Neuro-Imaging, Neuromonitoring, and Other Special Investigations

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Abstract: Modern neurosurgery is unimaginable without neuroimaging. Operating neurosurgeons can examine an intracranial pathology virtually (and conceptually) with the help of modern neuroimaging. Neurosurgery has become relatively easy to accomplish due to preoperative and perioperative neuroimaging. Neuroimaging helps in preoperative diagnosis and choosing a per-operative approach, and, perioperatively, it defines pathology precisely and can assess the completeness of resection. Neuromonitoring is very useful in functional preservation during cranial, spinal, and peripheral nerve surgery. In this chapter, X-rays, CT scans, MRI scans, and ultrasonograms are discussed, including with regard to their useful modified (including intraoperative uses) forms. Neuromonitoring (intraoperative neuromonitoring, EEG, ECoG, and neuronavigation) and other special investigations (NCS, EMG, and CSF studies and immunohistochemistry) are discussed briefly in the later part of this chapter.

Abbreviations

AED	anti-epileptic drugs	AFB	acid-fast bacillus
AVM	arteriovenous malformation	AVF	arteriovenous fistula
BAEP	brainstem auditory evoked potential	CBF	cerebral blood flow
CBV	cerebral blood volume.	CNS	central nervous system
CT	computed tomography	CTA	computed tomographic angiogram
CTV	computed tomographic venography	CSF	cerebrospinal fluid
CVST	cerebral vein and dural sinus thrombosis	DSA	digital subtraction angiogram
DTI	diffusion tensor imaging	EC-IC	extracranial–intracranial
ECoG	electrocorticogram	ECS	electrical cortical simulation
EEG	electroencephalogram	EMG	Electromyography
EZ	epileptic zone	fMRI	functional magnetic resonance imaging
GBS	Guillain–Barré syndrome	HF	hemifacial spasm
ICA	internal carotid artery	ICH	intracerebral hemorrhage
ICP	intracranial pressure	IEEG	intracranial EEG
IHC	Immunohistochemistry	IIH	idiopathic intracranial hypertension
MEG	magnetoencephalography	MRI	magnetic resonance imaging
MRA	magnetic resonance angiogram	MEP	motor evoked potential
MRV	magnetic resonance venography	MRS	magnetic resonance spectroscopy
MTP	mean transit time	NAA	N-acetyl aspartate
NSF	nephrogenic systemic fibrosis	PCR	polymerase chain reaction
PET	positron emission tomography	PNS	paranasal sinuses
PW	perfusion weighted	RF	Radiofrequencies
SAH	subarachnoid hemorrhage	SCA	superior cerebellar artery
SPECT	single-photon emission computed tomography	SPGR	spoiled gradient recall
SSEP	somatosensory evoked potential	TBI	traumatic brain injury
TCD	transcranial doppler	TIA	transient ischemic attack
TLE	temporal lobe epilepsy	TM	transverse myelitis
TN	trigeminal neuralgia	TTP	time to peak
USG	ultra sonogram	VEP	visual evoked potential
VA	vertebral artery	VBI	vertebrobasilar insufficiency

1. Neuro-Imaging

1.1. X-Ray

1.1.1. X-Ray—Cranium

A skull X-ray is one of the primary imaging techniques utilized to check the bones of the skull, including the bone structure of the face, the nose, and the paranasal sinuses. It is an easy, quick, and effective method that

has been used to view the area that contains the most vital organ of the human body—the brain. It is usually performed after a traumatic head injury. Apart from common AP and lateral views, other special views, such as occipito-mental, Towne's, and oblique views, can be used for different pathologies. An X-ray allows one to inspect any damage resulting from an injury. Other indications include the following:

1. Decalcification and bony tumors as well as osteolytic lesions of the skull and skull base;
2. Skull deformities;
3. Fractures of the skull base or vault or facial bones;
4. Headaches;
5. Osteomyelitis of the skull bones and paranasal sinus (PNS) infections;
6. Infection of the ear and mastoid process and hearing loss;
7. Chronic raised intracranial pressure (ICP) [beaten silver/beaten copper appearances] (Figure 1);
8. Neoplasia of the skull, skull base, brain, meninges, and nose, including the PNSs.

A CT scan of the head is commonly used instead of an X-ray due to its availability and its efficacy in the quick screening of the skull, brain, PNSs, soft tissues, and face.

1.1.2. X-Ray—Spine

X-rays of the spine are used to observe traumatic injuries of the spine, tumors, infections, bone-destructive lesions, and deformities. Besides AP and lateral views, other views such as oblique and open-mouth views can be used. Fractured bones; arthritis; spondylolisthesis; disc degeneration; neoplasms; disorders regarding the curvature of the spine, i.e., kyphosis or scoliosis; and congenital anomalies can all be discovered using neck, back, or lumbar spinal X-rays.

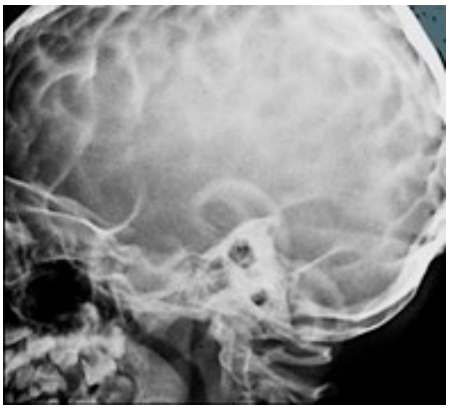

Figure 1. Skull X-ray (lateral view) showing beaten-silver/beaten-copper appearance due to chronic raised ICP. Source: Figure by authors.

1.1.3. Digital Subtraction Angiograms (DSAs) of Brain and Spinal Vessels

DSAs (digital subtraction angiograms) of cerebral and spinal vessels are used to delineate vascular pathologies of the brain and spine (both diagnostic and therapeutic) after injecting radio-opaque dye selectively in cerebral or spinal arteries with an angio-catheter, and X-rays are acquired simultaneously with the digital subtraction of bone.

1.1.4. Peroperative X-Ray/Fluoroscopy/C-Arm and O-Arm X-Rays

A peroperative X-ray is routinely and commonly utilized in spinal surgery for localization and instrumentation.

1.2. CT Scan

1.2.1. Principles of CT Scans

The first computed axial tomographic scanner was designed by Sir Godfrey Hounsfield and Dr. Allan Cormack in 1972, resulting in their receipt of the Nobel Prize in Medicine in 1979. CT scan machines have come a long way since then, with speed and resolution steadily rising (Grossman and Yousem 2003).

The CT scan is a non-invasive technique that has revolutionized research on intracranial diseases since its introduction in the 1970s. In a CT scan, a pencil beam of X-rays passes through the patient's head (spine or other body parts) and is measured by a diametrically oppositely placed detector. Calculation of absorption values for several small blocks of tissue is possible thanks to computer processing and several rotating beams and detectors grouped in a complete circle around the patient's head, spine, or other areas of body (voxels). The traditional CT scan images are created by reconstructing these locations on a two-dimensional screen (pixels). Slices are taken 3–5 mm apart for routine scanning. The most recent "spiral" or "helical" CT scanners utilize a large bank of detectors (multi-slice), and the patient moves through the field during scanning, causing the X-ray beams to follow a helical path. These scanners cut scanning time in half and are especially useful when slices with a length of 1–2 mm are used to provide more anatomical information. These 'high-definition' views enable comprehensive investigation and coronal and sagittal reconstructions. Changing the window level enhances the visibility of tissues with varying X-ray densities. For every scanned level of the spine and head, most centers produce two images: one to reveal bone structures (a bony window) and another to demonstrate soft tissue within and outside the spinal canal or cranium. This allows the creation of 3-D reconstruction images of the head and spine using CT scan data (Figure 2). When a plain CT scan reveals any abnormalities or if definite clinical indications are present, such as a vascular lesions or tumors, an intravenous iodin-containing water-soluble contrast injection is applied (Lindsay et al. 2011).

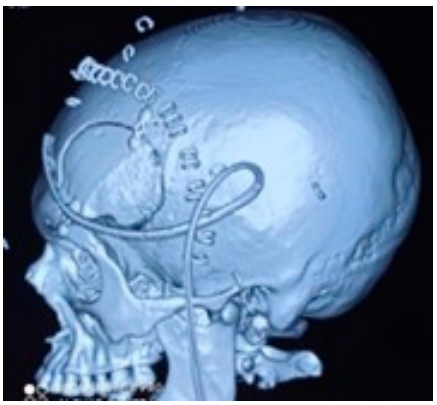

Figure 2. Three-dimensional reconstruction of a head via CT, constituting a lateral view of a post left supraorbital frontolateral craniotomy patient. Source: Figure by authors.

1.2.2. CT Scans of the Brain and Spine

CT scans of the brain and spine are extremely important imaging tools for the screening, diagnosis, and planning of treatment, including surgical intervention. In this modern era of neurosurgery, a neurosurgeon cannot conduct an intracranial operation without CT.

1.2.3. CTA and CTV of the Brain, Neck, and Spine

By using an intravenous contrast medium infusion during scanning, a non-invasive technique for revealing cerebral arteries in 2- and 3-D format can be devised. The capacity to rotate an image 360° allows for a clearer demonstration of vessels and any abnormalities. According to many studies, 3-D CT angiograms are just as good as traditional angiograms at detecting tiny aneurysms. CT arteriograms (Figures 3 and 4) and CT venograms are very useful neuroimaging techniques for the screening and diagnosis of cranial and spinal vascular pathologies including neck vessels (such as cerebral occlusive diseases, Moyamoya disease, carotid stenosis, intracranial aneurysm and AVM, AV fistula, cerebral venous sinus thrombosis, spinal AVM, and AV fistulae). These are essential for the planning of therapeutic options.

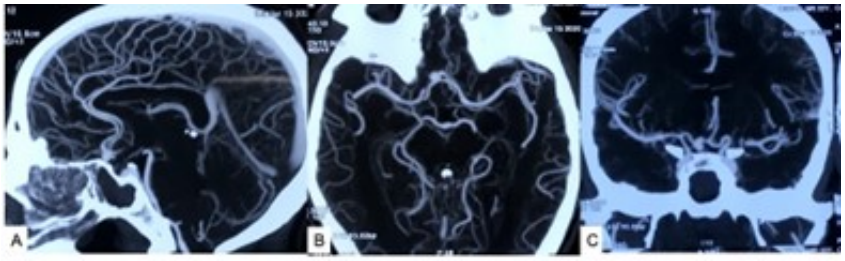

Figure 3. CTA of brain (showing the inside of the brain case); (**A**–**C**)—sagital, axial, and coronal views, respectively, showing an ACOM aneurysm with otherwise normal vasculature. Source: Figure by authors.

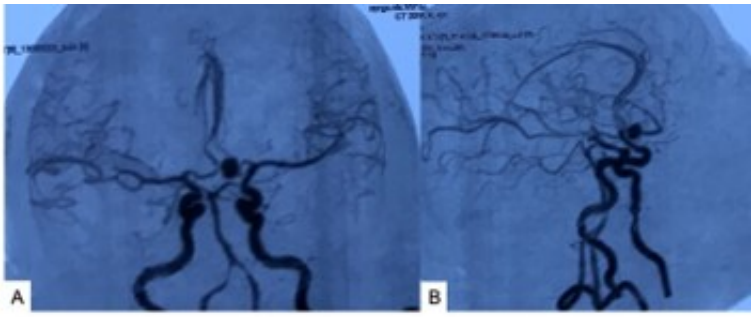

Figure 4. CTA of the brain (**A**—AP view and **B**—lateral view) showing a large ACOM aneurysm. Source: Figure by authors.

1.2.4. Perfusion CT of the Brain

After the intravenous injection of contrast media, it is possible to develop a brain perfusion map, which is very important in assessing acute and chronic ischemic conditions for achieving a diagnosis and selecting therapeutic options. For neurosurgeons, it is very important to create this map alongside conducting a Diamox challenge test in EC-IC bypass in ischemic conditions such as cerebral arterial stenosis/occlusion (Figure 5), Moyamoya disease, etc. Ischemic patches have less contrast and appear to have low density. This method is also useful in predicting the fate of an acute stroke.

1.2.5. SPECT

Single-photon emission computed tomography (SPECT) technology can be used to detect tumor spread in the brain, differentiate between tumor regrowth and radiation-induced necrosis, assess cerebral perfusion in cases of epilepsy and TBI, and diagnose secondary CNS diseases (Golanov et al. 2012).

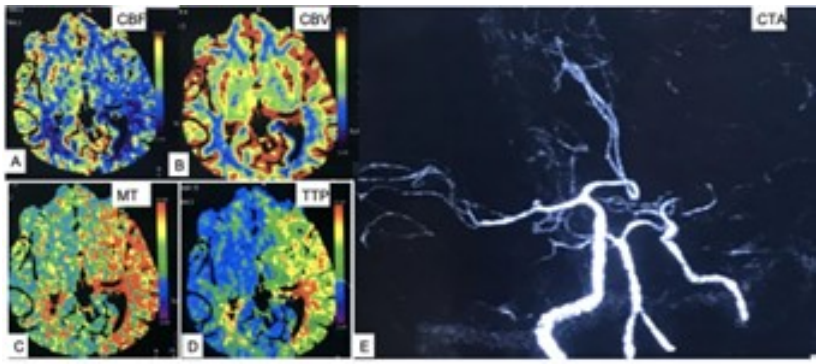

Figure 5. (**A**–**D**) Perfusion CT scan of the brain in a patient with left MCA occlusion (**E**), showing left MCA territory hypoperfusion. Source: Figure by authors.

1.2.6. PET

PET (positron emission tomography) is a sensitive imaging method that permits one to see real-time brain activity. It provides non-invasive brain measurements of cerebral blood flow (CBF), metabolism, and receptor binding. (Tai and Piccini 2004).

After radioactive "tracers" have been taken into the bloodstream, the FDG-PET/CT 18F-2-fluoro-2-deoxy-D-glucose (FDG) scan records images of cerebral activity. These tracers are "affixed" to a molecule such as glucose (sugar). Glucose is the brain's primary fuel source. The brain's active areas will use glucose at a faster pace than the brain's dormant portions. PET scanning offers a better explanation of how the brain works and aids in the detection of any anomalies. PET is used to detect malignant neoplasms; assess if cancer has spread to the cerebrum; diagnose dementias, e.g., Alzheimer's disease; distinguish between Parkinson's disease and other illnesses; and prepare a patient for epilepsy surgery.

1.2.7. Per Operative CT

A modern well-equipped neurosurgical operation room may have a CT scanner that can be used intra-operatively in cranial and spinal surgery to guide the approach and pathway to pathology or implantation (e.g., a DBS electrode in the brain and screw placement in the pedicle of the spine). It can also be used to check the completeness of the excision of a tumor.

1.2.8. CT Cisternography

In CT cisternography, intrathecal contrast is injected to better locate the source of a CSF leak, increasing the diagnostic yield of conventional CT (Figure 6). Unlike traditional CT imaging, only one investigation is usually required. In most patients with ongoing leaks, CT cisternography demonstrates the exact site of the CSF fistula.

1.3. Magnetic Resonance Imaging (MRI)

MRI is a noninvasive imaging method with superior soft-tissue contrast as well as physiological and functional applications. Since the 1980s, MRI has been a mainstay of non-invasive diagnostic imaging as it does not expose the body to radiation. To obtain comprehensive images, MRI involves the utilization of an intense magnetic field, a quickly altering magnetic field, radio waves, and a computer. However, there are some hazards associated with MRI. As the use of MRI in clinical practice has increased, healthcare workers must learn MRI safety protocols in order to safeguard patients against the hazards associated with this procedure (Feychting 2005).

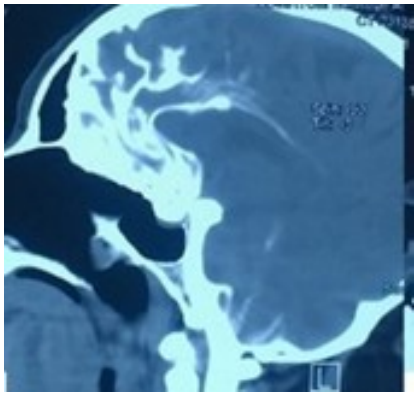

Figure 6. CT cisternogram (sagittal view) showing CSF cisterns at the base of the skull. Source: Figure by authors.

1.3.1. Principles of MRI

An atom's nucleus has angular momentum when it includes unpaired protons, neutrons, or both. Magnetic resonance imaging is based on this feature (MRI). Hydrogen is employed in clinical MRI because it is abundant in the human body. The atoms within the MR magnet are aligned with the magnet's magnetic field. The atoms are exposed to radiofrequency (RF) pulsations to form the MR signal, and the appearance of the image is governed by the pulse sequences utilized. The echo time (TE) is the time between the RF pulse and the signal recording, whereas the repetition time (TR) is the time between RF pulses. T1-weighted scans (short TR/short TE) provide the highest anatomical detail, although T2-weighted images (long TR/long TE) are more commonly used. In MR pictures, there can be a lot of strange artifacts. Unequal distributions in the magnetic field (e.g., those caused by metallic orthopedic devices or past surgical intervention), extraneous RF interference, and movement can all contribute to this. In musculoskeletal MR imaging, surface coils are widely employed to increase the quality of the test by boosting the signal-to-noise proportion over the area of interest (Lindsay et al. 2011; Seeger 1989).

1.3.2. Contraindications of MRI Scanning

Absolute Contraindications of MRI are listed in Box 1.

Box 1. Absolute contraindications of MRI (Seeger 1989).

- Intraocular metallic foreign objects
- Cochlear/ear implants
- Drug/chemical infusion pumps (analgesics, or chemotherapy pumps, insulin delivery)
- Catheters containing metallic parts (Swan–Ganz catheter)
- Residual metallic pieces such as bullets, metal shrapnel, and pellets
- Cerebral aneurysm clips (most of them are now MRI-compatible)
- Cardiac implantable electronic devices (CIEDs) [example: pacemakers]
- Implantable cardioverter defibrillators (ICDs), and cardiac
- Resynchronization therapy (CRT) devices
- Neurostimulator implants
- Piercings
- Dental magnetic implants
- Tissue expanders
- Artificial limbs
- Hearing aids

It is vital to understand that in MRI, some of these things are dangerous, while others are only safe at 1.5 tesla and 3 tesla. All gadgets and implants must be investigated using a certified MRI scanner safety website/the website of the manufacturer. Medical materials, equipment, and implants have been developed from non-ferromagnetic materials for decades and are typically labeled MR-safe or MR-conditional. A device or implant must be considered dangerous for MRI if there is no proof or information about its MRI safety (Seeger 1989).

Relative Contraindications of MRI

There are several relative contraindications (stressing the need for caution before conducting MRI) shown in Box 2.

Box 2. Relative contraindications for MRI (Seeger 1989).

- Peripheral and coronary artery stents
- Intrauterine devices (IUDs)
- Stapes implants
- Penis prostheses
- Inferior vena cava (IVC) filters;
- Medication patches
- Programmable shunts
- (Patients must be informed that they have to ask their providers to readjust their shunts after the scan)
- Tracheostomy/airway stent with metallic part
- Ocular prostheses
- Wire sutures/surgical clips
- Joint replacements/prostheses
- Harrington rods
- Claustrophobia

1.3.3. Gadolinium Contrast MRI

Gadolinium contrast is used to highlight the blood supply in a lesion seen in plain MRI. Gadolinium chelates with various viscosities, stabilities, and types of osmolality are used as MRI contrast agents. Gadolinium is a relatively harmless contrast; but it might induce hypersensitivity reactions in certain people and very rarely nephrogenic systemic fibrosis (NSF) in patients (Seeger 1989).

1.3.4. MRI in Pregnancy

MRI is a useful imaging method for evaluating obstetric and non-obstetric diseases throughout any trimester of pregnancy (Seeger 1989).

1.3.5. MRI Under General Anesthesia

General anesthesia may be needed for pediatric patients, patients with a psychiatric illness, restless patients who have suffered strokes or head injuries, and claustrophobic patients.

1.3.6. MRI of Brain and Spine

MRI of the brain or spine is the minimum requirement for neuro-investigation for a neurosurgeon in the screening, diagnosis, or planning of therapy/surgery of the brain or for spinal disorders including CNS tumors, trauma, stroke, neurovascular diseases, CNS infection, CSF disorders, and skull-base as well as cranial vault pathologies.

1.3.7. MRA and MRV of Brain, Neck, and Spine

MRA and MRV (Figure 7) of brain and neck vessels have almost become a routine investigation for a neurosurgeon. They are utilized in the diagnosis and treatment planning of vascular disorders of the neck and brain as well as in the selection of surgical methods and targets (i.e., cervical and intracranial carotid and vertebral arteries, anterior circulation and posterior circulation aneurysms, AVM, AV fistula, stenosis, occlusion, dissection, and arterial and venous involvement by tumors.) In cases of idiopathic intracranial hypertension (IIH) and cerebral sinus thrombosis, a venogram is recommended.

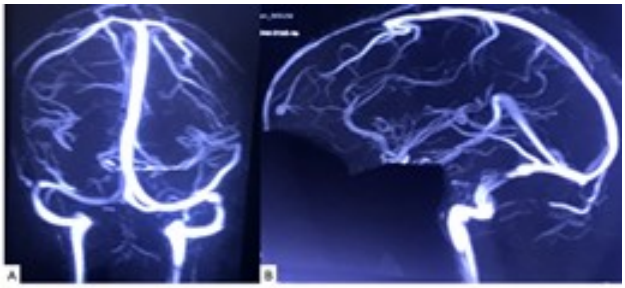

Figure 7. Normal MRV of the brain; (**A**) P/A view and (**B**) lateral view. Source: Figure by authors.

1.3.8. Perfusion MRI of the Brain (Especially for Ischemia)

MR perfusion imaging refers to a group of recently discovered techniques for measuring brain perfusion non-invasively using a variety of hemodynamic parameters. These approaches have become critical diagnostic and therapeutic tools for treating patients with cerebrovascular disease and other brain illnesses. The evaluation of tissues at risk following an acute stroke, the noninvasive histologic examination of cancers, the evaluation of neurodegenerative disorders like Alzheimer's disease, and the evaluation of the effects of medications used to treat these conditions are all possible applications (Petrella and Provenzale 2000).

This technique is very important in assessing acute (penumbra and infarcts) and chronic ischemic conditions (chronic ischemic brain parenchyma) for the diagnosis and selection of therapeutic options. For neurosurgeons, it is very essential to perform it along with a Diamox challenge test in EC-IC bypass in cerebral ischemic pathologies such as cerebral arterial stenosis/occlusion, Moyamoya disease, etc. Like perfusion CT of the brain, perfusion MRI is used to calculate hemodynamic measurements such as cerebral blood volume (CBV), time to peak (TTP), cerebral blood flow (CBF), and mean transit time (MTP).

1.3.9. DTI and Tractography

Diffusion-tensor imaging (DTI) is a noninvasive imaging technique for examining the connections between white matter tracts and connectomes. In DTI, signal contrast is created by variations in the Brownian movement of water molecules in the brain parenchyma. Postprocessed DTI scalars may be used to measure alterations in brain tissue generated by disease, disease progression, and therapeutic responses for a variety of neurological diseases and conditions, including gliomas, multiple sclerosis, Alzheimer's disease, Parkinson's disease, epilepsy, infarction, language or motor disorders, traumatic brain injuries, spinal cord trauma, and depression (Tae et al. 2018). In gliomas or other intra-axial tumors, the white matter tract can be displaced, split, infiltrated, or destroyed by the tumor; in this regard, preoperative DTI and tractography help in surgical planning (Figure 8), neuromonitoring during operation, and postoperative result prediction.

1.3.10. fMRI of Brain

By detecting variations in blood flow, functional MRI (fMRI) determines brain activities. The fact that cerebral blood flow as well as neural activation are chronologically linked is the basis for this approach (Logothetis et al. 2001).

When a part of the brain is working properly, blood circulation to that part of the brain increases. The blood-oxygen-level-dependent (BOLD) contrast (American College of Radiology and Radiological Society of North America 2011) was discovered by Seiji Ogawain in 1990 and is utilized in the primary version of fMRI. The cited researchers used functional magnetic resonance imaging (fMRI) to map the brain and uncover areas involved in critical tasks like moving, speaking, sensing, and planning. This is helpful for planning brain surgery as well as radiation therapy (Figure 9).

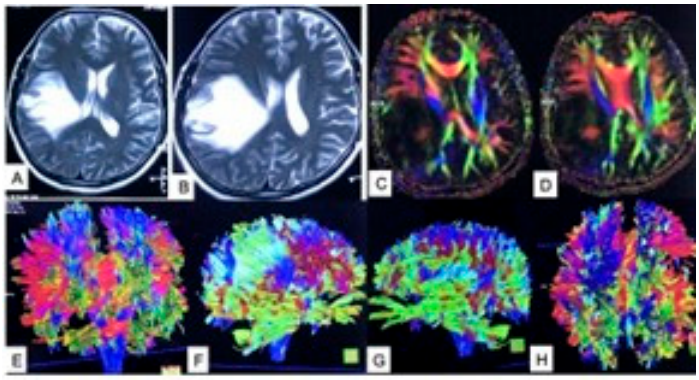

Figure 8. (**A**,**B**) MRI of brain T2W images showing right fronto-parieto-ganglionic glioma. (**C**,**D**) MR diffuse tensor imaging (DTI) of same patient in axial views showing displacement of adjacent white fiber tracts. (**E**–**H**) Tractography of the same patient in different views. Source: Figure by authors.

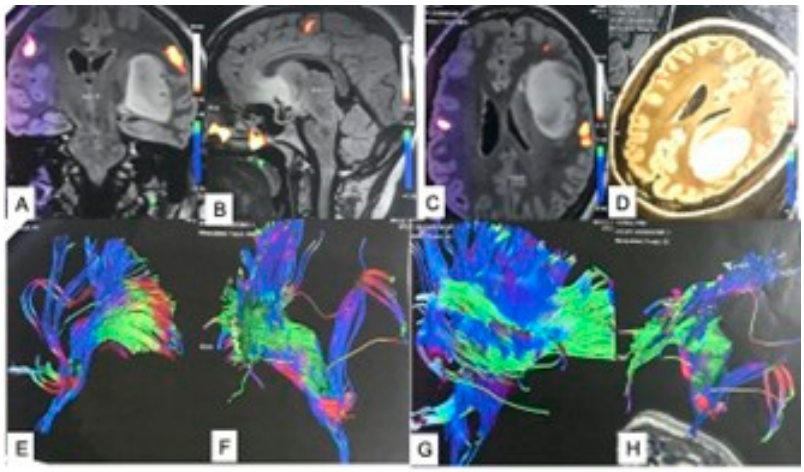

Figure 9. (**A**–**D**) fMRI of the brain, with coronal, sagittal, and axial views showing cortical functional areas in a patient with insular glioma. (**E**–**H**) MR tractography of same patient showing reduced and displaced cortico-spinal and cortico-nuclear tracts on the left side. Source: Figure by authors.

Clinicians can use fMRI to map the brain and identify the effects of tumors, strokes, head and brain trauma, diseases like Alzheimer's, and developmental anomalies like autism (Box 3) (American College of Radiology and Radiological Society of North America 2011; Subbaraju et al. 2018).

Box 3. Indications of fMRI.

- Intractable/drug-resistant epilepsy surgery
  Temporal lobe excision
  Epileptic lesion involving eloquent areas
  Cortical dysplasia (CD), involving eloquent areas causing intractable seizure
- Glioma involving eloquent areas
  (For planning surgery)
- Cerebral AVM and other intrinsic lesion involving eloquent areas
- To see the shifting of eloquent areas in diseased eloquent areas
  (i.e., low-grade gliomas, AVM, cavernoma, trauma, infarcts)
- Dementia
- Research in neurosciences

1.3.11. Magnetic Resonance Spectroscopy (MRS)

The predominant source of a signal in MRI is protons that stay within water, as well as molecules of fat, which are nearly a thousand times commoner than the molecules identified with MRS. As the more abundant signal is typically used in MRI to make very clear 2D images, whereas a signal is commonly collected from a single isolated spot known as a "voxel" in MRS, MRS can be utilized to analyze the relative quantities and physical qualities of a number of biochemicals usually referred to as "metabolites" due to their activity in metabolism (Figure 10).

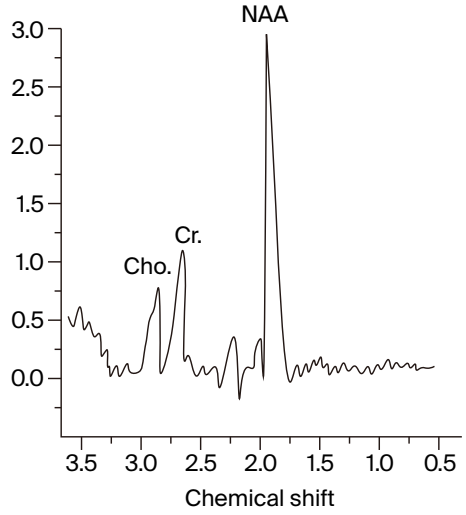

Figure 10. Schematic drawing showing normal MRS of brain. Cho.—choline, Cr.—creatine, and NAA—N-acetyl aspartate. Source: Figure by authors.

The biochemicals (metabolites) that can be studied in this regard include choline-containing molecules (used to construct cell membranes), creatine (an energy-metabolizing chemical), glucose and inositol (both sugars), alanine and lactate (both amino acids), and N-acetylaspartate (Tae et al. 2018).

MRS, also known as nuclear magnetic resonance (NMR) spectroscopy, is a non-invasive technique for studying metabolic changes in cerebral neoplasms, strokes, epilepsy, depression, Alzheimer's disease, and other brain diseases (Preul et al. 1996). MRS findings may be very confusing. MRS findings for different neurosurgical conditions are shown in Table 1.

1.3.12. iMRI (Intraoperative MRI)

Intraoperative MRI is available at only a few neurosurgical centers, where one can check the completeness of the excision of an intracranial tumor.

1.3.13. MR Cisternography

For a CSF fistula, MR cisternography can be performed, as is the case for CT cisternography. T1-weighted imaging is performed routinely in the axial, coronal, and sagittal planes. In the coronal, axial, and sagittal planes, a T2W spinecho sequence is acquired with fat saturation. To see how posture affects the distribution of CSF, MRI

is performed in both the supine and prone positions. In one case, a CSF leak was thought to have occurred when CSF was linked to the subarachnoid space outside the skull or herniation of the CSF was noticed (Wang et al. 2011).

Table 1. MRS findings for different neurosurgical conditions.

Conditions	Findings
Glioma (MRS can increase our ability to predict grades.)	NAA and creatine levels drop as the grade rises, whereas choline, lipid, and lactate levels rise. Choline levels are raised beyond the contrast enhancement margins in gliomas, indicating cellular invasion.
Non-glial neoplasms	Generally, non-glial neoplasms will have very few, if any, NAA peaks.
Radiation effects	It can be difficult to tell the difference between radiation alteration and tumor recurrence. Choline levels are elevated in a recurrent tumor, whereas NAA, choline, and creatine levels are all lower in a radiation transformation.
Infarction and ischemia	As the brain transitions to anaerobic metabolism, lactate levels will rise. When there is an infarction, lipids are released, and peaks appear.
Infection	NAA is not present in any of the processes that degrade normal brain tissue. Lactate, alanine, cytosolic acid, and acetate levels are all elevated/present in bacterial abscess cavities. Choline levels are low or nonexistent in toxoplasmosis but high in lymphoma, helping to distinguish between the two diseases.
White matter disorders	Increased myoinositol levels may be seen in progressive multifocal leukoencephalopathy (PML). Raised NAA levels are seen in Canavan illness.
Mitochondrial diseases	Leigh syndrome: high choline, low NAA, and, occasionally, high lactate levels

Source: Authors' compilation based on data from Horská and Barker (2010).

1.3.14. MRI for Cranial Nerves Protocol

Cranial nerve dysfunctions can be caused by disease processes inside the cranial nerves or by neoplasms, inflammation, infections, or traumatic damage to nearby structures. In the investigation of the cranial nerves, MRI is the gold-standard technique. The finest sequences for visualizing the cisternal segments are steady-state free procession (SSFP) images, which show dark cranial nerves on a brilliant cerebrospinal fluid background (CSF) (Romano et al. 2019).

The trigeminal nerve (TN) protocol for trigeminal neuralgia (Figure 11), the facial nerve protocol for hemifacial (HF) spasms, the glossopharyngeal and lower cranial nerve protocol for glossopharyngeal neuralgia and spasmodic torticollis, and the optic nerve (ON) protocol for idiopathic intracranial hypertension (IIH) are some of the most commonly used MRI protocols.

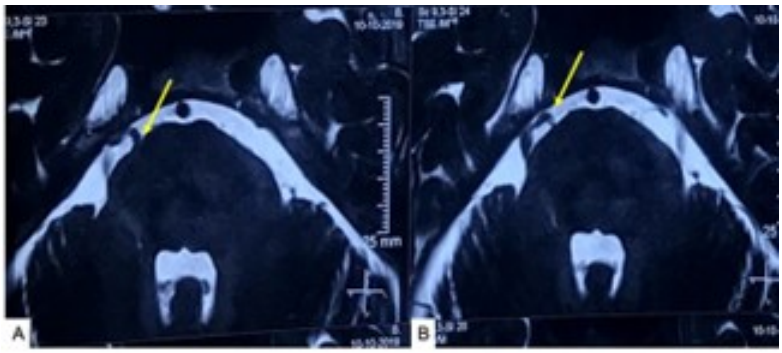

Figure 11. MRI in the TN protocol images (**A**,**B**) showing an artery at the REZ of the right trigeminal nerve causing neuralgia. Source: Figure by authors.

1.3.15. MRI in Epilepsy Protocol

Traditional MRI does not contain spoiled gradient recalled (SPGR) or magnetization prepared rapid gradient echo (MPRAGE) T1-weighted images that improve gray/white matter separation, which is important for understanding cortical architecture. If TLE is suspected, T1-weighted MPRAGE or SPGR pictures of the entire brain from nasion to inion and the epilepsy protocol MRI at 1.5T or 3.0T 1.5 mm slice thickness in the coronal oblique plane with no intervening gap in between are used. Coronal-and-axial-fluid-attenuated inversion recovery (FLAIR) sequences with a 2–3 mm slice thickness and a 0–1 mm interslice gap are also included in an epilepsy MRI protocol. The axial and coronal sequences are T2-weighted thin-slices (3 mm) (Passaro 2020).

1.3.16. MRI Cavernoma Protocol

The most sensitive sequences for cavernomas are gradient echo sequences. As a result, they are the ideal method for detecting cavernomas in patients with numerous lesions.

1.4. USG of the Head

When a probe (i.e., a transducer) with a frequency of 5–10 MHz is attached to the skin's surface, a portion of the ultrasonic waves produced are reflected back and detected by the same probe from structures with varying acoustic resistance. Electrical energy is converted from refracted waves and shown as a two-dimensional image (negative mode).

The reflected waves undergo a frequency shift proportional to the velocity of flowing blood when the probe is pointed towards moving entities, such as RBCs within a blood artery lumen (the Doppler effect). Either continuous wave (CW) or pulsed wave (PW) ultrasound is used Doppler ultrasonography. The former keeps track of frequency shifts over the probe's entire journey. A frequency shift is recorded using pulsed ultrasound at a given depth (Lindsay et al. 2011). Brain ultrasonography (duplex scanning, which includes B-mode and Doppler) can be utilized to assess brain architecture and disease, as well as cerebral circulation via blood flow velocity studies (Robba et al. 2019).

Ultrasound can penetrate the thinner sections of the skull at lower frequencies (2 MHz). When this is combined with a pulsed system, accurate flow velocity measurements in the posterior, middle, and anterior cerebral arteries, as well as the basilar artery, can be obtained. In extracranial stenotic/occlusive vascular disease, this procedure can be utilized to measure intracranial hemodynamics. Vasospasms are detected in subarachnoid hemorrhages (Lindsay et al. 2011). Thus, transcranial color-coded duplex sonography is a generally safe, non-invasive, repeatable bedside technique with a lot of potential for treating neurocritical care patients in a variety of clinical scenarios (Table 2), such as traumatic brain injury, hydrocephalus, aneurysmal subarachnoid hemorrhage, and the diagnosis of cerebral circulatory arrest (Robba et al. 2019).

Table 2. Common uses USG in neurosurgery.

Patients and the Method of USG Employed	Pathologies
In neonates, infants, and children—through an unclosed fontanel/through a burr hole	Congenital brain anomalies, hydrocephalus, cerebral aqueductal stenosis, vein Galan malformation
Older children and adults—through burr holes/bony defects/craniectomy	Congenital brain anomalies, hydrocephalus, cerebral aqueductal stenosis, vein Galan malformation, arachnoid cyst, tumour
Adults—focused ultrasound ablation	Lesioning in movement disorder
Adults—transcranial doppler (through thin bone)	Cerebral vasospasm in a subarachnoid hemorrhage
Children and adults—duplex scan	Carotid, vertebral, and other neck vessels; dissection; atherosclerosis; aneurysms; occlusion; and thrombosis
Children and adults—perioperative (after a burr hole and craniotomy)	For identification of lesions, especially deep, small lesions, and assessing the completeness of the resection of a tumor.
Children and adults—in ICU through TCD	Follow up on a head injury patient.

TCD—Transcranial doppler. Source: Table by authors.

2. Neuromonitoring (Perioperative Neuromonitoring, EEG, ECoG, and Neuronavigation) and Other Special Investigations (NCS, EMG, and CSF Studies and Immunohistochemistry)

2.1. Nerve Conduction Study (NCS)/Nerve Conduction Velocity (NCV) Analysis and Electromyography (EMG)

These methods are jointly used for neurosurgical conditions of peripheral nerves, especially peripheral nerve injuries and entrapments, for which surgery is commonly indicated. It is also indicated for the diagnosis of other peripheral neuropathies and to differentiate them from surgical etiologies.

2.2. Electroencephalography (EEG)

An electroencephalograph records the electrical activity of the brain in real time. Interictal scalp EEG is the first investigation carried out for seizure disorders. Routine EEG very rarely records actual seizures, except generalized absence seizures. However, routine EEG has important limitations. With multiple recordings, epileptiform EEG abnormality is detected in more than 90% of epilepsy patients (Salinsky et al. 1987).

Video-EEG Monitoring (VEM) is considered a cornerstone of the presurgical evaluation in epilepsy. Ictal EEG activity can be analyzed in the context of time-locked signs and symptoms. VEM gives better opportunities for the analysis of seizure semiology. The interpretations are more accurate when ictal events are analyzed in conjunction with simultaneously acquired EEG recordings.

Intracranial electroencephalography (IEEG)/Invasive EEG is an invasive procedure and utilized only when non-invasive tools fail to define EZ adequately (Jayakar et al. 2016).

There are subdural grid and strip electrodes and depth electrodes of multiple configurations for IEEG. Intracranial EEG signals may be recorded intraoperatively or extra-operatively. Craniotomy, the placement of subdural and depth electrodes, and the recording of electrical activity intraoperatively are collectively known as electrocorticography (EcoG) (Figure 12). Strips can be inserted through burr holes. Craniotomy is needed for grid placement. Depth electrodes can be placed through the burr, via craniotomy, or under neuronavigation guidance, but they are more commonly placed using the stereotactic method. Based on noninvasive evaluation, a hypothesis is made regarding a presumptive epileptic zone (EZ). Electrodes are placed to cover the EZ and an irritative zone and adjacent EC. Cortical stimulation mapping can be conducted through IEEG electrodes after EEG recording is completed. AED should be restarted before electrocortical stimulation (ECS).

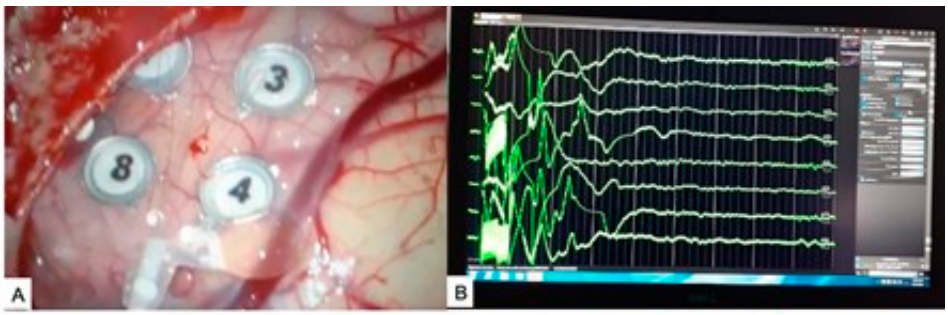

Figure 12. Perioperative electro-corticogram (ECoG). (**A**) Electrode on brain cortical surface after craniotomy and durotomy. (**B**) Tracing of ECoG. Source: Figure by authors.

2.3. Magnetoencephalogram (MEG)

A magnetoencephalogram is a promising noninvasive tool for defining the epileptogenic cortex and delineating the eloquent cortex. The neurophysiological process that generates the MEG signal is exactly the same as that which produces the EEG signal (Barth 1993). Magnetoencephaloghaphy is also useful in the localization of the sensory motor cortex, primary auditory cortex, and the language area. However, it has a huge operational cost.

2.4. Perioperative Neuromonitoring

2.4.1. Motor Nerve Monitoring

This technique is commonly used for the identification and preservation of motor cranial and spinal nerves in surgeries related to them. The levator palpabrae superioris muscle connected to the oculomotor nerve is used for cavernous sinus and superior orbital fissure surgery. Facial nerve monitoring is commonly conducted for

vestibular schwannoma (Figure 13) and petrous bone involving surgeries. Vagus, accessory, and hypoglossal nerve monitoring are used in jugular foramen and adjacent area surgery. For vagus monitoring, the cricothyroid muscle can be used. Spinal motor nerve monitoring is used for spinal tumors (especially intramedullary tumors), spinal instrumentations (especially deformity-corrective surgery, e.g., for scoliosis), myelomeningocele, myelocele, lipo-meningocele or tethered cord syndrome, peripheral nerve injury repair, or plexopathy surgery.

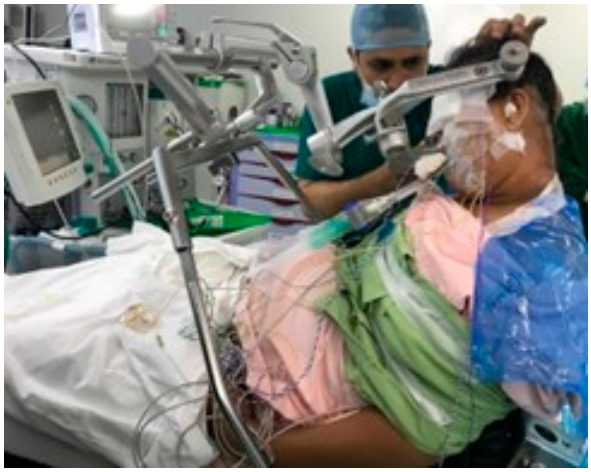

Figure 13. Placement of facial-nerve-monitoring equipment before removal of vestibular schwannoma in sitting posture. Source: Photo by authors.

2.4.2. Motor Evoked Potential (MEP) and Somato-Sensory Evoked Potential (SSEP)

These metrics are used during any surgery that may be related to complete motor (motor cortex to voluntary muscle) or sensory (peripheral sensory receptor to sensory cortex) pathways in order to check the integrity of the pathway.

2.4.3. Electrocorticogram (ECOG)

An ECOG is used during epilepsy surgery after opening a dura to identify the cortex responsible for the seizure (Figure 12) and to check for any residual responsible areas after cortical/lesional excision. It is also utilized for defining the central sulcus (as identified via phase reversal).

2.4.4. Visual Evoked Potential (VEP)

VEP can be used to ensure the safety and integrity of the visual pathway during surgeries related to visual pathways (i.e., visual apparatus tumors, occipital lobe surgery, etc.).

2.4.5. Brainstem Auditory Evoked Potential (BAEP) or Brainstem Auditory Evoked Potential (BAEP)

Brainstem auditory evoked potentials (BAEPs) are the electrical signals generated by the CNS within the first 10 ms after a transient acoustic stimulus. They are utilized for neurodiagnostic testing, intraoperative monitoring (e.g., acoustic schwannoma surgery and other surgeries related to hearing pathways), hearing screening/audiometry, head injuries, comas, brain death, and neurophysiological research.

2.4.6. Awake Craniotomy for Live Neuromonitoring

An awake craniotomy can be safely and expertly applied to psychologically stable patients for surgery involving the eloquent cortex (such as Broca's area, the primary motor area, etc.) or eloquent white mater (such as internal capsules, optic radiation, etc.) where the patient performs specific functions (such as limb movement, speech, etc.) at the time of the pathology's removal (Figures 14 and 15).

Figure 14. Pictures of awake craniotomy. (**A**) Position of patient and registration of neuronavigation. (**B**) Perioperative picture, showing the performance of an awake craniotomy. Source: Photos by authors.

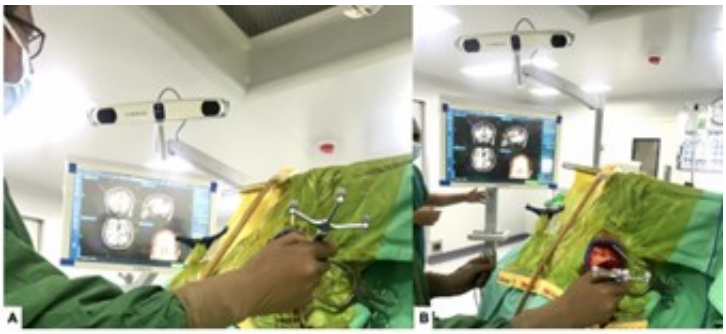

Figure 15. (**A**,**B**) Perioperative use of neuronavigation in awake craniotomy. Source: Photos by authors.

2.4.7. Stereotactic Navigation

The Cartesian coordinate system is based on three mutually perpendicular coordinate axes: the *xx* axis, the *yy* axis, and the *zz* axis. Thus, any point in space may be defined by *x*, *y*, and *z* values. Stereotactic surgery is based on the Cartesian coordinate system. By using computed tomography, magnetic resonance imaging (MRI), and Cartesian-co-ordinate-based stereotactic frames, anywhere deep in the brain can be reached/approached in a minimally invasive, precise, and reproducible manner. Modern stereotactic planning software helps in MRI and CT scan image fusion and trajectory planning, which eventually reduce surgical complications significantly. Biopsies, radiosurgery, deep-brain stimulation, radiofrequency ablation, the insertion of a depth electrode, and the suction of a hematoma or abscess are all indications for intracranial stereotactic surgery.

2.4.8. Neuronavigation

In image-guided neuronavigation, the concept of stereotaxis is applied. The brain is assumed to be a geometric volume that can be divided into three imaginary intersecting spatial planes that are orthogonal to each other using the Cartesian coordinate system (horizontal, frontal, and sagittal). Any site within the brain can be identified by measuring the distance between these three intersecting planes. This process provides precise neurosurgical guidance by transforming medical images into point-to-point maps of the corresponding locations within the brain by referencing this coordinate system of the brain with a parallel coordinate system of the 3-D image data of the patient, which are shown on the console of the computer workstation (Figures 14 and 15). Functional imaging methods such as magnetoencephalography (MEG), fMRI, and PET have been combined with neuronavigation to allow surgery in the vicinity of eloquent cerebral areas with little morbidity. The use of intraoperative MRI, which provides real-time images of residual lesions and allows for the testing of brain displacement during surgery, improves the spatial precision of today's neuronavigation systems (Ganslandt et al. 2002).

In order to relate the surgical techniques employed to images gathered both pre- and intraoperatively, each neuronavigation system follows the same steps: retrieving preoperative pictures; registration; intraoperative localization; intraoperative control; acquiring intraoperative images and fusing them with preoperative images; visualization; and operation (Ivanov and Ciurea 2009).

2.4.9. ICP Monitoring

An increased ICP can occur in cases with intracranial pathological conditions such as severe traumatic brain injuries, intracranial neoplasms, aneurysmal subarachnoid hemorrhage, and cerebral edema. The importance of the early detection and treatment of increased ICP cannot be overstated. ICP management has the ability to influence outcomes, especially when care is targeted, personalized, and supported with data from alternative monitors.

2.4.10. Jugular Venous Oximetry

This technique allows for intraoperative cerebral desaturation detection and anesthetic interventions such as improving hyperventilation therapy and managing perfusion pressure, fluids, and oxygenation to optimize cerebral physiology.

2.4.11. Intra-Operative Utilization of Dyes

Dyes are used in identifying CSF leakage, tumor identification, and intra-operative angiography. Fluorescein has been used intrathecally to identify CSF leaks, but there is risk of seizure associated with its use (Raza et al. 2016).

Fluorescein has also been used IV to help mark areas of the brain parenchyma where there is a breakage of the blood–brain barrier (BBB), e.g., in tumors. It has also been used to perform intraoperative "visible angiograms" during the removal of AVMs or during aneurysm clipping (Greenberg 2010).

Intraoperative angiography is performed using indocyanine green (ICG). This procedure can be performed under regular light; in some cases, near-infrared illumination can be used for a better view. It can only be applied to surface vessels. With big or wide-neck aneurysms or thick-walled atherosclerotic arteries, it may be less reliable (Greenberg 2010).

When tumor cells take up nonfluorescent 5-ALA, this process causes the production and accumulation of fluorescent protoporphyrin IX (PpIX). As a result of a broken BBB, enhanced neovascularization, and overexpression of membrane transporters in malignancy, there is greater ALA absorption in brain tumors. PpIX, which is collected specifically in malignant tissue, emits a red-violet light after being excited with blue light transmitted from a particular filter attachment on an operational microscope, allowing the surgeon to remove the red-violet tumor in a gross total fashion (Belykh et al. 2020).

2.4.12. CSF Study

CSF for research is often obtained via lumbar or ventricular taps, with a cisterna magna tap being used only very infrequently. A lumbar tap is contraindicated for an intracranial-space-occupying lesion (ICSOL), especially in the case of a posterior fossa tumor, wherein it may provoke tonsillar herniation through the foramen magnum, leading to death. A CSF study is commonly indicated for infective conditions (bacterial, viral, and fungal), including tuberculosis, demyelinating conditions (multiple sclerosis (MS), Guillain–Barre syndrome (GBS), and transverse myelitis (TM), wherein protein content is high), subarachnoid hemorrhages, etc. Very high protein content is found in GBS, bilateral acoustic schwannoma, and Froin's syndrome. Bacteria (including tuberculosis), viruses, and fungi can be identified by Gram and acid-fast bacillus (AFB) staining, the culturing of a precipitate of CSF in culture media, or by identifying genomic sequences (via PCR—polymerase chain reaction). CSF can also be used for serological studies, especially in neuro-cystocercosis, neuro-syphilis, hydatid disease, and toxoplasmosis (using ELISA, CFT, RIA, etc.).

2.4.13. Immunohistochemistry (IHC)

The IHC markers for CNS and PNS tumors can be broadly classified into three groups: (1) IHC markers utilized for diagnostic purposes, (2) IHC markers utilized for prognostic purposes, and (3) other IHC markers (Table 3) (Jaiswal 2016).

Table 3. IHC markers for CNS tumors.

Aims	Types	IHC Markers
For diagnosis	For glial cell tumors	S-100, GFAP
	For neuronal neoplasms	Synaptophysin, Beta-tubulin, NSE, Neurofilament, GFAP +/−, MAP-2
	For meningeal neoplasms	EMA, S-100, Vimentin, CK
	For choroid plexus neoplasms	CK, Transthyretin, S-100,
	For lymphomas	LAC, T-cell and B-cell markers
	For Schwann cell neoplasms	Leu 7, S-100,
	For germ cell neoplasms	AFP, PLAP, HCG, HPL
	For melanocytic neoplasms	HMB-45, MART-1(Melan-A), S-100, Microphthalmia transcription factor
	For vascular origin neoplasms	CD34, VEGF, Factor VIII, *Ulex europaeus*
	For pituitary neoplasms	PRL, ACTH, GH, MSH, FSH, LH, TSH
	For neuroendocrine neoplasms	Synaptophysin, Chromogranin
	For ATRT	INI-1/SMARCB-1
For prognosis	Cell cycle/proliferation markers	MIB-1, PNCA, Ki-67, BrdU,
	Tumor suppressor gene/oncogene protein	p53 tumor suppressor gene, C-myc oncogene, Retinoblastoma tumor suppressor gene (Rb)
	Growth factors/receptors	EGER
Other IHC markers		IDH-1and-2, BRAF, ATRX

IHC—Immunohistochemistry, GFAP—glial fibrillary acidic protein, CK—cytokeratin, NSE—neuron-specific enolase, MAP-2—Microtubule-associated protein-2, EMA—epithelial membrane antigen, LCA—leukocyte common antigen, AFP—alpha fetoprotein, HCG—human chorionic gonadotrophin, PLAP—placental alkaline phosphatase, HPL—human placental lactogen, HMB-45—human melanoma black-45, VEGF—vascular endothelial growth factor, PRL—prolactin, GH—growth hormone, ACTH—adrenocorticotrophin hormone, MSH—melanocyte-stimulating hormone, LH—luteinizing hormone, FSH—follicle-stimulating hormone, TSH—thyroid-stimulating hormone, ATRT—atypical teratoid/rhabdoid tumor, MIB-1—molecular immunology borstel-1, Ki-67—Kiel antibody-67, PCNA—proliferating cell nuclear antigen, BrdU—bromodeoxyuridine, EGFR—epidermal growth factor receptor, IDH-1&2—isocitrate dehydrogenase-1&2, ARTX—alpha-thalassemia/mental retardation syndrome X-linked (Jaiswal 2016). Source: Reprinted from Jaiswal (2016), used with permission.

Special molecular traits are part of the definition of a subset of CNS neoplasms in the 4th edition of the WHO Classification of CNS Tumors, which was published in 2016. This integrated 'histo-molecular' classification system provides for a significantly more exact diagnosis of diffuse gliomas and embryonal CNS malignancies, especially diffuse gliomas. IDH1/IDH2 mutations, 1p/19q codeletion, and mutations in histone H3 genes are all defining molecular markers for diffuse gliomas. According to the WHO's 2016 Classification, medulloblastomas, the commonest embryonal CNS neoplasms, are split into four molecularly characterized groups: WNT-signaling-pathway-activated, SHH-signaling-pathway-activated and tumor protein p53 gene (TP53) mutant, SHH-activated and TP53-wildtype, and non-WNT/non-SHH-activated. The diagnosis of various other CNS cancers, such as RELA fusion-positive ependymoma, atypical teratoid rhabdoid tumors (ATs/RTs), embryonal tumors with multilayered rosettes, and solitary fibrous tumors/hemangiopericytoma, is likewise dependent on molecular features. For further molecular characterization of several of these malignancies, immunohistochemistry is a useful alternative. Furthermore, genome-wide methylation profiling is a promising new approach to the diagnosis of CNS tumors (Kristensen et al. 2019).

2.4.14. Sample (Tissue/Granulation Tissue/PUS) for Histology, IHC, PCR, Cultures, and Staining

Sample specimens collected via/during surgical intervention should be collected appropriately. For histopathological examination, PCR, and immunohistochemistry, part(s) of specimens should be preserved in 10% formalin solution in container(s). For cultures, more than one specimen needs to be preserved in a sterile container without any preservative (including normal saline); commonly, three containers are used for 1. pyogenic aerobic bacteria, 2. fungal cultures (Sabouraud dextrose agar media), and 3. tubercular cultures. For anaerobic

cultures, collection, transport, and inoculation in Robertson cooked meat medium necessitate special techniques and preparation. For Gram, AFB, or fungal staining, more specimens (without preservative) in different containers are required.

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