

Imaging of Peripheral Nerves

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Abstract

Peripheral neuropathy is defined as any disorder affecting the peripheral nerves. Clinical examination along with electrophysiological studies form the gold standard for diagnosing peripheral neuropathy. Imaging of peripheral nerves has come a long way, beginning from plain ultrasound (USG) in early days to highly sophisticated magnetic resonance (MR) neurography in the current era. Direct visualization of the nerve along with secondary changes in muscles are well visualized with nerve imaging. USG acts as a screening modality allowing for quick comparison with the opposite side. MR imaging is the more objective and definitive modality for evaluating peripheral neuropathy; however, is underutilized due to its high cost and lack of expertise.

Keywords

- ▶ peripheral nerves
- ▶ ultrasound
- ▶ magnetic resonance imaging

Introduction

Imaging of peripheral nerves has come a long way beginning from plain ultrasound in early days to highly sophisticated magnetic resonance (MR) neurography in the current era. This has been made possible largely due to the advent of high-frequency ultrasonography (USG) probes, higher tesla MR machines, better coils, and specific neurography sequences. Almost 15 million people are affected worldwide by peripheral neuropathy and the degree of recovery depends on the grade of injury.¹ Conventionally, the diagnosis of peripheral neuropathies relied predominantly on clinical examination and electrophysiological studies, which is still considered the gold standard. However, imaging is gaining an important role in the management of peripheral nerve disorders and now has a well-established role. Imaging studies provide the spatial resolution and determine the site of pathology precisely. These features make imaging studies better than the electrophysiological studies. This has been a boon to the surgeons as now they know the exact site of pathology and can decide the management plan preoperatively.

Ultrasound

High-frequency probes with frequency ranging from 8 to 15 MHz are required to directly visualize the peripheral

nerves.² Ultrasound provides excellent spatial resolution for peripheral nerve imaging. It is a relatively inexpensive modality, apart from being quick and easy with not a very long learning curve. It is an excellent screening modality with the advantage of screening of the whole length of the nerve. It also allows comparison of the nerve with the nerve on the contralateral side. However, lack of specificity and failure in cases of deep-seated nerves and sometimes in post-traumatic cases (where there is architectural distortion and scarring) preclude its role as the imaging method of choice. Moreover, USG is operator-dependent and the ability to diagnose varies with the expertise of the operator.

On USG, normal nerve appears as a round to ovoid structure having fascicular appearance when imaged along transverse axis of the nerve (▶ Fig. 1). The fascicles are hypoechoic which

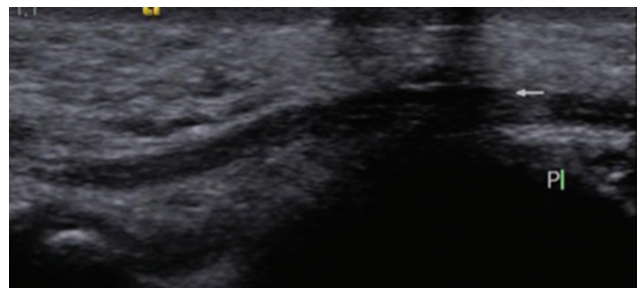


Fig. 1 Ultrasound image of a normal nerve in longitudinal plane.

are separated by echogenic septa representing the perineurium. All the fascicles are further surrounded by a hyperechoic covering—the epineurium. When imaged along the longitudinal axis, it appears as a tubular structure having multiple linear bands within, giving it a “bundle of straws” appearance.² The nerve can be differentiated from adjoining vessels by the lack of color flow and presence of fascicular appearance. It can be differentiated from adjoining tendons by its specific fascicular morphology vis-a-vis a fibrillar structure of tendons.³

Abnormal nerve shows abnormal caliber, morphology, and echotexture. Depending upon the pathology it can have altered caliber either focally or along the entire length of the nerve. Similarly, in most instances it usually appears hypoechoic when abnormal and loses its fascicular structure. Ultrasound can also give a clue to the diagnosis whether it is a primary nerve pathology or the nerve is involved secondarily due to pathology in adjoining structures.

Magnetic Resonance Imaging

It is due to excellent contrast resolution that magnetic resonance imaging (MRI) has emerged as the imaging modality of choice for peripheral neuropathy. In addition, development of higher strength magnets and specific neurography sequences has paved the way for direct visualization of nerves.

Peripheral nerves are best evaluated in axial plane. Thin sections of 3 to 4 mm thickness are acquired with 0 to 3 mm gap, depending on the thickness of nerve to be imaged. 3D sequences are also acquired for making multiplanar reformats for better understanding of surgeons.

Basic MR neurography protocol would include the following sequences:

1. T1 spin echo sequence, for the anatomical localization of the nerve. The nerve is usually isointense to muscle on T1-weighted sequence, having fascicular appearance (► **Fig. 2**). It is surrounded by fat which is hyperintense on T1. The nerve usually accompanies the vessel in intermuscular plane/fascia, from which it can be distinguished by lack of flow void and presence of perineural fat.

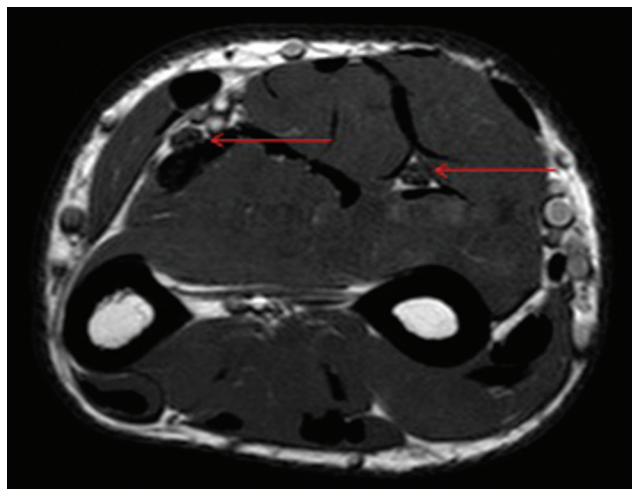


Fig. 2 T1w SE axial image depicting appearance of normal nerve (arrows).

2. T2 fat saturation/STIR sequence, for diagnosing the abnormal nerve. The normal nerve is isointense to mildly hyperintense to muscle on T2-weighted sequence (► **Fig. 3**). Abnormal nerves are usually hyperintense on T2-weighted sequence with loss of fascicular appearance. However, they can appear hypointense in long standing cases. Normal nerves can fallaciously show T2 hyperintensity due to magic angle effect. This can be corrected by acquiring images at high TE (~ 60 s).
3. 3D STIR (isovoxel) for making the 3D reformats.

The abnormality in MRI can be diagnosed by direct visualization of the nerves and also by secondary denervation of muscles supplied by the specific nerve. There can be change in the caliber of the nerve or change in the nerve signal. One can find other features of architectural distortion, nerve abscess, tumor of the nerve, adjoining nodes, in addition. Secondary denervation in the muscles supplied by the nerve can also be considered a useful sign of nerve pathology. Denervation can be acute when there the muscles show T2 hyperintensity, can be subacute when there is hyperintensity both in T1- and T2-weighted sequence or can be chronic when there is decrease in volume of muscle with fatty infiltration evidenced as T1 hyperintensity.

MRI also has a role in postoperative imaging to assess the persistent gap or nerve regeneration. In entrapment neuropathies, usually the signal intensity of entrapped nerve normalizes in 8 weeks after neurolysis or nerve release.⁴⁻⁶ Persistent nerve changes in MRI along with clinical deterioration would suggest re-entrapment.

The major advantages of MRI are that it is more objective, not operator-dependent. It gives excellent spatial and contrast resolution. It is possible to make 3D reformats with MRI. However, its major shortcomings include the cost and the long learning curve besides being cumbersome. The long duration of examination makes it uncomfortable to the patient. It cannot be performed in patients having contraindications to MRI, like having a pacemaker or metallic implant or if the patient is claustrophobic. In addition, a small area can be evaluated at a time and comparison with other side is difficult.

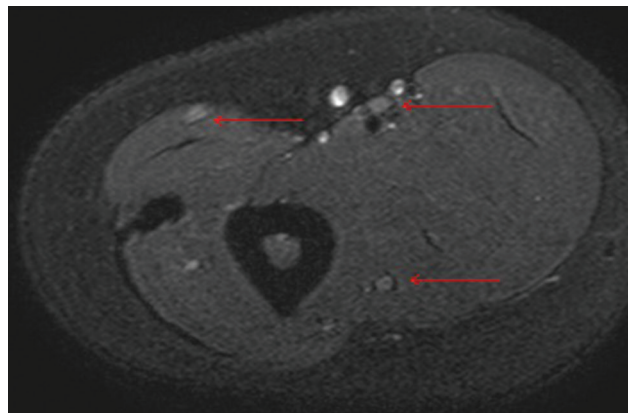


Fig. 3 T2w SE axial image depicting appearance of normal nerve (arrows).

Newer MR Sequences

Diffusion Tensor Imaging

This is a functional MRI imaging giving overview of micro-structure of nerves. Isotropic diffusion is when the protons show diffusion in all directions equally, whereas anisotropic diffusion is when there is preferential diffusion in one direction.

The application of motion probing gradients (MPGS) using diffusion-weighted MRI results in signal suppression from structures with relatively unimpeded diffusion such as blood vessels and cerebrospinal fluid and little suppression in structures with relatively impeded diffusion and, thus, will appear as relatively bright as the diffusion sensitizing gradient increases. As the peripheral nerves show relatively impeded diffusion orthogonal to the long axis of nerve fibers, hence they exhibit high signal intensity at DW-MRI.⁷ The difference in the water diffusivity being higher in the long axis of the nerves compared with the orthogonal short axes is known as anisotropy and is quantified by calculating the fractional anisotropy (FA). This ranges from 0 to 1, where 0 represents fully isotropic water diffusion (i.e., no difference in water diffusion in any of the neural axes) and 1 represents fully anisotropic water diffusion. This property of anisotropic diffusion is shown by peripheral nerves and forms the basis of diffusion tensor imaging (DTI). It gives quantitative assessment of the magnitude and direction of diffusion. Peripheral nerves show high FA values ranging from 0.599 to 0.80.^{8,9} Whenever there is injury to the nerve, this FA value starts decreasing.

It acts as a complementary tool in addition to basic MR neurography in detection of abnormal nerves. DTI also has a potential role in evaluating regeneration in the nerve. Post treatment/surgery if fractional anisotropy shows rise in value, it signifies the nerve is regenerating, thereby acting as a functional MRI technique.

Besides the FA value, we can also measure ADC (apparent diffusion coefficient) values. Normal nerves show ADC value in the range of $0.96 \pm 0.13 \times 10^{-3}$ mm²/s.¹⁰ Abnormal nerves would show reduction in ADC values.

Many studies have shown the utility of DTI in detecting median nerve neuropathy in carpal tunnel syndrome.¹¹⁻¹⁴ Also DTI has a role in early detection of neuropathy or in sub-clinical cases when the changes in basic MR sequences may be very subtle or not appreciable.¹⁵

With the help of DTI, the nerve fibers can be tracked and viewed in 3D, the technique is called MR tractography. It color codes the nerve fibers and gives excellent overview of the fibers. Reduced number of fibers is seen at the site of pathology.

Diffusion-Weighted Imaging with Background Suppression

Diffusion-weighted imaging with background suppression (DWIBS) is a newer sequence which is a quick sequence for imaging of whole body peripheral nerves at once. It gives PET-like images when we invert the gray scale. This is a 3D sequence and gives excellent overview of nerve pathology. There is suppression of muscles, blood, fat, and normal organs

in this sequence and hence structures showing high diffusion restriction can be easily appreciated. It gives thin sections and the imaging can be performed with free breathing.

Various Peripheral Nerve Pathologies

Trauma

Seddon classified nerve injuries into neuropraxia, axontomesis, and neurotmesis. Neuropraxia is when there is injury to the nerve with no discontinuation of the nerve. On imaging, there is altered signal intensity on MRI or echotexture on USG with or without change in the caliber of the nerve. However, the nerve can be completely traced proximal and distal to the site of injury. Axontomesis is moderately severe grade of injury when there is disruption of myelin sheath and the axons. On imaging, there can be focal partial disruption of the nerve with formation of side neuroma. Neurotmesis is the most severe grade of injury when there is complete transaction of the nerve. On imaging, there is a definite gap seen between the two nerve ends at the site of injury where there are no nerve fascicles. The prognosis would obviously vary with the grade of injury with near complete recovery of neuropraxia to least recovery in neurotmesis.

In traumatic peripheral neuropathy, electrophysiological studies would only determine the involved nerve and the approximate site. Imaging plays an important role in such cases by determining exact site of injury, grade of injury, distance between the two ends, neuroma formation, architectural distortion, other associated findings, and secondary denervation (► **Figs. 4** and **5**). Hence, imaging is almost always advocated presurgically in patients with traumatic neuropathy as it plays a decisive role in surgical management.

Tumors

The major tumors of peripheral nerves include benign tumors like schwannoma and neurofibroma, and malignant lesions like malignant peripheral nerve sheath tumors. Imaging is the modality of choice for the diagnosis of nerve tumors. There is presence of a well-circumscribed mass in relation to the nerve which can be eccentrically placed as in schwannoma or centrally placed as in neurofibroma. In addition, schwannomas are more heterogeneous with cystic changes whereas neurofibroma is relative homogenous tumors. These tumors are hypointense centrally due to their fibrous nature and hyperintense peripherally due to myxomatous component, giving what is called as the target sign. Split fat sign is also seen which presents as a peripheral rim of fat.

Malignant counterpart is the malignant peripheral nerve sheath tumors. Clinically when there is sudden increase in size or in pain, malignant transformation is suspected. It is difficult to differentiate these from benign tumor on imaging, except these are not so well defined.

Imaging can also differentiate primary versus secondary tumors. The nerve can be secondarily involved in tumors originating from surrounding structures.

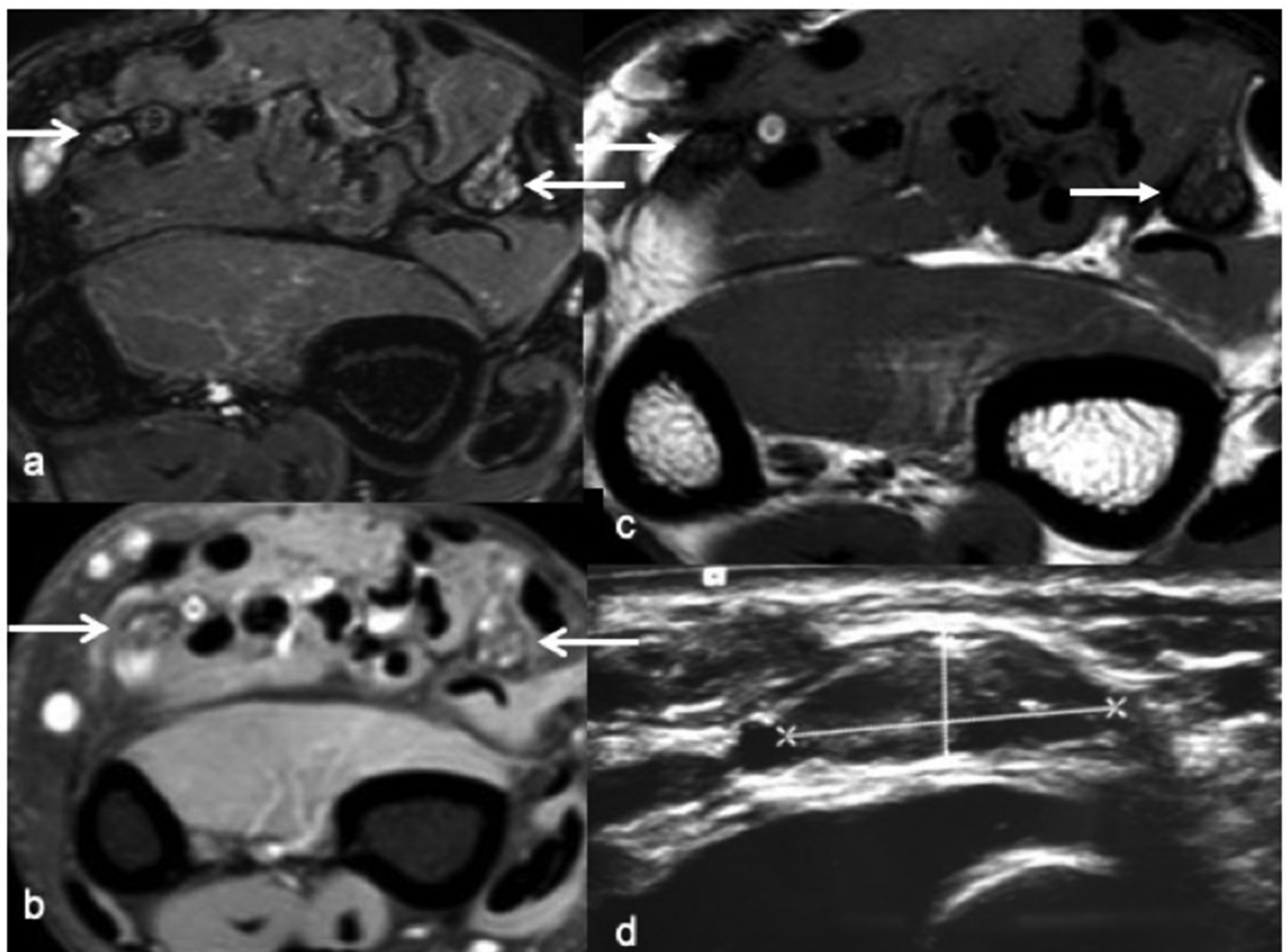


Fig. 4 Post-traumatic radial neuroma in continuity: A 32-year-old man presented with sensory loss in radial nerve distribution for 5 months following a road traffic accident. There was no fracture of any bone following the accident. (a–c) GRE 3D PD VISTA axial MR images showing (a) radial nerve having normal caliber and signal intensity (arrow) in the mid arm, (b) radial nerve neuroma (arrow) with altered signal intensity noted in mid-distal $\frac{2}{3}$ arm junction, no discontinuity in the nerve seen, (c) radial nerve regains its normal caliber distally though the signal alteration persists, and (d) STIR coronal (thin) image shows neuroma in continuity of the radial nerve in mid-distal arm (arrow).

Infections

Superficially located nerves are very commonly infected by *Mycobacterium leprae*, one of the common causes of peripheral neuropathy in India. Most commonly it infects the ulnar nerve in cubital tunnel. In infections, there is alteration in caliber and signal intensity of the involved nerve with or without formation of nerve abscesses on imaging. There can be associated nodes. Multiple nerve involvement is commonly seen.

Entrapment

Due to the course of peripheral nerves through certain anatomical constrains, they have a tendency to be compressed at those sites resulting in entrapment neuropathies. This is a common cause of pain and neural impairment which often goes unrecognized. Entrapment can also be caused by focal lesion in vicinity of nerve causing its compression, like soft tissue tumor/ganglion, cyst, and so forth.

On imaging especially on MRI, the diagnosis can be easily made with determination of exact site and cause of entrapment. The nerve is usually compressed and is small in caliber at the site of compression and thickened proximally and distally.

Most common entrapment neuropathies include carpal tunnel syndrome of median nerve at wrist joint, cubital tunnel syndrome of ulnar nerve at elbow, supinator syndrome of posterior interosseous nerve at proximal forearm, common peroneal nerve at fibular head, and posterior tibial nerve at foot.

Inflammation

Inflammation would usually involve long segment of nerve without any discontinuity or focal neuroma formation. Multiple nerves are seen to be thickened having altered signal intensity.

Changing Trends

In the past, electrophysiological studies were considered the gold standard for diagnosing peripheral neuropathy. However, these were long investigations, with indeterminate results at that time, uncomfortable for patients, and sometimes not feasible in deep-seated nerves^{16,17} or in case of dermatological disorders. In addition, the exact site of pathology and perineural changes could not be diagnosed with these.

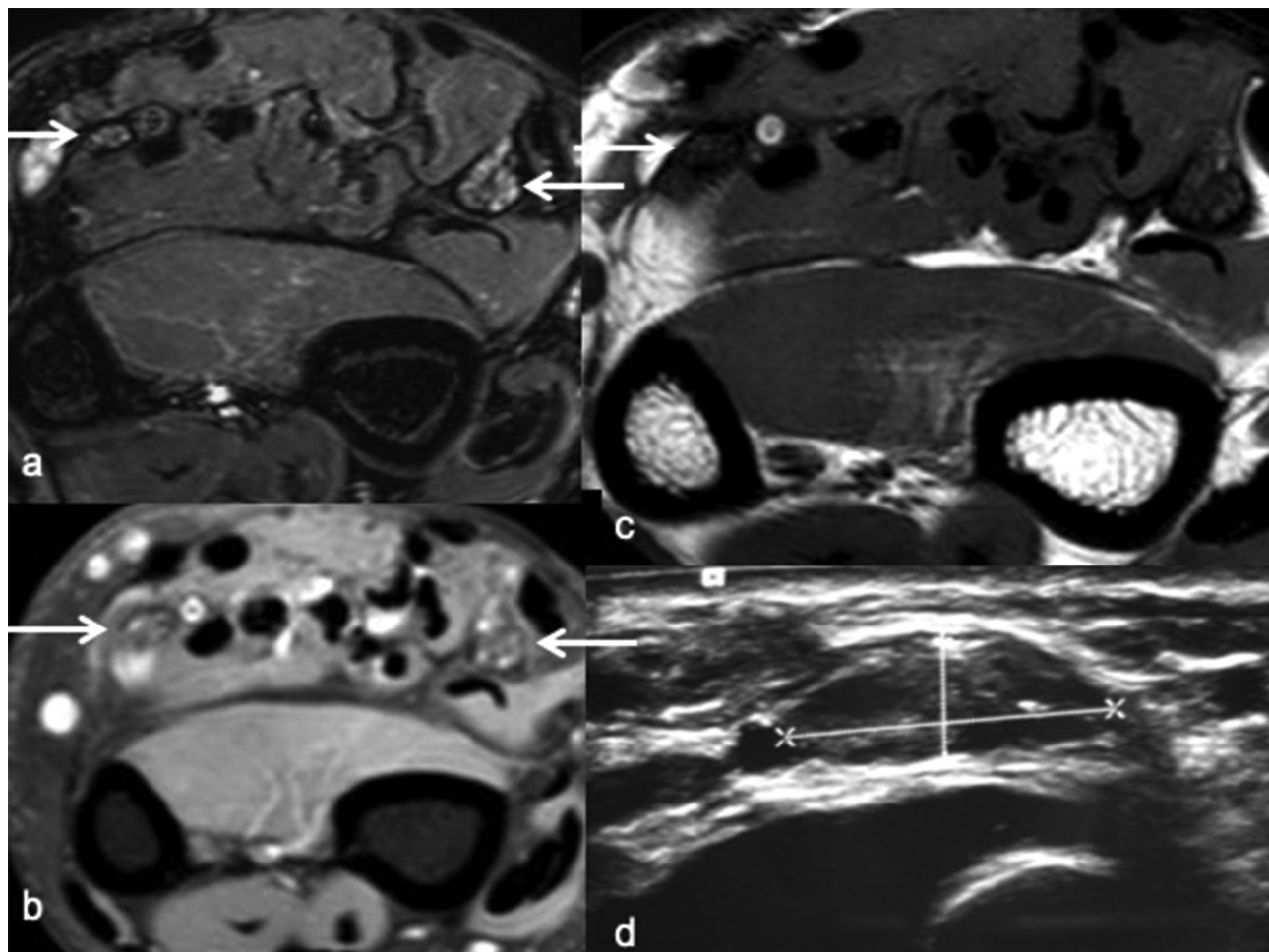


Fig. 5 Post-traumatic median and ulnar nerve neuroma in continuity; a 24-year-old man presented with complete claw hand with sensory loss following a road traffic accident 3 months back. (a) SE T2W axial fat suppressed MR image, (b) axial PD VISTA MR image, and (c) SE T1 W axial MR image showing globular median and ulnar nerve swellings with T2 hyperintensity in distal forearm (arrows). (d) Transverse sonogram showing hypoechoic ulnar nerve neuroma.

Somewhere in 1980s, imaging methods were being evaluated for visualization of nerves. Since then, due to advancements in hardware and software, MRI and USG have proven to be very useful in evaluation of peripheral neuropathies.

With the current standard of imaging, 3D anatomy and pathology of nerves can be excellently depicted.¹⁸ T1W SE axial, T2W FS SE axial, and 3D STIR form the mainstay of diagnosis as they give important information regarding the nerve morphology, focal disruption, alteration in caliber, signal intensity, fascicular pattern and surrounding architectural distortion, and secondary denervation. Multiplanar reformats can be constructed with 3D sequence which can assist in surgical planning. Advanced imaging with diffusion like DTI and DWIBS act as complementary tools to diagnosis by acting as functional imaging.

Contrast in peripheral neuropathies is utilized in limited conditions. Infection, inflammation, and tumors are the pathologies where the abnormal nerve would show enhancement after gadolinium administration.¹⁹ Also denervated muscles would also show post contrast enhancement.²⁰

In the coming years, the technique of MRI is set to give better results with introduction of 7 Tesla MRI. Newer nerve-specific contrast agents, like gadoflouride M, have been experimented in animals and have shown role in assessing demyelination and remyelination.²¹ Diffusion-based sequences have shown potential, acting as functional tools of imaging however more studies are required to further validate their usage.

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