# Table of Contents

Introduction .................................................................................................................................................. 5

Brain Anatomy .............................................................................................................................................. 6

Forebrain ................................................................................................................................................... 7

Cerebrum .............................................................................................................................................. 7

Cerebral Cortex .................................................................................................................................... 7

White Matter .................................................................................................................................... 8

Basal Ganglia ................................................................................................................................... 10

Lateral Ventricles ............................................................................................................................ 12

Limbic System ..................................................................................................................................... 13

Diencephalon ...................................................................................................................................... 14

Midbrain ................................................................................................................................................ 15

Superior and Inferior Colliculi .................................................................................................................... 15

Substantia Nigrae and Red Nuclei ............................................................................................................... 15

Fiber Tracts .......................................................................................................................................... 16

Diseases and Disorders ....................................................................................................................... 16

Hindbrain ................................................................................................................................................ 17

Pons ..................................................................................................................................................... 18

Medulla Oblongata ............................................................................................................................. 18

Cerebellum .......................................................................................................................................... 18

Meninges................................................................................................................................................. 19

Dura Mater .......................................................................................................................................... 20

Arachnoid Mater ................................................................................................................................ 20

Pia Mater ............................................................................................................................................. 20

Meningitis ........................................................................................................................................... 21

Ventricular System and Cerebrospinal Fluid (CSF).................................................................................. 21

Ventricular System ................................................................................................................................ 21

Cerebrospinal Fluid (CSF) .................................................................................................................. 23

Disorders of the Ventricles and CSF .................................................................................................... 24

Cranial Nerves ......................................................................................................................................... 25

Cerebral Vasculature .......................................................................................................................... 26
Introduction

Welcome to the Hitachi Medical Systems America, Inc. MRI Anatomy and Positioning Series. We offer teaching modules to allow users of Hitachi MRI scanners to review anatomy that will be seen on various MRI exams, and to enhance their positioning skills. Competent positioning ensures the best possible image quality for your studies.

In this seventh module, we will examine the anatomy of the brain, broken down into the forebrain, midbrain, and hindbrain. We will discuss the meninges, the ventricular system and cerebrospinal fluid, the cranial nerves, and cerebral vasculature. We will explore the relevance of MRI in the characterization and diagnosis of pathology and diseases of the brain, especially in relation to strokes and dementia.

We will also review the imaging sequences and post processing applications available for examinations of the brain on Hitachi MRI systems. We will examine Time of Flight Angiography, Diffusion Weighted Imaging, Diffusion Tensor Imaging, Blood Sensitive Imaging, Perfusion Imaging, MR Spectroscopy, and Functional MRI.

We will review proper patient positioning in the Hitachi head coils, keeping in mind that RF coil cables should always be routed in a manner that will avoid contact with the patient. We will discuss the use of the table and accessory pads in conjunction with proper patient positioning in the head coil, as well as their use to assist in eliminating, or at least minimizing, the amount of each patient’s skin-to-skin, skin-to-bore, or skin-to-cable contact. Reducing the amount of each of the aforementioned contacts reduces the patient’s chances of thermal injury. Please refer to the MR Patient Warming Prevention Plan published by Hitachi Medical Systems America, Inc. for more information concerning the prevention of patient warming.

**CAUTION:** Always route coil cables away from the patient, using pads and/or cable covers to eliminate or minimize the chances of contact between the coil cable and the patient. Failure to do so could result in a thermal injury.

**CAUTION:** Always use the pads that are provided to eliminate or minimize the patient’s skin-to-skin, skin-to-bore, and skin-to-cable contact. Failure to do so could result in a thermal injury.
Brain Anatomy

The brain is one of the largest and most complex organs in the human body. It weighs approximately one pound at birth, and grows to about two pounds during childhood. The average female adult brain weighs about 2.7 pounds, while the average adult male brain weighs approximately three pounds. The bony covering of the brain is referred to as the cranium. When combined with the bones that make up the face, the entire structure is called the skull. The three main structures of the brain are the cerebrum, the cerebellum, and the brainstem. These three main structures, and additional brain structures, are grouped in the following manner:

1. Forebrain- Cerebrum (or telencephalon), limbic system, and diencephalon (which includes the thalamus, hypothalamus, epithalamus, and subthalamus)
2. Midbrain- Two cerebral peduncles, cerebral aqueduct, superior cerebellar peduncles, superior and inferior colliculi, and reticular formation; also called mesencephalon
3. Hindbrain- Medulla oblongata (or myelencephalon), pons, and cerebellum (both included in metencephalon)

![Figure 1 Forebrain, midbrain, hindbrain](image.png)
Forebrain

Cerebrum

The cerebrum is the largest part of the brain. It is responsible for movement, body temperature, touch, vision, hearing, judgment, reasoning, problem solving, emotions, and learning. The cerebrum is divided into right and left hemispheres, which are connected inferiorly, and have a deep groove (longitudinal fissure) running between them. The hemispheres look like mirror images in structure, but not in function. The speech area typically develops fully only on the left side. In general, the right hemisphere controls the left side of the body, and the left hemisphere controls the right side. The right hemisphere concentrates on visual, spatial, and musical orientations (creativity and artistic abilities), while the left hemisphere deals with the higher mathematical, analytical, and verbal functions (logic and rational thinking). The cerebrum is further divided into four major elements:

1. Cerebral cortex- outer cortex of gray matter
2. White matter- underlying cerebral cortex
3. Basal ganglia- masses of gray matter at the base of the cerebrum
4. Lateral ventricles

Cerebral Cortex

The cerebral cortex is the most highly evolved area of the brain. It controls perception, memory, and all higher cognitive functions, including the ability to concentrate, reason, and think in abstract form. It is approximately 1/6” thick, and is characterized by fissures (deep grooves), gyri (bulges between grooves), and sulci (furrows or smaller grooves). Many of the gyri and sulci on the brain's surface have specific names, and various regions of the brain have specific functions, i.e. prefrontal cortex, primary taste area, primary visual area. The cortex is highly folded in order to increase the cortical surface area that is available within the confines of the cranial area. If unfolded, the highly convoluted cortex of the brain would extend over two square meters (21.52 feet squared). The cerebral cortex is divided into lobes with distinct borders formed by sulci. There are four lobes in both the right and left hemispheres of the brain. Lobes are named for the cranial bones that cover them- frontal, parietal, temporal, and occipital.

The frontal lobes are the largest of the four lobes. They are distinguished from the parietal lobes posteriorly by the central sulci. The frontal and parietal lobes are separated from the temporal lobes inferiorly by the lateral sulci (or fissures). The frontal lobes are responsible for many different functions, including motor skills, such as voluntary movement and speech, as well as intellectual and behavioral functions, such as problem solving and judgment. The primary motor areas in the frontal lobes produce movement in parts of the body. The premotor cortices guide eye and head movements, and account for a person’s sense of orientation. The prefrontal cortices areas play an important part in memory, intelligence, concentration, temper and personality. Broca’s area, which is important in language production, is also found in the frontal lobe, typically on the left side. The primary olfactory areas are located inferiorly in the frontal lobes.

The parietal lobes are located posteriorly to the frontal lobes. They are distinguished from the occipital lobes by the parieto-occipital sulci on their medial surfaces. The parietal lobes are concerned with body sensory awareness, including taste, the use of symbols for communication (handwriting), abstract
reasoning, and body imaging. A person’s memory combined with new sensory information that is received here gives meaning to objects.

The occipital lobes are located at the back of the brain, and are the smallest lobes. They are the brain’s visual processing system. The occipital lobes enable humans to receive and process visual information, influencing how we process shapes and colors. The right occipital lobe interprets visual signals from the left visual space, and the left occipital lobe performs that function for the right visual space.

The temporal lobes are located at the level of the ears, separated from the frontal and parietal lobes by the lateral sulci. An area in the right temporal lobe is involved in visual memory and helps humans recognize objects and people’s faces. An area in the left temporal lobe is involved in verbal memory and helps humans remember and understand language.

Figure 2 Lobes of cerebral cortex

**White Matter**

White matter accounts for almost one half of the brain’s volume, and forms most of the deeper parts of the brain. It is made up of densely packed collections of the myelinated projections of neurons (nerve cells) that course between the widely dispersed areas of gray matter. White matter joins all four lobes of the brain, and the brain’s emotion center in the limbic system, into complex brain maps. It appears that white matter provides the essential connectivity in the brain, uniting these different regions into networks that perform various mental operations. If this connectivity is disrupted by disease or other damage to white matter, the result is often a dramatic disturbance of normal mental function.

White matter is so named due to the appearance and composition of its nerve fibers. At the cellular level, brain functions are carried out by nerve cells called neurons. Attached to the body of each neuron are multiple short dendrites, which receive information from other neurons through electro-chemical impulses. The neuron body processes the information, then uses another electro-chemical impulse to send the information on to another cell via its axon. Axons are the longer nerve fibers (up to three feet in length), and each neuron generally has only one. Axons are lined with myelin, which serves as electrical insulation, and increases the speed of conduction of information. Myelin is roughly seventy percent lipid and thirty percent protein. The high percentage of fat in these myelin insulating sheaths, combined with the concept that millions of axons are closely packed together, gives certain areas of the
brain a whitish hue. The white matter areas of the brain are mainly composed of axons coated with myelin, while the gray matter areas are predominantly the cell bodies of the neurons.

![Diagram of a neuron](image)

Figure 3 Diagram of a neuron

The myelinated axons cluster together to form thicker bundles or fibers. The fibers are arranged in tracts within the white matter that serve to connect one part of the brain to another and to the spinal cord. Projection tracts extend vertically between the higher and lower brain and spinal cord centers, and carry information between the cerebrum and the rest of the body. The thalamus and the cortex communicate by this pathway. Association tracts connect structures in different regions within the same cerebral hemisphere. Long association fibers connect different lobes of a hemisphere to each other, while shorter association fibers connect different gyri within a single lobe. One of the roles of association tracts is to link perceptual and memory centers of the brain. Commissural tracts cross from one cerebral hemisphere to the other through bridges called commissures. These tracts enable the left and right hemispheres of the cerebrum to communicate with each other. The great majority of commissural tracts pass through the large corpus callosum, which is a collection of white matter fibers that joins the two cerebral hemispheres inferiorly. The corpus callosum also serves as a roof over the lateral ventricles. Smaller anterior and posterior commissures are present and accommodate a few commissural tracts. In the cerebrum, messages for movement and sensation cross to the other side of the brain, and cause the opposite limb to move or feel sensation. The right side of the brain controls the left side of the body and vice versa.

![Lateral view of projection, association, and commissural tracts (or fibers)](image)

Figure 4 Lateral view of projection, association, and commissural tracts (or fibers)
The major non-neuronal cells found in the brain and nervous system are the glial cells. They do not have dendrites and axons, but provide support and regulatory functions for neurons so that neurons can function more effectively. Glial cells supply nutrients and oxygen to the neurons. Evidence suggests that glial cells aid, or prevent recovery from neuronal injury, and are involved in a number of diseases, including Alzheimer’s and multiple sclerosis. The glial cells typically found in the brain and central nervous system include astrocytes, oligodendrocytes, and microglia. Astrocytes play a role in creating the blood-brain barrier, which allows certain substances to selectively pass from the capillary system. They are also responsible for reactive scar formation in the brain. Oligodendrocytes form myelin, which serves to electrically insulate the axons of the nerve cells, allowing for increased rates of conduction. Microglia function as the brain’s immune system. Glial cells are the most common cells found in primary brain tumors. The tumors are named based on the tissue type that is discovered after biopsy. The type of cells involved, and the type of tumor both have great impact on the patient’s treatment and prognosis.

References vary widely in their estimates of the number of glial cells vs. neurons in the brain. Some purport that glial cells outnumber neurons by about fifty to one, with over 100,000 million neurons in the brain. Estimates also state that there are more than 10,000 million cells in the cerebral cortex alone, and more than 100 billion nerves communicating in trillions of connections called synapses. Others hypothesize that glia and neurons are closer to a 1:1 ratio, but their numbers are different in different parts of the brain. They speculate that there are more neurons than glia in the cerebellum, while glia are in greater numbers in the white matter, with their highest numbers found in the gray matter of the cortex.

**Basal Ganglia**

The basal ganglia, or basal nuclei, are islands of gray matter in a sea of white matter. They are situated at the base of the hemispheres, on either side of and above the diencephalon, which is the area that contains the thalamus. The basal ganglia are responsible for a great deal of motor control and procedural learning. This area of the brain works in conjunction with the cerebral cortex, the thalamus, and the brainstem to help us make decisions, coordinate voluntary movements, and shift between activities. The gray matter in the basal ganglia acts like the brain’s traffic grid, directing the sensory and motor-related information from the sensory organs throughout the body. The basal ganglia are also
reported to have an effect on motivation, in both healthy and diseased states. Motivation can be helpful, or in some cases, harmful. This portion of the brain is known as the reward center, and is responsible for feelings of euphoria. Eating tasty food, having sex, and the use of certain drugs can all trigger pleasure responses deep in the brain. Cocaine and nicotine boost the dopamine receptors in this area of the brain, which increases the payoff of exposure to those substances. The larger components of the basal ganglia are named, and are associated with certain brain functions.

The putamen is the largest and outermost basal ganglia, located lateral to the thalamus on each side of the brain. Its main function is to regulate movements and influence various types of learning. The putamen does not appear to have a specialization, but is interconnected with many other structures, working with them to control many types of motor skills. The putamen and caudate nucleus together form the dorsal striatum, and are considered the “entrance” to the basal ganglia. The striatum receives input from many areas of the cerebral cortex, but only sends output to other components of the basal ganglia. The putamen is also paired with the globus pallidus to form the lenticular (or lentiform) nucleus.

As mentioned above, the caudate nucleus forms the dorsal striatum with the putamen. There is a caudate nucleus in each hemisphere of the brain, sitting astride the thalamus near the center of the brain. The caudate nucleus is involved with voluntary movement, learning, memory, sleep, and social behavior. MR studies have shown a decrease in the volume of the caudate nucleus in Alzheimer’s patients, as well as asymmetry of the caudate nuclei in patients with symptoms of ADHD (attention-deficit hyperactivity disorder). It has been theorized that the caudate nucleus may be dysfunctional in persons with OCD (obsessive compulsive disorder).

The globus pallidus was also previously mentioned due to its association with the putamen in forming the lenticular nucleus. The globus pallidus is located lateral to the thalamus and inferior to the caudate nucleus in each hemisphere. It has internal and external segments, with the external segment in the more lateral position, closest to the putamen. The globus pallidus is integral in the control of voluntary movements at the subconscious level, and is involved in posture control. It has a primarily inhibitory action that balances the excitatory action of the cerebellum. These two systems are designed to work in harmony with each other to allow people to move smoothly, with even, controlled movements.

The substantia nigra is a formation of basal ganglia, but is considered to be part of the midbrain rather than the forebrain. Humans have two substantiae nigrae, one on each side of the midline. They are found dorsal to the cerebral peduncles, and inferior to the thalamus. The substantia nigra is the brain’s largest dopamine-producing center. Dopamine is a neurotransmitter, which is a type of chemical that is essential for the movement of electrical signals between brain cells. This chemical has many roles in the brain, and can affect behavior, sleep, mood, and memory. The substantia nigra is divided into two parts that have very different connections and functions. The pars compacta, which lies more medially, serves as an input to the basal ganglia circuit, supplying the striatum with dopamine. The pars reticulata serves mainly as an output, and conveys signals from the basal ganglia to numerous other brain structures. The substantia nigra is important in brain function, especially with regards to eye movement, motor planning, reward-seeking, learning, and addiction. It also plays a role in Parkinson’s disease, schizophrenia, and cocaine addiction, due to its involvement with dopamine production.

The subthalamic nucleus is the remaining “named” nucleus of the basal ganglia. On a coronal image, it is located just inferior to the thalamus, and superior to the substantia nigra. The function of the subthalamic nucleus is associated with the globus pallidus, in that both act as pacemakers. They fire in sync with each other, exciting any neurons to which they are connected. Increased neuronal activity in
the subthalamic nucleus has been implicated in the motor dysfunction of Parkinson’s disease. Creating lesions in this structure improves motor function in patients with Parkinson’s disease, but can cause neurologic deficits. Some Parkinson’s patients that are no longer benefitting from medical therapy find improvement through deep brain stimulation of the subthalamic nucleus. This treatment simulates the effects of a lesion in this structure, which improves the patient’s motor function without destroying any brain tissue.

**Lateral Ventricles**

The lateral ventricles of the cerebrum are two of the total of four fluid-filled cavities found in the brain. They are the largest of the ventricles, and are the most superior portion of the brain’s ventricular system. One lateral ventricle is located in each of the brain’s two hemispheres. The ventricles, and the cerebrospinal fluid that they produce, will be discussed at greater length in the Ventricular System portion of this seminar.
Limbic System

The limbic system, also referred to as the limbic lobe, incorporates parts of the frontal, parietal, and temporal lobes. The limbic system is not a specific structure, but rather a series of nerve pathways that incorporates other structures, such as the hippocampus and the amygdala. It forms connections with the cerebral cortex, white matter, and brainstem. This system lies deep within the temporal lobes, buried under the cortex and on top of the brainstem. The limbic system is also called the “emotional brain”. It has a role in controlling emotions, decisions, learning, and motivation, particularly those that are related to survival. This system is also involved in the processing and storage of recent memory, and in control of appetite and emotional responses to food. All of these functions are frequently affected in patients suffering from depression, leading to the limbic system being implicated in the origins and effects of this disease. The limbic system is also linked with parts of the neuroendocrine and autonomic nervous systems. Certain nuclei within the cerebrum’s white matter are considered to be part of the limbic system, and are involved in the expression of emotions, the release of hormones from the pituitary gland, and in regulation of food and water intake. Some psychiatric disorders, such as anxiety, are associated with both hormonal and autonomic changes, which may further link them to the limbic system.

The limbic system integrates many additional brain structures. Both the amygdala and the hippocampus play important roles in memory. The amygdala is responsible for determining which memories are stored and where they are stored in the brain, as well as having involvement in emotional responses and hormonal secretions. It is theorized that the determination of memory storage is based on the size of the emotional response caused by an event. The hippocampus acts as a memory indexer- sending out memories to the appropriate part of the cerebral hemisphere for long-term storage, and retrieving them when necessary. Damage to this area of the brain may result in an inability to form new memories. The cingulate gyrus is a fold in the brain that is involved with sensory input concerning emotions, and the regulation of aggressive behavior. The olfactory cortex receives sensory information from the olfactory bulb and is involved in the identification of odors. The fornix is an arcing, fibrous band of nerve fibers that connects the hippocampus to the hypothalamus.
Diencephalon

The diencephalon is situated between the cerebral hemispheres, superior to the midbrain. It relays sensory information from the rest of the body to the cerebral cortex, and controls many autonomic functions, such as body temperature, heart rate and blood pressure. The diencephalon connects structures of the endocrine system with the nervous system, as well as working in conjunction with limbic system structures to generate and manage emotions and memories.

The structures of the diencephalon include the thalamus, hypothalamus, epithalamus, and subthalamus. The thalamus is a mass of gray matter cells divided into two lobes that are arranged around the third ventricle. It is the relay station for sensory impulses that come from other parts of the brain, and which are forwarded to other regions of the brain for interpretation. It plays a role in pain, touch, and temperature sensation, as well as attention and alertness. The optic nerve fibers cross over in the thalamus, so damage to this area can adversely affect vision.

The hypothalamus embraces the infundibular recess, which is the funnel-shaped floor of the third ventricle. It contains nerve connections that send messages to the pituitary gland, and handles information coming from the autonomic nervous system. The hypothalamus has a role in controlling many functions, including eating, sleeping, sexual behavior, body temperature, emotions, secretion of hormones, and movement. It also has close connections with various parts of the brain including the frontal lobe, the hippocampus, the thalamus, the brainstem, the spinal cord, the basal ganglia, and the pituitary gland. The pituitary gland develops from a downward extension of the hypothalamus in an area called the pituitary fossa or sella turcica. This gland is approximately the size of a dime, but is referred to as the “master gland” due to the many functions that it controls and coordinates. The pituitary gland is involved in the functioning of various body organs (kidneys, breast, uterus), the functioning of other glands (thyroid, gonads, and adrenal glands), as well as secreting the hormones responsible for normal growth and sexual maturation.

The epithalamus consists primarily of the pineal body, as well as related nuclei and tracts that have connections with the thalamus, hypothalamus, basal nuclei, and medial temporal cortex. The pineal gland is an outgrowth from the posterior portion of the third ventricle, and the only unpaired structure in the brain. This gland produces melatonin, which is a pigment-enhancing hormone, as well as a hormone that influences sexual development and sleep-wake cycles.

The subthalamus is located between the thalamus and the midbrain just superior to the hypothalamus. It is closely integrated with the basal ganglia, and contains two previously mentioned basal ganglia areas - the subthalamic nucleus and substantia nigra. The subthalamus plays a role in the modulation of movement. This area is also involved in sensory perception, which is the conscious mental capacity to register, process, and act upon sensory input. Due to this sensory involvement, the subthalamus and the thalamus region hold integral parts in the body’s sleep-wake cycle. They are involved in the brain’s ability to control when the body is at rest, or when consciousness is activated to sort out sensory stimuli during periods of being awake. Damage to the thalamus or subthalamus region can interfere with motor abilities, sensation, mood or sleep patterns.
Midbrain

The midbrain, or mesencephalon, is approximately two centimeters in length, and sits between the forebrain and hindbrain, specifically between the diencephalon and the pons. The midbrain forms the superior aspect of the brainstem, which is the portion of the brain that connects the spinal cord and the forebrain’s cerebral cortex. It contains several important reflex centers that help control posture and balance, hearing, movement of the head and eyes in a coordinated way, visual reflexes and responses to auditory stimuli.

Superior and Inferior Colliculi

The tectum is the dorsal roof of the midbrain, and controls visual and auditory reflexes. It is divided into the corpora quadrigemina, which consists of two superior and two inferior colliculi. The colliculi are the control centers for visual and auditory reflexes. They relay information to the thalamus, which sends the information on to the cerebral cortex. The superior colliculi are located below the thalamus, and are the visual reflex centers, coordinating head and eye movements during tracking of a moving object. The inferior colliculi are the auditory relay areas, and aid in sound localization. The tectum and the four colliculi are the first step of the neural pathway that determines how people react to what they see and hear.

Substantia Nigrae and Red Nuclei

The region beneath the colliculi is called the tegmentum, which forms the floor of the midbrain. The tegmentum surrounds the cerebral aqueduct, which connects the third and fourth ventricles. Motor skills and basic awareness are dependent on this part of the brain. The tegmentum also regulates autonomic functions, which are those acts that the body carries out without conscious thought. This would include digestion, heart rate, and breathing rate. Within the tegmentum are found the substantia nigrae, red nuclei, and nuclei of the reticular formation. The substantia nigrae are functionally linked to the basal ganglia, and were reviewed in the basal ganglia section of this seminar. They are the largest nuclei in the midbrain and are pigmented by melatonin. The substantia nigrae are located behind the cerebral peduncles, which are fiber tracts in the midbrain. The red nuclei are found between the
substantia nigra and the cerebral aqueduct. Their reddish color comes from iron in the form of hemoglobin and ferritin. They are involved in motions such as the crawling of babies, arm swinging in typical walking, and have minimal control over hand motion. Reticular formation nuclei are scattered in the tegmentum, and are also found in the brainstem. They have a role in stereotypical behavior patterns, as well as wakefulness, degree of arousal, and sleep patterns.

**Fiber Tracts**

Two large fiber tracts traverse the midbrain, which are the cerebral peduncles and the superior cerebellar peduncles. The cerebral peduncles are located on the ventral or anterior aspect of the midbrain. They divide the brain into two halves, with each half further divided into anterior and posterior parts by the substantia nigra. The cerebral peduncles are separated from the tectum by the cerebral aqueduct, also known as the aqueduct of Sylvius. The superior cerebellar peduncles are located posteriorly, and connect the midbrain to the cerebellum.

**Diseases and Disorders**

Common diseases and disorders of the midbrain include Parkinson’s disease, stroke, and a possible link to certain mental illnesses. Parkinson’s is a progressive illness that develops when dopamine-producing nerve cells in the pars compacta of the substantia nigra die off in large numbers. These nerve cells are important in regulating motor function and emotion, and their death leads to symptoms such as tremors, physical instability, and emotional changes. Medications used to treat Parkinson’s provide the brain with additional dopamine, but also have side effects and are not always effective.

A stroke in the midbrain typically occurs in the posterior cerebral artery, which is less common than those that affect the anterior or middle cerebral arteries. Midbrain strokes typically affect an individual’s motor and sensory functions, including speech, vision, body movement, and sensation. They are usually
the result of a cardioembolism and cause irreversible damage. Treatment is centered on rehabilitation and additional stroke prevention.

The midbrain is also linked to some forms of mental illness. Researchers have noted that dopamine production is often abnormally high in people with certain mental illnesses, such as schizophrenia. The most effective medications for the treatment of psychosis are those that reduce dopamine activity. In addition, the substantia nigra, where most dopamine is produced, has been seen to undergo structural and cellular changes in a person with schizophrenia.

**Hindbrain**

The hindbrain is located at the rear of the skull, and is the lowest portion of the brain. It consists of the pons, the medulla oblongata, and the cerebellum. These structures function collectively to support vital bodily processes. The pons and medulla of the hindbrain join the midbrain to form the brainstem, which extends from the upper cervical spinal cord to the diencephalon of the cerebrum. The brainstem is involved in alertness and in monitoring basic survival functions such as breathing, heartbeat, blood pressure, consciousness, cardiac function, involuntary muscle movements, swallowing, movement of the eyes and mouth, relaying sensory messages (pain, heat, noise, etc.), and hunger. Messages from the cerebral cortex to the spinal cord and nerves that branch from the spinal cord are sent through the pons and brainstem. Destruction of these regions of the brain will cause “brain death”. The cerebellum is highly involved in maintaining equilibrium and the coordination of muscle activities and movement. The fourth ventricle is also located in the hindbrain, posterior to the pons and the upper portion of the medulla oblongata.
Pons

The pons is a round protuberance on the brain stem that lies between the midbrain and the medulla oblongata, and forms the floor of the fourth ventricle dorsally. It is located in the upper hindbrain, serving as a bridge to connect the brainstem and the cerebellum, and relaying information between the medulla oblongata, cerebrum, and cerebellum. Fiber tracts called the middle cerebellar peduncles cross the fourth ventricle and the pons to reach the cerebellum. The pons contains centers that impact the rate and depth of respirations, and is involved with coordinating facial movements, facial sensation, hearing and balance. It receives information from visual areas to control eye and body movements, and plays a role in controlling patterns of sleep and arousal. The pons relays information to the cerebellum to control coordination of muscular movements and maintain equilibrium. Damage to the pons can result in an inability to close the mouth, chewing difficulty, atrophy of the muscles involved in chewing, visual problems, a serious loss of coordination in motor functions of the head, neck and face, and/or hearing problems.

Medulla Oblongata

The medulla oblongata, or simply medulla, is inferior to the pons, and is joined to the spinal cord. The medulla is located at the point where the spinal cord enters the skull. It serves as the connection between the brainstem and the rest of the brain, as well as connecting the brain to the spinal cord to allow communication between the brain and the rest of the body. The inferior cerebellar peduncles carry fiber tracts from the spinal cord and vestibular centers in the medulla. The medulla is home to many life-sustaining control centers- a respiratory center to regulate breathing, a cardiac center that can increase or decrease heart rate, and a vasomotor center that regulates how blood vessels dilate and constrict, thereby affecting blood pressure. It also has a role in regulating reflexes, and maintaining muscle tone and upright posture.

Cerebellum

The cerebellum is located at the back of the brain, beneath the occipital lobes and posterior to the brainstem. The cerebellum and brainstem occupy the area called the posterior fossa, and they are attached to each other by the cerebellar peduncles. The peduncles are paired bundles of nerves that carry impulses from one area of the brain to another. The superior cerebellar peduncles connect the cerebellum to the midbrain, the middle pair connect with the pons, and the inferior cerebellar peduncles connect the cerebellum with the medulla oblongata. The vermis, a word which means “wormlike structure”, is midline and connects the two hemispheres of the cerebellum. The cerebellum is separated from the inferior portions of the occipital lobes of the cerebrum by the tentorium cerebelli, which is an extension or fold of dura mater. The tentorium is clinically significant as brain tumors are often characterized as to their location in regards to the tentorium- supratentorial (above the tentorium) or infratentorial (below the tentorium). Different tumors occur with different frequencies in each location. In addition, most childhood primary brain tumors are infratentorial, while most adult primary brain tumors are supratentorial.

The cerebellum has a cortex of gray matter on its surface, with finely spaced parallel grooves that stand in contrast to the broad, irregular convolutions of the cerebral cortex. The cerebellar cortex is tightly folded in the style of an accordion, and divided into smaller “lobules”. Underneath the gray matter of the cortex are bands of white matter, made up largely of myelinated nerve fibers running to and from the cortex. The white matter is often referred to as the arbor vitae, which means tree of life, due to its
branched tree-like appearance in cross-section. Embedded in the white matter are four deep cerebellar nuclei composed of gray matter, which are motor-related. The cerebellum contains more nerve cells than both cerebral hemispheres combined, but takes up only about ten percent of the total brain volume. Unlike the cerebrum, the right side of the cerebellum controls the right side of the body, with the left side controlling the left. Right-side abnormalities will produce symptoms on the right side of the body.

The cerebellum has many important functions. It fine tunes motor activity or movement, helping one to maintain posture and a sense of balance or equilibrium by controlling the tone of muscles and position of limbs. The cerebellum is critical for the coordinated movements required for normal gait in walking or running. It is highly involved in position sense, which is the innate ability to know where your arms and legs are in space without having to see them. The cerebellum is important in one’s ability to perform rapid and repetitive actions that require fine motor skills, such as playing video games. It also coordinates sensory input from the inner ear and muscles to provide accurate control of position and movement.

![Figure 14 Lateral view of hindbrain](image)

**Meninges**

The meninges are the three layers of fibrous coverings that protect the central nervous system, which includes the brain and spinal cord. In the skull, they are found between the cranium and the brain, and include the dura mater, the arachnoid mater, and the pia mater.
Dura Mater

The dura mater is the dense, fibrous outermost meningeal covering. It consists of an outer periosteal layer, and an inner meningeal layer. The outer layer of the dura mater is closely applied to the cranial bone as periosteum. The inner layer contains four infolded areas, with the largest being the falx cerebri. This infolding of dura mater is created where the inner layer splits off the cranial roof in the midline bilaterally. It encloses the venous superior sagittal sinus, and descends in the longitudinal fissure between the cerebral hemispheres as the falx cerebri. This layer of dura mater is attached anteriorly at the crista galli and posteriorly at the internal occipital protuberance. The falx cerebri arches over the corpus callosum, and encloses the inferior sagittal sinus in its free border. The tentorium cerebelli is the second largest infolded area. It attaches to the falx cerebri, which gives it a tentlike appearance. The tentorium cerebelli separates the occipital lobes of the cerebrum from the cerebellum. Inferior to the tentorium cerebelli is the falx cerebelli, which is a vertical infolding. It separates the paired cerebellar hemispheres. The smallest infolding is the diaphragma sellae, which covers the pituitary gland and the sella turcica. The inner layer of dura mater is continuous with the spinal dura mater.

A potential space called the subdural space exists between the inner dura and the arachnoid mater, which is the meningeal layer that is deep to the inner dura. This space is only appreciable when there is underlying pathology, usually due to injury or illness. Bridging veins that drain from the underlying brain to the dura mater are easily placed under high tension. When the underlying brain becomes atrophic, as can occur in the elderly, these vessels are under higher than normal tension. Bleeding from these bridging veins can occur, and strip the dura away from the arachnoid mater, resulting in a blood collection known as a subdural hematoma.

Arachnoid Mater

The middle element of the meninges is the filmy and vulnerable arachnoid mater, so named because of its spider web-like appearance. It lies deep to and flush with the inner dura, and adheres to the dura via a series of tight junctions. The arachnoid mater is separated from the deeper pia mater by the subarachnoid space, which is filled with CSF. The subarachnoid space becomes voluminous at points around the brain, typically at areas where there are flexures. These areas are called cisterns, with names based on their locations. They include the superior cistern, found above the cerebellum; the cerebello-medullary cistern, located inferior to the cerebellum and adjacent to the medulla; the pontine cistern, found at the juncture of the pons and medulla; the interpeduncular cistern, located anterior to the cerebral peduncles. The subarachnoid space is the location of major blood arteries that supply blood to the brain. It is also the interface between vascular tissue and CSF, and is active in the blood brain barrier.

Pia Mater

The pia mater is a thin vascular layer of fibrous connective tissue. It is inseparable from the surface of the brain and cord, and is pierced by the blood vessels that travel to the brain and spinal cord. The subarachnoid space separates the pia and arachnoid layers, with the pia mater loosely connected to the arachnoid mater.
Meningitis

Meningitis is an inflammation of any of the above-mentioned meningeal layers that cover the brain and spinal cord. Meningitis typically develops in response to bacteria or viruses, but can also be caused by physical injury, cancer, certain drugs, or fungal infections. Viral meningitis is the most common and the least dangerous. It is caused by viruses, typically enteroviruses that live in the intestines. These viruses can be spread through food, water, or contaminated objects, occurring most often in babies and young children.

Bacterial meningitis is usually more severe, and can cause serious complications, such as brain damage, hearing loss, learning disabilities, and even death. The leading causes of bacterial meningitis in the US include Haemophilus influenza, Streptococcus pneumonia, and Neisseria meningitides. Different types of bacteria are prevalent with different age groups. Most of the bacteria that cause meningitis are not as contagious as the viruses that cause the common cold or flu. However, these bacteria can spread due to close or long contact with an infected person, or direct contact with a patient’s oral secretions. Bacterial meningitis can also occur due to a person’s risk factors, such as head trauma, or a compromised immune system. There are vaccines to prevent some forms of bacterial meningitis.

Ventricular System and Cerebrospinal Fluid (CSF)

Ventricular System

The ventricular system is involved in the production and circulation of cerebrospinal fluid (CSF). It consists of four interconnected cavities, or ventricles, in the brain- two lateral ventricles (the first and second ventricles) in the cerebrum, the third ventricle in the diencephalon, and the fourth ventricle in the hindbrain.

The two lateral ventricles are located in the cerebrum portion of the forebrain, with one ventricle in each hemisphere. They are roughly horseshoe shaped, with each lateral ventricle comprised of a central region and three horns. The horns are aptly named for their locations- the anterior or frontal horns, the posterior or rear horns, and the inferior or temporal horns. The corpus callosum lies above the anterior horns, serving as their roof. The curved shape of the lateral ventricles enables them to pass through all
four lobes of the brain—frontal, temporal, parietal, and occipital. The lateral ventricles are connected with the centrally located third ventricle by the small, paired interventricular foramina, also known as the Foramen of Monro. These foramina allow for flow of CSF from the lateral ventricles to the third ventricle.

The third ventricle is located in the diencephalon, which is also a part of the forebrain. It lies in the midline, with the thalamus and the hypothalamus located on its sides. The third ventricle circulates CSF to the fourth ventricle through the long, narrow cerebral aqueduct, or Aqueduct of Sylvius.

The fourth ventricle is found in the hindbrain, posterior to the pons and the upper half of the medulla oblongata, and is the most inferior of the ventricles. The fourth ventricle extends from the cerebral aqueduct to the caudal tip of the ventricle, which is called the obex. The obex is a marker for the level of the foramen magnum of the skull, and an “imaginary” dividing line between the medulla and the spinal cord. The roof of the fourth ventricle is formed by the cerebellum, the floor by the rhomboid fossa, and the side walls by the cerebellar peduncles. In cross-sections of the brain, the fourth ventricle has a characteristic diamond shape. CSF passes from the fourth ventricle into the subarachnoid space around both the brain and spinal cord via three small foramina—two lateral foramina of Luschka, and the single midline foramen of Magendie.

From the subarachnoid space that lines the cerebral hemispheres, CSF is absorbed into the venous circulatory system. Structures within the superior sagittal sinus called arachnoid villi release the CSF back into the venous sinuses. CSF then passes through the jugular vein and major venous system. CSF around the spinal cord can flow all the way down to the lumbar cistern around the cauda equina, which is the location for the performance of lumbar punctures.
Cerebrospinal Fluid (CSF)

Cerebrospinal fluid (CSF) is produced by a network of specialized cells called the choroid plexus. Choroid plexuses are found in the lining of all components of the ventricular system, except the anterior and posterior horns of the lateral ventricles, and the cerebral aqueduct. CSF is formed as plasma is filtered from the blood through the epithelial cells of the choroid plexus. These epithelial cells actively transport sodium, chloride, and bicarbonate ions into the ventricles, with water following the resulting osmotic gradient. The choroid plexuses also act as a filtration system, removing metabolic waste, foreign substances, and excess neurotransmitters from the CSF. These networks have a very important role in helping to maintain the delicate extracellular environment required by the brain to function optimally.

CSF is produced at a rate of about 450 mL/day. At any given time, about 150 mL can be found within the CSF spaces. The volume of CSF in most adults is turned over approximately three times per day. CSF is constantly absorbed and replenished, with the brain maintaining the balance between production and absorption.

Besides providing chemical stability and nutrients needed by the brain, CSF provides buoyancy and support to the brain against gravity. The brain and CSF are similar in density, so the brain floats in neutral buoyancy, suspended in the CSF. This allows the brain to grow in size and weight without resting on the floor of the cranium, which would destroy nervous tissue. CSF also helps to maintain the proper pressure around the skull, and acts as a shock absorber to protect the brain from injury when the head is jolted or struck.
Disorders of the Ventricles and CSF

The narrowness of the cerebral aqueduct and the foramina means that they can become easily blocked. Ventricular blockage or decreased CSF absorption can lead to high intracerebral pressure, which can cause significant brain damage if left unchecked. An increase in pressure in the ventricles and excessive accumulation of fluid in the brain are signs of hydrocephalus.

Hydrocephalus can be congenital or acquired, and affects about one out of every 500 children. It can lead to enlargement of the head, as the bones of a child’s skull are not yet fused. If CSF can still flow among the ventricles, the condition is termed communicating hydrocephalus. If CSF is blocked, the condition is called noncommunicating or obstructive hydrocephalus. Both conditions are most often treated by surgically inserting a shunt system. Normal pressure hydrocephalus is an obstructive hydrocephalus that is most commonly seen in the elderly. It may result from a subarachnoid hemorrhage, head trauma, infection, tumor, complications of surgery, or none of these factors.

Of the four ventricles, the lateral ventricles are the most likely to experience meningiomas, which are tumors that form on the membranes that cover the brain and spinal cord just inside the skull. Intraventricular meningiomas account for 0.5-3% of all intracranial meningiomas. These tumors are
usually benign, and often produce no symptoms at all. They can be surgically removed if they cause problems such as impaired vision or intracranial pressure. Other diseases of the ventricular system include meningitis, which is inflammation of the membranes, and ventriculitis, which is inflammation of the ventricles. These inflammations can be caused by infection or by the introduction of blood following trauma or hemorrhage in the cerebrum or subarachnoid areas. Enlarged ventricles have been associated with organic dementia as well as schizophrenia, but proof of cause and effect is not conclusive. MRI has replaced CT as the modality of choice for research into the role of ventricular abnormalities in psychiatric illness.

### Cranial Nerves

There are twelve pairs of cranial nerves. Cranial nerves I and II are derived from the forebrain, while all others are derived from the brain stem, including nerves V through VIII that originate from the pons. The cranial nerves are listed below with their names, numbers, and brief descriptions of their functions.

I. Olfactory- Sensory fibers that conduct impulses from the mucous membranes of the nose to the brain

II. Optic- Sensory fibers that conduct impulses from the retina to the brain

III. Oculomotor- Motor fibers that innervate most of the muscles of the eyeball; eye movements, eyelid opening

IV. Trochlear- Motor fibers that innervate the superior oblique muscle of the upper part of the eyeball

V. Trigeminal- Motor fibers that innervate the muscles of mastication (chewing) and sensory fibers that conduct impulses from the head and face to the brain; includes three divisions from face- ophthalmic, maxillary, and mandibular

VI. Abducens- Motor fibers that innervate the lateral rectus muscle of the eye

VII. Facial- Motor fibers that control muscles of the face, except those used in chewing; eyelid closing, facial expression, taste sensation
VIII. Vestibulocochlear- Vestibular part is sensitive to head balance and movement (equilibrium); cochlear parts supply the cochlea and semicircular canals of the internal ear and contribute to the sense of hearing; also referred to as Auditory/Vestibular, for hearing and sense of balance, or Acoustic nerve

IX. Glossopharyngeal- Motor fibers that innervate the muscles of the pharynx, the soft palate, and the parotid glands; sensory fibers that conduct impulses to the brain from the pharynx, the middle ear, and the posterior third of the tongue

X. Vagus- Motor fibers that innervate the muscles of the pharynx, larynx, heart, and thoracic and abdominal viscera; sensory fibers that conduct impulses from these structures to the brain; swallowing, taste sensation; controls some visceral functions such as heart rate and gastrointestinal motility

XI. Accessory- Spinal root is motor fibers from the spinal cord that innervate the pharyngeal, trapezius, and sternocleidomastoid muscles; cranial root is motor fibers from the brain that join the vagus nerve to innervate the thoracic and abdominal viscera

XII. Hypoglossal- Motor fibers that innervate the muscles of the tongue

Cerebral Vasculature

Arteries

The brain receives blood from two pairs of large vessels- the internal carotid arteries, which arise from arteries in the neck, and the vertebral arteries, which arise from arteries in the chest. The internal carotids supply the majority of the forebrain, passing into the skull, and giving off the ophthalmic arteries in the orbital regions. On each side, the internal carotids terminate into the anterior cerebral, middle cerebral, and posterior communicating arteries. These termination points are just lateral to the crossing of the optic nerves. The anterior cerebals form the anterior portion of the Circle of Willis, and supply the anterior aspect of the cerebrum. Small lenticulostriate arteries branch from the middle
cerebals at right angles, and supply the basal ganglia. They are also referred to as “stroke arteries”, as they are commonly the ruptured vessels in intracerebral hemorrhages, which often results in at least partial paralysis of the limb muscles on the side of the body contralateral to the hemorrhage. The posterior communicating arteries form a large portion of the posterior aspect of the Circle of Willis.

The vertebral arterial system supplies the brainstem, cerebellum, occipital lobe of the cerebrum and parts of the thalamus. The right and left vertebrals join to form the basilar artery, which gives rise to the posterior cerebral arteries and the cerebellar arteries. The anterior spinal artery, which is a major supplier of the spinal cord, arises from branches of the vertebral arteries.

An irregular vascular circle called the Circle of Willis, or circulus arteriosus, is formed by branches of both the internal carotid and the vertebral arteries. This important area of collateral circulation lies within the subarachnoid space, and is a common location for the formation of cerebral aneurysms. The internal carotids supply the anterior cerebral arteries, which are joined by the anterior communicating artery, to form the anterior portion of the circle. The posterior communicating arteries also branch from the internal carotids, and join the posterior cerebral arteries to form the posterior aspect of the circle. The posterior cerebals are branches of the basilar artery, which forms at the termination of the right and left vertebral arteries. The posterior aspect of the Circle of Willis is the location where blood originating from the internal carotids can mix with blood originating from the vertebral arteries. The arteries of the Circle of Willis act as anastomoses for each other. If any of the communicating arteries becomes blocked, blood can flow from another part of the circle to ensure that blood flow is not compromised.

The cerebral vasculature transports oxygen, nutrients, and other important substances to the brain to ensure its proper functioning. The brain uses about 20% of the oxygen absorbed by the lungs. Maintaining a constant blood supply to the brain is essential for normal brain function. Brain tissue being deprived of oxygen for less than one minute can result in a loss of consciousness, and it is at risk of becoming permanently damaged after approximately five minutes of blood deprivation.

Although the external carotid artery does not directly supply the brain, it has branches that supply the dura mater. The middle meningeal artery on the dura mater lies deep to the temporal bone, and is a potential site of rupture (epidural hematoma) with a hard fall on the side of the head. Cerebral hemorrhages usually involve the carotid system, while brain stem infarcts relate to the vertebral system.
Figure 24 Arterial circulation to the brain

Figure 25 Arteries involved in Circle of Willis

Figure 26 Axial image of arterial anatomy and Circle of Willis
Veins

The veins of the brain do not possess valves, and their walls are extremely thin, as they do not contain any muscular tissue. They pierce the arachnoid membrane and the inner or meningeal layer of the dura mater, and open into the cranial venous sinuses. The veins are considered tributaries of these large venous channels in the dura mater. They are typically divided into two sets, cerebral and cerebellar.

The cerebral veins are further divided into external and internal groups, as they drain either the outer surfaces, or the inner parts of the hemispheres. The external veins include the superior, middle and inferior cerebral veins. The superior cerebral veins number between eight and twelve, and drain the superior, lateral, and medial surfaces of the hemispheres. They are mainly lodged in the sulci between the gyri. The superior cerebral veins open into the superior sagittal sinus. They are also referred to as the “bridging” veins, and are known to rupture when placed under high tension. This situation occurs most often in the elderly, where the underlying atrophic brain places these vessels under higher than normal tension. Bleeding from the bridging veins may strip the dura from the arachnoid mater, resulting in a collection of blood known as a subdural hematoma. The subdural space is a “potential” space, and is appreciable only when there is underlying pathology. The middle cerebral vein begins on the lateral surface of the hemisphere, runs along the lateral cerebral fissure, and ends in the cavernous or sphenoparietal sinus. The middle cerebral vein also connects with the superior sagittal sinus and the transverse sinus. The inferior cerebral veins are of smaller size, and drain the under surfaces of the hemispheres. Those on the orbital surface of the frontal lobe join the superior cerebral veins, and, through them, open into the superior sagittal sinus. The inferior cerebals of the temporal lobe anastomose with the middle cerebral and basal veins, and join the cavernous, sphenoparietal, and superior petrosal sinuses.

There are two internal cerebral veins, which drain the deep parts of the hemisphere. Each is formed near the interventricular foramen by the union of the terminal and choroid veins. Just beneath the splenium of the corpus callosum, each internal cerebral receives the corresponding basal vein. At this point, the internal cerebri unite to form a short trunk called the great cerebral vein, which ultimately ends in the straight sinus.

The cerebellar veins are located on the surface of the cerebellum, and are grouped as superior and inferior. The superior cerebellar veins pass partly forward and medially to end in the straight sinus and internal cerebral veins, and partly laterally to the transverse and superior petrosal sinuses. The larger inferior cerebellar veins end in the transverse, superior petrosal, and occipital sinuses.

The dural venous sinuses are venous channels located intracranially between the two layers of dura mater. They form the major draining pathways from the brain, predominantly to the internal jugular veins, and on to the brachiocephalic veins and the superior vena cava. Some of the dural venous sinuses are unpaired, while others are paired. The main unpaired venous sinuses include the superior sagittal sinus, the inferior sagittal sinus, the straight sinus, the occipital sinus, and the intercavernous sinus. There is a confluence of sinuses posteriorly, where the superior sagittal, straight, and occipital sinuses meet. The main paired venous sinuses include the transverse sinuses, the sigmoid sinuses, the inferior petrosal sinuses, the superior petrosal sinuses, the cavernous sinuses, the sphenoparietal sinuses, and the basilic venous plexus. The cavernous sinuses offer significant collateral drainage of blood from the brain.
Figure 27 Veins and venous sinuses of brain
Brain Pathology

The brain can be the victim of numerous pathologies, including malignant tumors, strokes, infection, head injuries, disease, and dystonias. We will discuss the more common pathologies, as well as those that are uncommon, but may prove to be interesting.

Tumors

A brain tumor is a mass that is formed by an overgrowth of abnormal cells. Tumors that originate in the brain, the brain’s coverings, or its nerves are considered primary brain tumors, which are the type most commonly occurring in children. Metastatic or secondary brain tumors are more commonly found in adults, and are caused by cancer that has spread to the brain from the breast, lung, or other parts of the body. Nearly one in four people with cancer will get a secondary brain tumor.

Brain tumors are classified as benign or malignant. Benign tumors are composed of noncancerous cells that do not invade the brain or other tissues. However, some benign brain tumors can be life-threatening, due to the fact that the brain and spinal cord are housed within the skull and spinal column, which are bony structures that cannot expand. Benign brain tumors can grow large enough to put pressure on the sensitive areas of the brain, impair function, and lead to coma and death. Malignant brain tumors may contain benign-appearing cells that invade normal tissue, or contain cancerous cells either from the brain or other body cancers. The latter are typically life-threatening tumors, as they can spread throughout the brain or to the spinal cord.

Brain tumors are most commonly found in adults when they are between the ages of forty and seventy, with only two to three percent of new cancer cases attributed to primary brain tumors. The most common primary brain tumors in adults include pituitary tumors and meningiomas, both of which are typically benign, and glioblastomas. Children’s brain tumors are typically found between the ages of three and twelve, and account for approximately twenty five percent of all pediatric cancers. The most common pediatric primary brain tumors are medulloblastomas, astrocytomas, ependymomas, and brain stem gliomas. Treatment choices and chances of recovery depend on the type of brain tumor, and the patient’s general state of health.

Figure 28 Glioblastoma, which is highly malignant
Gliomas are the most common primary brain tumors involving the brain tissue, and they are typically malignant. They begin in glial cells, or their stem cells, which serve as support for the neurons in the brain. There are many types of gliomas, often named and distinguished by the type of cells they affect. Gliomas vary in their rate of growth, and their response to treatment.

Astrocytomas make up nearly sixty percent of all tumors. They resemble astrocytes, which are star-shaped cells that help feed neurons by drawing nutrients from blood vessels. Astrocytomas are typically found in the cerebellum in children, but in the cerebrum in adults. Most pediatric astrocytomas are low-grade, meaning they have slower growth. The majority of astrocytomas in adults are high-grade, which are faster growing tumors that can displace or replace local brain, while spreading into adjacent brain.

![Figure 29 Typical appearance of an anaplastic astrocytoma with high T2 signal; presence of enhancement suggests grade III tumor](image)

Oligodendrogliomas begin in the oligodendrocytes, which are the cells that make myelin. Myelin provides support and nourishment for the neurons. Oligodendrogliomas usually occur in the cerebrum and account for ten to twenty percent of all primary brain tumors, typically occurring in middle-aged adults. Most are slow-growing low-grade tumors that spread into surrounding brain tissue, often causing seizures.

![Figure 30 Anaplastic hemorrhagic oligodendroglioma; typically well-circumscribed, gelatinous gray masses; frequently have calcifications; fewer are cystic, but those can expand a gyrus and remodel the skull](image)
Ependymomas begin in the ependymal cells that line the cavities and passageways of the brain (ventricles) and spinal cord. These tumors can spread through a process called CSF seeding, in which cells break off from the tumor and spread to the spine through the cerebrospinal fluid. They are relatively uncommon, accounting for about six percent of all tumors affecting the central nervous system, with eighty five percent of them considered low-grade. Ependymomas are the third most common brain tumor in children, typically occurring between the ages of one and five. Tumors that begin in the central canal of the spinal cord are found more often in adults, usually those between the ages of thirty and thirty five.

Brain stem gliomas usually occur in the pons portion of the brain stem, and are called pontine gliomas. They rarely spread to other areas of the brain or to the spinal cord. Brain stem gliomas comprise ten to fifteen percent of pediatric brain tumors, and approximately two percent of all brain tumors in adults. In the United States, almost three fourths of patients with brain stem gliomas are below age twenty. Treatment of brain stem gliomas in the midbrain or medulla is usually more successful than treatment of pontine gliomas.
Additional types of brain tumors include medulloblastomas, which begin in the lower part of the brain, but can spread to the spine or to other parts of the body. Approximately one in five pediatric brain tumors are medulloblastomas, with seventy five percent of all cases of these tumors occurring in children. Meningiomas are typically benign, slow-growing tumors that occur in the membranes covering the brain. They account for fifteen to twenty percent of all primary brain tumors, and usually occur in people between the ages of forty and sixty. Meningiomas are more common in women than in men, and are rarely found in children. Schwannomas originate in the schwann cells of nerves. Vestibular schwannomas, also known as acoustic neuromas, are tumors of the nerve that controls balance and hearing in the inner ear. Acoustic neuromas typically occur in adults.
Strokes

Strokes, or cerebrovascular accidents (CVA), occur when blood vessels carrying oxygen and other nutrients to the brain become blocked or suddenly rupture. Brain cells served by these vessels become starved and begin to die off. The resulting damage may impair behavior or bodily functions controlled by the affected parts of the brain, although medical intervention can sometimes reduce stroke damage. Strokes are closely linked with cardiovascular diseases such as atherosclerosis, heart rhythm disorders, heart attacks, heart valve disorders, and especially hypertension. Additional risk factors include age, gender, race, and family history. Two thirds of strokes occur in people over the age of sixty five. Men are more likely to have strokes than women, with African-American males exhibiting the highest risk of stroke. Personal and/or family history of stroke also increases stroke risk. Strokes are the third leading cause of death in the United States, behind heart disease and cancer, but they are the number one leading cause of disability in America. Even though the number of strokes per year increases, the death rate has been decreasing, due in part to advances in diagnostic techniques and new treatments that allow physicians to intervene with less risk to the patient.

The interruption of blood flow to the brain that results in a stroke can occur in two different ways- by a blocked blood vessel (ischemic stroke), or by blood vessels that rupture (hemorrhagic stroke). Ischemic strokes account for roughly eighty percent of all strokes. They are further classified as either thrombotic or embolic strokes. A thrombotic stroke is a blockage caused by a blood clot that forms inside the brain or in the arteries of the neck. These strokes form most often in arteries damaged by atherosclerosis, where rough, fatty deposits build up in the walls of the arteries. These deposits gradually narrow the artery, slowing down or even occluding the blood flow. Thrombotic strokes are more severe when they occur in the larger arteries of the neck and brain, as they result in a more significant patient outcome. The larger arteries most commonly affected include the internal carotid artery, or the immediate large branches within the brain, which includes the middle and anterior cerebral arteries. Poor patient outcomes also typically follow thrombosis of the arteries in the back of the brain, including the vertebral, basilar, and posterior cerebral arteries. Thrombotic strokes that result from small-vessel disease are usually less severe. In these instances, the thrombosis occurs in a very small artery deep in the brain at the end of the arterial branches. These strokes are also referred to as lacunar strokes, as imaging performed later shows a small black or white space or gap, termed lacuna in Latin. Risk factors for lacunar strokes include hyperlipidemia, hypertension, and diabetes mellitus.

Figure 36 Plaque buildup and clot formation

Figure 37 Axial FLAIR images show posterior cerebral artery that can lead to ischemic stroke from thrombus territory infarct
Ischemic stroke is the most common neurological cause of severe disability and death. MRI reveals stroke biology in real-time, and may benefit the clinical management of patients, especially in the most severe strokes. Typically, the management of the acute ischemic stroke patient is driven by the concept of “time is brain”. If the time of stroke onset is known, that time becomes the decisive factor in the decision to treat. However, recent clinical studies are showing that each patient has his own time, meaning the rate of neuronal loss amongst patients is variable. This variability is best explained by differences in the adequacy of each patient’s collateral circulation, which can maintain brain viability if it receives adequate cerebral blood flow. Two “zones” can be delineated in the brain after occlusion of a major artery- the core and the penumbra. The core of the infarct is the area of brain tissue immediately beyond the occlusion that receives little or no flow, and quickly undergoes infarction. The penumbra includes other parts of the brain that are still alive, but receiving abnormally low blood flow and in danger of proceeding to infarction. The penumbra may give rise to significant neurological symptoms. Specific MR imaging techniques have invaluable roles in the evaluation of an ischemic stroke. MRA can be used to detect the initial arterial occlusion. The best current estimate of the infarct core is provided by DWI. The extent of the penumbra can be estimated using perfusion MRI. The relative sizes of the core and the penumbra are determined by the quality of the collateral flow. With the passage of time, there is shrinkage of the ischemic penumbra, and a corresponding growth of the core. With good collaterals, the shrinkage of the penumbra and growth of the core is slow, while with poor collaterals, very rapid growth of the core and shrinkage of the penumbra is observed. Research on a significant number of patients has shown changes of the ischemic penumbra occurring at a very slow rate, with the penumbra appearing to be stable for a long period of time. It has been proposed that more attention should be paid to each patient’s physiology, rather than to time alone, in the determination of stroke management, whether it involves the use of intravenous thrombolysis or intra-arterial intervention. This topic is discussed further in the Perfusion Imaging section.
Embolic strokes are the other classification of ischemic strokes, occurring due to a blockage from clots that form in another part of the body and travel to the brain. A clot, or embolus, can form in the heart or carotid arteries, and break loose to travel upstream towards the brain. The arteries that the clot moves through continuously branch off into smaller vessels, so the clot eventually reaches a point where it can go no further. The embolus then occludes the vessel, and blocks off blood supply to the brain in that area. Embolic strokes often result from heart disease or heart surgery, and occur rapidly, without any warning signs. Approximately fifteen percent of these strokes occur in people with atrial fibrillation, an abnormal heart rhythm in which the upper chambers of the heart do not beat efficiently.

Strokes that occur due to the rupture of a blood vessel in or around the brain are termed hemorrhagic strokes. The ruptured blood vessel not only deprives the brain of oxygen, but the accumulated blood from the ruptured artery clots, displacing normal brain tissue and disrupting function. Hemorrhagic
strokes can have very sudden onsets, which are typically catastrophic. Patient deaths are more frequent from these sudden strokes. If the patient survives, their disabilities from a hemorrhagic stroke are typically prolonged. The average age for hemorrhagic strokes is lower than that for ischemic strokes, but they are less common, accounting for approximately twelve percent of all strokes. Hemorrhagic strokes can occur within the brain itself (intracerebral hemorrhage), or in the subarachnoid space, which is in the meningeal layers between the brain and the skull (subarachnoid hemorrhage).

Intracerebral hemorrhages occur when a diseased blood vessel within the brain ruptures, allowing blood to leak inside the brain. The sudden increase in pressure within the brain can cause damage to the brain cells surrounding the blood, as well as leading to unconsciousness or death. Intracerebral hemorrhages are most often found in the basal ganglia, cerebellum, brain stem, or cortex. The most common cause of an intracerebral hemorrhage is hypertension, especially if it is uncontrolled. Less common causes include trauma, infections, tumors, blood clotting deficiencies, and abnormalities in blood vessels (arteriovenous malformations).

Subarachnoid hemorrhages occur when a blood vessel just outside the brain ruptures, causing bleeding in the area between the brain and the meningeal layers, particularly the subarachnoid space. This space
rapidly fills with blood, causing the patient to have a sudden, intense headache, neck pain, and nausea or vomiting. The sudden buildup of pressure outside the brain may also cause rapid loss of consciousness or death. Subarachnoid hemorrhages can be caused by bleeding from an arteriovenous malformation (AVM), bleeding from a cerebral aneurysm, a bleeding disorder, use of blood thinners, or a head injury. Trauma is the leading cause of subarachnoid hemorrhage. Subarachnoid hemorrhages due to injury are often seen in the elderly who have fallen and hit their head. In younger people, motor vehicle crashes are the most common injury leading to a subarachnoid hemorrhage. Important risk factors for subarachnoid hemorrhage include heavy alcohol use, cigarette smoking, hypertension, and possibly oral contraceptive use. A positive family or past personal history of subarachnoid hemorrhage also increases risk.

Arteriovenous malformations (AVM) are one type of cerebral vascular malformations characterized by a cluster of abnormal blood vessels. In an AVM, a tangle of blood vessels in or around the brain bypasses the normal brain tissue, and directly diverts blood from the arteries to the brain. Approximately ten percent of subarachnoid hemorrhages are attributed to AVM, vascular lesions, tumors, and less common disorders.

Cerebral aneurysms are abnormalities of the arteries, often found at the base of the brain. Eighty to eight five percent of these lesions are in the anterior cerebral circulation (internal carotid artery and its branches), with the remainder located in the posterior circulation (vertebral arteries and its branches). Multiple cerebral aneurysms are found in approximately twenty five percent of cases. Small areas of rounded or irregular swellings in the arteries can cause the vessel walls to become weak and prone to rupture, leading to a hemorrhagic stroke. Ruptured intracranial aneurysms account for approximately eighty percent of non-trauma subarachnoid hemorrhages. When an aneurysm ruptures, intracranial pressure rises precipitously. Cerebral perfusion may transiently cease, resulting in unconsciousness. Death can occur if the intracranial pressure is high enough to cause irreversible structural damage or halt cerebral perfusion. The prevalence of aneurysms is two hundred times higher than the annual incidence of subarachnoid hemorrhage, leading to the conclusion that most aneurysms do not rupture. Peak age at rupture is fifty years. Treatment of the ruptured aneurysm is recommended as soon as tolerable by the patient, with the goal of obliterating the aneurysm within one to three days after the hemorrhage. Microsurgical aneurysm clipping and endovascular coil embolization are two very popular treatments. In microsurgical clipping, the neurosurgeon opens the dura, identifies the parent vessel and the ruptured aneurysm, and clips the aneurysm to exclude it from circulation. Surgical clipping has a
high durability rating, with aneurysm recurrence reported at the low rate of two or three percent. Endovascular coiling uses a micro-catheter threaded through a guide catheter to the origin of the ruptured aneurysm. Once inside the aneurysm, platinum coils are inserted into the sac until the aneurysm is densely packed. Coil therapy requires serial monitoring of patients and follow-up cerebrovascular imaging to detect the occasional risk of coil compaction or aneurysm recanalization. Initial treatment yields approximately seventy percent of patients experiencing ninety five to one hundred percent occlusion of the aneurysm. However, twenty five to thirty percent of patients do not have complete obliteration of their aneurysms, and recanalization can occur. The decision to proceed with open surgical clipping or endovascular treatment of an intracranial aneurysm after subarachnoid hemorrhage depends on both aneurysm-specific factors (location, size, morphology, and presence of thrombus), and patient-specific factors (age, density of the subarachnoid hemorrhage, patient preference, and other medical comorbidities).

Figure 44 Extensive subarachnoid hemorrhage that is hyperintense on T1-weighted image, low signal on T2-weighted image, blooming on gradient echo image; MRA shows partially thrombotic aneurysm at right trifurcation of middle cerebral artery, suggesting rupture of aneurysm

Figure 45 A- Internal carotid artery angiogram shows giant aneurysm in internal cerebral artery; B- Post- coil embolization angiogram shows total obliteration of aneurysm sac; C- DW-MR shows high-signal intensity lesions in motor cortex, but patient had favorable clinical outcome

**Injury**

Each year in the United States, concussions, also known as mild traumatic brain injuries (mTBI), affect between 1.8 and 3.8 million people. Concussions occur when the head or body is hit hard, or violently jarred or shaken. This causes the brain to crash into the skull, resulting in a disturbance of brain function. Patients can experience a range of symptoms following a concussion including headache,
drowsiness, vomiting, dizziness, memory loss, attention deficit, depression, and anxiety. Problems can persist for months or even years in as many as thirty percent of patients. More than ten years ago, a federal study labeled concussions as “a serious public health problem”, costing the United States an estimated eighty billion dollars per year. Regardless of how a concussion occurs- whether it is due to an accident, athletic event, or combat- it can lead to permanent loss of higher level mental processes. As the media continues to keep the issue of concussions in the forefront of the news, researchers are working with imaging modalities to better detect the subtle brain damage that concussions can cause. By preventing and repairing the damage that accompanies mild traumatic brain injuries, we may be able to limit their long-term effects. Concussion researchers are finding that symptom resolution is not necessarily injury resolution. A concussion is not a single pathology, but many different injuries with different symptoms. Each patient needs to be treated individually.

Diffusion tensor imaging (DTI), a specialized MRI technique that establishes the direction of water flow through the white matter fiber tracts, has been increasingly used in post-concussion patients to show brain injury. One study using DTI showed evidence of injury to the corpus callosum, suggesting that concussions had caused edema or swelling in these fiber tracts, disrupting their normal ability to transmit messages in the brain. Patients with more severe symptoms, such as persistent headaches and difficulty concentrating or remembering things, showed the most substantial differences in their images. A concussion can place stresses and strains on the fiber tracts between the two halves of the brain that make up the corpus callosum, disrupting both the physical and functional connections between the two halves.
A 2012 study examined DTI results performed within two weeks of the patient’s mild traumatic brain injury, and a one-year follow-up with questionnaires to assess post-concussion symptoms and evaluate health status. The researchers measured the uniformity of water flow throughout the brain (called fractional anisotropy, or FA) and pinpointed areas with low FA or abnormally high FA. Low FA is indicative of axonal injury, as axons comprise the bundles of nerve fibers in the brain’s white matter. Abnormally low FA within white matter has been associated with cognitive impairment in patients with traumatic brain injuries. High FA is believed to be evidence of brain changes occurring in response to trauma, where the brain is actively compensating for its injuries. When the DTI data was compared to the one-year follow-up questionnaires, abnormally high FA was found to be a predictor of fewer post-concussion symptoms and higher functioning.
DTI has also shown regional white matter damage in the brains of those with chronic dizziness and other symptoms after concussion. Imaging data was reviewed for patients suffering with the concussion effects of vestibulopathy, which includes dizziness, imbalance, and visual problems, as well as those with ocular convergence insufficiency, a condition in which the eyes do not turn inward properly when focusing on a nearby object. Patients with vestibular symptoms displayed decreased FA values in the cerebellar area of the brain, which controls balance and movement. Previous thought held that vestibulopathy was related to the inner ear, rather than to a brain injury. Cerebellar injuries have been associated with longer recovery times. Decreased FA values were also found in the fusiform gyri, a part of the brain that integrates the visual fields of the right and left eyes, and is involved in spatial orientation. The use of DTI results such as these, along with neurocognitive testing, may help determine a patient’s prognosis and accelerate the delivery of appropriate treatment.

A 2013 study showed that approximately forty percent of a group of patients that underwent MRI brain scans after mild head injuries had imaging evidence of hemorrhage in the brain. After more advanced MR testing (sequence type was not mentioned), twenty percent of that group had microbleed lesions, and thirty three percent of the group had tube-shaped linear lesions. The microbleeds were distributed throughout the brain, whereas the linear lesions were found mainly in one area, and were more likely to be associated with injury to adjacent brain tissue. It was hypothesized that the linear lesions may represent a type of vascular injury seen in the brain tissue studies of people with more severe traumatic brain injury.

Functional MRI (fMRI) has been paired with a blood-oxygen-level dependent (BOLD) protocol to measure the levels of cerebrovascular reactivity (CVR) in certain brain regions of athletes that have had concussions. CVR is the ability of a blood vessel to change caliber in response to a stimulus. Since blood vessels widen with the introduction of carbon dioxide into the blood, CVR measurement can be performed by using simple breath-holds during an MRI scan, thus increasing carbon dioxide in the bloodstream. Researchers hypothesized that the increased levels of carbon dioxide would most closely simulate the physiologic challenge that occurs when physical activity is resumed. The BOLD fMRI results showed markedly increased CVR levels across all regions of interest in the brains of concussed athletes. The widening of blood vessels as a result of the increased carbon dioxide may be an indicator of acute injury and contribute to recurrent headache symptoms. The BOLD fMRI method may be used to help in the determination of when athletes could return to physical activity.
An addition to the fMRI family that has been used in the study of athletes’ recoveries from concussions is resting state functional MRI, or rsfMRI. When using traditional fMRI, the results are felt to be inconsistent, as the changes are measured in only a small fraction of overall brain activity, and only detectable when the subject is asked to perform a task that may not be consistently affected by a concussion. With rsfMRI, athletes that are recovering from concussions can be compared with control athletes. The test is performed at rest, where it can measure the brain’s overall level of activity. Researchers theorize that rsfMRI will allow them to look for larger, more consistent changes in brain activity after a concussion. Athletes who had experienced concussions without residual symptoms performed as well as control athletes on neuropsychological and mild exercise tests that are commonly used to determine if an athlete has recovered from a concussion. However, rsfMRI scans revealed altered patterns of brain activity in the concussed athletes. Activity representing the strength of connections between the left and right halves of the brain was lower, or weaker, suggesting that the injured athletes had not fully healed ten days after their concussions—symptom resolutions were not necessarily injury resolutions. Both sets of athletes were scanned again after mild exercise tests, which revealed similar brain activity in both groups. These results suggest that treating concussed athletes with certain mild exercises may warrant further study.

Figure 51 Resting state functional magnetic resonance imaging (rsfMRI) reveals potentially harmful changes in brain activity caused by a concussion vs. uninjured athlete
Resting state functional MRI has also been used to show changes in the brains of those with post-concussion syndrome (PCS). These patients showed increased frontal connectivity around the medial prefrontal cortex, which is thought to represent brain neuroplasticity operating in recovery and neural repair after injury. Neuroplasticity involves the formation of new neural connections throughout life. Increased frontal connectivity correlates with posttraumatic symptoms, such as depression, anxiety, fatigue, and PCS. Researchers also found reduced connectivity in the posterior cingulate cortex and parietal regions of the brain, which correlates clinically with neurocognitive dysfunction.

![Image](https://example.com/image.png)

Figure 52 A- healthy control group shows typical but enhanced connectivity pattern of the default mode network (DMN); B-disrupted DMN pattern in post-concussion syndrome patient group

Professional athletes in contact sports that are exposed to repetitive mild traumatic brain injuries may develop ongoing impairments, such as chronic traumatic encephalopathy (CTE). This is a degenerative condition caused by a buildup of tau protein that has been associated with memory loss, confusion, progressive dementia, depression, suicidal behavior, personality changes, abnormal gait and tremors. Tau proteins are also associated with Alzheimer’s disease. This non-invasive research method used a chemical marker called FDDNP, which binds to neurofibrillary tau “tangles”, as well as to deposits of amyloid beta plaques, both of which are hallmarks of Alzheimer’s. PET scans were then performed, which allowed researchers to pinpoint where in the brain these abnormal proteins accumulate. In the athletes that were studied, elevated levels of the FDDNP were found in the amygdala and subcortical regions of the brain, which are the areas that control learning, memory, behavior, emotions, and other mental and physical functions. Higher FDDNP levels were found in the athletes who had experienced a higher number of concussions. The FDDNP binding patterns seen in the athletes were consistent with the tau deposit patterns that have been observed at autopsy in chronic traumatic encephalopathy cases. The athletes also displayed more depressive symptoms, and scored lower on clinical assessment tests, demonstrating evidence of cognitive loss.
Infections

Infections in the cranium can affect the brain alone, or they can also affect the meninges. The brain is very prone to infection compared to other organs, such as the heart. Bacteria and viruses are the most common infections, but parasites, fungi, and other microorganisms can also invade the brain. An infectious agent can cause inflammation of the area that it invades; the area then lends its name to the infectious disease.

Meningitis is the inflammation of the meninges, which are the three layers of membranes that surround the brain and spinal cord, including the cerebrospinal fluid. Meningitis is typically either viral or bacterial, with viral infections being two to three times more common. Viral meningitis causes milder symptoms, requires no specific treatment, and typically goes away without complications. It can occur as a complication of mumps or measles. Bacterial meningitis is much more serious, and can result in a learning disability, speech defects, hearing loss, seizures, loss of extremity function or amputation, permanent brain damage, and even death. Up to fifteen percent of the survivors of bacterial meningitis are left with permanent complications and health issues. The overall incidence of bacterial meningitis in the United States has decreased significantly since 1998, as a result of widespread vaccination. It usually occurs in isolated cases, as opposed to epidemics, and approximately two-thirds of all cases are in children. Bacterial meningitis is more common in males, and occurs more often in late winter and early spring. From a worldwide perspective, bacterial meningitis is still common, and is a serious threat to global health. It particularly affects the African continent, with regular epidemics in sub-Saharan and West Africa, areas also known as “the meningitis belt.” Particular signs of meningeal infection in someone with a fever include neck pain or stiffness with neck flexion or with knee extension, and involuntary flexion of both hips with neck flexion. Advanced meningitis can also cause increased intracranial pressure.
The three types of bacteria that are the most common causes of bacterial meningitis in all age groups (except newborns) include:

- Streptococcus pneumonia, which causes pneumococcal meningitis
- Neisseria meningitides, which causes meningococcal meningitis
- Haemophilus influenza type b (Hib)

Bacterial meningitis in newborns usually comes from Escherichia coli or Listeria, which are coliform bacterias in the gut that are contracted at birth. A vaccine against pneumococcal meningitis can also prevent other forms of infection. It is not effective in children under the age of two years, but it is recommended for all those over the age of sixty five, and for younger people with certain chronic medical conditions. A vaccine against meningococcal meningitis is available in the U.S., and is recommended for those ages eleven to eighteen, as well as people at high risk for disease. The meningococcal vaccine is used to control outbreaks in certain regions of the country, in overcrowded environments (such as college dormitories), and as a preventive measure for travelers outside the U.S. Hib vaccines are now part of routine pediatric immunizations, and have significantly reduced the occurrence of serious Hib disease.

Most of the bacterias that cause meningitis are not very contagious, requiring the exchange of respiratory and throat secretions through coughing, sneezing, or kissing, to spread the bacteria. The exception is meningococcal meningitis, which has an increased risk of spreading to those in the same household, those with prolonged contact, or those in direct contact with a patient’s oral secretions. Bacterial meningitis most commonly affects infants and small children, and is an increased risk for those with weakened immune systems, diabetics, chronic alcoholics, IV drug abusers, and all those over sixty years of age.

![Figure 54 Contrast-enhanced T1-weighted axial MR image shows a right frontal parenchymal low intensity (edema), leptomeningitis (arrowheads), and a lentiform-shaped subdural empyema (arrows)](image)

Brain infections can also be caused by parasites and various types of worms. Toxoplasmosis is caused by the parasite Toxoplasma gondii, which can be acquired by eating unwashed vegetables or undercooked meat, by direct contact with cat feces, or from an infected mother to an unborn baby. Toxoplasmosis is the reason pregnant women are warned to not clean cat litter boxes, and why they should not eat undercooked meat. Symptoms are similar to a mild form of bacterial meningitis. Prognosis is poor for
affected infants if passed to them before birth. It is also more severe for those with weakened immune systems, such as people who are HIV positive.

![FLAIR image of toxoplasmosis](image)

Figure 55 FLAIR image of toxoplasmosis, characterized by multiple lesions in gangliobasal and subcortical locations, with a "target" sign

Neurocysticercosis, or cerebral cysticercosis, is caused by the pork tapeworm, and is acquired when people eat the larvae, or eat food contaminated by feces. This is the most common neuroparasitic infection in humans. It is seen worldwide, but is most common in Central and Latin America, Mexico, Asia, Africa, Spain, Portugal, and Eastern Europe, as well as in the southwestern U.S. Clinical presentation is highly variable, and depends on the number, size, and location of the cysts that develop from the tapeworm larvae. Neurocysticercosis is a common cause of seizures. Subarachnoid lesions may cause meningitis, while intraventricular or aqueductal lesions may lead to hydrocephalus. Signs of increased intracranial pressure, such as headache, vomiting, and confusion, may also be present. An acute inflammatory response may occur when the larvae degenerate, with the inflammation becoming granulomatous, and finally forming a fibrous scar. Treatment of neurocysticercosis has evolved from surgical therapy to anticysticercal chemotherapy, with steroid treatment for the inflammatory response.

![MRI image](image)

Figure 56 Patient was an Indian national, residing in the US for 7 months, presented after a seizure and increasing headaches; MRI with contrast showed poorly demarcated nodular enhancement with overlying dural enhancement; suspected primary glial neoplasm; microscopic description of mass after craniotomy showed a parasite; final diagnosis was neurocysticercosis
Trichinosis is caused by the roundworm Trichinella spiralis, acquired by eating larvae in raw or undercooked pork. Symptoms may be similar to encephalitis, with confusion and delirium, or, in more severe cases, may include coma, seizures, paralysis and other signs of neurologic loss. Recovery is usually complete within a few days or weeks, with no long-term problems. Treatment is usually geared to the symptoms.

An abscess is an accumulation of infectious material and offending microorganisms that can occur in the brain. A cerebral abscess can be a complication of chronic sinus or middle-ear infections, or can be the distant spread from another infection, such as pneumonia. An abscess can also be the consequence of head trauma or a neurosurgical procedure. Symptoms will depend on the location of the abscess, but typically include a severe headache, fever, or generalized malaise. Treatment includes IV antibiotics, and possible surgical drainage.

Encephalitis is an inflammation of the brain itself. It can occur in varying degrees of severity as a complication of measles and mumps, or it can be quite severe when associated with the transmission of rabies. Encephalitis is also seen in conjunction with AIDS and HIV, where it is sometime called AIDS dementia.

Rabies is a viral infection, most commonly transmitted to humans by the bite of an infected animal. Rabies encephalitis has a classic clinical presentation, so neuroimaging is rarely performed. It typically begins with malaise, fever, and paresthesia at the site of the bite, followed by classic neurologic
symptoms of agitation, hydrophobia, aerophobia, hypersalivation, and seizures. In approximately one in five cases, rabies occurs in a paralytic form, which does not exhibit the classic symptoms and may mimic other diseases. MRI of the brain may be a useful diagnostic tool in the diagnosis of paralytic rabies, as it displays a distinct abnormal pattern. In a case study of paralytic rabies, a patient was bitten by a wild fox. The wound was cleaned, and antirabies vaccines were given. Three weeks later, the patient was experiencing fever, vomiting, and progressive quadriplegia, but not the classic rabies signs of hydrophobia or aerophobia. MRI of the brain at that time showed bilateral symmetrical hyperintensities in the thalamus, basal ganglia, midbrain, pons and medulla on T2-weighted and FLAIR images. These changes were restricted to the gray matter. When MRI is performed in cases of rabies encephalitis, it typically demonstrates hyperintensities in the globus pallidi, putamen, and thalami bilaterally on both T1- and T2-weighted images, as well as brainstem and hippocampus abnormalities. Hyperintensity on the T1-weighted images may be due to extracellular methemoglobin, as necropsy of the brain can show scattered hemorrhages. The patient with paralytic rabies did not have hemorrhagic lesions on MRI or pathology, which may be due to the less severe and sudden response in patients with paralytic rabies. Basal ganglia hyperintensities on T2-weighted and FLAIR sequences are seen in other encephalopathies, but the selective involvement of only the gray matter can differentiate paralytic rabies. Although this patient’s wounds were adequately cleaned, and antirabies vaccines were given, post-exposure antirabies immunoglobulin was never given, and the patient died from the paralytic rabies infection.

AIDS and HIV encephalopathy, also known as AIDS dementia complex (ADC), is caused by the human immunodeficiency virus (HIV). It is characterized by the slow onset of behavioral, intellectual, and motor impairment. Early symptoms include confusion, loss of libido, social withdrawal, decreased concentration, poor balance, and weaknesses. In the late stage, severe dementia, inability to control urine flow, and an inability to speak and walk are found. Treatment includes standard antiviral drugs, with variable results.
Another AIDS-related encephalopathy is progressive multifocal leukoencephalopathy (PML). This is a disease of the white matter of the brain, caused by a virus infection that targets cells that make myelin, which insulates neurons. PML is most common among those with HIV/AIDS, but is rarely described as the “presenting sign” of AIDS. Overall, the disease is considered to be rare, occurring mainly in those undergoing chronic corticosteroid or immunosuppressive therapy for organ transplant, or individuals with certain cancers (Hodgkins disease or lymphoma). Additional individuals considered at risk are those with autoimmune conditions such as multiple sclerosis, rheumatoid arthritis, and systemic lupus erythmatosis. PML has diverse symptoms, as they are related to the location and amount of damage in the brain, and may evolve over the course of several weeks to months. The most prominent symptoms include clumsiness, progressive weakness, and visual, speech and personality changes. The progression of deficits associated with PML can lead to life-threatening disabilities, and frequently, death. Progressive multifocal leukoencephalopathy has a mortality rate of thirty to fifty percent in the first few months following diagnosis, depending on the severity of the underlying disease, and the treatment received. Those who survive PML can be left with severe neurological disabilities. A diagnosis of PML can be made following brain biopsy, observations of a progressive course of the disease, or consistent white matter lesions visible on an MRI scan.
Diseases of the Brain

As the space in this section will not allow for an all-inclusive report on brain diseases, we will focus on diseases that may be more commonly seen in MRI. We will discuss Parkinson’s disease, Alzheimer’s disease, dementias other than Alzheimer’s disease, multiple sclerosis, and dystonia.

Parkinson’s Disease

Parkinson’s disease is a neurodegenerative disease and motor system disorder, caused by the loss of dopamine-producing brain cells. Dopamine is a neurotransmitter, acting as a chemical messenger that helps in the transmission of signals in the brain and other vital areas. It is produced in several areas of the brain, including the substantia nigra, and is released by the hypothalamus. If a protein called alpha-synuclein forms aggregates, or clumps, in the substantia nigra, these protein clumps can cause degeneration of the nerve cells that produce dopamine. Dopamine can also be used as a medication. It acts on the sympathetic nervous system, leading to increased heart rate and blood pressure. Dopamine cannot cross the blood-brain barrier, so when it is given as a drug, it does not affect the central nervous system. When dopamine is needed in the brain, due to diseases such as Parkinson’s, levodopa is used. It is a precursor of dopamine, and is able to cross the blood-brain barrier.

The primary symptoms of Parkinson’s disease include:

- tremors of the hands, arms, legs, jaw, and face
- rigidity of the limbs and trunk
- bradykinesia, or slowness of movement
- postural instability, or impaired balance and coordination

Parkinson’s usually affects people over the age of fifty. Early symptoms are typically subtle, and may occur gradually, but the disease can progress at varying rates. Additional symptoms may include visual hallucinations, depression and other emotional changes, difficulty in swallowing, chewing, and speaking, urinary problems and sleep disruptions. Dementia may be evident before, concurrently, or at most within twelve months of onset of Parkinsonian symptoms. The majority of Parkinson’s cases are
considered sporadic, with only ten to fifteen percent of patients having a positive family history for this disease. Research has found at least eleven genes that have been implicated in various forms of Parkinson’s, with the prominence of specific clinical features dependent on which genes are involved. A diagnosis of Parkinson’s is based on medical history and neurologic examination, as there are currently no blood or laboratory tests proven to help in diagnosing sporadic Parkinson’s. MRI research on 7T, and more recently on 3T systems has revealed a promising diagnostic sign- the absent swallow tail sign. The substantia nigra normally shows a susceptibility signal pattern that has the appearance of a swallow’s tail. This sign is absent when Parkinson’s disease is present, and the diagnostic accuracy of this sign is reported to be greater than ninety percent. Iron accumulation and loss of neuromelanin also affect the appearance of the substantia nigra on T1 and T2-weighted images. MRI research results are promising in regards to the discovery of a diagnostic test for Parkinson’s disease.

Alzheimer’s Disease

Alzheimer’s is a progressive disease that damages the neurons in the parts of the brain involved in memory, learning, language, and reasoning. It is the most common type of dementia, accounting for an estimated sixty to eighty percent of dementia cases, and is more prevalent among women than men. The two basic types of Alzheimer’s are early-onset and late-onset. Early-onset tends to strike people under age sixty five, and is more likely to run in families. It occurs in fewer than ten percent of all Alzheimer’s disease patients. Late-onset Alzheimer’s is the more common type, afflicting people after age sixty five, and occurring in almost half of all people over the age of eighty five. An extremely rare type of Alzheimer’s disease that is known to be entirely inherited is called Familial Alzheimer’s disease (FAD). This type accounts for less than one percent of all cases, with onset often seen in the forties.

The hippocampus, located in the temporal lobe, is thought to be where short-term memories are converted into long-term memories. It has been found to be atrophied in the brains of Alzheimer’s patients. In addition, the hippocampus, as well as other areas of the brain involved in thinking and decision making are filled with two types of abnormalities- beta-amyloid plaques and neurofibrillary tangles. The plaques are deposits found outside and around the neurons, made up of dense fragments of the beta-amyloid protein mixed with other cellular material. The neurofibrillary tangles are made up
of twisted microtubules, which are nerve cell fibers that are part of the transport system inside nerve cells. Plaques and tangles are both associated with damage to healthy brain cells, and result in brain atrophy. Another characteristic of Alzheimer’s disease is the reduced production of certain chemicals in the brain that are necessary for communication between nerve cells. These chemicals are called neurotransmitters, and include acetylcholine, serotonin, and norepinephrine.

Early symptoms of Alzheimer’s disease include failure of short-term memory, apathy, and depression. Over time, long-term memory, language, and reasoning decline. Impaired communication, disorientation, confusion, behavior changes, and difficulty speaking, swallowing and walking are often seen in later stages. There is currently not a cure for Alzheimer’s disease, only drug and non-drug treatments that may help with both cognitive and behavioral symptoms. Alzheimer’s is a disease, not a normal part of aging, and research for a cure is ongoing. A study published in January, 2015 using high-resolution MRI found vascular leakage in the hippocampus of older brains, with more damage to the blood-brain barrier in the hippocampal area among people with dementia. The hippocampus is a critical area for learning and memory, and is damaged by Alzheimer’s. MRI scans of the brain may be helpful in detecting changes in blood vessels in the hippocampus before they cause irreversible damage.

**Additional Dementias**

Although Alzheimer’s disease is the most common type of dementia, additional types of dementia exist that affect the brain in a variety of ways. We will discuss vascular dementia, dementia with Lewy bodies, mixed dementia, and frontotemporal dementia.

Vascular dementia accounts for approximately ten percent of dementia cases, and was previously known as multi-infarct or post-stroke dementia. This type of dementia occurs because of brain injuries such as microscopic bleeding and blood vessel blockage. The location, size and number of brain injuries determines how the individual’s thinking and physical functioning are affected. Initial symptoms may include impaired judgment or impaired ability to make decisions, plan, or organize, as opposed to the initial symptoms of memory loss found with Alzheimer’s. Brain imaging can often detect the blood vessel problems implicated in vascular dementia. Pathologic evidence has shown that the various types of dementia are not considered mutually exclusive, as their “hallmark” brain changes are found simultaneously.
Dementia with Lewy bodies (DLB) occurs when abnormal aggregations of the protein alpha-synuclein (Lewy bodies) develop in the cortex of the brain. Lewy body aggregates are also seen in the brains of people with Parkinson’s disease, but in a pattern that is different from dementia with Lewy bodies. Symptoms of dementia with Lewy bodies are memory loss and thinking problems, which are similar to Alzheimer’s. However, dementia with Lewy bodies also causes early symptoms such as sleep disturbances, well-formed visual hallucinations, and muscle rigidity or other parkinsonian movement features.

Mixed dementia involves the simultaneous occurrence of abnormalities that can be linked to more than one type of dementia. Most commonly, the brain changes are abnormalities associated with Alzheimer’s and vascular dementia, but dementia with Lewy bodies cannot be excluded. Recent studies suggest that mixed dementia is more common than previously thought.
Frontotemporal dementia (FTD) is a group of disorders caused by progressive cell degeneration in the brain’s frontal or temporal lobes. The cell damage caused by these disorders leads to tissue shrinkage and reduced function in the brain’s frontal and temporal lobes, which control planning and judgment, emotions, speaking and understanding speech, and certain types of movement. Each of the specific disorders in the frontotemporal group has different core symptoms, but they display significant symptom overlap as these disorders progress. Frontotemporal dementia accounts for approximately ten to fifteen percent of all dementia cases, and usually develops when people are in their fifties or early sixties. The three main types of FTD include behavioral variant frontotemporal dementia (bvFTD), primary progressive aphasia (PPA), and FTD movement disorders. BvFTD mainly affects personality and behavior. As it progresses, those affected may develop disinhibition, which is a loss of restraint in personal relations and social life. Primary progressive aphasia affects language skills in its early stages, and behavior as it advances. FTD movement disorders affect certain involuntary, automatic muscle functions, and may also impair language and behavior. Frontotemporal dementia remains a “clinical” diagnosis, as there are currently no tests that can conclusively diagnose this disorder. MRI often plays a key role in its diagnosis, as it can detect shrinkage in the brain’s frontal and temporal lobes, which are hallmark signs of FTD.
Multiple Sclerosis

Multiple sclerosis (MS) is a disease that causes demyelination of the brain and spinal cord nerve cells. Myelin acts like insulation on electrical wires, helping the axon portion of the nerve cells to conduct impulses to other cells. As more areas or nerves are affected by demyelination, the impulses are diminished or lost, and patients begin to develop symptoms. Specific symptoms are related to the area of injury, and may affect the axon of the nerve as well. The areas of injury from demyelination are called lesions or plaques, and are readily apparent on MRI.

Multiple sclerosis is considered to be an autoimmune disorder, in which the body’s immune system attacks and destroys healthy body tissue by mistake. It occurs predominantly in younger persons, with diagnosis usually taking place between the ages of fifteen and forty five. Women are almost twice as likely to develop MS as men. Genetic factors do not seem to play a large role in multiple sclerosis, although people with a first-degree relative with MS are at slightly higher risk for developing this disease. Lifestyle factors do no play a role in the risk of developing MS.

A diagnosis of MS requires objective evidence of lesions disseminated in both time and space, which is where the important role of MRI comes into play. MRI can show multiple lesions (dissemination in space), some of which can be clinically occult, and MRI can show new lesions on follow-up scans (dissemination in time). MS has a typical distribution of white matter lesions, which is helpful in differentiating them from vascular lesions. MS involvement is typically seen in the corpus callosum, U-fibers (myelinated fibers found at the junction of gray and white matter), temporal lobes, brainstem, cerebellum, and spinal cord. This pattern of involvement is uncommon in other diseases. Small vessel disease may involve the brainstem, but it is usually symmetrical and central, while it is typically peripheral in MS.
Symptoms of multiple sclerosis are dependent on the area of demyelination. If the optic nerve is impacted, patients may experience visual changes, including loss of vision. Numbness, tingling, or weakness may be described, which can be severe enough to cause paralysis of one side of the body. Patients may become incontinent, or unable to empty their bladders. Muscle spasticity, or an involuntary painful contraction of certain muscles, may be found as MS progresses.

Four types of multiple sclerosis are described in the literature. The most common form is relapsing-remitting multiple sclerosis (RRMS), in which patients develop symptoms which respond to treatment, and then resolve. Symptom development is often referred to as an exacerbation of the disease. Episodes of remission may last for weeks to years. Secondary-progressive multiple sclerosis (SPMS) occurs when the problems caused by an exacerbation do not fully resolve during a remission. Over time, patients are identified with a progressive debility. Primary-progressive multiple sclerosis (PPMS) progresses over time, without episodes of remission or improvement of symptoms. Progressive-relapsing multiple sclerosis (PRMS) is identified when patients experience escalating symptoms over time, as well as intermittent episodes of remission.

Treatments for multiple sclerosis include IV steroids for acute exacerbations, while disease-modifying therapy is recommended once an MS diagnosis has been confirmed. These therapies may help to decrease the severity of exacerbations, as well as to decrease the potential for long-term disability. Approved medications can also be used to treat the many symptoms caused by multiple sclerosis, such as spasticity, fatigue, memory loss, pain, etc. The life expectancy of those with MS is felt to be the same as those not afflicted by this disease; however, for patients with severe, progressive forms of MS, problems caused by disability may lead to complications, such as pneumonia. For those that are not treated, over thirty percent may develop pronounced problems with mobility. Multiple sclerosis tends to have two extremes- the first being a “benign” syndrome, in which numerous lesions are identified on MRI, but the patient has few, if any, symptoms, even decades after their diagnosis. A condition called the Marburg variant of MS is at the other end of the spectrum, which involves rapidly progressive symptoms, and may include death after a brief time. Evaluations of drugs that may eliminate lesions, or prevent new MS lesions from forming, are ongoing. Stem cell therapy is also being investigated, in which a patient’s immune system is “rebooted” so that MS lesions no longer form.
Dystonia

Dystonia is a disorder characterized by involuntary muscle contractions that cause slow repetitive movements or abnormal postures. Individuals may have a tremor or other neurologic features. Dystonia may affect one muscle, groups of muscles, or muscles throughout the body. Some forms of dystonia are genetic, but the cause for the majority of cases is unknown. Researchers believe that dystonia results from an abnormality in, or damage to, the basal ganglia or other brain regions that control movement. There may be abnormalities in the brain’s ability to process neurotransmitters, which are the chemicals that help neurons communicate. There also may be abnormalities in the way the brain processes information and generates commands to move.

Dystonia can be divided into three groups, which are idiopathic, genetic, and acquired. Idiopathic dystonia does not have a clear cause, but this grouping includes many dystonias that occur. Genetic dystonia can be inherited in a dominant manner, with widely varying symptoms and severity. Acquired dystonia, or secondary dystonia, can result from environmental or other damage to the brain, or from exposure to certain types of medications. Birth injuries, infections, trauma, and strokes can all cause acquired dystonia. Dystonia can occur at any age, but are typically classified as early onset or adult onset. It can progress through various stages, with the patient eventually displaying dystonic postures and movements even when relaxed.

Dystonia is also classified based on the regions of the body that are affected. Generalized dystonia affects most or all of the body. Focal dystonia is localized to a specific part of the body. The most common focal dystonia is cervical dystonia, or spasmodic torticollis, which involves the muscles in the neck causing the head to turn to one side or be pulled forward or backward. The second most common focal dystonia is blepharospasm, which is the involuntary, forcible contraction of the muscles controlling eye blinks. Multifocal dystonia involves two or more unrelated body parts. Segmental dystonia affects two or more adjacent parts of the body. Hemidystonia involves the arm and leg on the same side of the body. A variety of dystonias have been identified that have a genetic cause, and mutations in specific genes have been linked to specific dystonic syndromes.

There are no medications to prevent dystonia or slow its progression, but treatment options exist that can ease some of the symptoms. Botulinum toxin injections into affected muscles prevent muscle contractions and provide temporary improvement in the abnormal postures and movements that characterize dystonia. This toxin injection blocks the release of the neurotransmitter acetylcholine, which causes muscle contraction. Off-label usage of certain classes of medications can block or regulate various neurotransmitters. Deep brain stimulation (DBS) can be used if medications do not sufficiently alleviate symptoms. DBS involves the use of controlled amounts of electricity that are sent into the region of the brain that is generating the dystonic symptoms to interfere with and block the electrical signals that are causing the symptoms. Surgery may be performed to interrupt the pathways responsible for the abnormal movements. Small regions of the thalamus, globus pallidus, or other deep centers in the brain can be purposely damaged to reduce symptoms of dystonia.

Dystonia abnormalities are typically not visible on MRI. However, dystonia that is associated with neurodegeneration with brain iron accumulation (NBIA) displays in a specific manner on MRI. NBIA is a group of rare genetic disorders characterized by abnormal accumulations of iron in the basal ganglia, which is the region of the brain that assists in regulating movements. The high brain iron is typically seen in the part of the basal ganglia called the globus pallidus, as well as the substantia nigra. On a T2-weighted MRI image of a patient with NBIA, the center of the globus pallidus will display high signal...
Low signal intensity is seen in the surrounding region due to the abnormal accumulation of iron. This is termed the “eye of the tiger” sign in MRI.
MRI of the Brain

Time of Flight (TOF) Angiography

Time of flight (TOF) angiography is an MRI technique that allows visualization of flow within vessels, without the need to administer contrast. It is based on the phenomenon of flow-related enhancement of spins entering into an imaging slice (inflow effect). These spins are unsaturated, and therefore give more signal than the surrounding stationary spins. This is accomplished through the use of gradient echo sequences with very short TR times, which cause saturation of the stationary tissue signal. TOF can also be considered “flow direction sensitive” when presats are used. Placement of a presat on one side that is parallel to the slice can selectively destroy the MR signal from the in-flowing blood from this side of the slice, allowing for imaging of only arterial or only venous flow. The strength of the vascular signal depends on the type of flow and its velocity, the length and orientation of the vessel being imaged (vascular signal is better if the slice is perpendicular to the axis of the vessel), and the sequence parameters (TR, flip angle, TE, slice thickness). One of the limitations associated with TOF is signal loss when flows are complex or turbulent, when flows are too slow, or when they are oriented parallel to the slice plane. Additionally, limitations include longer acquisition times, ghosting and susceptibility artifacts, and poor signal suppression of stationary tissues that have short T1 relaxation times (i.e. fat, hematoma, thrombus).

TOF can be performed as 2D or 3D acquisitions, with 3D the method of choice for imaging the Circle of Willis in the brain. In 2D, multiple thin imaging slices are acquired with a flow-compensated gradient echo sequence. The images can be combined using a post-processing technique such as maximum intensity projection (MIP) to obtain an angiographic appearance. The advantages of 2D, with its thinner slices, are better sensitivity to slow flow, better stationary tissue saturation through the use of high flip angles, and an increased vascular signal. However, spatial resolution along the axis of the slice stack may be poor. With 3D imaging, a volume of images is obtained simultaneously by phase-encoding in the slice-select direction. Each repetition excites the volume, which produces a progressive saturation of the flows. However, if flows are too slow, they may disappear entirely. Flow saturation can be reduced by dividing the 3D acquisition into slabs, and by using a variable flip angle. The flip angle should be smaller as the flow enters the volume, and larger as the flow leaves the volume to compensate for the relaxation of short T1 tissues. On Hitachi systems, this variable flip angle is carried out by the Slope Slab Profile parameter. As with 2D, post-processing performance of a MIP results in the angiographic appearance of the vessels. 3D TOF provides better spatial resolution with increased SNR when compared to 2D acquisitions.
Diffusion Weighted Imaging (DWI)

Diffusion weighted imaging (DWI) has become an important tool in assessing and diagnosing acute stroke, and is excellent at detecting small and early infarcts. It is reliable even one hour immediately after the stroke has occurred. In one comparison of non-contrast CT and MRI, the sensitivity of DWI for ischemic acute stroke ranged from 73% three hours after the event to 92% more than twelve hours after the event. In those same time frames, CT’s sensitivities were 12% and 16%, respectively. MRI’s specificity for stroke detection was 92% at three hours, and 97% after more than twelve hours. False negatives can and do occur, but at a greatly reduced rate when compared to CT. DWI has a major role in many additional clinical situations, including the differentiation of acute from chronic stroke, the differentiation of epidermoid cyst from arachnoid cyst, the differentiation of abscess from necrotic tumors, the assessment of the extent of diffuse axonal injury, and the assessment of active vs. old MS plaques (old plaques will not be bright).

DWI is based on the random Brownian motion of water molecules within a voxel. Water molecules are equally likely to move about, or diffuse, in any direction, and are only hindered in the brain by cell membrane boundaries, ligaments, and other molecules. Diffusion weighted imaging uses an EPI T2-weighted spin echo sequence that includes the application of large motion probing gradients before and after the 180° refocusing pulse. The strength and timing of these gradients are reflected in the B-value, which is the factor that controls the degree of weighting of the DWI. The higher the B-value, the stronger the diffusion weighting effects, allowing diffusion to become the dominant mechanism of tissue contrast. Moving water molecules acquire phase information by the first motion probing gradient, but are not rephased by the second motion probing gradient, and therefore lose their signal. Stationary water molecules are unaffected by the diffusion gradients, and retain their signal. These water molecules are not diffusing throughout the brain as they should be, and will appear hyperintense on DWI. Old strokes or reoccurring strokes will appear hypointense on DWI, because there are no hydrogen molecules (and little or no blood supply) in those areas at all. Diffusion weighted images are subject to
“T2 shine-through”, as they are based on a T2-weighted sequence. T2 shine-through means that fluid that would normally be bright on a T2-weighted image could also appear bright on a DWI. DWI lesions can help identify stroke etiology, as certain lesion patterns are associated with specific stroke subtypes. Cardioembolism is associated with single corticosubcortical lesions, multiple lesions in the anterior and posterior circulation, and multiple lesions in multiple cerebral territories. Large-artery atherosclerosis is associated with multiple lesions in the unilateral anterior circulation, and small scattered lesions in one vascular territory, particularly in a watershed distribution. These imaging patterns, combined with additional MRI sequences, may help in the selection of the most appropriate measures for secondary prevention of stroke.

Acute ischemic lesions have been shown to be dynamic on DWI- they grow with time. The ischemic core may evolve to irreversible infarction without effective reperfusion or cytoprotection. Some of the DWI lesion could be reversible if blood flow is promptly restored. Studies show that the initial diffusion lesion volume correlates well with the final infarct volume, as well as with the neurological and functional outcomes. This suggests that DWI can provide important early prognostic information, as well as detection of early recurrent strokes. It is reported that patients with multiple DWI lesions of different ages have a high risk of recurrent stroke.

Along with the restricted diffusion of water that results from ischemia-induced membrane dysfunction and cytotoxic edema, a decrease in the apparent diffusion coefficient (ADC) occurs. ADC is a physiological measure of the rate of water movement through brain tissue. Acute focal ischemia, or areas of restricted diffusion, will be hypointense or dark on ADC maps, as the rate of water movement will be slower in an ischemic area. Areas of normal diffusion will be bright on the ADC map, as the regular flow of spins giving off signal will be hyperintense.

Decreased diffusion in ischemic brain tissue is observed within a few minutes after arterial occlusion and progresses through a stereotypic sequence of ADC reduction, followed by subsequent increase, pseudo normalization, and, finally, permanent elevation. The appearance of DWI and ADC depends on the timing of imaging, with changes observed as follows:

- **Acute (0-7 days)**
  - ADC value decreases, with maximal signal reduction at 1-4 days
  - Marked hyperintensity on DWI and hypointensity on ADC

- **Subacute (1-3 weeks)**
  - ADC pseudo normalization occurs in the second week (7-15 days); ADC values rise and return to near baseline
  - Irreversible tissue necrosis is present despite normal ADC values
  - DWI remains hyperintense due to T2 shine through
  - After 2 weeks, ADC values continue to rise above normal parenchyma and the region appears hyperintense

- **Chronic (>3 weeks)**
  - High ADC signal
  - Low DWI signal (T2 hyperintensity, and thus T2 shine through resolve)

Post processing of the DWI sequence is performed with the Diffusion Analysis task. On the Oasis, Echelon, and Echelon OVAL systems, this task can be set up to be performed automatically. The
parameters for the DWI trace and the ADC map, as well as distortion correction settings can all be established prior to initiating the DWI sequence. The ADC maps can be generated in all 3 axes- anterior-posterior, head-foot, and right-left.

![Image of brain scans](image)

**Figure 74** DWI and ADC performed in less than 2 hours from initial onset of patient’s symptoms; 
a- DWI sequence shows an area of hyperintensity in right temporal, insular, and frontal lobes; 
b- ADC map shows matching area of hypointensity, confirming that DWI lesion is due to acute ischemia; clot was found in right middle cerebral artery

**Diffusion Tensor Imaging (DTI)**

Diffusion tensor imaging (DTI) can improve our understanding of the brain structures and neural connectivity. DTI measures are thought to be representative of brain tissue microstructure, and are useful for examining organized brain regions, such as white matter tract areas. DTI data offers information regarding the directions of the neural connections, inferring which brain areas are connected with each other. It can also reveal the integrity of these connections, and enable mapping of the orientation of the white-matter tracts.

When diffusion motion is symmetric, or equal in all directions, it is referred to as isotropic. In DTI, diffusion motion in the white matter is asymmetric, or not the same in all directions, and is referred to as anisotropic. This asymmetry occurs because diffusion is restricted in the direction that is perpendicular to the long axis of the axons. The resulting degree of anisotropy in a white matter region, as seen on a Fractional Anisotropy map, can be viewed as a reflection of the degree of the structural integrity of the white matter. Since DTI is limited in its ability to demonstrate directional anisotropy, advanced methods such as color coding and tractography (fiber tracking) have been used to investigate directionality.
Where good diffusion exists, there is signal loss along the direction in which a gradient is applied. In order to determine the diffusion status in all directions, multiple diffusion weighted gradients in different directions must be applied. The minimum number of directions is six, which would involve diffusion weighting measurements in the anterior, posterior, superior, inferior, right and left directions. Hitachi currently offers DTI in 6, 7, 13, or 21 directions, with 21 being the recommended number. Information from all the diffusion weighted images in the various directions is collected to determine where water is able to diffuse to in each voxel. An ellipsoid represents where water can go, with a long thin ellipsoid indicating good diffusion for water along the long axis of that ellipsoid. The mathematical way to describe the ellipsoid for each voxel is called the tensor. The mathematics used to describe the tensor/ellipsoid for each voxel are used to produce parametric maps, which are images where the pixel values represent some parameter other than signal intensity. The parametric maps that are produced from Diffusion Tensor Analysis post processing on Hitachi’s systems are Fractional Anisotropy (FA) and Mean Diffusivity (MD). Fractional Anisotropy maps can communicate information concerning the orientation of the underlying structure of the fiber tracts in the brain. Mean Diffusivity is a measure of the average molecular motion, independent of any tissue directionality. This measurement can be affected by cellular size and integrity.
DTI can provide useful information regarding the myelination of white matter, as anisotropy is greater in ordered structures, such as myelinated axons. In many pathologic conditions, FA may vary because of altered diffusivity and disorganization of the white matter fibers, leading to decreased anisotropy. The FA measurement may become abnormal before the lesion is morphologically apparent on conventional MRI, and may therefore help in early detection and in defining the extent of these lesions. DTI has been used extensively to detect acute ischemic brain injury. In the acute phase of ischemia, FA values are increased. In chronic stroke, diffusion anisotropy remains significantly lower in the infarcted area than in the similar contralateral region of the brain, even 2-6 months after an ischemic stroke. FA data combined with ADC information may aid in the assessment of the severity of strokes, as well as helping to distinguish between acute and ischemic changes. Better understanding of stroke severity and acute vs. ischemic changes can affect stroke treatment determination.

Imaging on patients with chronic epilepsy may display mesial temporal sclerosis or hippocampal sclerosis. DTI findings on these patients may include increased diffusivity and decreased anisotropy caused by the loss of structural organization, and expansion of the extracellular fluid space. Changes in DTI may extend to areas of the brain that appear morphologically normal on conventional MRI. In this way, DTI may define the true extent of pathology, and improve preoperative planning.

DTI has demonstrated a potential in distinguishing gliomas and solitary metastasis in the brain parenchyma. Significantly higher Mean Diffusivity and lower FA, as compared with levels in normal-appearing white matter, have been demonstrated in the peritumoral regions of both gliomas and metastases. Peritumoral Mean Diffusivity of metastases and meningioma is significantly higher than that of gliomas, whereas the FA values are similar, which confirms the infiltrative nature of gliomas.

Many studies have shown potential advantages of DTI in the diagnosis and follow-up of MS lesions, as multiple sclerosis harms neural integrity. In MS, Fractional Anisotropy values are more sensitive than ADC values with regard to white matter abnormalities. Lesions with destructive pathology or acuity generally have increased diffusivity and decreased FA values. On conventional T2-weighted and FLAIR images, normal-appearing white matter adjacent to the MS lesions may also demonstrate abnormality, bringing to light the actual extent of the lesions. In some cases, the gray matter around the white matter lesions is abnormal, suggesting that disease may not be isolated to the white matter.
DTI is playing an increasingly important role in research into mild traumatic brain injury and mild cognitive impairment. In cases of mild traumatic brain injury, symptoms of brain damage typically involve mood changes or confusion, while neurological exams and standard brain imaging techniques may show no signs of damage. In one study, DTI revealed white matter abnormalities in patients with mild traumatic brain injuries, with no abnormal DTI findings in the control group. Conventional MRI had not revealed any differences between the two groups. Additional evaluations were performed 3-5 months later, as this is the typical recovery timeframe for mild brain injuries. The patients showed improvements on some of their DTI measures, while control subjects showed no differences. The study proposes that DTI may be used as a potential biomarker of injury that may assist in classification and tracking of mild traumatic brain injury and its effects. Another study involved high school football players whose helmets were fitted with head impact telemetry accelerometers to assess the frequency and severity of helmet impacts. None of the athletes showed signs of concussion during their season. They were divided into heavy-hitter and light-hitter groups, based on information from their helmet devices. Both groups showed increases in fractional anisotropy before and after the season, likely due to the effects of adolescent brain development. Higher FA values result when the direction of water movement is fairly uniform, as seen in healthy white matter. However, the heavy-hitting football players showed statistically significant decreases in FA after the season in specific areas of the brain, including the corpus callosum and deep white matter tracts. Decreases in fractional anisotropy indicate that water movement is more random, suggesting the existence of microstructural abnormalities. Again, the heavy-hitting players showed no signs or symptoms of clinically diagnosed concussion. These results raise concerns about potential white matter injury or delayed brain development, as similar MRI changes in previous research have been associated with mild traumatic brain injury.

A Duke University study combined DTI with functional MRI and PET scans, resulting in the detection of differences in the brains of patients with mild cognitive impairment. The researchers constructed connectomes - maps of the brain’s neural connections- for each subject in the study. The connectomes were created by mapping neural connections and networks using DTI to evaluate brain structure, and adding information from functional MRI to see the way the brain connections occurred. Study subjects also had PET amyloid imaging at baseline, and at two-year follow-up. The study brought together two of the major changes in the Alzheimer’s brain- structural tissue changes, and pathological amyloid plaque deposition. DTI may have a promising role as a diagnostic adjunct in the use of structural network topology as an imaging biomarker of Alzheimer’s disease. The structural connectome offers a way to characterize and measure brain connections, and how they change through disease or age. This information may lead to the application of therapy earlier in the course of Alzheimer’s disease.

**Blood Sensitive Imaging (BSI)**

Blood sensitive imaging (BSI) uses a susceptibility weighted sequence that is sensitive to compounds that distort the local magnetic field, making it useful in detecting blood products, calcium, etc. It exploits the magnetic susceptibility differences of these tissues as a source of contrast enhancement. Compounds that have paramagnetic, diamagnetic and ferromagnetic properties all interact with the local magnetic field, distorting it, and thus altering the phase of local tissue, which results in loss of signal. Paramagnetic compounds include deoxyhemoglobin, ferritin, and hemosiderin. Diamagnetic compounds include bone minerals and dystrophic calcifications. BSI on Hitachi systems is performed with a 3D RSSG EPI sequence that is T2* weighted. When performed on higher field strength systems, and by using longer echo times, the sensitivity to susceptibility effects increases. A phase mask obtained from the phase images is multiplied with magnitude images in order to increase the visualization of the smaller veins and other sources of susceptibility effects. This is helpful in the detection of calcifications.
and microhemorrhages, which are both characterized by low signal. Calcifications will appear bright because of a positive phase shift, and hemorrhages appear dark, because of a negative phase shift. The 3D dataset is best displayed after post-processing with the minimal intensity projection (minIP) algorithm, and the Sliding projection setting on Hitachi’s Oasis, Echelon, and Echelon Oval systems.

![Figure 78 Echelon Oval BSI source images on left, BSI image after post processing on right](image)

Blood sensitive imaging (BSI) in the brain has been found to be a useful tool for the identification of microbleeds and vascular malformations, as well as for a better understanding of many cerebrovascular diseases. Susceptibility weighted imaging methods are used to demonstrate cerebral microbleeds. These are relatively common in the general elderly population, and are more frequently observed in patients with Alzheimer’s disease. Hypertensive encephalopathy is characterized by multiple cerebral microbleeds, which are usually silent. They may be discovered when MRI is used to understand the cause of intraparenchymal hemorrhage located outside the basal ganglia. Blood sensitive imaging is more sensitive than routine T2*-weighted GE sequences for cerebral microbleeds in blood pressure-related small vessels disease. Cerebral microbleeds are usually discovered both in deep basal ganglia and subcortical white matter. They are indicative of previous extravasation of blood, and are often associated with the presence of a symptomatic hemorrhage in the corresponding area. The number of cerebral microbleeds, which remain detectable for years, is significantly associated with blood pressure levels. The presence of deep cerebral microbleeds can be a useful marker of blood pressure-related small vessels disease, which can help in the differential diagnosis of cerebral amyloid angiopathy.

![Figure 79 Patient with long-standing hypertension; a- T2-weighted image shows a thin hypointense band in the right thalamus, which represents hemosiderin deposition (solid white arrow); b- GE T2*-weighted image shows multiple microbleeds, with the largest one in the right thalamus (solid white arrow); c- Post processing with minIP demonstrates increased number of identifiable microbleeds compared with GE images; they can be seen bilaterally in the basal ganglia and in the subcortical temporal white matter (solid black arrows)](image)
BSI is also well suited for showing increased iron content in the brain. Iron deposition increases in the brain as a function of age, but abnormally elevated iron levels are evident in many neurodegenerative disorders, including Parkinson’s disease, Alzheimer’s disease, Huntington’s disease, and amyotrophic lateral sclerosis (Lou Gehrig’s disease). BSI can be proposed as a useful imaging tool to identify iron deposition as a biomarker for Parkinson’s disease progression. In 70-98% of patients with Alzheimer’s disease, cerebral microbleeds are commonly observed, and intravascular amyloid deposition is found at autopsy. Patients with multiple cerebral microbleeds have more white matter hyperintensities and perform worse on mini mental state examinations compared with patients with no microbleeds.

![Figure 80 GE T2*-weighted image on left demonstrates small punctate hypointense foci in right parietal cortex (white open arrow); Post processing with miniIP on right demonstrates increased visualization of markedly hypointense foci surrounding white matter abnormalities, which correspond to multiple cerebral microbleeds](image1)

BSI is quite useful in the acute phase of a stroke, as it is very sensitive to the presence of cerebral microbleeds, which may predict the probability of potential hemorrhagic transformation after thrombolytic treatment. Cerebral microbleeds may represent a link between cerebral hemorrhage and ischemia. In addition, BSI can identify the acute intravascular clot in the main and distal branches of the cerebral arteries. BSI can be used in the assessment of tissue viability in patients with hyperacute cerebral ischemia, as it can provide functional information about the ischemic penumbra.

![Figure 81 Left internal carotid artery dissection; miniIP image on left shows improved visualization of veins of left cerebral hemisphere, related to increased oxygen extraction in ischemic penumbra; corresponds to hypoperfusion deficit shown by mean transit time perfusion map on right; delayed transit time in left middle cerebral artery territory](image2)

![Figure 82 Mean transit time perfusion map on left performed 24 hours after stent placement shows complete resolution of perfusion deficit; miniIP on right shows normalization of venous drainage of left hemisphere](image3)
Blood sensitive imaging (BSI) has become a functional method for evaluating cerebral venous sinus thrombosis by demonstrating engorgement of the venous system as a result of venous hyper tension and collateral slow flow. Dural sinus thrombosis causes an increase in deoxyhemoglobin concentration in the veins involved that appears as a prominent area of hypointense signal intensity. BSI can also depict the features of parenchymal or extra-axial hemorrhages that can occur in the case of infarction.

Cerebral arteriovenous malformations (AVMs) are easily displayed by conventional MRI and MRA due to their characteristic high flow. However, venous malformations mainly consist of slow flow small vessels, so their visualization is better suited to BSI. It plays a substantial role in their identification and characterization by improving their detection rate, as well as aiding in therapeutic planning.

MRI with GE sequences has been extensively used for investigating traumatic brain injuries, either in the acute phase, when the clinical picture of a severe coma is not explained by CT, or months after trauma, in order to understand the causes of an unsuccessful recovery. In both cases, diffuse axonal injuries can be responsible for the clinical picture. BSI has been used in the identification of smaller hemorrhages due to a shear-strain mechanism of injury, thus refining the prediction of outcome. Hemorrhagic diffuse axonal injury lesions can be six-times better detected on BSI vs. conventional T2*-weighted GE sequences, and the recognizable volume of hemorrhage is approximately twofold greater. Both number and volume of hemorrhagic lesions correlate with neuropsychological deficits.

Figure 83 Diffuse axonal injury with sever traumatic brain injury after motorcycle crash; GE T2*-weighted image on left shows hemorrhagic shearing injuries barely visible in right fronto-opercular and parieto-occipital regions (solid black arrows); miniIP on right shows additional microhemorrhages at gray matter-white matter junction of frontal lobes and in right parieto-occipital white matter (solid black arrows)

Mild traumatic brain injuries commonly display microbleeds on BSI, which are associated with worse neuropsychological performance. Some mild traumatic brain injuries lead to prolonged disability, with BSI showing great accuracy in detecting trauma-related injuries, such as diffuse axonal and vascular injuries. BSI may have the potential to become an imaging biomarker for mild traumatic brain injuries. One study involved 111 patients with mild traumatic brain injuries that were all negative for hemorrhage on CT and standard MRI. The 111 healthy controls had no history of head trauma, and were age- and sex-matched to the injured patients. All subjects underwent BSI, with testing on the brain injured patients performed between one and eight weeks after their injury. A total of 60 microbleeds
were found in 26 mild traumatic brain injury patients, while 15 microbleeds were found in 12 control subjects. In the brain injury patients, 87% of the microbleeds were found in the cortex and subcortical white matter, compared with only 20% of the control subjects. Central brain area microbleeds were more common among the controls, which are commonly attributed to hypertension or vascular abnormalities. The number of microbleeds may be an indicator of the severity of a mild traumatic brain injury, as more blood extravasation means more underlying injury to neurons and vascular tissues.

BSI can provide a thorough assessment of the internal angioarchitecture of brain tumors by displaying any increased microvasculature inside and beyond the tumor margins, as well as identifying the foci of hemorrhage and calcification.

Figure 84 T2-weighted image on left demonstrates mass that is irregularly hyperintense with cystic changes and small hypointensities representing small vessels and calcifications; contrast enhanced minIP on right displays calcifications as punctate hypointensities, unchanged after gadolinium injection (solid white arrows); post processing with minIP algorithm allows simultaneous visualization of arteries (hyperintense, solid black arrows) and veins (linear hypointensities, open white arrow) around and inside the tumor; contrast enhanced BSI is superior in demonstrating a diffuse blood-brain barrier rupture in the lateral necrotic area (bright signal, asterisk); histopathology revealed a primary neuroectodermal tumor with extensive cystic and necrotic changes and increased vascularity.

This imaging method offers an additional tool in the neuroradiological grading of cerebral neoplasms. Overall, BSI has increasing indications for use in neuroradiology, and should be considered for inclusion in routine imaging protocols for trauma and vascular abnormalities.

Perfusion Imaging

The ultimate goal of perfusion MRI is to measure or assess the blood flow that is irrigating the organ in question. Perfusion MRI gives access to information concerning the capillary microcirculation of tissue, and allows for quantitative measurements of parameters such as blood volume, blood flow, and transit time. This flow corresponds to microcirculatory tissue perfusion, rather than the flow of the main blood vessels. MR perfusion imaging of the brain is performed most often on acute stroke patients, at a time when treatment decisions based on perfusion measurements may dramatically affect patient outcomes. It is used to refine the selection of patients for thrombolysis, particularly the use of tPA (tissue plasminogen activator). tPA is a thrombolytic drug whose purpose is to restore brain perfusion, but which was initially approved for use only in those very few acute stroke patients who can be treated...
within three hours of symptom onset. This drug offers both the potential for lifesaving rescue of underperfused tissue, as well as the risk of catastrophic intracranial hemorrhage. Perfusion imaging has additional potential roles in ischemic cerebrovascular disease, including establishing diagnosis, predicting prognosis, and guiding non-thrombolytic therapies designed to maintain cerebral perfusion.

An important principle in ischemic pathophysiology is that the time it takes for ischemic damage to become irreversible is inversely related to the severity of the ischemia. Brain tissue dies after just a few minutes without any blood flow, but moderately ischemic or “at-risk” tissue may remain potentially viable for hours before becoming irreversibly injured. One approach that is used to help identify this “at-risk” tissue is called the diffusion-perfusion mismatch. A diffusion abnormality identifies the infarct core, which is irreversibly injured tissue. A perfusion abnormality identifies the tissue at risk of eventual infarction. The “mismatch” between them represents the ischemic penumbra, so named because this mildly ischemic tissue sometimes forms a ring-like shape surrounding the infarct core. Tissue in the ischemic penumbra is still structurally intact, and hence viable, but electrically dysfunctional, as the neurons have ceased their electrical transmission. Problems with the diffusion-perfusion mismatch approach include the perfusion abnormality overestimating the final infarct volume, the mismatch region overestimating the amount of tissue actually at risk, and the assumption that the initial diffusion lesion represents irreversibly infarcted tissue. Diffusion lesions may be reversed if blood flow is restored at an early time point.
Figure 86 Perfusion deficiency on perfusion weighted image on left includes infarct core plus penumbra and region of benign oligemia (deficiency in volume of blood in organ); early abnormality on diffusion weighted image in center equals infarct core plus a part of the tissue at risk (penumbra); perfusion-diffusion mismatch in image on right does not optimally define the ischemic penumbra.

Dynamic susceptibility contrast imaging is the technique used in most clinical centers for MR perfusion imaging of acute stroke. Gadolinium chelates are used for their magnetic susceptibility effect at high concentration: the heterogeneities of the magnetic field created by the presence of the contrast agent in the vessels leads to a decrease in the T2 and T2* relaxation times of the surrounding tissue. As the contrast agent arrives in the brain and then washes out again, first the large arteries demonstrate a transient loss in signal intensity, followed by transient parenchymal signal loss as the contrast agent moves through smaller vessels, and then finally signal loss in the large intracranial veins. In order to create high-quality perfusion maps, the passage of the contrast agent in each part of the brain must be measured with high temporal resolution, obtaining images no less frequently than one every 1.5 seconds. Echo planar imaging (EPI) pulse sequences are typically used, with gradient echo EPI used more often than spin echo EPI. Dynamic susceptibility contrast produces different degrees of signal change for similar quantities of gadolinium in blood vessels of different sizes. Gradient echo EPI is more sensitive to contrast agents in larger vessels, while spin echo EPI demonstrates greater sensitivity to contrast agents in smaller vessels.
Elapsed time since contrast injection appears below each perfusion source image; at 14.0 and 15.5 seconds, contrast appears in some large arteries, which become hypointense; by 20.0 seconds, gadolinium in small vessels causes loss of parenchymal signal intensity in normally perfused right hemisphere; arrival of contrast is delayed and prolonged in left hemisphere.

Figure 87 Elapsed time since contrast injection appears below each perfusion source image; at 14.0 and 15.5 seconds, contrast appears in some large arteries, which become hypointense; by 20.0 seconds, gadolinium in small vessels causes loss of parenchymal signal intensity in normally perfused right hemisphere; arrival of contrast is delayed and prolonged in left hemisphere.

Individual dynamic susceptibility images undergo additional post-processing to produce maps of various perfusion-related parameters. Perfusion analysis on Hitachi MR systems produces cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) maps. It is important to understand the hemodynamics of ischemic stroke in order to appreciate the interrelationships of cerebral blood measurements. The changes in perfusion that occur in acute stroke are driven by changes in cerebral perfusion pressure (CPP). CPP is basically the difference between mean arterial pressure and venous pressure, the latter of which is usually equal to intracranial pressure. The cerebral vasculature responds to small reductions in CPP by dilating small arteries, thereby reducing cerebrovascular resistance, and maintaining normal cerebral blood flow (CBF) over a wide range of perfusion pressures. This vasodilatory response results in an increase in cerebral blood volume (CBV), which is the volume of the intravascular space within a particular volume of brain tissue, such as that within a single image voxel. However, the increase in CBV may be subtle and difficult to detect in MR perfusion images. Vasodilation also results in an increase in mean transit time (MTT), which is the average amount of time that red blood cells spend within a particular volume of tissue. The central volume theorem states the relationship between CBF, CBV, and MTT as MTT=CBV/CBF. Cerebral blood flow (CBF) is the most directly connected to tissue viability, as it measures the rate of delivery of oxygen and glucose to ischemic brain tissue. Tissue with elevated mean transit time (MTT) and reduced cerebral blood flow (CBF) is more severely and immediately threatened by ischemia, whereas tissue with elevated MTT but normal CBF experiences some smaller and perhaps less urgent degree of risk. The risk of infarction for tissue with an elevated mean transit time is dependent on the associated cerebral blood flow, so both CBF and MTT maps should be consulted.
Testing is ongoing for the use of arterial spin labeling as a non-invasive tool for the assessment of brain perfusion in patients with contraindications to gadolinium-based contrast agents. Currently, negative aspects of using this method include reduced signal-to-noise ratio, overestimation of tissue perfusion, and residual signal from labeled spins in arterial vessels. However, it is well suited for exploring one specific area, as in the case of strokes, so research using arterial spin labeling for perfusion will continue.

**MR Spectroscopy**

Proton magnetic resonance (MR) spectroscopy of the brain is a non-invasive, in vivo technique that allows investigation into brain metabolism. The generation of a spectrum of brain metabolites by MR spectroscopy provides the clinician with information on the regional chemical environment. It provides valuable insights into brain tumor characteristics, progression, and response to treatment. In addition, because of its sensitivity to brain dysfunction in the presence of apparently normal structural imaging, interest has increased in the use of spectroscopy as a biomarker of neurodegenerative disorders such as Alzheimer’s disease.

The hydrogen nucleus is abundant in certain neurometabolites, and has high sensitivity, so it is the principle nucleus applicable to spectroscopic investigation associated with clinical MR imaging of the brain. The proton MR spectrum comprises a set of resonances (peaks) distributed along the x-axis of the graph, labelled in parts per million (ppm). The amplitude of the resonances is measured on the y-axis, typically using an arbitrary scale. The three prominent peaks that are consistently seen include N-acetyl aspartate (NAA), creatine (Cr), and choline (Cho). The positions of the resonances along the x-axis are constant, while the relative heights of the resonances can differ depending on various MR imaging parameters. Additional compounds may be detected due to pathological conditions that increase their concentrations, as well as due to changes in parameters.

The biological significance of the prominent compounds includes:

- **N-acetyl Aspartate (NAA)** - Largest signal in the normal adult brain spectrum; one of the most abundant amino acids in the central nervous system; breakdown product of N-acetylaspartylglutamate (NAAG), which is a neurotransmitter; good surrogate marker of
neuronal health; reliable marker for monitoring neuronal energy impairment and dysfunction; displays a natural physiological increase in concentration during brain development and maturation in infancy; higher concentration within gray matter compared to white matter in adult brain

- **Creatine (Cr)** - Primary creatine resonance is combination of creatine (Cr) and phosphocreatine (PCr); smaller creatine peak found at higher ppm on x-axis; involved in energy metabolism; lower levels in white matter than in gray matter in normal brain; higher levels in cerebellum compared to supratentorial regions; concentration shows little variations between differing pathologies

- **Choline (Cho)** - Composite peak representing soluble constituents of cell membrane including choline, phosphocholine (PC), and glycerophosphocholine (GPC); involved in membrane synthesis and degradation; elevated in disease states where increased membrane turnover is involved, such as malignancy and demyelination; slightly higher concentration in white matter compared to gray matter; concentration in astrocytes may be twice that found in neurons; levels are high in glial cells, low in hepatic encephalopathy

- **Myo-Inositol (mI)** - Resonance found on spectra obtained at short echo times; synthesized in glial cells, absent from neurons, incapable of crossing blood-brain barrier; increases in resonance peak thought to represent increase in glial cell size or glial proliferation, both of which occur in inflammation; increased in Alzheimer’s dementia and demyelinating diseases, reduced in hepatic encephalopathy

- **Glutamate and Glutamine (Glu and Gln)** - Complex spectral appearance, appearing as multiple resonances in various regions; best appreciated at short echo times; glutamate is most abundant amino acid in brain, and dominant neurotransmitter; glutamate is increased in patients with multiple sclerosis (in both demyelinating lesions and apparently normal white matter; glutamine is astrocyte marker, may be elevated in hepatic encephalopathy, Reyes syndrome, hypoxic-ischemic events; glutamine decreased in Alzheimer’s disease and hyponatremia

- **Lactate** - Not detectable in brain under normal conditions; often detected in pathological conditions such as acute hypoxic or ischemic injury, brain tumors, or mitochondrial diseases

- **Lipids** - There should be little lipid signal in the healthy brain, unless the voxel is contaminated by fat in subcutaneous tissues, meninges, or the scalp; elevated lipid levels have been observed within high-grade brain tumors and metastasis reflecting areas of necrosis or hypoxia, as well as within various hereditary leukodystrophies

Many additional compounds have been detected in proton spectra of the human brain. Some compounds are present in the normal human brain, but are difficult to detect routinely because they are small and/or have overlapping peaks. Some compounds are only detected under disease or other abnormal conditions. Alcohol is one of the more familiar of these additional compounds.

Spectroscopy can be performed by acquiring one single voxel per scan, two voxels per scan, or a large volume voxel. In single voxel spectroscopy, the operator places the voxel within a lesion, obtaining the metabolic profile of the lesion in an attempt to characterize it. It is recommended that a second single voxel spectroscopy be performed over the contralateral side, in order to obtain comparable information.
over normal tissue. In dual voxel spectroscopy, only one spectroscopy scan is performed, with one voxel placed over the lesion, and the second voxel placed over normal tissue on the contralateral side. The larger volume voxel is scanned using chemical shift imaging. In general, single and dual voxel spectroscopies are performed when localized accurate measurements of neurometabolites are required, whereas chemical shift imaging is used when information on spatial distribution is desired.

Figure 89 Single voxel spectroscopy setup with voxel within lesion on left; recommended second single voxel setup on right with voxel placed over contralateral side

Figure 90 Dual voxel spectroscopy setup with one voxel placed over lesion, and second voxel placed over normal tissue on contralateral side

Figure 91 CSI (chemical shift imaging) spectroscopy setup; orange box is volume of interest; green grid area is field of view region

Single and dual voxel spectroscopy can be performed using either PRESS or STEAM sequences. Both involve selecting a volume of interest by applying three sequential RF pulses. Each RF pulse is combined with a gradient in the X, Y, or Z direction to allow the selection of a slice in each plane. This generates a rectangular volume of interest, and only the signal within the volume where all three slices overlap is refocused and acquired. The PRESS (Point RESolved Spectroscopy) sequence uses one 90° RF pulse, and
2-180° RF pulses. PRESS uses a spin echo, and has twice the SNR and less susceptibility to motion as compared to STEAM. A STEAM (STimulated Echo Acquisition Mode) sequence uses 3-90° RF pulses, and can accommodate shorter TE times. A CSI (Chemical Shift Imaging) sequence is used for larger volume spectroscopy, where many voxels are each giving rise to a spectrum simultaneously. Like PRESS, one 90° and 2-180° RF pulses are combined with a gradient in the X, Y, or Z direction, and only the signal within the volume where all 3 slices overlap is refocused and acquired. In CSI, the chemical information is phase encoded, analogous to the spatial information that is phase encoded in conventional MR imaging. Chemical shift is basically a difference in frequency due to the fact that chemical environments and electron bonds within them affect nuclei differently. Additionally, phase encoding is applied in 2 directions in the field of view (FOV), and the FOV is significantly larger than the volume of interest in chemical shift imaging.

Shimming is performed prior to spectroscopy to optimize the magnetic homogeneity over the voxels. Water suppression is also applied to minimize the water peak for better detection of metabolite signals. A CHESS (CHEmical Shift-Selective) pulse is used to suppress water.

The concentration of a metabolite is linearly proportional to its spectral peak area. However, peak area measurements in in vivo spectroscopy are complicated by resonance overlap, baseline distortions, and non-ideal line shapes. The measurements also depend on factors such as relaxation times, pulse sequence used, and scanner hardware. Rather than trying to quantify metabolite concentrations, a technique has been established in which relative amounts (ratios) of each metabolite are reported, often using creatine as a reference. However, creatine can show regional variations, and can be affected by disease or pathology, so caution must be used when interpreting ratios of metabolites to creatine. Normal variations in neurometabolite concentration exist between different age groups and between different parts of the brain. Age-related variations are attributed to myelination, and are at their greatest in the first few years of life. NAA/Cr ratios are at their highest in children, peaking at approximately 10-14 years, then gradually falling in the elderly. NAA concentration is typically higher in gray matter compared to white matter, while the reverse is true for choline.
The clinical applications of MR spectroscopy cover a wide variety of neuropathological conditions, including traumatic brain injury, neonatal hypoxic ischemic brain injury, epilepsy, multiple sclerosis, infection and metabolic disorders. The two conditions for which it has shown its greatest clinical potential are brain tumors and Alzheimer’s disease. Single voxel spectroscopy performed on brain tumors typically involves placement of the voxel within the neoplasm, with the inclusion of a reference voxel in the corresponding region of the contralateral hemisphere. Brain tumors generally show an elevated level of choline, attributable to increased cancer cell proliferation, and reduced NAA, which reflects the loss of neuronal integrity, and the fact that most brain tumors are non-neuronal in origin. Due to this reciprocal relationship, changes in the ratio of the two metabolites (Cho/NAA) are often studied to identify regions of abnormality. A Cho/NAA ratio greater than one has shown to have a positive correlation with neoplasia. Much of the work on the spectral analysis of neoplasms has concentrated on differentiating high-grade from low-grade tumors. Approximately 9-45% of apparently structurally benign lesions on conventional MRI are actually malignant. In addition, the ability to detect transition from low-grade to high-grade could have serious implications for patient management. Cellular heterogeneity can introduce overlap between tumor grades, but multivoxel spectroscopy can help by indicating the most aggressive part of the lesion on the spatial distribution maps. Typically, higher Cho/Cr and lower NAA/Cr ratios suggest high-grade as opposed to low-grade tumors. Myoinositol decreases when tumor grade worsens, while the presence of lactate within the tumor is believed to suggest transformation to a higher grade. A recent systematic review indicated that MR spectroscopy resulted in accurate diagnoses in 78% to 96% of cases when differentiating low-grade from high-grade gliomas. MR spectroscopy has also found success in differentiating brain abscess from cystic tumor, as well as differentiating recurrent tumor from radionecrosis.
Alzheimer’s disease shows predilection for the hippocampi and anteromedial temporal lobes. However, reproducibility of high quality spectra is difficult due to susceptibility artifact encountered when imaging the medial temporal lobes. The voxel is typically placed in the posterior cingulate gyrus, which is a spectroscopically homogeneous region. Reduced NAA and elevated myoinositol are consistently demonstrated on the spectra, even in the early stages of Alzheimer’s. It is thought that elevated myoinositol levels may provide the earliest imaging indicator of the disease, as glial proliferation typically precedes significant neuronal loss or mitochondrial dysfunction. MR spectroscopy is also proving useful in the diagnosis of mild cognitive impairment, which is recognized as preceding the development of Alzheimer’s disease. It is capable of predicting which patients with mild cognitive impairment will go on to develop Alzheimer’s disease. A significant decline in NAA/Cr ratio or rise in Cho/Cr ratio measure in the paratrigonal white matter may be detected before the clinical onset of dementia. These findings could have significant implications in the management of the condition.

MR spectroscopy has a great role to play in the world of personalized medicine, with the concept of regarding each patient as their own internal standard, and predicting/managing diseases before they become life threatening. Technical advances must be coupled with a greater understanding of the biochemistry behind the MR visible neurometabolites, so that conclusions drawn from spectroscopic data are based in facts, rather than assumptions.

**Functional MRI (fMRI)**

Functional magnetic resonance imaging (fMRI) is a technique for measuring brain activity. It works by detecting the changes in blood oxygenation and flow that occur in response to neural activity- when a brain area is more active it consumes more oxygen, and to meet this increased demand, blood flow increases to the active area. fMRI can be used to produce activation maps showing which parts of the brain are involved in a particular mental process. It is becoming the diagnostic method of choice for learning how a normal, diseased or injured brain is working, as well as for assessing the potential risks of surgery or other invasive treatments of the brain.

When discussing fMRI, most people are referring to its use for brain mapping, and the evaluation of brain function using Blood Oxygenation Level-Dependent (BOLD) imaging, which involves hemodynamics. Neuronal activation requires energy for cell function, which is delivered by the vascular system in the forms of oxygen and glucose. Oxyhemoglobin (oxygen-carrying hemoglobin) in capillary red blood cells delivers oxygen to the neurons. When neuronal activity increases, there is an increased demand for oxygen, leading to increased cerebral blood volume and increased cerebral blood flow. Cognitive activity and sensory stimulation cause increased flow within a few seconds into the involved segments of the brain. These hemodynamic responses bring an excess of oxygenated blood to the area. When the oxygen is extracted from the blood by active neurons, it results in the creation of deoxyhemoglobin, which causes local dephasing of proton spins, and signal loss. This early signal loss has been called the “initial dip”, occurring approximately 0.5-2 seconds after stimulus onset. Following this initial dip, there is an increase in cerebral blood flow that is at least twice as large as the proportional increase in oxygen consumption by the nerve cells. This overperfusion with oxygenated blood results in a relative increase in oxyhemoglobin and corresponding relative decrease in deoxyhemoglobin in capillaries and veins in the area. The decrease in deoxyhemoglobin causes an increase in signal on T2*-weighted images that begins a few seconds after neuronal activation and peaks at or near 5 seconds. This positive BOLD response to stimulus is most obvious in and near large vessels, whereas the initial dip is more localized to the capillary bed. Although the first few seconds of the positive BOLD response provide better spatial resolution, the signal-to-noise ratio (SNR) is lower when
compared to the latter part of the positive BOLD response. There is often a “signal undershoot” after the latter part of the BOLD response, where the signal dips and then recovers to baseline.

![Figure 94 BOLD signal shows initial dip, then more prolonged "positive" signal](image)

Oxyhemoglobin is diamagnetic, meaning it has a very slight magnetic susceptibility when exposed to a strong external magnetic field. When oxygen disassociates from hemoglobin, it leaves the heme iron exposed, resulting in a molecule called deoxyhemoglobin, which is paramagnetic. Paramagnetic substances have greater magnetic susceptibility than diamagnetic substances, and attract and enhance the magnetic field. Blood that is completely deoxygenated has approximately 20% more magnetic susceptibility than blood that is completely oxygenated. Deoxyhemoglobin can therefore be considered an endogenous contrast agent, or one with no external cause. Gadolinium compounds that are injected into the body are exogenous contrast agents, as they originate outside the system. Since deoxyhemoglobin and gadolinium are both paramagnetic substances, both create inhomogeneities within the local environment of a single voxel. This causes dephasing of proton spins within that voxel, which reduces signal. fMRI pulse sequences create images with emphasis on contrast based on blood oxygen levels. BOLD contrast is a functional type of contrast, delineating active versus non-active areas based on local changes in blood oxygen level. The imaging is dynamic, measuring a change in local blood oxygenation over a period of time. The temporal resolution of fMRI depends on the sampling rate, which is commonly one image every few seconds. The correlation of a measured physiologic change to the mental process causing the change is called functional resolution.
The BOLD signal is a very weak signal, and is very susceptible to motion of the head, as well as respiratory and cardiovascular motions. Gradient echo EPI sequences are used most often for fMRI. Echo planar imaging (EPI) allows for very fast imaging, providing good temporal resolution. Gradient echo sequences produce T2*-weighted images that are susceptible to even the small, localized spatial variation in the magnetic field caused by deoxyhemoglobin. Spin echo EPI is sometimes used for fMRI, as it offers superior resolution, but lower SNR. Voxel size must be large enough to give good SNR, as the BOLD signal is very weak. fMRI is most often performed on 3T or higher strength systems. In theory, there is a quadratic (4 times) increase in signal at 3T compared to 1.5T, while the increase in noise is linear with the increasing field strength. This results in better SNR at the higher field strength. In addition, the increased effects of magnetic susceptibility at 3T provide better imaging, as the contrast depends on very small differences in local magnetic susceptibility due to the exposed iron atoms on deoxyhemoglobin.

The BOLD signal that is currently used for most fMRI is essentially a qualitative signal, and is dependent on the combined physiological changes of blood flow and oxygen metabolism. The BOLD signal is actually a signal change between two conditions, such as tapping your fingers compared to resting. BOLD imaging cannot tell us anything about the actual level of blood flow before the task started. An alternative MRI method, Arterial Spin Labeling (ASL), can be used to measure blood flow changes directly. ASL manipulates the MR signal of arterial blood before it is delivered to different areas of the brain, making it possible to measure the absolute level of blood flow in any condition. By subtracting two images in which the arterial blood is manipulated differently, the static signal from all the hydrogen nuclei in the rest of the tissue subtracts out, leaving only the signal arising from the delivered arterial blood. In some diseases, such as Alzheimer’s, the hypothesis that blood flow decreases as Alzheimer’s disease develops could be detected with ASL methods, but not with BOLD imaging. ASL is more sensitive and less variable for tasks that are repeated at low frequency, but can explore less volume than BOLD. ASL and BOLD can be used together to provide a more quantitative probe of brain function, including assessment of oxygen metabolism changes. This combination may be the next generation of fMRI methods.
The experimental design of fMRI involves the use of 2 types of variables: the dependent variable, which is the measured data (i.e. the increased signal seen with BOLD contrast), and the independent variable, which may be some type of motor, cognitive, or sensory task, whose performance in the MR scanner is called a paradigm. Examples of motor tasks include finger tapping, lip pursing, and toe curling. Cognitive tasks include word rhyming, word generation, decision making, and responding to questions. Sensory tasks can include visual, tactile, and/or auditory stimuli. Visual input includes photic stimulation using lights, patterns, photographs, or illustrations of people or objects. Some fMRI scans use purely sensory stimuli, such as an alternating checkerboard pattern flashed briefly to activate the visual cortex. This type of primary sensory stimulation can produce 5 to 10 times the neural activation compared with a paradigm that involves a higher-level cognitive task.

In addition to the 2 types of variables, there are 2 types of experimental designs used in fMRI: the blocked design and the event-related design. Selection of an experimental design should be based on the type that best elicits a detectable difference in BOLD signal, which is indicative of neuronal activation. Timing is also very important, in order to get maximum response from one stimulus, and allow enough time for recovery before initiating a hemodynamic response to another stimulus. The block design involves 2 conditions: the experimental condition and the control condition. In the experimental condition, the independent variable (the task) is present, and the block is called a task or stimulus block. In the control condition, the stimulus is either not present at all, or much less evident. These are called control, baseline, or rest blocks, and this period of time is called the Inter-Stimulus Interval (ISI). The experimental and control blocks are alternated, allowing the BOLD response to occur and be quantified. Statistical comparison of the two states is done, with background neuronal activity that occurs during the rest block being subtracted from the activity elicited by the independent variable. The experimental blocks may be the same each time, or may consist of different tasks. The time between the tasks can also be varied. Blocks of 10-15 seconds, which is the approximate length of the hemodynamic response to a single stimulus, provide a good compromise between good signal and minimal noise. Blocked designs are good at detecting active voxels, but not good at estimating the timing of the hemodynamic response. They do provide strong, statistically relevant results, and are the most frequently used design for clinical fMRI.

The event-related experimental design is best suited for stimuli that generate brief bursts of neural activity, such as a flash of bright light that elicits a burst of activity in the occipital cortex. The stimuli are known as “events”, and are separated by an ISI. The ISI can be fixed at a constant length of time, or it can be “jittered”, meaning the ISI is random and varies between each event. Currently, event-related designs are used mainly for research fMRI. They are good at estimating the timing of the hemodynamic response, and can be optimized to be equivalent to blocked designs for the detection of active voxels. Mixed experimental designs that incorporate elements of both blocked and event-related designs can also be used.

Post-processing of fMRI can be highly complex, but commercial software packages are available for pre-processing, post-processing, and statistical analysis. The end result of statistical evaluation is often presented as a map of brain activation with different colors representing different levels of significance. The voxels are color-coded according to the probability that the data collected from that voxel represents a chance happening only. Low significance levels (result is likely the result of chance) are usually represented by dark colors, with high significance levels (the result is not likely to have happened just by chance) represented by bright colors. Color maps are displayed over 2D anatomical slices, or over 3D rendered brain images.
fMRI has many uses in the clinical setting. It can be used to examine the anatomy and organization of the brain, to help access the effects of stroke, trauma or degenerative disease, to monitor the growth and function of brain tumors, and to guide the planning of surgery, radiation therapy, or other surgical treatments for the brain. Brain mapping can help determine the manner in which a specific patient’s brain is structurally and functionally arranged. Motor areas are typically similar across individuals, but portions of the language areas can be quite variable. The dominant hemisphere for language functions (called lateralization) is the left side for a majority of people, with a minority having right lateralization, and some people considered bilateral. If a brain injury occurs early in life, the brain can reorganize and recruit undamaged areas to carry out the functions of the lost tissue. Adults affected by trauma or stroke may experience some recovery of function in corresponding areas in the unaffected hemisphere, so fMRI can be used to help predict their functional outcomes. It can also be used to map the dominant language areas prior to surgery for aphasia or temporal lobe epilepsy. fMRI can provide functional information about tissue that could be affected by neurosurgery or stereotactic radiosurgery, and can help predict the clinical outcome if nearby tissue is inadvertently damaged. It may be somewhat unreliable in patients with brain tumors, as the vascular response to neural activation may be absent or less than expected, due to changes the tumor makes to the local environment. However, intraoperative brain mapping with fMRI or conventional MRI can be quite useful, as the surgeon is actually changing the anatomy during surgery. Functional MRI has been used to explore memory impairment resulting from diseases such as schizophrenia, Alzheimer’s disease, and dementia. It is able to detect changes in neural function in individuals with a genetic risk of Alzheimer’s disease long before they are clinically affected. It is hoped that early detection may lead to prevention or improved treatment of this disease, although it is difficult to distinguish the early changes of Alzheimer’s from mild cognitive impairment and normal aging.

fMRI has been used to study the effects of addictive drugs on the brain. Cocaine, nicotine, alcohol, cannabis, and amphetamine abusers have been studied with functional MRI. It is also the basis for a newer field called “neuromarketing”, where a volunteer’s BOLD responses are analyzed to determine if movie trailers and television advertisements are maintaining their interest. fMRI can evaluate sensory, emotional, and cognitive responses to ensure that the volunteer remains engaged in what they are viewing. Researchers are particularly interested in neural activity in the amygdala, which are the paired structures in the brain that are important in producing, processing, and storing emotional reactions. Functional MRI is definitely an evolving and improving imaging method.
Figure 97 BOLD cerebrovascular reactivity maps obtained after admission of patient with cocaine-induced cerebral vasculitis; A- BOLD cerebrovascular reactivity maps acquired 2 days after admission show reduced reactivity in left middle cerebral artery territory; absence of color indicates exhausted reactivity, blue represents steal phenomenon, and red, orange, and yellow represent normal reactivity; B- BOLD cerebrovascular reactivity maps at 4-week follow-up show definite interval improvement in BOLD cerebrovascular reactivity on the left side; reduced cerebrovascular reactivity with steal phenomenon can be independent predictor for stroke, and may indicate tissue exposed to episodic low-grade ischemia after exhaustion of cerebrovascular reserve capacity
Head Coils and Positioning

A head coil is supplied with each of Hitachi’s MRI systems. Proper positioning and immobilization of the patient’s head inside the coil, along with isocenter positioning of the head coil in the magnet result in excellent quality brain imaging, whether for routine brain scans, or more advanced applications.

The Oasis is a vertical field magnet, and is equipped with laser lights for positioning purposes in all three planes or directions- head-to-foot (horizontal plane), right-to-left (longitudinal plane), and anterior-to-posterior (coronal plane). The Echelon Oval and the Echelon systems are both horizontal field magnets, and have laser lights for positioning purposes in the longitudinal and horizontal planes.

Oasis MR System

The Oasis system utilizes a 5-channel RAPID Head coil. It should be placed directly on the table, at the end of the table closest to the magnet. Trough and/or table pads should be placed on the table for patient comfort. The head coil is mounted on a base, and can slide forward and backwards over the head holder. Locking levers are located on both sides of the coil at the bottom. Push the lever on either side backwards (towards the magnet) to unlock the head coil, and slide the coil backwards on the base
to reveal the head holder. Head holder pads should be placed on the head holder before the patient’s head is positioned. Once the patient is lying supine with his or her head on the head holder, the head coil should be slid forward over the patient’s head, and locked in place by pushing either of the locking levers forward. Positioning pads can be inserted through the openings in the back of the coil to further immobilize the patient’s head in a straight position in the coil. The longitudinal alignment light should lie in the midline of the patient’s head, and the horizontal alignment light should pass through the nasion. The head coil should be properly aligned with the coronal centering light when the coil is placed directly on the patient table.

**Echelon Oval MR System**

![Figure 100 Echelon Oval WIT Posterior Head/Neck coil with WIT Anterior Head Attachment](image)

The head coil for the Echelon Oval is part of the WIT (Workflow Integrated Technology) group. For brain imaging, the 15-element WIT Posterior Head/Neck coil, and the 4-element WIT Anterior Head Attachment are used. The WIT Posterior Head/Neck coil sits directly on the patient table, and can be plugged into either end of the table for head-first or feet-first imaging. Table pads should be placed on the table for patient comfort, as well as to cover the WIT spine coils, which can remain plugged into the table. The pad that is designed for and fitted to the Posterior Head/Neck coil should be placed in the coil before the patient’s head is positioned. Typically, the patient should slide up into the head coil as far as possible. The WIT Anterior Head Attachment is then placed on the WIT Posterior Head/Neck coil and pushed firmly into place to lock the coil pieces together. Positioning pads can be placed alongside the patient’s head inside the coil to further immobilize their head in a straight position. The longitudinal alignment light should lie in the midline of the patient’s head, and the horizontal alignment light should pass through the nasion.
Echelon MR System

The Echelon XL system utilizes an 8-channel RAPID Head coil, while the Echelon XLS uses a 16-channel RAPID Head coil. The 8-channel head coil for the Echelon XL system is mounted on a base, which should be placed directly on the patient table. The coil can be located at either the head or foot end of the table. Table pads should be placed on the table for patient comfort. Locking latches are located on both sides of the coil base, which can be pulled up to unlock the coil. The head coil can then be pulled backwards on the base to expose the head holder. The pads that are designed to fit the head holder should be in place before the patient’s head is positioned in the brain coil. Once the patient is lying supine with his or her head on the head holder, the head coil should be slid forward over the patient’s head, and locked in place by pushing down on the latches. Positioning pads can be inserted through the openings on the coil to further immobilize the patient’s head in a straight position in the coil. The longitudinal alignment light should lie in the midline of the patient’s head, and the horizontal alignment light should pass through the nasion.

The components of the 16-channel head coil for the Echelon XLS system include a head holder and a 16-channel coil, which are separate items, but may be stored together. Both items should be placed directly on the patient table, and can be located at either the head or foot end of the table. For positioning purposes, the head coil and the head holder should be separated. This can be accomplished by pressing the large button on the top of the head coil, and sliding the coil backwards. The pad that is designed to fit the head holder should be in place before the patient’s head is positioned in the coil. Once the patient is lying supine with his or her head on the head holder, the head coil should be slid forward over the patient’s head by pressing down on the button on the top of the coil, and sliding the coil forwards. Positioning pads should be inserted to further immobilize the patient’s head in a straight position in the coil. The longitudinal alignment light should lie in the midline of the patient’s head, and the horizontal alignment light should pass through the nasion.
Scan Setups

Routine Brain

Sagittal Scans

A sagittal scan of the brain is typically the first sequence that is acquired. The slices can be set up using the axial and coronal scanogram images. Slices should be positioned parallel to the midline of the brain. If angulation is necessary due to the position of the patient’s head, the angled slice lines prescribed in the coronal plane should be parallel to the third ventricle and brain stem. The slice number should be sufficient to cover the brain from right temporal lobe to left temporal lobe, and should include the area from the foramen magnum to the top of the head.

Axial Scans

Axial slices can be set up using sagittal and coronal images or scanograms. Slices should be positioned parallel to the genu and splenium of the corpus callosum. If angulation is necessary due to the position of the patient’s head, the angled slice lines prescribed in the coronal plane should be perpendicular to the third ventricle and brain stem. The slice number should be sufficient to cover the entire brain from the vertex to the line of the foramen magnum.
Coronal Scans

Coronal slices can be set up using sagittal and axial images or scanograms. Slices should be positioned parallel to the brain stem. If angulation is necessary due to the position of the patient’s head, the angled slices prescribed in the axial plane should be perpendicular to the midline of the brain. The slice number should be sufficient to cover the entire brain from the frontal sinus to the line of the occipital protuberance.

Time of Flight (TOF)

3D TOF scans are typically acquired in the axial plane, and can be set up using routine sagittal and coronal images or scanograms. The volume block or slabs should be positioned parallel to the genu and splenium of the corpus callosum. If angulation is necessary due to the position of the patient’s head, the angled block prescribed in the coronal plane should be perpendicular to the line of the third ventricle and brain stem. The volume block should be large enough to cover the entire Circle of Willis, from the corpus callosum to the line of the foramen magnum. A walking saturation band placed superior to the volume block will reduce venous contamination. Post processing of TOF scans is performed using a MIP task. Under the Projection tab, the Projection is set to Rotating, and the Mode is set to MIP. Clipping is performed to eliminate excess tissue and small vessels around the Circle of Willis.
Diffusion Weighted Imaging (DWI)

DWI scans are typically acquired in the axial plane, and can be set up using routine sagittal and coronal images or scanograms. Slices should not be angled on Hitachi MRI systems, as the DWI sequence stresses the gradients, and angulation stresses the gradients even further. The slice number should be sufficient to cover the entire brain from the vertex to the foramen magnum. Post processing of DWI information is performed using the Diffusion Analysis task, which can be set up to run automatically after reconstruction of the DWI sequence. Diffusion Analysis tasks can be set up to include DWI, ADC, and ADC in all 3 planes (A-P, H-F, R-L).

Diffusion Tensor Imaging (DTI)

DTI scans are typically acquired in the axial plane, and can be set up using routine sagittal and coronal images or scanograms. Slices should not be angled on Hitachi MRI systems, as the DTI sequence stresses the gradients, and angulation stresses the gradients even further. The slice number should be sufficient to cover the entire brain from the vertex to the foramen magnum. The scan setup for DTI is the same as DWI; however, DTI is performed in multiple directions, and is used to evaluate diffusion in various directions. Post processing of DTI information is performed using the Diffusion Analysis task, with image
results reported as DWI Trace, Fractional Anisotropy Map, and Mean Diffusivity Map. DTI Analysis can be set up to run automatically after reconstruction of the DTI sequence.

![Figure 108 DTI scan setup using coronal and sagittal images; slices should not be angled](image)

**Blood Sensitive Imaging (BSI)**

BSI scans are typically acquired in the axial plane, and can be set up using a routine sagittal image or scanogram. These are 3D, or volume, acquisitions. The volume block should be adequate in size to cover the brain anatomy from the vertex to the foramen magnum. Post processing of BSI scans is performed using a MIP task. Under the Projection tab, the Projection is set to Sliding, and the Mode is set to minIP.

![Figure 109 BSI scan setup using a sagittal image](image)

**Perfusion**

Perfusion scans are typically acquired in the axial plane, and can be set up using routine sagittal and coronal images or scanograms. The reference images should be reviewed to locate the images that optimally display the area of interest. Centering and angulation should be performed as needed to provide optimal coverage of the area of interest. The slice number should be sufficient to adequately cover the area of interest. Perfusion studies involve a contrast injection during the scan, and post processing using the Perfusion Analysis task. Perfusion Analysis results include a Cerebral Blood Flow
(CBF) analysis map, a Cerebral Blood Volume (CBV) analysis map, and a Mean Transit Time (MTT) analysis map.

Figure 110 Perfusion scan setup using coronal and sagittal images

Spectroscopy

Spectroscopy begins with routine brain scans, with a 3-plane scanogram, and the sequence best suited to localize and display the area of interest. Data concerning the brain metabolites is collected using either a Single Voxel or Dual Voxels. If Single Voxel spectroscopy is performed, it is recommended that two scans be performed- one with the voxel positioned over the lesion, and another with the voxel positioned over the contralateral side. This enables metabolite comparisons to be made between the lesion and normal tissue. In Dual Voxel spectroscopy, voxel 1 is placed over the lesion, while voxel 2 is placed over the contralateral side. Whenever possible, the voxels should be positioned away from fat, bone, air, ventricles, vessels, and cerebral spinal fluid. Spectroscopy Analysis results include a graph or graphs displaying the peak values of primary metabolites, and a metabolite list which includes the signal ratio of each metabolite to Creatine, the standard deviation of each metabolite against the standard signal value, and the signal value (intensity).

Figure 111 Single voxel spectroscopy scan setup using sagittal and axial images; as recommended, positioning is demonstrated for two scans- one with the single voxel centered over the lesion, and one with the single voxel positioned over the contralateral side
Figure 112 Dual voxel spectroscopy scan setup using sagittal and axial images

Figure 113 Chemical shift imaging (CSI) spectroscopy scan setup using sagittal and coronal images

This concludes the Brain Imaging module of the Hitachi Medical Systems America’s MRI Anatomy and Positioning Series. You must complete the post-test for this activity in order to receive your Continuing Education credits.
Appendix A: References for Neuro Seminar

• DiMuzio, Dr. Bruno, Maingard, Dr. Julian et al. (n.d.). *Subdural space*. Retrieved from http://radiopaedia.org/articles/subdural-space


• Luijkx, Dr. Tim, Gaillard, Dr. Frank, et al. (n.d.). *Dural venous sinuses.* Retrieved from http://radiopaedia.org/articles/dural-venous-sinuses


• Mandal, Dr. Ananya, M.D. (Last Updated 18July2013). *What is Dopamine?* Retrieved from http://www.news-medical.net/health/What-is-Dopamine.aspx


• Mayfield Clinic for Brain and Spine. (Updated February2013). *Brain mapping: functional MRI and DTI.* Retrieved from http://www.mayfieldclinic.com/PE-fMRI_DTI.htm#VW3xb03wv0


• UC San Diego School of Medicine, Center for Functional MRI. (n.d.). What is fMRI? Retrieved from http://fmri.ucsd.edu/Research/whatismri.html
Appendix B: References for Anatomy Pictures

- Figure 1- [http://www.midbrainpower.in/technical-details/supersonic-human-brain/parts-and-functions-of-human-brain/]
- Figure 2- [http://projectflexner.sites.medinfo.ufl.edu/how-we-learn/]
- Figure 3- [http://www.wisegeek.com/what-are-white-matter-tracts.htm]
- Figures 4, 11, 15, 16, 17, 18- [http://classes.midlandstech.edu/carterp/Courses/bio210/Chap12/lecture1.htm]
- Figure 5- [http://www.cortjohnson.org/blog/2014/04/15/low-dose-naltrexone-inflammation-pain-different-approach-fibromyalgia/]
- Figure 6- [http://www.intechopen.com/books/basal-ganglia-an-integrative-view/clinical-motor-and-cognitive-neurobehavioral-relationships-in-the-basal-ganglia]
- Figure 7- [http://www.buzzle.com/articles/ventricles-of-the-brain.html]
- Figure 8- [http://graulab.tamu.edu/J-Grau/Psyc606/Figures/Limbic%20System.png]
- Figure 9- [http://www.3icreative.com/psych/forebrain-telencephalon-diencephalon.html]
- Figure 10- [https://www.studyblue.com/notes/note/n/structure-cns-take-2/deck/2996759]
- Figure 12- [http://droualb.faculty.mjc.edu/Lecture%20Notes/Unit%2020/chapter_15_the_brain%20Spring%202007with%20figures.htm]
- Figure 13- [http://163.178.103.176/Fisiologia/neurofisiologia/Objetivo_9/brain.html]
- Figure 14- [http://www.cerebellum.us/wordpress/wp-content/uploads/gallery/cerebellum/cerebellum-cerebellum-8.jpg]
- Figure 19- [http://images.radiopaedia.org/images/525965/542fbedc4c234ae8aed8cedfa96fb.jpg]
- Figure 20- [http://images.radiopaedia.org/images/632565/9aede97c6aaf00558ddc74adf16c6.jpg]
- Figure 21- [http://radiopaedia.org/cases/third-ventricular-cyst]
- Figure 22- [http://www.upmc.com/services/neurosurgery/brain/treatments/neuroendopod-surgery/clinical-case-studies/pages/intraventricular-meningioma.aspx]
- Figure 23- [http://healthfixit.com/vagus-nerve/]
- Figure 24- [http://www.reboundhealth.com/cms/articles/systems-of-the-body/image-arterial-circulation-of-the-brain-including-carotid-arteries.html]
- Figure 26- [https://mrimaster.com/anatomy%20brain%20cerebral%20arteries.html]
- Figure 27- [https://www.studyblue.com/notes/note/n/venous-drainage--stroke-related-deficits/deck/2090466]
- Figure 28- [http://radiopaedia.org/images/606263]
- Figure 29- [http://radiopaedia.org/cases/anaplastic-astrocytoma]
• Figure 30- http://radiopaedia.org/articles/oligodendroglioma
• Figure 31- http://path.upmc.edu/divisions/neuropath/bpath/cases/case11/images/gross6.jpg
• Figure 32- http://www.ccyp.medicine.net.au/clinical/Radiology/Radiolog2276.html
• Figure 33- http://www.broadinstitute.org/news/2837
• Figure 34- http://usmlepathslides.tumblr.com/post/53614674770/meningioma-head-mri-the-dural-tail-sign-is
• Figure 35- http://dizziness-and-hearing.com/disorders/tumors/acoustic_neuroma.htm
• Figure 36- http://www.snays.com/medical-coding-2/246/
• Figure 37- http://www.neuroradiologycases.com/2012/09/ischemic-stroke-and-vascular.html
• Figure 38- http://www.hxbenefit.com/lacunar-infarct-lacunar-stroke.html
• Figures 40, 41- http://nhlbi.nih.gov/health/health-topics/topics/stroke/types
• Figure 42- http://www.medscape.com/viewarticle/550817_5
• Figure 43- http://webeye.ophth.uiowa.edu/eyeforum/cases/93-PseudoabducensPalsy.htm
• Figure 44- http://emedicine.medscape.com/article/344973-overview#aw2aab6b7
• Figure 45- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2588251/figure/F3/
• Figure 46- http://www.moveforwardpt.com/SymptomsConditionsDetail.aspx?cid=4f2ebb00-f1c0-4691-b2ab-742df8dfb99#.VXcOB03wvs0
• Figure 47- http://news.byu.edu/archive08-Mar-concussion.aspx
• Figure 48- http://www2.rsna.org/timssnet/rsna/media/pr2012/Lipton/JPG/Figure-1.jpg
• Figure 49- http://www.auntminnie.com/index.aspx?sec=sup&sub=mri&pag=dis&ItemID=107124
• Figure 50- http://www.auntminnie.com/index.aspx?sec=sup&sub=mri&Pag=dis&ItemID=109880&wf=6362
• Figure 51- http://www.ninds.nih.gov/news_and_events/news_articles/rsfMRI_athlete_concussion.htm
• Figure 52- http://www.healthimaging.com/topics/diagnostic-imaging/mri-shows-brain-coping-mechanism-post-concussion-syndrome
• Figure 53- http://www.newswise.com/articles/ucla-study-first-to-image-concussion-related-abnormal-brain-proteins-in-retired-nfl-players
• Figure 54- http://emedicine.medscape.com/article/341971-overview
• Figure 55- http://radiopaedia.org/cases/toxoplasmosis
• Figure 56- http://path.upmc.edu/divisions/neuropath/bpath/cases/case28/images/gross1.jpg
• Figure 57- http://neuropathology-web.org/chapter5/chapter5aSuppurative.html
• Figure 58- http://medicalpicturesinfo.com/encephalitis/
• Figure 59- http://pmj.bmj.com/content/79/932/352.full.pdf+html?sid=03b80493-50d2-4343-b29c-07541242b477
• Figure 60- http://radiopaedia.org/articles/aids-dementia-complex
• Figure 61- http://radiopaedia.org/cases/progressive-multifocal-leukoencephalopathy-pml
• Figure 62- http://www.nottingham.ac.uk/news/pressreleases/2014/april/tell-tail-mri-image-diagnosis-for-parkinsons.aspx
• Figure 63- http://radiopaedia.org/blog/new-tell-tail-mri-sign-of-parkinsons-disease-1
• Figures 67, 68- http://www.bmj.com/content/343/bmj.d5568
• Figure 69- http://frontotemporaldementia.info/frontotemporal-dementia/
• Figure 70- http://www.medicinenet.com/multiple_sclerosis_pictures_slideshow/article.htm
• Figure 71- http://www.urmc.rochester.edu/libraries/courses/neuroslides/lab3a.cfm
• Figure 72- http://www.ajnr.org/content/27/6/1230/F1.expansion.html
• Figure 73- http://www.technology.org/2013/07/31/migraine-is-associated-with-variations-in-structure-of-brain-arteries/
• Figure 74- http://www.medscape.org/viewarticle/728124_3
• Figure 75- https://www.medphysics.wisc.edu/research/fmri/research/dti.php
• Figure 76- http://bme240.eng.uci.edu/students/08s/jlisinsk/DTI.html
• Figure 77- http://www.martinos.org/neurorecovery/technology.htm
• Figure 79- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3259351/figure/Fig3/
• Figure 80- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3259351/figure/Fig2/
• Figures 81, 82- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3259351/figure/Fig5/
• Figure 83- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3259351/figure/Fig13/
• Figure 84- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3259351/figure/Fig15/
• Figure 85- http://www.nih.gov/science/imaging/stroke.htm
• Figure 86- http://www.wjgnet.com/1949-8470/full/v4/i3/WJR-4-63-g001.htm
• Figure 87- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135980/figure/F1/
• Figure 88- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135980/figure/F6/
• Figure 94- http://www.ijri.org/viewimage.asp?img=IndianJRadiolImaging_2008_18_3_210_41829_1.jpg
• Figure 95- http://www.martinos.org/neurorecovery/technology.htm
• Figure 96- http://web.hksh.com/clinical_services/radiology/en/multimedia.php#advanced_brain_imaging
• Figure 97- http://www.nature.com/nrneurol/journal/v4/n11/fig_tab/ncpneo0918_F2.html