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Utility and Limitations of Multimodality Imaging for the Evaluation of Neuromas-in-Continuity in the Preoperative and Intraoperative Settings

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KEYWORDS

- Neuroma-in-continuity
- Ultrasound-guided methylene blue injection
- MR neurography
- Diffusion tensor imaging
- Ultrasound

KEY POINTS

- Identification of neuroma-in-continuity is a challenging diagnosis that traditionally has relied on surgical exploration using both anatomic and electrophysiologic criteria.
- Improved preoperative diagnostic imaging and intraoperative localization have the potential to reduce the extent of surgical exploratory dissection and, hence, damage to surrounding tissues as well as surgical times.
- Multimodality imaging helps neurosurgeons with preoperative planning as well as locating the nerve intraoperatively with ultrasound. Additionally, ultrasound-guided methylene blue injection provides neurosurgeons with a direct surgical pathway to the damaged nerve.

INTRODUCTION

Traumatic neuromas develop after injuries when the fibroneural tissue becomes disorganized and a damaged nerve attempts to repair itself [1,2]. If the nerve and its supporting structures are completely transected, a terminal or end-bulb neuroma typically forms [2,3]. If the nerve is damaged but overall continuity of the nerve is maintained, however, a neuroma-in-continuity is produced [1,2]. Neuromas-in-continuity can range in severity; the mildest grade of peripheral nerve injury, neurapraxia, is characterized by a conduction block due to focal demyelination; a more severe grade, axonotmesis, is one in which the axons at and distal to the neuroma degenerate but supporting extracellular matrix structures, called the bands of Büngner, are present, which can allow for axonal regeneration to occur; and the most severe grade, neurotmesis, produces sufficient intraneural fibrosis to block axonal regeneration [4]. The neuropraxic and axonotmetic grades of neuroma-in-continuity are treated with surgical decompression and neurolysis. On the other hand, the neurotmetic grade requires resection

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of the fibrotic segment of nerve and repair either with or without a graft depending on the length of the intervening gap between the proximal and distal stumps of the nerve [4]. Identifying neuromas-in-continuity can be challenging and traditionally has involved surgical exploration with exposure of the damaged segment of the nerve and intraoperative assessment using both anatomic and electrophysiologic criteria, such as the presence or absence of a nerve conduction response. Typically, there can be significant scarring in the region of a neuroma-in-continuity, which may make it difficult to localize. Radiologic imaging of the injured nerve, using both magnetic resonance imaging (MRI) and ultrasound, can help the neurosurgeon identify a neuroma-in-continuity prior to surgery. The addition of diffusion tensor imaging (DTI) also may allow for evaluation of axonal continuity within the neuroma preoperatively, potentially resulting in improved specificity of diagnosis [5]. DTI may further allow for indirect imaging of the nerve microstructure, via the calculation of quantitative parameters, such as fractional anisotropy (FA) [5].

Furthermore, intraoperative ultrasound can be performed to localize the neuroma-in-continuity, commonly followed by ultrasound-guided percutaneous injection of methylene blue to further direct the surgeon to the area of concern. Methylene blue guides the surgeon by staining a tract from the nerve to the skin surface, allowing the surgeon to dissect down directly to the neuroma. This technique thereby reduces damage to the surrounding tissues in addition to decreasing surgical times [6,7]. The purpose of this article is to describe the use of both preoperative and intraoperative imaging as well as intraoperative methylene blue injection to help localize and better characterize the neuroma-in-continuity for neurosurgeons.

PATHOPHYSIOLOGY

Traumatic injuries can result in nerves that are partially or completely transected [1]. After an axon is injured, the proximal portion of the nerve attempts to regenerate, growing at a rate of 1 mm per day to 2 mm per day, whereas the distal damaged portion concurrently undergoes wallerian degeneration, including axonal degeneration, followed by myelin sheath degradation and infiltration by macrophages and Schwann cells [1,3]. The proximal portion of the regenerating nerve does not reach the distal portion but instead continues to proliferate, forming a neuroma [1]. If the nerve was completely transected, it forms a terminal (or end-bulb) neuroma [3]. If the proximal and distal margins of the damaged nerve are connected by the surrounding epineurium, however, a neuroma-in-continuity can form. Neuromas-in-continuity can be subdivided further into spindle neuromas, in which the perineurium is also intact, and lateral neuromas, in which there is partial perineurium disruption that often occurs after repairs of the nerve [1,2,5,8]. Neuromas-in-continuity are believed to represent approximately 60% to 70% of all peripheral nerve injuries [1]. These can be profoundly symptomatic, including causing great pain in patients, and many times are identifiable as small palpable masses [3].

TREATMENT

Management of these lesions is difficult. Various techniques have been performed to try to prevent the formation of neuromas-in-continuity. The main surgical approach for a neuroma-in-continuity is microsurgery, including nerve decompression with or without neurolysis for lower-grade injuries, with en bloc resection reserved for cases of neurotmetic injuries [1]. Typically, however, there is scarring due to prior trauma or surgery in the region of the neuroma, which can make it difficult to identify the offending lesion at the time of surgery. For this reason, appropriate knowledge and use of a multimodality imaging strategy can be helpful in the preoperative and intraoperative evaluations of neuromas-in-continuity and to effectively and efficiently guide surgical management.

IMAGING STRATEGY

Magnetic resonance (MR) neurography provides high spatial resolution and high-contrast resolution imaging of nerves that allow for better anatomic assessment and internal signal characterization by using a combination of non–fat-suppressed T1-weighted and fluid-sensitive (heavily T2-weighted and short-tau inversion recovery [STIR]) pulse sequences. MR neurography studies are preferentially performed on a 3T MRI scanner to optimize signal-to-noise ratio and contrast-to-noise ratio. Imaging at a high-field strength also allows for more aggressive optimization of spatial resolution, which can be essential in the diagnosis of small or subtle pathology centered within an anatomically complex background. The fluid-sensitive sequences generally are fat suppressed, which suppresses the signal from normal structures and allows for increased conspicuity of nerve pathology [5,9]. Additionally, thin-section isotropic 3-D fluid-sensitive sequences can be used to allow multiplanar reformatted imaging along the long axis of the

desired nerves, to better detect areas of nerve pathology. Images can be reconstructed further using a maximum intensity projection technique, to improve lesion perceptibility. These thin-section 3-D images ideally are obtained after the injection of gadolinium-based intravenous contrast medium, utilizing STIR technique rather than chemically selective fat suppression, in order to null the otherwise bright vascular signal that typically is seen adjacent to the nerves of interest, improving visualization of these nerves and therefore diagnostic confidence. If there is a contraindication to intravenous injection of gadolinium-based contrast medium, such as an allergy or renal dysfunction, alternative imaging strategies exist, such as high-resolution 3-D STIR imaging with multiplanar reformats.

On T1-weighted images, the neuroma-in-continuity usually is isointense to skeletal muscle, whereas on fluid-sensitive sequences, it is heterogeneously hyperintense [2]. Additional MRI findings of nerve injury include enlargement and edema of the entire nerve; edematous, enlarged fascicles; and frank nerve discontinuity [5]. With high-resolution MR neurography, neuromas-in-continuity can be seen as focal, fusiform masses continuous with the proximal and distal segments of the nerve, whereas a terminal neuroma is diagnosed when the neuroma is discontinuous with the nerve distally [5,10]. Additionally, MR neurography, including T1-weighted and fluid-sensitive sequences, allows for assessment of end-organ damage in the setting of subacute or chronic nerve injury; depending on the acuity of the nerve injury, evidence of muscle denervation may be seen, including edema-like signal (manifested as increased signal intensity on fluid-sensitive sequences) to muscle fatty infiltration and/or atrophy (seen best on T1-weighted sequences) [5]. Assessment for evidence of other soft tissue injury, including perineural scarring, or bone pathology also is possible.

During the MR neurography examination, additional functional imaging sequences can be obtained using DTI [9]. In brief, DTI uses a series of noncollinear diffusion-sensitizing gradients to capture a diffusion tensor matrix, quantified mathematically as eigenvalues and eigenvectors, detailing the magnitude and direction, respectively of diffusion in any given imaged voxel. Simply stated, diffusion tensor imaging allows for evaluation of the microstructure of the nerve by utilizing the differences in motion of water protons between the nerve and the surrounding tissues [5,9]. In tissues with low barriers to diffusion (such as muscles or adipose), diffusion should be isotropic, that is, equal in all directions, resembling a sphere. In intact, myelinated nerves, however, there is a constraint to diffusion in the radial axis, directing diffusion along the longitudinal axis and resulting in anisotropic diffusion (ie, resembling an elongated, football-shaped or cigar-shaped ellipsoid). Multiple quantitative measures can be derived from the diffusion indices, such as FA, apparent diffusion coefficient, and axial diffusivity, among others [5,9]. These values can be visualized by color-encoded maps or arrows or as ellipsoids, among other visualization strategies. Tractography is the 3-D graphic representation of the direction of maximum diffusivity of water molecules [5,9,11], and, therefore, it can be used to help evaluate the courses of nerve bundles and individual nerves [12,13]. It has been suggested that FA positively correlates with axonal density and diameter; therefore, this quantitative analysis can be used to assess changes of axonal density to quantify evidence for both nerve injury and potentially nerve regeneration or repair during follow-up imaging [12,14]. Tractograms represent a mathematical representation of diffusivity and do not represent individual axons. Therefore, in practice, FA maps should be coregistered with dedicated anatomic imaging to localize fiber tracts.

Preoperative ultrasound also is a valuable tool in the evaluation of neuromas. Advantages of ultrasound include that it is low cost, is quickly obtained, and allows for dynamic examination to be performed; and assessment of the asymptomatic contralateral side can be obtained for comparison [15]. Additionally, imaging is performed in real time and can be correlated with physical examination to better localize clinically relevant pathology. Given the improved resolution of ultrasound with high-frequency probes, assessment of small peripheral nerves can be performed, including localization, evaluation of morphology, and evaluation of surrounding structures [6,16]. In general, traumatic neuromas-in-continuity appear as fusiform hypoechoic thickening of the injured nerve, in contiguity with the nerve proper both proximally and distally. When only a portion of the nerve cross-sectional area is injured (partial-thickness injury), the normal-appearing nerve fibers may be seen coursing along the periphery of the neuroma-in-continuity. This information may be useful for the treating neurosurgeon to plan a surgical approach, such that as many nerve fibers as possible may be preserved.

Given these advantages of ultrasound, this imaging modality also is ideal for intraoperatively localizing neuromas [6,15]. Osorio and colleagues [6] have described a technique using intraoperative ultrasound to identify the nerve of interest and to inject methylene blue adjacent to the nerve and along the tract. In this technique, an ultrasound-guided needle electrode also

was used to stimulate the nerve, which in turn stimulated the muscle, thus confirming the desired position. Methylene blue injections are particularly useful when the regional anatomy is distorted due to scarring, anatomic variation, or obesity. Anecdotally, the authors' surgical colleague has noted preoperative ultrasound may underestimate the depth of some nerve lesions, most likely due to compression of the skin and deep tissues by the transducer head during insonation; therefore, methylene blue injection is advantageous in that it allows the surgeon to precisely identify the nerve by providing a direct trajectory from the skin to the lesion. This, in turn, can reduce operative times and trauma to the tissues in the surgical bed [7].

INJURY-GRADE SPECIFIC IMAGING FINDINGS AND PITFALLS

Example: Identifying Severe Injury

A 24-year-old man with a gunshot to the left leg subsequently developed weakness in the left foot, with burning and numbness along the bottom of his left foot as well as numbness along the lateral aspect of his left calf, 1 month after the injury. Preoperative evaluation included an electromyogram demonstrating severe left sciatic neuropathy at or proximal to the long head of the biceps femoris muscle with continuity to all muscles tested except the tibialis anterior. Physical examination demonstrated weak motor function in this foot, including 1/5 foot eversion, 1/5 to 2/5 plantar flexion and no definite foot or toe dorsiflexion, and absent sensation along the dorsum of the foot, with intact sensation along the sole of the foot.

Preoperative imaging included MR neurography of his left upper leg approximately 6 months after his injury. The imaging demonstrates a left sciatic neuroma within the midthigh that is continuous with the nerve, with edema within the nerve distally, with a focal defect in the nerve representing a bullet tract (Fig. 1A, B). There is fatty atrophy of the muscles in the posterior compartment of the midthigh and edema and enhancement within the muscles of the distal thigh medial compartment. The DTIs demonstrate a large gap mainly within the peroneal segment of the sciatic nerve with the distal peroneal nerve fibers degenerated and disorganized; additionally, these images show that the tibial nerve fibers of the sciatic nerve are intact (see sFig. 1C).

Two weeks prior to the surgery, an ultrasound of the left thigh and knee was performed. The left sciatic nerve was identified, and demonstrated a 3.3-cm fusiform, hypoechoic neuroma within the nerve (see Fig. 1D).

Surgery was performed approximately 7 months after the injury. Intraoperative ultrasound was performed identifying the left sciatic neuroma, and methylene blue was injected along the superficial surface of the nerve and along the tract to the skin surface (see Fig. 1E, F). Electrodes were placed in the left lower leg muscles supplied by the peroneal and tibial nerves. Exploration, extensive decompression, and circumferential neurolysis of the damaged left sciatic neuroma-in-continuity with internal neurolysis under the microscope was performed (see Fig. 1G). The neuroma was not resected because stimulation of the internal portion of the nerve did not give rise to motor response in the peroneus longus muscle. Additionally, stimulation of the tibial component of the nerve resulted in mild somatosensory evoked response in the contralateral cortex, whereas stimulation of the peroneal component of the nerve did not result in somatosensory evoked response. Intact lateral sciatic fascicles, however, were visible on direct inspection, and, therefore, the neuroma-in-continuity was not resected.

Four weeks after surgery, physical examination revealed improvement in the patient's left foot plantar flexion and toe flexion. Additionally, he had return of sensation along the dorsum of his foot.

Example: Identifying Lower-grade Injury and Visualizing Nerve Healing/Regeneration

A 24-year-old woman suffered an open laceration to her right median nerve in the proximal forearm from glass presented 3 months after the initial injury, with a positive Tinel sign over her curvilinear incision in her proximal forearm radiating into her right first to third fingers in a median nerve distribution. Motor function in her right pronator teres was 4+, wrist flexors 4+, abductor pollicis brevis 0, opponens pollicis 4, and flexor pollicis longus 0. Her sensation along the volar aspects of her right thumb and index and middle fingers was absent.

Preoperative imaging included MR neurography, which demonstrated a focal segment of median nerve attenuation within the proximal forearm. Just proximal to this attenuated portion, the median nerve was bulbous, whereas distal to the attenuated portion, the nerve appeared edematous (Fig. 2A, B). There was mild diffuse flexor compartment muscle edema without atrophy, and a flexor carpi radialis central tendon complex partial tear with granulation tissue. DTI demonstrated a few intact fibers (see Fig. 2C).

A subsequent preoperative ultrasound of the right forearm also was performed, demonstrating injury to the median nerve in the proximal forearm with a bulbous neuroma. The thin intact nerve fibers, however,

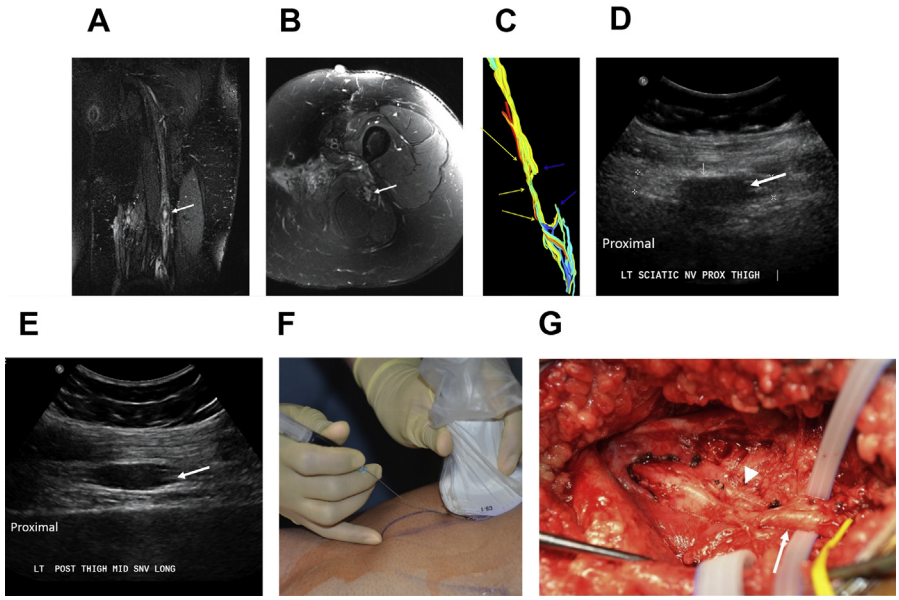

FIG. 1 Sciatic nerve neuroma-in-continuity in a 24-year-old man with sciatic neuropathy after gunshot wound. (**A**) Coronal STIR SPACE image through the posterior thigh on MR neurography demonstrates focal fusiform thickening of the sciatic nerve with central brighter signal (*arrow*) that was believed to represent a gap within the nerve either filled with fluid or granulation tissue. (**B**) Axial T2 fat-suppressed image of the midthigh shows a longitudinally oriented defect in the sciatic nerve representing the bullet tract (*arrow*). (**C**) Coronal diffusion tensor tractogram shows partial discontinuity of the diffusivity tracts within the sciatic nerve. This peroneal nerve fibers are predominantly degenerated and disorganized, leading to a gap in the tracts (*blue arrows*), whereas the tibial nerve fibers appear intact (*yellow arrows*). (**D**) Preoperative long-axis ultrasound image of the sciatic nerve performed 2 weeks later demonstrates a 3.3-cm segment of hypoechoic fusiform thickening of the nerve (*arrow*). The calipers to the left and right of the lesion indicate the normal caliber of the proximal and distal segments of the sciatic nerve. (**E**) Intraoperative long-axis ultrasound image of the sciatic nerve performed 7 months after the initial injury redemonstrates the sciatic nerve lesion (*arrow*). A needle was advanced to the superficial surface of the lesion under sonographic guidance as part of a methylene blue injection to aid intraoperative localization. (**F**) Intraoperative photograph that shows a musculoskeletal sonologist using a 5-MHz curved array transducer to advance a 25-gauge spinal needle connected to a syringe containing methylene blue to the superficial surface of the sciatic nerve lesion. (**G**) Intraoperative photograph of the posterior thigh with surgical dissection to the sciatic nerve. There is a gray-colored tie coursing under the segment of the sciatic nerve just distal to the lesion (*arrow*). The lesion itself is marked by an arrowhead.

were not recognizable on ultrasound in this surgically proved neuroma-in-continuity. An apparent 1.7-cm gap was seen on preoperative ultrasound (see Fig. 2D, E).

Surgery was performed approximately 5.5 months after the initial injury. Intraoperative ultrasound demonstrated the right median neuroma, and methylene blue was injected percutaneously adjacent to the nerve and along the tract under ultrasound guidance (see Fig. 2F). Electrodes were placed in the right upper extremity for sensory and motor function monitoring. Exploration and extensive circumferential neurolysis and decompression of the right median nerve were performed. Under microscopic evaluation, the neuroma was noted to be continuous with the median nerve, diagnostic of a neuroma-in-continuity (see Fig. 2G).

One month postprocedure, the patient's pain and strength improved significantly, although the abductor pollicis brevis was still weak. Despite a persistent sensory deficit, the patient did note improvement in sensation in this median nerve distribution.

MR neurography of the right forearm performed 6 months postoperatively demonstrated scarring and granulation tissue in the surgical bed; the previously

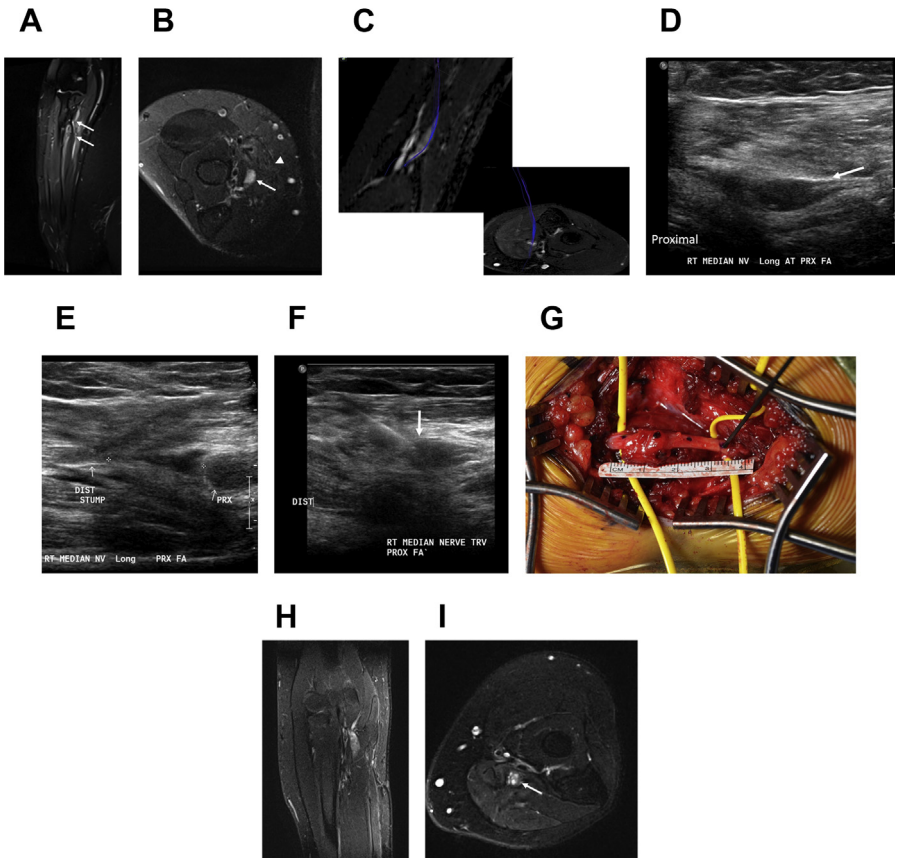

FIG. 2 Median nerve neuroma-in-continuity in a 24-year-old woman after forearm laceration. (**A**) Coronal STIR image of an initial right forearm MRI reveals a 1.8-cm thinned segment of the nerve (*between arrows*). (**B**) Axial T2-weighted fat-suppressed image from the same study shows fusiform thickening of the median nerve just proximal to the thinned segment (*arrow*). There is mild flexor forearm muscle edema without atrophy (*arrowhead*). (**C**) Diffusion tractography images using thin-section coronal and axial STIR SPACE images to provide anatomic context show intact diffusion tracts along the course of the nerve, indicating at least partial fiber continuity. (**D**) Long-axis ultrasound of the median nerve at the site of prior laceration shows a 1.0-cm long hypoechoic fusiform segment of the nerve that represents the neuroma-in-continuity (*arrow*). (**E**) Just distal to the lesion, on the same study, there is an apparent 1.7-cm gap in the nerve with proximal and distal stumps labeled (*between calipers*). (**F**) Intraoperative long-axis ultrasound of the median nerve shows the long axis of a 25-gauge needle connected to a syringe containing methylene blue extending to the superficial surface of the neuroma-in-continuity (*arrow*). Methylene blue was injected at the surface of the lesion and along the needle path as it was slowly withdrawn to the skin surface. (**G**) Intraoperative surgical exploration of the forearm shows yellow ties proximal and distal to the abnormal segment of the nerve. There is fusiform thickening of the nerve proximally. (**H**) Repeat forearm MR neurography performed 6 months after neurolysis shows fusiform thickening of the nerve in the segment of the nerve in which there was an apparent gap, which was believed to present granulation tissue and fibrosis. The gap was much less conspicuous, suggesting healing. (**I**) Axial T2-weighted fat-suppressed image of the upper forearm shows persistent nerve fasciculation (*arrow*). The previously noted flexor muscle edema has resolved, however, consistent with the functional improvement the patient reported.

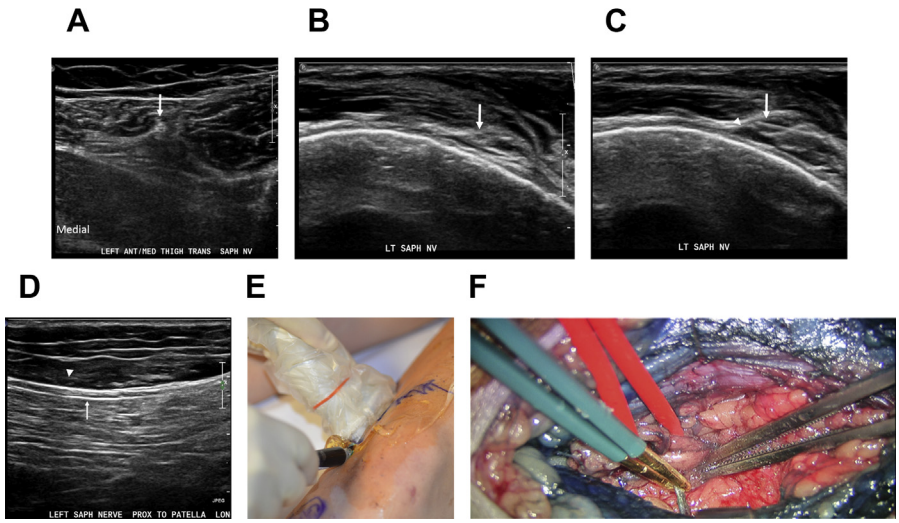

FIG. 3 Saphenous nerve neuroma-in-continuity in a 32-year-old woman who experienced medial left knee pain after arthroscopic surgery. (**A**) Initial transverse ultrasound image of the medial knee at the level of the medial femoral condyle shows the saphenous nerve has a normal course, caliber, and echotexture (*arrow*). The nerve was obscured at the level of the knee due to soft tissue architectural distortion at an operative site but was again visible distal to the knee joint (not shown). (*B*) Transverse sonographic image of the saphenous nerve at the level of the medial femoral condyle immediately prior to sonographically guided hydrodissection demonstrates the nerve (*arrow*). (*C*) Subsequent transverse sonographic image of the saphenous nerve shows a 25-gauge needle (*arrow*) with soft tissue distension (*arrowhead*) due to perineural saline injection. (**D**) Intraoperative ultrasound image of the medial knee demonstrates the long axis of the saphenous nerve (*arrow*). A 25-gauge needle was advanced to the superficial surface of the nerve using an out-of-plane approach, and there is a small hypoechoic halo surrounding the tip of the needle representing methylene blue injection (*arrowhead*). (**E**) Intraoperative photograph of the medial knee demonstrates advancement of a 25-gauge needle to the saphenous nerve using sonographic guidance with a 12-MHz linear transducer. (**F**) Photograph of the surgical bed after dissection of the saphenous nerve. There are forceps grasping the distal segment of the nerve, which has a slightly bluish color that is, related to the methylene blue injection, and there is a red tie coursing under the more proximal segment of the nerve.

identified nerve gap was less conspicuous, suggesting functional improvement. The median nerve neuroma was similar in size and location to the prior examination (see Fig. 2H, I). Decreased muscle edema within the flexor digitorum superficialis and flexor carpi radialis also was noted.

Example: Identifying Subtle Injury, Confirming Preoperative Diagnosis with Ultrasound-guided Percutaneous Intervention

A 32-year-old woman underwent left knee revision arthroscopy and partial medial meniscectomy for medial knee pain. She continued to experience pain with numbness, however, at the medial aspect of her knee and distal to the patella, with sharp shooting pain down her medial lower leg to her ankle in the saphenous nerve distribution. Diagnostic local anesthetic injection in the region of the infrapatellar branch of the saphenous nerve was performed with subsequent 1-day temporary relief.

Physical examination was notable for allodynia along the left medial lower leg above, at, and below the knee in the distribution of the saphenous nerve and/or infrapatellar nerve distribution. The patient walked with a limp. Knee reflexes were decreased.

Additional work-up included ultrasound of the distal left thigh and knee. The saphenous nerve was obscured at the level of the medial knee joint, and the nerve appeared normal proximally in the thigh and distally within the calf (Fig. 3A). Concurrently, the patient received diagnostic ultrasound-guided left saphenous nerve block, with the patient reporting 2 days of symptom relief. One week later, the patient underwent

ultrasound-guided hydrodissection of the left saphenous nerve adjacent to the medial femoral condyle, in which a 23-gauge needle was placed adjacent to the nerve and 7 mL of saline was injected to free the nerve from the adjacent scar tissue (see Fig. 3B, C). Again, the patient reported 2 days of partial symptom relief.

The patient underwent exploratory surgery. Intraoperative ultrasound demonstrated the abnormal segment of the left saphenous nerve and ultrasound-guided percutaneous methylene blue injection was performed (see Fig. 3D, E). Circumferential decompression and neurolysis of the left saphenous nerve adjacent to the knee were performed using intraoperative ultrasound and microscope, in which a neuroma-in-continuity was identified (see Fig. 3F).

CURRENT IMAGING LIMITATIONS

Because of difficulties a treating physician may have in preoperative assessment of traumatic peripheral nerve injuries, a multimodality approach to identifying and characterizing these injuries, including preoperative MRI often with DTI and/or ultrasound, could be helpful. Using 1 imaging modality may be helpful to identify the site of nerve damage but may not provide a comprehensive understanding of the anatomy and function of the nerve, and the combination of modalities may help confirm or at least suggest the diagnosis of neuroma-in-continuity.

In the example given of severe nerve injury, both preoperative MRI and ultrasound correctly showed that the neuroma was continuous with the sciatic nerve and that the tibial component of the nerve appeared intact. The tractography suggested a gap in the nerve at the site of the neuroma (see Fig. 1C); however, some intact fibers were identified at surgery. This discrepancy illustrates some of the current challenges of tractography. In order to develop tracts, thresholds for certain parameters, such as FA and angular deviation, need to be selected. If the parameters are too strict, few tracts are seen, and an area of discontinuity can be diagnosed. On the other hand, if the parameters are too inclusive numerous, spurious tracts in addition to the expected tracts are seen, providing a false over-representation of intact nerve fibers or a false direction of the fibers. At current, this field is in its infancy in terms of its understanding, with tractography based on multiple mathematical assumptions and requiring substantial manual optimization. Although the techniques utilized in central nervous system imaging can be adapted to a certain degree to the peripheral nervous system, the very small structures involved and the tortuous courses they follow introduce an additional layer of complexity typically not seen in the tracts of the central nervous system. Moreover, other factors, such as magnetic field strength, voxel size, and number of diffusion gradients, can have a great impact on the quality of the DTI information and subsequent tractograms [17]. Optimization of matrix size, field of view, and signal-to-noise ratio is a common challenge in MRI, but when imaging small peripheral nerves, it becomes even more important, because introduction of even a small amount of noise can nullify the validity of tractography [18]. One strategy to improve the fidelity of the tractography performed is to identify an asymptomatic healthy nerve of similar size and course within the data set obtained, such that internal quality assurance and control can be performed and selection of tractography parameters can be optimized.

Local edema at the site of injury, such as that seen in the acute phase of injury, may sufficiently reduce FA to interfere with the tractography algorithms, resulting in spurious truncation of imaged fiber tracts, which may improve with subsequent serial examinations as the degree of localized edema resolves. Additionally, local magnetic field inhomogeneity can have a disproportionate effect on diffusion-weighted imaging, and, therefore, tractography should be obtained in conjunction to assess for causes of susceptibility artifact, such as metallic surgical clips, mineralization, or prior hemorrhage.

In other instances, the anatomic imaging may not demonstrate the continuity of the neuroma with the proximal and distal portions of the nerve. Although the resolution in ultrasound and MRI has greatly improved with recent technical advances, very small structures nevertheless may be difficult to perceive. Furthermore, the diagnosis of neuroma-in-continuity and the implications of different degrees of nerve injury on surgical management are not always well-known to imagers. In the second example (lower-grade injury), the thin intact nerve fibers were not appreciated and apparent nerve gaps were reported on both MRI and ultrasound studies, findings that were not confirmed at surgery. Despite improvements in spatial resolution, very small intact nerve fibers still may not be appreciated, resulting in the incorrect interpretation as complete nerve transection or discontinuity.

SUMMARY

Multiple imaging modalities, when used in conjunction, can be helpful to surgeons not only to preoperatively characterize neuromas-in-continuity both

anatomically and functionally but also to assist in preoperative planning. Intraoperative ultrasound and ultrasound-guided methylene blue injection can be used to assist the surgeon in identifying the neuroma efficiently by providing a tract for the surgeon to follow to the neuroma. Although there have been significant advances in imaging, some neuromas-in-continuity may have only a few intact fascicles, which may be too small to resolve by MR neurography or ultrasound or may be obscured by perineural scarring. At present, the use of multiple imaging modalities provides additional preoperative information to that obtained from electromyogram and clinical examination but does not provide definitive diagnosis with sufficient positive and negative predictive value to match the gold standard of intraoperative findings. It is anticipated that advances in imaging will increase sensitivity and specificity of the imaging diagnosis of neuroma in continuity, such that only those cases that would most benefit undergo invasive surgery. It is anticipated that commercialization and automation of DTI data processing will result in increased standardization and improved quality assurance of tractography metrics.

Intraoperative identification of neuroma-in-continuity using ultrasound and percutaneous injection of ultrasound-guided methylene blue allows radiologists to add value to patient care and assists referring clinicians by reducing surgical times and potentially damage to other tissues in the surgical bed. Progressive improvements in minimally invasive techniques have the potential to further reduce trauma to surrounding structures, potentially decreasing complication rates and improving recovery times.

Last, but not least, further investigation is needed into postoperative imaging strategies to monitor for nerve regeneration/repair and response to therapy, which has the potential to guide patients' ongoing management during recovery.

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