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The Utility of Multimodality Perioperative Imaging in Peripheral Nerve Interventions

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ABSTRACT

Recent advances in peripheral nerve imaging provide a more complete understanding of the extent of nerve injury and pathology. High-resolution ultrasound and, more recently, MR neurography, are being increasingly used in preoperative planning for treatment of both trauma and peripheral nerve tumors. The addition of more advanced imaging, such as diffusion tensor imaging and tractography has further improved preoperative planning. We review the current techniques in imaging assessment of peripheral nerve pathology, including their relative strengths and drawbacks, and describe the utility of a multimodality approach to perioperative peripheral nerve imaging. This allows the surgeon to more confidently make a decision on whether a surgical treatment is indicated and plan for a more effective and efficient surgical approach.

Keywords: Peripheral nerve, Neurography, Ultrasound, Diffusion tensor, Tractography

INTRODUCTION

Recent advances in imaging have provided increasingly detailed characterization of peripheral nerve pathology. Magnetic resonance neurography (MRN), diffusion tensor imaging (DTI) and high-resolution ultrasound provide a more complete understanding of the nerve pathology or injury, and thus, enable more efficient pre-operative planning [1]. This in turn, has improved outcomes in treatment and repair of nerve pathology and injuries [2]. In the past, detailed preoperative assessment of nerve integrity was limited. Although the use of MRN and nerve conduction studies have allowed for some understanding of the extent of nerve injury or tumor involvement, it has been difficult to determine whether surgical repair or conservative management would be more appropriate. Furthermore, without detailed understanding of the extent or, at least, location of nerve pathology, operative planning has been difficult. This has resulted in long and more technically challenging procedures with risks of complications [1].

Advanced imaging can help characterize nerve integrity in a variety of peripheral neuropathies, most notably with tumors and traumatic injuries. With these conditions, a multimodality approach may better characterize the extent of nerve involvement, the relationship of nerve fibers with the tumor or site of injury, the integrity of particular nerve fibers and whether surrounding structures, such as vessels, are involved. With this understanding, the surgeon can determine the most appropriate approach for repair or resection in order to avoid injury to intact nerve fibers during surgery. Furthermore, ultrasound can be used both preoperatively and intraoperatively to localize the nerve and more accurately guide the operative approach.

In this review, we describe the utility of advanced multimodality imaging to characterize nerve pathology both preoperatively and intraoperatively.

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Ultrasound

With excellent tissue contrast, MRI is often seen as superior to ultrasound in peripheral nerve imaging. In fact, ultrasound has many benefits over MRI and should rather be thought of as a complementary imaging modality. Ultrasound is a real-time, dynamic modality that allows for active interaction between the examiner and patient. Sonographic imaging can be quickly and easily tailored to the location and situation of the patient's symptoms. Sonographic evaluation of a patient while performing provocative maneuvers that reproduce symptoms may demonstrate nerve abnormalities that cannot be detected during static imaging, such as MRI. Under optimal conditions, ultrasound has the added benefit of higher spatial resolution than currently available MRI scanners, which aids assessment of smaller caliber, distal peripheral nerves. Finally, ultrasound is well-tolerated by patients, and can be performed comfortably on patients for whom MRI may be contraindicated or suboptimal, including those with pacemakers or cochlear implants. Ultrasound can be performed quickly and comfortably, obviating the need for sedation which is otherwise commonly required for MR imaging of pediatric and claustrophobic patients.

High resolution ultrasound is typically performed with a high frequency linear transducer (12-18 MHz) to maximize visualization of fascicular structure. However, various factors, such as deep location of the nerve or a larger patient body habitus, may require the use of lower frequency transducers. Transverse images of the nerve better delineate its fascicular structure, whereas images along the longitudinal plane of the nerve may be useful to determine extent of injury, the degree of caliber change that is often seen with nerve pathology, and show the relative position of the area of nerve pathology to anatomic landmarks. Expertise in nerve sonography is essential as suboptimal technique can mimic nerve pathology. This is particularly the case with anisotropy, in which incorrect angle of the transducer results in a more hypoechoic appearance of the nerve and loss of its fibrillar pattern [3]. To verify nerve pathology, imaging must be performed by keeping the transducer angle as close to the perpendicular axis of the target nerve as possible, which allows optimal detection and characterization of peripheral nerve internal architecture.

Ultrasound is readily able to distinguish the perineural fat, which appears hyperechoic, from the hypoechoic fascicles (**Figure 1).** In short axis, the nerve fibers are round, generally similar in cross-sectional area and separated by the more echogenic perineurium. In long axis, the hypoechoic nerve fibers are oriented in parallel along the long axis of the nerve, again separated by the more echogenic perineural connective tissue. When injured, there is disruption of the normal fascicular architecture of the nerve and, with increasing degree of injury, enlargement of the nerve and discontinuity of the fibers [4] (**Figure 2).** In cases of compressive neuropathy, the nerve develops an "hour-glass morphology" when seen in long axis, with the nerve swelling proximal to the point of compression, narrowing at the point of compression, and normal or slightly thickened nerve caliber distally.

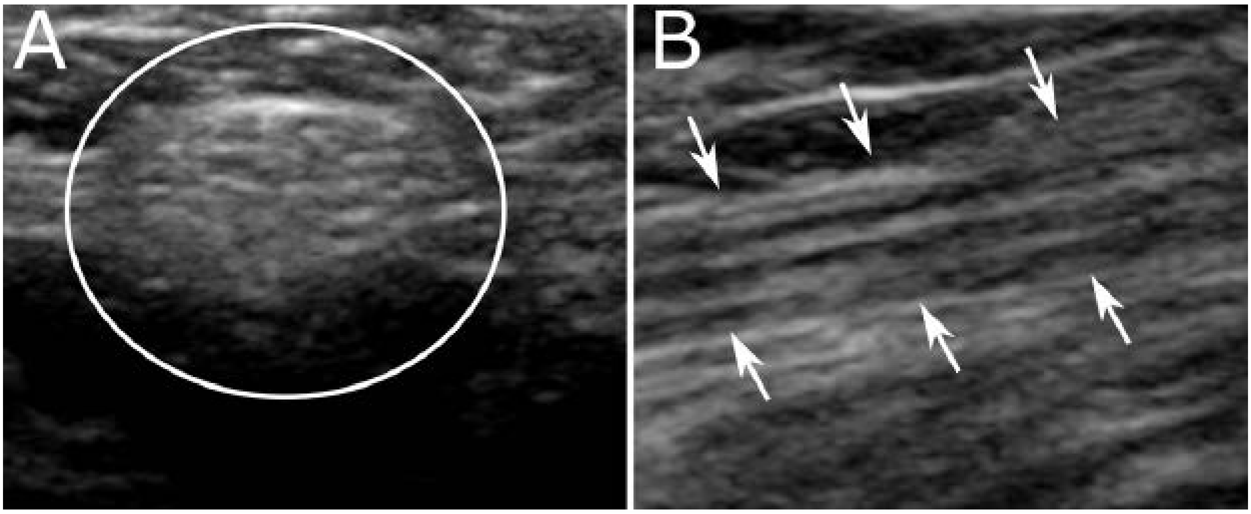

Figure 1. Normal ultrasound appearance of the sciatic nerve. Transverse image (A) demonstrates small rounded hypoechoic fascicles surrounded by hyperechoic perineural fat. Longitudinal image (B) demonstrates a "tram-track" appearance of the nerve, with alternating hypoechoic fascicles and hyperechoic perineural fat.

Ultrasound has proven to be an especially promising technique for preoperative and intraoperative planning and localization of peripheral nerve pathology [5].Without the aid of imaging, accessing the peripheral nerve at the site of pathology requires a long procedure with a wide dissection. While traditional preoperative ultrasound can improve procedure times, differences in patient positioning between the preoperative imaging study and surgery, can result in dramatic changes in location of the nerve with respect to the dominant anatomic landmarks. Anecdotally, the nerve is often deeper at surgery than the preoperative ultrasound may suggest. Therefore, ultrasound can be used intraoperatively to better localize the region of concern, identify potentially intact nerve fibers, and localize tumors [6] thereby helping the peripheral nerve surgeon to determine the best surgical approach.

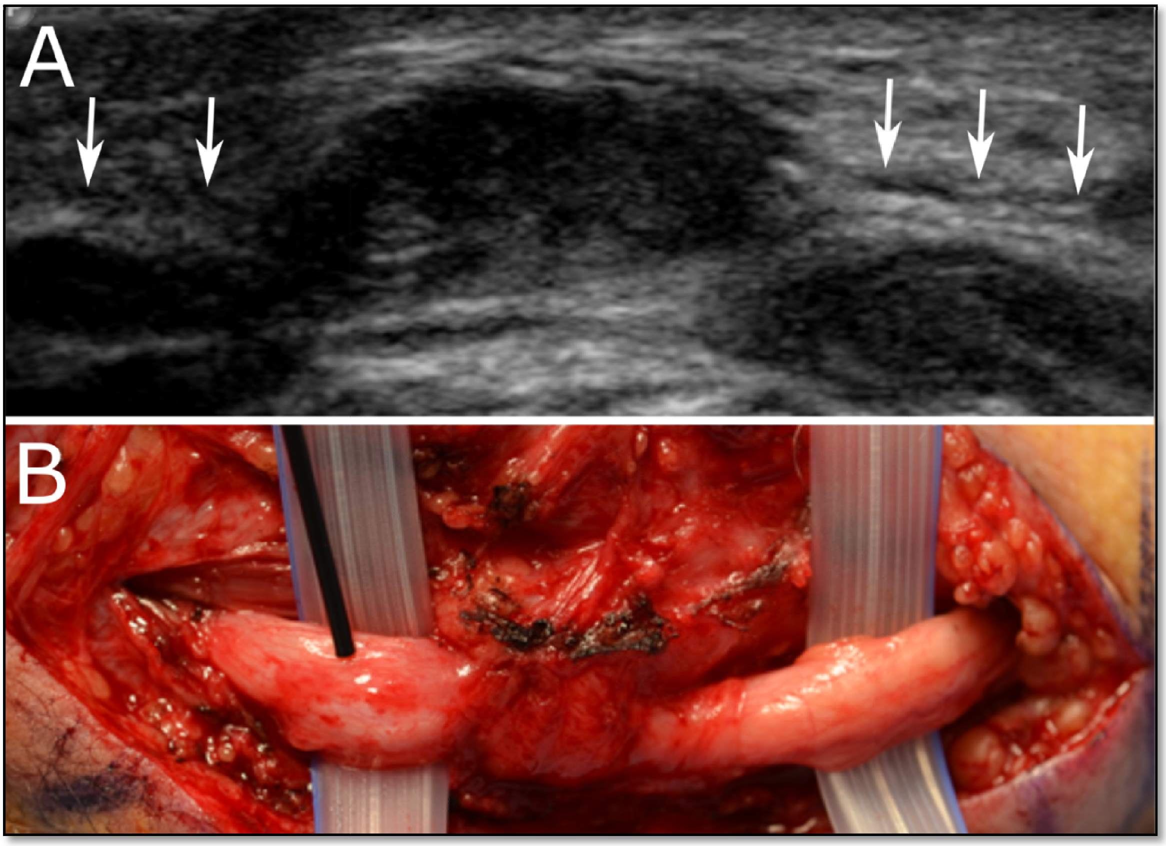

Figure 2. Laceration of the ulnar nerve. Longitudinal ultrasound at the site of a laceration (A) demonstrates a large hypoechoic focus along the course of the ulnar nerve with complete loss of fibrillar structure. Arrows delineate the normal segments of the ulnar nerve. Intraoperative image (B) demonstrates discontinuity of the nerve corresponding to the hypoechoic focus.

Recently, a technique using ultrasound-guided percutaneous injection of dilute methylene blue has emerged, providing surgeons with a better ability to both mark the site of peripheral nerve pathology and direct surgical exploration in a more efficient manner without the use of intraoperative imaging [7]. By injecting methylene blue near the nerve of interest and as one is slowly withdrawing the needle, one is able to create a surgical corridor that better directs the surgical trajectory down to the nerve of interest. This allows for more efficient identification of the diseased portion of the nerve (**Figure 3)** and can potentially reduce operative times. Additionally, it can provide a more accurate measure of the depth of the nerve from the skin surface, which can also aid in more rapid surgical exposure. Combined with the use of electrical stimulation, it has been hypothesized that this new technique will demonstrate clinical benefits, especially in regions of variable anatomy [5]. While outcomes and complication rates associated with this technique have yet to be extensively studied, a number of cases reported by Osorio and colleagues with procedures ranging from repair of impingement syndromes to tumor resection and nerve explorations have shown promising results. Furthermore, there were no reported associated complications, such as permanent skin discoloration, nerve injury or hematoma [7]. While promising, further prospective studies will be necessary to identify whether this new perioperative imaging technique will decrease operative complications and improve surgical outcomes.

The limitations of ultrasound include the fact that it is highly operator dependent. Expertise in peripheral nerve sonography is required to identify the nerve of interest and recognize nerve pathology. Factors such as the patient's body habitus and abnormalities in the tissue surrounding the area of concern, including post-traumatic or postsurgical architectural distortion or scarring, can limit the sonographic visualization of the nerve. Finally, ultrasound has limited tissue contrast compared to MRI, which may reduce the ability of the imager to clearly identify smaller caliber or deeper peripheral nerves. Additionally, evaluation of masses or downstream effects of nerve pathology, such as muscle edema or atrophy can be more difficult to identify with ultrasound.

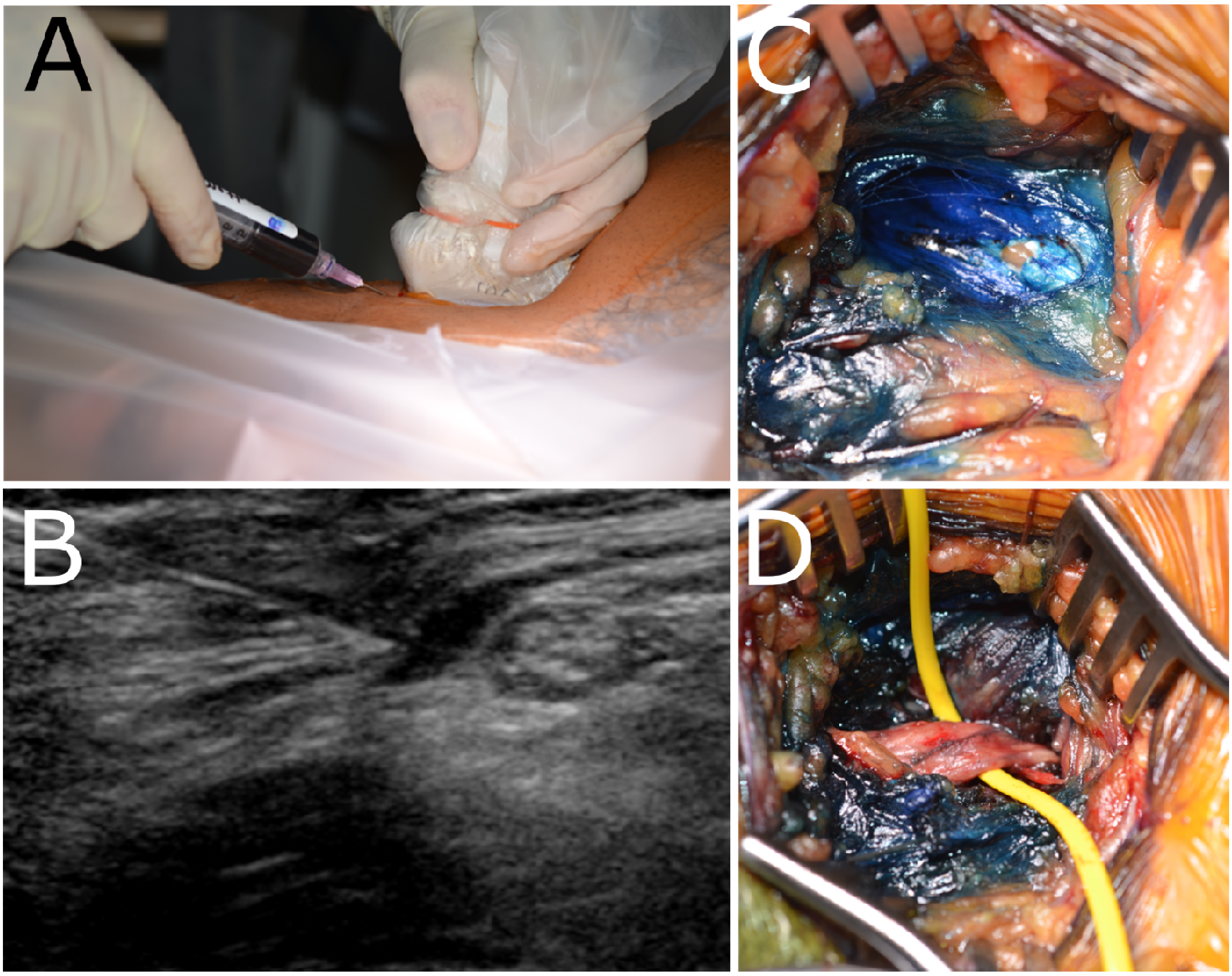

Figure 3. Ultrasound-guided methylene blue injection for peripheral nerve localization. Using ultrasound guidance, methylene blue was injected immediately proximal to the site of an enlarged lateral femoral cutaneous nerve (A and B). This allowed for rapid dissection to immediately proximal to the affected nerve (C), followed by careful dissection to access the nerve (D).

Magnetic Resonance Neurography

MRN is useful to determine the extent, degree and location of nerve injury. Typical MRN utilizes both T1-weighted nonfat-suppressed and fluid-sensitive imaging. On T1-weighted images bright signal of the perineural fat serves as a natural contrast to the darker nerve fascicles. This enables excellent assessment of fascicular structure and nerve caliber (**Figure 4a**). Normally there is visible circumferential perineural fat that can be effaced when the nerve is extrinsically compressed. In cases of tumor involvement, loss of the perineural fat can indicate impingement, encasement, and even invasion. T1-weighted imaging is also useful in assessment of muscular fatty atrophy as a consequence of nerve pathology, and the pattern of involved muscles can often indicate neuropathy due to a specific peripheral nerve. Fluid-sensitive sequences include T2-weighted or short-tau inversion recovery (STIR) sequences and are commonly performed with fat suppression to diminish normal hyperintense fat signal. This increases the contrast between the nerve and surrounding tissues and facilitates better assessment of signal alterations within individual fascicles, which can indicate neuropathy.

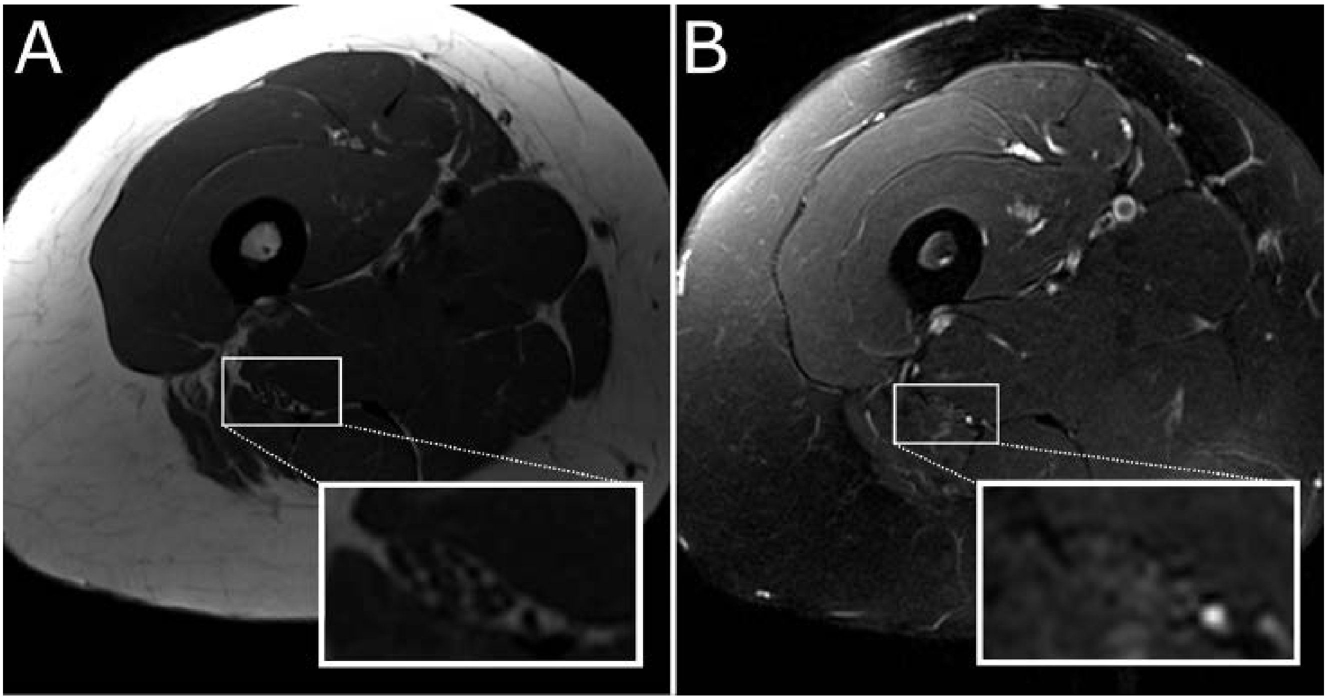

Figure 4. Normal MRI appearance of the sciatic nerve. On the T1-weighted image (A), the sciatic nerve is well visualized as a collection of individual hypointense fascicles surrounded by hyperintense perineural fat. On the T2 fat saturated image (B), the nerve is isointense to minimally hyperintense to the adjacent muscle. The bright focus medial to the nerve is a small adjacent vessel.

The fascicles in a normal peripheral nerve are generally round and have a similar cross-sectional area. On fluid-sensitive sequences, the fascicles are either similar to or slightly brighter than skeletal muscle (**Figure 4b).** Nerve pathology often initially presents as fascicular edema, indicated by T2 hyperintensity when compared to other, uninvolved segments of the nerve or other regional peripheral nerves. Occasionally, fascicular swelling can lead to effacement of the perineurium and enlargement of the nerve. In some neuropathies, individual fascicles may be abnormal, leading to varying sizes and signal intensities of these fascicles. In cases of early myopathy from nerve injury, the affected muscle also appears hyperintense on T2-weighted imaging (**Figure 6).** The utility of intravenous gadolinium-based contrast agents is not clear, as most peripheral nerve pathologies demonstrate T2 hyperintensity as well as enhancement. Of course, contrast is necessary for detection and characterization of any associated tumor. In addition, contrast can be helpful to diagnose cases of active neuritis [8]. Furthermore, when imaging smaller peripheral nerves that course adjacent to similarly-sized blood vessels, intravenous contrast can help distinguish the nerve from the blood vessels.

Unless clinically contraindicated or not available, MRI at 3 Tesla is essential for optimal assessment of nerves in MRN. The small size of the nerves requires the higher signal-to-noise ratio (SNR) that 3 Tesla provides. Higher SNR serves to increase contrast and spatial resolution, and to decrease scan times, which can become long depending on the area of coverage needed. 3 Tesla imaging also accentuates certain artifacts, notably metal susceptibility artifact, which may limit assessment of nerves when there is an adjacent implant or metallic foreign bodies. In such cases, the choice of field strength must be determined on a case-by-case basis. The choice of coil type is another decision that must be made prospectively and varies with the specific nerve and suspected extent of nerve injury [9]. The selected coil should be optimal for the particular area of coverage and is a major determinant of SNR. Ultimately it should be tailored to the individual clinical question.

The Seddon and Sunderland classifications of nerve injury have been correlated with changes in size, signal and architecture of the nerve on MRI [10]. Neuropraxia, or conduction block within the nerve without structural injury, typically is occult on imaging. Axonotmesis, which ranges from axonal injury to perineural disruption, can range from T2 hyperintensity with intact fascicular architecture in low grade injuries, to nerve enlargement and fascicular disruption in higher grade injury **(Figure 5).** Neurotmesis, describes nerve disruption, which appears as discontinuity of the nerve on imaging (**Figure 6).** Furthermore, injury involving specific groups of fascicles can be identified, particularly within larger nerves, such as with the sciatic nerve (**Figure 7).** When only nerve signal is altered, without underlying structural abnormalities, the potential for recovery without operative repair is high. As fascicular structure is lost, the potential for spontaneous recovery without operative repair declines [11]. Furthermore, as the nerve heals, normalization of MR characteristics of the nerve correlates with recovery of nerve function as determined by clinical examination and electromyography. Although traditional MRN has been limited to more proximal, larger caliber nerves, recent use of high-resolution 3D techniques improves visualization of the fascicular structure within nerves, allowing for more distal nerves to be imaged and permits reconstructions in multiple planes [12], including along the plane of the nerve (curved multiplanar reformatting; **Figure 6).**

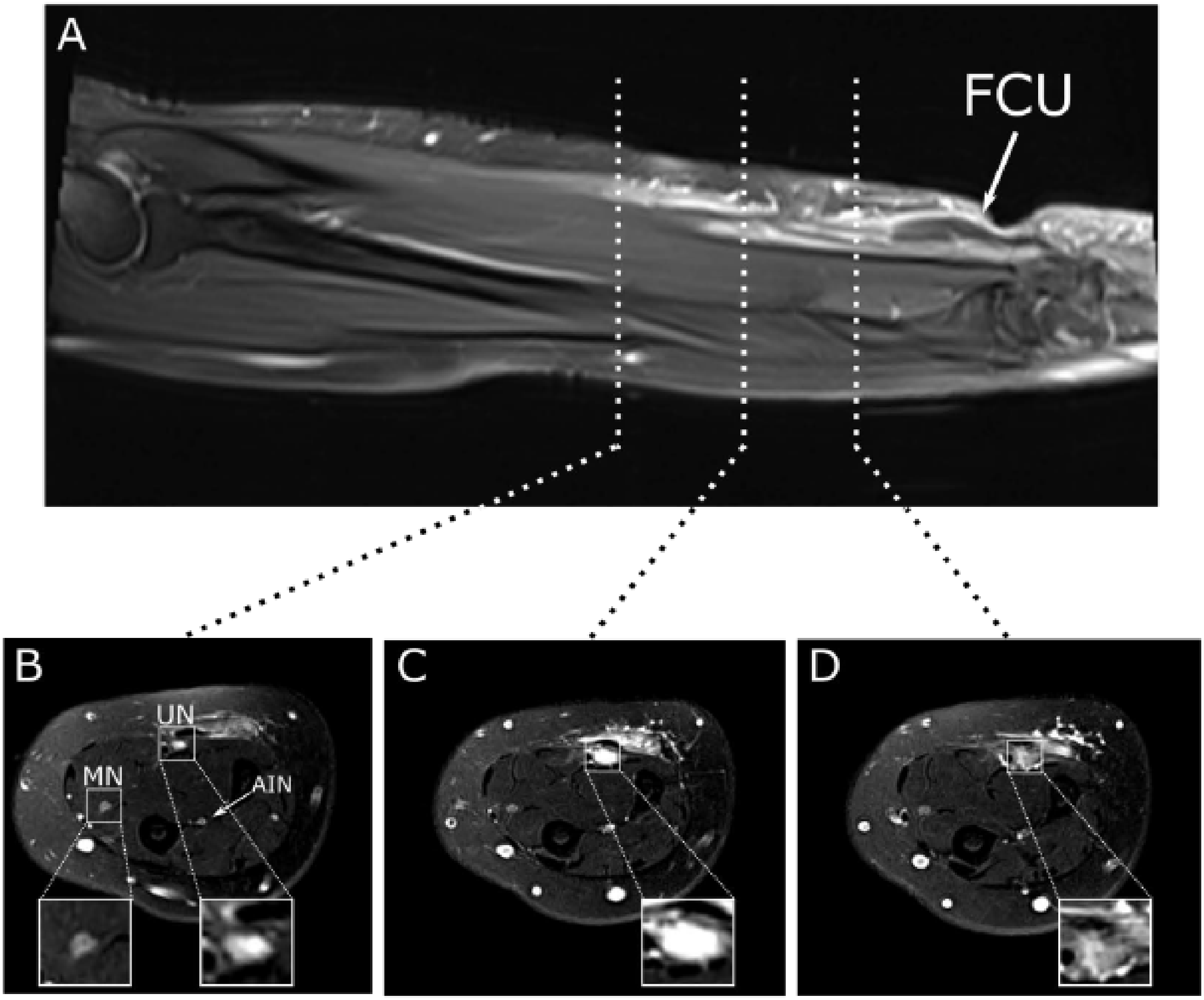

Figure 5. Ulnar nerve laceration. Sagittal T2 fat saturated image (A) demonstrates extensive edema in the subcutaneous tissues and muscles subjacent to the site of laceration, along the course of the ulnar nerve. A torn, retracted flexor carpi ulnaris tendon (FCU) can also be seen. Proximal to the site of laceration (B), the ulnar nerve (UN) maintains its size, but is diffusely T2 hyperintense with the fascicles difficult to visualize. The normal median (MN) and anterior interosseus (AIN) nerves are shown for comparison. Closer to the site of laceration (C), the ulnar nerve is larger and its fascicular structure completely lost. At the site of the laceration (D), the ulnar nerve is not visualized. Only diffuse edema is seen. Comparison with normal nerves within the same field of view or corresponding contralateral side can be helpful in distinguishing nerve pathology.

Figure 6. Brachial plexus avulsion. Coronal 3D T2 SPACE curved multiplanar reformat along the course of the right brachial plexus (A) demonstrates discontinuity of the right C5 nerve root and at least partial tear of the C4 and C6 nerve roots as indicated by the prominent T2 hyperintensity (arrows). The more distal right brachial plexus demonstrates a lesser degree of T2 hyperintensity, corresponding to stretch injury. Axial 3D T2 SPACE image (B) demonstrates the avulsed right C5 nerve root. Sagittal T2 fat saturated image (C) demonstrates resultant muscle edema from denervation injury of the right rotator cuff muscles.

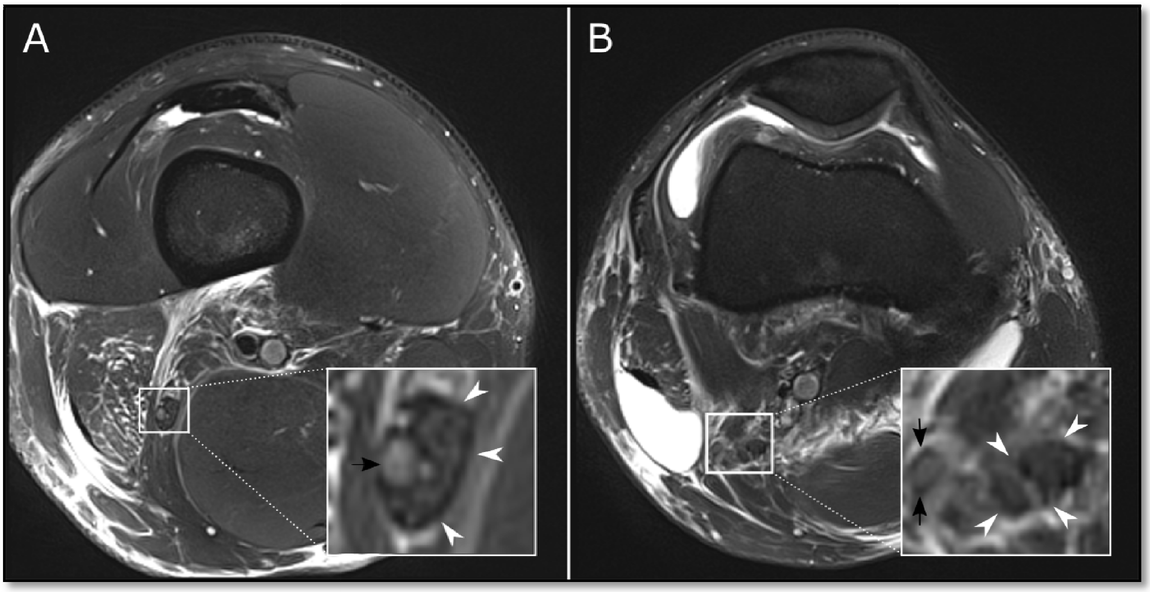

Figure 7. Low grade common peroneal nerve injury. At the level of the distal femur, axial T2 fat saturated image (A) demonstrates hyperintense signal (black arrow) in only a small group of fascicles within the sciatic nerve. The fascicular structure remains intact. At the level of the knee (B), the common peroneal (black arrow) and tibial (white arrowheads) components of the sciatic nerve have split and the edematous components of the sciatic nerve correspond to the common peroneal component, whereas the larger, tibial component is normal in signal. This is due to a posterolateral corner injury resulting in low grade injury of the adjacent common peroneal nerve.

In addition to detailed assessment of nerve pathology, MRI is essential in evaluating the surrounding structures. Rather than direct injury to the nerve, nerve irritation can be reactive to injury of adjacent structures (**Figure 7),** due to constriction by adjacent structures (**Figure 8),** or due to a mass. MRI can characterize these adjacent abnormalities and establish their relationships with the nerve. This helps the surgeon to optimize operative approach and minimize potential damage to the nerve during surgery.

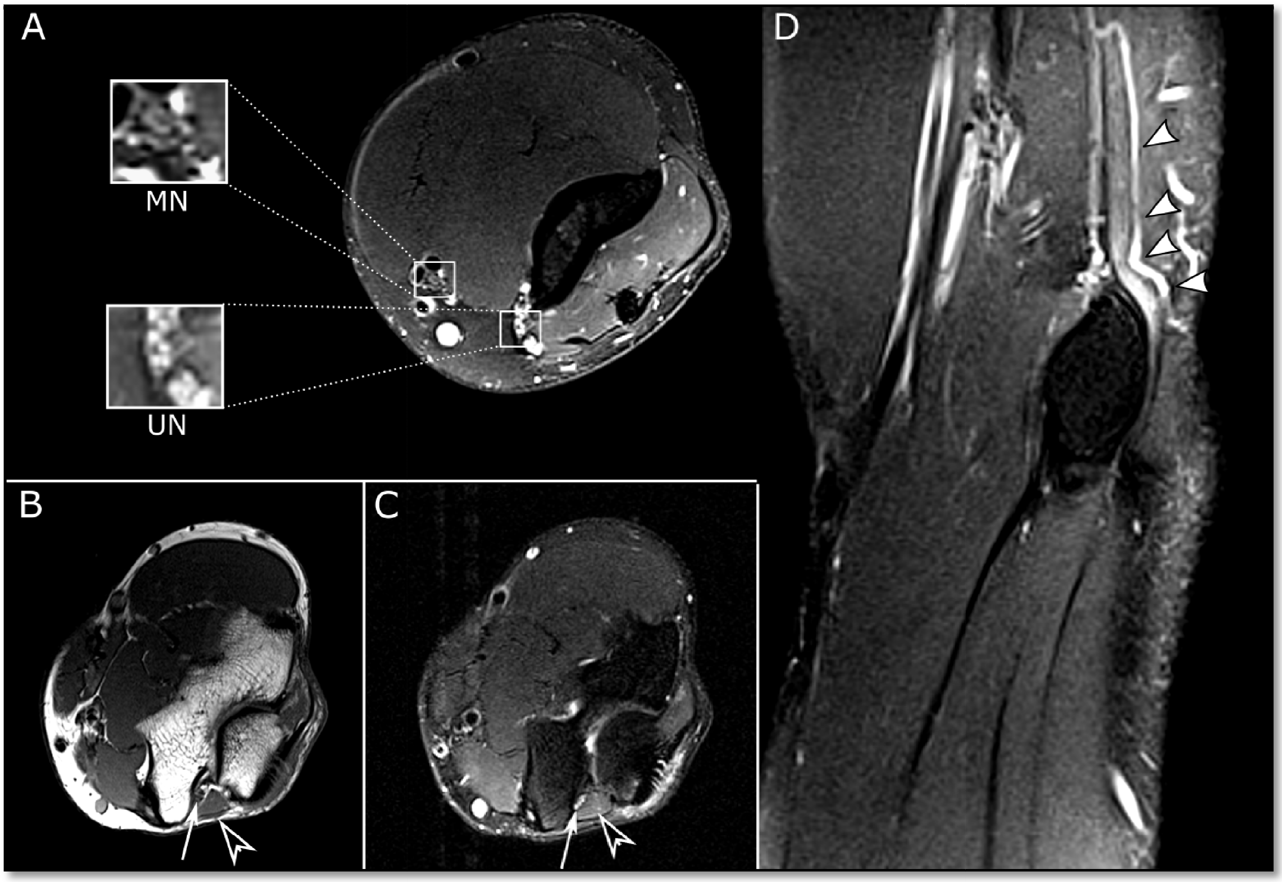

Figure 8. Nerve impingement. Axial T2 fat saturated image (A) displays marked hyperintensity in the ulnar nerve (UN) at the level of the distal humerus. This can be compared to the normal signal median nerve (MN). T1-weighted image at the level of the cubital tunnel (B) demonstrates an accessory anconeus epitrochlearis muscle (open arrowhead) along the medial aspect of the olecranon, adjacent to the ulnar nerve (small arrow). Axial and coronal T2 fat saturated images (C and D) demonstrate focal compression of the ulnar nerve at the level of the accessory muscle.

Limitations of traditional MRN lie in the fact that, despite newer 3D techniques with higher field-strength magnets, assessment of the extent of nerve fiber injury and tumor involvement is limited. In traditional MRN, with high-grade nerve injury, extensive edema within nerve fibers can make it difficult to determine whether there is complete disruption of the nerve or whether some intact fibers remain. Occasionally, tissue architectural distortion or perineural scarring can prevent adequate visualization of the nerve. Electromyography at the time of MRN can be useful to detect whether some response is still present. A similar problem arises with imaging of nerve sheath tumors, with abnormal signal from the tumor obscuring normal nerve fibers as they pass along or through the tumor. More advanced imaging techniques, notably, diffusion tensor imaging can be used to address some of these issues.

Diffusion Tensor Imaging

Traditional MRN techniques and ultrasound are anatomic techniques, and primarily evaluate the morphology and anatomic relationships of peripheral nerves. More recently there has been emphasis on functional assessment of the nerves. Electrodiagnostic studies, such as nerve conduction studies and electromyography, have been mainstays in characterizing nerve function. However, these studies can be affected by temperature and metabolic conditions, and may not accurately determine the location of nerve pathology [12,13]. A recent addition to peripheral nerve imaging is the use of DTI and tractography in characterizing anatomy and pathology of peripheral nerves. DTI is routinely used in assessment of the integrity of white matter tracts and their relationships to pathology in the brain. More recently, this technique has been shown to be particularly useful in preoperative planning for peripheral nerve tumor resection in order to balance maximal tumor resection with sparing of the surrounding nerve fibers [14]. With higher field magnets and stronger magnetic gradients, DTI is becoming more effective in distinguishing normal nerve fibers from tumor during operative planning.

DTI uses the principle of limitations in direction of water diffusivity within the constraints of a nerve. Because of the parallel arrangement of nerve fibers, the bulk movement of water molecules is highly limited in the transverse axis of the nerve, but is free to move along its longitudinal axis [15]. This limitation in directionality of water movement, or anisotropy, can be measured with MRI by exposing the water molecules to magnetic gradients in multiple directions. The degree of anisotropy, fractional anisotropy (FA), is high in normal nerves and diminishes with nerve edema [16]. The degree of loss of FA in peripheral nerves has been correlated with the extent of nerve injury and diminished potential for spontaneous recovery of function. Furthermore, improvement of FA after nerve injury has been correlated with improved nerve function seen both clinically and as measured by electromyography [16]. Alterations in FA appear earlier than changes in T2 signal and can detect subclinical neuropathy [17].

The direction of the vector describing water movement at each location in the imaged nerve can be used to generate tracts modeling the nerve fibers, a technique referred to as tractography. Tractography allows for more detailed visualization and assessment of nerve fibers by following direction of FA [18]. This can provide detailed visualization of the site and extent of nerve injury as well as determine whether intact fibers remain (**Figure 9).** In cases of peripheral nerve tumors, tractography further allows for detailed evaluation of the relationship between nerve fibers and tumors (**Figure 10 and 11**). This may allow the surgeon to modify the surgical approach in order to minimize injury to uninvolved nerve fibers.

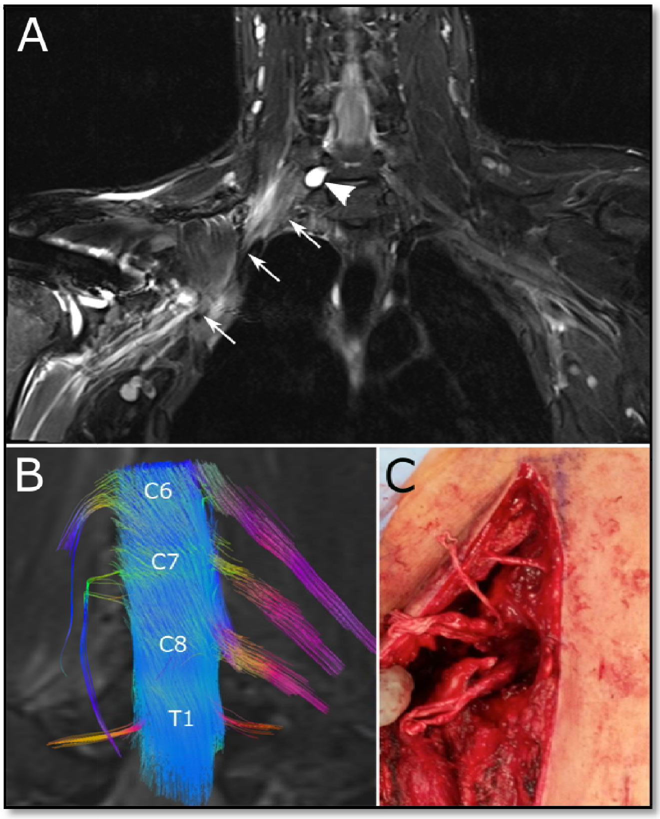

Figure 9. Lacerated brachial plexus nerve root. Coronal STIR image (A) shows diffuse enlargement and hyperintensity of the right brachial plexus (arrows). A pseudomeningocele at C7-T1 on the right (arrowhead) is suggestive of C8 nerve avulsion. However, the integrity of adjacent nerve roots is not well assessed. Tractography (B) demonstrates complete loss of the C8 nerve root fibers, but demonstrates some intact fibers of the right C6 and C7 nerve roots. This can be compared with the normal left sided nerve roots. Surgical photograph (C) confirms the injuries with complete disruption of C8 shown. The remaining intact brachial plexus nerve roots allowed for cadaveric graft repair of the injury.

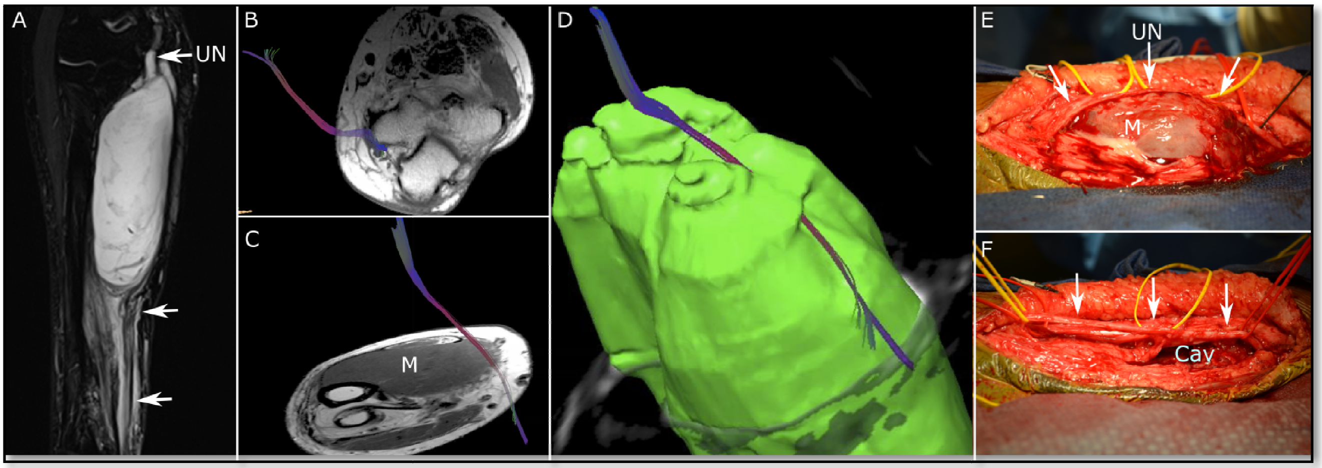

Figure 10. Ulnar nerve myxoid neurofibroma. Sagittal STIR image (A) showing a large T2 hyperintense mass along the course of the ulnar nerve (UN, arrows). Tractography superimposed on T1-weighted images (B and C) demonstrates the ulnar nerve to be predominantly along the superficial aspect of the mass (M), which is better appreciated with 3D reconstruction (D) of the tumor (green) and the ulnar nerve (blue and purple fibers). Surgical photograph (E) confirms that the majority of the ulnar nerve (UN, arrows) is superficial to the mass (M). Following resection (F), the ulnar nerve (arrows) remains intact, shown lifted above the resection cavity (Cav).

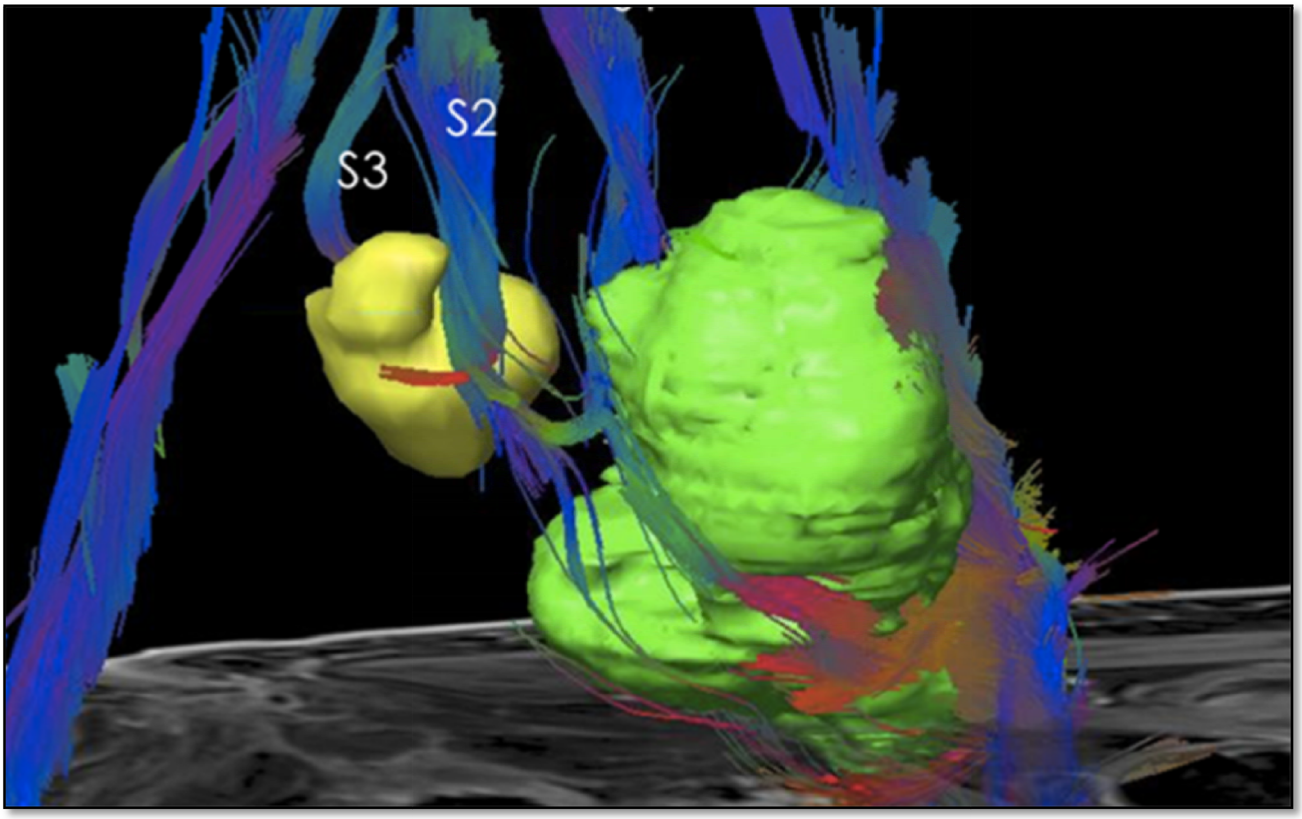

Figure 11. Two lumbosacral plexus peripheral nerve sheath tumors. Tractography of the lumbosacral nerve roots with models of two peripheral nerve sheath tumors demonstrates the complex relationship between the nerve roots and the tumors.

DTI is a technique that relies on high signal to noise ratio and should ideally be performed on 3 Tesla scanners. Furthermore, extensive post processing is required to remove motion and magnetic field inhomogeneity artifacts.

Thus, the technique may not be an option in patients with metallic implants or in cases with excessive patient motion. Tractography can be performed with various techniques and, most notably, requires appropriate selection of FA and angle thresholds. Improper selection of these thresholds can overestimate or underestimate nerve integrity (**Figure 12).** It should be noted the tracts generated represent mathematical constructs detailing the direction of bulk flow of water molecules and do not directly represent individual nerve fibers [15]. As such, the tractograms generated can be helpful adjunctive information to the anatomic imaging of traditional MRN and ultrasound, and should not be used exclusively without proper understanding of the nerve morphology and course.

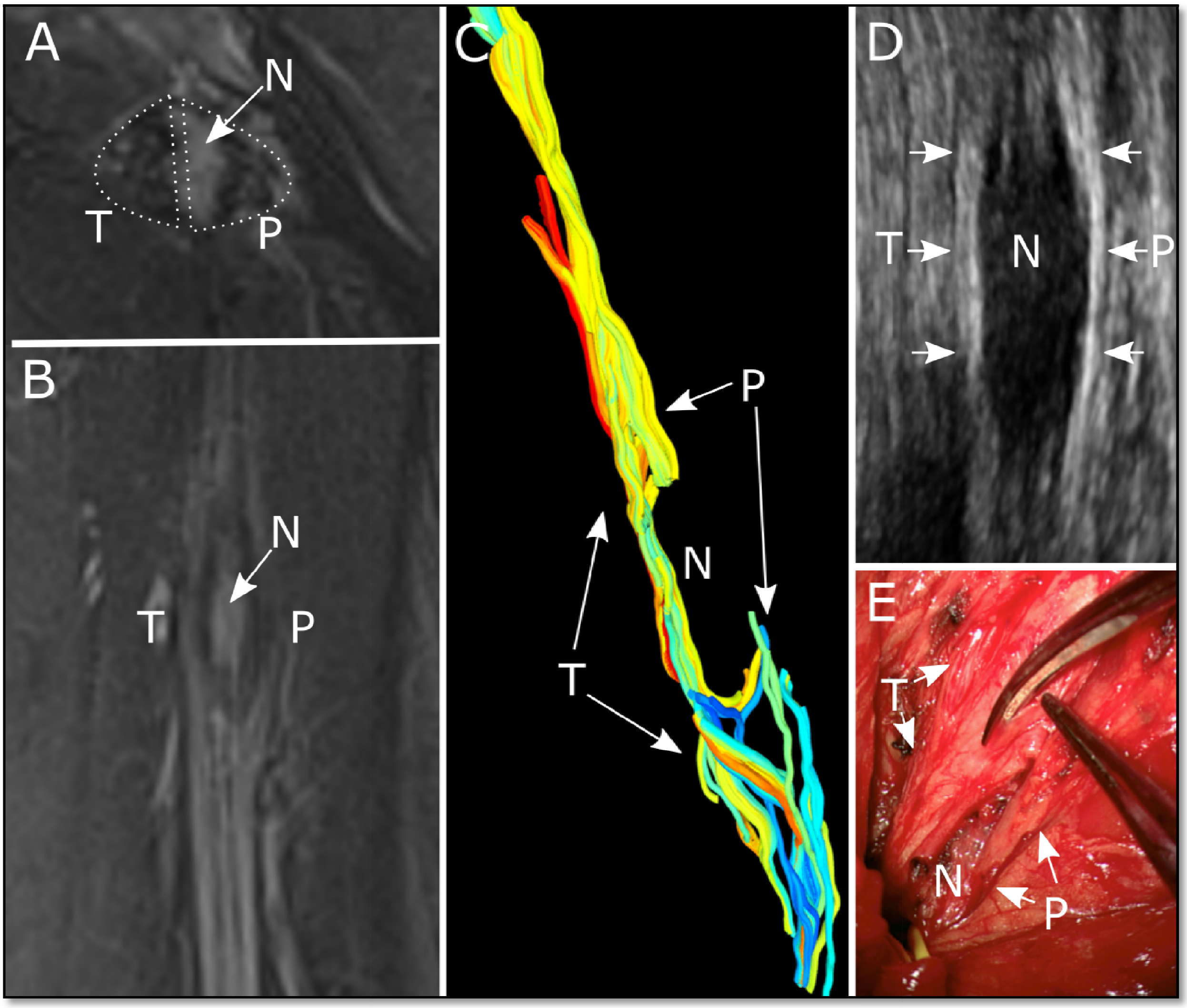

Figure 12. Complementary nature of ultrasound and MRI. Axial and coronal T2 fat saturated images (A and B) of the sciatic nerve after a gun-shot injury to the thigh with a relatively intact appearance of the tibial component (T), but hyperintensity and loss of fascicular structure in the common peroneal component (P). There has been complete loss of the fibers comprising the medial aspect of the common peroneal component with subsequent neuroma formation (N), which appears as confluent T2 hyperintensity. The extent of intact common peroneal fibers is difficult to assess with traditional MRN. DTI tractography (C) suggests a complete discontinuity of the common peroneal fibers at the site of injury. However, high-resolution ultrasound (D) is able to distinguish some remaining intact common peroneal fibers. Surgical exploration confirmed the ultrasound findings (E).

A Complimentary Approach

Each of the peripheral nerve imaging modalities has their particular strengths and drawbacks. The choice of which modality on which to rely should be made on a case by case basis. However, these modalities often serve as complimentary methods that, when used in combination, can be useful to more confidently characterize nerve pathology.

For example, although MRN is excellent for assessing characterization of peripheral nerve tumors, the relationship between individual nerve fibers and the tumor may be difficult to delineate. The addition of ultrasound or DTI can elucidate this relationship. Although DTI and tractography alone are helpful tools to evaluate the integrity of damaged nerves, the subjectivity of choosing FA and angle thresholds with which to define intact nerve fibers may lead to overestimation or underestimation of the extent of nerve injury. Similarly, scar tissue from prior surgery or trauma, calcifications, metallic implants, or even a deep location may prevent adequate visualization of the nerve in question with ultrasound, thus potentially overestimating the degree of injury. The use of advanced imaging techniques for preoperative planning in the setting of peripheral nerve pathology involves a thorough understanding of the strengths and limitations of each imaging modality and should utilize a combination of available imaging tool to ensure a more accurate understanding of the nerve pathology.

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