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SCHOOL OF BIOMEDICAL AND ALLIED HEALTH SCIENCES

ELECTROENCEPHALOGRAPHY IN SEIZURE DIAGNOSIS AND THE PREDICTION OF FUNCTIONAL OUTCOMES OF STROKE PATIENTS AT KORLE BU TEACHING HOSPITAL

BY

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DECLARATION

I Ruth Yemorkor Laryea, do hereby declare that apart from literature cited and acknowledged, this thesis is my own work produced from research under the supervision of Rev. Dr Charles Antwi Boasiako of the Department of Physiology and Dr Albert Akpalu of the Department of Medicine and Therapeutics, College of Health Sciences, University of Ghana.

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DEDICATION

I dedicate my thesis to God almighty- my sun and shield, to my family and to my mentors.

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LIST OF ABBREVIATIONS

ADL	Activities of daily living
AED	Anti-epileptic drug
BI	Barthel Index
BSI	Brain symmetry index
Ca^{2+}	Calcium
CEEG	Continuous electroencephalography
CNS	Central nervous system
CT	Computed tomography
DAR	Delta/ Alpha ratio
EEG	Electroencephalography
fMRI	Functional magnetic resonance imaging
GABA	Gamma amino-butyric acid
KBTH	Korle Bu Teaching Hospital
MDT	Multidisciplinary team
mNIHSS	Modified National Institute of Health stroke scale
MRS	Modified Rankin Scale
Na^{+}	Sodium
NIHSS	National Institute of Health Stroke Scale
pdBSI	Pairwise derived brain symmetry index
PNS	Peripheral nervous system
PSE	Post stroke epilepsy
QEEG	Quantitative electroencephalography

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RAP	Relative alpha power
SME	Surgical and Medical Emergency unit
SPSS	Statistical Product for Service Solution
SSA	Sub-Saharan Africa
TIA	Transient ischaemic attack

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ABSTRACT

Background: As compared to developed economies, stroke is a rising epidemic affecting mostly the younger workforce in Sub-Saharan Africa (SSA), exerting a severe toll on the physical, psychoemotional, cognitive and social lives of its victims with a 3-year mortality rate of 84%. The occurrence of seizures lead to poor prognosis and increased mortality in stroke patients.

Early screening for seizures and effective prognostication of the functional outcome of stroke may improve the outcomes of patients.

General aim: This study aimed to determine the incidence of seizures in 30 stroke patients and how quantitative electroencephalography (QEEG) indices prognosticate their one-month functional outcome.

Methodology: Electroencephalography (EEG) is a non-invasive analysis of brain function available at Korle Bu Teaching Hospital. Stroke outcome was measured using the modified National Institute of Health Stroke Scale (mNIHSS), modified Rankin Scale (MRS) and Barthel Index (BI).

In this study, routine EEG of thirty (30) consenting acute stroke patients was recorded using the 10/20 standardized format within ten days of stroke onset. The EEG patterns were characterized by a neurologist and then delta/alpha ratio (DAR), relative alpha power (RAP) and the pairwise derived brain symmetry index (pdBSI) were calculated using the EEGLAB software. On the day of recording EEG, the mNIHSS, MRS and Barthel Index scores of the patients were measured and again a month later.

Clinical and EEG findings were displayed on bar charts and statistical tables while Spearman's rank correlation and linear regression was used to determine predictors of one-month outcome using the Statistical Product for Service Solution (SPSS) version 20.

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Results: The 30 participants of this study consisted 60% aged 60years or below, 66.7% male and 33.3% haemorrhagic stroke. Clinical seizures occurred in 13.3% of study participants, electrographic seizure occurred in 46.7% (with 92.9% being generalized seizures) and cerebral dysfunction was diagnosed in 56.7% of the participants. The MRS, mNIHSS and BI measured at recruitment significantly correlated to their measures at one-month ($p < 0.01$); the least being between MRS and mNIHSS scores at recruitment (rho = 0.753) and the highest was between MRS and BI scores at recruitment (rho = -0.932). The only correlation for QEEG indices was between RAP and DAR (rho = -0.988, $p < 0.001$), the highest in the entire analysis. Overall, mNIHSS score at recruitment was the best predictor of all three functional outcome measures at one-month- MRS_1 (beta = 0.471, p = 0.001), $mNIHSS_1$ (beta= 0.753, p = 0.001) and BI_1 (beta= -0.556, p = 0.001).

Conclusion: There was a high incidence of electrographic seizure in stroke patients of Korle Bu Teaching Hospital than what could be clinically diagnosed. The QEEG indices- DAR, RAP and pdBSI did not significantly predict post-stroke functional outcomes measures (MRS, mNIHSS or BI) at one-month across all stroke types. Relative alpha power (RAP) measured at recruitment was the only QEEG index useful in the prediction of neurological deficit (mNIHSS) in ischaemic stroke at one-month post stroke. The mNIHSS measured at recruitment was the most significant predictor of all functional outcome measures (MRS, mNIHSS and BI) assessed at one-month post stroke.

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1.0 BACKGROUND

1.1 Introduction

Stroke is the damage of brain cells which occurs when the blood supply to that part of the brain is interrupted. This interruption can be due to blockage of the blood vessels (ischaemic stroke) by local or migrating thrombus or rupture of the blood vessels (haemorrhagic stroke) at the site of an aneurysm or due to high blood pressure (Barrett, Brooks, Boitano, & Barman, 2010; Mehta & Vemuganti, 2014; Sherwood, 2010). Despite advances in medical practice, World Health Organization statistics reports that each year, a third of the over 15 million stroke victims die and another third live with permanent disabilities (Mehta & Vemuganti, 2014; Offner, Ihara, Schäbitz, & Wong, 2017), emphasizing the importance of all measures to prevent stroke or reduce its impact on lives. Common complications of stroke includes seizures (Nkusi et al., 2017; Silverman, Restrepo, & Mathews, 2002) among others.

Seizures are transient abnormal synchronous discharges of electrical activity from brain cells which cause involuntary spasms and altered behaviour or sensation in the patient (Barrett et al., 2010). Epilepsy is the term used when a person has two or more seizures due to persisting neurological abnormality (Fisher et al., 2005). Seizures are either generalized or partial/focal and are common in stroke patients (Barrett et al., 2010; Silverman et al., 2002). Within the first week or two after stroke, the consequent metabolic dysfunction in the brain can induce seizures (early seizures) while persisting changes in neuronal excitability could also cause seizures beyond two weeks after stroke (late seizures) (Siddiqui et al., 2008; Silverman et al., 2002). The occurrence of seizures in stroke patients increase disability and mortality after stroke (Koubeissi, 2015);

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however, these seizures can occur without observable signs and symptoms (subclinical seizures) putting these patients in inconspicuous danger.

Till date, the electroencephalogram (EEG) remains the most common and most affordable tool in the diagnosis of seizures, especially subclinical seizures (Feldwisch-Drentrup et al., 2011) be it routine or continuous EEG (Finnigan & van Putten, 2013; Koren et al., 2016).

Piotr Olejniczak defined EEG as "a graphic representation of the difference in voltage between two different cerebral locations plotted over time" (Olejniczak, 2006). EEG can be recorded on the scalp, on the brain's surface or inside the brain tissue (Barrett et al., 2010) and interpreted primarily by visual characterization or analysed computationally (a process known as QEEG) for diagnosis or cognitive assessment (Kaiser, 2007).

Recent studies on EEG shows QEEG indices significantly predict the functional outcome of stroke patients at day 7 (Sheorajpanday, Nagels, Weeren, & De Deyn, 2011) and even 6 months after stroke (Sheorajpanday, Nagels, Weeren, van Putten, & De Deyn, 2011)- a tool that could be useful in informing clinical management (Finnigan & van Putten, 2013).

According to the World Health organization, changes in the health status, well-being or quality of life of individuals as a result of a process/ intervention is the definition of health outcome (Mukuha, 2017). (Kwakkel et al., 2010) termed health outcomes which measure a person's ability to perform tasks as functional outcomes. These outcomes can be measured as ability to perform activities of daily living after stroke (Barthel Index) (Kwakkel et al., 2010) and functional deficits using the National Institute of Health Stroke Scale (NIHSS) (Martin-Schild et al., 2011) and the Modified Rankin Scale(MRS) (Cincura et al., 2009).

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Despite the clinical relevance of seizures to stroke survival and recovery (Tanaka & Ihara, 2017), EEG is not routinely done on stroke patients in Ghana; a factor which might significantly impact functional recovery from stroke. Knowledge on the occurrence of seizures in stroke patients in Ghana could go a long way in deciding the use of antiepileptic drug (AED) prophylaxis (Sheth et al., 2015; Zandieh, Messé, Cucchiara, Mullen, & Kasner, 2016; Zelano, 2016), or increased vigilance in seizure identification or prevention (Sudalaimani et al., 2016).

1.2 Problem statement:

It is firmly established that seizures in stroke patients lead to poorer chances of survival and higher morbidity (Koubeissi, 2015). Seizures are more common in haemorrhagic than ischaemic stroke (Nkusi et al., 2017; Tanaka & Ihara, 2017). With the higher incidence of haemorrhagic stroke in sub-Saharan Africans (Owolabi et al., 2017) including Ghanaians, the incidence of seizures are likely to be higher (Nkusi et al., 2017), leading to post stroke epilepsy (PSE) which will further decrease the quality of life of stroke survivors (Lahti et al., 2017) and increase mortality. How common clinical and subclinical seizures are in Ghanaian stroke patients is a question that needs answering. Early seizure diagnosis can direct clinical management during hospitalization to improve outcomes (Koubeissi, 2015), but routine seizure monitoring with EEG is not done in Ghana for stroke patients. Will the EEG be useful in diagnosing seizures in stroke patients and prognosticating their recovery at one-month?

1.3 Justification/Relevance:

In the Korle Bu Teaching Hospital, stroke persistently ranks as the leading cause of medical mortalities. Considering the negative impact of seizures on survival, a study that could result in prevention and early management of seizures could improve stroke survival rates. Also, there is scarcity of literature on the occurrence and impact of seizures (both clinical and subclinical) in

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Ghanaian stroke patients, this study will contribute to knowledge and form the basis for further research.

Although several studies have been done on the correlation of electroencephalography (EEG) indices with stroke outcomes , they were done in other populations such as in the Belgium (Sheorajpanday, Nagels, Weeren, van Putten, et al., 2011), China (Xin, Gao, Zhang, Cao, & Shi, 2012), Australia (Finnigan & van Putten, 2013) and the U.S.A (Wu et al., 2016), but not in the Ghanaian population. Furthermore, these studies mentioned above made use of the NIHSS scale to measure the stroke outcome. There is the need for such a study to be carried out in the Ghanaian population, using the more reliable modified NIHSS (mNIHSS) which could even be extracted from medical records to measure the stroke outcome (Meyer & Lyden, 2009).This is the scale this study intends to use.

Stroke recovery relies significantly on neuroplasticity. In resource-poor countries like Ghana, QEEG can be a cost-effective tool for giving patients feedback on their neurological recovery during rehabilitation to motivate them to continue therapy (Kanna & Heng, 2009). Although it is not the gold-standard- functional magnetic resonance imaging (fMRI), it is non-invasive, easy to maintain, can be done at the patient's bedside, does not require a high level of expertise to record and is affordable enough to be made available in many hospitals (Kanna & Heng, 2009; Piersson & Gorleku, 2017). To top it off, it measures brain activity in milliseconds, an ability fMRI is yet to achieve (Wu et al., 2016).

1.4 Study Hypothesis:

Seizures in stroke patients on admission may be diagnosed with EEG and QEEG indices may be useful in prognosticating one-month functional outcome of stroke patients of the Korle Bu Teaching Hospital.

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1.5 Aim

The aim of this study was to determine the incidence of electrographic seizures in stroke patients and how QEEG indices prognosticate one-month functional outcome.

1.6 Specific objectives

The specific objectives of this study were as follows:

- Determine the occurrence of seizures (clinical and subclinical) in 30 stroke cases within one month of stroke onset using clinical observations and routine EEG recorded during admission
- To compare the prognostic correlation of QEEG indices (RAP, DAR, pdBSI) measured at recruitment with post stroke functional outcomes in 30 stroke patients, measured at one-month using the MRS, mNIHSS and Barthel Index scores.
- To compare the prognostic correlation of MRS, mNIHSS and Barthel Index scores measured at recruitment with post stroke functional outcomes in 30 stroke patients, measured at one-month using the MRS, mNIHSS and Barthel Index scores.

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2.0 LITERATURE REVIEW

Stroke leads to the premature death of victims and lost productivity for survivors and their caregivers; this results in a huge financial loss to individuals and states (Offner et al., 2017). With increasing population age projected to increase the financial burden stroke has on the economy (Hsieh, Wu, & Sung, 2017), all efforts must be made to improve stroke outcomes.

This chapter reviews the normal function of brain cells, pathophysiology of stroke, stroke-related seizures, functional status of stroke patients and the use of electroencephalography in seizure diagnosis and functional status prediction at one-month post-stroke.

2.1. The homeostatic brain

Control and coordination of activities of the body such as tasting, seeing, talking, walking digestion and respiration is the primary role of the nervous system. The brain and spinal cord form the central nervous system (CNS) while nerve fibres and sensory organs throughout the body make up the peripheral nervous system (PNS). At any particular time, many afferent nerves of the PNS send sensory input from all parts of the body to the CNS and the CNS sends responses back to the peripheries through the efferent nerves of the PNS (Sherwood, 2010). The ability to maintain homeostasis through these complex and extensive communication networks depends on the functioning and interactions of the neurons, glial cells and the vascular endothelial cells that make up the CNS.

Neurons (e.g. pyramidal cells and retinal bipolar cells) are specially equipped to carry the rapid signals within the nervous system because of their ability to maintain a potential gradient while at rest (resting membrane potential); with a slightly negative intracellular and a slightly positive extracellular environment (Barrett et al., 2010). The release of chemical messengers (neurotransmitters) by the axon of a pre-synaptic neuron into the synaptic cleft causes a change in

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the membrane potential of the post-synaptic neuron (excitation or inhibition) with a resultant cascade of activities that result in signal transduction to target cells (Costanzo, 2011). Glial cells on the other hand, are specialized to support the functioning of neurons. Some enhance transduction of neuronal signals by formation of myelin sheaths around neuronal axons to enhance conductivity (oligodendrocytes) or take up excess neurotransmitters from the extracellular space (astrocytes) to maintain the membrane potential at the junctions. Others help maintain the blood-brain barrier, participate in inflammatory response and scar formation at sites of injury (astrocytes, microglia) or formation of new synapses and circuits after brain injury (synaptic plasticity) (Barrett et al., 2010). These activities of neurons and glial cells are highly metabolic and require constant supply of huge quantities of oxygen and nutrients as well as clearance of the by-products of those metabolic activities. These are the essential functions of the brain's endothelial vasculature (Guyton & Hall, 2006).

2.2. Pathophysiology of stroke

When a stroke occurs, be it ischaemic or haemorrhagic, brain cells are damaged from the interruption of blood supply to the brain (Mehta & Vemuganti, 2014). Hypoxia resulting from this interruption causes neurons to release large quantities of neurotransmitters like dopamine, serotonin and glutamate extracellularly (Tanaka & Ihara, 2017) and cells at the core of the ischaemia quickly die through necrosis. Though cells near the core injury site (ischaemic penumbra) maintain metabolism and low neuronal damage through blood supply from adjacent arteries, they lose the ability to maintain sodium (Na^+) gradient due to ion channel dysfunction; therefore, intracellular Na^+ levels become elevated, making astrocytes unable to reuptake glutamate from the extracellular fluid (Barrett et al., 2010). Glutamate continues to stimulate calcium (Ca^{2+}) influx (glutamate excitotoxicity) and cells in the penumbra die (apoptosis) from the

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activities of calcium-dependent catabolic enzymes like proteases and nucleases (Mehta & Vemuganti, 2014). Also, proteases and oxidants are released from leukocytes activated by the restoration of blood flow to the ischaemic penumbra, causing cytokine-mediated inflammation and cell death, further increasing the area of damage (Pan, Konstas, Bateman, Ortolano, & Pile-Spellman, 2007).

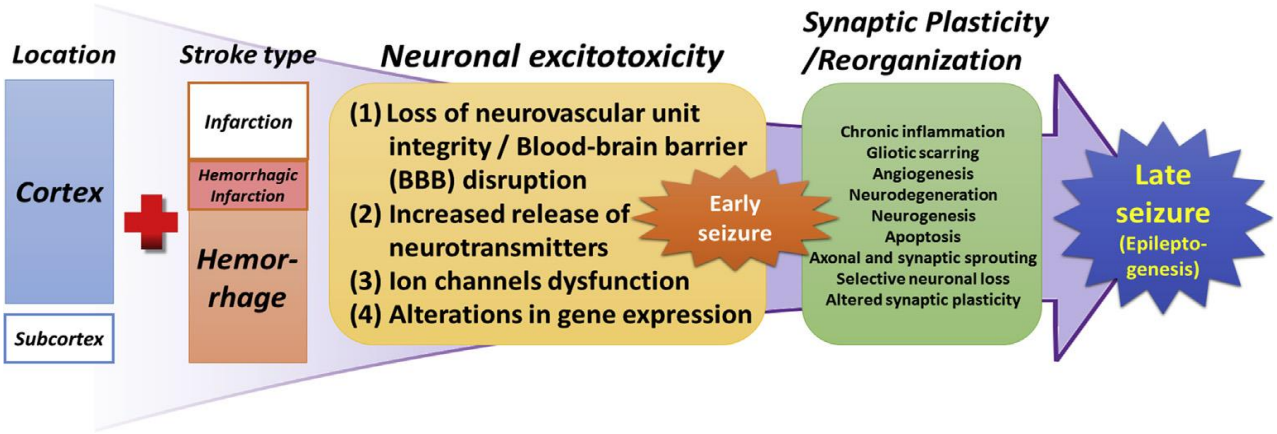

Figure 1: Mechanisms of seizure generation after stroke (adapted from Tanaka & Ihara, 2017)

2.3. Synaptic plasticity after stroke

Be it ischaemia or haemorrhage, the effect of stroke is infarction of brain tissue and neuronal damage (Mehta & Vemuganti, 2014). These damages include physical, psychological and neurological debilitations such as muscle stiffness, paralysis, language difficulties and cognitive impairment (Tanaka & Ihara, 2017) and is dependent on the location, severity, and duration of loss of blood supply to the brain tissues (Mehta & Vemuganti, 2014).

Neural plasticity is the structural and functional changes that occur in the central nervous system (CNS) in response to external or internal stimuli (Cohen, Quarta, Bravi, Granato, & Minciacchi, 2017). These changes can be in molecules, cells or networks such that a single change in either of

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these can result in changes in the functioning of the CNS. Neural plasticity is how the CNS maintains homeostasis and also allows for developmental changes (such as learning) (Feinberg, Koresko, & Heller, 1967; Sherwood, 2010).

Recent studies have established that formation of new neurons (neurogenesis) occurs after birth and throughout life (Barrett et al., 2010; Cohen et al., 2017). These new cells are formed from stem cells in the dentate gyrus (hippocampus) and the subventricular zone of the lateral ventricles (Barrett et al., 2010). Afferent input to the brain maintains homeostasis of this neuronal proliferation; with increasing input reducing proliferation while balanced input increases proliferation- as over-proliferation can lead to disruptions in neuronal networks (Cohen et al., 2017).

When harmful stimuli such as stroke strikes and unbalances the homeostatic state of the brain, synaptic plasticity is triggered and the brain attempts to regain its balance through creation of new synapsis (synaptogenesis), spreading of dendrites to sub-layers (dendritic arborisation) and the recruitment of synapses and axons (Sheorajpanday, Nagels, Weeren, & De Deyn, 2011; Sherwood, 2010) to the damaged region for reformation of lost connections needed for body functions. This is the principle behind rehabilitation therapy (Kanna & Heng, 2009).

2.4. Seizures in stroke

Generally, the intracellular influx of calcium and sodium due to glutamate excitotoxicity, creates a hyperosmolar environment for neurons, depolarizing the cell membrane to a threshold low enough for seizure activation (Mehta & Vemuganti, 2014; Tanaka & Ihara, 2017). This is especially true for the hippocampus (a highly excitable part of the brain) where focal seizures with symptomatic hallucinations occur (Guyton & Hall, 2006). The increase in neuronal excitability

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could also be enabled by stroke-induced down-regulation of the inhibitory gamma-aminobutyric acid (GABA) receptors (Nudo, 2013; Tanaka & Ihara, 2017).

Various mechanisms are thought to be responsible for seizure occurrence in stroke patients. These include a large size of the area of damage, cortical location of the stroke and the type of stroke. Haemorrhagic strokes have been found to be more likely to develop seizures (Tanaka & Ihara, 2017) through mechanism thought to be due to hemosiderin deposition which irritates the site where they are deposited, making the brain tissue more excitable and increasing the likelihood of focal seizures (Silverman et al., 2002; Tanaka & Ihara, 2017).

2.4.1. Early seizures

Early seizures are thought to be due to metabolic mechanisms like glutamate excitotoxicity, calcium overload and oxidative stress (Silverman et al., 2002; Tanaka & Ihara, 2017). As the size of damage increases, the levels of excitotoxins released increase with increasing risk of early seizures (Mehta & Vemuganti, 2014; Pan et al., 2007) as in Figure 1 above. In haemorrhagic strokes, these seizures are associated with reduced consciousness or a history of seizures in patients (Naidech, 2011).

2.4.2. Late seizures

Beyond two weeks of stroke onset, changes in neuronal networks are now persistent and neuroglia and immune cells have replaced the formerly healthy neurons. This gliotic scarring has been implicated as the main reason for the manifestation of late seizures in stroke patients (Silverman et al., 2002; Tanaka & Ihara, 2017).

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In addition, mechanisms of synaptic plasticity such as synaptogenesis, dendritic arborisation and the recruitment of synapses and axons (as described in the next section) increase brain excitability and the risk of seizures (Sheorajpanday, Nagels, Weeren, & De Deyn, 2011).

2.4.3. Subclinical seizures- EEG as a diagnostic tool

In their study on the impact of seizures on stroke morbidity and mortality in 5076 stroke cases, Burneo, Fang and Saposnik (2010) stated that "electrographic seizures are common after stroke and that most patients with electrographic seizures may not have clinical correlates" (subclinical), a situation that can undermine the true incidence and impact of seizures on stroke and subsequently, clinical management. In such cases, continuous EEG (CEEG) is the recommended diagnostic tool (Naidech, 2011). In monitoring 570 consecutive critically ill patients with CEEG, Claassen *et al.* (2004) reported 19% subclinical seizures of which 84% was recorded on the first day of recording and another 5% on the second day. A study by Miskin *et al.* (2015) concurs that though 20 minutes of EEG recording is sufficient for capturing EEG abnormalities, a 40 minutes recording significantly increases the yield by 11%. In extrapolation, it can be said that the odds of capturing electrographic seizures in stroke patients using about 30 minutes of routine EEG is fair (as used for this study).

2.5. Relationship between EEG and action potential

Poitre Olejniczak (2006) in his review on the Neurophysiologic basis of EEG said that synaptic activity is the most relevant source of the electrical potential recorded by the EEG; specifically, from apical dendrites of cortical neurons. He said that scalp electrodes record the summation of the excitatory and inhibitory postsynaptic potentials from these neurons. And also that other possible contributors to EEG potentials in synchronous events like sleep transients and epileptiform discharges are calcium mediated action potentials (calcium spikes) and individual

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high-amplitude, fast action potentials (sodium) which are short-acting (Olejniczak, 2006). The oscillatory waves recorded by the EEG are grouped according to frequency bands (delta, alpha, beta, gamma etc.) (Sheorajpanday, Nagels, Weeren, van Putten, et al., 2011). Depending on the status of the individual at the time of recording, the appearance of these frequency bands can be physiologic or pathologic (Guérit et al., 1999).

2.6. Measures of functional outcome in stroke patients

In clinical care and rehabilitation therapy after stroke, assessment of deficit and recovery is essential. The NIHSS is a well-validated tool for assessing neurological deficits (Kwah & Diong, 2014) and a good predictor of the likelihood of recovery from stroke (Saposnik et al., 2011) but has items with imbalances in scoring based on the hemisphere in which stroke occurs. These items have been eliminated in the more reliable mNIHSS which has scoring between 0 for normal neurological function and 31 for no neurological function (Meyer & Lyden, 2009). However, neither the NIHSS nor mNIHSS has the ability to assess difficulties such as bed mobility, sitting, standing, walking nor upper limb function (Kwah & Diong, 2014). The Barthel Index (BI) is an ideal measure of these activities of daily living (ADL) such as eating, bathing, grooming and toilet use, with scores ranging from 0 to 20 (between no ability and normal function). Neither mNIHSS nor BI clearly indicates whether a patient is alive or dead by their scores. The Modified Rankin Scale (MRS) is a descriptive measure of survival with scores from 0 (normal) to 6 (dead) and is primarily used to assess disability status of stroke patients as described in Appendix 3 (Martin-Schild et al., 2011; Veerbeek, Kwakkel, Van Wegen, Ket, & Heymans, 2011).

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2.7. Quantitative EEG (QEEG)- another measure of functional outcome

Studies carried out proves that EEG recordings (in either acute or sub-acute stage of stroke) generated from a standard number of electrodes (10/20 system), when quantitatively analysed is a clinically relevant measure of post-stroke status and outcome, independent of comorbidities and stroke type (Sheorajpanday, Nagels, Weeren, van Putten, & De Deyn, 2009).

In brain ischaemia, delta waves (1-4Hz) with high amplitudes are usually observed at the regions of ischaemia showing slowing of brain activity with a converse reduction in the occurrence of faster waves like alpha (8-12Hz) (Sheorajpanday et al., 2009). The QEEG indices used in monitoring brain activity after stroke is based on mathematical derivatives of these frequency band measures. Examples are the delta/alpha ratio (DAR) and relative alpha power (defined as equations 1 and 2 in the methodology section). Delta activity is not characteristic of a normal awake brain (Table 2) so the higher the ratio of delta to alpha spectral power, the greater the abnormality and vice versa while a low relative alpha power is indicative of abnormality in brain activity (Finnigan & van Putten, 2013; Kanna & Heng, 2009; Sheorajpanday, Nagels, Weeren, van Putten, et al., 2011).

The brain symmetry index (BSI) is another QEEG index defined by Van Putten & Tavy, 2004 and modified by Sheorajpanday et al., 2009 as the pairwise derived brain symmetry index (pdBSI) for comparison of spectral power in contralateral brain locations (such as frontal left to frontal right) over a specified frequency range (1-4Hz, 1-7Hz, 1-13Hz, 1-25Hz etc.) to determine the presence of asymmetry- an indicator of abnormal brain activity at the location with higher asymmetry (Sheorajpanday et al., 2009).

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Significant correlations have been established between QEEG indices and stroke outcomes such as pairwise derived brain symmetry index's (pdBSI) correlation with NIHSS in discriminating between stroke and transient ischaemic attack (TIA) or controls (Sheorajpanday et al., 2009); pdBSI in predicting early worsening of outcome (Sheorajpanday, Nagels, Weeren, De Surgeloose, & De Deyn, 2010); delta/alpha power ratio (DAR) and relative alpha power (RAP) were also significantly associated with NIHSS score at 30 days post stroke (Finnigan & van Putten, 2013). Even without using the quantitatively obtained EEG indices, the presence of slow wave activity has also been found to correlate with worsening functional outcome in patients with intracranial haemorrhage (Grays et al., 2016). Since increasing population age is projected to increase the financial burden stroke has on the economy (Hsieh et al., 2017), all efforts must be made to improve stroke outcome; more so as elderly people living with seizures have been reported in the United States of America to spend double the amount those without seizures spend on health care (Lekoubou, Bishu, & Ovbiagele, 2018).

In this study, the QEEG variables used were relative alpha power (RAP), the delta/alpha ratio (DAP) and the pairwise derived brain symmetry index (pdBSI) (Sheorajpanday et al., 2009) described in the next chapter. Each of these indices have been found to correlate and even predict functional outcome in stroke patients when measured on admission or some time in their recovery in more than one study (Agius Anastasi, Falzon, Camilleri, Vella, & Muscat, 2017; Finnigan & van Putten, 2013; Kanna & Heng, 2009).

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3.0 METHODOLOGY

3.1 Study Design:

This was a longitudinal study where all patients who met the eligibility criteria and consented were recruited.

3.2 Study Site:

The study was conducted at the stroke unit of the Korle Bu Teaching Hospital. The hospital is the first of the three Teaching Hospitals to be established in Ghana. It is a tertiary care facility with a bed capacity of 2000. It receives referrals from other regional and district hospitals especially in the southern sector of the country.

Korle Bu Teaching Hospital has a surgical and medical emergency facility run jointly by the Surgical and Medical Departments of the hospital. It is the first point of call for patients coming into the hospital with non-trauma emergency where patients are admitted for a few hours or days till they can be discharged or transferred to other wards for further management.

From the SME and other hospital departments, patients diagnosed with stroke confirmed by neuroimaging are admitted to the stroke unit, a 20-bed facility which is part of the medical department of KBTH. The stroke unit is equipped with specially trained multidisciplinary team (MDT) of clinical staff who assess and manage patients admitted to the unit. Patients for this study were recruited from this unit.

In addition, the hospital has a Neurophysiology unit where EEGs are recorded and a radiology department where Computed Tomography scans and Magnetic Resonance Imaging for stroke patients are done by competent experts.

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3.3 Study population:

All patients admitted to the stroke unit of the Korle Bu Teaching Hospital with stroke confirmed by neuroimaging (CT (computed tomography) scan or MRI) within 10 days of symptom onset.

3.4 Inclusion Criteria

Subjects were eligible if they satisfied the following criteria:

- They meet the definition of stroke
- Evidence of infarction or haemorrhage on Head with CT scan or MRI
- First ever symptomatic stroke irrespective of level of consciousness
- Presentation within 10 days of stroke onset.
- Aged 18 or above
- Given informed consent or consent by next of kin to participate in study.

3.5 Exclusion Criteria

Subjects were excluded if they had any of the following:

- Previous symptomatic stroke
- History of chronic disability (physical, mental) prior to illness.
- No evidence of infarct or haemorrhage on CT scan or MRI.
- Neuroimaging shows other stroke mimics such as tumours, cerebral abscess and other mass lesions.
- Did not satisfy inclusion criteria.

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3.6 Sample size:

The sample size was calculated using the software by Sergeant, 2018 from http://epitools.ausvet.com.au/content.php?page=cohortSS&P1=0.05&RR=10&Conf=0.95&Power=0.8 with the following parameters:

- Expected incidence in unexposed population= 0.05
- Assumed relative risk= 10
- Confidence level= 0.95
- Power= 0.8

This calculation yielded a sample size of twenty four (24), which has been approximated to thirty to cater for potential drop outs.

3.7.0 Procedures

3.7.1 Selecting study participants

Doctors of the Korle Bu Teaching Hospital stroke team are routinely called to see stroke cases in the hospital's wards and emergency unit (SME). The names of patients diagnosed with stroke (by neuroimaging) were obtained from these doctors and their eligibility was assessed using the criteria stated above. Consecutive patients who met the eligibility criteria were selected for inclusion in the study.

3.7.2 Obtaining consent

Eligible patients who were lucid and gave consent were informed about the study and given an opportunity to ask questions. Those who agreed to participate were asked to sign the consent form (Appendix 1) and recruited into the study. For patients who could not comprehend or give consent, the study was explained to their next of kin and if they consented, they signed on behalf of the patient (as clearly shown in Appendix 1).

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3.7.3 Demographic data

Questionnaires (as in Appendix 2) were used to gather participant demographics including participant ID, date of birth and age. The contact details of participants and their proxy were stored on a separate document for one-month follow-up visit. Details on the incidence of clinical seizures before stroke occurred and within the one month of study were documented on the questionnaire. Patients' use of antiepileptic drugs within the study period were also documented as they may reduce the occurrence of seizures in stroke patients (Tanaka & Ihara, 2017).

3.7.4 Stroke classification

The inclusion criteria for this study required participants' stroke status to have been confirmed by neuroimaging (CT scan or MRI). Patients neuroimaging reports reviewed and approved by stroke specialists prior to admission were used to fill in details on stroke classification in the questionnaire (Appendix 2) such as stroke type, cortical location, hemispheric location and subcortical structures affected.

3.7.5 Outcome measures

Modified Rankin Scale (Appendix 3) was measured for each patient recruited to rank their level of disability after the stroke, both at recruitment (MRS_0) and a month (MRS_1) after stroke started (Cincura et al., 2009; de Haan, Limburg, Bossuyt, van der Meulen, & Aaronson, 1995).

The modified National Institute of Health Stroke Scale (Appendix 4) was filled for each patient at recruitment ($mNIHSS_0$) and a month ($mNIHSS_1$) after stroke started (Lyden et al., 2001; Meyer & Lyden, 2009) as a measure of neurological deficit.

The Barthel Index (Appendix 5) was recorded at recruitment (BI_0) and at one-month (BI_1) as a measure of activities of daily living (Kwakkel et al., 2010; Liu, Unick, Galik, & Resnick, 2015).

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The three outcome measures were then categorized in the order in Table 1 below into three comparable categories of mild, moderate or severe (Govan, Langhorne, & Weir, 2009).

Table 1: Categorization of outcome measures

Stroke Severity Categorization			
	Categories		
Scale	**Mild (1)**	**Moderate (2)**	**Severe (3)**
Modified NIHSS	0-5	6-14	15-31
Modified Rankin Scale	0-3	4	5
Barthel Index (20 point scale)	10-20	3-9	0-2

3.7.6 EEG recording

The 32 channel portable EEG Maximus 24/32* ("RMS-Maximus Electroencephalograph," 2013) was used to record the electrical activity of the brain. The scalp of each participant was thoroughly cleaned with abrasive gel to remove all dirt and dead cells to enhance connectivity of electrodes. Electrodes were connected to the scalp with conductive gel according to the international 10/20 system of electrode placement (Kaiser, 2007). A 19 channel awake-EEG recording (with electrode positions Fz, Cz, Pz, Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4, P3, P4, T5, T6, O1 and O2) was done for patients in the 'eyes-open' and 'eyes-closed' states for 30 minutes including a 3 minutes period of photic stimulation. Patients who were conscious and cooperative did another brain activation test by hyperventilation. The EEG recordings were stored on the recording computer as well as a hard-drive (after appropriate de-identification).

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3.7.7 EEG pattern classification and seizure diagnosis

Each recording was visually characterized by a neurologist with attention to the general pattern and characteristics of the recording including comments on seizure activity and slow wave activity (characteristics which point to pathophysiology). This data was entered using the questionnaire (Appendix 2).

The frequency bands to be used for EEG characterization and quantification are as in Table 2:

Table 2: EEG frequency bands

EEG frequency	Typically observed during
Delta (1-4Hz)	Dominant during deep sleep. High delta levels show more stable sleep state
Theta (4.1-8Hz)	Light sleep or extreme relaxation state
Alpha (8.1-12.5Hz)	Relaxed wakefulness.
Beta (12.6-30Hz)	Wide awake and focused
Gamma (≥30.1Hz)	Formation of ideas, memory processing and learning

Another characteristic EEG activity is the 'spike and wave' activity known as epileptiform discharge (Boro, 2016).

Since slow wave activity has also been found to correlate with worsening functional outcome in patients with intracranial haemorrhage, all EEGs recorded were analysed to determine presence of slow wave activity (Grays et al., 2016).

The recordings were quantitatively analysed on the EEGlab software in MATLAB for relative alpha power (RAP), delta/ alpha power ratio (DAR) (Finnigan et al., 2007; Kanna & Heng, 2009) and pairwise derived brain symmetry index (pdBSI) which have been found to be significantly correlated with 30-day NIHSS score in ischaemic stroke (Sheorajpanday et al., 2009).

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3.7.8 EEG pre-processing

EEG recordings were de-identified and imported into the EEGlab software (Delorme & Makeig, 2004; Sheorajpanday, Nagels, Weeren, & De Deyn, 2011) in EDF format, choosing default (BESA) channel locations (Budzynski, Budzynski, Evans, Abarbanel, & Thatcher, 2009; Phillips, Rugg, & Friston, 2002) with exclusion of channels which were not part of the conventional 19-channel EEG recording electrodes. All electrodes were re-referenced to average reference (Sheorajpanday et al., 2009; Sheorajpanday, Nagels, Weeren, van Putten, et al., 2011; Thatcher & Lubar, 2009). The recording was then filtered using a highpass filter of 0.3Hz and a lowpass filter of 30Hz (Sheorajpanday et al., 2009), after which line-noise was removed by means of the CleanLine toolbox (Mullen, 2012) in EEGlab. Sections of the recording which had high artifacts were automatically selected and after visual inspection, they were deleted. Although no channels were deleted, at this stage, channels with high voltage artifacts even after filtering were excluded from spectral analysis.

3.7.9 Quantitative EEG analysis

For each patient, 5 minutes of artifact-free EEG data was selected from the recording for spectral analysis according to the QEEG experts recommendation (Budzynski et al., 2009). Delta/ Alpha Ratio (DAR), Relative Alpha Power (RAP) and the pairwise derived Brain Symmetry Index (pdBSI) were computed from EEG recordings using modified algorithms on the EEGlab software according to the formulae below.

Equation 1:

$$\textbf{Delta}:\textbf{Alpha Ratio} = \frac{\sum_{1}^{K}\sum_{N/fs}^{4N/fs} P}{\sum_{1}^{K}\sum_{8N/fs}^{13N/fs} P}$$

Equation 2:

$$\textbf{Relative Alpha Power} = \frac{\sum_{1}^{K}\sum_{8N/fs}^{13N/fs} P}{\sum_{1}^{K}\sum_{N/fs}^{25N/fs} P}$$

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Where:

- **P** is the absolute power at a given frequency
- **K** is the discrete number of channels
- **N** is the Fast Fourier Transform (NFFT)
- **fs** is the sampling frequency rate in Hertz

Equation 3:

pdBSI = $\frac{1}{MN} \sum_{j=1}^{M} \sum_{i=1}^{N} \left| \frac{R_{ij} - L_{ij}}{R_{ij} + L_{ij}} \right|$ where:

- $\mathbf{R_{ij}}$ = the FFT based power spectral density using Welch's method of signal obtained from the right channel homologue
- $\mathbf{L_{ij}}$ = the FFT based power spectral density using Welch's method of signal obtained from the left channel homologue
- **i**= the pair of homologous channels (1, 2,...,M)
- **j**= the frequency (Fourier coefficient with index j= 1, 2,…,N)
- **M**=8 and
- **N**= 1-4Hz, 1-8Hz, 1-12.5Hz, 1-30Hz for (delta, theta, alpha and beta respectively)

3.8 Data handling

All EEG recordings were de-identified and secured on an external hard-drive with password and locked in a steel cabinet in a secure room when not in use.

Consent forms and questionnaires generated were also secured in separate locations to maintain patient privacy and confidentiality.

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3.9 Statistical analysis

Data collected were analysed using the Microsoft Excel (version 2013) and the Statistical Product for Service Solution (SPSS) version 20. Bar charts frequency tables were used to represent categorical data collected and tables of means with standard deviations were used to summarize data on continuous variables, including p-values for proportions at a significance level of 95%. To determine predictors of one-month functional outcomes, Spearman's correlations and linear regressions were analysed at a significance level of 95% ($p < 0.05$).

3.10 Ethical issues

Ethical clearance was sought from the Ethical and Protocol Review Committee (EPRC) of the College of Health Sciences (Appendix 6).

The details of the research were explained to potential participants before enrolment, emphasising that participation is voluntary and their choice will not affect the quality of care the hospital gave them.

Data obtained was de-identified and coded to maintain confidentiality, stored in secure rooms with locks and on computers with passwords.

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4.0 RESULTS

This chapter displays data collected from 30 stroke patients in bar charts and statistical tables to answer the objectives of this research. Data that answers the first objective are in the first four sub-sections and most of the data for the second research objective are in the last three subsections.

4.1 Patient demographics: Age and gender characteristics of 30 stroke patients

Of the 30 stroke patients studied, 18 were 60 years old or below (60%) and 12 patients were older than 60 years (40%), but the difference between the two proportions was not significant ($p = 0.12$). From the student's t-test for unpaired data, the mean age of patients who had ischaemic stroke (63.1 ± 15.3years) was significantly higher than those who had haemorrhagic stroke (48.1 ± 15.1years), ($p = 0.02$) as shown in Table 3. There was also a significant difference in the gender ratio of the patients, 10 females (33.3%) and 20 males (66.7%), ($p = 0.01$).

Table 3: Patients' demographic characteristics

	Age group		
	≤ 60 years	**> 60 years**	p-value
Number (percentage)	18 (60%)	12 (40%)	0.12
	Stroke type		
	Ischaemic (Mean ± SD)	**Haemorrhagic (Mean ± SD)**	**p-value**
Mean age (years)	63.1 ± 15.3	48.1 ± 15.1	0.02*
	Gender		
	Female	**Male**	**p-value**
Number (percentage)	10 (33.3%)	20 (66.7%)	0.01*

*significant at $p < 0.05$; SD= standard deviation

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4.2. Clinical characteristics of patients

According to neuroimaging findings (shown in Figure 2), of the 20 ischaemic and 10 haemorrhagic stroke patients studied, 21 had lesions in the cerebral cortex (16 ischaemic and 5 haemorrhagic strokes, p = 0.17) and 17 patients had lesions in subcortical structures (13 ischaemic and 4 haemorrhagic strokes, p = 0.29); including patients who had no cortical lesions. The differences in proportions were not significant (at 95% significance level) after performing the z-test for two proportions.

In terms of hemisphere where stroke occurred, 10 patients had left hemisphere lesions (8 ischaemic, 2 haemorrhagic), 13 had right hemisphere lesions (8 ischaemic, 5 haemorrhagic), 4 had bilateral hemispheric lesions (2 ischaemic, 2 haemorrhagic) but 3 patients had no hemispheric categorization of stroke. However, none of the difference in proportions of ischaemic to haemorrhagic were significant.

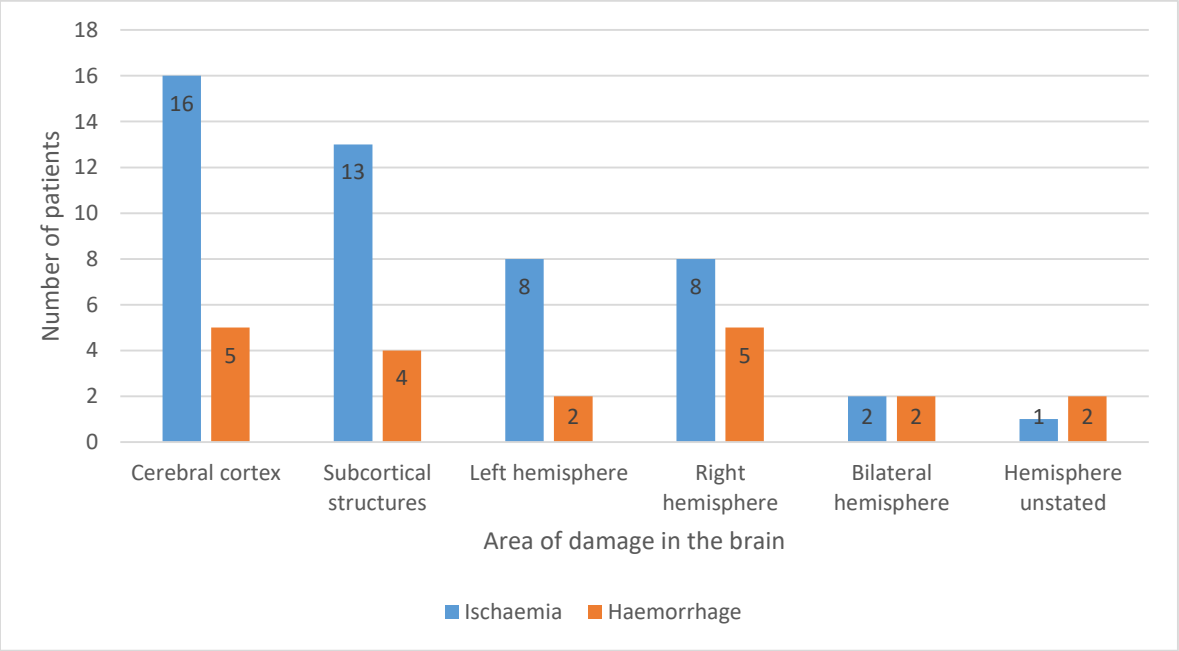

Figure 2: Neuroimaging findings of study participants

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Table 4 shows the distribution of functional status among patients at recruitment and one-month post stroke. At recruitment, 36.7% had mild disability on MRS, 36.7% had moderate disability and 26.7% had severe disability. These percentages improved to 63.3% mild, 20.0% moderate and 16.7% severe disability for assessment done at one-month post stroke. The distribution of neurological deficit (mNIHSS) in the patients at recruitment was 41.4% mild, 44.8% moderate and 13.8% severe neurological deficit which improved to 71.4% mild, 21.4% moderate and 7.1% severe neurological deficit a month later. Inability to perform activities of daily living at recruitment was in a ratio of 53.3% mild inability, 13.3% moderate inability and 33.3% severe inability at recruitment with increase in the percentage who had mild and moderate inability as 73.3% and 20% respectively, and a decrease in the percentage with severe inability as 6.7% at one-month.

Table 4: Functional status of 30 stroke cases at recruitment and follow-up

Outcome measure	Severity at recruitment				Severity at one-month		
	Mild	Moderate	Severe		Mild	Moderate	Severe
MRS	36.67%	36.67%	26.67%		63.33%	20.00%	16.67%
mNIHSS	40.00%	46.67%	13.33%		66.67%	26.67%	6.67%
BI	53.33%	13.33%	33.33%		73.33%	20.00%	6.67%

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4.3.0 Occurrence of seizures

4.3.1 Diagnostic parameters of EEG recordings

Based on the neurologist's report on the 30 EEG recordings in Table 5, a significantly lower number of patients (36.7%) had normal readings (p = 0.04), 14 patients (46.7%) had EEG activity diagnostic of electrographic seizures (13 generalized seizures and 1 focal seizures) and 17 (56.7%) had activity signifying cerebral dysfunction (these patients had abnormal EEG recordings with or without electrographic seizure activity). Further details on the EEG findings and occurrence of clinical seizures in the patients studied are displayed in Figure 3 below.

Table 5: EEG findings in 30 stroke patients

	Normal EEG activity	**Abnormal EEG Activity**	**p-value**
Number (percentage)	11 (36.7%)	19 (63.3%)	0.04*
	Generalized seizures	**Focal seizures**	**p-value**
Number (percentage)	13 (92.9%)	1 (7.1%)	< 0.001*
	Cerebral dysfunction	**No cerebral dysfunction**	**p-value**
Number (percentage)	17 (56.7%)	13 (43.3%)	0.302

* Significant at p <0.05

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4.3.2 Occurrence of seizure and EEG abnormalities in ischaemic and haemorrhagic stroke patients

Figure 3 shows that, of the 19 patients with aberrant brain activity on recorded EEGs, 12 were from ischaemic stroke patients and 7 from haemorrhagic strokes. Electrographic seizures were seen in 9 ischaemic stroke patients and 5 haemorrhagic stroke patients. Clinical seizures were observed in 4 patients in a 1:1 ratio for ischaemic and haemorrhagic strokes including 2 patients who also had seizure activity on EEG (1 ischaemic and 1 haemorrhagic stroke); however none of these difference in proportions were significant.

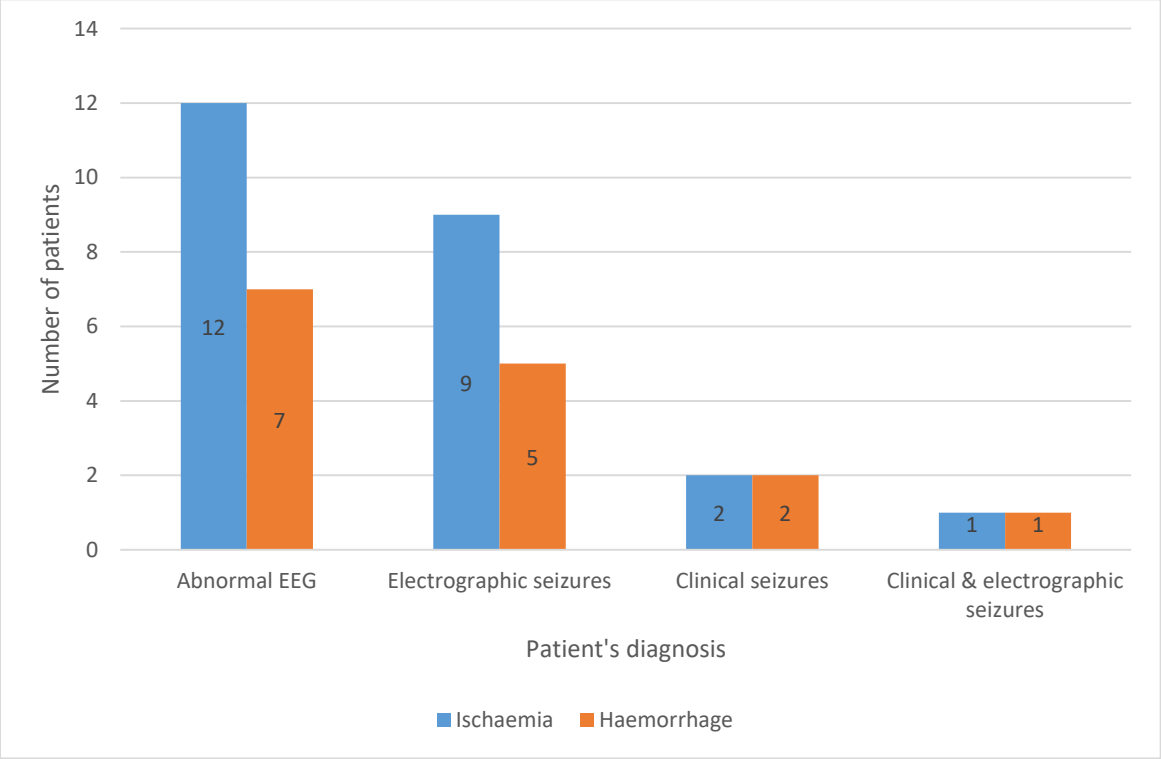

Figure 3: Electroencephalographic and clinical details on seizures

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4.3.3 Details on patients with clinical seizures

Further details on the 4 cases who had clinical seizures (in Table 6 below) showed that the two ischaemic stroke patients had only early seizures (1 each), one of the two haemorrhagic stroke patients had early seizures (3) while the other patient had both early and late seizures (2 each). Three of the four patients were given anti-epileptic drugs (Levetiracetam, Phenytoin and both Levetiracetam and Carbamazepine respectively). Of the two who had no seizure activity on EEG, one had a normal EEG recording while the other had evidence of cerebral dysfunction on EEG and one of the two who had seizure activity on EEG also had evidence of cerebral dysfunction.

Table 6: Early seizures, late seizures and the use of anti-epileptic drugs in stroke patients

ID	Stroke type	Early seizures	Late seizures	Total No. of seizures	AEDs	EEG comments
004	Ischaemia	1	0	1	Levetiracetam	Normal EEG
006	Ischaemia	1	0	1	None	GS,CD
010	Haemorrhage	2	2	4	Phenytoin	CD
028	Haemorrhage	3	0	3	Levetiracetam, Carbamazepine	GS

GS = generalized seizure activity; CD = cerebral dysfunction activity; AEDs = anti-epileptic drugs

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4.4.0: Visual characterization of EEG recordings

4.4.1 Characterization of electrographic seizure activities

Observing the types of EEG activity seen in the 14 patients that led to a diagnosis of electrographic seizures (in Figure 4), almost all patients (13) had spike and slow wave activity, 11 had sharp waves on recording, 5 patients also had spike and wave activities but only one patient had diffuse slowing characteristic of seizures.

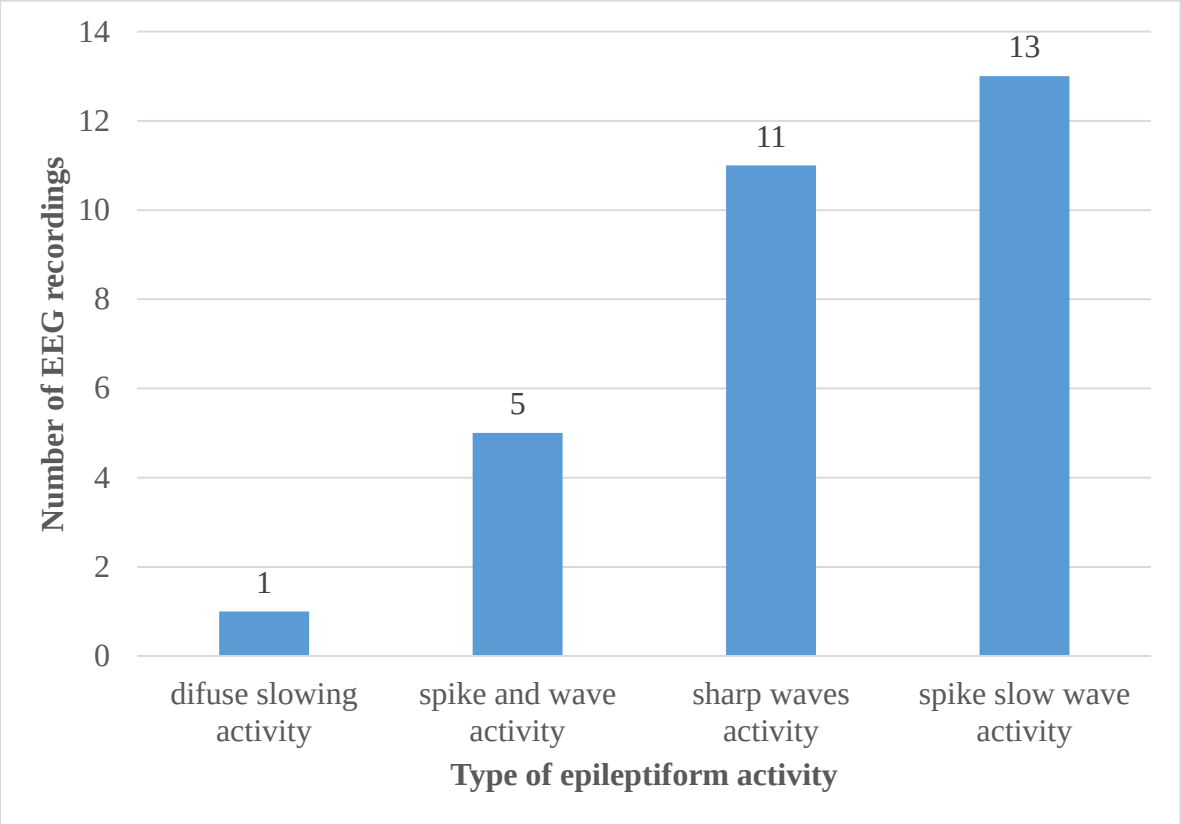

Figure 4: Categories of epileptiform activity seen on EEG

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4.4.2 Electrographic indications of cerebral dysfunction

Of the three types of EEG activities showing cerebral dysfunction in 17 patients, the most prevalent was diffuse slowing (found in 14 patients), followed by focal slowing (in 10 patients) but only one patient had slow burst activity.

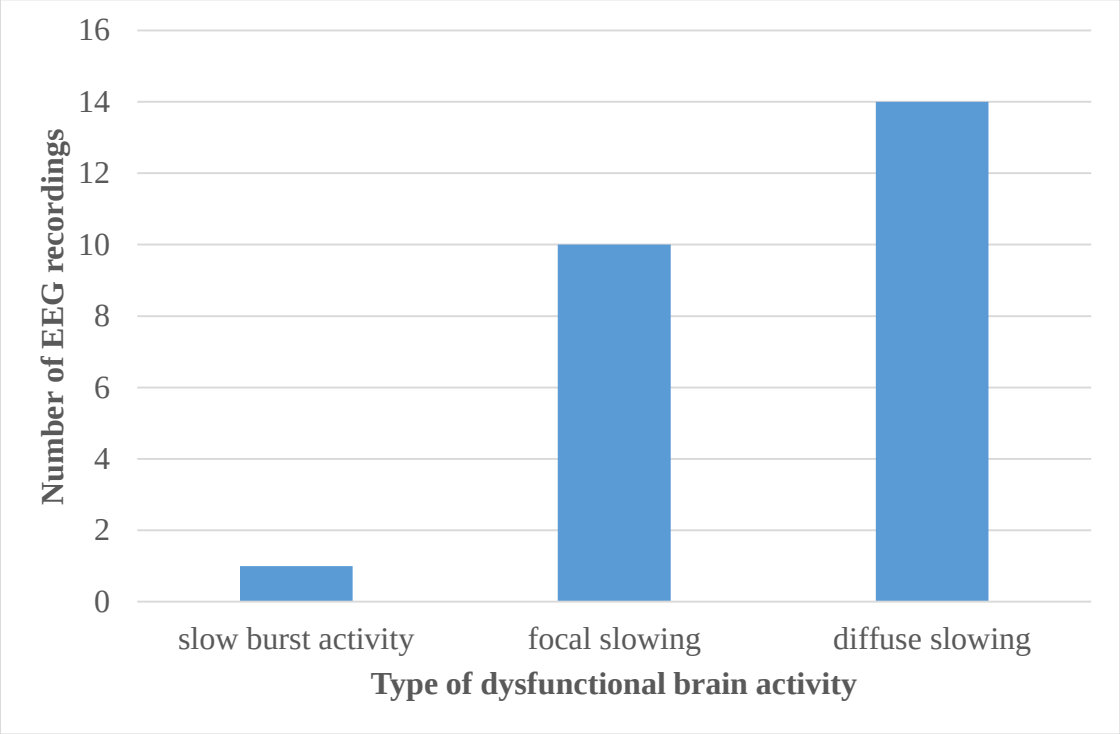

Figure 5: Distribution of dysfunctional brain activity on EEG

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4.5.0 Comparison of functional outcome at recruitment to one-month measures

4.5.1 Relationship between mean functional status at recruitment and one-month after stroke

The mean MRS of patients one-month after stroke (2.9 ± 1.4) was significantly lower ($p = 0.001$) than the mean MRS at recruitment (3.6 ± 1.3) as was the mean mNIHSS a month after stroke (5.2 ± 7.0) to the mean mNIHSS at recruitment (7.4 ± 5.8) with $p = 0.007$. The mean Barthel Index at one-month post stroke (13.4 ± 7.6) was however significantly higher ($p = 0.001$) than the mean Barthel Index at recruitment (9.4 ± 7.3) as displayed in Table 7.

Table 7: Mean functional status measures at recruitment and one-month post stroke

	At recruitment	One-month after stroke	p-value
MRS	3.6 ± 1.3	2.9 ± 1.4	0.001*
mNIHSS	7.4 ± 5.8	5.2 ± 7.0	0.007*
Barthel Index	9.4 ± 7.3	13.4 ± 7.6	0.001*

*Significant at $p < 0.05$

4.6. Correlation between recruitment measures of functional status and functional outcome values at one-month

Two-tailed Spearman's rank correlation analysis (Table 8) with significance level set at 95% showed the following relationships between the variables of interest: At $p < 0.001$, MRS_0 showed a significant positive correlation to $mNIHSS_0$ (rho = 0.753), $mNIHSS_1$ (rho = 0.754) and MRS_1 (rho = 0.847) and a significantly negative correlation to BI_0 (rho= -0.932) and BI_1 (rho = -0.813); with its strongest correlation being to BI_0.

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Apart from its correlation with MRS_0, $mNIHSS_0$ showed strong and significant negative correlation to BI_0 (rho = -0.800) and BI_1 (rho = -0.896) and a significantly strong positive correlation with MRS_1 (rho= 0.883) and $mNIHSS_1$ (rho= 0.877). Other significant negative correlations for BI_0 were to MRS_1 (rho= -0.853) and $mNIHSS_1$ (rho= -0.769), while a significant positive correlation was with BI_1 (rho= 0.852).

In addition to the correlations with functional status measures at recruitment (MRS_0, $mNIHSS_0$ and BI_0), there was a significant positive correlation between MRS_1 and $mNIHSS_1$ (rh0 = 0.917) and a significant negative correlation between $mNIHSS_1$ and BI_1 (rho = -0.895) all at $p < 0.001$.

Of the 3 QEEG indices analysed (DAR, RAP and pdBSI), there was no significant correlation to known functional measures (MRS_0, MRS_1, $mNIHSS_0$, $mNIHSS_1$, BI_0 and BI_1) or among the QEEG indices, except for a negative correlation between DAR and RAP (rho= -0.988, $p < 0.001$), which was the highest correlation coefficient in the entire analysis.

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Table 8: Correlations between measures of functional status

		MRS_0	$mNIHSS_0$	BI_0	MRS_1	$mNIHSS_1$	BI_1	DAR	RAP	pdBSI
MRS_0	rho	1.000	0.753*	-0.932*	0.847*	0.754*	-0.813*	-0.190	0.189	0.049
	p-value		0.000	0.000	0.000	0.000	0.000	0.316	0.316	0.796
$mNIHSS_0$	rho	0.753*	1.000	-0.800*	0.883*	0.877*	-0.896*	-0.048	0.021	-0.057
	p-value	0.000		0.000	0.000	0.000	0.000	0.800	0.912	0.765
BI_0	rho	-0.932*	-0.800*	1.000	-0.853*	-0.769*	0.852*	0.126	-0.125	-0.074
	p-value	0.000	0.000		0.000	0.000	0.000	0.508	0.512	0.698
MRS_1	rho	0.847*	0.883*	-0.853*	1.000	0.917*	-0.959*	-0.099	0.089	0.052
	p-value	0.000	0.000	0.000		0.000	0.000	0.601	0.638	0.785
$mNIHSS_1$	rho	0.754*	0.877*	-0.769*	0.917*	1.000	-0.895*	-0.039	0.004	-0.126
	p-value	0.000	0.000	0.000	0.000		0.000	0.839	0.984	0.506
BI_1	rho	-0.813*	-0.896*	0.852*	-0.959*	-0.895*	1.000	0.096	-0.077	-0.007
	p-value	0.000	0.000	0.000	0.000	0.000		0.614	0.686	0.970
DAR	rho	-0.190	-0.048	0.126	-0.099	-0.039	0.096	1.000	-0.988*	0.124
	p-value	0.316	0.800	0.508	0.601	0.839	0.614		0.000	0.512
RAP	rho	0.189	0.021	-0.125	0.089	0.004	-0.077	-0.988*	1.000	-0.070
	p-value	0.316	0.912	0.512	0.638	0.984	0.686	0.000		0.714
pdBSI	rho	0.049	-0.057	-0.074	0.052	-0.126	-0.007	0.124	-0.070	1.000
	p-value	0.796	0.765	0.698	0.785	0.506	0.970	0.512	0.714	

**significant at $p < 0.01$ (2-tailed)*

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4.7.0 Prediction of functional outcome of patients at one-month post-stroke

Regression analysis of all patients (Table 9) showed that none of the three QEEG indices significantly predicted functional outcomes (MRS_1, $mNIHSS_1$ or BI_1), however $mNIHSS_0$ positively predicted MRS_1 (beta = 0.471, p = 0.001) and $mNIHSS_1$ (beta = 0.753, p = 0.001) and negatively predicted BI_1 (beta= -0.556, p = 0.001) as shown in Table 9. In addition, BI_0 positively predicted BI_1 (beta = 0.519, p = 0.001). These predictions were significant at $p < 0.05$.

Table 9: Regression analysis between functional outcomes and QEEG indices of all patients

	MRS_1		**$mNIHSS_1$**		**BI_1**	
	Beta	**p-value**	**Beta**	**p-value**	**Beta**	**p-value**
DAR	-0.051	0.849	-0.051	0.849	0.105	0.701
RAP	-0.146	0.594	-0.146	0.594	0.044	0.873
pdBSI	-0.146	0.464	-0.146	0.464	0.021	0.917
MRS_0	0.257	0.131	0.030	0.905	0.163	0.410
$mNIHSS_0$	0.471*	0.001	0.753*	0.001	-0.556*	0.001
BI_0	-0.260	0.176	-0.027	0.925	0.519*	0.026

** Beta (standardized coefficient) is significant at $p < 0.05$*

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4.7.1 Regression analysis according to stroke type

In a sub-analysis of linear regression between recruitment parameters (MRS_0, $mNIHSS_0$, BI_0, DAR, RAP and pdBSI) and functional outcome measures in ischaemic strokes (Table 10) significantly, $mNIHSS_0$ positively predicted $mNIHSS_1$ (beta = 1.104, p = 0.003), and negatively predicted BI_1 (beta = -0.694, p = 0.012) while RAP negatively predicted $mNIHSS_1$ (beta = -0.668, p = 0.021).

For haemorrhagic strokes, MRS_0 positively predicted MRS_1 (beta = 0.536, p = 0.033) and $mNIHSS_0$ positively predicted MRS_1 (beta = 0.961, p = 0.012). There were no other significant predictions. The import of all the results displayed in this section are discussed in the next section.

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Table 10: Regression analysis between outcome measures by stroke type

	Ischaemic stroke						Haemorrhagic stroke					
	MRS_1		**$mNIHSS_1$**		**BI_1**		**MRS_1**		**$mNIHSS_1$**		**BI_1**	
	Beta	*p-value*	*Beta*	*p-value*	*Beta*	*p-value*	*Beta*	*p-value*	*Beta*	*p-value*	*Beta*	*p-value*
MRS_0	0.116	0.666	-0.024	0.939	0.171	0.509	0.536*	0.033	0.237	0.522	0.052	0.849
$mNIHSS_0$	0.323	0.218	1.104*	0.003	-0.694*	0.012	0.961*	0.012	0.99	0.09	-0.959	0.051
BI_0	-0.525	0.105	0.188	0.609	0.42	0.168	0.446	0.072	0.346	0.427	0.062	0.843
DAR	-0.031	0.881	-0.458	0.083	0.358	0.091	-0.058	0.642	-0.029	0.917	-0.005	0.983
RAP	-0.001	0.996	-0.668*	0.021	0.318	0.144	-0.117	0.335	-0.35	0.235	0.274	0.224
pdBSI	0.093	0.478	-0.109	0.482	-0.034	0.786	0.103	0.387	-0.134	0.609	0.026	0.895

** Beta (standardized coefficient) is significant at $p < 0.05$*

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5.0 DISCUSSION

The implications of the findings of this research are discussed below

5.1. Patient demographics and clinical characteristics

A high number of patients in this study were in the pre-retirement age (≤60years) and according to stroke type, a significant number of them were haemorrhagic strokes. A report on the global burden of stroke by Feigin, Norrving, & Mensah (2017) documented that in low and middle income countries like Ghana, 68% of strokes which occurred in 2010 were in persons younger than 75years. This two-decade (1990-2010) analysis of the global burden of stroke showed a 25% increase in the percentage of young and middle aged adults (20-64years) who suffered stroke, contributing to 31% of all stroke cases (Feigin et al., 2017). These stroke in young adults have been attributed to high body mass index, low vegetable intake and air pollution from household fuels while in middle aged adults systolic blood pressure and other metabolic factors have been attributed to the cause of stroke. The implication of these findings is that low and middle income countries like Ghana may lose a number of their younger work-force to stroke associated morbidity and mortality causing further diminution of the nation's productivity (Feigin et al., 2016).

Haemorrhagic stroke patients formed 33.3% of the stroke cases studied. This finding was similar to findings from the INTERSTROKE study of stroke in 22 countries worldwide, which found haemorrhagic stroke accounted for 34% of stroke in Africa (O'Donnell et al., 2010) and the SIREN study of stroke in Ghana and Nigeria, which found the frequency of haemorrhagic stroke to be 32% (Kengne & Mayosi, 2018). When compared to high income countries such as Canada which reported 18.7% (Burneo et al., 2010) and the report from the INTERSTROKE study which showed strokes caused by haemorrhage to contribute as low as 9% of all strokes (O'Donnell et al., 2010),

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it becomes imperative that more focus be given to the reduction of the occurrence and impact of haemorrhagic strokes in Ghana and Africa at large (Feigin et al., 2017). This high percentage of haemorrhagic stroke in middle and low income countries has been attributed to changes in life-style and increase in urbanization in Africa (Feigin et al., 2016).

The male stroke patients in this study were twice the number of female patients. This finding follows the trend in the review of global stroke statistics given by Thrift et al. in 2017 for 205 countries (including some African countries but not Ghana) in all of whom incidence was more in males than females. This variation has been attributed to difference in risk factors for stroke by gender (Roth et al., 2017).

In this study, 70% of the patients had lesions in the cerebral cortex; especially the ischaemic stroke patients (though the difference in proportions between ischaemic and haemorrhagic strokes was not significant). In terms of hemispheric location of brain lesion, this study found no significant difference between ischaemic and haemorrhagic strokes; though the group was a mixture of left, right and bilateral hemisphere strokes. As cortical location of damage is one of the known risk factors of post stroke epilepsy, the occurrence of cortical damage in the study participants may have increased the likelihood of seizure occurrence in them (Packiaseeli et al., 2017; Tanaka & Ihara, 2017). When the connections between the two brain hemispheres are damaged in subcortical lesions, the degeneration of these connections could even provoke post stroke seizures (Klein et al., 2018; Tanaka & Ihara, 2017). Subcortical lesions may also lead to secondary degeneration of the cerebral cortex, therefore the occurrence of purely subcortical lesions in a few of the patients in this study did not exempt them from cortical damage (Tanaka & Ihara, 2017).

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Majority of the group had mild to moderate stroke severity at recruitment with improvement in one-month variables (MRS, mNIHSS and BI). More severe neurological deficits at the initial stages of stroke (as measured by NIHSS) have been found to be associated with the occurrence of epilepsy after stroke (Klein et al., 2018; Tanaka & Ihara, 2017) and death (Nkusi et al., 2017); though no death was recorded within this study. This is because the larger the cortical area of damage, the greater the severity and hence the greater the risk of post stroke epilepsy.

5.2. Seizure occurrence in stroke patients

The 13.3% frequency of seizures found in this study was slightly higher than the 11% stroke occurrence in over 530 stroke cases from the Korle Bu Teaching Hospital's stroke unit (unpublished data) and much higher than the 8.9% found in a multicentre study of over 2000 stroke patients in Canada, Australia, Israel and Italy (Bladin et al., 2000). As discussed above, most patients in this study were young (≤60years), most had lesions in the cerebral cortex and the percentage with haemorrhagic stroke was high. These are three of the most consistent risk factors for post stroke epilepsy (Bladin et al., 2000; Zelano, 2016).

Although four patients in this study had early seizures, only one patient developed late seizures- a haemorrhagic stroke patient. This finding concurs with the report from a study in India from which the most common seizure type in stroke patients was early seizures (Packiaseeli et al., 2017). As that one patient had more than one unprovoked seizure in over 24 hour interval, by the definition of the International League Against Epilepsy, this patient has developed post-stroke epilepsy (Fisher et al., 2005). Early seizures is a known risk factor for late seizures and late seizures is a known risk factor for post stroke epilepsy (Klein et al., 2018). Also, stroke has been found to be the main cause of late-onset seizure disorder in African adults (Owolabi, Akinyemi, Owolabi, Sani,

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& Ogunniyi, 2013); a risk that is increased by the aetiology of haemorrhagic stroke (Zelano, 2016). Seizures are known to increase post stroke morbidity and mortality (Bladin et al., 2000), but no death was recorded within the one-month period of this study and most patients had slight improvement in functional status at one-month post stroke.

Apart from the occurrence of clinical seizures, many more patients had electrographic seizures suggestive of generalized seizure disorder. These seizures which are generally as a direct result of the cortical insult to the brain when stroke occurs are more common than clinical seizures and likely lead to worse outcomes (Bleck, 2012). These seizures, which are sometimes inappropriately called subclinical seizures (Fisher et al., 2005) have been found to be a sensitive predictor of clinical seizures (Feldwisch-Drentrup et al., 2011). If the occurrence of these seizures is an indicator of the likelihood of patients to manifest clinical seizures (Feldwisch-Drentrup et al., 2011), then at least 46% of the patients in this study were at risk of post stroke seizures (though only 14% of that number had associated clinical seizures). In addition, with information on the presence of electrographic seizure status of their patients, clinicians could readily provide interventions to reduce the risk of post stroke epilepsy and associated worsening of outcomes.

Almost all the electrographic seizures recorded in this study were generalized seizures. Of the numerous aberrant electrographic activity categorized in this study, the most common which was diagnostic of seizures was generalized spike and wave activity and for the diagnosis of cerebral dysfunction, diffuse slowing was the most characteristic. These findings have some similarities to the findings of Siddiqui et al. (2008) in their observational study of EEG recordings in post stroke seizures; though their commonest seizure activity was focal not generalized. Their study also had some similarities to a study of seizure semiotics in Nigeria, which found the most common seizure associated electroencephalographic brain activity to be focal epileptiform discharge followed by

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focal slowing (L. Owolabi et al., 2013). These findings of aberrant electroencephalography activities are explained by the impairment of neuronal metabolism, neuronal death and mechanisms of plasticity that occur after stroke (Brain Science International [BSI], 2017; Tanaka & Ihara, 2017).

5.3. Predictors of post stroke functional outcome at one-month in 30 stroke patients

Despite the good correlations between functional status measures at recruitment and their corresponding one-month measures, only the modified National Institute of Health Stroke Scale turned out to be a good predictor of all the three outcome measures used, and the Barthel Index score at recruitment was able to predict the Barthel Index score at one-month. The ability of NIHSS (or its modified version (mNIHSS) to predict different measures of post stroke functional outcome has been proved over and over by many studies, including a study on post stroke cognitive impairment in a some Ghanaians (Sarfo, Akassi, Adamu, Obese, & Ovbiagele, 2017) and another on measures of activities of daily living (Kwakkel et al., 2010; Veerbeek et al., 2011).

There was no significant correlation between any of the QEEG indices studied (DAR, RAP and pdBSI) and other measures of functional status at recruitment or their outcome scores at one-month when measured for all stroke types; none of the indices predicted outcome measures of activities of daily living (BI), death and disability status (MRS) or neurological deficit (mNIHSS). When assessed by stroke type, only RAP significantly predicted mNIHSS score at one-month in ischaemic strokes. Since the mechanisms of damage and repair in the two stroke types differ, the variability in brain activity according to physiological mechanisms in each stroke type may have contributed to the poor correlations of QEEG indices with functional outcomes in this study. Perhaps an analysis with larger samples by stroke type may yield significant QEEG predictors of functional outcome for each stroke type.

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For this study, EEGs were recorded with scalp-electrode impedance between 20-50kΩ; as opposed to various studies which have found significant associations between the three QEEG indices and functional status measured at admission or at different stages of recovery (Finnigan & van Putten, 2013). The researchers for those studies maintained impedance at levels below 5kΩ or not more than 15kΩ during recording (Finnigan et al., 2007; Sheorajpanday, Nagels, Weeren, & De Deyn, 2011; Sheorajpanday et al., 2009; Sheorajpanday, Nagels, Weeren, van Putten, et al., 2011; Xin, Chang, Gao, & Shi, 2017). Though measures were taken during EEG pre-processing in this study to filter out noise as well as rejecting bad electrodes from the analysis and Ferree, Luu, Russell, & Tucker (2001) concluded that the use of high input impedance-amplifiers and digital-filters for EEG processing eliminates the impact of scalp impedance on EEG recordings, ensuring EEGs are recorded with impedance below 5kΩ may improve study findings.

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6.0 CONCLUSION

From a discussion above it can be concluded that:

- There was a high incidence of electrographic seizure in stroke patients of Korle Bu Teaching Hospital than what could be clinically diagnosed.
- The QEEG indices DAR, RAP and pdBSI did not significantly predict post-stroke functional outcomes measures (MRS, mNIHSS or BI) at one-month across all stroke types.
- Relative alpha power (RAP) measured at recruitment was the only QEEG index useful in the prediction of neurological deficit (mNIHSS) in ischaemic stroke at one-month post stroke
- The mNIHSS measured at recruitment was the most significant predictor of all functional outcome measures (MRS, mNIHSS and BI) assessed at one-month post stroke.

STUDY LIMITATIONS

A longitudinal study of electroencephalography characteristics of stroke patients during hospitalization and at recovery could not be carried out due to high cost of EEG and time limitation.

RECOMMENDATIONS

- Electroencephalography should be routinely done for all stroke patients as a surveillance measure for seizure prediction. Perhaps it may help improve the vigilance in clinical seizure detection.
- Electroencephalography recordings for studies on QEEG predictors of functional outcome in stroke patients should be recorded at scalp-electrode impedances below 5kΩ.
- Prospective studies measuring QEEG indices predictive of stroke at admission and subsequent recovery months should be done to monitor neuronal recovery after stroke.

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- Further studies should be done to determine respective QEEG indices predictive of functional outcome for ischaemic and haemorrhagic stroke using a large sample size.

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APPENDIX

Appendix 1: Information and Consent form

Title of research: Association between EEG findings and functional outcomes in stroke patients at the Korle Bu Teaching Hospital

Investigators: Ruth Y. Laryea

MPhil student, University of Ghana- School of Biomedical and Allied Health Sciences (mobile number: +233 243722940)

Rev Dr Charles Antwi-Boasiako

Senior lecturer, University of Ghana- School of Biomedical and Allied Health Sciences

Dr Albert Akpalu

Senior Lecturer, University of Ghana School of Medicine and Dentistry

You are being invited to participate in a study of the association between EEG findings and functional outcomes of stroke patients at the Korle Bu Teaching Hospital.

When someone suffers from a stroke, the brain of that person sustains some injury which can affect the brain's ability to do its work which includes coordination of body functions. The injury from stroke can also cause the patient to have seizures which could worsen the health status of the patient

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and slow down recovery. Sometimes these seizures do not show any outward signs for the doctors to see.

The EEG (electroencephalography) is a painless and non-invasive diagnostic test (like the ECG test) that records the electrical activity of the brain, which shows how the brain is functioning. The EEG is a unique test that can show if someone's brain is having a seizure (even when the doctor cannot see it).

The purpose of this study is to use the EEG to measure the type of brain activity (seizures, normal etc.) of those who have had stroke while they are on admission and to see if the recorded brain activity can tell us how well the patients will be able to perform their body functions like walking and talking after one month.

If you agree to participate in this study, I will record your age, gender, type of stroke you have then a routine EEG test will be done for you. This test will take not more than 30 minutes. In addition, I will ask you to say and do a few things so I can assess how much the stroke has affected your ability to function. This assessment will be done again one month after you do the EEG at which time I will give you a copy of your EEG report.

To protect your privacy, I will separate your name from any data I will collect from you. In place of your name, I will give you a code which cannot be traced back to you. All data collected from you will be stored on a password protected computer which will be kept in a locked room.

Participation in this research is purely voluntary. If you choose not to participate in this study, it **will not** affect the care you receive from this facility; you will still receive the quality of care as any other patient here.

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Consent and Signature

The details of the study titled "Association between EEG findings and functional outcomes in stroke patients at the Korle Bu Teaching Hospital" have been explained to me and I have understood it. **I agree to participate** in this research, knowing that my participation involves a follow-up visit at one month.

Name of Participant……..

Name of Proxy……..

(if participant cannot sign)

Contact details (*telephone*)……

Signature……

Date Signed (DD/MM/YYYY)…….

Name of Investigator: Ruth Y. Laryea

Signature……

Date Signed (DD/MM/YYYY)…….

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Appendix 2: Study Questionnaire

Date:___/___/2018

Demographics

Participant ID:_____ **Age (yrs):**_____ **Sex:** Male/Female

Date of Birth:_____**(DD/MM/YYYY)**

Neuroimaging Report

Stroke type:

a. Haemorrhage
b. Infarct

Volume of lesion:

I. 0-3
II. 3.1-5.0
III. 5.1-7.0
IV. 7.1-10.0
V. >10.0

Cortical location *(one or more)*:

A. Frontal lobe
B. Temporal lobe
C. Parietal lobe
D. Occipital lobe
E. Brainstem

Hemispheric location of lesion:

a) Left b) Right

Subcortical structures affected:

□ Thalamus □ Pituitary gland
□ Basal ganglia

Functional Assessment

MRS at recruitment:_____ **MRS at one-month:**_____

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mNIHSS at recruitment:_____ **mNIHSS at one-month:_____**

Barthel Index at recruitment:_____ **Barthel Index at one-month:_____**

EEG Pattern Report

Type of EEG: a) Awake b) Drowsy c) Asleep d) Sedation e) Sleep deprived

Activations done: a) None b) Hyperventilation c) Photo stimulation

EEG activity

1. Normal activity
2. Epileptiform activity
   - i Spike and slow waves
   - ii Sharp waves
   - iii Spikes
   - iv Diffuse slowing
3. Cerebral dysfunction
   - i. Focal slowing
   - ii. Diffuse slowing
   - iii. Others……

Have you ever had a seizure before this stroke? (Yes/ No) If yes, how many_____

How many seizures has the patient had since stroke occurred? _____

When did they occur? a)Within two weeks b) After two weeks c) Both

Are you currently on any anti-epileptic drugs? (Yes/ No)

If yes, name them_____

EEG Quantification

pdBSI_____ RAP_____ DAR_____

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Appendix 3: Modified Rankin Scale (MRS)

MODIFIED RANKIN SCALE	
	Participant ID:
	Date assessed:
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

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Appendix 4: Modified National Institute of Health Stroke Scale (NIHSS)

Modified National Institute of Health Stroke Scale (mNIHSS)				
Participant ID:_____	**Date assessed:_____**			
Instructions	**Scale definition**		**Score**	
			1	**2**
1b. LOC Questions: The patient is asked the month and his/her age. The answer must be correct - there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier, or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or non-verbal cues.	0	**Answers** both questions correctly.		
	1	**Answers** one question correctly.		
	2	**Answers** neither question correctly.		
	0	**Performs** both tasks correctly.		

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1c. LOC Commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to him or her (pantomime), and the result scored (i.e., follows none, one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored	1	**Performs** one task correctly.		
	2	**Performs** neither task correctly.		
2. Best Gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored, but caloric testing is not done. If the patient has a conjugate	0	**Normal.**		
	1	**Partial gaze palsy;** gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present.		

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deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV or VI), score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or fields should be tested with reflexive movements, and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy	2	**Forced deviation,** or total gaze paresis not overcome by the oculocephalic maneuver.		
3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat, as appropriate. Patients may be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or	0	**No visual loss.**		
	1	**Partial hemianopia.**		
	2	**Complete hemianopia.**		
	3	**Bilateral hemianopia** (blind including cortical blindness).		

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enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia, is found. If patient is blind from any cause, score 3. Double simultaneous stimulation is performed at this point. If there is extinction, patient receives a 1, and the results are used to respond to item 11.					
5. Motor Arm: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine). Drift is scored if the arm falls before 10 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0	**No drift;** limb holds 90 (or 45) degrees for full 10 seconds.	Right		
	1	**Drift;** limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support.			
	2	**Some effort against gravity;** limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity.			
	3	**No effort against gravity;** limb falls	Left		
	4	**No movement.**			

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		UN= **Amputation** or joint fusion, explain: _____			
6. Motor Leg: The limb is placed in the appropriate position: hold the leg at 30 degrees (always tested supine). Drift is scored if the leg falls before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic leg. Only in the case of amputation or joint fusion at the hip, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0	**No drift;** leg holds 30-degree position for full 5 seconds.	Right		
	1	**Drift;** leg falls by the end of the 5-second period but does not hit bed.			
	2	**Some effort against gravity;** leg falls to bed by 5 seconds, but has some effort against gravity.			
	3	**No effort against gravity;** leg falls to bed immediately.	Left		
	4	**No movement.**			
		UN = **Amputation** or joint fusion, explain: _____			
8. Sensory: Sensation or grimace to pinprick when tested, or withdrawal from	0	**Normal;** no sensory loss.			

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noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas (arms [not hands], legs, trunk, face) as needed to accurately check for hemisensory loss. A score of 2, "severe or total sensory loss," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will, therefore, probably score 1 or 0. The patient with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in a coma (item 1a=3) are automatically given a 2 on this item.	1	**Abnormal;** patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick, but patient is aware of being touched. Or patient is not aware of being touched in the face, arm, and leg.		
9. Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. For this scale item, the patient is asked to describe what is	0	**No aphasia;** normal.		
	1	**Mild-to-moderate aphasia;** some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of		

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happening in the attached picture, to name the items on the attached naming sheet and to read from the attached list of sentences. Comprehension is judged from responses here, as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in a coma (item 1a=3) will automatically score 3 on this item. The examiner must choose a score for the patient with stupor or limited cooperation, but a score of 3 should be used only if the patient is mute and follows no one-step commands.		expression. Reduction of speech and/or comprehension, however, makes conversation about provided materials difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content from patient's response.		
	2	**Severe aphasia;** all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response.		
	3	**Mute, global aphasia;** no usable speech or auditory comprehension.		
11. Extinction and Inattention (formerly Neglect): Sufficient information to identify neglect may be	0	**No abnormality**		
	1	**Visual, tactile, auditory, spatial, or personal inattention** or extinction to		

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obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.		bilateral simultaneous stimulation in one of the sensory modalities.		
	2	**Profound hemi-inattention or extinction to more than one modality;** does not recognize own hand or orients to only one side of space.		
	TOTAL SCORE AT RECRUITMENT (SCORE 1)			
	TOTAL SCORE AT ONE-MONTH (SCORE 2)			

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Appendix 5: Barthel Index

BARTHEL INDEX OF ACTIVITIES OF DAILY LIVING			
ITEM	**RANKING**	**SCORE 1**	**SCORE 2**
Bowels	0 = incontinent (or needs to be given enemata) 1 = occasional accident (once/week) 2 = continent		
Bladder	0 = incontinent, or catheterized and unable to manage 1 = occasional accident (max. once per 24 hours) 2 = continent (for over 7 days)		
Grooming	0 = needs help with personal care 1 = independent face/hair/teeth/shaving (implements provided)		
Toilet use	0 = dependent 1 = needs some help, but can do something alone 2 = independent (on and off, dressing, wiping)		
Feeding	0 = unable 1 = needs help cutting, spreading butter, etc. 2 = independent (food provided within reach)		
Transfer	0 = unable – no sitting balance 1 = major help (one or two people, physical), can sit 2 = minor help (verbal or physical) 3 = independent		
Mobility	0 = immobile		

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	1 = wheelchair independent, including corners, etc. 2 = walks with help of one person (verbal or physical) 3 = independent (but may use any aid, e.g., stick)		
Dressing	0 = dependent 1 = needs help, but can do about half unaided 2 = independent (including buttons, zips, laces, etc.)		
Bathing	0 = dependent 1 = independent (or in shower)		
Stairs	0 = unable 1 = needs help (verbal, physical, carrying aid) 2 = independent up and down		
	Total Score		

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Appendix 6: Copy of Ethical clearance

UNIVERSITY OF GHANA
COLLEGE OF HEALTH SCIENCES
ETHICAL AND PROTOCOL REVIEW COMMITTEE

29th March, 2018

Ref. No.:.....

Ruth Y. Laryea
Department of Physiology
SBAHS
Korle-Bu

ETHICAL CLEARANCE

Protocol Identification Number: **CHS-Et/M.6 – P1.11/2017-2018**

The Ethical and Protocol Review Committee of the College of Health Sciences on the 1st of March, 2018 unanimously approved your research proposal.

TITLE OF PROTOCOL: **"Association between EEG Findings and Functional Outcomes in Stroke Patients at the Korle- Bu Teaching Hospital."**

PRINCIPAL INVESTIGATOR: **Ruth Y. Laryea**

This approval requires that you submit six-monthly review reports of the protocol to the Committee and a final full review to the Ethical and Protocol Review Committee at the completion of the study. The Committee may observe, or cause to be observed, procedures and records of the study during and after implementation.

Please note that any significant modification of this project must be submitted to the Committee for review and approval before its implementation.

You are required to report all serious adverse events related to this study to the Ethical and Protocol Review Committee within seven (7) days verbally and fourteen (14) days in writing.

As part of the review process, it is the Committee's duty to review the ethical aspects of any manuscript that may be produced from this study. You will therefore be required to furnish the Committee with any manuscript for publication.

This ethical clearance is valid till 29th March, 2019.

Please always quote the protocol identification number in all future correspondence in relation to this protocol.

Signed: .....
PROFESSOR ANDREW A. ADJEI
CHAIRPERSON, ETHICAL AND PROTOCOL REVIEW COMMITTEE

cc: Provost, CHS
Dean, SBAHS
Head of Department

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