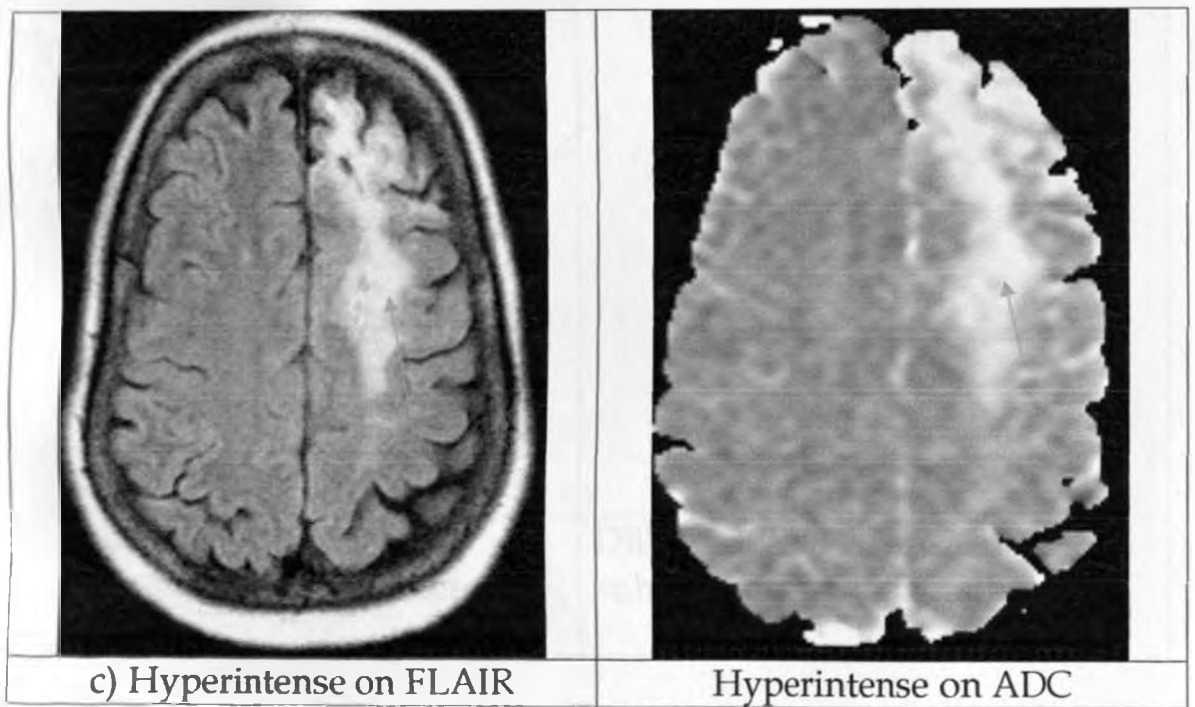
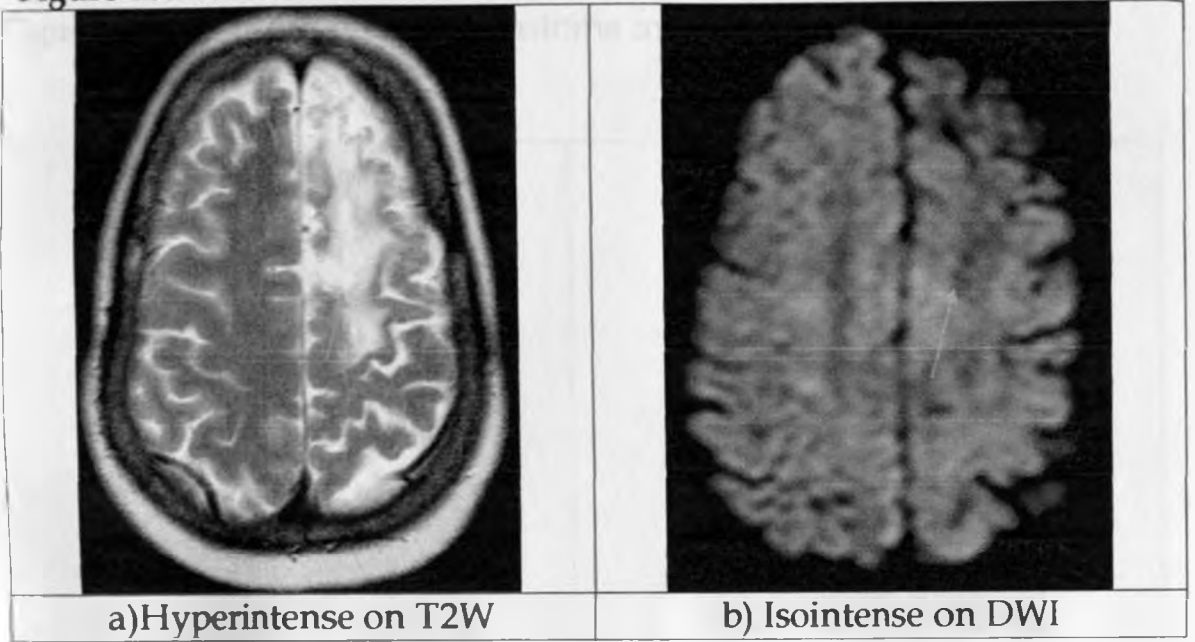


Figure 19.11: Multicentric glioblastoma multiforme ddx multiple Abscesses



A) Hypointense lesions T1W



B) Hyperintense lesions-T2W



C) Heterogenous but predominantly hypointense DWI



D) Largest lesion show ring enhancement with gadolinium

Figure 19.12: Artifacts(two cases)

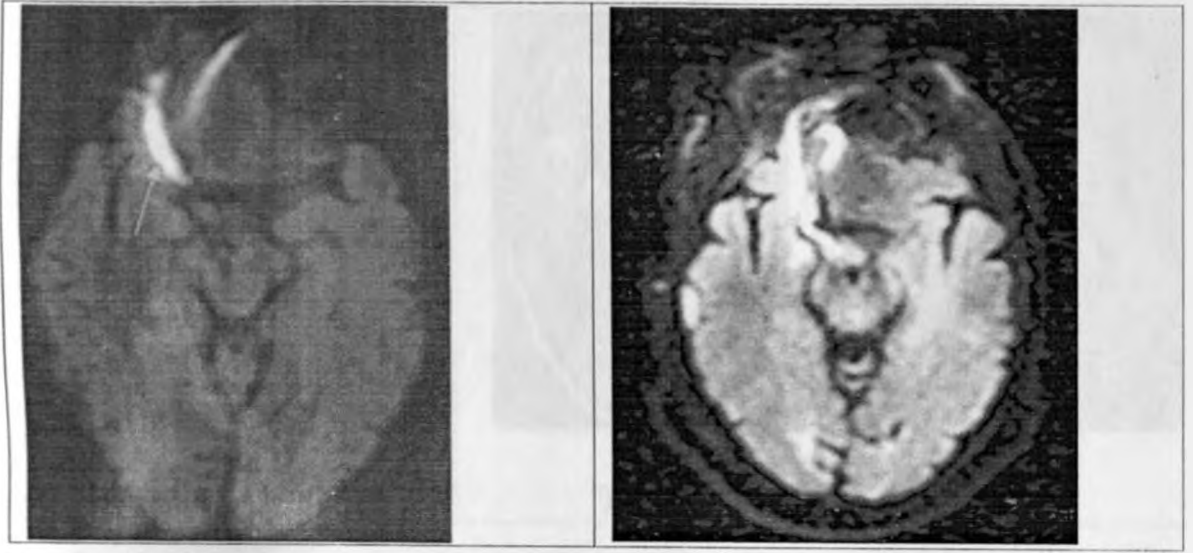


Figure 19.13 : CSF spaces-Cisterna magna

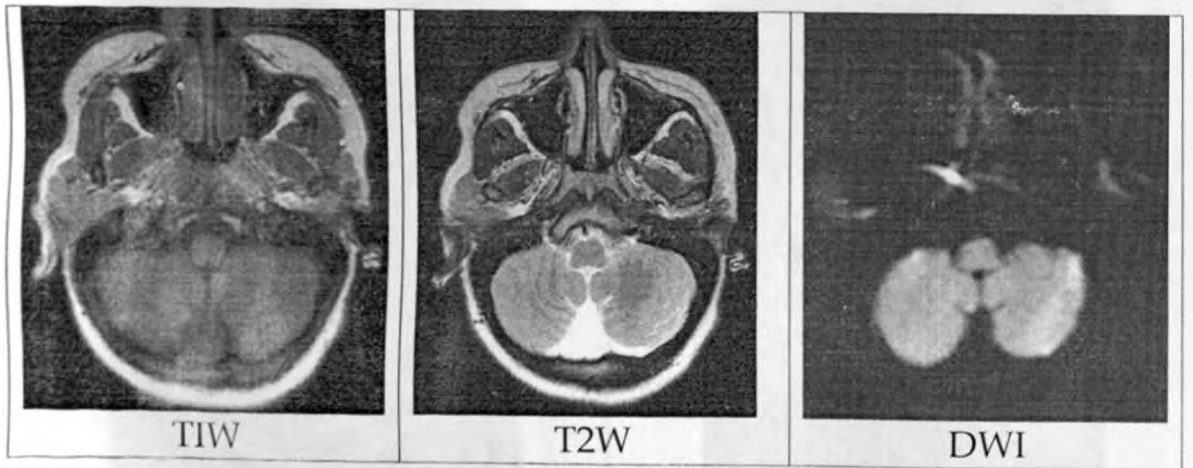
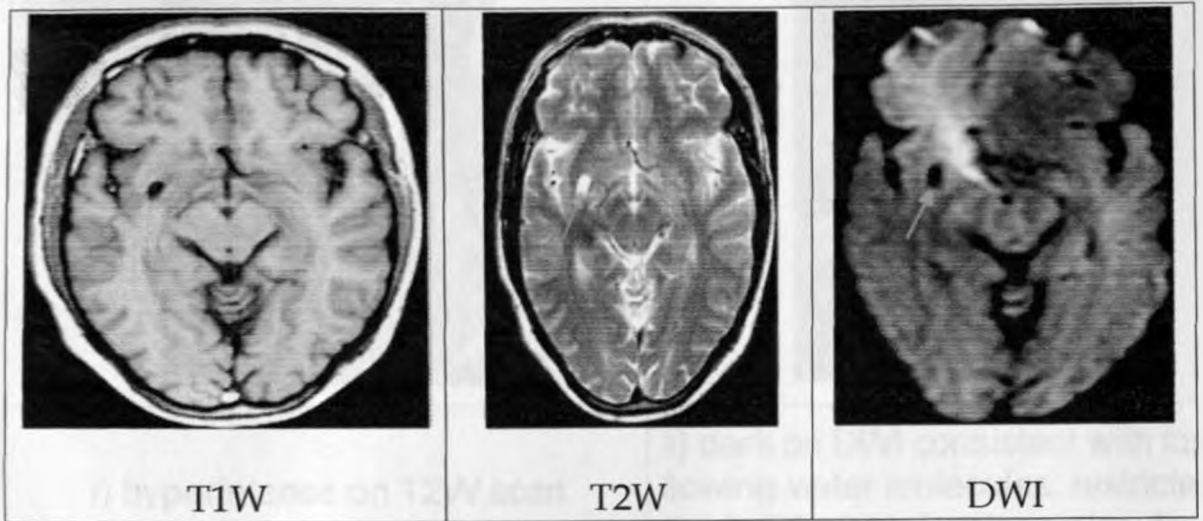


Figure 19.14: Cystic masses



**Figure 19.15 : Non specific hyperintensities (DDX Multiple sclerosis
in this case)**

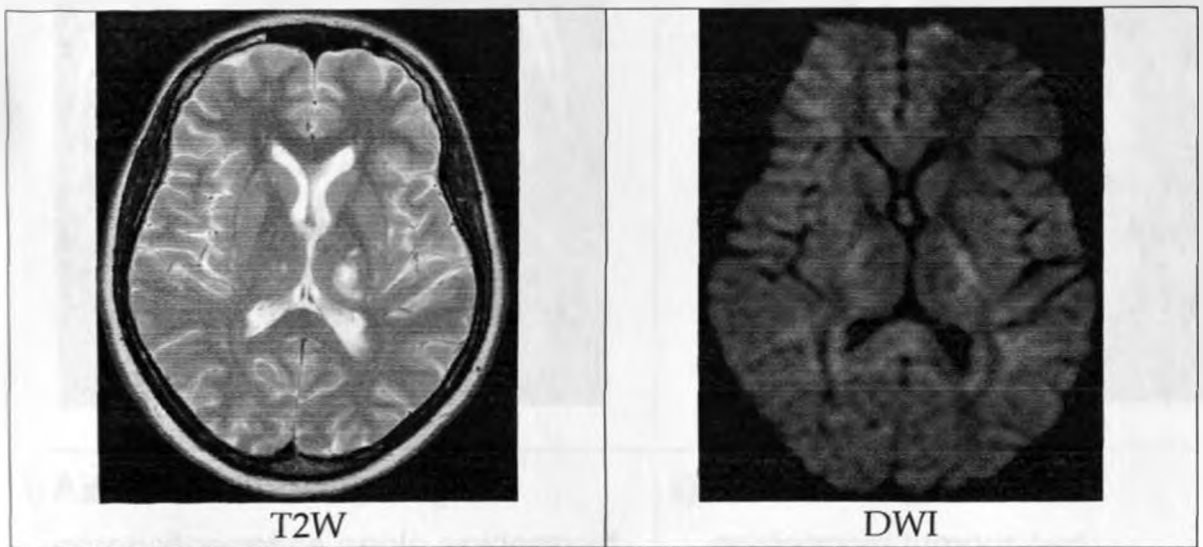
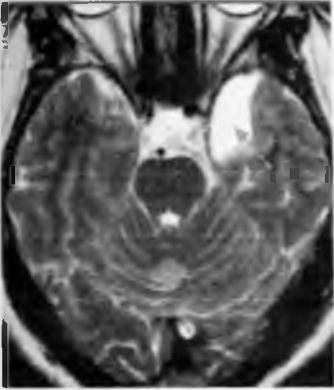


Figure 19.16 (A): Middle-fossa arachnoid cyst

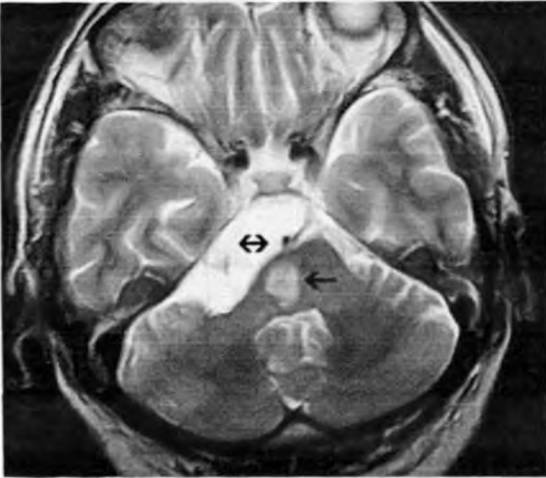


i) hyperintense on T2W scan

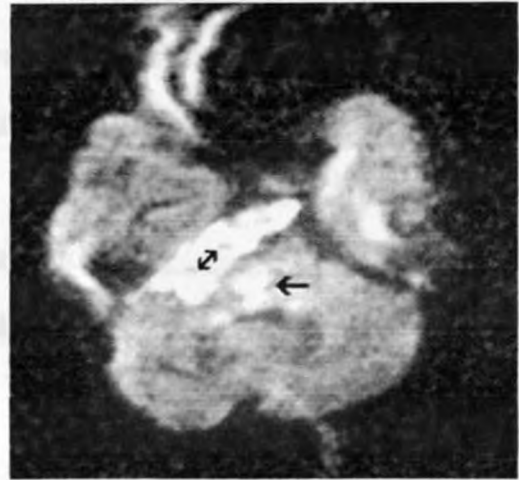


ii) dark on DWI consistent with fast-flowing water molecules. restricted (low) diffusion of water molecules would appear bright on dwi scans.

Figure 19.16 (B) : Right cerebellopontine angle epidermoid tumour.



i) Axial T2W showing a right cerebellopontine angle epidermoid tumour and mid-pontine infarct



ii) DWI showing the same epidermoid tumour and infarct as in (i)

20.0 APPENDIX: 1

Questionnaire

Patients study number _____

Patients IP/OP number _____

A. Patients demographic

1) **Age** _____

2) **Sex** _____

3) **Date of Imaging** _____

4) **Duration of illness** _____

B. Presenting Complaint (s) as per the request form

Headache **Duration**_____

Convulsions **Duration**_____

Visual disturbances **Duration**_____

Cerebellar signs **Duration**_____

Focal neurological signs **Duration**_____

Other (Specify)

C. Suspected brain lesion

Clinically (Tumour/Infective/stroke) _____

D. MRI findings

Description of the Lesions

- i. Site** _____
- ii. Size** _____
- iii. Shape** _____

iv. Intensity

<i>Sequence</i>	<i>Intensity</i>
T1W	
T2W	
FLAIR	
ADC	
DWI	
OTHER (<i>Specify</i>)	

Final Diagnosis

Differential diagnosis

21.0 APPENDIX: 2

BUDGET

No.	Requirement	Cost (KShs.)
1.	Stationary, photocopying,	15,000
2.	Typing	5,000
3.	Data management	20,000
4.	Computer printing (using coloured desk jet printer)	20,000
5.	Image acquisition (using scanner and digital camera)	20,000
6.	Binding	5,000
7.	Data collection	10,000
8.	Transport	10,000
9.	Contingency	50,000
TOTAL		160,000

The researcher will meet the above expenses.

The contingency allocation provided is to cater for any unforeseen expenditure.

22.0 References

1. Li F, Han SS, Tatlisumak T, et al. **A new method to improve in-bore middle cerebral artery occlusion in rats: demonstration with diffusion- and perfusion-weighted imaging.** *Stroke*1998; 29: 1715 -1720
2. Li F, Han SS, Tatlisumak T, et al. **Reversal of acute apparent diffusion coefficient abnormalities and delayed neuronal death following transient focal cerebral ischemia in rats.** *Ann Neurol*1999; 46: 333 -342
3. Warach S, Gaa J, Siewert B, Wielopolski P, Edelman RR. **Acute human stroke studied by whole brain echo planar diffusion-weighted magnetic resonance imaging.** *Ann Neurol*1995; 37: 231 -241
4. Gonzalez RG, Schaefer PW, Buonanno FS, et al. **Diffusion-weighted MR imaging: diagnostic accuracy in patients imaged within 6 hours of stroke symptom onset.** *Radiology*1999; 210: 155 -162
5. Helpert JA, Huang N. **Diffusion-weighted imaging in epilepsy.** *Magn Reson Imaging*1995; 13: 1227 -1231
6. Hanuy H, Sakurai H, Iwamoto T, Takasaki M, Shindo H, Abe K. **Diffusion-weighted MR imaging of the hippocampus and temporal white matter in Alzheimer's disease.** *J Neurol Sci*1998; 156 :195 -200

7. Tievsky AL, Ptak T, Farkas J. Investigation of apparent diffusion coefficient and diffusion tensor anisotropy in acute and chronic multiple sclerosis lesions. *AJNR Am J Neuroradiol*1999; 20: 1491 -1499
8. Cercignani M, Iannucci G, Rocca MA, Comi G, Horsfield MA, Filippi M. Pathologic damage in MS assessed by diffusion-weighted and magnetization transfer MRI. *Neurology*2000; 54: 1139 -1144
9. Adachi M, Hosoya T, Haku T, Yamaguchi K, Kawanami T. Evaluation of the substantia nigra in patients with Parkinsonian syndrome accomplished using multishot diffusion-weighted MR imaging. *AJNR Am J Neuroradiol*1999; 20: 1500 -1506
10. Le Bihan D, Breton E, Lallemand D, Grenier P, Canabis E, Laval-Jeantet M. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurological disorders. *Radiology*1986; 161: 401 -407
11. Sakuma H, Nomura Y, Takeda K, et al. Adult and neonatal human brain: diffusional anisotropy and myelination with diffusion-weighted MR imaging. *Radiology*1991; 180: 229 -233
12. Ulug AM, Beauchamp N Jr, Bryan RN, van Zijl PCM. Absolute quantitation of diffusion constants in human stroke. *Stroke*1997; 28: 483 -490

13. Xing D, Papadakis NG, Huang CL, Lee VM, Carpenter TA, Hall LD. **Optimized diffusion-weighting for measurements of apparent diffusion coefficient (ADC) in human brain.** *Magn Reson Imaging*1997; 15: 771 -784
14. Burdette JH, Elster AD, Ricci PE. **Calculation of apparent diffusion coefficients (ADCs) in brain using two-point and six-point methods.** *J Comput Assist Tomogr*1998; 22: 792 -794
15. Gideon P, Thomsen C, Henriksen O. **Increased self-diffusion of brain water in normal aging.** *J Magn Reson Imaging*1994; 4: 185 -188
16. Tanner SF, Ramenghi LA, Ridgway JP, et al. **Quantitative comparison of intrabrain diffusion in adults and preterm and term neonates and infants.** *AJR Am J Roentgenol*2000; 174: 1643 -1649
17. Harada K, Fujita N, Sakurai K, Akai Y, Fujii K, Kozuka T. **Diffusion imaging of the human brain: a new pulse sequence application for a 1.5-T standard MR system.** *AJNR Am J Neuroradiol*1991; 12: 1143 -1148
18. Van Everdingen K, van der Grond J, Kappelle LJ, Ramos LM, Mali WP. **Diffusion-weighted magnetic resonance imaging in acute stroke.** *Stroke*1998; 29: 1783 -1790
19. Shellock FG, Morisoli S, Kanal E. **MR procedures and biomedical implants, materials, and devices: 1993 update.** *Radiology*1993; 189: 587 -599

20. Salonen O, Autti T, Raininko R, Ylikoski A, Erkinjuntti T. **MRI of the brain in neurologically healthy middle-aged and elderly individuals.** *Neuroradiology*1997; 39: 537 -545
21. Le Bihan D, Turner R, Douek P, Patronas N. **Diffusion MR imaging: clinical applications.** *AJR Am J Roentgenol*1992; 159: 591 -599
22. Baird AE, Warach S. **Magnetic resonance imaging of acute stroke.** *J Cereb Blood Flow Metab*1998; 18: 583 -609
23. Bakshi R, Caruthers SD, Janardhan V, Wasay M. **Intraventricular CSF pulsation artifact on fast fluid-attenuated inversion-recovery MR images: analysis of 100 consecutive normal studies.** *AJNR Am J Neuroradiol*2000; 21 :503 -508
24. Sherman JL, Citrin CM, Gangarosa RE, Bowen BJ. **The MR appearance of CSF flow in patients with ventriculomegaly.** *AJR Am J Roentgenol*1987; 148: 193 -199
25. Dardzinski BJ, Sotak CH, Fisher M, Hasegawa Y, Li L, Minematsu K. **Apparent diffusion coefficient mapping of experimental focal cerebral ischemia using diffusion-weighted echo-planar imaging.** *Magn Reson Med*1993; 1994 :318 -325
26. Brockstedt S, Thomsen C, Wirestam R, Holtas S, Stahlberg F. **Quantitative diffusion coefficient maps using fast spin-echo MRI.** *Magn Reson Imaging*1998; 16: 877 -886

27. Chien D, Buxton RB, Kwong KK, Brady TJ, Rosen BR. **MR diffusion imaging of human brain.** *J Comp Assist Tomogr*1990; 14: 514 -520
28. Pierpaoli C, Jezzard P, Basser PJ, Barnett A, Di Chiro G. **Diffusion tensor MR imaging of the human brain.** *Radiology*1996; 201: 637 -648
29. Mintorovitch J, Moseley ME, Chileuitt L, Shimizu H, Cohen Y, Weinstein PR. **Comparison of diffusion- and T2-weighted MRI for the early detection of cerebral ischemia and reperfusion in rats.** *Magn Reson Med*1991; 18: 39-50
30. Roussel SA, van Bruggen N, King MD, Houseman J, Williams SR, Gadian DG. **Monitoring the initial expansion of focal ischemic changes by diffusion-weighted MRI using a remote controlled method of occlusion.** *NMR Biomed*1994; 7: 21 -28
31. Davis D, Ulatowski J, Eleff S, et al. **Rapid monitoring of changes in water diffusion coefficient during reversible ischemia in cat and rat brain.** *Magn Reson Med*1994; 31: 454 -460
32. Hoehn-Berlage M, Norris DG, Kohno K, Mies G, Leibfritz D, Hossmann KA. **Evolution of regional changes in apparent diffusion coefficient during focal ischemia of rat brain: the relationship of quantitative diffusion NMR imaging to reduction in cerebral blood flow and metabolic disturbances.** *J Cereb Blood Flow Metab*1995; 15: 1002 -1011
33. Takano K, Tatlisumak T, Formato JE, et al. **A glycine site antagonist attenuates infarct size in experimental focal**

- ischemia: postmortem and diffusion mapping studies. *Stroke*1997; 28: 1255 -1263
34. Marks MP, de Crespigny A, Lentz D, Enzmann DR, Albers GW, Moseley ME. **Acute and chronic stroke: navigated spin-echo diffusion-weighted MR imaging.** *Radiology*1996; 199: 403 -408
35. Nagesh V, Welch KM, Windham JP, et al. **Time course of ADCw changes in ischemic stroke: beyond the human eye!** *Stroke*1998; 29: 1778 -1782
36. Shimony JS, McKinstry RC, Akbudak E, et al. **Quantitative diffusion-tensor anisotropy brain MR imaging: normative human data and anatomic analysis.** *Radiology*1999; 212: 770 - 784
37. Sorensen AG, Wu O, Copen WA, et al. **Human acute cerebral ischemia: detection of changes in water diffusion anisotropy by using MR imaging.** *Radiology*1999; 212:785 -792
38. Conturo TE, Lori NF, Cull TS, et al. **Tracking neuronal fiber pathways in the living human brain.** *PNAS*1999; 96: 10422
39. Bykowski J, Shellinger PD, Warach S; **Diffusion and perfusion MRI**, in Edelman, Hesselink, Zlatkin and crues, eds, *clinical Magnetic Resonance imaging* 3rd edition, saunders- Elsevier Philadelphia, 2006, pp 1538-70.
40. Callaghan, P.T., *Principles of Nuclear Magnetic Resonance Microscopy.* 1993, Oxford: Oxford University Press. 492.

41. Basser, P.J., J. Mattiello, and D. Lebihan, *Estimation of the Effective Self-Diffusion Tensor from the NMR Spin-Echo*. Journal of Magnetic Resonance Series B, 1994. 103(3): p. 247-254.
42. Basser, P.J., *Inferring microstructural features and the physiological state of tissues from diffusion-weighted images*. Nmr in Biomedicine, 1995. 8(7-8): p. 333-344.
43. Chepuri, N.B., Y.-F. Yen, J.H. Burdette, H. Li, D.M. Moody, and J.A. Maldjian, *Diffusion Anisotropy in the Corpus Callosum*. American Journal of Neuroradiology, 2002. 23: p. 803-808.
44. Basser, P.J., S. Pajevic, C. Pierpaoli, J. Duda, and A. Aldroubi, *In vivo fiber tractography using DT-MRI data*. Magnetic Resonance in Medicine, 2000. 44(4): p. 625-632.
45. Pajevic, S., A. Aldroubi, and P.J. Basser, *A Continuous Tensor Field Approximation of Discrete DT-MRI Data for Extracting Microstructural and Architectural Features of Tissue*. Journal of Magnetic Resonance, 2002. 154: p. 85-100.
46. Broderick J, Brott T, Kothari R, et al. **The Greater Cincinnati/ Northern Kentucky Stroke Study: preliminary first-ever and total incidence rates of stroke among blacks**. Stroke. 1998;29(2):415-421.
47. American Heart Association. **2000 Heart and Stroke Statistical Update**. Dallas, Tex.: American Heart Association, 1999.

48. Adams HP Jr, Brott TG, Furlan AJ, et al. **Guidelines for thrombolytic therapy for acute stroke: a supplement to the guidelines for the management of patients with acute ischemic stroke.** A statement for healthcare professionals from a Special Writing Group of the Stroke Council, American Heart Association. *Circulation*. 1996;94(5):1167-1174.
49. Tissue plasminogen activator for acute ischemic stroke. **The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group.** *N Engl J Med*. 1995; 333(24): 1581-1587.
50. Zeumer H, Freitag HJ, Zanella F, Thie A, Arning C. **Local intra-arterial fibrinolytic therapy in patients with stroke: urokinase versus recombinant tissue plasminogen activator (r-TPA).** *Neuroradiology*.1993; 35:159-162.
51. Bryan RN, Levy LM, Whitlow WD, Killian JM, Preziosi TJ, Rosario JA. **Diagnosis of acute cerebral infarction: comparison of CT and MR imaging.** *AJNR Am J Neuroradiol*. 1991; 12(4): 611-620.
52. Rowley HA, Roberts HC, Dillon WP, et al. **Early CT signs in 177 angiographically proved MCA occlusions-PROACT II findings.** Proceedings of 38th Annual Meeting of the ASNR, April 3-8, 2000, Atlanta GA, page 47.
53. Ricci PE, Burdette JH, Elster AD, Reboussin DM. **A comparison of fast spin-echo, fluid-attenuated**

- inversion-recovery, and diffusion-weighted MR imaging in the first 10 days after cerebral infarction. *AJNR Am J Neuroradiol.*1999;20(8):1535-1542.**
54. Yuh WT, Crain MR, Loes DJ, Greene GM, Ryals TJ, Sato Y. **MR imaging of cerebral ischemia: findings in the first 24 hours. *AJNR Am J Neuroradiol* 1991;12(4):621-629.**
55. Schuier FJ, Hossmann KA. **Experimental brain infarcts in cats. II. Ischemic brain edema. *Stroke.* 1980; 11(6):593-601.**
56. LeBihan D, Breton E, Lallemand, Grenier P, Cabanis E, Laval-Jeantet M. **MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurological disorders. *Radiology.* 1986;161: 401-407.**
57. Mintorovitch J, Moseley ME, Chileuitt L, Shimizu H, Cohen Y, Weinstein PR. **Comparison of diffusion- and T2-weighted MRI for the early detection of cerebral ischemia and reperfusion in rats. *Magn Reson Med.* 1991; 18(1): 39-50.**
58. Gonzalez RG, Schaefer PW, Buonanno FS, et al. **Diffusion-weighted MR imaging: diagnostic accuracy in patients imaged within 6 hours of stroke symptom onset. *Radiology.*1999; 210(1):155-162.**
59. Burdette JH, Ricci PE, Petitti N, Elster AD. **Cerebral infarction: time course of signal intensity changes on diffusion-weighted MR images. *AJR Am J Roentgenol.* 1998; 171(3): 791-795.**

60. Villringer A, Rosen BR, Belliveau JW, et al. **Dynamic imaging with lanthanide chelates in normal brain: contrast due to magnetic susceptibility effects.** *Magn Reson Med.* 1988; 6(2): 164-174.
61. Finelli DA, Hopkins AL, Selman WR, Crumrine RC, Bhatti SU, Lust WD. **Evaluation of experimental early acute cerebral ischemia before the development of edema: use of dynamic, contrast-enhanced and diffusion-weighted MR scanning.** *Magn Reson Med.* 1992; 27(1):189-197.
62. Sorensen AG, Copen WA, Ostergaard L, et al. **Hyperacute stroke: simultaneous measurement of relative cerebral blood volume, relative cerebral blood flow, and mean tissue transit time.** *Radiology.* 1999;210(2):519-527.
63. Ueda T, Yuh WT, Maley JE, Quets JP, Hahn PY, Magnotta VA. **Outcome of acute ischemic lesions evaluated by diffusion and perfusion MR imaging.** *AJNR Am J Neuroradiol.* 1999; 20(6):983-989.
64. Barber PA, Darby DG, Desmond PM, et al. **Prediction of stroke outcome with echoplanar perfusion- and diffusion-weighted MRI.** *Neurology.* 1998; 51(2): 418-426.
65. Neumann-Haefelin T, Wittsack HJ, Wenserski F, et al. **Diffusion- and perfusion- weighted MRI. The DWI/PWI mismatch region in acute stroke.** *Stroke.* 1999;