Anatomical Variations of the Circle of Willis as seen at the University Teaching Hospital, Lusaka, Zambia

By

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DECLARATION

I, Hilda Zulu, hereby declare that this dissertation herein presented for the degree of Master of Science in Human Anatomy has not been previously submitted either in whole or in part for any other degree at this or any other University, nor being currently submitted for any other degree.

Signature …… Date…….

CERTIFICATE OF COMPLETION OF DISSERTATION

I, Professor Erzingatsian Krikor, having supervised and read this dissertation is satisfied that this is the original work of the author under whose name it is being presented. I confirm that the work has been completed satisfactorily and approve it for final submission.

Signature……..……. Date……..……

Head of Department

Signature……..……Date…….

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CERTIFICATE OF APPROVAL

The University of Zambia approves this dissertation of Hilda Zulu in partial fulfilment of the requirements for the award of the degree in Master of Science in Human Anatomy.

Examiner I

Signature……Date……

Examiner II

Signature……..Date……...……

Examiner III

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ABSTRACT

BACKGROUND: The ideal distribution of blood to the brain and the collateral potential of the Circle of Willis (CW) is believed to be dependent largely on the morphology and the presence of all the component vessels of the CW. However, there is a considerable individual variation in the pattern and calibre of vessels that make up the CW. The anatomical variations of the CW that have been observed may affect the occurrence and severity of symptoms of cerebrovascular disorders such as stroke, aneurysms, infarctions among others. The study aimed to determine the anatomical variations of the CW as seen at the University Teaching Hospital, Zambia.

METHODS: A cross-section design was used to ascertain variations in 185 postmortem brains with respect to completeness of the circle, aneurysms and external diameter of the posterior communicating arteries (PcoA). The circle completeness was observed whereas the external diameter of the PcoA was measured using a digital vernier caliper. The median diameter was chosen to describe hypoplasia with a cutoff point at less than 1mm chosen based on earlier reports from other autopsy studies. Photographs were taken after dissection using a digital camera Canon power shot SX400IS 16 mega pixels. The brain specimen was placed back into the cranium upon completion of the examination. STATA version 12.0 was used for data analysis.

RESULTS: Out of a sample of 185, the proportion of males 149 (80.5%) were significantly higher ($p < 0.0001$) than females 36 (19.5%). Complete CW was found in 90.3% of the cadavers. Hypoplasia of the PcoA was noted in 30.3% on the right and 36.2% on the left side. The median age for individuals with hypoplasia (<1.0mm) of the right PcoA was 48 years (range; 17-86) and those without it was 34 years (17-72); the medians were statistically different ($p < 0.0001$). In case of hypoplasia of the left PcoA, the median age for the affected was 46 years (range; 17-86) and for those unaffected was 33 years (range; 17-75); there was a statistical difference, $p < 0.0001$. Multivariate analysis showed that one unit increase in age statistically increased the likelihood of having hypoplasia of the left and right PcoA by 9% (OR 1.09; 95%CI 1.06, 1.12; $p < 0.001$) and 10% (OR 1.10; 95%CI 1.06, 1.13; $p < 0.001$) respectively.

CONCLUSION: The study revealed significant variations in the CW in the brain specimens studied at the University Teaching Hospital, Zambia. Hypoplasia in the PcoA was the most common noted variation with CW incompleteness in a few cases. No aneurysm was observed. These anomalies could predispose one to developing neurological deficit especially in patients with internal carotid artery (ICA) occlusion. Studying the variability of the CW is important academically and for clinical reasons because such considerations can influence the mode of presentation, plan of investigation and treatment of various neurological disorders.

Key Words: Circle of Willis, Anatomical Variations, Hypoplasia, Posterior communicating arteries.

DEDICATION

I dedicate this work to my husband and my sons Zengani and Chawanzi. My boys you are a precious gift from God. You give me courage, strength and a reason to persevere in life.

I love you and may God continue to bless you.

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Lastly but not the least, I thank all those who helped me with this study directly or indirectly. May the grace of our Lord Jesus Christ, the love of God and the fellowship of the Holy Spirit be with you all.

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DEFINITIONS OF TERMS USED

Anastomosis - Means a direct or indirect connection of separate parts of a branching system to form a network, especially among blood vessels.

Aneurysm - Is a weak point in a blood vessel where the pressure of he blood causes the vessel wall to bulge outwards.

Anomaly - Refers to an abnormality or aberration from common finding of an anatomic structure.

Autopsy/Postmortem- Refers to inspection and dissection of a body after death in order to determine the cause of death.

Cadaver - A dead human body that may be used by physicians and other scientists to study anatomy identify disease sites and determine causes of death.

Cerebral hemodynamics- relates to the physical aspects of the blood circulation.

Cerebrovascular - Diseases refers to a group of conditions that affect the circulation of blood to the brain, causing limited or no blood flow to affected areas of the brain.

Circle of Willis - Is a vascular circulatory anastomosis at the base of the brain formed by the interconnection of the middle cerebral, anterior cerebral, posterior cerebral, basilar, anterior communicating and posterior communicating arteries.

Hypoplasia - Refers to underdevelopment or incomplete development of a tissue or an organ.

Interpeduncular fossa- Is a rhomboid-shaped area at the base of the brain, limited in front by the optic chiasma, behind by the antero-superior surface of the pons, antero-laterally by the converging optic tracts, and postero-laterally by the diverging cerebral peduncles.

Lilliequist's membrane- Is the thick arachnoid membrane between the interpeduncular cisterns inferiorly and the chiasmatic and carotid cisterns superiorly.

Variations Means a difference or deviation (e.g. in structure, form, function) from the recognized norm or standard.

ACRONYMS AND ABBREVIATIONS

ACA	-	Anterior cerebral artery
AcoA	-	Anterior communicating artery
CVA	-	Cerebrovascular accidents
CVD	-	Cerebral vascular disease
CW	-	Circle of Willis
ICA	-	Internal carotid Artery
MRA	-	Magnetic resonance Angiograpghy
PCA	-	Posterior cerebral artery
PcoA	-	Posterior communicating artery
UTH	-	University Teaching Hospital

CHAPTER ONE

1.1 INTRODUCTION

The brain is a highly vascular organ with its profuse blood supply characterized by a densely branching arterial network (Standring 2008). Standring further states that the brain is supplied by two internal carotid arteries and two vertebral arteries that form a complex anastomosis (circulus arteriosus or Circle of Willis) at the base of the brain. The Circle of Willis (CW) described by Thomas Willis in 1664, is a polygonal structure of collateral blood vessels located in the subarachnoid space within the interpeduncular cistern. It surrounds the optic chiasma and infundibulum at the base of the brain (Figure 1).

Moorehead et al., (2005) pointed out that the CW vessels diverge from this anastomosis to distribute oxygen-rich arterial blood to various cerebral regions. Moorehead et al also stated that blood is delivered to the brain through two internal carotid arteries that contribute 80% of the blood supply and two vertebral arteries that join intracranially to form the basilar artery. Anteriorly, the two internal carotid arteries branch at the medial end of the Sylvian fissure to form the middle and anterior cerebral arteries, with the two anterior cerebral arteries joined at the anterior end of the longitudinal fissure by the small anterior communicating artery which supply blood to the front and the sides of the brain (the frontal, temporal, and parietal regions of the brain). Posteriorly, there are two posterior cerebral arteries, formed by the division of the basilar artery, joined to the ipsilateral internal carotids by a posterior communicating artery. These perfuse and supply the posterior aspect of the brain (the occipital lobes, cerebellum and the brain stem).

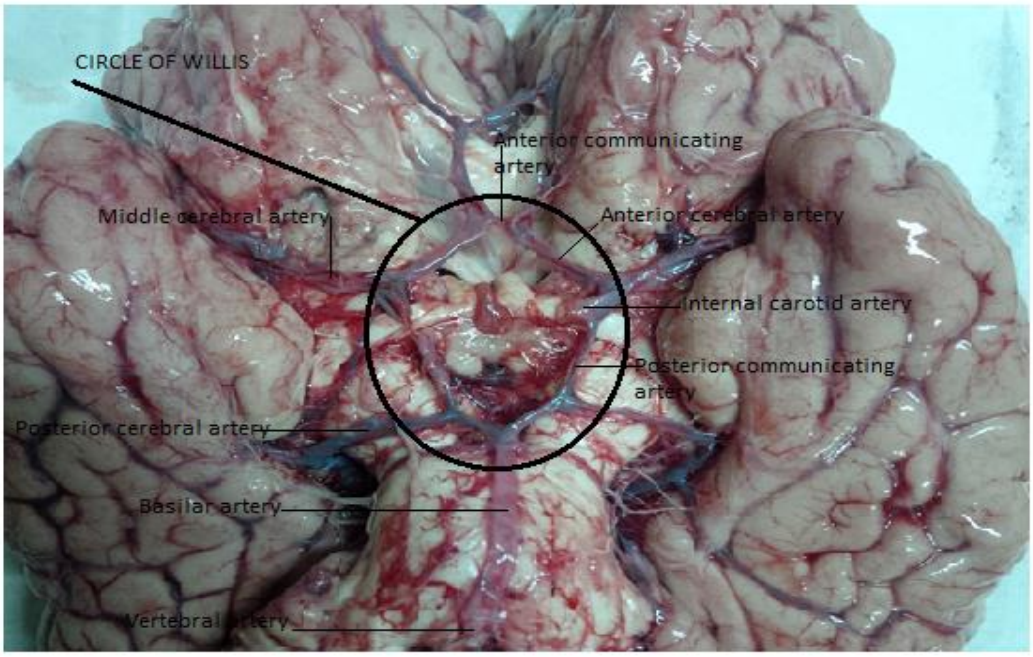

Figure 1: Inferior view of the brain showing the interconnection of vessels, forming the CW. (Photograph obtained from postmortem laboratory, University Teaching Hospital, Lusaka, Zambia)

Paul and Mishra (2004) pointed out that the ideal distribution of blood to the brain and the collateral potential of the CW is believed to be dependent largely on the morphology and the presence of all the component vessels of the CW. However, there is a considerable individual variation in the pattern and calibre of vessels that make up the CW. Although a complete circular channel almost always exists, one vessel is usually sufficiently narrowed to reduce its role as a collateral route thus potentially compromising circulation (Standring, 2008). It has been shown that in more than 50% of healthy brains and in more than 80% of dysfunctional brains, the CW contains at least one artery that is absent or underdeveloped (Macchi et al., 2005). A complete configuration of the CW on the other hand is present in 42–52% of healthy individuals (Hoksbergen et al., 2003; Schomer et al., 1994). Schomer et al (1994) further added by stating that there is evidence suggesting that a well-functioning complete CW is protective against cerebral ischemia in patients with carotid artery occlusive disease.

Many variations have however been reported in the arteries forming the CW in their formation, development and size (Paul and Mishra, 2004). Different abnormalities such as absence, split, hypoplastic and accessory vessels had been observed (Kapoor et al., 2008; Tanaka et al., 2006). Hartkamp et al (1999) indicated that since the anterior and posterior communicating arteries are designated as primary collateral pathways, they present with frequent anomalies. Wu and Chuang (2011) also noted that on the anterior side, the anterior communicating arteries or one of the proximal segments of the anterior cerebral arteries (ACA) can be missing or hypoplastic whereas on the posterior side, the posterior communicating arteries (PcoA) can be absent unilaterally or bilaterally. In light of this the integrity of the CW may be compromised because anomalies and hypoplasia in the anterior and posterior communicating arteries of the CW are common (Merkkola et al., 2006).

Furthermore, the anatomical variations of the CW that had been observed may affect the occurrence and severity of symptoms of cerebrovascular diseases (CVD) such as cerebrovascular accidents or stroke, aneurysms and infarctions among others (Iqbal, 2013). Hoksbergen et al (2003) added by also stating that several studies had shown that these variations play an important role in the development of cerebrovascular diseases (CVD) and can exacerbate the problem. Identification of such variations in a specific population is therefore important in the evaluation of cerebral vascular morbidity for appropriate management.

1.2 STATEMENT OF THE PROBLEM

There is a correlation between the pattern of the CW and cerebrovascular diseases (Iqbal, 2013; Miralles, 1995). Despite, several studies having shown that variations play an important role in the development of Cerebral Vascular Diseases (CVD), this researcher has not come across documentation on anatomical patterns or variations in the CW in the Zambian population. In developed countries however, anatomical variations of the CW have been extensively studied while in Sub-Saharan Africa, Zambia included, there is lack of information on the subject.

1.4 MAIN OBJECTIVE

To determine the anatomical variations of the CW as seen at the University Teaching Hospital.

1.4.1 SPECIFIC OBJECTIVES

i. To determine the completeness of CW.
ii. To ascertain the calibre of the PcoA in the CW.
iii. To establish the presence of aneurysms in the CW.

1.5 RESEARCH QUESTION

What is the anatomical morphology of the CW seen at the University Teaching Hospital?

1.6 SIGNIFICANCE OF THE STUDY

The study will provide information regarding the importance of knowing the variations in the configuration or branching pattern of the CW in a selected group representing the population of Zambia. Henderson et al (2000) emphasised that the knowledge about variations of the CW is clinically important as it plays an important role in cerebral hemodynamics. It also provides relevant data on these variations for its possible implications. To this effect, knowing the state of the circle becomes vital in determining the adequacy of the brain circulation in operations for cerebral aneurysms and also in ligation of the internal carotid artery (Sande and Wanjari, 2014). Additionally, this may have special value to neurosurgeons as well as those who perform advanced procedures while maintaining constant blood supply to the brain.

Banerjee (2000) also pointed out that the association between aneurysms and anomalies of the CW suggests that structural malformations may provide a mechanical basis for the development of aneurysm in congenitally weak portions of the vascular wall. These problems make it necessary to have a wide knowledge of the variations in the anatomy of the CW.

It is therefore important to try to correlate these anomalies to the occurrence of certain common clinical conditions such as stroke, aneurysms and arterio-venous malformations. Hoksbergen et al (2003) further stated that patients with effective collateral circulations have a lower risk of transient ischemic attack and stroke than those with ineffective collaterals.

Furthermore, the possibility of by-passing or shunting effects in occlusion of one of the cerebral vessels and the adequacy of recovery or lack of recovery after vascular occlusions may be explained in part by variations in the anatomy of the CW (Miralles, 1995). Therefore, based on these scientific reports, it has been persuasively argued that it is essential to properly assess the anomalies in the vessels that form the CW in the general population. This is in order to determine the capacity of the brain circulation in operations for cerebral aneurysms as well as in interventions involving the internal carotid artery (Iqbal, 2013). Lastly, the inferences that will be obtained from this study will be useful to anatomists and other health practitioners in enhancing their knowledge in teaching and research.

CHAPTER TWO

2.1 LITERATURE REVIEW

Several studies have reported a range of variations in the anatomy of the CW as a whole. However, it is not clear whether the frequency of manifestation of the different variations of the CW is similar in the studies done in different racial populations (Eftekhar, 2006). An autopsy study that aimed at identifying the anatomical variations in the CW in adult Pakistani population was conducted on 51 human brains by Siddiq (2010). The results were as follows; 37 (72.5%) of the 51(100%) cerebral arterial circles were complete; 15 (29.4%) had typical configuration; 25 (49%) had symmetrical arrangement and 39 (76.4%) had different types of variations in their component vessels. Variations were most common in the posterior communicating arteries followed by anterior communicating arteries then pre-communicating segments of the posterior cerebral and lastly in the pre-communicating segments of the anterior cerebral arteries. No circle was found with aneurysms. To this effect, the study concluded that different variations in the formation of the CW and in its component vessels were common in the local adult population of Pakistan. The results of the study emphasised the effects of variations in CW in producing hypoxia of the brain in many clinical conditions. Siddiq recommended that these effects should be taken into consideration during angiographic evaluation and neurosurgical procedures.

Ranil et al (2009) in their study on the prevalence of a typical CW and the variation in the anterior communicating artery in the Sri Lankan population revealed a high incidence of hypoplastic vessels (193 of 225; 86%) and with multiple anomalies (127 of 225; 56.4%). The most frequent site of abnormal diameters was seen in the posterior half of the circle. The assumption was that this could be related to the embryological development of the posterior half of the CW, where the basilar and the internal carotid arteries anastomose during development of the cerebral arteries. Furthermore, the findings of the anomalies of the anterior communicating artery in their study was similar to the studies conducted in India and from those of more diverse populations reported in the literature.

There was a wide range in the prevalence of typical configuration between Indian and Sri Lankan studies and this was attributed to the belief that Sri Lankans have a common origin from India. Additionally, Ranil et al (2009) reported that the results warranted further studies to ascertain influence of genetic, racial, regional, environmental, hemodynamic factors, or a combination of any of these.

A study conducted in India by Iqbal (2013) on 50 brain specimens, showed that the majority of the circles (52%) had anomalies. Cerebrovascular hypoplasia involving some vessels in the CW was the most frequent anomaly and was found in 24% of the brains whereas accessory vessels in the form of duplications/ triplications of the anterior communicating artery were seen in 12% of the circles. On the other hand, the embryonic origin of the posterior cerebral arteries from the internal carotid persisted in 10% of the circles. Lastly, an incomplete circle due to the absence of one or the other posterior communicating arteries was found in 6% of the specimens. Variations were also seen to be more frequent in the posterior half of the circle just like in most reviewed studies.

A dissection study undertaken by Sande and Wanjari (2014) on variations in the arterial CW on 30 adult cadavers revealed that the circle was complete in 24 (80%) cases and incomplete in 6 (20%) cases. The circle was incomplete in one of the 30 (3.33%) cases in the anterior part and in 5 (16.66%) of the cases in the posterior part. Sande and Wanjari also found that the anomalies were more common in the posterior part (43.33%) than in the anterior part (16.66%) of the circle. This was similar to previous studies by Jain et al (1990), Hartkamp et al (1999) and many more studies that reported more anomalies in the posterior part of the circle specifically absence or hypoplasia of PcoA. Sande and Wanjari also emphasised that knowledge of anatomical variations of the CW is of importance in surgery, with the aim being to preserve arteries in unusual locations, which if injured can lead to debilitating consequences.

A study conducted by Saha et al (2013) on variation of PcoA in human brain showed absence in 38.2% and hypoplasia in 23.3% cases.

To define hypoplasia a cutoff point of 0.5mm was used. Their reason was that if 1mm (vessel diameter) is taken as a cut off point for hypoplasia almost one fourth of the brain specimens become hypoplastic. Furthermore, it was observed that other researchers who utilized 0.5mm as the upper limit of hypoplasia found almost similar incidences.

Nevertheless, a minimal variation in between them was observed and the difference was attributed to technical or racial reasons. The study showed a wide variability in the posterior arterial component of the CW with absence and significant hypoplasia in a considerable number of cases. In light of the above, it was emphasised that exact knowledge of the variation of PcoA is necessary not only to explain various neurological symptoms but also for successful microvascular surgery in this region.

A Magnetic Resonance Angiography (MRA) imaging scan study was conducted by Maaly and Ismail (2011) on 250 patients. Their aim was to evaluate the different anatomical variations of the CW and to determine average vessel diameters in an Egyptian population. The study revealed complete CW in 46.7% cases. The prevalence of the circle completeness in the younger subjects was higher than the older ones (50% versus 45% respectively) and in females (52.8%) more than males (42.6%). Furthermore, the anterior part of circle was complete in 75% (younger subjects) and 65% (older subjects) while the posterior part was complete in 40% (younger subjects) and 37.5% (older subjects). Maaly and Ismail found statistically significant differences between the mean vessel diameters between males and females in the vessels forming the CW. Additionally, the average diameters of the proximal vessels supplying the CW were larger in the order subjects. On the contrary, the distal branches of the circle had smaller mean diameters in the older subjects. The study illustrated that there were statistically significant differences in some vessel diameters according to age and gender. They concluded that some of the variations could be related to aneurysmal development and significantly correlate with relative contributions of the flow rates of the proximal arteries.

CHAPTER THREE

3.1 METHODOLOGY

3.1.1 STUDY DESIGN

A cross sectional study was used.

3.1.2 STUDY SETTING

The study was conducted in the Department of Pathology at the University Teaching Hospital, Lusaka, Zambia from August 2015 to February 2016. The site was selected purposefully because of the convenience and ease of access to the human brains during postmortem.

3.1.3 STUDY POPULATION

The study population included all brains from human cadavers that underwent postmortem.

3.1.4 INCLUSION CRITERIA

All intact brains of human cadavers that was available during routine autopsy at the University Teaching Hospital (UTH).

3.1.5 EXCLUSION CRITERIA

Any brain specimen with evidence of pathology or trauma (severe haemorrhage, tissue damage and mass lesions) of the brain and its blood supplying vessels that may have affected the topography of the arteries was excluded from the study.

3.1.6 STUDY SAMPLE

The sample size was calculated as follows;

$$N = \frac{Z^2 \times P\,(1-P)}{(E)^2}$$

N = Sample required

Z = Z statistic for a given level of confidence = 1.96 when using a 95% CI

P = the expected prevalence of the condition in the population being studied; if unsure, then

use 0.5 to give the most conservative sample size

E = confidence interval, usually 0.05= this refers to the accuracy range (+/- 5%)

$$\frac{1.96^2 \times 0.86\,(1-0.86)}{(0.05)^2}$$

=185 sample size

The assumption for the sample size was obtained from De Silva et al (2011) who used a cross sectional study design similar to one adapted in this study. De Silva et al found the prevalence of a typical circle in a Sri Lankan population to be 14%. Therefore a prevalence of the variation used in this study was to be 86% or 1-0.14=0.86, giving a sample size of 185 brain specimens.

3.1.7 DATA COLLECTION PROCEDURE

Data was collected immediately after removal of the brain from the cranial cavity. After opening each calvaria by saw, dura was incised carefully with special attention given to the interpedencular fossa to preserve the CW which lies in the subarachnoid cistern. After that the brain was detached from the spinomedullary junction and removed from the calvaria. The brain specimen was washed and the base of the brain cleaned by peeling off the arachnoid mater in order to expose the component vessels. The CW was studied in detail in each specimen with reference to parameters such as completeness, hypoplasia or absence of the PcoA and presence of aneurysm.

The external diameter was measured using a digital vernier calliper (figure 2 below) with a cutoff point for hypoplasia at less than 1mm chosen based on earlier reports from other postmortem studies (Tanaka et al., 2006; Kapoor et al., 2008; Eftekhar et al., 2006). Photographs were taken after dissection using a digital camera canon power shot SX400IS 16 mega pixels. The photos were later used to study the CW in detail. The brain specimens were placed back into the cranium upon completion of the examination. Finally, the pattern was recorded in a data collecting sheet, coded and entered in Microsoft excel.

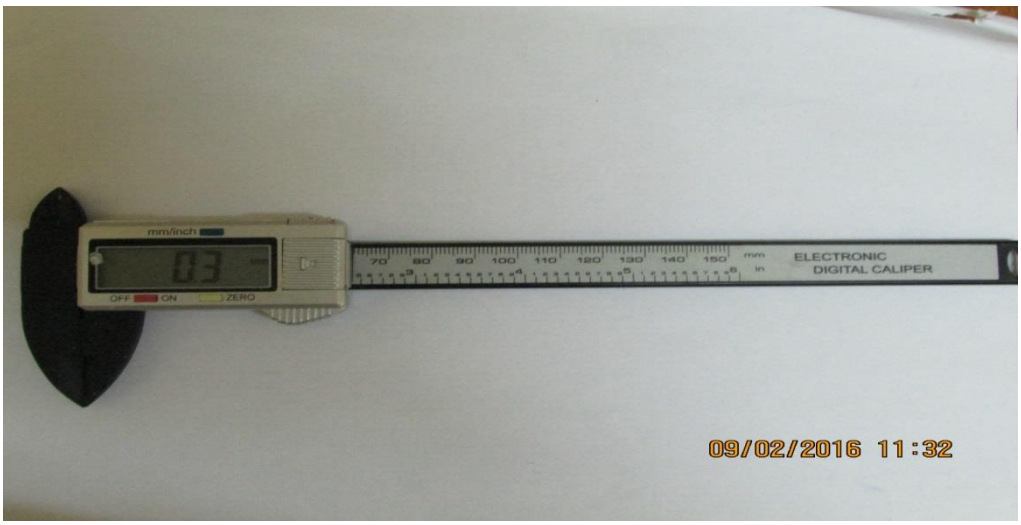

Figure 2: Digital Vernier Caliper: Instrument that was used to measure external diameter of the PcoA

3.1.8 RESEARCH VARIABLES

Variable (Dependent)	Indicator	Scale Measurement
Variation of COW from typical configuration	-completeness	0=yes 1=no
	-External diameter for PcoA	< 1mm= hypoplasia
	-Aneurysm	Yes or no
Independent		
Age	>17	Continous
Gender	Male	0=male
	Female	1=female

3.2 DATA MANAGEMENT

3.2.1 DATA COLLECTION TOOL

A structured checklist was used to collect biographic data, measured variables and then entering in Microsoft excel sheet.

3.2.2 DATA ANALYSIS

The analysis of the anatomical pattern and variations of the CW was performed using Stata version 12. A two sample test of proportion for gender was used giving an equal proportion of male and female. To test for differences in the median, two sample Wilcoxon Rank Sum (Mann Whitney) test was used. The median diameter was chosen to describe hypoplasia with a cut off of point less than 1mm. Logistic regression was used to determine factors associated with right and left hypoplasia. All statistical tests was performed at 5% significance level or 95% confidence interval with p-value of <0.05 to determine statistical significance.

3.2.3 DATA PRESENTATION

After processing and analysing the data, it was presented in contingency tables and numerical descriptions were given to show the relationships of variables so as to make the data more meaningful.

3.2.4 PLANS FOR DISSEMINATION OF THE FINDINGS

The findings of this research will be disseminated to neurosurgeons and pathologists at the University Teaching Hospital (UTH). Furthermore, the information obtained will also be disseminated to the Anatomy Department at the University of Zambia, School of Medicine for learning purposes.

3.2.5 ETHICAL CONSIDERATION

Ethical approval was sought from Excellence in Research Ethics and Science (ERES) CONVERGE IRB. Furthermore, permission to conduct the study was sought from University Teaching Hospital Management and the head of the Department of Pathology for authorisation. The study was performed as part of the routine postmortem examinations and to this effect, the researcher used the approval already obtained by pathologists. The information obtained from this study was used strictly for research purposes and high confidentiality was maintained. In order to guarantee the privacy of study, the samples were coded and no names used.

CHAPTER FOUR

4.1 RESULTS

The total sample size was 185 of human cadavers with the median age of 37 years (range; 17-86). The proportion of males 149 (80.5%) were significantly higher ($p < 0.0001$) than their female 36 (19.5%) counterparts. The median age for individuals with hypoplasia (<1.0mm) of the right PcoA was 48 years (range; 17-86) and those without it was 34 years (17-72); the medians were statistically different ($p < 0.0001$). In case of hypoplasia of the left PcoA, the median age for the affected was 46 years (range; 17-86) and those unaffected it was 33 years (range; 17-75); there was a statistical difference, $p < 0.0001$.

4.1.1 BASIC STATISTICAL ANALYSIS

The basic statistical analysis of the posterior communicating artery (PcoA) on both sides in the CW of human cadavers of different ages and genders are shown in table 1 below. Average values and the standard deviations for right and left PcoA are 1.4 (±0.8) mm and 1.3 (±0.7), respectively. The means and standard deviations for males and females with regards to right and left PcoA were 1.4 (±0.8) mm and 1.3 (±0.7) mm and 1.4 (±0.7) mm and 1.4 (±0.6), respectively (see table 1). However, the t-test showed that there was no statistical difference in the means of both right ($p = 0.7191$) and left ($p = 0.6650$) side of the PcoA with respect to gender.

Table 1: Statistical parameters of posterior communicating arteries (PcoA) in human cadavers

Characteristics	Age (in years)	PcoA Rt (in mm)	Pcoa Lt (in mm)
Mean	38.9	1.4	1.3
SE	1.1	0.1	0.1
Median	37	1.3	1.2
SD	15.1	0.8	0.7
Minimum	17	0	0
Maximum	86	3.2	3.1
CI (95%)	36.7, 41.1	1.3, 1.5	1.2, 1.4
Male			
Mean	38.3	1.4	1.3
SE	1.2	0.1	0.1
Median	37	1.3	1.2
SD	14.4	0.8	0.7
Minimum	17	0	0
Maximum	79	3.2	3.1
CI (95%)	35, 40.6	1.3, 1.6	1.2, 1.4
Female			
Mean	41.3	1.4	1.4
SE	3.0	0.1	0.1
Median	37	1.3	1.2
SD	17.8	0.7	0.6
Minimum	17	0	0.4
Maximum	86	3.1	2.9
CI (95%)	35.3, 47.3	1.1, 1.6	1.2, 1.6

4.1.2 BASIC CHARACTERISTICS OF THE STUDY VARIABLES

Table 2 below shows the basic characteristics of the study variable of the human cadavers. When the PcoA measurement is below 1.0mm, then there is hypoplasia. In the right and left of the PcoA, hypoplasia was 30.3% and 36.2%, respectively. These were proportions of less than 1mm (figure 3 below). Complete CW was found in 90.3% of the cadavers (figure 2 below). Of all the human cadavers examined, there was no aneurysm, see table 2.

Table 2: Basic characteristics of study variables

Characteristics	**N (%)**
Total	185 (100%)
Gender	
Male	149 (80.5)
Female	36 (19.5)
PcoA Rt	
< 1.0mm	56 (30.3)
≥ 1.0mm	129 (69.7)
PcoA Lt	
< 1.0mm	67 (36.2)
≥ 1.0mm	118 (63.8)
Circle of Willis	
Complete	167 (90.3)
Incomplete	18 (9.7)
Aneurysm	
Yes	0 (0.0)
No	185 (100%)

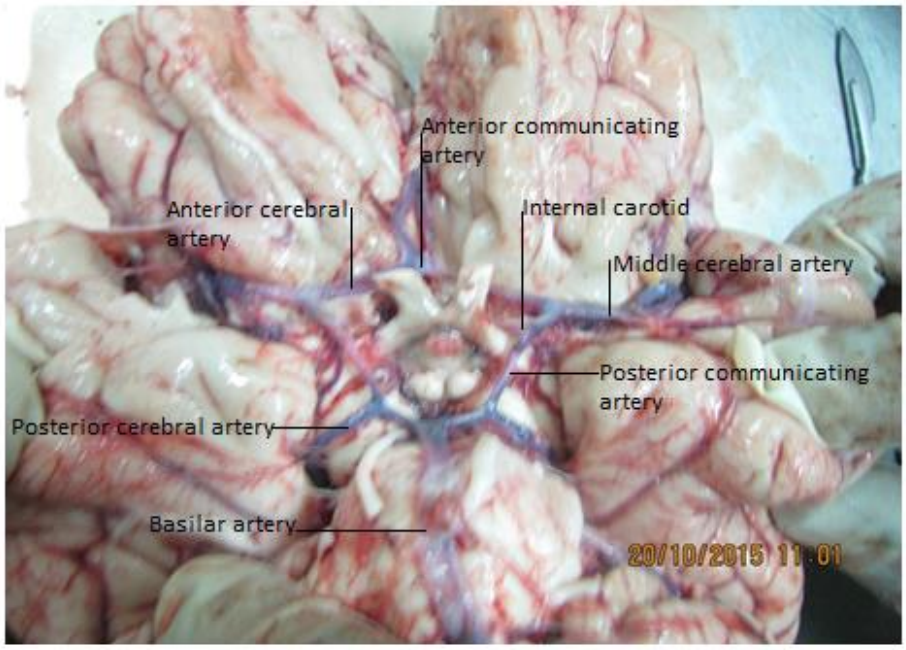

Figure 3 showing a complete circle: Posterior part: All components, PCoA, PCA segments and BA present; normal in their origin and size. Bifurcation of BA is equal and symmetric. Anterior part: all the components, A1 segment and ACoA present; normal in their origin and size.

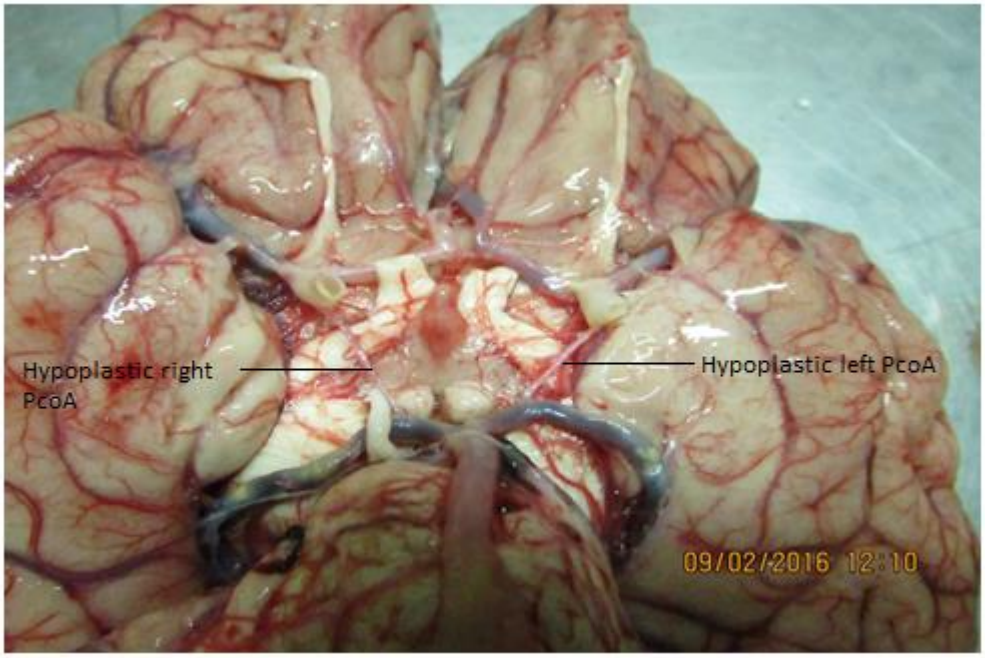

Figure 4 showing bilateral hypoplasia of the PcoA with diameters less than 1mm measured during postmoterm examination at the University Teaching Hospital.

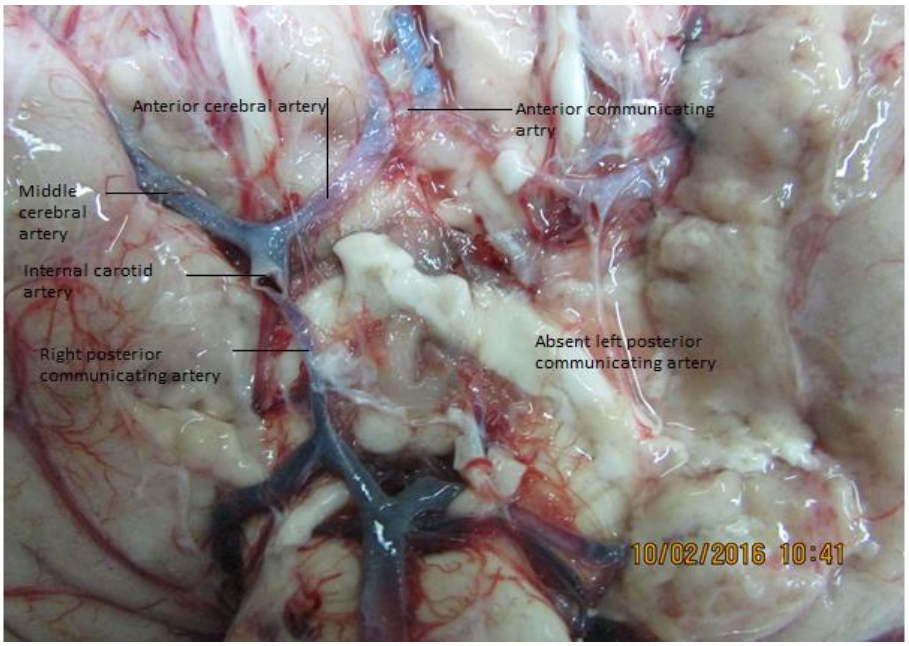

Figure 5 showing absent left PcoA (incomplete circle)

4.1.3 FACTORS ASSOCIATED WITH HYPOPLASIA

Table 3, shows the univariate and multivariate analysis of the factors associated with hypoplasia for both left and right PcoA. A multivariate analysis showed that one unit increase in age statistically increased the likelihood of having hypoplasia of the left PcoA by 9% (OR 1.09; 95%CI 1.06, 1.12; $p < 0.001$). At univariate analysis, gender was not associated with hypoplasia of the left PcoA (OR 0.52; 95%CI 0.23, 1.19; $p = 0.123$). However, during multivariate analysis, females had a statistically reduced odds of having hypoplasia of the left PcoA by 72% (OR 0.28; 95%CI 0.10, 0.80; $p = 0.017$) compared to their male counterpart. Hence, making age and gender as the factors associated with hypoplasia of the left PcoA.

In case of hypoplasia of the right PcoA, multivariate analysis showed that a unit increase in age statistically increased one's odds of having hypoplasia by 10% (OR 1.10; 95%CI 1.06, 1.13; $p < 0.001$). Gender was not statistically significant at both univariate and multivariate analysis (OR 1.02; 95%CI 0.46, 2.24; $p = 0.967$ and OR 0.70; 95%CI 0.26, 1.88; $p = 0.477$). Therefore, making age as the only variable associated with hypoplasia of the right PcoA.

Table 3: Factors associated with left and right posterior communicating arteries

	Univariate analysis		**Multivariate analysis**	
Characteristics	**OR (95%CI)**	**P-value**	**OR (95%CI)**	**P-value**
Hypoplasia for left PcoA				
Age	1.08 (1.05, 1.11)	< 0.001**	1.09 (1.06, 1.12)	< 0.001**
Gender				
Male	0.00	0.00	0.00	0.00
Female	0.52 (0.23, 1.19)	0.123	0.28 (0.10, 0.80)	0.017**
Hypoplasia for right PcoA				
Age	1.09 (1.06, 1.13)	< 0.001**	1.10 (1.06, 1.13)	< 0.001**
Gender				
Male	0.00	0.00	0.00	0.00
Female	1.02 (0.46, 2.24)	0.967	0.70 (0.26, 1.88)	0.477

Abbreviations: OR = odds ratio; CI = confidence interval; PcoA = posterior communicating artery; **p-value < 0.05

CHAPTER FIVE

5.1 DISCUSSION

CW is formed at the base of the brain in order to preserve the cerebral perfusion and to avoid the symptoms of ischemia in case of blockage of part of the cerebral arterial system. The study looked at the completeness of the circle, presence of aneurysms and also the calibre of vessels in the posterior communicating arteries with external diameters less than 1mm as hypoplasia. Additionally, the study discovered factors such as age and gender to be associated with hypoplasia.

5.1.1 COMPLETENESS OF THE CIRCLE

The prevalence of the typical circle (normal textbook polygon) ranges from 4.6% to 7.2% (Ranil, 2009 and Iqbal, 2013). A reason for the difference in range could have been due to the diversity in classification and the definition of hypoplastic vessels. In the present study a high proportion of completeness of the CW was observed (90.19%). These findings were consistent with studies by Sande and Wanjari (2014) and Eftekhar et al (2006) who also found a high prevalence of completeness 80% and 90% respectively. This was compared to studies by Iqbal (2013); Kapoor et al (2008) both in India; Maaly and Ismail (2011) in Egypt who found that almost half of the circles were complete. On the other hand, De Silva et al (2011) in Sri Lanka found a low prevalence of completeness in the CW (14.2%). Iqbal pointed out that the wide range in the prevalence of the typical configuration could be attributed to the influence of genetic, regional, environmental, hemodynamic factors and also the diversity in the classification of hypoplastic vessels.

Ranil (2009) defined a circle as typical if all the component vessels of the CW were present, origin of the vessels forming the CW was from its typical source and the size of a component vessel more than 1 mm in diameter. However, in the present study a circle was considered complete if all the component vessels were present, whether hypoplastic or duplicated but not absent (figure 2) below.

This is supported by Hartcamp etal (1999) who based their classification system on the continuity of the circular configuration (morphological completeness) in order to assess the potential for collateral flow development.
On the other hand the CW was found to be incomplete in a few cases and this was mostly due to absence of the PcoA unilaterally or bilaterally. This incompleteness could pose a risk factor for ischaemic stroke especially in internal carotid occlusion.

5.1.2 HYPOPLASIA IN THE POSTERIOR COMMUNICATING ARTERIES

The PcoA connects the two systems that supply the brain (internal carotid and vertebro-basilar systems). Therefore, making the PcoA very important vessels and worthwhile to study since they provide collaterals in the cerebral circulation so that if one system is blocked, the other can take over (Saha et al., 2013). To define hypoplasia of the PcoA, various authors used different measurement. In the present study, the vessel was considered hypoplastic if the external diameter was less than 1mm, chosen based on various autopsy studies ((Tanaka et al., 2006; Kapoor et al., 2008; Eftekhar et al., 2006 and Ardakani, 2008).

In contrast, Radiological studies by Three Dimensional Time of Flight Magnetic Resonance (3DTFMR) angiography considered hypoplasia if the diameter of the vessel is less than 0.8mm (Hoksbergen et al., 2003). Hoksbergen et al argues that threshold diameter for supplying collateral flow is even smaller, namely between 0.4mm to 0.6mm. PcoA variations are regarded as the most common variations in brain circulations. They are either hypoplastic or missing in 10% to 46% of the cases (Merkolla et al., 2006; Eftekhar et al., 2006). Similarly, hypoplasia was seen in 30.3% and 36.2%, in the left and right PcoA respectively in the present study. While absent vessels were seen in 9.7%. This is also in line with Standring (2008) who stated that the greatest variation in calibre between individuals occurs in the posterior communicating artery, which is normally very small, so that only limited flow is possible between the anterior and posterior circulations.

The findings in the present study were also consistent with the study by Saha et al (2013) who found 37 specimens (61.6%) out of 60 brain specimens of the PcoA were either absent or hypoplastic. Furthermore, they reported that the average diameter of PcoA varied between 1.0 -1.5 mm with some specimens having very narrow diameters of less than 0.5 mm. Similarly, the means in the present study varied from 1.3mm and 1.4 mm for the left right PcoA respectively, with minimum diameter of 0mm which meant absent vessel.

According to most literature, hypoplasia of PcoA is a congenital variation and does not lead to any symptoms if other component vessels of the CW are functioning normally. This observation could explain its presence in otherwise normal persons. However, PcoA becomes a risk factor in ischaemic stroke in the presence of internal carotid artery (ICA) occlusion (`Wu and Chuang 2011). Saha et al (2013) emphasised that that anomalies of the PcoA have a great significance since it forms a link between two major arterial systems (the internal carotid and the vertebrobasilar circuit). Consequently, a hypoplastic PcoA may be a risk factor for developing neurological deficit in patients with ICA occlusion. Schomer et al (1994) also found a definitive correlation between narrow or absent PcoA and cerebral infarction in persons with internal carotid artery occlusion. Ultimately, Saha et al (2013) highlighted that studying the variability of the PcoA is important for academic reasons and in clinical practice since variations can influence the mode of presentation, plan of investigation and treatment of various neurological disorders.

5.1.3 FACTORS ASSOCIATED WITH HYPOPLASIA

In the present study, a significant association was observed between age and hypoplasia of the PcoA. However, gender was only statistically significantly associated with hypoplasia of the left PcoA. It was established that one unit increase in age statistically increased the likelihood of having hypoplasia by 9% and 10% for left and right PcoA respectively. This was consistent with findings by Baskaya et al (2004) who found Larger PcoA to be more in children (39–75%) than in adults (8–29%). Therefore, concluded that this observation supports that the calibre of this vessel diminishes with age.

In contrast, a study by Vasović et al (2011) found the smallest calibre of the right and left PcoA (0.30 and 0.45 mm) in a 44-year-old and in a 64-year-old woman, while the largest calibre (2.86 and 3.31 mm) was found in an 80-year old woman. This observation can be explained in line with literature that states that segments of the CW which are narrow or string-like, or even absent are a result of agenesis or involution during embryonic development (Saikia et al., 2014). Gender however, was not associated with hypoplasia of the right PcoA, but at multivariate analysis it was found to be a factor associated with hypoplasia of the left PcoA only. Macchi et al (2005) in his Magnetic Resonance angiography (MRA) study in 100 healthy subjects (50 men and 50 women) found no statistical significant gender difference between the frequencies of variations.

5.1.4 ANEURYSM

Standring (2008) describes aneurysms as balloon-like swellings which occur on arteries as a result of defects in the vessel wall. They are most commonly found on the vessels of the CW particularly at or near the junctions of vessels. Siddiq (2013) pointed out that there is a definite correlation between asymmetrical proximal segments of the anterior cerebral arteries and aneurysms of anterior communicating artery. This association between aneurysms and anomalies of CW suggests structural basis for the development of aneurysms in congenitally weak portions of the vascular wall. However, most intracranial aneurysms are asymptomatic and remain undetected until the time of rupture (Vega et al., 2002).

The current study did not find any aneurysm in the CW of all the human cadavers examined. Similarly, Pradhan et al (2009) in a morphological study of the CW also did not find any aneurysms. The incidence of aneurysms of the CW reported in published literature is 0.25% to 4.9%. This is in line with the findings by Saikia et al (2014) who found a single aneurysm (1.42%) in the proximal segment of the right anterior cerebral (ACA). The lower incidence of aneurysms reported in most published literature could be one of the reasons attributed to the finding in the present study. Another reason could be a small sample size and short period allocated to the study.

5.2 LIMITATIONS OF THE STUDY

The limitation for this study was the possible change that could have occurred in the diameter of the vessels during postmortem which could have affected the measurements.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

The study revealed a high prevalence in the completeness of the circle and no aneurysm was noted.

A wide variability in the posterior arterial component of the CW was observed. The variability was mainly hypoplasia or absent vessels in the PcoA. It was also established that age was significantly associated with hypoplasia of both the right and left PcoA. Hypoplasia in the PcoA can predispose one to developing neurological deficit especially in patients with ICA occlusion. Ultimately, variations of the CW have the potential to influence the mode of presentation, plan of investigation and treatment in various neurological disorders. Knowledge of these variations is therefore important not only to explain various neurological symptoms but also for successful micro-vascular surgery in this region.

6.2 RECOMMENDATIONS

As a measure to maintain cerebral haemodynamics for neurosurgeons during cerebrovascular microsurgery and in prevention of CVDs, the following recommendations are made based on the findings of this study:

1. Surgeons who perform head and neck operative procedures should be aware of CW variations in order to reduce the potential hazards associated with interventions.
2. Future research should include clinical data of disease patterns such as CVDs and the cause of death.

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8.1 APPENDICES

APPENDIX 1: DATA COLLECTION FORM

Code number …….

Age (years) …….

Completeness of the CW……...

Presence of aneurysm Yes ☐

No ☐

Artery	**Diameter (mm)**		**Other finding**
Anterior communicating artery			
Posterior cerebral arteries	Right		
	Left		
Anterior communicating arteries	Right		
	Left		
Posterior communicating arteries	Right		
	Left		
Middle cerebral artery	Right		
	Left		

APPENDIX 2: APPROVAL FROM ERES CONVERGE

33 Joseph Mwilwa Road
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Tel: +260 955 155 633
+260 955 155 634
Cell: +260 966 765 503
Email: eresconverge@yahoo.co.uk

I.R.B. No. 00005948
F.W.A. No. 00011697

7th July, 2015

Ref. No. 2015-May-006

The Principal Investigator
Ms. Hildah Zulu
The University of Zambia
School of Medicine
Dept. of Anatomy
P.O. Box 50110,
LUSAKA.

Dear Ms. Zulu,

RE: ANATONOMICAL VARIATIONS OF THE CIRCLE OF WILLIS IN THE ZAMBIAN POPULATION.

Reference is made to your corrections dated 2nd July, 2015. The IRB resolved to approve this study and your participation as principal investigator for a period of one year.

Review Type	Ordinary	Approval No. **2015-May-006**
Approval and Expiry Date	Approval Date: 7th July, 2015	Expiry Date: 6th July, 2016
Protocol Version and Date	Version-Nil	6th July, 2016
Information Sheet, Consent Forms and Dates	• N/A	6th July, 2016
Consent form ID and Date	Version-Nil	6th July, 2016
Recruitment Materials	Nil	6th July, 2016
Other Study Documents	Data Collection Form.	6th July, 2016
Number of participants approved for study	230	6th July, 2016

Specific conditions will apply to this approval. As Principal Investigator it is your responsibility to ensure that the contents of this letter are adhered to. If these are not adhered to, the approval may be suspended. Should the study be suspended, study sponsors and other regulatory authorities will be informed.

Conditions of Approval

- No participant may be involved in any study procedure prior to the study approval or after the expiration date.
- All unanticipated or Serious Adverse Events (SAEs) must be reported to the IRB within 5 days.
- All protocol modifications must be IRB approved prior to implementation unless they are intended to reduce risk (but must still be reported for approval). Modifications will include any change of investigator/s or site address.
- All protocol deviations must be reported to the IRB within 5 working days.
- All recruitment materials must be approved by the IRB prior to being used.
- Principal investigators are responsible for initiating Continuing Review proceedings. Documents must be received by the IRB at least 30 days before the expiry date. This is for the purpose of facilitating the review process. Any documents received less than 30 days before expiry will be labelled "late submissions" and will incur a penalty.
- Every 6 (six) months a progress report form supplied by ERES IRB must be filled in and submitted to us.
- ERES Converge IRB does not "stamp" approval letters, consent forms or study documents unless requested for in writing. This is because the approval letter clearly indicates the documents approved by the IRB as well as other elements and conditions of approval.

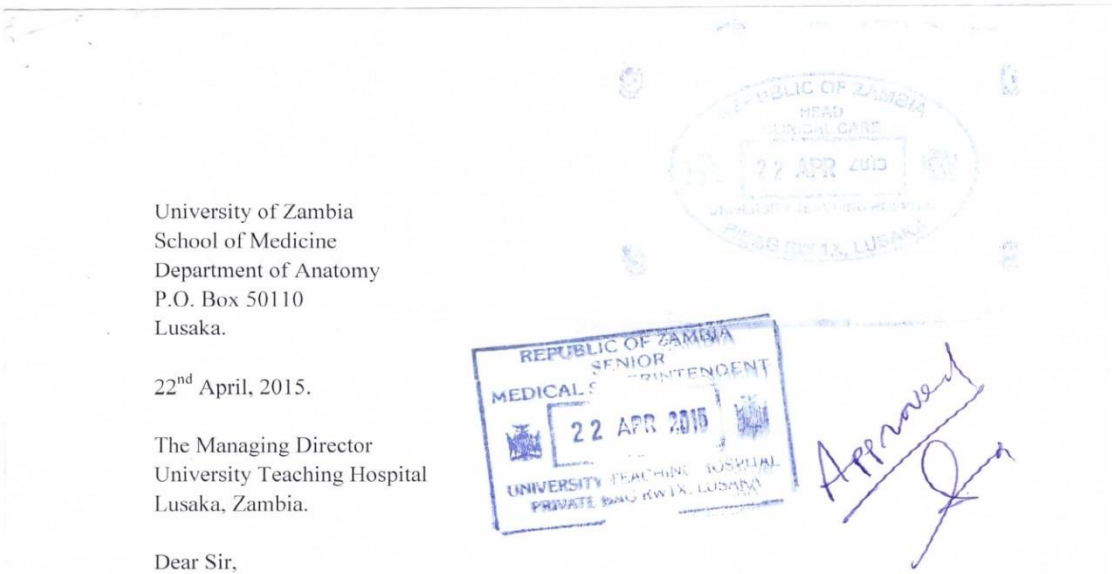
Should you have any questions regarding anything indicated in this letter, please do not hesitate to get in touch with us at the above indicated address.

On behalf of ERES Converge IRB, we would like to wish you all the success as you carry out your study.

Yours faithfully,
ERES CONVERGE IRB

Dr. E. Munalula-Nkandu
BSc (Hons), MSc, MA Bioethics, PgD R/Ethics, PhD
CHAIRPERSON

APPENDIX 3: APPROVAL LETTER FROM UNIVERSITY TEACHING HOSPITAL



University of Zambia
School of Medicine
Department of Anatomy
P.O. Box 50110
Lusaka.

22nd April, 2015.

The Managing Director
University Teaching Hospital
Lusaka, Zambia.

Dear Sir,

REF: PERMISSION TO CONDUCT A RESEARCH AT THE UNIVERSITY TEACHING HOSPITAL

Reference is made to the above captioned subject.

I am a second year student, pursuing a Master of Science degree in Anatomy. I write to request for permission to conduct a research on the Anatomical Variations of the Circle of Willis at the University Teaching Hospital. The research will be a cross sectional post-mortem based study to be conducted at the Pathology department.

Your favourable consideration regarding this matter will be highly appreciated.

Yours faithfully,

Hilda Zulu

APPENDIX 4: CLEARANCE LETTER FROM PATHOLOGY DEPARTMENT

REPUBLIC OF ZAMBIA

MINISTRY OF HEALTH
University Teaching Hospital

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OFFICE OF THE SENIOR MEDICAL SUPERINTENDENT

Our Ref:
Your Ref:

University Teaching Hospital,
Department of Pathology and Microbiology,
P.O Box 50110,
Lusaka.

29th June, 2015

The Chairperson,
ERES Converge IRB,
33 Joseph Mwilwa,
Lusaka,
Zambia.

Dear Sir/Madam,

RE: REQUEST TO FOREGO THE NEED TO OBTAIN INFORMED CONSENT FROM RELATIVES OF THE DECEASED DURING THE POST MORTEM BASED STUDY.

Reference is made to the above noted subject and to the concerns expressed by ERES about obtaining consent from relatives to undertake the study on anatomical variations of the Circle of Willis at the University Teaching Hospital by Hilda Zulu as Principal Investigator.

We write to advise and assure ERES that brain examination is done as part of routine examination during post mortem. To this effect, all autopsy examinations which are carried in the Department of Pathology are in line with the provisions of regulations practiced in the Department. The Principal Investigator therefore will use the permission obtained by the pathologists since the study will be conducted as part of the routine autopsy examination.

Furthermore, we wish to advise that the examination will be done immediately the brain specimen is removed and will not be stored but replaced in the cranium following completion of the examination.

We look forward to your favourable consideration on this request.

Yours faithfully,

Dr Aaron Lunda Shibemba

Consultant Anatomical Pathologist

Histopathology Unit Head