بسم الله الرحمن الرحيم

Sudan University for Sciences and Technology

College of Graduate Studies

Optimization of the MRI Brain Protocol for Multiple Sclerosis.

تحسين برتكول تصوير الدماغ بالرنين المغناطيسي لمرض التصلب المتعدد.

A thesis Submitted for Partial Fulfillment of the Requirement of PHD. in Diagnostic Radiologic Technology

By:

MOHANAD ABDALLAH OMER

Supervisor:

Dr. IKHLAS ABDALAZIZ

(Associate professor)

2018

الآيـة

قال تعالى:

﴿اللَّهُ نُورُ السَّمَاوَاتِ وَالأَرْضِ مَثَلُ نُورِهِ كَمِشْكَاةٍ فِيهَا مِصْبَاحٌ الْمِصْبَاحُ فِي زُجَاجَةٍ الزُّجَاجَةُ كَأَنَّهَا كَوْكَبٌ دُرِّيٌّ يُوقَدُ مِنْ شَجَرَةٍ مُبَارَكَةٍ زَيْتُونَةٍ لا شَرْقِيَّةٍ وَلا غَرْبِيَّةٍ يَكَادُ زَيْتُهَا يُضِيءُ وَلَوْ لَمْ تَمْسَسْهُ نَارٌ نُورٌ عَلَى نُورٍ يَهْدِي اللَّهُ لِنُورِهِ مَنْ يَشَاءُ وَيَضْرِبُ اللَّهُ الأَمْثَالَ لِلنَّاسِ وَاللَّهُ بِكُلِّ شَيْءٍ عَلِيمٌ﴾

صدق الله العظيم

سورة النور: الآية (36)

Dedication

With my love and appreciation I dedicate this thesis to:

My ***all family***

My ***all teacher***

My ***all friends, family, and to all people those I love and respect***

Acknowledgement

I would like to express my sincere gratitude to

Dr.Ikhlas AbdAziz, DR. Amaa,Elamin, ABdalrahman Alamas *who have given me great advice and help in the whole process of my thesis for his fruitful day to day supervision, guidance, endless help and encouragement that built confidence in my work for his valuable and continuous help, his patience through all the years that made this work possible for giving this opportunity of study, and for endless encouragement and unlimited support .*

My thanks extend also to colleagues in every radiological department who gave their gold time to help others, to my College, for contributing in the sample collections and my friends for their assistance in many social activities through all the periods of the study. I would like to thank everyone who assisted by one way or another to bring this study to the light.

Abstract

Multiple Sclerosis (MS) is a chronic autoimmune inflammatory disease of the central nervous system, which can be diagnosed by magnetic resonance imaging (MRI).

This study is an analytical study, which conducted in many diagnostic centers from May 2015 to Mars 2018, MRI brain scan were done for 64 patients (male 18) and female(46) their age range 17 year to 46 year. Patients known case of multiple sclerosis the aim of this study was to evaluate the of routine MRI brain protocol for MS comparing with modified protocol and advanced protocol. The study used image analysis texture and reveal protocol 3 (3D volume) signal intensity increase with age more than routine protocol (5 mm gap 1) and modified protocol (3mm gap 0) were R^2 = o.11 ,0.012 and 0.007 P1,p2 and P3 respectively. T test used to differentiate between protocols T-test (Cl =995%) and (p-value = 0.05) Resulted about significant different between P1 (routine protocol) and P2 (modified protocol) and the mean of them 38.4 and 52.2 respectively. And also there was a significant different between P1 and P3, The mean between them 38.4 and 69.00 respectively. The study was arrived for more accurate discrimination of signal intensity between different brain tissues. Using texture analysis for each DICOM image, then was used Linear discriminant analysis ,classify feature to brain tissues ,CSF and MS.to differentiate between the classes using LDA accuracy of classification 96.7% and sensitivity for each class is 99.7% ,96.8% and for 92.2% (brain tissues, CSF and MS respectively). This program clearly different between these classes which match the routine protocol. Clearly different in signal intensity between CSF, brain tissues and MS, when using the mean, the higher signal noted for MS. The

results revealed the advanced protocol (3D volume) is the best in diagnose MS and then modified protocol. Patients for follow up, the best sequence to detected new plaque, was the volume T1 with contrast substance. The most patients have MS have vitamin D deficiency 57% have vitamin D deficiency and 42% not having.

المستخلص

التصلب المتعدد هو مرض التهابي ذاتي مزمن في الجهاز العصبي المركزي ، والذي يمكن تشخيصه عن طريق التصوير بالرنين المغناطيسي. هذه الدراسة هي دراسة تحليلية أجريت في العديد من مراكز التشخيص من مايو 2015 إلى مارس 2018 ، وتم إجراء مسح للدماغ بالرنين المغناطيسي ل 64 مريضا (الذكور 18) والإناث (46) أعمارهم تتراوح بين 17 سنة إلى 46 سنة. كل المرضى لديهم حالة التصلب المتعدد. كان الهدف من هذه الدراسة هو تقييم بروتوكول الرنين المغناطيسي للدماغ لمرض التصلب العصبي المتعدد مقارنة مع البروتوكول المعدل والبروتوكول المتقدم. استخدمت الدراسة تركيبة تحليل الصور وكشف زيادة كثافة البروتوكول 3 (حجم ثلاثي الأبعاد) مع تقدم العمر أكثر من البروتوكول الروتيني (الفجوة 5 مم 1) والبروتوكول المعدل (الفجوة 3 مم 0) كانت R2 = o.11 و 0.012 و 0.007 P1 و p2 و P3 على التوالي. استخدم اختبار T للتفريق بين البروتوكولات T-test (Cl = 995٪(و (p-value = 0.05) نتج عنه اختلاف كبير بين P1 (البروتوكول الروتيني) و P2 (بروتوكول معدل) ووسطها 38.4 و 52.2 على التوالي. وأيضا كان هناك اختلاف كبير بين P1 و P3 ، المتوسط بين 38.4 و 69.00 على التوالي. توصلت الدراسة للحصول على تمييز أكثر دقة لشدة الإشارة بين أنسجة الدماغ المختلفة. باستخدام تحليل الملمس لكل صورة DICOM ، ثم تم استخدام تحليل التمييز الخطي ، تصنيف ميزة أنسجة المخ ، CSF و MS. للتمييز بين الطبقات باستخدام دقة LDA للتصنيف 96.7 ٪ والحساسية لكل فئة 99.7 ٪ ، 96.8 ٪ ولل 92.2 ٪ (أنسجة المخ ، CSF و MS على التوالي). هذا البرنامج يختلف بوضوح بين هذه الفئات التي تتطابق مع البروتوكول الروتيني. يختلف اختلاف شدة الإشارة بين CSF وأنسجة المخ و MS بشكل واضح عند استخدام المتوسط ، إشارة أعلى ملحوظة لـ MS. كشفت النتائج أن البروتوكول المتقدم (حجم ثلاثي الأبعاد) هو الأفضل في تشخيص مرض التصلب العصبي المتعدد ومن ثم تعديل البروتوكول. كان المرضى الذين يقومون بالمتابعة ، أفضل تسلسل للوحة جديدة تم اكتشافها ، هو حجم T1 مع مادة متباينة. معظم المرضى الذين يعانون من مرض التصلب العصبي المتعدد لديهم نقص فيتامين (د) 57 ٪ لديهم نقص فيتامين (د) و 42 ٪ لا يعانون. كانت النسبة بين الجنسين 71.9 ٪ من الإناث و 28.1 ٪ من الذكور وهذا هو متوسط نسبة الإناث أكبر. تم تسجيل أعلى معدل للمرضى الذين يشكون من الصداع والدوار والخدر 28.1 ٪ ل 18 مريضا. أظهرت الدراسة أن الفئة العمرية الأكثر تعرضًا لمرض التصلب العصبي المتعدد هي 22.8 - 28.5 و 34.4 - 40.2. من ناحية أخرى أظهرت نتائج هذه الدراسة أن المرضى الذين تتراوح أعمارهم بين 34.4 و 40.2 كانوا الأكثر تأثراً بنقص فيتامين د. كانت النساء الأكثر تأثراً بنقص فيتامين (د) ، مع 30 امرأة و 7 رجال. خلصت الدراسة إلى أن: خلصت الدراسة إلى أن: البروتوكول المتقدم هو الأفضل في تشخيص التصلب المتعدد المتبع في ترتيب البروتوكول المعدل

List of Tables

List of Figures

List of abbreviations

CSF	Cerebro Spinal Fluid
MS	Multiple Sclerosis
FLAIR	Fluid Attenuation Inversion Recovery
P1	Protocol 1 (routine protocol).
P2	Protocol 2 (modified protocol).
P3	Protocol 3 (advance 3D volume).
IDL	Interactive Data Language
LDA	Linear Discriminant Analysis
MRI	Magnetic Resonance Imaging
3D	Three dimension
Vit D	Vitamin D
FOS	First-Order Statistical Texture Analysis:
CNS	Central nervous system

Table of contents

Chapter one

1-1 Introduction

MS is a chronic, progressive, degenerative disorder of the central nervous system (CNS) characterized by disseminated demyelization of nerve fibers of the brain and spinal cord, MS usually affects young to middle- aged adults, with onset between 15 and 50 years of age the women affected more than men it's unknown etiological cause it's may be related to infectious, immunologic, and genetic factors possible precipitating factors include (physical injury, emotional stress, pregnancy, poor state of health. Pathophysiology of mylelin sheath affected by segmented lamination that wraps axons of many nerve cells increases velocity of nerve impulse conduction in the axons, composed of myelin, a substance with high lipid content (Kalb & P. D.R.C 2008). Characterized by chronic inflammation, demyelination, and gliosis (scarring) in the CNS, initially triggered by a virus in genetically susceptible individuals subsequent antigen-antibody reaction leads to demyelination of axons .Disease process consists of loss of myelin, disappearance of oligodendrocytes, and proliferation of astrocytes changes result in plaque formation with plaques scattered throughout the CNS, initially the myelin sheaths of the neurons in the brain and spinal cord are attacked, but the nerve fiber is not affected, patient may complain of noticeable impairment of function, myelin can regenerate, and symptoms disappear, resulting in a remission (Kalb & P. D.R.C 2008).

The characteristic abnormalities of MS in the brain consist of multiple white matter lesions with a high signal intensity (SI) on fluid attenuation inversion recovery (FLAIR), proton density (PD)-weighted image (WI), and T2-WI and low signal intensity (SI) on T1-WI. Lesions are found predominantly in a periventricular distribution, Centrum semiovale, and the callososeptal interface. Additional sites of involvement include other parts of the cerebral white matter such as

the sub cortical a penetrating medullary vein. Atypical lesions and mass-like lesions occur with sufficient frequency to cause diagnostic errors. MS lesions may enhance after contrast administration on T1-WI, depending on the age and activity of the lesion. New and active lesions commonly show contrast enhancement, due to BBB breakdown. New lesions tend to show solid enhancement, whereas reactivated lesions enhance in a ring-like fashion (Fazekas et al., 1999).

After 2 months, the integrity of the BBB is restored, and the majority of lesions no longer show contrast enhancement. As with unenhanced lesions, the contrast-enhancing lesions are smaller than the corresponding lesions on the T2-W scan. The discrepancy between the size of the lesion on T1-WI and T2-WI reflects the different components of the local process: edema, inflammation, and demyelization. The poor correlation between the MRI findings and the clinical events is demonstrated by the frequent finding of enhancing lesions in clinically stable patients. White matter, optic nerves, corpus callosum, internal capsule, cerebellar peduncles, brainstem, and spinal cord. Demyelinating lesions appear smaller on T1-WI than on T2-WI. Occasionally, they show a hyper intense border on T1-WI (Fazekas et al 1999).

Lesions in MS can be small, large, or confluent the typical configuration is that of an ovoid lesion extending perpendicularly from the ventricular surface (Dawson's finger).This probably reflects the perivascular inflammation along found in the corpus callosum. Typically, these lesions occur along the inner callosal-ventricular margin, creating an irregular ventricular surface of the corpus callosum. This aspect can be differentiated from callosal atrophy due to the lobar white-matter lesions. The existence of callosal lesions improves both the sensitivity and the specificity of MRI for the diagnosis of MS. The absence of callosal lesions renders the diagnosis of MS less likely, but does not exclude it. A frequent initial presentation of MS is optic neuritis, although there is controversy regarding the likelihood of definitive MS developing in patients

who have had an optic neuritis. Brainstem lesions are common, and a lesion in the medial longitudinal bundle affects approximately one-third of MS patients. In patients with clinically possible MS and a normal MRI study of the brain, a spinal MRI study should be performed. MS is an inflammatory demyelinating disease of the CNS. It is the most common demyelinating disease after vascular- and age-related demyelination. MS is characterized by multiple "plaques" of demyelination in the white matter of the brain and spinal cord. The primary lesions are found in the perivascular spaces along penetrating veins. Though the etiology of MS is not fully understood, the destruction of myelin is most likely caused by an autoimmune process. Initial symptoms can sometimes be triggered by trauma or a viral infection, but a convincing link to the disease has not been made. (Gray, et al., 2004).

The clinical course of MS is highly variable. The age of symptom onset in MS is usually between 18 and 40 years; onset is uncommon in childhood and after the age of 50 years. Initial symptoms may include numbness, dysesthesia, double vision, or problems with balance and coordination. Loss of motor function is also a frequent initial presentation. Less commonly, spinal-cord-related symptoms constitute the initial presentation of MS. There is a female: male ratio of 3:2. The most common clinical presentation is "relapsing- remitting" MS (70% of cases) (Rae-Grant et al., 1999).

Patients experience symptomatic episodes (known as "attack"), which can last from 24 h to several weeks, followed by complete or partial disappearance of symptoms (remission). The interval between relapses may be weeks to years (and even decades). As white-matter lesions increase over time, and neurologic disabilities increase, the disease frequently becomes "secondary progressive." Accumulating neurological deficits eventually lead to permanent disability. The evolution from relapsing-remitting to secondary-progressive MS occurs in

approximately half of patients within 10 years after onset. Alternatively, in 10–20% of cases, MS can follow a “primary progressive” course; in this type of disease, there is a continuous, gradual evolution from the beginning, rather than relapses (Rae-Grant et al., 1999).

1-2 Problem of the study:

Increasing the incidence of patient with multiple sclerosis was one of the critical area of examination in MRI department but in routine MRI brain protocols a hidden small MS does not seen due to a thicker slice (5 mm) and slice gab (1mm), in some cases enhanced T1w with using contrast is the necessary to view active MS and to aid the deferential diagnosis between the MS and small vascular disease. Therefore using modified MRI protocol to detect such case in conjunction with IDL image processing program can increase the sensitivity of detection using its character and texture.

1-3 objectives of the study:

1-3-1 General objectives:

The general aims of this study was to evaluate the routine MRI brain protocol for MS comparing with modified protocol and advanced protocol.

1-3-2 Specific objectives

To find the signal in the routine, modified and advanced image protocol.

To find the significant differences between the routine and optimized protocol

To evaluate agreed role of gadolinium to provides useful additional information about new activity.

To optimize MS protocol.

Correlate patient age, symptoms with MRI finding.

To correlate between vitamin D deficiency with MS disease.

To classify MS and brain tissue using texture analysis.

1-4 Significance of the study:

This study was highlighted on the characterization of multiple sclerosis in patient with clinically suspected disease (MS) for purpose of early detection and management using both routine and standardized MRI protocol and the comparing such result with the finding of texture analysis of multiple sclerosis.

1-5 Thesis outline

This study was consist of five chapters; Chapter one consist of introduction, statement of the problem, objectives of the study, significance of the study and thesis outline. Chapter two was the literature review contained the theatrical background Anatomy, Physiology, Pathology of the brain, and previous studies. Chapter three consist of methods and materials Chapter four: result presentation, Chapter five was contain dissection, Conclusions, and recommendation in addition to References and Appendices.

Chapter Two

Literature Review

2-1 Theoretical background

2-1-1Anatomy:

The human nervous system consists of the central nervous system (CNS) and peripheral nervous system (PNS). The former consists of the brain and spinal cord, while the latter composes the nerves extending to and from the brain and spinal cord. The primary functions of the nervous system are to monitor, integrate (process) and respond to information inside and outside the body. The brain consists of soft, delicate, non-replaceable neural tissue. It is supported and protected by the surrounding skin, skull, meninges and cerebrospinal fluid. (Martini et al., 2007).

Structures protect the brain: The cranium: Depending on their shape, bones are classified as long, short, flat or irregular. Bones of different types contain different proportions of the two types of osseous tissue: compact and spongy bone. While the former has a smooth structure, the latter is composed of small needle-like or flat pieces of bone called trabeculae, which form a network filled with red or yellow bone marrow. Most skull bones are flat and consist of two parallel compact bone surfaces, with a layer of spongy bone sandwiched between. The spongy bone layer of flat bones predominantly contains red bone marrow and hence has a high concentration of blood. The skull is a highly complex structure consisting of 22 bones altogether. These can be divided into two sets, the cranial bones (or cranium) and the facial bones. While the latter form the framework of the face, the cranial bones form the cranial cavity that encloses and protects the brain. All bones of the adult skull are firmly connected by sutures. The frontal bone forms the forehead and contains the frontal sinuses, which are air filled cells within the bone.

Most superior and lateral aspects of the skull are formed by the parietal bones while the occipital bone forms the posterior aspects. The base of the occipital bone contains the foramen magnum, which 27 is a large hole allowing the inferior part of the brain to connect to the spinal cord. The remaining bones of the cranium are the temporal, sphenoid and ethmoid bones. (Martini et al., 2007).

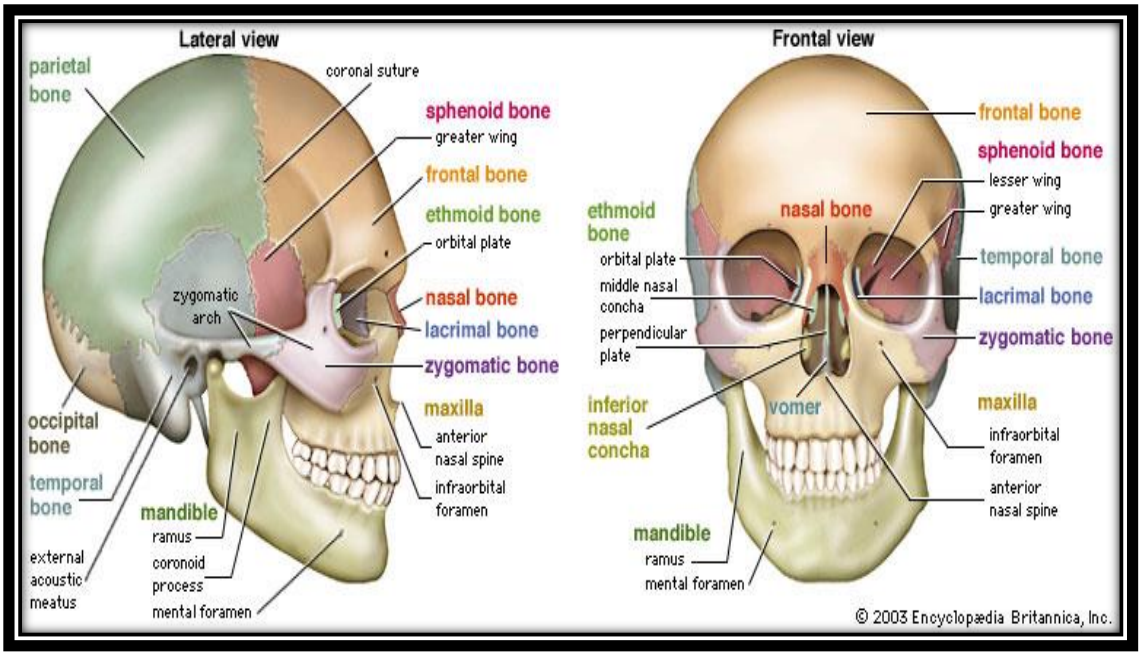


Figure (2-1) Lateral and Anterior View of Human skull (http://www.drpulp.com/)

Meninges: The brain and spinal cord are covered and protected by three layers of tissue called meninges. From the outermost layer inward they are: the dura mater, arachnoid mater, and pia mater (Figure 2.2). The dura mater is a strong, thick membrane that closely lines the inside of the skull; its two layers, the periosteal and meningeal dura, are fused and separate only to form venous sinuses. The dura creates little folds or compartments. There are two special dural folds, the falx and the tentorium. The falx separates the right and left hemispheres of the brain and the tentorium separates the cerebrum from the cerebellum. The arachnoid mater is a thin, web-like

membrane that covers the entire brain. The arachnoid is made of elastic tissue. The space between the dura and arachnoid membranes is called the subdural space.

The pia mater hugs the surface of the brain following its folds and grooves. The pia mater has many blood vessels that reach deep into the brain. The space between the arachnoid and pia is called the subarachnoid space. It is here where the cerebrospinal fluid bathes and cushions the brain. (Martini et al., 2007).

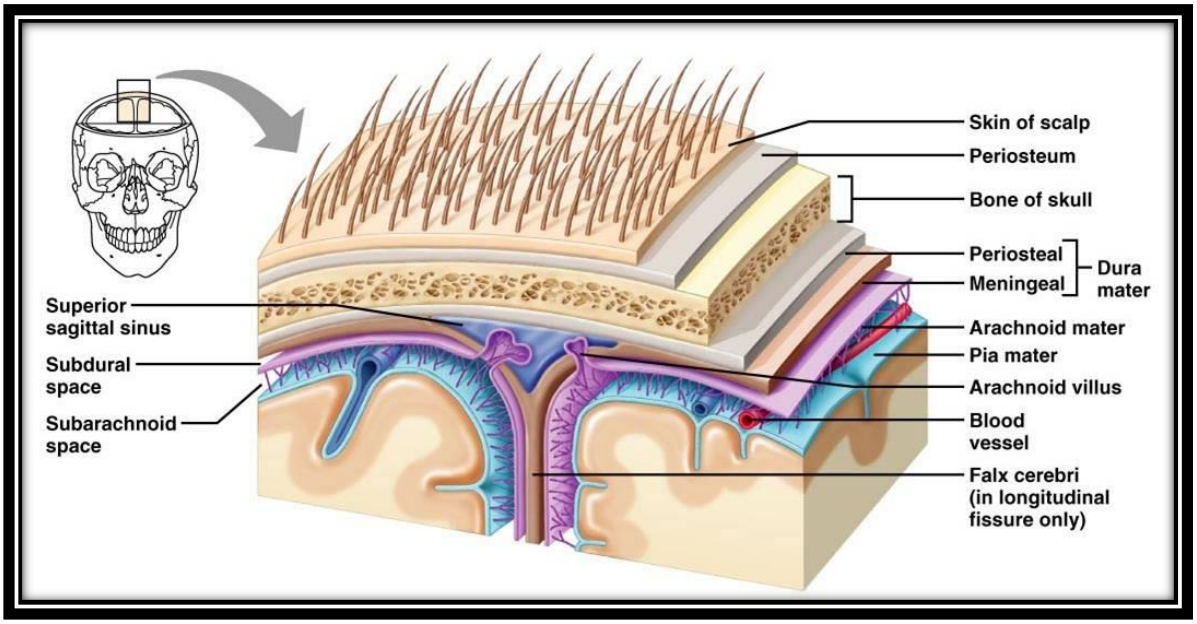


Figure 2.2 Meninges (http://faculty.irsc.edu.com**)**

Ventricles and cerebrospinal fluid*:* The brain has hollow fluid-filled cavities called ventricles (Fig. 2.3). Inside the ventricles is a ribbon-like structure called the choroid plexus that makes clear colorless cerebrospinal fluid (CSF). CSF flows within and around the brain and spinal cord to help cushion it from injury. This circulating fluid is constantly being absorbed and replenished. There are two ventricles deep within the cerebral hemispheres called the lateral ventricles. They both connect with the third ventricle through a separate opening called the foramen of Monro. The third ventricle connects with the fourth ventricle through a long narrow

tube called the aqueduct of Sylvius. From the fourth ventricle, CSF flows into the subarachnoid space where it bathes and cushions the brain. CSF is recycled (or absorbed) by special structures in the superior sagittal sinus called arachnoid villi. A balance is maintained between the amount of CSF that is absorbed and the amount that is produced. A disruption or blockage in the system can cause a build-up of CSF, which can cause enlargement of the ventricles (hydrocephalus) or cause a collection of fluid the spinal cord (syring omyelia). (Martini et al., 2007)

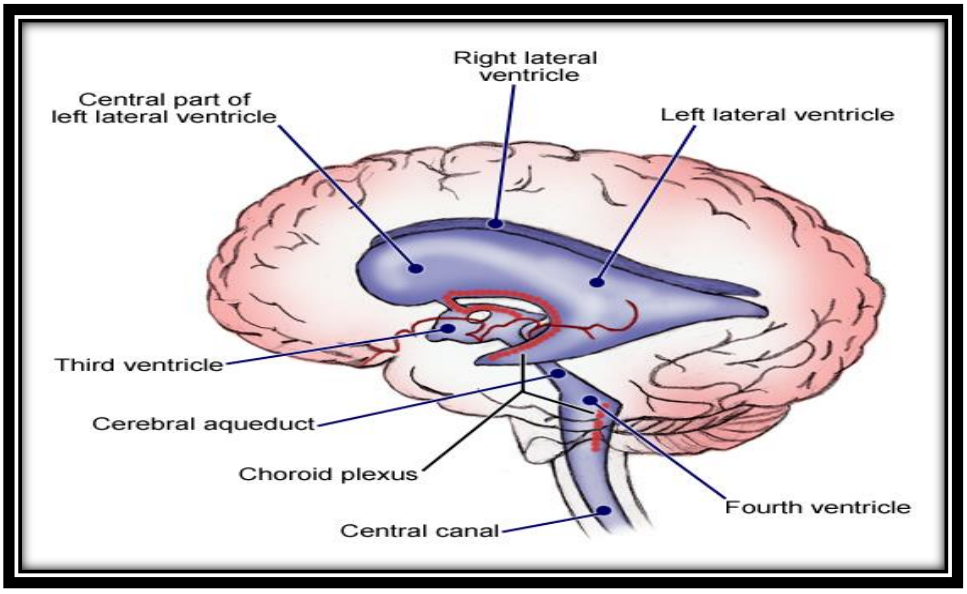


Figure (2-3) Ventricle of the brain (http://withealth.net)

Cerebrum: The cerebral hemispheres are narrower posteriorly, at the occipital pole, than anteriorly,at the frontal pole. They are large, oval structures that superficially resemble the surface of a shelled walnut .The midline longitudinal cerebral fissure, occupied in life by the falx cerebri, incompletely separates the two cerebral hemispheres from one another. The floor of the cerebral fissure is formed by the corpus callosum, a largemyelinated fiber tract that forms an anatomical and functional connection between the right and left hemispheres. The surface few millimeters of the cerebral hemisphere arecomposed of a highly folded collection of gray matter, known as the cerebral cortex. This folding increases the surface area and presents elevations,

gyri, and depressions, sulci. Deep to the cortex is a central core of white matter that forms the bulk of the cerebrum and represents fiber tracts, supported by neuroglia, ferrying information destined for the cortex and cortical responses to other regions of the central nervous system (CNS). Buried within the mass of white matter are collections of neuron cell bodies, some of which are lumped together under the rubric of basal ganglia, even though, technically,they are nuclei. Large collections of gray matter are also present in the diencephalons, namely, the epithalamus, thalamus, hypothalamus, and subthalamus. The cerebrum is a hollow structure and the cavities within the cerebral hemispheres are called the right and left lateral ventricles, which communicate with the third ventricle via the interventricular foramen (foramen of Monro). The two lateral ventricles are separated from one another by two closely adjoined non-nervous membranes, each known as a septum pellucidum. Ependymal cells line each lateral ventricle, and protruding into each ventricle is a choroid plexus that functions in the manufacture of cerebrospinal fluid. (Maria et al, 2006)

Lobes of the cerebral hemispheres: Each cerebral hemisphere is subdivided into five lobes: the frontal, parietal, temporal, and occipital lobes, and the insula. Additionally, the cortical constituents of the limbic system are also considered to be a region of the cerebral hemisphere and some consider it to be the sixth lobe, the limbic lobe. Viewed from the side, each cerebral hemisphere resembles the shape of a boxing glove, where the thumb is the temporal lobe and is separated from the parietal lobe by the lateral fissure (fissure of Sylvius) .The floor of the lateral fissure is formed by the insula (island of Reil) that is hidden by the frontal, parietal, and temporal opercula regions of the same named lobes. Although the geographic distributions of many of the sulci and gyri are relatively inconsistent, some regularly occupy specific locations, are recognizable in most brains, and are named. The sulci are generally smaller and shallower than

the fissures, and one of these, the central sulcus (central sulcus of Rolando), separates the frontal lobe from the parietal lobe. The division between the parietal and occipital lobes is not readily evident when viewed from the lateral aspect because it is defined as the imaginary line between the preoccipital notch and the parieto-occipital notch. However, it is clearly delimited on the medial aspect of the cerebral hemisphere, where the boundary between these two structures is the parieto-occipital sulcus and its continuation, the calcarine fissure. (Maria et al, 2006)

Frontal lobe: The frontal lobe extends from the frontal pole to the central sulcus on its lateral aspect, the frontal lobe extends from the frontal pole to the central sulcus, constituting the anterior one-third of the cerebral cortex. Its posteriormost gyrus, the precentral gyrus, consists of the primary motor area and is bordered anteriorly by the precentral sulcus and posteriorly by the central sulcus. The region of the frontal lobe located anterior to the precentral sulcus is subdivided into the superior, middle, and inferior frontal gyri. This subdivision is due to the presence, though inconsistent, of two longitudinally disposed sulci, the superior and inferior frontal sulci. The inferior frontal gyrus is demarcated by extensions of the lateral fissure into three subregions: the pars triangularis, pars opercularis, and pars orbitalis. In the dominant hemisphere, a region of the inferior frontal gyrus is known as Broca's area, which functions in the production of speech. (Maria et al, 2006)

On its inferior aspect, the frontal lobe presents the longitudinally disposed olfactory sulcus. Medial to this sulcus is the gyrus rectus (also known as the straight gyrus), and lateral to it are the orbital gyri. The olfactory sulcus is partly occupied by the olfactory bulb and olfactory tract. At its posterior extent, the olfactory tract bifurcates to form the lateral and medial olfactory striae. The intervening area between the two striae is triangular in shape and is known as the olfactory trigone and it abuts the anterior perforated substance. On its medial aspect, the frontal

lobe is bordered by the arched cingulate sulcus, which forms the boundary of the superior aspect of the cingulate gyrus. The quadrangular-shaped cortical tissue anterior to the central sulcus is a continuation of the precentral gyrus and is known as the anterior paracentral lobule. (Maria et al, 2006)

Parietal lobe: The parietal lobe is interposed between the frontal and occipital lobes and is situated above the temporal lobe. On its lateral aspect, its anteriormost gyrus, the postcentral gyrus, is the primary somesthetic area to which primary somatosensory information is channeled from the contralateral half of the body. The remainder of the parietal lobe, separated from the postcentral gyrus by the postcentral sulcus, is subdivided by the inconsistent intraparietal sulcus, into the superior and inferior parietal lobules. The former is an association area involved in somatosensory function, whereas the latter isseparated into the supramarginal gyrus, which integrates auditory, visual, and somatosensory information, and the angular gyrus, which receives visual input. On its medial aspect, the parietal lobe is separated from the occipital lobe by the parieto occipital sulcus and its inferior continuation, the calcarine fissure. This region of the parietal lobe is subdivided into two major structures, the anteriorly positioned posterior paracentral lobule (a continuation of the postcentral gyrus) and the posteriorly situated precuneus. (Maria et al, 2006).

Temporal lobe*:* The temporal lobe, the "thumb of the boxing glove," is situated inferiorly to the lateral fissure and anterior to the parieto-occipital sulcus. The temporal lobe is separated from the frontal and parietal lobes by the lateral fissure and from the occipital lobe by an imaginary plane that passes through the parieto-occipital sulcus. The anteriormost aspect of the temporal lobe is known as the temporal pole. On its lateral aspect, the temporallobe exhibits three parallel gyri, the superior, middle, and inferior temporal gyri, separated from each other by the inconsistently

present superior and middle temporal sulci. The superior temporal gyrus of the dominant hemisphere contains Wernicke's area, which is responsible for the individual's ability to speak and understand the spoken andwritten word. Hidden within the lateral fissure is the superior aspect of the temporal lobe whose surface is marked by the obliquely running transverse temporal gyri (of Heschl), the primary auditory cortex. The inferior aspect of the temporal lobe is grooved by the inferior temporal sulcus that is interposed between the inferior temporal gyrus and the lateral occipitotemporal gyrus (fusiform gyrus). The collateral sulcus separates the fusiform gyrus from the parahippocampal gyrus of the limbic lobe. (Maria et al, 2006)

Occipital lobe: The occipital lobe extends from the occipital pole to the parieto-occipital sulcus. On its lateral aspect, the occipital lobe presents the superior and inferior occipital gyri, separated from each other by the horizontally running lateral occipital sulcus On its medial aspect, the occipital lobe is subdivided into the superiorly located cuneate gyrus (cuneus) and the inferiorly positioned lingual gyrus, separated from each other by the calcarine fissure. The cortical tissue on each bank of this fissure is known collectively as the striate cortex (calcarinecortex), and forms the primary visual cortex. (Maria et al, 2006).

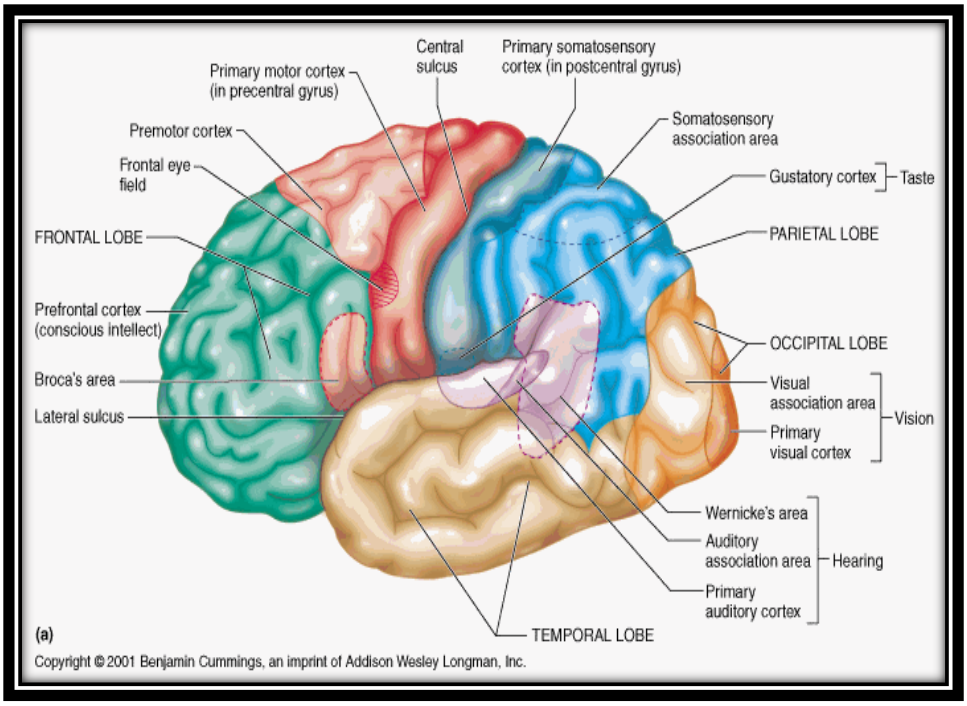


Figure (2-4) lobe of cerebral hemispheres (http://legacy.owensboro.kctcs.edu)

Insula: The insula forms the floor of the lateral sulcus .In order to view the insula the frontal, temporal, and parietal opercula have to be pulled apart, since this lobe is submergedwithin and forms the floor of the lateral sulcus. It is completely circumscribed by the circular sulcus. The lateral surface of the insula is subdivided into several short and longgyri, the most prominent of which is located posteriorly. The insula is believed to be associated with taste, and perhaps other visceral functions. (Maria et al, 2006).

Limbic lobe: The limbic lobe is a complex region and includes the cingulate gyrus, para-hippocampalgyrus, hippocampal formation, subcallosal gyrus, parolfactory gyrus, and the preterminal gyrus. The following description is a view of the medial aspectof the hemisected brain and the various regions of the corpus callosum are obvious landmarks. Therefore, the corpus callosum will now be described, even though it is not a part of the limbic lobe. The anterior extent of the corpus callosum, known as the genu, bends inferiorly and turns posteriorly, where it forms a slender connection, the rostrum, with the anterior commissure. The posterior

extent of the corpus callosum is bulbous in shape, and is known as the splenium. The cingulate gyrus is located above the corpus callosum and is separated from it by the callossal sulcus. As the cingulate gyrus continues posteriorly, it follows the curvature of the corpus callosum and dips beneath the splenium to continue anteriorly as the isthmus of the cingulate gyrus. The anterior continuation of the isthmus is the parahippocampal gyrus whose anteriormost extent is known as the uncus. Above the parahippocampal gyrus is the hippocampal sulcus, which separates the parahippocampal gyrus from the hippocampal formation (composed of the hippocampus, subiculum, and dentate gyrus). Just beneath the rostrum of the corpus callosum is thesubcallosal gyrus. The connection between the anterior commissure and the optic chiasma is the lamina terminalis and the cortical tissue anterior to the lamina terminalis is the parolfactory gyrus and preterminal gyrus. The subcallosal, parolfactory, and preterminal gyri are referred to as the subcallosal area. (Maria et al, 2006).

White matter of the cerebral hemispheres: The central core of white matter that forms the substance of the cerebrum is composed of myelinated nerve fibers of varied sizes and their supporting neuroglia.

Fibers: These fibers may be classified into the following three categories: commissural, projection, and association fibers.

Commissural fibers: Commissural fibers are bundles of axons that connect the right and left cerebral hemispheres .it interconnect the right and left cerebral hemispheres. There are four bundles of commissural fibers, the corpus callosum, anterior commissure, posterior commissure, and hippocampal commissure (see Fig. 2.5). The largest group of the commissural fibers, the corpus callosum, is comprised of four regions: the anteriormostrostrum, the curved genu, the relatively flattened body, and its posteriormost region, the splenium. The corpus callosum

connects the neocortex of the right hemisphere with that of the left. The anterior commissure connects the right and left amygdalas, the olfactory bulbs, and several cortical regions of the two temporal lobes. The posterior commissure connects the right and left pretectal region and related cell groups of the mesencephalon. The hippocampal commissure (commissure of the fornix) joins the right and left hippocampi to one another. (Maria et al, 2006).

Projection fibers: Projection fibers are restricted to a single hemisphere and connect the cerebral hemispheres with lower levels Projection fibers are restricted to a single hemisphere and connect the cerebral cortex with lower levels, namely the corpus striatum, diencephalon, brainstem, and spinal cord. The majority of these fibers are axons of pyramidal cells andfusiform neurons. These fibers are component parts of the internal capsule, which is subdivided into the anterior limb, genu, posterior limb, retrolentiform, and sublentiformregions. The projection fibers may be subdivided into corticopetal and corticofugal fibers. Corticopetal fibers are afferent fibers that bring information from the thalamus to the cerebral cortex. They consist of thalamo-cortical fibers. Corticofugal fibers are efferent fibers that transmit information from the cerebral cortex to lower centers of the brain andspinal cord. They consist of the corticobulbar, corticopontine, corticospinal, and corticothalamic fibers. (Maria et al, 2006).

Association fibers: Association fibers connect regions of a hemisphere to other regions of the same hemisphere it also known as arcuate fibers, are restricted to a single hemisphere and are subdivided into two major categories, short arcuate fibers and long arcuate fibers They are the axons of pyramidal cells and fusiform neurons. Short arcuate fibers, which connect adjacent gyri, do not usually reach the subcortical white matter of the cerebral cortex; most of them are confined to the cortical gray matter. The long arcuate fibers, which connect nonadjacent gyri,

consist of the following fiber tracts (the uncinate fasciculus, cingulum, superior longitudinal fasciculus, inferior longitudinal fasciculus, and fronto-occipital fasciculus. .(Maria et al, 2006).

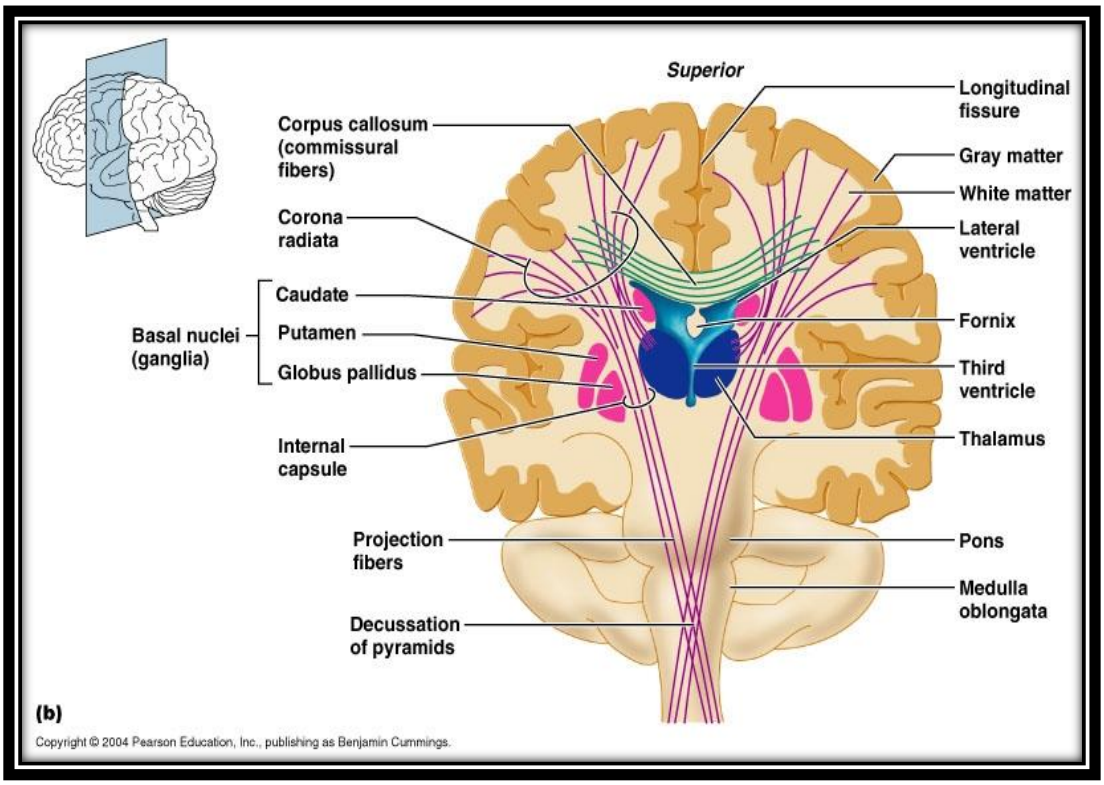


Figure 2.5 types of fibers (http://apbrwww5.apsu.edu)

Basal ganglia: The basal ganglia, called ganglia even though they are nuclei, are large collections of cell bodies that are embedded deep in the white matter of the brain (Fig. 2.6). These soma include those deep nuclei of the brain and brainstem which, when damaged, produce movement disorders. Thus the basal ganglia are composed of the caudate nucleus, lenticular nucleus (putamen and globus pallidus), subthalamic nucleus of the ventral thalamus, and the substantia nigra of the mesencephalon (the caudatenucleus and the putamen together are referred to as the striatum). These nuclei have numerous connections with various regions of the CNS; some receive input and are categorized as input nuclei, some project to other regions and are

referred to as output nuclei, whereas some receive input, project to other regions of the CNS, and have local interconnections and these are known as intrinsic nuclei. (Maria et al, 2006).

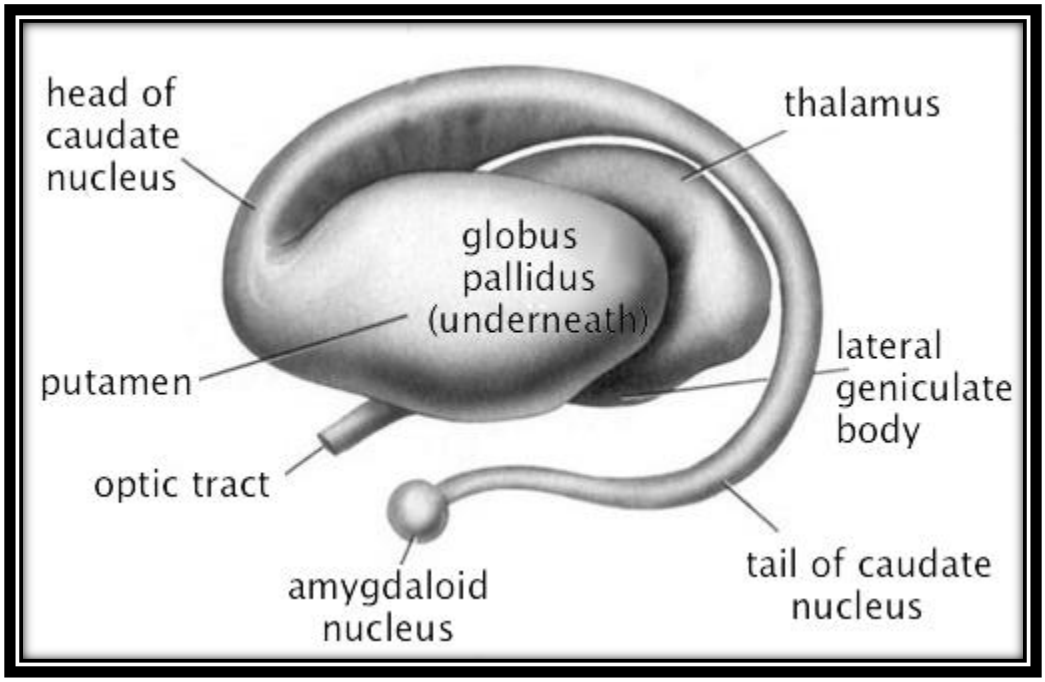


Figure (2-6) basal ganglia (http://webspace.ship.edu)

Diencephalon: The diencephalon, interposed between the cerebrum and the midbrain, has four regions: the epithalamus, thalamus, hypothalamus, and subthalamus. The right and left halves of the diencephalon are separated from one another by a narrow slit-like space, the ependymal-lined third ventricle. Rostrally, the interventricular foramina (of Monro) leads from the lateral ventricles into the third ventricle, whereas caudally, the third ventricle is connected to the fourth ventricle by the cerebral aqueduct (of Sylvius). The epithalamus, composed of the pineal body, stria medullaris, and habenular trigone, constitutes the dorsal surface of the diencephalon. The right and left thalami compose the bulk of the diencephalon and form the superior aspect of the lateral walls of the third ventricle. The two thalami, structures composed of numerous nuclei, are connected to each other by a bridge of gray matter, the interthalamic adhesion (massa

intermedia). Some of the nuclei of the thalamus form distinctive bulges on its surface, namely the pulvinar and the medial and lateral geniculate bodies. The boundary between the thalamus and the hypothalamus is marked by a groove, the hypothalamicsulcus, located along the lateral walls of the third ventricle. Structures associated with the hypothalamus are the pituitary gland and its infundibulum, the tuber cinereum, andthe two mammillary bodies. The hypothalamic nuclei and fiber tract form the hypothalamus. (Maria et al, 2006).

Cerebellum: The cerebellum is located in the posterior aspect of the brain, just below the occipital lobes of the cerebrum (Figs 2.7). It is separated from the cerebrum via a horizontal dural reflection, the tentorium cerebelli. The cerebellum is connected to the midbrain, pons, and medulla of the brainstem via three pairs of fiber bundles, the superior, middle, and inferior cerebellar peduncles, respectively. Viewing the cerebellum, it can be seen that it is composed of the right and left cerebellar hemispheres and the narrow, intervening vermis. The vermis is also subdivided into a superior and an inferior portion, where the superior portion is visible between the two hemispheres, while its inferiorportion is buried between the two hemispheres. The surface of the cerebellum has horizontal elevations, known as folia, and indentations between the folia, known assulci. Some of these sulci are deeper than others and they are said to subdivide each hemisphere into three lobes, the small anterior lobe, the much larger posterior lobe, and the inferiorly positioned flocculonodular lobe (formed from the nodule of the vermis and the flocculus of each cerebellar hemisphere). The anterior lobe is separated from the posterior lobe by the primary fissure, and the postero-lateral fissure separates the flocculonodular lobe from the posterior lobe. Similar to the cerebrum, the cerebellum has an outer rim of gray matter, the cortex, and an inner core of nerve fibers, the medullary white matter, and the deep cerebellar nuclei, located within the white matter. The cortex and white matter are easily distinguished from

each other in a midsagittal section of the cerebellum, where the white matter arborizes, forming the core of what appears to be a tree-like architecture, known as the arbor vitae. (Maria et al, 2006).

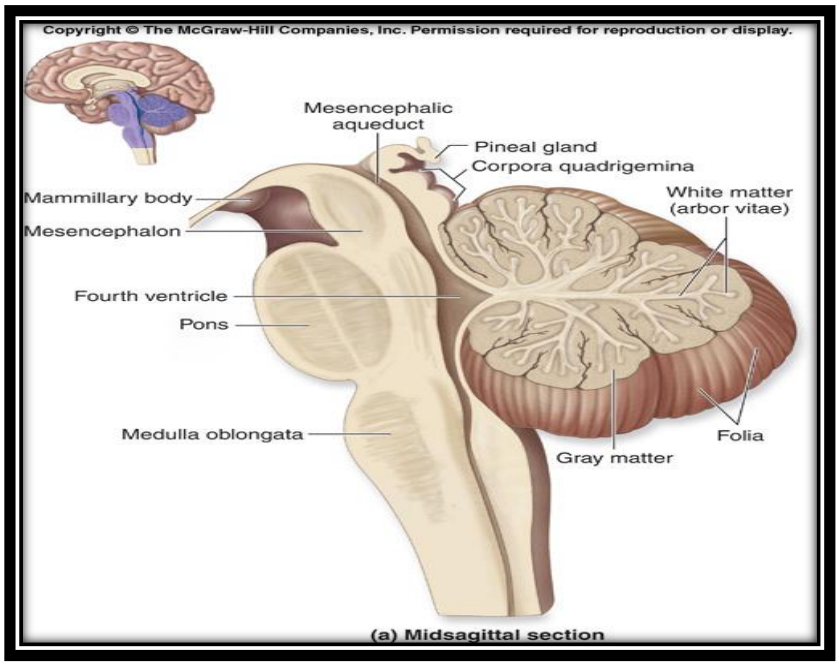


Figure (2-7) midsagittal section of the cerebellum (http://academic.kellogg.edu/)

Brainstem: The brainstem, the oldest part of the CNS, is composed of the mesencephalon, metencephalon, and myelencephalon (although some authors also include the diencephalon) (Figs 2.8). Since these are embryologic terms, one may also state that the brainstem is composed of the mesencephalon, pons, cerebellum, and medulla oblongata. As parts of it have been overgrown by the cerebrum and the cerebellum, its dorsal aspect is mostly hidden from view in the whole brain, whereas its ventral and lateral aspects are visible. Removal of the cerebral and cerebellar hemispheresexposes the brainstem in its entirety and it is usually examined in that fashion as well as by hemisecting the entire brain. (Maria et al, 2006).

Mesencephalon: The mesencephalon (midbrain) is a relatively narrow band of the brainstem surrounding the cerebral aqueduct, extending from the diencephalon to the pons. The dorsal aspect of the midbrain is known as the tectum and incorporates the paired superior and inferior colliculi (also known as the corpora quadrigemina). The sestructures are associated with the lateral and medial geniculate bodies, respectively, and they are all associated with visual and auditory functions. The trochlear nerve (CN IV) exits the dorsal aspect of the mesencephalon just below the inferior colliculus. All other cranial nerves exit the ventral aspect of the brainstem. The region of the mesencephalon below the cerebral aqueduct is known as the midbrain (mesencephalic) tegmentum. The cerebral hemispheres are connected to the brainstem by two large fiber tracts, the cerebral peduncles, and the depression between the peduncles is known as the interpeduncular fossa, the site of origin of the oculomotor nerve (CN III). (Maria et al, 2006).

Metencephalon*:* The cerebellum overlies and hides the dorsal aspect of the brainstem, but its ventral aspect, the pons, is clearly evident. Rostrally, the superior pontine sulcus acts as theboundary between the metencephalon and the midbrain and the inferior pontine sulcus as the boundary between the metencephalon and the myelencephalon. Part of the floor ofthe fourth ventricle is formed by the dorsal aspect of the pons, and is known as the pontine tegmentum, the structure that houses the nuclei of the trigeminal, abducent, facial, and vestibulocochlear nerves. Cranial nerves VI, VII, and VIII leave the brainstem at the inferior pontine sulcus, whereas the trigeminal nerve exits the brainstem through the middle cerebellar peduncle. (Maria et al, 2006).

Myelencephalon: The caudal-most portion of the brainstem, the myelencephalon, also known as the medulla oblongata, extends from the inferior pontine sulcus to the spinal cord. The boundary between them is the region where the lateral walls of the fourth ventricle converge in a V shape at the midline obex (at the level of the foramen magnum). The ventral surface of the

myelencephalon displays the anterior midline fissure, bordered on each side by the pyramids and crossed by the pyramidal decussations, connecting the right and left pyramids to each other. The olives are olivepit-shaped swellings lateral to each pyramid. (Maria et al, 2006).

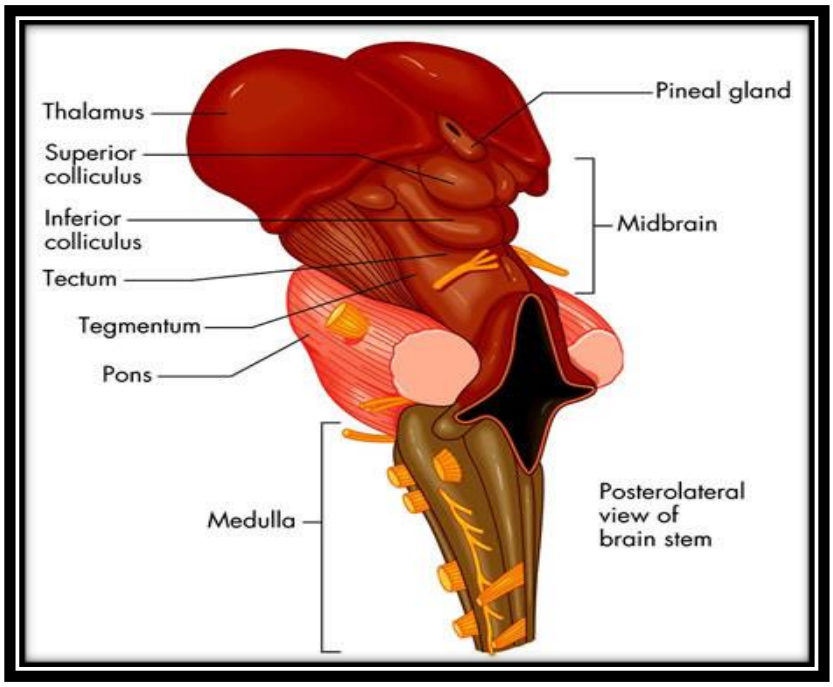


Figure (2-8) Brainstem (http://fultoncountybraininjurysupportgroup.health.officelive.com/)

Blood supply of the Brain*:* Normal function of the brain's control centers is dependent upon adequate supply of oxygen and nutrients through a dense network of blood vessels. Blood is supplied to the brain, face, and scalp via two major sets of vessels: the right and left common carotid arteries and the right and left vertebral arteries. The common carotid arteries have two divisions. The external carotid arteries supply the face and scalp with blood. The internal carotid arteries supply blood to the anterior three-fifths of cerebrum, except for parts of the temporal and occipital lobes. The vertebra-basilar arteries supply the posterior two-fifths of the cerebrum, part of the cerebellum, and the brain stem. Any decrease in the flow of blood through one of the internal carotid arteries brings about some impairment in the function of the frontal lobes. This impairment may result in numbness, weakness, or paralysis on the side of the body opposite to

the obstruction of the artery. Occlusion of one of the vertebral arteries can cause many serious consequences, ranging from blindness to paralysis. (Richards 1987).

Circle of Willis: At the base of the brain, the carotid and vertebrobasilar arteries form a circle of communicating arteries known as the circle of Willis. From this circle other arteries – the anterior cerebral artery (ACA), the middle cerebral artery (MCA), the posterior cerebral artery (PCA) – arise and travel to all parts of the brain (Fig. 2.9). Posterior Inferior Cerebellar Arteries (PICA), which branch from the vertebral arteries, are not shown. Because the carotid and vertebrobasilar arteries from a circle, if one of the mine arteries is occluded, the distal smaller arteries that it supplies can receive blood from the other arteries (collateral circulation). (Krabble, 1994).

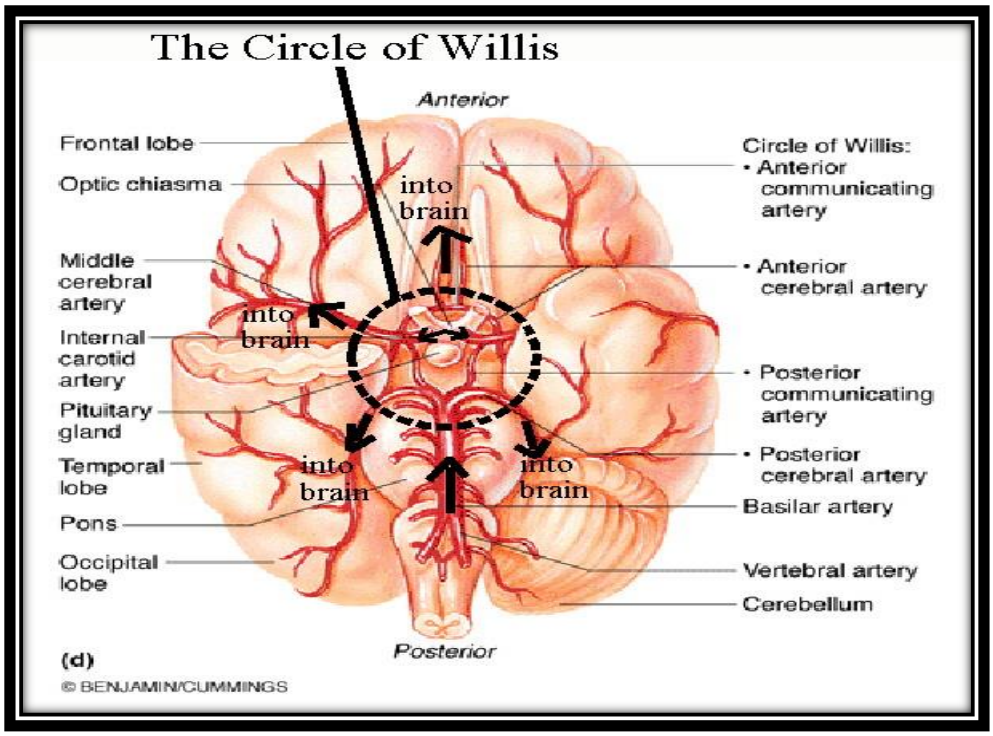


Figure (2-9) Circle of Willis (http://yazoqem.hostoi.com/blood-flow-to-the-brain.php)

Cranial nerves: The brain communicates with the body through the spinal cord and twelve pairs of cranial nerves (Fig. 2.10). Ten of the twelve pairs of cranial nerves that control hearing, eye movement, facial sensations, taste, swallowing and movement of the face, neck, shoulder and tongue muscles originate in the brainstem. The cranial nerves for smell and vision originate in the cerebrum.

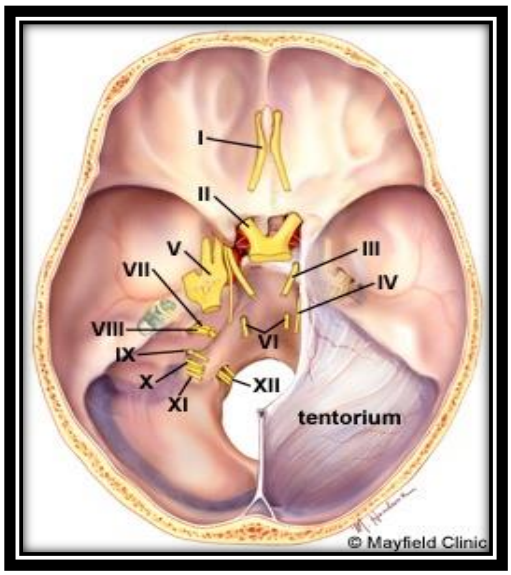


Figure (2-10) The Roman numeral, name, and main function of the twelve cranial nerves.

Table 2.1 The Roman numeral, name, and main function of the twelve cranial nerves.

Number	Name	Function
I	Olfactory	smell
II	Optic	sight
III	oculomotor	moves eye, pupil
IV	trochlear	moves eye
V	trigeminal	face sensation
VI	abducens	moves eye
VII	Facial	moves face, salivate
VIII	vestibulocochlear	hearing, balance
IX	glossopharyngeal	taste, swallow
X	Vagus	heart rate, digestion
XI	accessory	moves head
XII	hypoglossal	moves tongue

2-1-2 Physiology of the Brain

Frontal Lobes: The frontal lobes are considered our emotional control center and home to our personality. There is no other part of the brain where lesions can cause such a wide variety of symptoms (Kolb & Wishaw, 1990). The frontal lobes are involved in motor function, problem solving, spontaneity, memory, language initiation, judgment, impulse control, and social and sexual behavior. The frontal lobes are extremely vulnerable to injury due to their location at the front of the cranium, proximity to the sphenoid wing and their large size. MRI studies have shown that the frontal area is the most common region of injury following mild to moderate traumatic brain injury (Levin et al., 1987).

Functions: Consciousness, Initiation of activity in response to our environment. Judgments what occurs in activities, Controls emotional response. , Controls expressive language, Assigns meaning to the words we choose, Involves word association, Memory for habits and motor activities.

Parietal Lobes: The parietal lobes can be divided into two functional regions, one involves sensation and perception and the other is concerned with integrating sensory input, primarily with the visual system. The first function integrates sensory information to form a single perception (cognition). The second function constructs a spatial coordinate system to represent the world around us. Individuals with damage to the parietal lobes often show striking deficits, such as abnormalities in body image and spatial relations The main Functions are ;Location for visual attention, Location for touch perception, Goal directed voluntary movements, Manipulation of objects, Integration of different senses that allows for understanding a single. (Kandel et al., 1991).

Temporal Lobes: Kolb & Wishaw (1990) have identified eight principle symptoms of temporal lobe damage: disturbed of auditory sensation and perception, disturbance of selective attention of auditory and visual input, disorders of visual perception, impaired organization and categorization of verbal material, disturbance of language comprehension, impaired long-term memory, altered personality and affective behavior, altered sexual behavior. The main Functions are Hearing ability, Memory acquisition, some visual perceptions, Categorization of objects. (Kandel et al., 1991).

Occipital Lobes: The occipital lobes are the center of our visual perception system. They are not particularly vulnerable to injury because of their location at the back of the brain, although any significant trauma to the brain could produce subtle changes to our visual perceptual system, such as visual field defects and scotomas. The main Function is theVision. (Kandel, et al., 1991).

Cerebellum: The cerebellum is involved in the coordination of voluntary motor movement, balance and equilibrium and muscle tone. It is located just above the brain stem and toward the back of the brain. It is relatively well protected from trauma compared to the frontal and

temporal lobes and brain step. The main Functions are Coordination of voluntary movement, Balance and equilibrium, some memory for reflex motor acts.

Brain steam: The brain stem plays a vital role in basic attention, arousal, and consciousness. All information to the from our body passes through the brain stem on the way to or from the brain. Like the frontal and temporal lobes, the brain stem is located in an area near bony protrusions making it vulnerable to damage during trauma. The main Functions are Breathing, Heart Rate, Swallowing, and Reflexes to seeing and hearing (Startle Response), Controls sweating, blood pressure, digestion, temperature (Autonomic Nervous System), Affects level of alertness, Ability to sleep, Sense of balance (Vestibular Function). (Kandel, Schwartz & Jessel, 1991).

2.1.3 Pathology of the brain

Brain Hemorrhage: Brain Hemorrhage is a more serious type of brain attack and accounts for 20% of the cases of strokes occurring due to the faults in blood vessels. The remaining occur due tothromboembolism. This is a serious disease of the brain in which there is bleeding in the brain either due to the rupture of a blood vessel or some other reason. Most of the patientsbecome unconscious in minutes and if timely treatment is not given, it proves fatal for many patients.Brain hemorrhage can be classified into two groups:

Intra Cerebral Hemorrhage: Rupture of blood vessels deep inside the brain due to high blood pressure is called intracerebral hemorrhage. This hemorrhage occurs at some particular locations in the brain (like Putamen, Thalamus, and Cerebellum) and usually while examining the patient; the physician can easily identify the location, by its specific signs and symptoms. Amyloid Angiopathy is a kind of cerebral hemorrhage occurring mostly in elderly people and it can recur frequently. If all these hemorrhages are diagnosed quickly and immediate treatment is initiated to reduce the edema of the brain and control of blood pressure, the death rate in the cases of

cerebral hemorrhage can be brought down considerably. At present the death rate is as high as 50% to 60%. In some cases of cerebellar hemorrhage, e.g. temporal lobe hemorrhage or putaminal hemorrhage, lives can be saved by surgery done by a neurosurgeon. (Sudhir et al, 2008)

Symptoms of brain hemorrhage: Sudden headache, vomiting, vertigo, blackouts (these can be due to high blood pressure also), seizures, stumbling, paralysis, and loss of consciousness within a few minuteswith rapid breathing; are the usual symptoms of brain hemorrhage.

Diagnosis of brain hemorrhage; It is essential to get an immediate diagnosis with a CT scan or MRI scan. These tests can also identify the location of the hemorrhage, the size of the clot, edema of the brain and the cause of the same. It is better to get a CT scan done even before admission, if the facility is available in the city or town, provided the patient is stable with normal respiration and B.P. This is for confirmation of the hemorrhage. Even if clinically, a hemorrhage is suspected, the scan sometimes may reveal a thrombosis, tumor, subdural or cerebral infection' and that would make a major difference in the line of treatment.

Subarachnoid Hemorrhage: This type of hemorrhage is completely different from the one discussed before. Most of these patients do not suffer from high blood pressure. Many of them are young and in most of them there is a congenital weakness in the blood vessels causing ballooning of the blood vessel (Saccular aneurysm) or entanglement of the vessels (AV. Malformation). These which rupture at a particular age due to sudden exertion or unknown causes, with oozing of blood into the subarachnoid spaces between the membranes of the brain. This is known as the subarachnoid hemorrhage. (Sudhir et al, 2008)

The main symptoms of this disease: Subarachnoid hemorrhage are that the patient experiences a never-before kind of severe headache, sometimes accompanied by a seizure and he might even

become unconscious momentarily due to the edema in the brain. Usually the patient regains consciousness in a short while, but may again start losing consciousness after some time, suffer from paralysis and there may be irregularities in the vital functions like espiration, blood pressure or heart. Many such patients die immediately or within 14 to 30 days. Therefore, if the patient feels that he/she has never experienced such a splitting headache before along with other signs and symptoms, it is all the more important for the patient to see a neurologist so that timely treatment may save his / her life. (Sudhir et al, 2008)

Investigation of Blood Vessels of the Brain: Angiography is the most important test. MR Angiography makes the use of the MRI magnet for the examination of the blood vessels In this test no catheter is required to be introduced in the blood vessels. Therefore, it is called a Non Invasive test. For coronary angiography, a catheter has to be introduced in a blood vessel and therefore there is a slight risk involved, which is not the case in a MR Angiography. This test can give an accuracy of only 90 to 95% and therefore, can be used only as a screening test. The gold standard tests are the conventional 4 vessel angiography or Digital Substraction Angiography (DSA). An aneurysm is immediately detected on angiography. In 15% cases more than one aneurysm can be present and so it is imperative that the angiography is done on all the four blood vessels of the brain, so that if surgery becomes necessary it can be planned keeping all the aneurysms in mind. The angiography can also detect another vascular condition, i: e the entanglement of blood vessels known as arteriovenous malformation (AV. Malformation). These patients have a history of severe headache; with an occasional seizure, and some of them may already be suffering from the paralysis of a limb. In some cases of sub-arachnoid hemorrhage DSA angiography may show normal results. Out of these cases a few may have a very small aneurysm or a cryptic AN. malformation or a vasospasm, which may not be detected on

angiography. Therefore in such cases angiography is repeated after 3 months. Only then it can be confirmed that these are not the causes of hemorrhage. This kind of hemorrhage is termed as Idiopathic Sub-arachnoid Hemorrhage. (Sudhir. et al, 2008)

Multiple Sclerosis: The diseases of the brain and spinal cord in which myelin sheath or white matter is affected are known as demyelinating diseases. The cells of the human nervous system are anatomically and physiologically divided into grey matter and white matter. The white matter can be compared to the electrical wires that perform the important function of transporting the sensations or commands originating from gray matter cells to other parts of the nervous system. The electrical wires have an outer cover for insulation. Similarly, the white matter has a myelin sheath for insulation. The diseases damaging the myelin coating of the white matter are known as demyelinating diseases. The most important, strange and painful demyelinating disease is called multiple sclerosis. In simple language some type of allergy or disturbance in metabolism of brain, damages the white matter. This is called as demyelination and gliosis. In this disease specific symptoms are seen in the brain, spinal cord and mainly the sensory nerves of the eyes. This disease is twice more common in females than in males. l It is generally seen in age group of 15 to 50 years. Generally it is not found in children and elderly people. The causes of this disease are also awkward and still not properly understood. In a few cases it seems to be hereditary, but in other cases the reasons may not be hereditary. This disease may occur due to some virus, environmental factors or irregularities in lifestyle and food habits. (Sudhir et al , 2008)

Symptoms of multiple sclerosis: Paralysis of one or more parts of the body: in 35% cases, Loss of vision or diplopia: in 36% cases, Loss of sensation in some parts of the body (in 37% cases) or abnormal sensations like pricking of needles (in 26% cases) ,Loss of balance, vertigo, problems

of bowel and bladder movements, Loss of memory and seizures and Tremors of limbs, pain, and problems in sexual life, mental disorders ranging from insanity to depression may be seen. Multiple sclerosis may start with one or more of the above symptoms and it may either be cured completely, recover and recur again (relapsing variety) or gradually go on increasing in intensity after a mild beginning (chronic progressive variety) or l Initially relapsing disease may become permanent after a few years. (Sudhir et al, 2008)

Diagnosis of multiple sclerosis:It is important to contact a physician/neurologist immediately, if the patient is suffering from above mentioned symptoms, especially the ones related to eyesight, paralysis or equilibrium. Diagnosis mainly requires some specific blood tests and Magnetic Resonance Imaging (MRI). Besides this C.S.F. (lumbar puncture) examination is also important. The C.S.F. test shows increase in cell count, increase in protein levels, specifically gamma globulin. Oligoclonal band (1gG) is seen with increase in the myelin basic protein level. V.E.P, S.S.E.P, B.E.R.A tests are helpful in confirmation of diagnosis. Thus, physical examination and above-mentioned tests can help in accurate diagnosis. (Sudhir et al., 2008).

Brain tumours: Brain tumor is an extremely serious neurological disease and it is very important to know about it. There are various types of brain tumors. They cause various common and specific symptoms depending on their size, type, location, properties and histology. Some tumors destroy the brain and some increase the pressure on the brain. Tumors are one ofthe main reasons of raised intracranial pressure. Improvement in the surgical techniques and anesthesia, developments in stereo tactic and the micro neurological techniques, remarkable advances in radiation as well as chemotherapy have brightened the future of patients of brain tumors. Brain tumor is a wellknown disease and in a highly developed country like USA approximately 1 lakh people die per year due to it, so the plight of our country is unimaginable. Out of these many, are

cases of cancer –that originate in the brain (primary) like glioma or spread from other parts of the body to the brain. (Secondary). Rest of the tumors are relatively benign like meningioma, pituitary tumor etc. Tumors occurring due to infectious diseases like tuberculoma, abscess, cysticercosis, AIDS etc. also need to be mentioned, though they have different symptoms, diagnosis and treatments. (Sudhir et al, 2008)

Symptoms of brain tumors: The symptoms of brain tumors worsen gradually, depending upon the quality, location, size, and type of tumor as well as the severity of the accompanying edema.

Increased Intracranial pressure: Increase in the size of the tumor increases the pressure inside the skull (a fixed vault) as well as on the brain, causing symptoms like headache on both sides, nausea-vomiting, blackouts, uneasiness and diplopia. All cases of headache do not indicate brain tumor, only in 1 % of the cases, the cause of headache is brain tumor. But if a healthy individual starts experiencing headaches of increasing intensity, it is essential to get examined by a specialist. The symptoms of brain tumor depend upon the location of the tumor. Therefore there can be a gradual increase of paralysis, speech loss, memory loss or lack of bodyco-ordination. In some patients there is only a behavioural or a personality change, or loss of bowel or bladder control, Seizures or unconsciousness can also be an important symptom especially if it is accompanied by headache or paralysis; if so immediate investigations are necessary and Sometimes a je,prrjage in the tumor can create an emergency situation for the patient. Usually, only if there is more than one of the above symptoms, the possibility -of a brain tumor in the patient is high. (Sudhir et al, 2008)

Diagnosis of brain tumors: In most of the cases the following investigations are done to confirm diagnosis of tumor. CT Scan Brain (with contrast): This is a complete investigation in itself, but if the tumor is small or is present at the posterior of the brain or the type of the tumor

cannot be confirmed on a CT Scan, MRI is required, MRI (Magnetic Resonance Imaging**)** can be done for confirmation and is in fact essential in some cases. For accurate diagnosis, sometimes angiography is also needed. If a person has a pace maker or a metal implant in the body MRI cannot be done and in such cases diagnosis has to be based only on CT scan. Some patients find it difficult to sleep in the MRI chamber for 20 to 30 minutes (claustrophobia). In this condition as well as in small children a sedative or low dose of anesthesia is given and the investigation is carried out and Lumbar puncture: Lumbar puncture is done for the investigation of the cerebrospinal fluid. But if the edema in the brain is high this investigation can be dangerous. Therefore in the cases of brain tumor, there is very little scope for this investigation. This investigation is very useful in the diagnosis of the infectious diseases of the brain like meningitis, encephalitis etc. (Sudhir et al, 2008).

Types of brain tumors: As mentioned earlier, there are two types of brain tumors, cancerous and the benign (non-cancerous). The brain tumor in the upper part of the brain is called supratentorial. The tumor in the posterior or inferior part of the brain is called infratentorial. These two kinds of cancerous and benign tumors also occur in the spinal cord. Some cancerous tumors grow very rapidly and are serious, in which the patient's lite span is only six months to 3 years e.g. malignant glioma (Anaplastic glioma, glioblastoma multifor-me etc....), whereas some cancerous tumors spread slowly like Astrocytoma, Oligodendroglioma etc.

Apart from this there are tumors of lymphoma kind in the brain, which are found mostly in the patients suffering from AIDS. The main benign tumors are meningioma, schwannoma and the tumors of the pituitary glands. If these are diagnosed in early stages and operated upon by a capable surgeon thelife of the patient can be saved. Not only this, the patient can lead a near normal life, apart from some minor problems and weakness At the most he may have to take

drugs for prevention of seizures for the rest of his life. If the cancer spreads from any other part of the body to the brain, it is known as metastatic tumor. Sometimes it so happens, that the symptoms of brain tumor may point out the presence of cancer in some other part of the body, but it is too late by then. Locating the primary cancer and treating it may increase the life span of the patient. (Sudhir et al., 2008)

Tuberculosis of the Brain: Usually, tuberculosis infection of the brain comes from other parts of the body like lungs or stomach. There is a possibility that the tuberculosis in the chest may be there for a long time, but a decrease in the immunity of the body due to any cause may result in TB of the brain. This disease is so common in our country that the TB organism is present in the bodies of most of the people, having entered through milk or air and its immunity is already there in the body. When the immunity of the body is compromised due to any reason, .and the body becomes weak, active disease develops. A patient of AID Scan get infected with innumerable organisms causing variety of diseases in which TB organisms are the main germs. Tuberculosis infection in the membranes of the brain is called TB Meningitis and the TB tumor in brain is called as Tuberculoma. The infection of the cortex of the brain is called Encephalitis (Encephalopathy). Headache, low-grade fever, vomiting, loss of appetite, excessive weakness or anxiety are the initial symptoms of this disease. Gradually, seizures, paralysis of one or more limbs can occur and in advanced stage, coma due to the edema of the brain and even death may occur. If there is an obstruction in any small or big blood vessel of the brain due to TB, it is known as TB arteritis. TB can also cause paralysis. If the pathways of the C.S.F are obstructed, the result is hydrocephalus, in which the cerebral ventricles dilate leading to unconsciousness or loss of eyesight. A tubercular infection in the spinal cord or vertebra may lead to paralysis of the lower limbs. (Sudhir et al, 2008)

Diagnosis: In order to diagnose this disease, a detailed medical examination as well as blood tests are required. The CT Scan or/and M.R.I are useful. Lumbar Puncture is almost an essential test for the confirmatory diagnosis of the infectious diseases of the brain. In tubercular meningitis the examination of the C.S.F shows high protein levels, low sugar levels and high lymphocyte (a type of white blood cell) count. In some complicated cases, C.5.F.-P.C.R, C.S.F.-C.R.P, C.S.F-A.D.A tests are conducted for accurate diagnosis. This accuracy is necessary because once the diagnosis is confirmed the patient requires proper treatment for a minimum of one and a half years to two years. Initially, the C.S.F reports may sometimes present a picture of a viral or pyogenic infection and if there is a laxity in the treatment of any of the three infections due to lack of proper diagnosis, it could lead to dangerous consequences. Hence, proper investigations are very essential in these infectious diseases. Almost all the specialist physicians agree that the diagnosis should never be done with guesswork. But in situations where the edema in the brain is considerable, respiration is inadequate and the general condition of the patient is fragile, lumber puncture test can be dangerous and at such times the treatment should be immediately initiated on the basis of CT Scan, MRI and other supportive facts. Lumbar Puncture can be done later, when general condition permits. (Sudhir et al, 2008)

Stroke and paralysis: Stroke is the major cause of death after heart attack, cancer and road accidents. It is really sad and surprising that there is very little awareness among the general public regarding this disease. Like heart attack, knowledge of the risk factors can prevent the occurrence of the disease in majority of cases. If the warning signs are identified in time, immediate safety measures can be taken easily, so that in future any major stroke can be averted.

After a stroke it is essential that immediate diagnosis and correct treatment be given to prevent permanent disabilities. This will be beneficial socially, personally, financially, family wise and nationally. The high fat and sweet diet pattern, sedentary lifestyle, lack of exercise, excessive fat deposition on the abdominal area, hereditary (racial) causes, and excessive lipids in the blood Stroke means sudden paralysis of the right or left side of the body. During stroke, sometimes the ability of speech, comprehension and/or sight can also get affected. Due to the obstruction of some of the arteries of the brain, the blood circulation is affected leading to reduced nutrition and oxygen to brain cells, which hampers the normal working of these brain cells leading to a stroke. Some fortunate people get a transient paralytic attack, which is completely cured within 24 hours. In medical terminology this is known as TIA (Transient Ischemic Attack). In 30% of these kind of patients there is a possibility of getting a bigger stroke attack in next five years. Thus, this serves as a warning for such patients to take good care of themselves in order to avoid future strokes. The doctors evaluate the extent, type and location of the damage to the brain on the basis of the signs and the severity of the paralytic attack. If the left side of the brain is affected then the right side of the body is paralyzed, and usually speech is also affected. Similarly, if the right side of the brain is affected, the left side of the body gets paralyzed. The brain receives blood from four major arteries. The two arteries in the anterior portion of the neck are called the Carotid arteries and the arteries in the posterior part of the neck are called the vertebral arteries, which provide uninterrupted blood supply to the brain. The posterior arteries then merge to form the basilar artery, which is one of the most important arteries of our body. If there is a constriction or obstruction in the main artery supplying blood to the brain due to a clot, the circulation of blood in the brain is hampered. If the heart stops beating for some minutes, then the brain suffers damage. Sometimes thrombosis of blood in the veins can also cause paralysis. With advancing

age the inner lining of the damaged arteries thickens causing an obstruction or reduction in the blood flow. Such a condition is known as Arteriosclerosis. Thus cells of the brain can be damaged in two ways. Increase of lipids in the blood can cause thickening of blood and a local clot formed resulting in Thrombosis, or a clot from the heart or any other part of the body may travel to the arteries of the brain, obstructing blood supply to the brain. This is known as Embolism. In 20% of the cases rupture of a blood vessel due to high blood pressure or any other reason, causes paralysis. This condition is called Brain Hemorrhage. Symptoms similar to stroke can also occur in other diseases like infections of brain, brain tumor, lymphomas, multiple sclerosis, hysteria, head injuries etc...In these cases there may be paralysis of one or both sides. This paralysis is different from stroke and other associated symptoms can usually help in differential diagnosis. (Sudhir et al, 2008)

Risk factors responsible for occurrence of a stroke are as under: High blood pressure**,** Diabetes **,** High lipids (fats) in the blood, Obesity (excess weight) **,**Smoking, tobacco or alcohol abuse **,**Heart disease (IHD), diseases of the valve, irregular pulse (AF) **,** Previous stroke or T.I.A,Use of Contraceptive pills ,Hectic lifestyle, stress or sedentary life and lack of exercise ,Genetic causes ,Diseases of the blood that result in clotting or increased viscosity of the blood **,**Diseases like collagen disease, anticardiolipin syndrome **,**Metabolic diseases like Homocysteinuria, and Addiction to cocaine and other drugs.

Many of the above mentioned risk factors are common to heart disease and stroke. These factors can be effectively controlled by regular treatment and preventive measures. People beyond the age of 40, need regular medical examinations. If any of the family member has suffered from a heart disease or a stroke, it is necessary for the other members to take extra precautions. There are some of less-known but potential factors, which may cause a stroke. Presence of infectious

disease in the body, electrolyte imbalance (Sodium-Potassium), low hemoglobin levels, environment, hardness of water etc... maybe some of the reasons for stroke, but they are not yet accepted universally.

It should also be noted that 40% of the patients of stroke have no apparent and visible risk factors worth accounting for the stroke. (Sudhir et al, 2008)

The warning signals of an impending stroke (T.I.A.): Feeling of weakness in one side of the body; the limbs of the affected side may stop working or become numb, Momentary loss of vision in one or both the eyes, Confusion, difficulty in speech or comprehension. Far a short period of time and Vertigo, blurring of vision, diplopia, sudden headaches, nausea or vomiting, weakness in both the legs, stumbling, sudden momentary unconsciousness or falling down.

These symptoms prevail for certain period of time and if the symptoms are ignored and if no treatment is commenced, paralysis of a whole side ensues, with loss of speech and the patient may be unconscious. Ignoring these symptoms can prove fatal.

Diagnosis of stroke and paralysis: Paralysis is a disease of the brain and therefore it is necessary to get proper and timely treatment from an experienced Physician or a Neurophysician. In order to locate the lesion and the extent of damage these doctors conduct necessary Physical examinations and use related diagnostic tools like a CT scan or MRI for proper diagnosis and decision of the appropriate line of treatment. It is advisable to get a CT scan done in the initial few hours of a stroke, in order to find out whether the patient is suffering from a hemorrhage or thromboembolism. Hemorrhage can readily be detected in a CT scan very easily.

In the cases of thrombosis, CT scan is normal in the first few hours. Therefore, in cases of paralysis if the CT scan does not show a hemorrhage, then usually, immediate treatment for thrombosis is started. Another CT scan done after 24 to 36 hours, with a contrast dye confirms

thrombosis along with the extent of damage. With the help of this, one can predict the future of the patient. Sometimes there can be another disease with similar symptoms and a scan will diagnose the same, preventing a fatal mistake e.g. Tumor, abscess. (Sudhir et al, 2008)

In addition to this, hematological tests, biochemistry (sugar, tests related to kidney etc.), E.C.G. and other important tests are also done to assess the physical condition of the patient. Lipid profiles are done regularly. For the assessment of heart diseases 2D Echo test can also be done. As observed earlier the risk factors of stroke as well as heart diseases are the same and heart disease is comparatively more prevalent than stroke. Therefore, investigations relating to heart disease are essential in patients of paralysis to prevent heart disease. According to a scientific research, number of paralytic patients dying due to heart disease is far more than the deaths caused by stroke. For young patients of paralysis, who do not have blood pressure or diabetes, special investigations like anticardiolipin test, homocysteine tests etc. are advisable. The damage to the blood vessels can be ascertained by Carotid Vertebral Doppler or MR angiography (or DSA Angiography). The decision of the investigations required for the patient, is better left to the doctor. (Sudhir et al, 2008).

2.1.4. Texture Analysis:

Texture analysis refers to the branch of imaging science that is concerned with the description of characteristic image properties by textural features. However, there is no universally agreed-upon definition of what image texture is and in general different researchers use different definitions depending upon the particular area of application (Tuceryan & Jain, 1998). In this chapter texture is defined as the spatial variation of pixel intensities, which is a definition that is widely used and accepted in the field. The main image processing disciplines in which texture analysis techniques are used are classification, segmentation and synthesis. In image

classification the goal is to classify different images or image regions into distinct groups (Pietikainen, 2000).

Texture analysis methods are well suited to this because they provide unique information on the texture, or spatial variation of pixels, of the region where they are applied. In image segmentation problems the aim is to establish boundaries between different image regions (Mirmehdi et al., 2008).

By applying texture analysis methods to an image, and determining the precise location where texture feature values change significantly, boundaries between regions can be established. Synthesizing image texture is important in three-dimensional (3D) computer graphics applications where the goal is to generate highly complex and realistic looking surfaces. Fractals have proven to be a mathematically elegant means of generating textured surfaces through the iteration of concise equations (Pentland, 1984). Conversely the ability to accurately represent a textured surface by a concise set of fractal equations has led to significant advances in image compression applications using fractal methods (Distani et al., 2006)

An example of image classification is presented in Fig. 2.1 in which it is possible to uniquely identify the two different textures (left, grass; right, water) by eye. In Fig. 2.2 the image on the left is a composite image formed from eight Brodatz textures, all of which are represented in approximately equal proportions. The right image is a grey-level texture map showing the ideal segmentation of the textures (Weber, 2004).

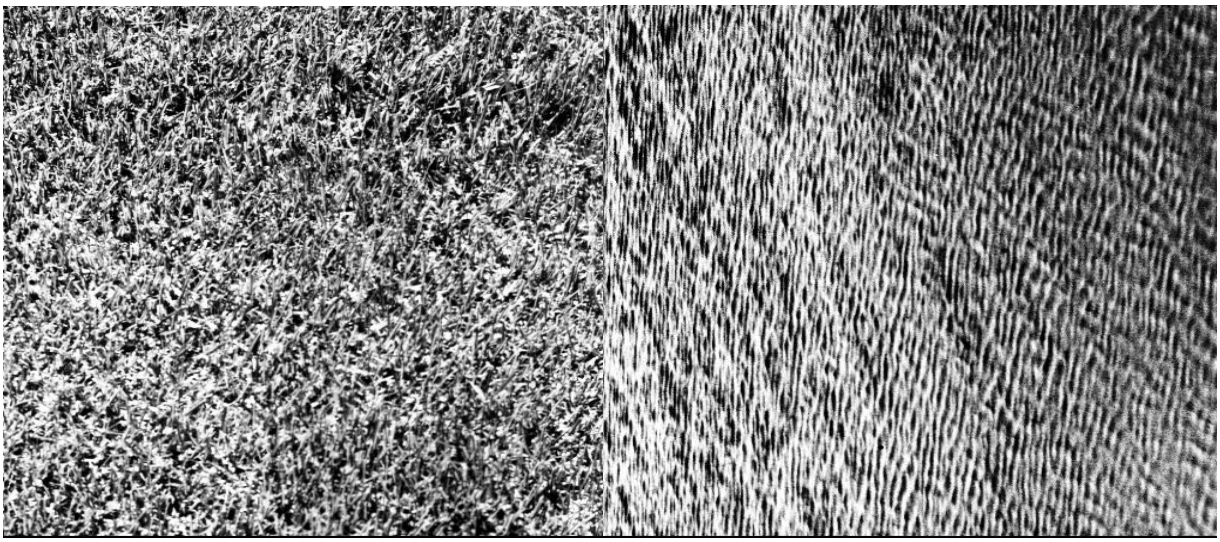


Figure. 2.11. Digital images of two visibly different textured regions extracted from the Brodatz texture database (Brodatz, 1966). Left, image of grass (1.2.01, D9 H.E.). Right, image of water (1.2.08, D38 H.E.) (Weber, 2004).

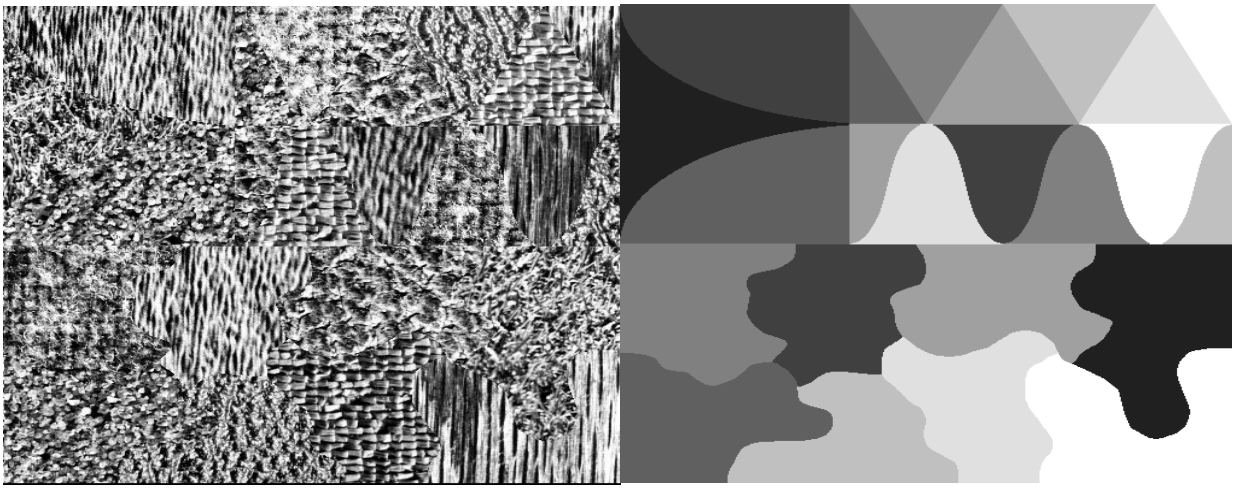


Fig. 2.12. Example of image segmentation using texture analysis to determine the boundary between distinct regions of texture. Left, mosaic image of eight Brodatz textures represented in approximately equal proportions. Right, grey-level texture map showing the ideal segmentation of the textures (Weber, 2004).

2.1.4.1 The Visual Perception of Texture:

Much of our understanding of machine vision algorithms is a result of attempts to overcome the failings of the human visual system to detect certain textured patterns. This understanding has proven vital in evaluating and comparing the performance of human vision against machine-

based texture analysis approaches. Julesz, an experimental psychologist, was an early pioneer in the visual perception of texture (Julesz, 1975). He was responsible for establishing authoritative data on the performance of the human vision system at discriminating certain classes of texture. He verified that discriminating between two image textures depends largely upon the difference in the second-order statistics of the textures. That is, for two textures with identical second-order statistics a deliberate amount of effort is required to discriminate between them. In contrast little effort is required when the second-order statistics of the textures are different. However, this observation does not extend to textures that differ in third- or higher-order statistics, which are not readily discriminated by eye. This is illustrated in Fig. 2.3 in which each of the main textured images (left and right) has a smaller area of similar, but subtly different, texture embedded within it. In the image on the left both the main and embedded areas have identical first-order statistics, however, their second-order statistics are different making it straightforward to discriminate both regions. In the image on the right both textures have identical first- and second-order statistics and therefore it is only after careful scrutiny that the different textured regions become visible. (Julesz, (1975)).

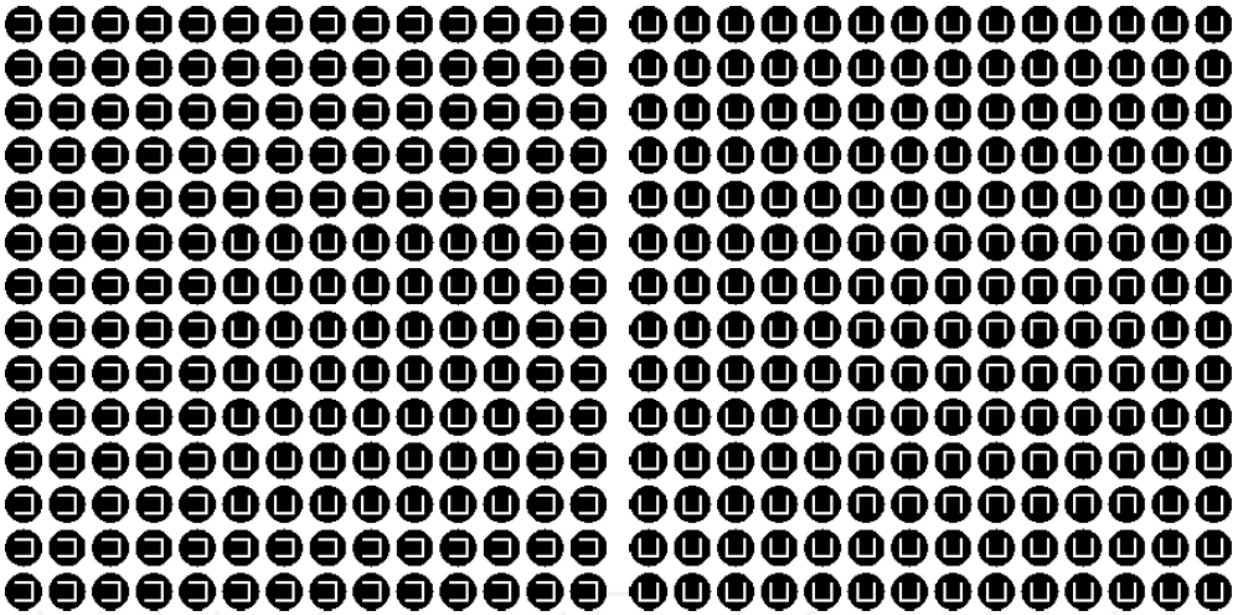


Fig. 2.13. The images on the left and right have a main area of texture embedded within which is a smaller area of similar, but subtly different, texture. In the left image both textures have the same first-order statistics and different second-order statistics, which makes it straightforward for an observer to distinguish between them. In the image on the right both textures have identical first- and second-order statistics and hence only after careful scrutiny are the different patterns visible (Julesz, 1975).

Although our understanding of the cognitive process of human vision is constantly expanding much has been learned from experiments in the visual perception of digital image information (Bruce et al, 2003). Such work is vital, particularly in medical imaging where the misinterpretation of image information can have a serious impact on health (ICRU, 1999). This is particularly apparent in radiotherapy, the treatment of cancer by ionizing radiation, where the aim is to deliver as high a radiation dose as possible to diseased tissue whilst limiting the radiation dose to healthy tissue. Delineation of the tumour volume is based primarily on visual assessment of computerized tomographic (CT) and magnetic resonance (MR) image data by a radiation oncologist. Accurately defining the tumour, and potential areas of tumour involvement, on CT and MR data is a complex image interpretation process requiring considerable clinical

experience. As a result significant inter- and intra-clinician variability has been reported in the contouring of tumours of the lung, prostate, brain and esophagus (Weltens et al., 2001; Steenbakkers et al., 2005).

This variability has been shown to be significant and heavily correlated with the digital imaging modality used and the image settings applied during the assessment. Texture analysis is presented here as a useful computational method for discriminating between pathologically different regions on medical images because it has been proven to perform better than human eyesight at discriminating certain classes of texture. (Julesz, (1975)).

2.1.4.2. Statistical Approaches for Texture Analysis

To examine an image using texture analysis the image is treated as a 3D textured surface. This is illustrated in Fig. 2.4 which shows the textured intensity surface representation of a (2D) medical image. In first-order statistical texture analysis, information on texture is extracted from the histogram of image intensity. This approach measures the frequency of a particular grey-level at a random image position and does not take into account correlations, or co-occurrences, between pixels. In second-order statistical texture analysis, information on texture is based on the probability of finding a pair of grey-levels at random distances and orientations over an entire image. Extension to higher-order statistics involves increasing the number of variables studied.

Many conventional approaches used to study texture have concentrated on using 2D techniques to compute features relating to image texture. This traditional approach has been used extensively to describe different image textures by unique features and has found application in many disparate fields such as: discrimination of terrain from aerial photographs (Conners & Harlow, 1980); in vitro classification of tissue from intravascular ultrasound (Nailon, 1997); identification of prion protein distribution in cases of Creutzfeld-Jakob disease (CJD) (Nailon &

Ironside, 2000); classification of pulmonary emphysema from lung on high-resolution CT images (Uppaluri et al., 1997; Xu et al., 2004; Xu et al., 2006); and identifying normal and cancerous pathology (Karahaliou et al., 2008, Zhou et al., 2007; Yu et a., 2009). Higher-order approaches have been used to localise thrombotic tissue in the aorta (Podda, 2005) and to determine if functional vascular information found in dynamic MR sequences exists on anatomical MR sequences (Winzenrieth, 2006). Extension of these approaches to 3D is continuing to develop within the machine vision community. Several authors have reported the application of 2D texture analysis methods on a slice-by-slice basis through volumetric data, however, it has been reported that with this approach information may be lost (Kovalev et al., 2001; Kurani et al., 2004). Findings reported by Xu et al., on the use of 3D textural features for discriminating between smoking related lung pathology, demonstrate the power of this approach for this particular application (Xu et al., 2006). Kovalev et al., showed that an extended 3D co-occurrence matrix approach can be used for the classification and segmentation of diffuse brain lesions on MR image data (Kovalev et al., 2001).

Texture analysis has also been used to identify unique pathology on multi-modality images of cancer patients. Using the local binary operator to analyze the weak underlying textures found in transrectal ultrasound images of the prostate, Kachouie and Fieguth demonstrated that the approach was suitable for segmentation of the prostate (Kachouie & Fieguth, 2007). In another cancer-related study of 48 normal images and 58 cancer images of the colon, Esgiar et al., demonstrated that by adding a fractal feature to traditional statistical features the sensitivity of the classification improved (Esgiar et al., 2002).

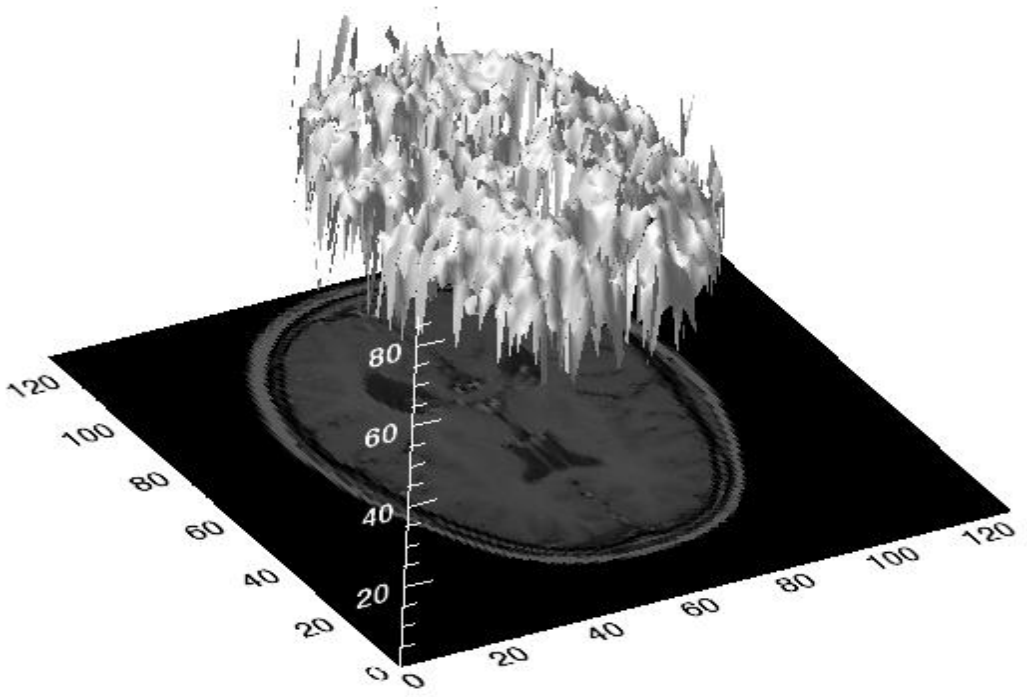


Fig. 2.14. Three-dimensional textured intensity surface representation of a medical image. A: Two-dimensional MR image of the brain. B: Pixel values of the MR image plotted on the vertical axis to produce a 3D textured surface.

With the proliferation of 3D medical image data of near isotropic quality there is an increasing demand for artificial intelligence methods capable of deriving quantitative measures relating to distinct pathology. The remaining sections of this chapter provide a review of statistical and fractal texture analysis approaches in the context of medical imaging and provide comprehensive real-world examples, in the form of two case studies, on the use of these approaches in clinical practice. In case study 1 texture analysis is presented as a means of classifying distinct regions in cancer images, which could be developed further towards automatic classification. In case study 2 texture analysis is presented as an objective means of identifying the different patterns of prion protein found in variant CJD (vCJD) and sporadic CJD. Two contrasting methods are presented in the case studies for evaluating the performance of the texture analysis methodologies. (Nailon et.al (2010))

2.1.4.3. First-Order Statistical Texture Analysis:

First-order texture analysis measures use the image histogram, or pixel occurrence probability, to calculate texture. The main advantage of this approach is its simplicity through the use of standard descriptors (e.g. mean and variance) to characterize the data (Press, 1998). However, the power of the approach for discriminating between unique textures is limited in certain applications because the method does not consider the spatial relationship, and correlation, between pixels. For any surface, or image, grey-levels are in the range $0 \leq i \leq Ng - 1$, where Ng is the total number of distinct grey-levels. If N (i) is the number of pixels with intensity i and M is the total number of pixels in an image, it follows that the histogram, or pixel occurrence probability, is given by,

$$P(i) = \frac{N(i)}{M}.$$

In general seven features commonly used to describe the properties of the image histogram, and therefore image texture, are computed. These are: mean; variance; coarseness; skewness; kurtosis; energy; and entropy.

2.1.4.4. Second-Order Statistical Texture Analysis

The human visual system cannot discriminate between texture pairs with matching second order statistics (Julesz, 1975). The first machine-vision framework for calculating second-order or pixel co-occurrence texture information was developed for analyzing aerial photography images (Haralick et al., 1973).

In this technique pixel co-occurrence matrices, which are commonly referred to as grey-tone spatial dependence matrices (GTSDM), are computed. The entries in a GTSDM are the

probability of finding a pixel with grey-level *i* at a distance *d* and angle α from a pixel with a grey-level *j*. This may be written more formally as *P* (*i, j: d,*α). An essential component of this framework is that each pixel has eight nearest-neighbors connected to it, except at the periphery. As a result four GTSDMs are required to describe the texture content in the horizontal ($H_p = 0^0$), vertical ($P_v=90^0$) right- ($P_{RD}=45^0$) and left diagonal ($P_{LD}= 135^0$) directions. This is illustrated in Fig. 5.

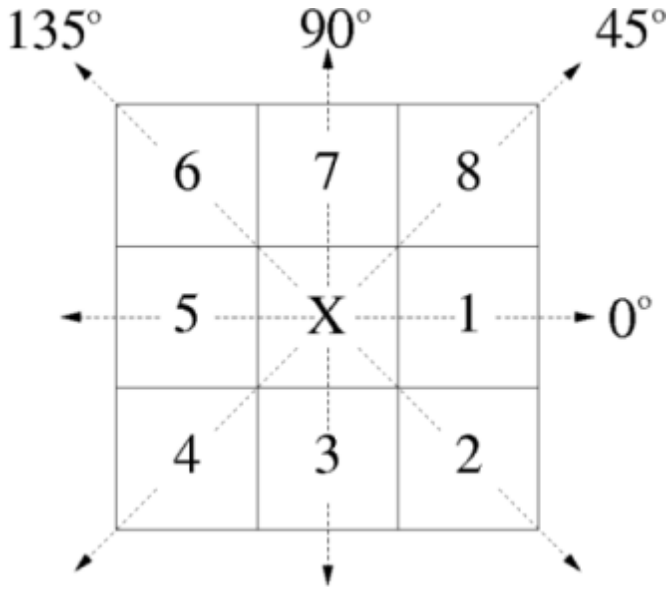


Fig. 2.15. Eight nearest-neighbor pixels used in the GTSDM framework to describe pixel connectivity. Cells 1 and 5 show the horizontal (H_p), 4 and 8 the right-diagonal (P_{RD}), 3 and 7 the vertical (P_v) and 2 and 6 the left-diagonal (P_{LD}) nearest-neighbors. Haralick et al., 1973.

An example of the calculation of a horizontal co-occurrence matrix (***H_p***) on a 4x4 image containing four unique grey-levels is shown in Fig. 2.6. A complete representation of image texture is contained in the co-occurrence matrices calculated in the four directions. Extracting information from these matrices using textural features, which are sensitive to specific elements of texture, provides unique information on the structure of the texture being investigated. Haralick et al., proposed a set of 14 local features specifically designed for this purpose (Haralick et al., 1973).

In practice the information provided by certain features may be highly correlated or of limited practical use. A feature selection strategy is therefore useful with this approach to take account of redundant, or irrelevant, information. It is also interesting to note that prior to any processing the GTSDMs, which are symmetric, can provide some useful information on the characteristics of the image being studied. For example, the co-occurrence matrix entries for a coarse texture will be heavily focused along the diagonals relative to the distance d between the pixels studied.

0	2	2	2
0	3	2	2
1	2	2	2
3	0	3	0

(P_H)

Grey-Level	Grey-Level			
0^0	0	1	2	3
0	0	0	1	4
1	0	0	1	0
2	1	1	10	1
3	4	0	1	0

Fig. 2.16. Simple example demonstrating the formation of a co-occurrence matrix from an image. Left, 4x4 image with four unique grey-levels. Right, the resulting horizontal co-occurrence matrix (P_H).

To illustrate the computational requirements of this framework, three of the 14 features proposed by Haralick et al., 1973, are presented in equations 2 to 4.

Angular second moment,

$$f_1 = \sum_{i=1}^{N_q} \sum_{j=1}^{N_q} p'(i,j)^2. \tag{2}$$

Contrast,

$$f_2 = \sum_{i=0}^{N_q-1} n^2 \left[\sum_{i=1}^{N_q} \sum_{j=1}^{N_q} p'(i,j) \right]_{i-j=n} \tag{3}$$

Correlation,

$$f_3 = \sum_{i=1}^{N_q}\sum_{j=1}^{N_q}\frac{(i-\mu_x)(j-\mu_y)p'(i,j)}{\sigma_x\sigma_y}, \quad (4)$$

Where, Nq is the number of distinct grey-levels in the input and μ_x, μ_y, σ_x and σ_y are the means and standard deviations of p' (i, j). Throughout, p' (i, j) P' (i, j)/R, where P (i, j) is the average of (P_H, P_V, P_{LD} and P_{RD}) and R is the maximum number of resolution cells in a GTSDM. (Nailon et.al (2010)).

2.1.4.5. Higher-Order Statistical Texture Analysis:

The grey-level run length method (GLRLM) is based on the analysis of higher-order statistical information (Galloway, 1975). In this approach GLRLMs contain information on the run of a particular grey-level, or grey-level range, in a particular direction. The number of pixels contained within the run is the run-length. A coarse texture will therefore be dominated by relatively long runs whereas a fine texture will be populated by much shorter runs. The number of runs *r´* with gray-level *i*, or lying within a grey-level range *i*, of run length *j* in a direction α is denoted by {*R* (α) = *r´ (i, j*| α)}. This is analogous to the GTSDM technique (Haralick et al., 1973) as four GTRLMs are commonly used to describe texture runs in the directions (0^0, 45^0,90^0 and 135^0) on linearly adjacent pixels. An example of the calculation of a horizontal GLRLM is shown in Fig. 2.7.

0	1	2	2
0	3	2	2
1	2	2	2
3	0	3	0

Grey-Level	Run-Length			
	0^0	1	2	3	4
0	4	0	0	0
1	2	0	0	0
2	0	2	1	0
3	3	0	0	0

Fig. 2.17. Simple example demonstrating the formation of a GLRLM. Left, 4 x4 image with four Unique grey-levels. Right, the resulting GLRLM in the direction 0^0.

A set of seven numerical texture measures are computed from the GTRLMs. Three of these measures are presented here to illustrate the computation of feature information using this framework.

Short Run Emphasis,

$$f_{SR} = \frac{1}{T_R} \sum_{i=0}^{N_g-1} \sum_{j=1}^{N_r} \frac{r'(i,j \mid \alpha)}{j^2}. \quad (5)$$

Long Run Emphasis,

$$f_{LR} = \frac{1}{T_R} \sum_{i=0}^{N_g-1} \sum_{j=1}^{N_r} j^2 r'(i,j \mid \alpha). \quad (6)$$

Grey-Level Distribution,

$$f_{GD} = \frac{1}{T_R} \sum_{i=0}^{N_g-1} \left[\sum_{j=1}^{N_r} r'(i,j \mid \alpha) \right]^2, \quad (7)$$

Where *g N* is the maximum number of grey-levels, *r N* is the number of different run lengths in

the matrix and, *T* serves as a normalizing factor in each of the run length equations.

$$T_R = \sum_{i=0}^{N_g-1} \sum_{j=1}^{N_r} r'(i, j \mid \alpha). \tag{8}$$

2-2 Previous Studies:

Asma et al (2015) studied : Modified Magnetic Resonance Imaging (Mri) Brain Protocol For Diagnosing Multiple Sclerosis (Ms) GJRA - Global Journal For Research Analysis, Volume-4, Issue-10, Oct-2015 • Issn No 2277 – 8160.

this study founded the best protocol to visualize all the M.S in the new and old (follow up) brain cases by using modified protocols, Axial, Sagittal and Flair with 3 mm slice thickness instead of 5 mm and slice gab 0.00 zero instead of 1 mm were used to cover any MS that might be missed in routine protocol and discover a new MS. Out of 20 patients scanned by MRI, 11 (55%) were males and 9 (45%) were females. The patients' ages ranged from 24 to 60 years. Concluded of this study The best MRI protocol for detection and diagnoses of M.S is the modified protocol suggested by this study. The result showed that 55 % of the affected patients were males and 45%. Were females.

J.H. Simon D. LiA. Traboulsee et al (2006) Standardized MR Imaging Protocol for Multiple Sclerosis: Consortium of MS Centers Consensus Guidelines - AJNR Am J Neuroradiol 27:455–461 Feb 2006

The study concluded the development of consensus guidelines is a challenging process that, when done well, balances advantages and disadvantages. In this case, the advantages of standardized indications and imaging are to allow diagnosis and follow-up within and between imaging centers and practices. Disadvantages include compromises in choosing methodology, removing choice, and in some cases asking practices to move from the methodology in which they have the most experience. Ultimately, although initially slightly painful, the hope is that standardization will benefit the individual MS patient, which after all is the goal of any medical imaging. These recommendations are provided with the understanding that they will likely require modification as instrument capabilities change, new pulse sequences are developed, and more quantitative methodologies become validated in individuals and feasible in practice.

Paul D. Molyneux, Niall Tubridy et al(1998) The Effect of Section Thickness on MR Lesion Detection and Quantification in Multiple Sclerosis - AJNR Am J Neuroradiol19:1715–1720, October 1998

This study found that progressive reduction in section thickness led to detection of smaller lesions, resulting in a significant (8%) increase in lesion volume on MR images as section thickness was reduced from 5 mm to 3 mm. However, despite a further increase in lesion detection at a section thickness of 1 mm, this did not result in an increase in total lesion volume. This finding indicates that the relationship between section thickness and lesion volume on MR images is not linear. Scan-rescan reproducibility was improved by reducing section thickness, at the cost of increased analysis time.

This study concluded shows that acquisition of very thin sections increases the sensitivity and precision of MS lesion measurement. Serial studies assessing lesion changes over time are needed to define the impact of this increase on sample size requirements for MS treatment trials.

Bink ,A., Schmitt,M.,J et al EUR Radiol (2006) Detection of lesion in multiple sclerosis by 2D FLAIR and single –slab 3D FLAIR sequence at 3.0 T: initial result- EUROPEAN Radiology May 2006.

The aim of this study was to compare conventional 2D FLAIR and single-slab 3D FLAIR sequences in the detection of lesions in patients with multiple sclerosis. Eight patients with MS were examined at 3.0 T by using a 2D FLAIR sequence and a single-slab 3D FLAIR sequence. A comparison of lesion detectability was performed for the following regions: periventricular, nonperiventricular/juxtacortical and infratentorial. The contrast-to-noise ratios (CNRs) between lesions and brain tissue and CSF were calculated for each sequence. A total of 424 lesions were found using the 2D FLAIR sequence, while with the 3D FLAIR sequence 719 lesions were found. With the 2D FLAIR sequence, 41% fewer lesions were detected than with the 3D FLAIR sequence. Further, 40% fewer supratentorial and 62.5% fewer infratentorial lesions were found with the 2D FLAIR sequence. In images acquired with the 3D FLAIR sequence, the lesions had significantly higher CNRs than in images acquired with the 2D FLAIR sequence. These are the first results using a single-slab 3D FLAIR sequence at 3.0 T for detection of lesions in patients with MS. With the 3D FLAIR sequence significantly higher CNRs were achieved and significantly more lesions in patients with MS were detected.

Wolter L. de Graaf & Jaco J. et al (2011) Lesion detection at seven Tesla in multiple sclerosis using magnetisation prepared 3D-FLAIR and 3D-DIR-Eur Radiol (2012) 22:221 –231 DOI 10.1007/s00330-011-2242-z

Resulted of this study Evaluation of the acquired images showed incomplete attenuation of CSF in some areas of the brain for 3D-MP-FLAIR and 3D-MP-DIR. Perivascular spaces were depicted hyperintense and were not attenuated by the inversion recovery pulses. They were depicted hypointense visible on 3D-T1 images. The contrast ratio for GM/WM was highest for the 3DMP-DIR (93%), while the conventional sequences and 3DMP-FLAIR showed intensity differences ranging between 23% and 40%. The variation in CR between sequences was much higher for lesions than between GM/ WM. The 3D-MP-DIR and 3D-MP-FLAIR sequences showed in general the highest CR for lesion vs. GM or WM. Only the 2D-T2 sequence had a higher CR for the lesion/WM than either DIR or FLAIR. Lesion contrast (for both GM and WM lesions) was quite low on both 2D-PD and 3D-T1 images, although the negative contrast and sharp delineation on the T1 images helped correct localisation on these images. Outlined regions of interest were drawn in areas with good image quality on the 3D-MP-FLAIR sequence for all subjects and copied to the other sequences. All sequences showed higher signal intensities of frontal and occipital brain areas compared with the temporal lobes for both WM and GM. However, signal intensities were high enough for proper GM/WM and lesion contrast. On 3D-MP-FLAIR and 3D-MP-DIR images, the cortex showed an intensity gradient with the outer cortical layers being visualized with higher signal intensity compared to the inner layers. In addition to this hyperintense rim, a hypo-intense line was visible in the pre- and post-central cortex, resulting in a banding pattern. This effect could be seen in all orientations.

S. V. Ramagopalan, et al (2009) Sex ratio of multiple sclerosis and clinical phenotype

European Journal of Neurology, 17: 634–637. doi:10.1111/j.1468-1331.2009.02850.x

Resulted of this study year of birth was a significant predictor for sex ratio in RR MS ($P < 0.0001$, $\chi^2 = 21.2$; Spearman's rank correlation $r = 0.67$), but not for PP MS ($P = 0.44$, $\chi^2 = 0.6$; Spearman's rank correlation $r = 0.11$).

We concluded that an increase in the number of female RR MS patients over time accounts for the increasing sex ratio of MS. This has implications for pathogenesis, for assessment of clinical trial results and for disease prevention. The factors underlying the selective increase in MS in females need to be uncovered.

Brandis M, Reitman NC, Gruenewald D et al (2008) Aging with Multiple Sclerosis 2011 National Multiple Sclerosis Society

Considering the evidence that life expectancy of people with MS is essentially normal, and that the number of older individuals in the general population is growing, it is likely we will see increasing numbers of older individuals with MS. A recent estimate based on weighted data from the Sonya Slifka Longitudinal Multiple Sclerosis Study places the percentage of MS patients over the age of 65 at 9% (Minden et al., 2004). Despite the projected growth of this population, relatively little MS research has targeted, or even included, older individuals. In fact, in published trials of diseasemodifying agents, the highest mean age of participants was 47 years (Stern, 2005). A few recent studies have examined the older MS population; however, "older" has been defned differently by different investigators. In this report we discuss research that specifically focused on the older population—the youngest age for inclusion in any study was 45 years. However, the mean ages of the samples was typically between 60 and 70 years.

Duquette, P., Pleines, J., Girard, M et al (1992) The Increased Susceptibility of Women to Multiple Sclerosis. Canadian Journal of Neurological Sciences / Journal Canadien Des Sciences Neurologiques, 19(4), 466-471. doi:10.1017/S0317167100041664

Many diseases with an auto-immune etiology have a skewed sex distribution. In the majority of instances, women are affected more frequently than men. A review of population studies demonstrates that the preponderance of women in multiple sclerosis (MS) is almost constant. We show that this preponderance is further increased in early as well as in late-onset cases, in familial cases as well as in MS twin pairs and that the HLA-DR2 allele, which has been associated with MS in Caucasian populations, is significantly more frequent in women than in men with MS. "Rules" have been established for multifactorial diseases; MS contravenes most of

those rules. The skewed sex distribution in MS could be attributed to the known hormonal and gender influences on the immune response, as well as to genetic influences.

Ender Uysal1 Sukru Mehmet Erturk1 et al (2007) Sensitivity of Immediate and Delayed Gadolinium-Enhanced MRI After Injection of 0.5 M and 1.0 M Gadolinium Chelates for Detecting Multiple Sclerosis Lesions. AJR:188, March 2007

RESULTS. Significantly fewer enhancing lesions were seen on MR images immediately after the injection of 0.5- and 1.0-mol/L gadolinium chelates ($n = 18$ and $n = 36$, respectively; $p < 0.05$) than at 5 minutes ($n = 32$ and $n = 54$; $p < 0.05$) and 10 minutes ($n = 34$ and $n = 55$; $p < 0.05$) after the injection ($p < 0.05$). Likewise, significantly fewer patients with at least one enhancing lesion after the injection of 0.5- and 1.0-mol/L gadolinium chelates ($n = 10$ and $n = 16$; $p < 0.05$) were found immediately after injection than were found 5 minutes ($n = 18$ and $n = 24$; $p < 0.05$) and 10 minutes ($n = 18$ and $n = 24$; $p < 0.05$) after injection ($p < 0.01$). We concluded the use of 1.0-mol/L gadolinium chelate enables us to detect an increased number of enhancing lesions and patients with active disease. A delay of 5 minutes after the injection of the gadolinium chelate might be sufficient to detect active lesions in patients with MS.

Alberto Ascherio, MD, DrPH; Kassandra et al (2014) Vitamin D as an Early Predictor of Multiple Sclerosis Activity and Progression - JAMA Neurology March 2014 Volume 71, Number 3.

Higher 25(OH)D levels predicted reduced MS activity and a slower rate progression. A 50-nmol/L (20-ng/mL) increment in average serum 25(OH)D levels within the first 12 months predicted a 57% lower rate of new active lesions ($P < .001$), 57% lower relapse rate ($P = .03$), 25% lower yearly increase in T2 lesion volume ($P < .001$), and 0.41% lower yearly loss in brain volume ($P = .07$) from months 12 to 60. Similar associations were found between 25(OH)D measured up to 12 months and MS activity or progression from months 24 to 60. In analyses using dichotomous 25(OH)D levels, values greater than or equal to 50 nmol/L (20 ng/mL) at up to 12 months predicted lower disability (Expanded Disability Status Scale score, -0.17; $P = .004$) during the subsequent 4 years.

CONCLUSIONS AND RELEVANCE of this studies Among patients with MS mainly treated with interferon beta-1b, low 25(OH)D levels early in the disease course are a strong risk factor for long-term MS activity and progression.

Terry DiLorenzo, PhD (2011) Aging with Multiple Sclerosis - © 2011 National Multiple Sclerosis Society

Considering the evidence that life expectancy of people with MS is essentially normal, and that the number of older individuals in the general population is growing, it is likely we will see increasing numbers of older individuals with MS. A recent estimate based on weighted data from the Sonya Slifka Longitudinal Multiple Sclerosis Study places the percentage of MS patients over the age of 65 at 9% (Minden et al., 2004). Despite the projected growth of this population, relatively little MS research has targeted, or even included, older individuals. In fact, in published trials of diseasemodifying agents, the highest mean age of participants was 47 years (Stern, 2005). A few recent studies have examined the older MS population; however, "older" has been defned differently by different investigators. In this report we discuss research that specifically focused on the older population—the youngest age for inclusion in any study was 45 years. However, the mean ages of the samples was typically between 60 and 70 years.

Tina gissel et al (2009) Global vitamin D levels in relation to age, gender, skin pigmentation and latitude: an ecologic meta-regression analysis - Published online: 6 May 2008 # International Osteoporosis Foundation and National Osteoporosis Foundation 2008

Chapter three

Materials and Methods

3.1 Materials:

3.1.1 Patients (Study sample)

This study was a practical study which include a samples of 64 patients 18 male and 46 female under went to MRI department for brain MRI known case of MS disease in different genders and age groups. whom will be referred to the radiology department in modern medical centers in Khartoum with a known case of multiple sclerosis, undergone MRI examination, to standardize protocol to diagnose MS, child's, HTN and patient with brain tumor excluded from the study, all patients will informed to obtain their consent before the exam and their information's will be used in this study, the data will be collected and interpreted by radiologist reports.

3.1.2 Machines used

Machine used in this study MRI scanner TOSHIPA, ALLTECH (1.5 tesla), and GE. TOSHIPA machine in Almoalem medical city, ALLTECH machine in sharg alneel hospitsal, and GE machine in Asia hospital Coil used neurovascular head coil, ear plug, and immobilization bad.**:**

3.2 Methods

3.2.1. MRI protocol used

The following MRI technique was used: Field Strength: **1.5 T.** Sequences: 1st: Sagital volume FLAIR, 2nd: Axial T2. 3rd: Axial FLAIR. 4th: Gadolinium enhanced in volume T1 fat saturation

3.2.2. Data collection variables:

The study variables was consisted of parameters related to the MS in which the data was categorized into two main groups as (patient disease and demographic data and images containing

the pathology for further evaluation using CAD programs) the patient data include (age, gender, clinical diagnosis, signal intensity……

All brain images was collected including all sequences in case of MRI scan. Which include the FOS, which are; Result: The calculated texture measures as described below; FOS texture (mean, energy, entropy, variance, Skewness and kurtosis) features exstracted

3.2.3 Data Interpretation:

The data result collected from the MRI scan finding and supported the result by radiologist reports. Determine by SI as hyper, hypo and iso compare to normal brain area by observation and by measuring SI of affected area.

3.2.4. Method of data analysis and presentation:

The data were stored in computer programs than containing all parameters related to the MS in which the data was categorized into two main groups as (patient disease and demographic data and images contacting the pathology for further evaluation using computer aided diagnosis programs. IDL). After that MRI images were stored in computer disk were viewed by the Radiant, Ant DICOM viewer in computer to selected the axial images that suit the criteria of research population then uploaded into the computer based software Interactive Data Language (IDL) where the DICOM image converted to JEPG format to suit IDL platform in order to preserve the quality of the image. Then the image were read by IDL in JEPG format and the user clicks on areas represents the background, grey matter, white matter, CSF and MS plaques in case of test group; in these areas a window 3×3 pixel were generated and textural feature for the classes center were generated. These textural features includes FOS; (coefficient of variation, stander deviation, variance, signal, energy, and entropy), these features were assigned as classification center used by the Euclidian distances to

classify the whole image. The algorithm scans the whole image using a window; 3×3 pixels and computes the above mentioned textural features and then computes the distance (the Euclidean distance) between the calculated features during the scanning and the class's centers and assigns the window to the class with the lowest distance. Then the window interlaced one pixel and the same processes started over again till the entire image were classified and classification maps were generated. After all images were classified the data concerning the brain tissues (CSF, grey, and white matter) and MS plaques entered into SPSS with its classes to generate a classification score using stepwise linear discriminate analysis; to select the most discriminate features that can be used in the classification of brain tissues in MRI images. Where scatter plot using discriminate function were generated as well as classification accuracy and linear discriminate function equations to classify the brain tissues into the previous classes without segmentation process for unseen images in routine work.

Ethical considerations:

3.2.5. Data collection:

Data will be collected from findings which appear in different MRI cuts and the data will be represented in tables and graphs. The data's will include the general patients data (Age, genders and weight) and will be accompanied by the related to Symptoms and clinical information such as clinical signs (A numb or weak feeling in the face, trouble speaking, blurred or poor vision, loss of balance, headache,

The risk factors and patients history (hypertension, D.M, heart disease).

Chapter Four

Results

This study was aimed to standardize MRI protocols in which used to characterize the brain MS in suspected patient in order to increase the detection accuracy and assist in early management of such case the data were collected from asset of patient including different variability and images also was extracted for purpose of texture information extraction. The result will summarized as:

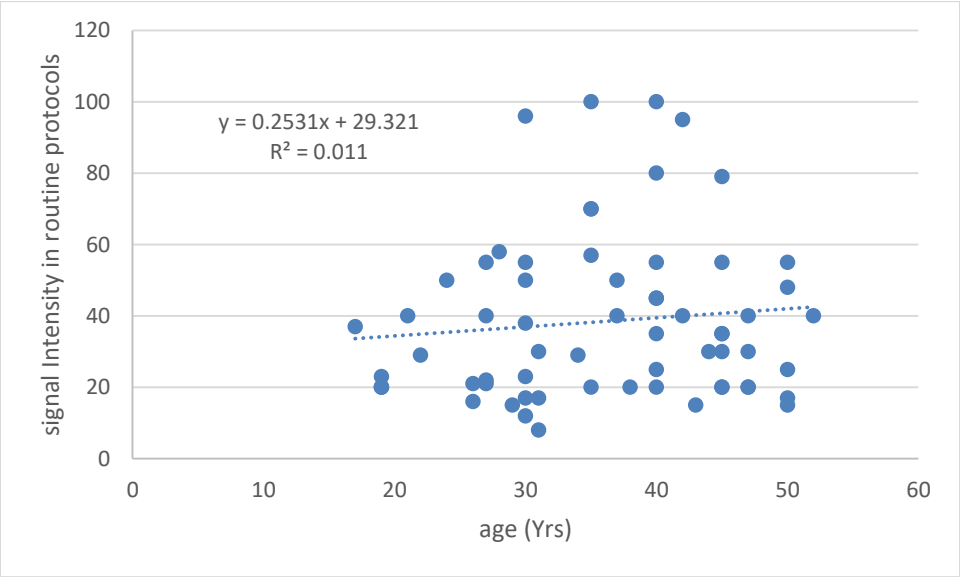


Figure (4.1) scatter plot showed the correlation between signal intensity with age of the patients in protocol 1.

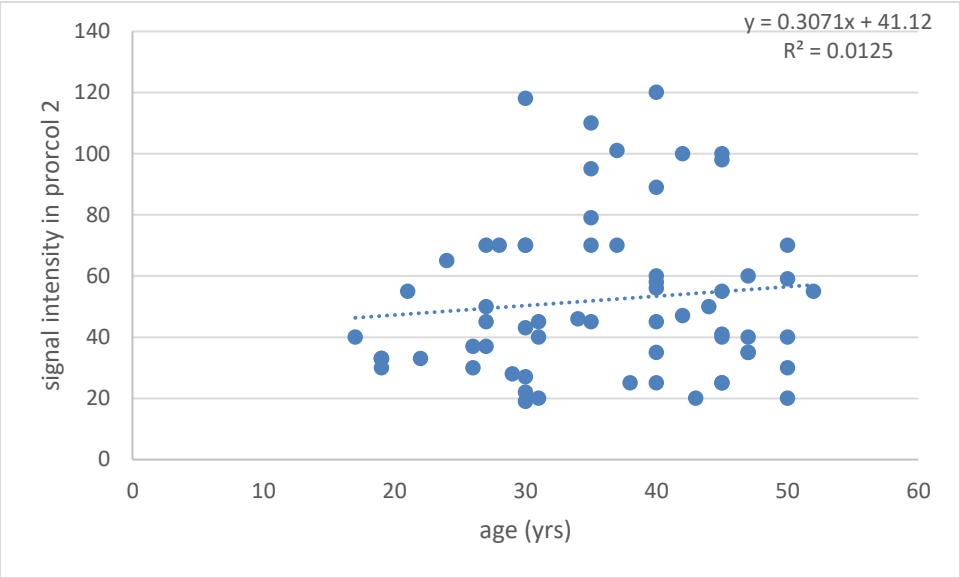


Figure (4.2) scatter plot showed the correlation between signal intensity with age of the patients in protocol 2.

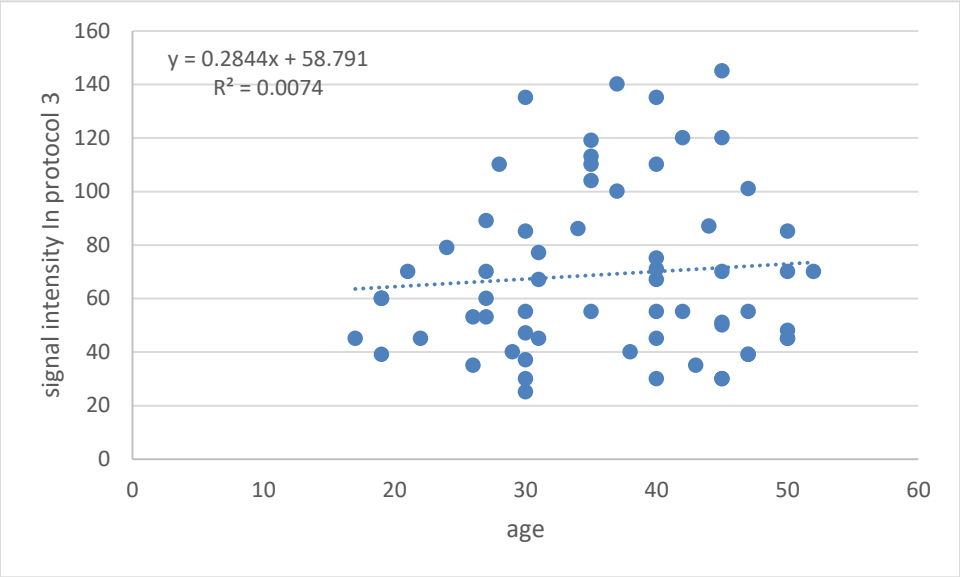


Figure (4.3) scatter plot showed the correlation between signal intensity with age of the patients in protocol 3.

Table (4.1) Paired Samples Statistics protocol 1 (routine protocol) & protocol 2 (modified protocol)

Paired Samples Statistics				
		Mean	N	Std. Deviation
Pair 1	Protocol 1 finding	38.41	64	22.860
	Protocol 2 finding	52.14	64	26.030

Table (4.2) pair sample T- test between protocol 1 (routine protocol) & protocol 2 (modified protocol)

Paired Samples Test						
		Paired Differences				Sig. (2-tailed)
		Mean	Std. Deviation	95% Confidence Interval of the Difference		
				Lower	Upper	
Pair 1	Protocol 1 finding – Protocol 2 finding	-13.734	8.803	-15.933	-11.535	.000

Table (4.3) Paired Samples Statistics protocol 1 (routine protocol) & protocol 3 (advance 3d volume protocol)

Paired Samples Statistics				
		Mean	N	Std. Deviation
Pair 1	Protocol 1 finding	38.41	64	22.860
	Protocol 3 finding	69.00	64	31.316

Table (4.4) pair sample T- test between protocol 1 (routine protocol) & protocol 3 (advance 3d volume protocol)

Paired Samples Test						
		Paired Differences				Sig. (2-tailed)
		Mean	Std. Deviation	95% Confidence Interval of the Difference		
				Lower	Upper	
Pair 1	Protocol 1 finding - Protocol 3 finding	-30.594	16.909	-34.818	-26.370	0.000

Table (4.5) represents frequency of sign & symptoms in patients with multiple sclerosis.

Sign & symptoms	Frequency	Percent
Headache + vertigo	17	26.6
Headache + Vertigo + numbness	18	28.1
Headache + numbness	3	4.7
Headache + vertigo +paraplagic	8	12.5
Headache + vertigo + diploma	6	9.4
Headache + numbness + double vision	5	7.8
Headache +Vertigo + bluring vision	7	10.9
Total	64	100.0

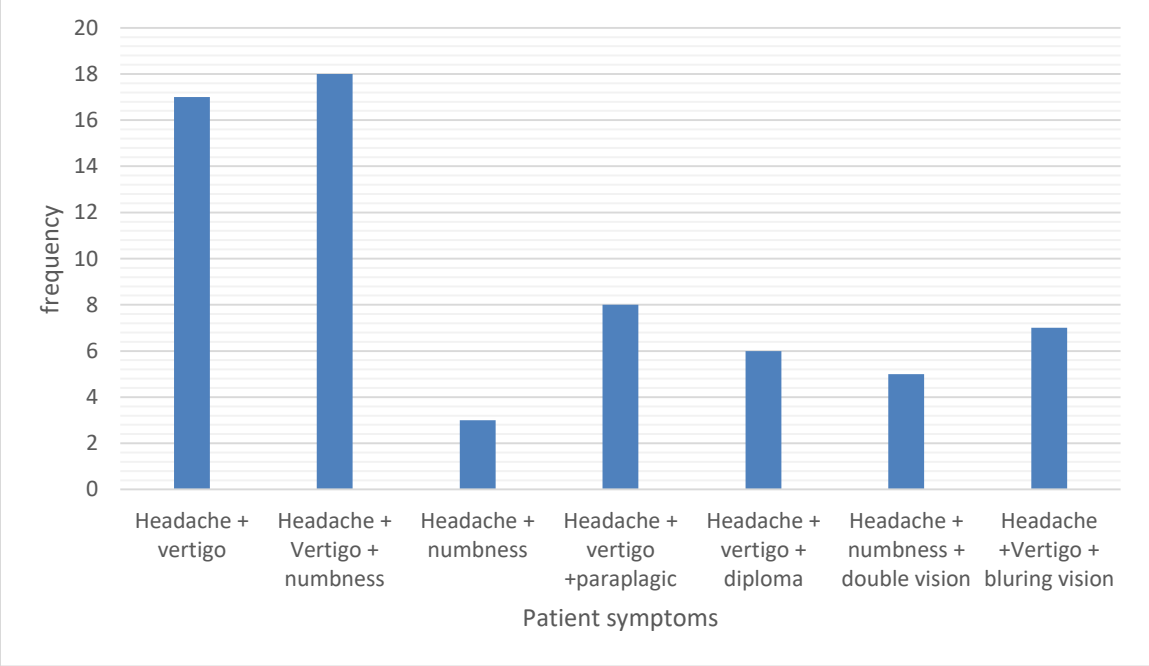


Figure (4.4) illustrate frequency of Sign & symptoms in patients with multiple sclerosis.

Table (4.6) illustrates the frequency of multiple sclerosis patients according to the gender.

gender	Frequency	Percent
Male	18	28.1
Female	46	71.9
Total	64	100.0

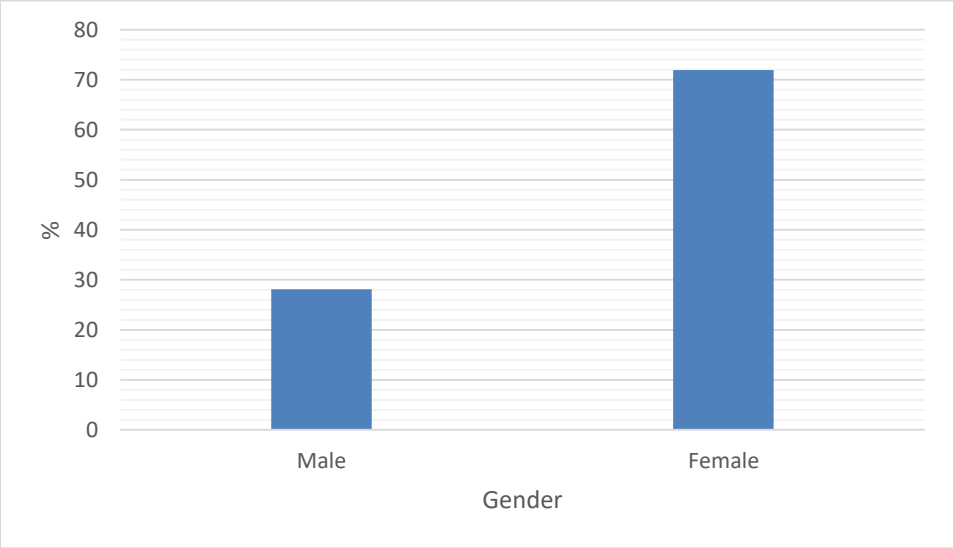


Figure (4.5) illustrates the frequency of multiple sclerosis patients according to the gender.

Table (4.7) shows the contrast substance.
Enhanced and non-enhanced scan after injection the contrast substance immediate

Contrast Immediate	Frequency	Percent
enhanced	4	6.3
Non enhanced	60	93.8
Total	64	100.0

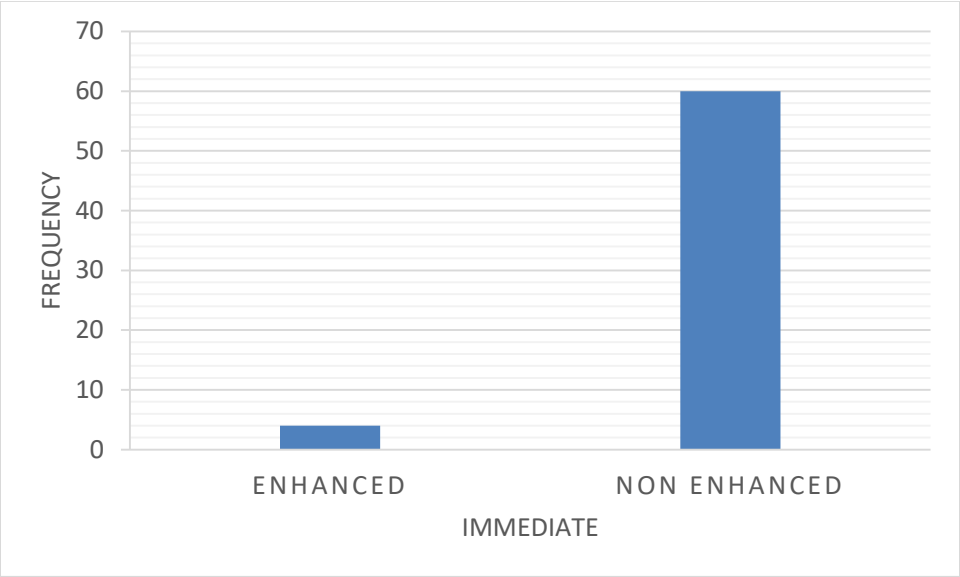


Figure (4.6) shows the contrast substance.
enhanced and non-enhanced scan after injection the contrast substance immediate

Table (4.8) shows the contrast substance.
Enhanced and non-enhanced scan 5 minute after injection the contrast substance immediate

contrast after 5 min	Frequency	Percent
High Enhancement	4	6.3
Non Enhancement	60	93.8
Total	64	100.0

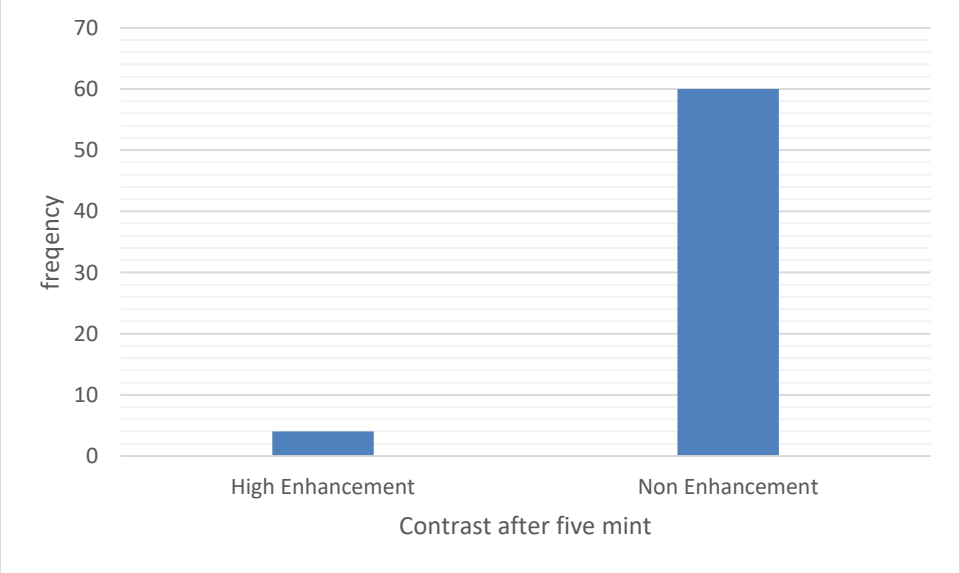


Figure (4.7) shows the contrast substance.
Enhanced and non-enhanced scan 5 minute after injection the contrast substance immediate

Table (4.9) shows frequency of vitamin D deficiency in multiple sclerosis patients

Vitamin D Deficiency	Frequency	Percent
yes	37	57.8
no	27	42.2
Total	64	100.0

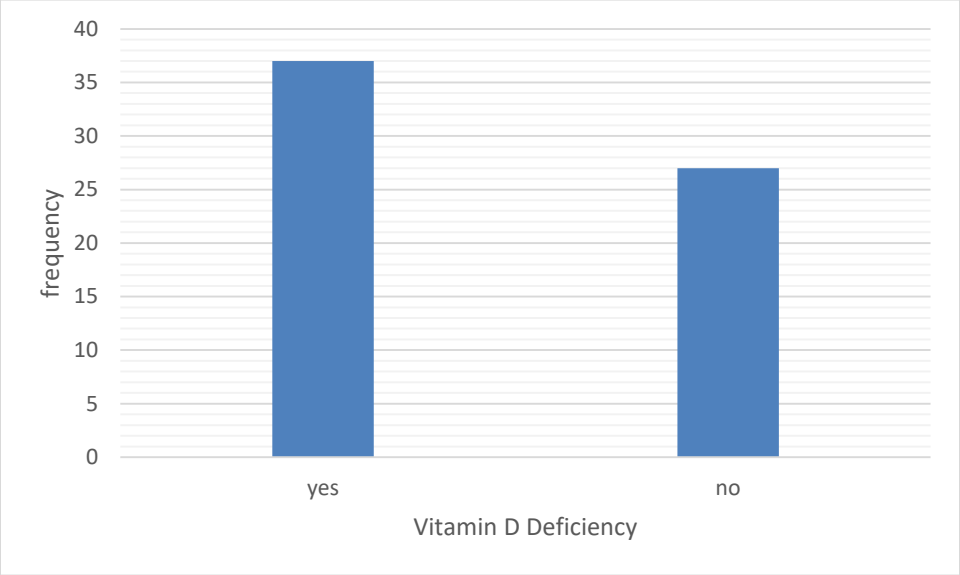


Figure (4.8) shows frequency of vitamin D deficiency in multiple sclerosis patients

Table (4.10) represented frequency of age groups

age	Frequency	Percent
17-22.8	8	12.5
22.8-28.5	18	28.1
28.5-34.4	9	14.1
34.4-40.2	19	29.7
40.2-46	10	15.6
Total	64	100.0

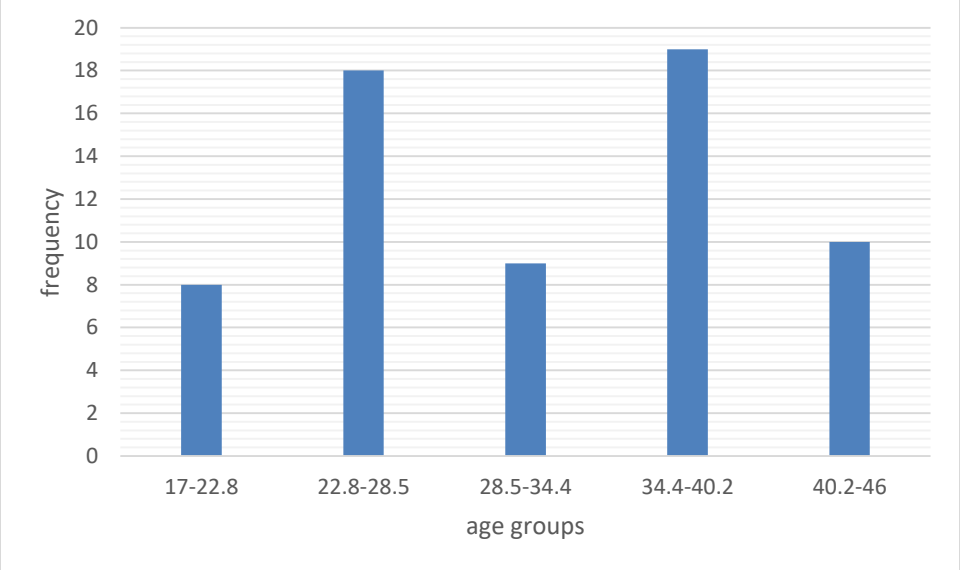
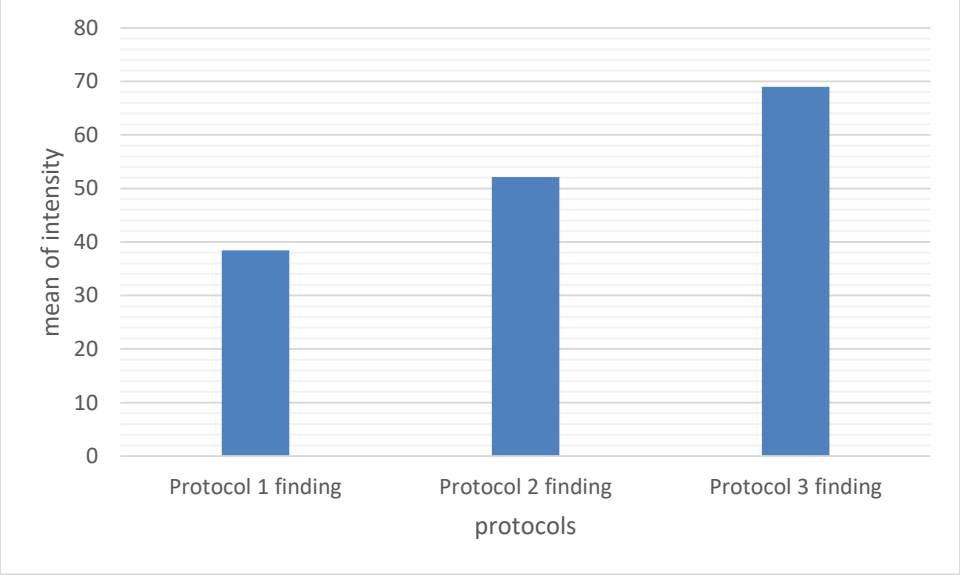


Figure (4.9) represented frequency of age groups

Table (4.11). illustrates the MS findings in protocol 1 (routine protocol 2d flair slice thickness 5mm gap 1mm), protocol 2 (modify protocol 2d flair slice thickness 3mm and slice gap 0mm) and advanced protocol3 (3Dvolume flair).

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
age	64	17	52	35.89	9.5
Protocol 1 finding	64	8	100	38.41	22.860
Protocol 2 finding	64	19	120	52.14	26.030
Protocol 3 finding	64	25	145	69.00	31.316



Figure(4.10) Illustrates the MS finding in protocol 1 (routine protocol 2d flair slice thickness 5mm gap 1mm), protocol 2 (modify protocol 2d flair slice thickness 3mm and slice gap 0mm) and advanced protocol3 (3Dvolume flair).

Table (4.12) shows cross tabulation between age and vitamin D deficiency.

Cross tabulation		Vitamin D Deficiency		Total
		yes	no	
age	17-22.8	6	2	8
	22.8-28.5	11	7	18
	28.5-34.4	5	4	9
	34.4-40.2	11	8	19
	40.2-46	4	6	10
Total		37	27	64
p-value equal =0.668				

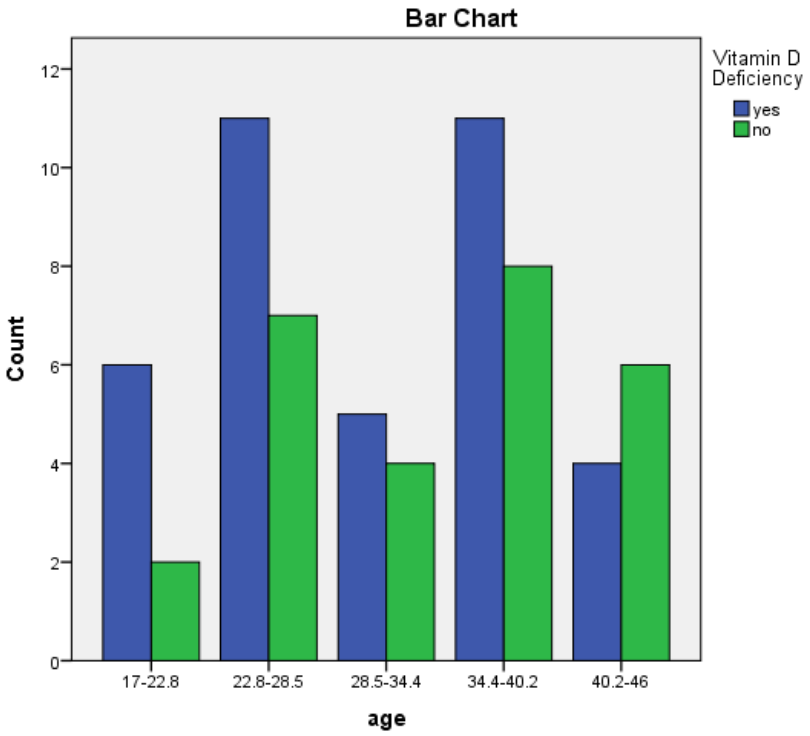


Figure (4.11) shows cross tabulation between age and vitamin D deficiency.

Table (4.13) shows cross tabulation between gender and vitamin D deficiency.

		Vitamin D Deficiency		Total
		yes	no	
gender	Male	7	11	18
	Female	30	16	46
Total		37	27	64
p-value equal =0.055				

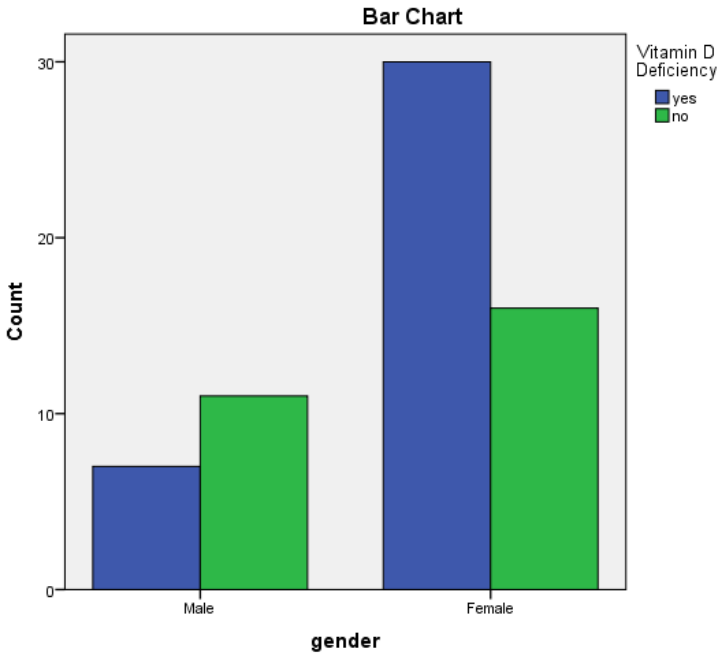


Figure (4.12) shows cross tabulation between gender and vitamin D deficiency.

Table (4.14) show cross tabulation sign & symptoms and vitamin D deficiency.

		Vitamin D Deficiency		Total
		Yes	no	
Clinical diagnosis	Headache + vertigo	9	8	17
	Headache + Vertigo + numbness	8	10	18
	Headache + numbness	2	1	3
	Headache + vertigo +paraplegic	6	2	8
	Headache + vertigo + diploma	4	2	6
	Headache + numbness + double vision	4	1	5
	Headache +Vertigo + blurring vision	4	3	7
Total		37	27	64
p-value=0.710				

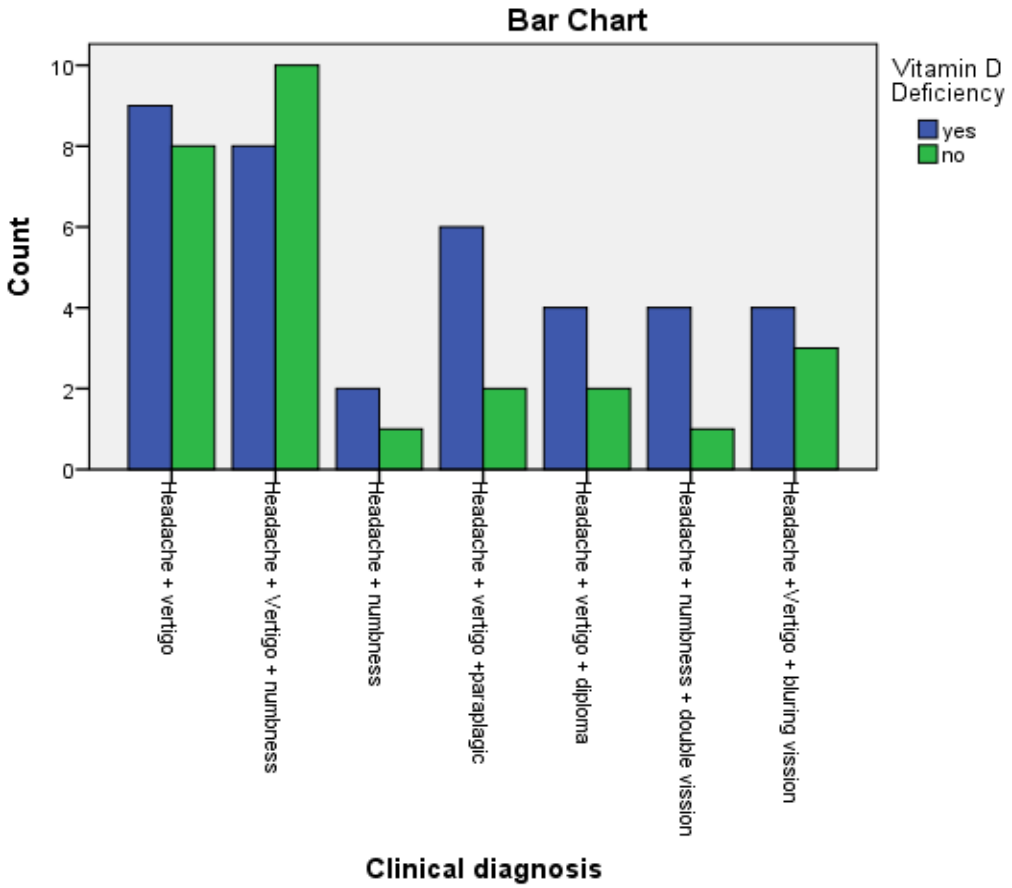


Figure (4-13) show cross tabulation between clinical diagnosis and vitamin D deficiency.

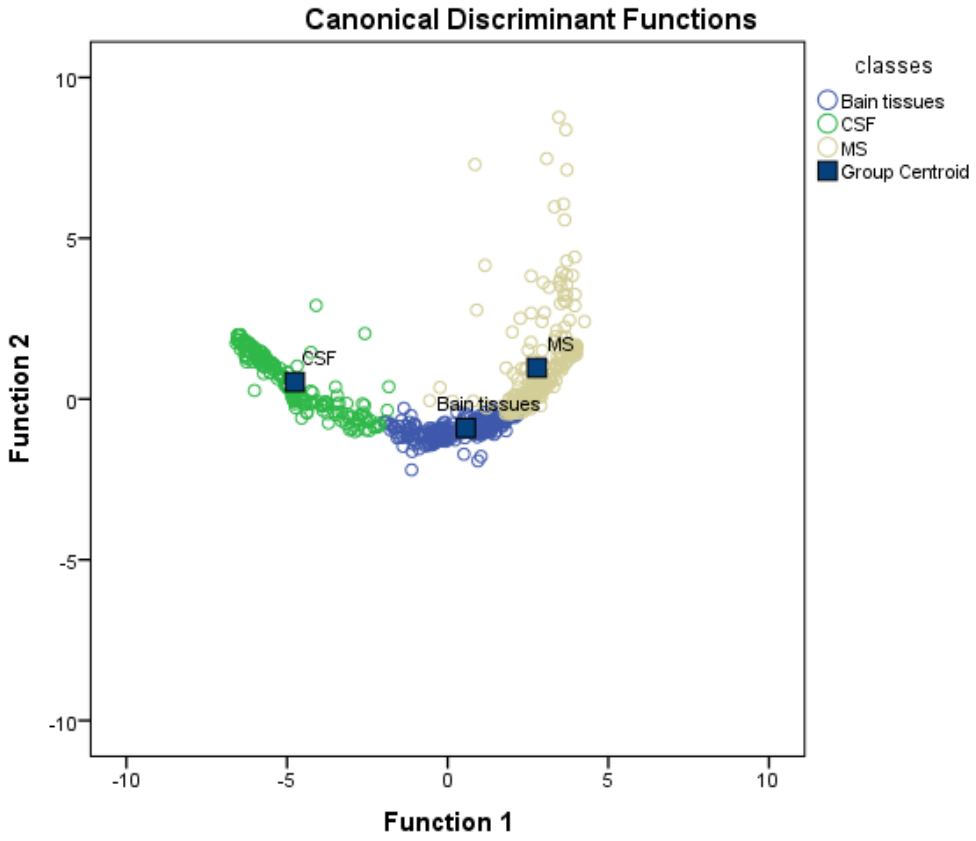


Figure (4-14) classification Map that created using linear discriminant analysis function for MS and brain tissues

Table (4.15) Cross-tabulation table show the classification results tissues using linear discriminate analysis

96.7% of original grouped cases correctly classified

Classification Results[a]						
		classes	Predicted Group Membership			Total
			Bain tissues	CSF	MS	
Original	Count	Bain tissues	369	0	1	370
		CSF	6	180	0	186
		MS	19	0	224	243
	%	Bain tissues	99.7	0.0	0.3	100.0
		CSF	3.2	96.8	0.0	100.0
		MS	7.8	0.0	92.2	100.0

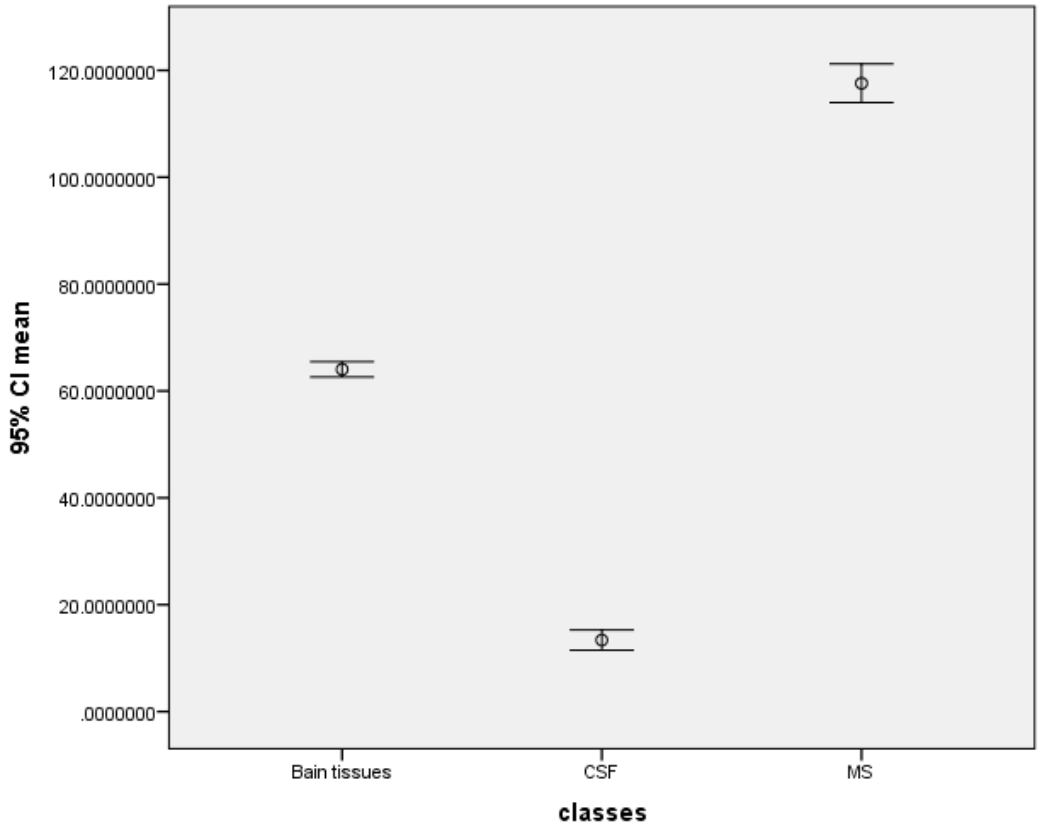


Fig 4-15: Error bar plot show the discriminate power of the mean textural feature distribution for the selected classes

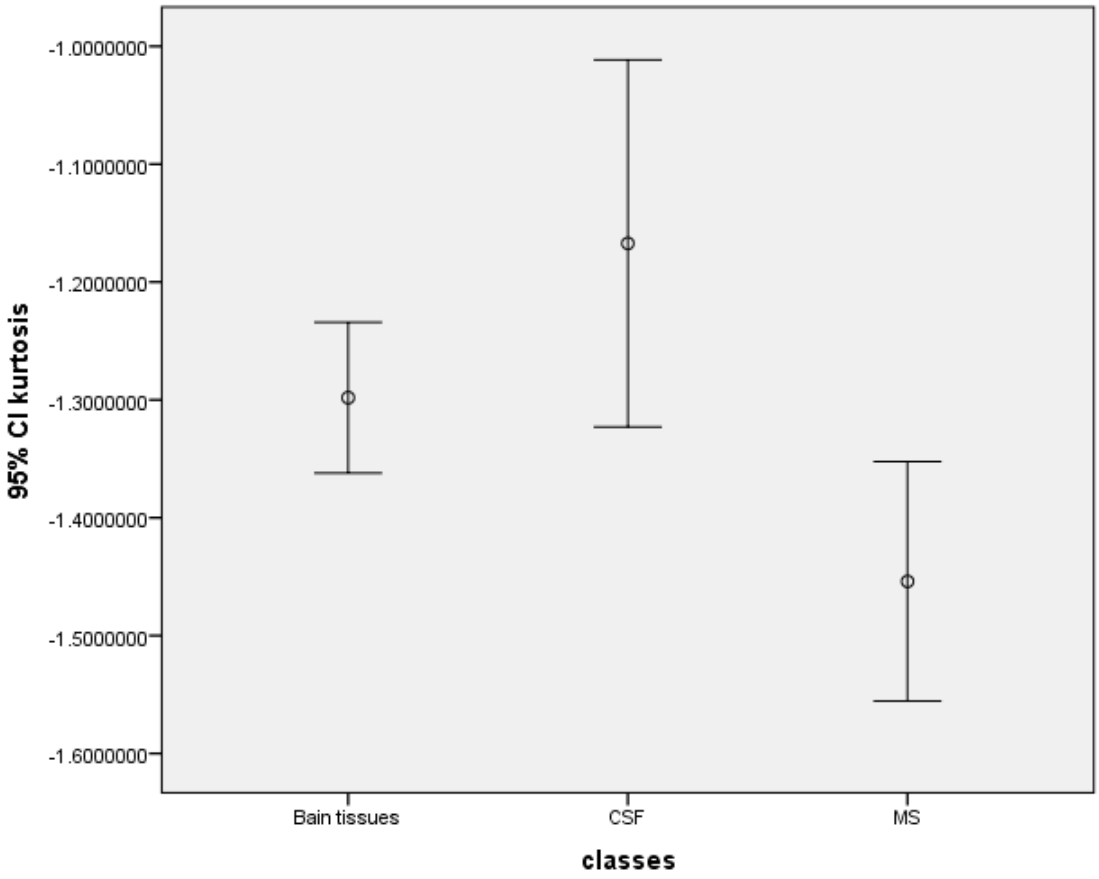


Fig 4-16: Error bar plot show the discriminate power of the kurtosis textural feature distribution for the selected classes

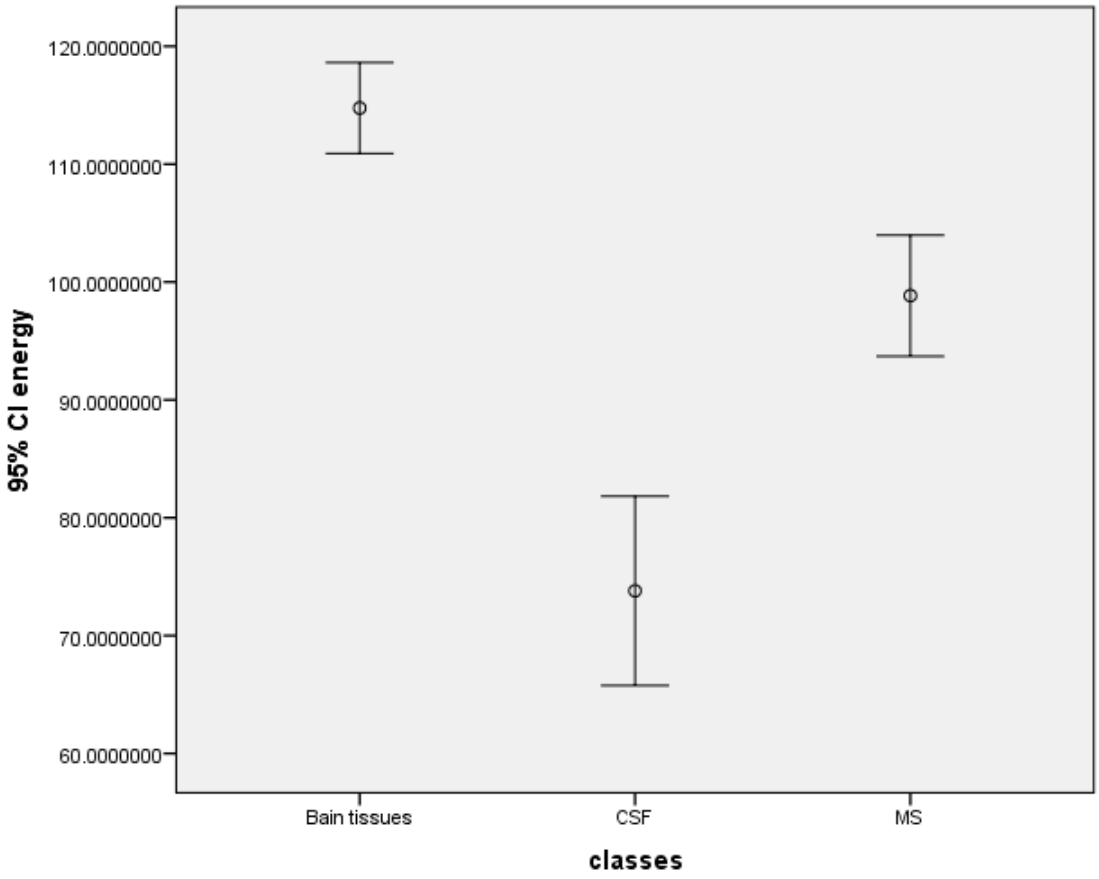


Fig 4-17: Error bar plot show the discriminate power of the energy textural feature distribution for the selected classes

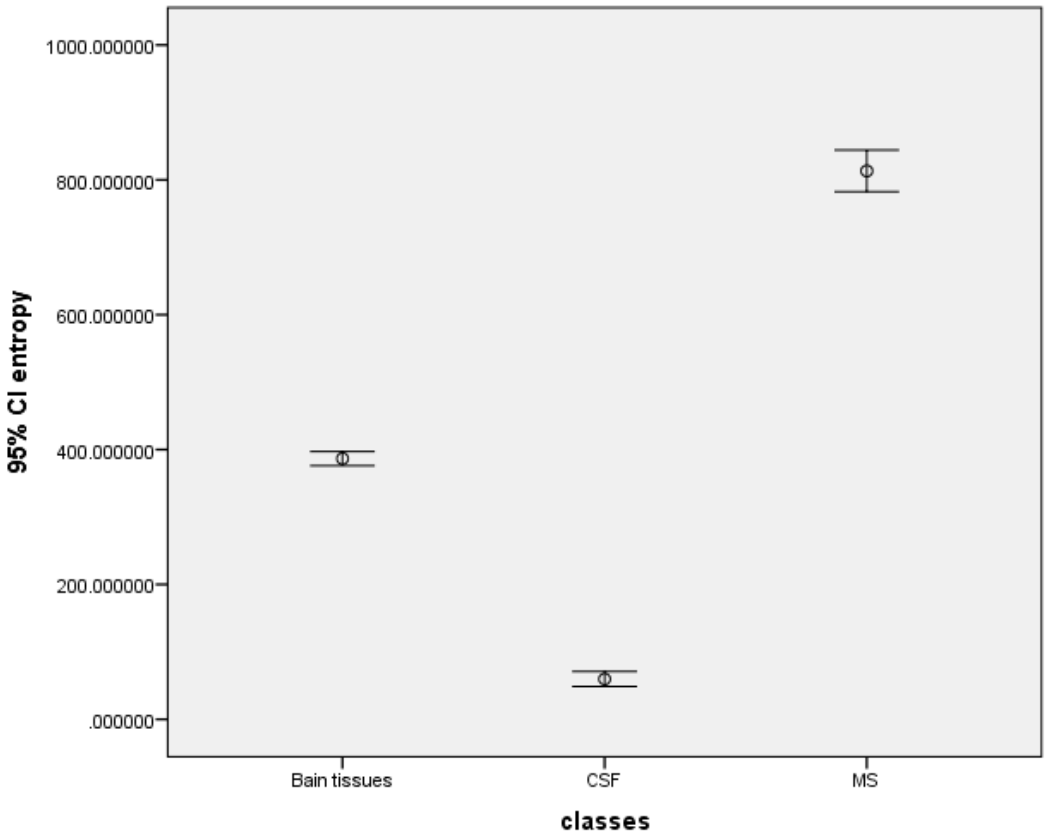


Fig 4-18: Error bar plot show the discriminate power of the entropy textural feature distribution for the selected classes

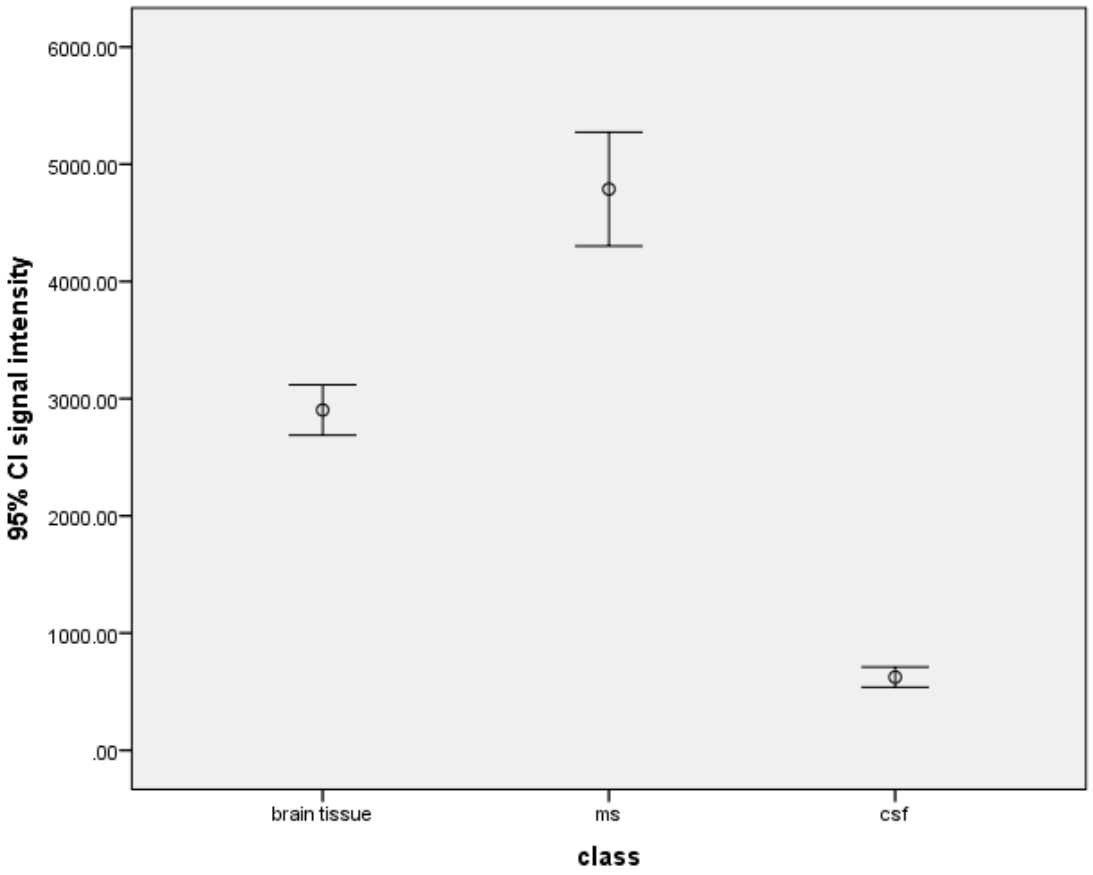


Fig 4-19: Error bar plot show the discriminate power of the signal intensity textural feature distribution for the selected classes

CHAPTER FIVE

5.1 Discussion

A correlation was made between the signal intensity in routine MRI protocol (5mm) and patient age where the signal increase by 0.253 every one year. while in the second protocol for the same patients the relationship were also direct but the signal increase by 0.307 for every one year but when we used the volume protocol the signal increase by 0.28 for every one year .where the slice in P.1 = 5mm slice thickness and gap =1

P2 = 3mm slice thickness and slice gap =0 and P3= volume flair 3D we recommended that the slice thickness has significant effect on the signal changes with age. R2 = 0.011, 0.012 and 0.007 for P1, P2 and P3 respectively.

In refer to T. Test the significant differentiate for the protocols used (p1, p2 and p3), pair sample T.Test was used.

(Cl = 95%) and (P – value = 0.05) which significant when ≤0.005. the result showed that there was a significant differences between P1 and P2 where the mean value for signal in P1 = 38.4 and P2 = 52.14.

P =0.0000.

Also pair sample used to differentiate between (p1 and P3) result showed there was a significant different between them. The mean value for signal in P1= 38.4 and P3 = 69.00.

P = 0.000

In this study, we found a significant result in terms of clinical diagnosis of patients with MS, that patients with headaches + vertigo and numbness are the most frequent

Followed by sufferers of headaches and vertigo only that ,was as follows Proportion of patients suffering from head +vertigo + numbness are 28.1% , headache + vertigo 26.6% , headache + + paraplegic 12.5% , headache +vertigo +blurring vision 10.9% headache +vertigo +diploma 9.4% ,headache + numbness +double vision 7.8% and headache +numbness 4.7%.

The preliminary investigations obtained from this study revealed that the patients participated in this study's women's with being more affected than men in regards with M S disease 28.1% male and 71.9% female, in this study including 18males and 46 females , this result was agree with Duquette, et al (1992).

regarding to this study we found that the delayed injection in the contrast substance 5 minute is more sensitive to the active MS plaque and the volume T1 is more accurate and sensitive to detecting MS plaque, and this remarks are agree with Ender Uysal1 Sukru Mehmet Erturk1 et al (2007).

Looking to this study, vitamin D deficiency results were as follows 57.8% yes and their number was 37, And 42.2 NO and their number was 27. This result indicates to relation between MS patients and vitamin D deficiency and there was one of the reason this disease and this results matches with Alberto et al (2014)

Concerning to this study we found the age group was more affected to this disease in ages between 34.4 to 40.2 and this result same within Terry DiLorenzo

In this study the most sensitive and efficient protocol in the detection of MS plaque was protocol 3 (3Dvolume FLAIR).

Protocol 3 1st: 3Dvolume FLAIR, 2nd: Axial T2 – Sagittal T2. 3rd: Gadolinium enhanced in 3Dvolume T1 fat saturation and T1 sequence. The modified protocol applied in this study represented by protocol 2 and this protocol was less efficient than protocol 3 in the detection of MS lesion, but can be applied in the absence of protocol 3 in the MRI machine used in hospitals.

Protocol 2: 1st FLAIR slice thickness 3mm slice gap 0 mm, 2nd: Axial T2 – Sagittal
3rd: Gadolinium enhanced in T1 slice thickness 3mm slice gap 0mm.
The routine protocol common applied in hospitals and radiological centers to detect MS was represented by protocol 1 .This protocol in this study showed a weak detection of MS lesion and active MS, but it is good in brain survey although it cannot cover all MS in the brain.
Protocol 1 : 1st Sagittal FLAIR slice thickness 5mm slice gap 1 mm , 2nd: 2DAxial T2 -sagittal T2, 3rd: Gadolinium enhanced in T1 slice thickness 5mm slice gap 1mm. The recent results of this study similar with the results of (Wolter.et al 2011) and (bink, A.,schmit,)et al (2006).

According to the results, obtained by the analysis the mean MS findings in protocol 1 was 38.41, in protocol 2 was 52.14 and in protocol 3 was 69.00 and this was strong significant value in protocol 3.

According to this study showed the vitamin D deficiency more affected them age group 22.8 - 28.5 and 34.4 - 40.2.

In this study the most important risk factor in MS disease was vitamin D deficiency, cross tabulation between gender and vitamin D deficiency showed female was more affected than male this finding matches with (Tina gissel et a 2009)

According to this study patient have a clinical diagnosis (headache + vertigo +numbness) was more affected by vitamin D deficiency.

For more accurate discrimination of signal intensity between different brain tissues texture analysis was use using 3*3 window for each DICOM image extracted for different.

A FOS (mean, variance, standard deviation, energy, entropy, skewness) was entered then using linear decrement analysis the selected feature was classes using LDA.

A classification accuracy of 96.7% was obtained, which the sensitivity for each class was 99.7%, 96.8% and 92.2% (brain tissues, CSF and MS respectively).This program clearly differentiate between different between these classes which match the routine protocol result .

But the classification map reveal some similarity between MS and brain tissue because the new MS plaques look like brain tissue.

CSF with brain step wise technique in LDA reveal the most significant feature that can be used for classification purpose is mean variance. Clear difference in signal

By using the mean, higher signal intensity noted for MS.

Signal intensity was the main focus to differentiate between different tested images regions of the brain structure as it key point to demonstrate that different.

A classification using signal intensity in error bar was reveal that the higher signal was for MS followed by brain tissue in which match the texture feature (mean)

As it calculated from these images and there was mark difference between MS-CSF-brain tissues.

And using homogenous signal acquired from CSF with mark deference between all classes using entropy feature, but energy reveal range of CSF and high energy value for brain tissue.

5.2 Conclusions:

The study concluded that: the advanced protocol is best in diagnosis multiple sclerosis Followed in the order modified protocol. Both protocol can be reconstructed in Multi planner reconstruction (MPR) and control slice thickness to detect any MS plaque old or new.

Volume T1 with contrast also very informative in new MS plaque, we suggest that there must be provided these protocols in MRI machine at least one protocol and working it for MS patients.

5.3 Recommendations

- Large sample can be used to have better overall accuracy using representative data set
- MRI technologist must training and aware importance about MS and MS protocol in diagnosis of MS
- MRI radiologist must training about MS protocol and diagnosis from it.
- Neuro physician must be aware about MS protocol and request form written it MS protocol.

References

- AJNR Am J Neuroradiol 27:455–461 Feb 2006

- AJNR Am J Neuroradiol19:1715–1720, October 1998

: initial result- EUROPEAN Radiology May 2006.

© 2011 National Multiple Sclerosis Society

AJR:188, March 2007

Canadian Journal of Neurological Sciences / Journal Canadien Des Sciences Neurologiques, 19(4), 466-471. doi:10.1017/S0317167100041664

Charles R.N. Norman L . S . Robert J . D , David .A.R , 2005 , The human nervous system: structure and function , human press , Sixth edition , New jersy , pag 2 -10 .
Eur Radiol (2012) 22:221 –231 DOI 10.1007/s00330-011-2242-z

European Journal of Neurology, 17: 634–637. doi:10.1111/j.1468-1331.2009.02850.x

Global Journal For Research Analysis, Volume-4, Issue-10, Oct-2015 • Issn No 2277 – 8160.

http://academic.kellogg.edu/herbrandsonc/bio201_mckinley/Nervous%20System.htm
http://apbrwww5.apsu.edu/thompsonj/Anatomy%20&%20Physiology.htm
http://faculty.irsc.edu/FACULTY/TFischer/AP1/AP%201%20resources.htm
http://fultoncountybraininjurysupportgroup.health.officelive.com/stem.aspx
http://legacy.owensboro.kctcs.edu/gcaplan/anat/Notes/API%20Notes%20L%20Central%20Nervous%20System-Brain.htm
http://legacy.owensboro.kctcs.edu/gcaplan/anat/Notes/API%20Notes%20L%20Central%20Nervous%20System-Brain.htm
http://megromancereviews.blogspot.com/2008/04/technical-difficulties-please-stand-by.html
http://radiology.rsna.org/content/196/2/505.short
http://webanatomy.net/anatomy/circulatory_notes.htm
http://webspace.ship.edu/cgboer/basalganglia.html
http://withealth.net/en/anatomy-of-the-ventricles-of-the-brain)
http://www.drpulp.com/2011/05/anatomy-and-osteology-of-cranium.html)
http://www.ncbi.nlm.nih.gov/pubmed/12637695
http://www.ncbi.nlm.nih.gov/pubmed/15304574
http://www.neurology.org/content/54/8/1557.abstract
http://yazoqem.hostoi.com/blood-flow-to-the-brain.php

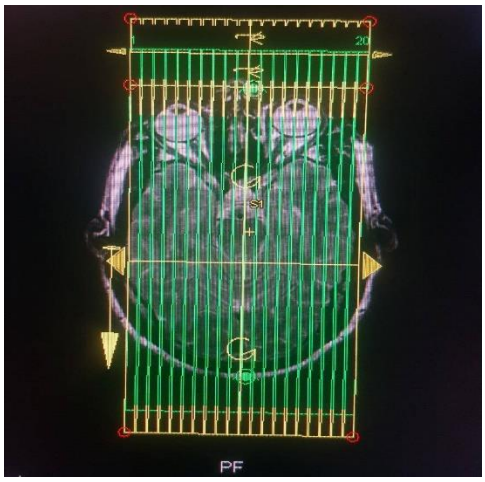
JAMA Neurology March 2014 Volume 71, Number 3.

Maria Antoniou , Patestas, Leslie P. Gartner, 2006, Textbook of neuroanatomy, first edition, , blackwell , Australia , 68-80

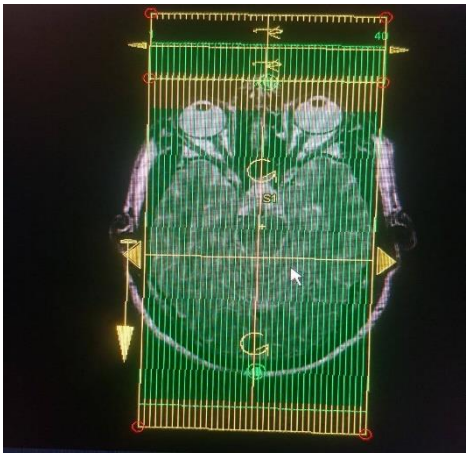
Martini, Frederic H, 2007, Anatomy and Physiology , pearson education , first edition , Singapore , pag 346- 348
National Multiple Sclerosis Society

O'R . rahilly , M uller , Carpenter and Swanson , 2008 , Basic Human Anatomy, 1st edition , O'Rahilly , Rand Swenson
Richards.s., second edition , clinical Nero-anatomy for medical study, (1987).,little Broun company, Boston, Torinto
Sudhir. V. Shah , 2008, Diseases of The Brain and Nervous System (A Health Education Guide) , 1st edition , Team Spirit ,India,25- 143

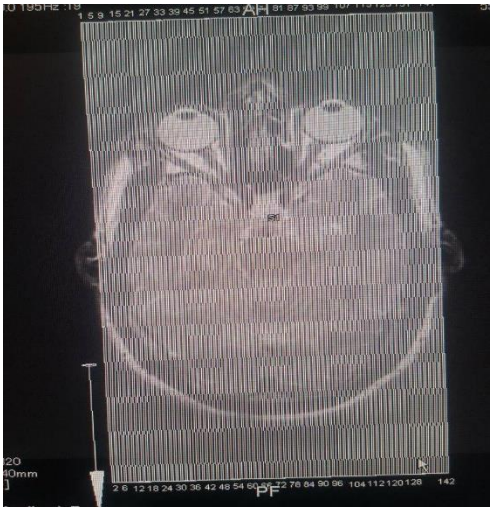
Appendix



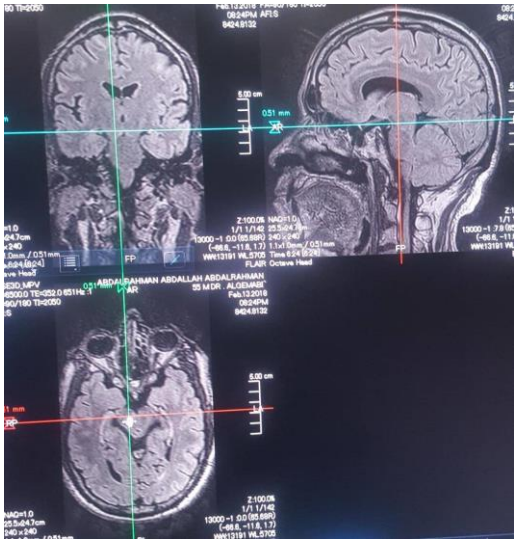
Routine protocol (5mm, gap 1mm)



modified protocol (3mm,gap 0.0)



Advance protocol (3D volume FLAIR)



MPR volume FLAIR