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REVIEW ARTICLE

NEUROIMAGING IN CLINICAL PRACTICE: AN OVERVIEW

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Abstract:

Neuroimaging is a specialization of imaging technique that produce images of the brain or other parts of the Central Nervous System (CNS) in a noninvasive manner that directly or indirectly assess the structural or functional activity of the nervous system. Computed tomography (CT) and magnetic resonance imaging (MRI) are the most widely used modalities in routine clinical practice. Neuroimaging can be divided into two broad categories, namely, structural and functional neuroimaging. This article discusses the basics and applications of various traditional, as well as emerging neuroimaging techniques, considering their strengths and limitations with this rapidly expanding field.

Keywords: *Neuroimaging in clinical practice , Structural imaging Functional imaging , Technique of Neuroimaging*

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Introduction:

Neuroimaging is the use of varied ways to either directly or indirectly image the structure, functional activities of the nervous system. Neuroimaging plays a vital part in the determination of CNS diseases. Main modalities of neuroimaging approaches are CT scan and MRI.[1] The pioneer method for imaging brain structure was CT. It remains useful because of short imaging times, wide vacuity, ease of access, sensitive spotting of calcification and hemorrhage, and resolution of bony detail. MRI provides excellent detailed structural information and enables the naked eye to distinguish argentine matter (neuronal cell bodies) from white matter (myelinated tracts).[2] MRI offers superior soft- tissue contrast, excellent visualization of vascular structures, minor artifacts, and imaging in any plane. New anatomical methods, similar as diffusion tensor imaging, have been developed to specifically image myelinated tract. These approaches can be used to trace the normal and anomalous evolution of neural pathways in children. Now a day, CT and MRI operations that concentrate on functional and physiologic display of the CNS will add greatly to the clinical usefulness of these imaging tools. Neuroimaging techniques are growing increasingly sophisticated and as a result there is a high demand in both clinical and research settings for individuals with neuroimaging skills.[4]

Indications:[5]

1. To investigate a patient who has or may have a neurological disorder such as stroke, headache, syncope, seizure disorder etc.
2. It is indicated for CT-, MRI- and PET-guided stereotactic surgery or radiosurgery for treatment of intracranial tumors, arteriovenous

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malformations and other surgically treatable conditions.

3. It is helpful to diagnose metabolic diseases and degenerative diseases (such as Alzheimer's disease, Parkinson's diseases etc.) and also for neurological and cognitive psychology research.

Types of Neuroimaging: (Figure: 1)[6]

A. Structural imaging :
Structural imaging refers to approaches that are specialized for the visualization and analysis of anatomical properties of the brain. Structural approaches are particularly useful for detecting brain damage and abnormalities. It deals with the structure of the nervous system and the diagnosis of gross (large scale) intracranial disease (such as stroke, tumor, infection, demyelinating disease etc.) and injury. It also shares detailed information regarding brain integrity, microstructure, and white matter connections.

B. Functional imaging :
Functional imaging has been the dominant force in cognitive neuroscience because it ables to determine when and where neural activity in the brain is associated with the ability to perform a particular cognitive task. It localizes the activity of brain associated with performing a cognitive task and/or behavior. It is used to diagnose metabolic diseases and lesions on a finer scale (such as Alzheimer's disease) and also for neurological and cognitive psychology research and building brain-computer interfaces.

Technique of Neuroimaging:[7]

A. Computed tomography (CT) or Computed Axial Tomography (CAT)
B. Magnetic resonance imaging
C. Functional magnetic resonance imaging
D. Magnetoencephalography
E. Positron emission tomography
F. Single-photon emission computed tomography
G. Computed tomography angiography
H. Magnetic resonance angiography
I. Magnetic resonance venography
J. MR Neurography / MR Imaging of Peripheral Nerves (PNI)
K. Cerebral Digital Substraction angiography.

Guidelines for selecting of neuroimaging techniques:[8]

- Neuroimaging techniques have advantages and disadvantages that are based on the strengths and limitations of each. The different neuroimaging techniques in terms of the degree of invasiveness, tasks that can be performed, spatial resolution, and temporal resolution. Spatial resolution refers to how accurately the measured activity is localized within the brain, and temporal resolution refers to how closely the measured activity corresponds to the timing of the actual neural activity. The following guidelines are used for selecting of neuroimaging techniques in Table: 1.[8]

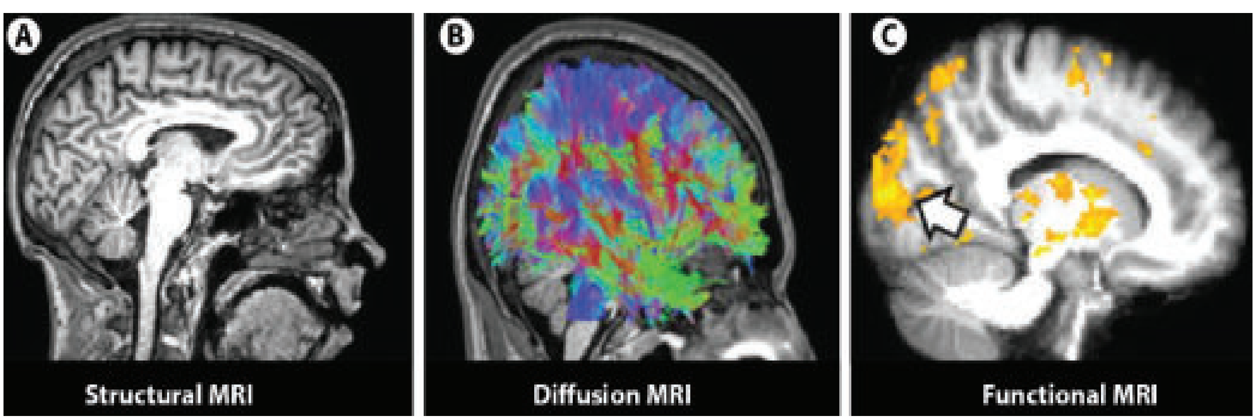

Figure 1: *MRI based imaging techniques:(A) Structural MRI reveals the gross anatomical structure of the brain with high detail (B) Diffusion MRI reveals the overall layout of white matter connections and pathways within the brain (known as Diffusion tractography). (C) Functional MRI reveals areas of the brain that are active when and individual is asked to perform a particular task. In this case, an individual who is congenitally blind was asked to identify a tactile pattern through touch. Note areas of activation identified throughout the brain (yellow) including within the occipital cortex which is normally associated with visual information processing (arrow).*

Table-I

Guidelines for selecting of Neuroimaging techniques[9] Conditions

Condition	Recommended Technique
Hemorrhage	
Acute parenchymal	CT, MR
Subacute/chronic	MRI
Subarachnoid hemorrhage	CT, CTA, lumbar puncture angiography
Aneurysm	Angiography > CTA, MRA
Ischemic infarction	
Acute infarction	MRI > CT
Hemorrhagic infarction	CT or MRI
Carotid or vertebral dissection	MRI/MRA
Vertebral basilar insufficiency	CTA, MRI / MRA
Carotid stenosis	CTA > Doppler ultrasound, MRA
Suspected mass lesion	
Neoplasm, primary or metastatic	MRI + contrast
Infection/abscess	MRI + contrast
Immunosuppressed with focal findings	MRI + contrast
Vascular malformation	MRI +/– angiography
White matter disorders	MRI
Demyelinating disease	MRI +/– contrast
Dementia	MRI > CT
Trauma	
Acute trauma	CT (noncontrast)
Shear injury/chronic hemorrhage	MRI
Headache/migraine	CT (noncontrast) / MRI
Seizure	
First time, no focal neurologic deficits	?CT as screen +/– c ontrast
Partial complex/refractory	MRI with coronal T2W imaging
Cranial neuropathy	MRI with contrast
Meningeal disease	MRI with contrast
Spine	
Low back pain	
No neurologic deficits	MRI or CT after 4 weeks
With focal deficits	MRI > CT
Spinal stenosis	MRI or CT
Cervical spondylosis	MRI or CT myelography
Infection	MRI + contrast, CT
Myelopathy	MRI + contrast > myelography
Arteriovenous malformation	MRI, myelography/ angiography

Computerized tomography (CT) Scan of Head

Introduction: [7-10]

CT Scan is an imaging modality that uses X-rays to obtain structural and functional information about the human body. It is also called a computed axial tomography (CAT) scan. [8] The word Tomography is derived from a Greek word where tomos represents "slice" or section and graphia meaning "description". The term Tomography refers to a process for generating 2D image slices of an examined organ of three dimensions (3D). [8] CT scans can expose patients to levels of radiation 100-500 times higher than traditional x-rays, with higher radiation doses producing better resolution imaging.[9] CT scanning uses a computer program that performs a numerical integral calculation (the inverse Radon transform) on the measured x-ray series to estimate how much of an x-ray beam is absorbed in a small volume of the brain. [9]

Typically the information is presented as cross-sections of the brain. It uses a series of x-rays of the head taken from many different directions. Clinicians oftentimes take multiple scans, with 30% of individuals undergoing at least 3 scans in one study of CT scan usage.[10] While easy to use, increases in CT scan use, especially in asymptomatic patients, is a topic of concern since patients are exposed to significantly high levels of radiation. Computed Tomography (CT or CAT scan) is a noninvasive diagnostic imaging procedure that uses a combination of x-rays and computer technology to produce horizontal (axial) and vertical (Sagittal/ coronal) images (often called slices) of the head. A computed tomography is a display of the anatomy of thin slide of the body developed from multiple x-ray absorption measurement made around the body's periphery.[11] Routine head CT is performed in an axial axis with 15-20 degree angulations of the gentry to orbitomeatal plane. This angulation provides superior visualization of brainstem & cerebellum. This angulation also decreases radiation to eyes. Routine CT examination of brain involves making (9-10) axial section.[11]

A CT scan shows detailed images of any part of the brain including the hemorrhage, infraction, calcification and other pathological conditions. CT scans are more detailed than standard x-rays. Indications of CT Scan of brain in Box: 2

Indications of CT Scan of Head:[12]

A CT brain is considered to look at the structures of the brain and evaluate for the presence of pathology, such as mass/tumor, abscess, and stroke (Box: 2). It is particularly good for hemorrhage, trauma or fracture to the skull and for hydrocephalus.

Box: 2 Indications of CT Scan of Head

1. Head injury or skull fractures,
2. Stroke,
3. Suspected hydrocephalus,
4. Suspected intracranial hematoma,
5. Evaluation of Headaches,
6. Diseases or malformations of the skull.
7. Initial evaluation for space-occupying lesions
8. Seizures and
9. Unexplained change in mental status.

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It will usually exclude non-stroke lesions, including subdural haematomas and brain tumours. It will demonstrate intracerebral haemorrhage within minutes of stroke onset. CT changes in cerebral infarction may be completely absent or very subtle within the first few hours after symptom onset, though changes usually evolve over time (12- 24 hrs). Contraindications of CT scan of Head in Box:3

Box: 3 Contraindications of CT scan of Head

1. CT scan has no absolute contraindications.
2. Caution is indicated in pregnant women, particularly during the first trimester to avoid fetal abnormalities.
3. Repeated x-ray exposure may increase the patient's risk for cancer..

Magnetic Resonance Imaging (MRI):

Magnetic resonance imaging (MRI) is an imaging technique used primarily in medical settings to produce high quality images of the soft tissues of the human body. Magnetic resonance imaging (MRI) is based on the magnetic characteristics of the imaged tissue. It involves creation of tissue magnetization (which can then be manipulated in several ways) and detection of tissue magnetization as revealed by signal intensity.[13] Imaging is created by the motion of hydrogen protons in response to the applied radiofrequency.[14]

It is useful in a wide range of clinical situations; for example, imaging the optic chiasm; small intracanalicular acoustic neuroma; detection of meningiomas which are sometimes isointense with normal central nervous system tissue on T2- and T1-weighted unenhanced sequences; intramedullary spinal tumours; leptomeningeal disease and in demonstrating acute inflammation in multiple sclerosis plaques.[15] Indications for Brain MRI in Box:4. Contraindications for Brain MRI in Box:5

Box 4: Indications for Brain MRI[15]

1. Vascular (ischemic and hemorrhagic stroke, AVM, aneurysm, venous thrombosis)
2. Infection (abscess, cerebritis, encephalitis, meningitis)
3. Inflammatory/Demyelinating Lesions (multiple sclerosis, sarcoidosis, etc.)
4. Tumor (primary CNS and metastatic)
5. Trauma (epidural hematoma, subdural hematoma, contusion)
6. Hydrocephalus

Box 5: Contraindications for Brain MRI[15]

1. Implanted devices and other metallic devices
   a) Pacemakers and other implanted electronic devices
   b) Aneurysm clips and other magnetizable materials
   c) Cochlear implants
   d) Some artificial heart valves
   e) Intraocular metallic foreign bodies
   f) Screening CT of the orbits if history suggests possible metallic foreign body in the eye.
2. Unstable patients (most resuscitation equipment cannot be brought into the scanning room).
3. Other relative contraindication – severe agitation or claustrophobia (may require anesthesia assistance

MRI Compatible Metals:[16]

1. Titanium: Titanium's nonmagnetic properties make it compatible for use with an MRI as well. Joint replacements, surgical screws, bone plates and pacemaker cases all use titanium.
2. Cobalt-Chromium: Though cobalt has magnetic properties, implants such as coronary stents made of cobalt-chromium alloy have tested safe during an MRI. The alloy also tests safe for larger items, such as knee and hip replacements.
3. Copper: Researchers have tested intrauterine contraceptive devices (IUDs) for MRI safety. Some of these devices have a small copper coil. Copper wiring for pacemakers has also tested safe for an MRI.
4. Stainless Steel: Some stainless steel alloys have a very low reaction, or susceptibility, to magnetic fields. Medical supply companies sell stainless steel tools and accessories that staff can safely use in the MRI room. Stainless steel items such as dental braces can distort MRI images, however. If the metal interferes too much with the MRI image, the doctor may recommend you have your braces removed.

Limitations of MRI:[15]

1. Subject to motion artifact
2. Inferior to CT in detecting acute hemorrhage
3. Inferior to CT in detection of bony injury
4. Requires prolonged acquisition time for many images

MRI of Spine:

Magnetic resonance imaging (MRI) of the spine uses radio waves, a magnetic field and a computer. It creates clear, detailed pictures of the spine and surrounding tissues. [17] MRI does not use radiation and may require an injection of gadolinium contrast material. MRI scan was developed in the 1980's and has revolutionized our ability to see normal and abnormal spinal structures and help diagnose those spinal disorders.[18] MRI of the spine can be useful in evaluating symptoms such as neck or back pain, leg pain, numbness, tingling or weakness, or problems with bladder and bowel control.[17] It can assess the disks to see whether they are bulging, ruptured, or pressing on the spinal cord or nerves. It can also help to diagnose tumors, bleeding, swelling, developmental or structural abnormalities, and infections or inflammatory conditions in the vertebrae or surrounding tissues. The indications of MRI spine in Box:.4

Box 6: Indications of MRI Spine[18]

1. Assess spinal anatomy and alignment.
2. Detect congenital anomalies of vertebrae or the spinal cord.
3. Detect bone, disc, ligament or spinal cord injury after spine trauma.
4. Assess lower back pain due to intervertebral disk disease (degenerated, bulging or herniated) and intervertebral joint disease, compression fracture or bone swelling).
5. Assess compression of spinal cord and nerves.
6. Assess inflammation of the spinal cord or nerves.
7. Assess infection involving the spine, disks and spinal contents including spinal cord or its coverings (meninges).
8. Assess tumors that arise from or have spread to the vertebrae, spinal cord, nerves or the surrounding soft tissues.

MRI with or without contrast:[19]

MRI without contrast cannot generally help in evaluating the given tumor condition. MRI images with contrast are clearer than the images of MRI without contrast. Due to the high clarity of images gathered by MRI with contrast, they are easier for a medical specialist to evaluate and interpret. Non-contrast MRI is great option for patients for whom dye is not recommended, pregnant women and kidney-compromised patients. Non-contrast also provides greater images of blood vessel activity, detecting aneurysms and blocked blood vessels.

Functional imaging:

Positron Emission Tomography (PET) Imaging:

Positron emission tomography (PET) is a type of nuclear medicine procedure that measures metabolic activity of the cells of body tissues.[20] This imaging technique employs radioactive isotopes and can study a variety of functional or chemical features in normal and pathological brain which are inaccessible to other imaging modalities. [21] A positron is a positively charged electron, and in positron emission tomography (PET) imaging, a biological tracer is labelled with a positron-emitting radionuclide. PET scans of the brain are used to detect or highlight tumors and diseased tissue, measure cellular and/or tissue metabolism, show blood flow, evaluate patients who have seizure disorders that do not respond to medical therapy and patients with certain memory disorders, and determine brain changes following injury or drug abuse, among other uses.[22] The imaging of cerebral metabolism indirectly via perfusion directly with PET using [F-18] fluorodeoxyglucose (FDG) is clinically well established. Using radio-isotopes such as [^{15}O] or [^{18}F] deoxyglucose, it has been possible to quantify cerebral blood flow and metabolism in vivo. [23] The tracer is given by intravenous injection or gaseous inhalation, and its distribution in the brain can be demonstrated on tomographic images. Radio-isotope labels are also used in PET studies to evaluate receptor binding, e.g. the study of dopaminergic receptors in extrapyramidal disease.

Advantages of PET Imaging: 23

1. PET studies, provided considerable insights into aspects of normal brain function and as well disease pathogenesis and pathophysiology.
2. Valuable insights have been obtained into the varying anatomical patterns of altered metabolism and flow in a wide range of neurodegenerative diseases, and the patterns of flow and oxygen utilization in infarcts and their surrounding ischaemic penumbra.
3. Amyloid PET in AD in figure:2

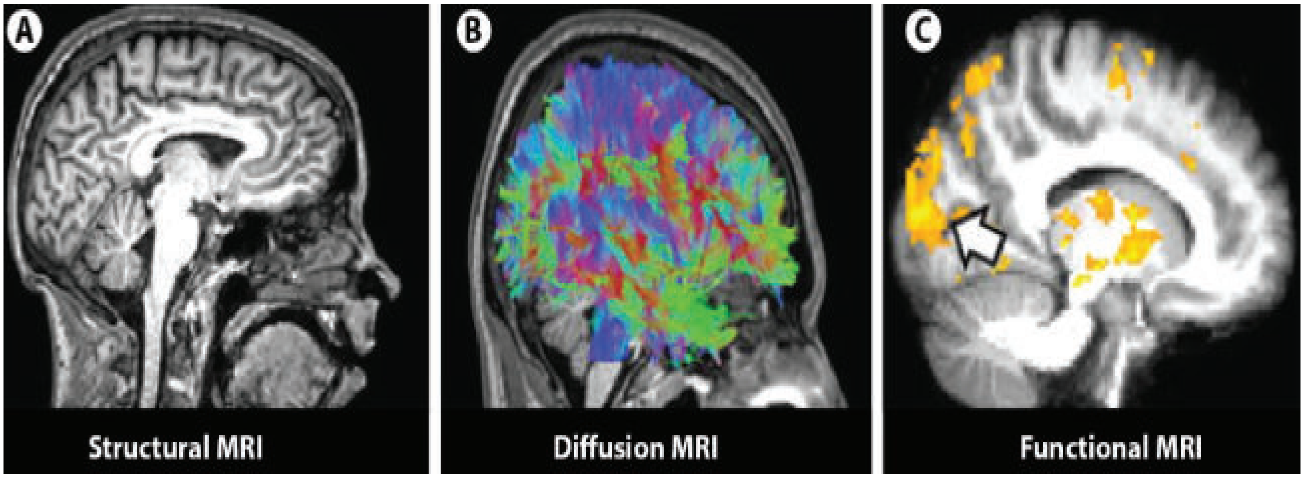

Figure 2: *PET using fluorodeoxyglucose (FDG), which is taken up by active mitochondria, to measure the metabolic activity of the brain. Patients with Alzheimer's disease show evidence of near-global decreases in metabolic function, particularly in the temporoparietal regions.*

Disadvantages of PET Imaging :[23]

1. It is an expensive tool, requires immediate access to a cyclotron.
2. The opportunity for serial examinations is limited by the constraints of radiation exposure.

Single photon emission computed tomography (SPECT) (Figure: 3)

It is a functional nuclear imaging technique performed to evaluate regional cerebral perfusion. Because cerebral blood flow is closely linked to neuronal activity, the activity distribution is presumed to reflect neuronal activity levels in different areas of the brain.[24] A lipophilic, PH-neutral radiopharmaceutical (most commonly 99m Tc hexamethylpropyleneamine oxime [HMPAO] and 99m Tc-ethylene cysteine diethyl ester [ECD], with a half-life of 6.02 hours) is injected into the patient, which crosses the blood-brain barrier and continues to emit gamma rays.[25] A 3-dimensional representation of cerebral blood flow can be literated using gamma detectors, allowing for interpretation.

Acetazolamide increases local pCO2 and causes arteriolar dilation, allowing for assessment of cerebrovascular reserve in transient ischemic attack (TIA), stroke, and vascular anomalies and distinguishing vascular from neuronal causes of dementia.[26] Indications of SPECT in Box:7

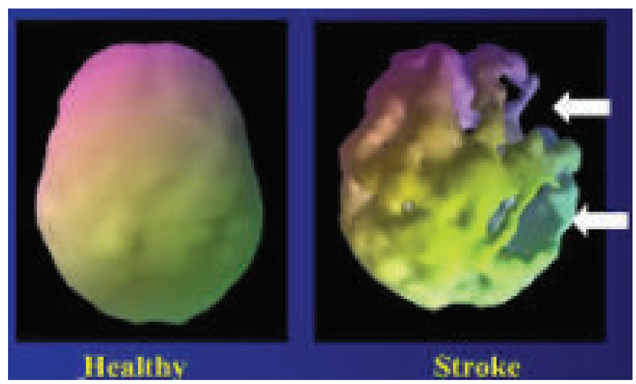

Figure 3: *Single photon emission computed tomography (SPECT).*

Box 7: *Indications of SPECT*[27]

1. Detection and evaluation of cerebrovascular disease.
2. Aid in the diagnosis and differential diagnoses of suspected dementia.
3. Detection of seizure focus.
4. Assessment of brain death.
5. Evaluating suspected brain trauma.
6. Neuropsychiatric disorders: Mood disorders, evaluating and sub typing attention-deficit disorder.
7. Substance abuse.
8. Infection/inflammation.

Limitations:[27]

1. SPECT is technically less sophisticated and demanding when compared with PET, but provides lower-resolution images.
2. It can be used to evaluate regional variations in blood flow, but its role in everyday clinical practice is, like that of PET, a small one.

Magnetic Resonance Neurography :

Magnetic resonance neurography (MRN) or MR Neurography, also known as MR Imaging of Peripheral Nerves (PNI), is an advanced technique that is useful for diagnosing disorders of the peripheral nerves beyond the spinal canal.[28] MRN is a relatively new non-invasive imaging technique for dedicated assessment of peripheral nerves.[28] It is the direct imaging of nerves in the body by optimizing selectivity for unique MRI water properties of nerves. It is a modification of magnetic resonance imaging. It is used to assess peripheral nerve entrapments and impingements as well as localization and grading of nerve injuries and lesions.[29]

Nerve trauma, tumor, inflammation, radiation damage, compression related to disc disease or entrapment are some of the more common nerve diseases that are evaluated with MRN. MRN can image nerves anywhere in the body, although it is most commonly used in the diagnosis of abnormalities of the brachial plexus, lumbosacral plexus, thoracic outlet, and sciatic nerves.[27] MRN is mostly used to assess major nerve compressions such as those affecting the sciatic nerve (e.g. piriformis syndrome), the brachial plexus nerves (e.g. thoracic outlet syndrome), the pudendal nerve, or virtually any named nerve in the body.[29] Many nerves, such as the median and ulnar nerve in the arm or the tibial nerve in the tarsal tunnel, are just below the skin surface and can be tested for pathology with electromyography, but this technique has always been difficult to apply for deep proximal nerves.[30]

So MRN can characterize nerve morphology, longitudinal variations in signal intensity and caliber, and connections and relations to other nerves or plexuses to help identify pathology in correlation with the patient's clinical history, physical examination, and electrophysiological studies.[31]

Clinical applications: [32]

It is especially beneficial for patients with:

1. Persistent nerve-related symptoms despite normal or equivocal routine spine imaging, and
2. Specific nerve abnormalities on electromyelography.

MRN Protocol:[33]

Dedicated high-resolution MR sequences are utilized to optimally increase the conspicuity of nerve tissue signal. Exact parameters, planes and reconstructions will vary according to anatomical location, scanner constraints and local preference. Commonly used imaging protocols include:

- o Axial T1-weighted
- o Axial fat-suppressed T2-weighted
- o 3D STIR (short tau inversion-recovery)
- o 3D PSIF (reversed fast imaging in steady state precession)

Diffusion tensor imaging (DTI) and high-resolution balanced steady-state sequences (e.g. 3D CISS) may also be useful. Use of intravenous gadolinium contrast is usually restricted for assessment of infection, perineural involvement by tumor of to further assess mass lesions. Pitfalls and Technical Limitations of MRN in Box:8

Box 8: Pitfalls and Technical Limitations of MRN[34]

- Differentiating nerves from adjacent vessels
- Increased perineural T2 signal from adjacent vessels
- Magic angle effect
- Inhomogeneous fat suppression
- Increased specific absorption rate (SAR) at 3 T
- Increased susceptibility artifact at 3 T

Summary:

Neuroimaging includes the use of various techniques to either directly or indirectly image the structure, function, or pharmacology of the brain. Neuroimaging falls into two broad categories: structural imaging and functional imaging. CT scan is used to visualize of gross brain abnormalities, malformations, hemorrhagic stroke and bone structure. Magnetic resonance imaging (MRI) scans use echo waves to discriminate among grey matter, white matter, and cerebrospinal fluid. Electroencephalography (EEG) is used to show brain activity under certain psychological states, such as alertness or drowsiness. Positron emission tomography (PET) scans show brain processes by using the sugar glucose in the brain to illustrate where neurons are firing. Functional magnetic resonance imaging (fMRI) scans are a series of MRIs measuring brain function via a computer's combination of multiple images taken less than a second apart.

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Conclusion:

Neuroimaging is an important crucial approach in clinical neuroscience and modern cognitive of the human brain. long with the quantitative examination of the structure, blood flow, blood volume, electrical activity, metabolism, oxygen consumption, and many other physiological activities inside the central nervous system, it may give a variety of directly or indirectly derived graphical representations. It plays a role in the investigation structural lesions as well as the physiological underpinnings of mental processes and is crucial to the identification, diagnosis, and treatment of neurological and psychiatric disorders as well as the testing of novel therapeutic interventions.

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