INTRODUCTION

Advances in field of ultrasound over the past twenty years have generated increasing interest in utilizing the technology in neuromuscular assessment and diagnosis. High-resolution ultrasound offers a noninvasive, real-time, static and dynamic examination of the peripheral nervous system, yielding information which complements the neurological examination, electrodiagnostic testing (EDX), and other established imaging modalities such as Magnetic Resonance Imaging (MRI).

ULTRASOUND BASICS

Ultrasonography involves transmitting sound-wave pulses into tissue and analyzing the temporal and acoustic properties of the reflected wave, or echo. Echoes occur at tissue interfaces. Reflected energy is a product of the difference in adjacent tissue densities (acoustic impedance), as well the angle of the ultrasound beam (angle of incidence) relative to the interface.

A fraction of a transmitted sound-wave energy is reflected whenever there is a change in acoustic impedance within tissue. Larger differences in acoustic impedance result in more profound reflection. Unreflected sound travels deeper into the tissue, generating echoes from layers at a greater depth. A portion of the ultrasound energy never returns to the transducer, either being transformed into heat (absorption), refracted or scattered at nonperpendicular tissue interfaces. When the sound wave encounters a significantly different tissue density, analysis of deeper structures is not possible. For example, ultrasound cannot evaluate structures deep to air-filled cavities or bone due to the acoustic impedance of these regions.

An ultrasound probe (transducer) is capable of both emitting and receiving these pulses and converting them into electrical signals for analysis. Since the average velocity of sound through soft tissue is known (1540 m/s), the time interval between transmitting and receiving a sound wave is used to estimate the depth of each tissue interface. This information can be envisioned as a single vertical line of a two dimensional image, with the amplitude of each returning echo corresponding to the brightness of the pixel displayed on the ultrasound screen at that level. Successive activation of the elements within the ultrasound transducer generate a series of vertical lines across the area of interest, completing the two dimensional image (B-mode ultrasound).

Image quality depends on many factors, including the insonation frequency. Higher frequencies (7-15 MHz) provide improved axial resolution (the ability to distinguish two objects in tandem along the axis of the ultrasound beam), but are less capable of penetrating into deeper tissues due to greater absorption and scattering. Thus, high-resolution ultrasound is particularly well suited to study small, superficial structures such as most peripheral nerves.

Transducer frequency is important to facilitate imaging of the peripheral nervous system, but more recent software enhancements and increasing computer processor speeds further improve image quality. For example, compound imaging sonography can reduce noise/artifacts by overlapping slightly different image frames and averaging them into a single image in real-time. Tissue harmonic imaging makes use of resonant tissue frequencies, providing better signal-to-noise ratios particularly when imaging deeper structures. Moreover, larger, panoramic images can be created as a transducer is moved across the patient using extended field of view ultrasound imaging.

For a more in-depth understanding of ultrasound physiology and techniques, a variety of excellent texts are available.
The principle advantages of ultrasonography are summarized in Table 1. Technical limitations of ultrasound include inability to image through bone (e.g., the brachial plexus beneath the clavicle), difficulty with imaging deeper nerves at high-frequencies, and poor visualization of nerves surrounded by tissues of similar acoustic impedance (e.g., fat). In addition, practical limitations must be considered, such as operator dependence, a need for significant hands-on experience with scanning and ultrasound machine settings, and a required depth of anatomical knowledge.

Physicians with neuromuscular training, particularly those with experience performing the electrodiagnostic examination, are well suited to learn neuromuscular ultrasound, given the neuroanatomical knowledge and familiarity of surface landmarks required to perform nerve conduction studies and the needle electrode examination. Supplementing this knowledge with a hands-on ultrasound training course can provide a solid foundation for becoming a competent ultrasound examiner. However, the importance of access to an ultrasound machine for ongoing practice to increase skill and confidence cannot be overstated. Of note, some neuromuscular/electrodiagnostic fellowships offer exposure to neuromuscular ultrasound, a trend which will likely continue going forward.

### Table 1: Advantages of ultrasound

- Painless, harmless, comfortable
- Relatively low cost
- Excellent resolution with high-frequency transducers
- Flexible field-of-view for imaging the entire course of a nerve
- Comparison to contralateral limb
- Dynamic examination: observe nerve movement, subluxation, dislocation
- Ability to identify areas of interest in “real time”
- Imaging adjacent to hardware

**Ultrasound and EDX**

EDX within the proper clinical context is the diagnostic “gold standard” for many disorders affecting the peripheral nervous system. Ultrasound is a valuable adjunct to electrophysiological studies, adding valuable and often diagnostic structural information. These tests are complementary, in much the same way that electroencephalography and MRI are used together in the field of epilepsy.

A study by Padua et. al. examined outcomes when neuromuscular ultrasound was added to the electrodiagnosis in evaluation of mononeuropathy. Diagnosis and treatment were meaningfully impacted in 20 cases (26%), including identification of nerve tumors, adjacent pathology (e.g., synovial cysts), and variant anatomy responsible for the patient’s symptoms. In 35 cases (47%), findings supported the electrodiagnostic test impression, but did not impact treatment (e.g., focal nerve swelling at an entrapment site identified by EDX). An additional 20 cases were considered “inconclusive” (i.e., no definite abnormalities identified), although the lack of evidence of nerve entrapment and exclusion of relevant adjacent pathology obviously did yield useful clinical information in these cases. Overall, the study supported the notion that ultrasound can meaningfully impact patient care when combined with the EDX in selected patients.

**Ultrasound and MRI**

There have been no large scale, high-quality studies comparing ultrasound and MRI in peripheral nervous system evaluation. MRI has the advantage of being well established, widely available, offering a large field of view, and affording the opportunity to utilize intravenous contrast to identify pathology. In some cases, MRI and ultrasound can be used together to more effectively utilize health care resources. For example, due to the high cost and extensive scan time required to complete an MRI of a nerve along its course, ultrasound may be useful for localizing pathology and focusing the MR to a segment of interest, reducing scan time and cost.

In recent expert commentary, Dr. Levon Nazarian, a radiologist from Thomas Jefferson University with extensive experience in ultrasound, presented his “top 10 reasons musculoskeletal sonography is an important complementary or alternative technique to MRI.” These included availability for patients in whom MRI is contraindicated (e.g., pacemaker, metal implants), as well as the advantages listed in Table 1, among others. He emphasized the usefulness of real-time patient interaction for localization in diagnostic ultrasound, allowing the examiner to “place the probe exactly where it hurts,” and to dynamically visualize movement of relevant anatomy, such as ulnar nerve dislocation at the elbow. Dr. Nazarian also referenced studies documenting superior axial resolution of high frequency ultrasound, suggesting a 10-MHz probe can resolve 150 micrometers, compared with
a 1.5-T MR scanner with a field of view or 12 x 6 cm, a matrix of 256 x 256, and a slice thickness of 0.5 cm yielding a resolution of 469 x 469 micrometers.

In summary, MRI and ultrasound each have specific advantages, and will both likely become increasingly important tools in neuromuscular diagnosis as the technologies evolve.

ULTRASOUND OF NERVE

Normal anatomy

In short-axis, healthy nerves have a "honeycomb" appearance, comprised of continuous bundles of hypoechoic (dark) neuronal fascicles surrounded by an echogenic (bright) perineurium and epineurium (Figure 1). In long-axis, nerve has a “tram track” appearance (Figure 2).

Differentiating adjacent anatomy is fairly straightforward with ultrasound. Arteries and veins are characteristically hypoechoic, compressible, and in the case of arteries, pulsatile. Adding color or power Doppler ultrasound can further distinguish blood vessels. Nerves and tendons can have a similar appearance in static cross section, particularly when they lie adjacent to one another (i.e., median nerve and flexor tendons in the carpal tunnel), although nerve fascicles are typically thicker and less numerous than tendon fibrils. Tendons can be differentiated by their greater anisotropy (greater tendency to scatter sound with changes in the angle of the transducer), causing them to appear more hypoechoic than adjacent nerves.(9)

Identifying Peripheral Nerve Pathology

Nerve pathology may be reflected as breaks in the connective tissue, loss of fascicular architecture, or swelling (increased cross-sectional area), among other potential findings. Table 2 summarizes causes of focal nerve swelling described in the literature. Ultrasound can also identify adjacent pathology affecting nerve continuity, such as aneurysms, cysts, or non-neural soft tissue tumors. Any of these findings can aid precise localization and may reveal specific etiology.

<table>
<thead>
<tr>
<th>Table 2: Causes of focal nerve enlargement on ultrasound</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Entrapment neuropathies</td>
</tr>
<tr>
<td>• Peripheral nerve tumors/neuromas</td>
</tr>
<tr>
<td>• Hereditary neuropathies: HNPP, CMT, Refsum’s, Familial amyloidosis</td>
</tr>
<tr>
<td>• Inflammatory neuropathies: GBS, CIDP, MMNCB</td>
</tr>
<tr>
<td>• Acquired amyloid neuropathy</td>
</tr>
<tr>
<td>• Sarcoidosis</td>
</tr>
<tr>
<td>• Neuropathy in leprosy</td>
</tr>
</tbody>
</table>
**Entrapment Neuropathy**

The utility of ultrasound for identifying nerve entrapment is well documented in the literature as discussed below. Although many diagnostic parameters have been studied in entrapment neuropathy, focal peripheral nerve enlargement proximal to the area of entrapment is the most reproducible and widely accepted. Normal cross sectional values have been published for most nerves of interest.(10-13)

Interestingly, the pathophysiology of nerve enlargement in entrapment is incompletely understood, but theories based on animal studies suggest the cause varies over the course of the disease. The earliest changes responsible for increased nerve size likely include endoneurial edema, proliferation of fibroblasts and capillary endothelial cells, fibrin deposition, damming of axon transport, and Schwann cell proliferation/apoptosis. Later, endoneurial invasion of mast cells and macrophages, fibrosis, distal axon degeneration, axon regrowth, demyelination/remyelination, and thickening of the endoneurium and perineurium likely predominate.(14, 15) Due to variability in the underlying cause of nerve swelling throughout the course of entrapment, the precise relationship between the degree of enlargement and clinical symptoms at various stages of the disease is likely complex. This notion is supported by a recent study in patients with carpal tunnel syndrome, suggesting a correlation between nerve size and clinical impairment as well as neurophysiological classification, albeit with increasing variability in cross sectional area in more severe/advanced disease.(16)

1. **Carpal tunnel syndrome**

Carpal tunnel syndrome (CTS) is the most common peripheral nerve entrapment syndrome. Anatomy of the carpal tunnel is easily delineated by ultrasound and many ultrasonographic findings have been evaluated for diagnostic potential in CTS, including: changes in the echotexture of the median nerve beneath the flexor retinaculum (i.e., loss of fascicular discrimination, and less distinct outer margins), abrupt caliber change (“notch sign”) at the proximal margin of the retinaculum, flattening of the nerve within the distal carpal tunnel, reduced mobility of the nerve with wrist flexion, bowing and thickening of the flexor retinaculum, and “increased vascularization” within the nerve on color Doppler.(17-19)

However, increased cross sectional area (CSA) of the median nerve at the level of the pisiform bone (marker of the proximal carpal tunnel) is considered the most reliable and clinically useful parameter (Figure 3, long arrows identify the enlarged median nerve; the broad arrow indicates a flexor tendon).

In one of the largest studies of ultrasound in idiopathic CTS to date, 275 patients (414 wrists) with a clinical history and neurological examination findings consistent with CTS underwent nerve conduction studies (median sensory and motor distal latencies) and ultrasound CSA at three locations within the carpal tunnel and at the distal forearm for comparison. These findings were compared with 408 healthy volunteers (408 wrists). Diagnosis of CTS by nerve conduction criteria alone yielded a sensitivity of 73% and a specificity of 96%, compared with ultrasound findings (mean CSA > 0.12 cm²) yielding a sensitivity of 67% and a specificity of 97%. Combining the evaluation to include diagnostic abnormalities in either NCS or ultrasound resulted in a sensitivity of 84% and a specificity of 94% for diagnosis of CTS. Importantly, when motor and sensory responses were absent, thus limiting the localizing value of the EDX (8%), ultrasound provided localizing information in all cases.(20)

Another study prospectively examined 74 consecutive patients (110 wrists) referred to a tertiary care center for suspected CTS, and compared CSA in patients with and without electrodiagnostic evidence of nerve entrapment. Good correlation between median nerve distal motor latency and CSA within the carpal tunnel was found, and analysis suggested that the posttest probability of CTS was > 90% for patients with a CSA > 12 mm² and approached 100% for patients with a CSA > 14 mm².(21)

Subsequent studies have confirmed the accuracy of using increased median nerve CSA at the pisiform bone in the diagnosis of CTS when compared with EDX,(22), and correlations are present between ultrasonographic findings and electrophysiological stage as well as MUNE.(16, 23) There is also evidence that a median wrist-to-
forearm CSA ratio may be of additional value, although the utility of this measurement requires further study.(11, 24)

Regarding the prognostic value of ultrasound findings prior to carpal tunnel release surgery, a recent study suggested that preoperative nerve size alone is not a useful prognostic factor for postoperative outcome, although the ability of the study to detect a difference may have been limited by a relatively small number of patients with a poor postoperative outcome.(25) The study did reveal a significant decrease in nerve size in post-operative patients with a good outcome, compared with no change in symptomatic patients treated conservatively, lending further support for a relationship between entrapment, nerve size, and clinical symptoms in carpal tunnel syndrome.

In addition to diagnosis of CTS, ultrasound can identify structural causes of CTS, or important anatomic variations, impacting surgical approach. Compression of the median nerve by synovitis, aberrant muscle, ganglia, and tumors within the carpal tunnel have been reported. Persistent median artery (PMA) within the carpal tunnel (estimated incidence 10 – 26%), can also be demonstrated. PMA when not identified preoperatively can complicate an endoscopic carpal tunnel release, or an open release if a tourniquet is used.(26) Ultrasound imaging can thus help to guide CTS surgical planning and may improve patient outcomes.

2. Ulnar nerve entrapment

Insonation of the ulnar nerve is possible throughout its course, and normal cross sectional values have been published at key locations from the axilla to the wrist.(12) Cubital tunnel syndrome (synonymous with ulnar neuropathy at the elbow [UNE] for the purposes of this review), the second most common nerve entrapment, has traditionally been diagnosed by clinical findings and EDX. There is increasing evidence that ultrasound can be localizing when EDX is equivocal, and may identify relevant pathology and anatomic variants which alter clinical management.

The literature supporting the use of ultrasound in UNE, includes a study of 123 patients (136 elbows) referred for clinical symptoms suggestive of UNE, comparing ulnar nerve diameter at three locations across the elbow segment by ultrasound, with EDX criteria and clinical history/examination findings. The highest diagnostic yield for ultrasound was observed in patients with slowing across the elbow (without conduction block) on nerve conduction studies (86%), and in cases with normal or nonlocalizing EDX testing (85%), supporting the localizing value of ultrasound in these patients. Good interobserver agreement was also documented. In addition, patients with axon loss changes (i.e., spontaneous activity on needle electrode examination, and/or low/absent CMAPs) had significantly larger nerves than those with a pure demyelinating pattern.(27) Another study of 102 patients (109 elbows) using the same ultrasound criteria for diagnosis, suggested that adding sonography to EDX increased the sensitivity from 78% (for EDX alone) to 98%, and ultrasound localized the lesion to the elbow in 22 of 24 cases with a nonlocalizing or normal EDX.(28) Utilizing CSA of the ulnar nerve at the elbow, a more recent study found a mean size of 19 (9-37) mm² in UNE, versus 6.5 (5-10) mm² in controls, and suggested that a cut-off 10 mm² or higher, yields a sensitivity 93% and specificity 98% for the diagnosis.(29)

With regard to the prognostic value of ultrasound in UNE, one a study followed 74 affected elbows with ultrasound for a median of 14 months after diagnosis. Independent predictors of outcome included slowing or conduction block at the elbow (associated with a good outcome), and increased ulnar nerve diameter (associated with a poor outcome, OR 2.9 [1.3 to 6.4]). Patients with an initial ulnar nerve diameter > 3.5 mm were never symptom free regardless of management approach. Surgically treated cases showed a decrease in mean ulnar nerve diameter, supporting a relationship between entrapment and nerve size.(30)
In addition to localizing lesions within the ulnar nerve, ultrasound as has been used to document relevant adjacent pathology, including occult ganglia,(31) an anconeus epitrochlearis muscle,(32) and perineuroma mimicking entrapment,(33) as well as ulnar nerve subluxation and dislocation with or without “snapping triceps syndrome.” (34, 35) Dislocation of the ulnar nerve may expose the nerve to trauma with arm in the flexed position, and may complicate the electrodiagnostic examination by altering conduction velocity measurements (due to an alteration in nerve length across the elbow), as well as causing false positives in short segment nerve conduction studies.(36)

3. Peroneal mononeuropathy

Entrapment neuropathy of the common peroneal nerve can be caused by compression at the head of the fibula, although localization can be difficult with EDX in pure axon loss lesions (i.e., conduction block may not present), and challenging to differentiate from sciatic nerve lesions when the peroneal division is predominantly affected.

One recent study compared ultrasound of the nerve at the fibular head in 8 patients with foot drop with 20 healthy controls. Three patients with normal ultrasound findings of the peroneal nerve a the fibular head were diagnosed with other neuromuscular problems based on EDX and MRI. In the 6 symptomatic limbs of the remaining 5 patients, all were found to have an increased cross sectional area of the peroneal nerve at the fibular head (0.21 – 0.31 cm2) compared with the control patients (mean 0.10 cm2, ranging 0.06 to 0.14 cm2). Measurement of a transverse nerve breadth-to-length ratio was not consistently different from controls in this study. All of these patients had EDX evidence of peroneal nerve dysfunction, and in 5 of the 6 symptomatic limbs, localization to the fibular head was supported by ultrasound due to a lack of conduction block on nerve conduction studies.(37)

In another series of 28 patients with foot drop and EDX findings consistent with an isolated peroneal neuropathy, 5 patients (18%) were found to have an intraneural ganglion. Four of the 5 had pure axon loss changes on EMG, and one had conduction block across the fibular head. Full recovery was achieved in 4 of these patients after surgical removal,(38) suggesting that ultrasound can identify underlying pathology which can have a significant impact on patient outcomes in peroneal mononeuropathy.

4. Other entrapment neuropathies and mononeuropathies

A number of smaller studies and case reports have been published supporting the usefulness of ultrasound in iatrogenic accessory neuropathy,(39) radial nerve entrapment at the spiral groove,(40-42) supinator syndrome,(43) iatrogenic femoral neuropathy,(44) lateral femoral cutaneous neuropathy (malignant peripheral nerve sheath tumor and sural mononeuropathy. Among others.

Peripheral Nerve Tumors

Peripheral nerve tumors can also be identified by ultrasound. Tumor types include lesions derived from nonspecific neural tissue, such as fibrolipomas, peripheral nerve sheath ganglia, and intraneural perineuroma, as well as benign peripheral nerve sheath tumors (e.g., schwannomas, neurofibromas and granular-cell tumor) and malignant peripheral nerve sheath tumors.(52) In addition to continuity with the nerve, most nerve tumors appear hypoechoic, fairly homogenous, and have posterior acoustic enhancement (i.e., area deep to the lesion appears more echogenic than its surroundings).(53) Although the most commonly encountered tumor types have an expected “typical” ultrasound appearance (Table 3), no parameters on B-mode imaging have been consistently found to correlate with tumor type in the few small studies published to date.(54)

<table>
<thead>
<tr>
<th>Table 3: Ultrasound features suggestive of specific nerve sheath tumor types</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurofibroma:</strong> Centrally positioned and diffusely involving the nerve, “target appearance” (hyperechoic core)</td>
</tr>
<tr>
<td><strong>Schwannoma:</strong> Eccentrically positioned and focal within the nerve, fusiform to round in shape, echogenic capsule, cavitation within the mass</td>
</tr>
<tr>
<td><strong>Malignant peripheral nerve sheath tumors:</strong> Focal mass, variable findings on ultrasound, power Doppler signal</td>
</tr>
</tbody>
</table>
The usefulness of power Doppler ultrasound in differentiating malignant and benign musculoskeletal tumors has been suggested. In one study, increased vascularity was present in 2 of 2 malignant peripheral nerve sheath tumors studied, but was also present in 2 of 4 schwannomas, suggesting that this finding is not specific for malignant lesions. Of note, it has been suggested that tumors < 1.5 cm in diameter may not induce ultrasound-detectable malignant vascularity, and that tumor necrosis may limit the usefulness of Doppler analysis. Thus, the primary role of ultrasound in nerve tumor management, may be limited to precise localization for biopsy planning as opposed to predicting underlying pathology. Serial evaluation of asymptomatic lesions to monitor for change in size or morphology may prove useful, and has been utilized effectively in a neurofibromatosis clinic in Italy.

**Nerve trauma**

Identification of complete nerve transection would be helpful in guiding the decision to pursue earlier surgical intervention. Importantly, EDX cannot differentiate axonotmesis from complete nerve transaction (i.e., neurotmesis) until reinnervation begins beyond 6 weeks. In a recent proof-of-concept study, a blinded US examiner studied 20 fresh cadaver arms with randomly placed median, ulnar, and/or radial nerve transections and sham incisions. The study revealed an 89% sensitivity and a 95% specificity for transection identification with high-frequency ultrasound, despite the special challenges associated with examining cadavers (i.e., loss of pulsatile vessels as landmarks, etc.). Interestingly, the study used disarticulated cadaver arms in all except two arms (one cadaver). In the intact cadaver a 1 cm gap was present between transected ends facilitating transaction identification, and suggesting that the natural tension present across nerves in living patients would further enhance the sensitivity of the test.

A study of 14 patients undergoing microsurgical repair for traumatic neuropathies involving the ulnar (50%), median (14%), and sciatic (36%) nerves demonstrated “good or excellent” results when utilizing preoperative US for diagnosis of a stump neuroma (3 of 3 patients), localizing of the proximal/distal nerve stumps (8 of 9 patients), identifying the type and site of injury (10 of 14 patients), and revealing excessive perineural scar tissue in chronic cases (4 of 5 patients). A study of 18 patients with various iatrogenic nerve injuries involving the spinal accessory, radial, ulnar, or femoral nerves reported similar success.

**Figure 6: Radial nerve stump neuroma**

Patients who remain symptomatic after peripheral nerve exploration and surgical intervention present a special challenge for clinicians. Although delayed recovery is expected, early identification graft discontinuity, nerve encasement by scar tissue, or neuroma formation may prompt surgical revision and potentially improve patient outcomes. A study of patients status-post primary repair of transected median, ulnar, and/or radial nerves (19 patients, 26 nerves) with persistent symptoms, evaluated the utility of serial ultrasound to identify neuroma formation, nerve discontinuity, fascicular alignment, and compression by scar formation. Assessment was inhibited by excessive scar formation in 4 of 19 patients, which was the main limiting factor. Of the 11 patients (13 nerves) undergoing reoperation, findings on US were confirmed in most cases, and were found to be particularly useful in identifying neuroma formation (11 of 13 confirmed surgically).
Brachial Plexopathy

A number of excellent reviews have been published describing the ultrasonographic evaluation of the brachial plexus,(61-64) and the utility of ultrasound in plexus trauma, tumor identification (primary and metastatic), and radiation fibrosis have been described.(65) Although the brachial plexus sonology is technically feasible, it can be challenging even for an experienced examiner, and thus will likely remain a useful primarily in guiding anesthetic procedures, and as a diagnostic adjunct to MRI.

Peripheral Polyneuropathy

Application of ultrasound has been described in both hereditary and acquired and neuropathies, as well as in neuropathy associated with leprosy.(66) The most common finding in the peripheral polyneuropathies studied to date is a diffuse increase in nerve cross sectional area (CSA). However, the specificity of this findings is not known, and more studies are needed.

In chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), one study demonstrated larger C5 and C6 nerve root diameters in 9 of 13 CIDP patients (69%) versus normal control patients (n=35), and found nerve root size correlated with CSF protein levels.(67) A separate case report of a patient with CIDP detailed symmetric increases in brachial plexus size, as well as increased median, sciatic, and femoral nerve diameter, sparing the tibial and vagus nerves.(68)

Findings have also been described in multifocal motor neuropathy (MMN) (Figure 7). Multiple sites of nerve enlargement were identified in 21 MMN patients, including lesions affecting nerves which were both clinically and electdiagnostically normal, suggesting the disease is more widespread than the traditional assessment would indicate.(69) Another study showed that ultrasound is as sensitive as MRI for identifying focal enlargement within brachial plexus in MMN,(70) supporting its usefulness for identifying proximal lesions difficult to assess with nerve conduction studies.

Among hereditary neuropathies, comparison of the median nerve at the forearm in genetically-confirmed Charcot-Marie-Tooth (CMT) disease versus controls revealed significantly larger CSA and fascicular diameter (FD) in CMT, and found that patient with CMT 1A (n=12) had a mean CSA and FD double CMT 2 (n=7) and CMT type X (n=5) patients.(71) A case report of a patient with hereditary neuropathy with liability to pressure palsies revealed diffuse enlargement of peripheral nerves, and a disproportionate increase in CSA at entrapment sites.(72) These findings raise the possibility of using ultrasound as a screening tool in asymptomatic family members of kindreds affected by hereditary neuropathies, to assist genetic counseling and to direct definitive testing.

ULTRASOUND OF MUSCLE

Normal Muscle

The appearance of normal muscle in short-axis is relatively echolucent (dark) and is divided by hyperechoic streaks representing supporting fibrous tissue (Figure 8). In long-axis (Figure 9), hyperechoic fascial lines typically form either a parallel or pennate configuration. Muscles can vary considerably in size, depth, and echogenicity, dependent on many factors including age.

Subcutaneous fat can be identified superficial to muscle as a more echolucent and compressible layer, typically containing irregular septa of connective tissue. Tendons become more obvious closer to muscle origin and insertion, and are differentiated from muscle by tightly packed fibrils, gliding movements with muscle activation in
long-axis, and anisotropy (described above). Bone is easily identified by its profound echogenicity (very bright) and by the shadowing of deeper layers of tissue.(1)

**Figure 8**: Normal biceps muscle in short-axis

**Figure 9**: Normal biceps muscle in long-axis

**Muscle Pathology**

Ultrasound has been used for many years to identify muscle rupture, trauma, and hematoma as well as soft tissue neoplasms and infections affecting the musculoskeletal system. Involuntary muscle movements, including fasciculations, can also be observed with a sensitivity rivaling the needle electrode examination due to a large sampling area of ultrasound.(73-75) Muscle ultrasound has also been suggested to be useful for selecting the optimal muscle for biopsy in order to avoid sampling error due to focal muscle involvement.(76)

Using ultrasound to diagnose muscle diseases of interest to neurologists, is a more recent phenomenon which continues to gain acceptance. An excellent review of the literature was recently published.(77) An overview of ultrasound in muscle disease is provided below.

Neuromuscular disorders impact muscle morphology, which can be visualized on ultrasound. Atrophy, fatty infiltration, and fibrous tissue changes increase muscle echogenicity over time. The "brightness" of a muscle on ultrasound is referred to as echo intensity, which increases with normal aging and disproportionately in pathological states. A visual echo intensity grading scale has been described,(78) although interobserver agreement is suboptimal. To address the shortcomings of subjective visual rating scales, quantitative methods of measuring echo intensity using computer-assisted gray-scale analysis have been developed. The quantitative method is objective and more accurate for differentiating normal from abnormal muscle.(79) In order to facilitate reproducibility across different imaging platforms, ideal standards for machine configuration, calibration, probe positioning, and selection of the region-of-interest have been studied.(80) This technique has become a powerful research tool, and as reproducibility is confirmed and more widespread experience is gained, it will likely come into more common clinical practice.

Ultrasound findings predictive of various types neuromuscular disorders have been proposed, based on specific muscles affected, relative changes in muscle thickness, patterns of increased echo intensity within muscle, and the presence or absence of fasciculations or other involuntary movements. For example, focal and asymmetric increases in muscle echo intensity and more marked atrophy on ultrasound have been described in inclusion body myositis when compared with other inflammatory myopathies.(81) This same study suggested a sensitivity of muscle ultrasound in detecting histopathologically proven disease of 83%, which was not significantly different from electromyography or serum creatine kinase activity. Prospective studies in children showed neuromuscular disorders can be detected with a sensitivity of 67-81% and a specificity of 84-92% using visual evaluation of muscle echo intensity, and quantitative methods further improve sensitivity to the 87-92% range.(77) Overall, the high sensitivity for identifying muscle disease, combined benefits of a well tolerated, low cost procedure, suggest a bright future for ultrasound, going forward.
REFERENCES


8. Nazarian LN. The top 10 reasons musculoskeletal sonography is an important complementary or alternative technique to MRI. AJR Am J Roentgenol 2008;190:1621-1626.


