Detection of peripheral nerve pathology

Comparison of ultrasound and MRI

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ABSTRACT

Objective: To compare accuracy of ultrasound and MRI for detecting focal peripheral nerve pathology, excluding idiopathic carpal or cubital tunnel syndromes.

Methods: We performed a retrospective review of patients referred for neuromuscular ultrasound to identify patients who had ultrasound and MRI of the same limb for suspected brachial plexopathy or mononeuropathies, excluding carpal/cubital tunnel syndromes. Ultrasound and MRI results were compared to diagnoses determined by surgical or, if not performed, clinical/electrodiagnostic evaluation.

Results: We identified 53 patients who had both ultrasound and MRI of whom 46 (87%) had nerve pathology diagnosed by surgical ($n = 39$) or clinical/electrodiagnostic ($n = 14$) evaluation. Ultrasound detected the diagnosed nerve pathology (true positive) more often than MRI (43/46 vs 31/46, $p < 0.001$). Nerve pathology was correctly excluded (true negative) with equal frequency by MRI and ultrasound (both 6/7). In 25% (13/53), ultrasound was accurate (true positive or true negative) when MRI was not. These pathologies were typically (10/13) long (>2 cm) and only occasionally (2/13) outside the MRI field of view. MRI missed multifocal pathology identified with ultrasound in 6 of 7 patients, often (5/7) because pathology was outside the MRI field of view.

Conclusions: Imaging frequently detects peripheral nerve pathology and contributes to the differential diagnosis in patients with mononeuropathies and brachial plexopathies. Ultrasound is more sensitive than MRI (93% vs 67%), has equivalent specificity (86%), and better identifies multifocal lesions than MRI. In sonographically accessible regions ultrasound is the preferred initial imaging modality for anatomic evaluation of suspected peripheral nervous system lesions. *Neurology*® 2013;80:1634-1640

Nerve imaging augments patient management by providing information regarding lesion morphology, anatomic location, relationship of lesions to surrounding soft tissue, and evaluation of areas difficult to evaluate by electrodiagnostic testing. Imaging can also identify peripheral nerve lesions that are not apparent on electrodiagnostic testing. Types of peripheral nerve abnormalities suited to visualization by imaging include changes in nerve caliber, continuity, and echogenicity or magnetic resonance signal characteristics.¹⁻³ Imaging can identify peripheral nerve tumors, traumatic neuromas, lacerations, entrapments with nerve damage, inflammation, demyelinating features, and infections.⁴⁻¹⁵ Ultrasound and MRI are the most commonly used methods for visualizing peripheral nerves. Ultrasonography of nerve lesions impacts management beyond the electrodiagnostic findings in as many as 43% of patients¹⁶ and, by identifying nerve continuity, can change surgical decisions after traumatic neuropathies.¹⁷ MRI visualizes nerves, characterizes soft tissue structures when evaluating atypical sites of compression, identifies features of malignancy in peripheral nerve tumors, and provides information on the presence of muscle denervation and atrophy.^{11,12,18} MRI can describe nerve lesions in areas that are difficult to localize using electrodiagnostic studies^{8,19,20} or visualize using ultrasound. Depending on the specific clinical question, MRI or ultrasound can be a peripheral nerve imaging modality of choice.^{4,6,16,21} In this retrospective study of 53 patients with clinical/pathologic diagnoses of

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peripheral nerve lesions other than ulnar or median nerve entrapments, we compared the accuracy of ultrasound and MRI evaluations.

METHODS We retrospectively searched our database of 849 patients referred for neuromuscular ultrasound from June 2007 to October 2011. We excluded patients referred with only idiopathic carpal tunnel syndrome, ulnar neuropathy at the elbow, hereditary neuropathies, acquired inflammatory polyneuropathies, or idiopathic peripheral neuropathies. We reviewed charts of 145 patients evaluated for suspected brachial plexopathy or single or multiple mononeuropathies. Of these, we identified 53 patients who had MRI studies of the same limb and for the same indication as the ultrasound. Diagnosis was based on surgical exploration or histopathology or, if no surgery was performed, the presence or absence of localized nerve pathology was determined by the clinical and electrodiagnostic evaluation (table 1). The sensitivity (test positive/total positive) and specificity (test negative/total negative) of ultrasound and MRI was determined by comparing the reported imaging findings to the diagnostic standard. Imaging studies that were either true-positive or true-negative were termed accurate. Images from

inaccurate (false-positive or false-negative) ultrasound and, if available, MRI cases, were reviewed by C.M.Z. (ultrasound) and J.C.B. (MRI). Results of this review are reported but were not utilized to determine sensitivity and specificity because only images of select cases were reviewed. Nerve pathology identified by MRI or ultrasound was typically based on qualitative abnormalities in nerve size, contour, and abnormal signal characteristics.

Multifocal pathology of nerves, defined as more than one discrete abnormality in either the same or multiple nerves in a limb, was identified based on the review of the ultrasound and MRI reports. In these cases, a diagnostic gold standard for each of the multiple lesions identified with ultrasound or MRI was not achievable. We limited sensitivity and specificity analysis of ultrasound and MRI to a single lesion in each patient, identified by surgical exploration. We also report the ultrasound and MRI findings of cases with multifocal pathology and inferred the pathologic cause for each lesion from the histopathologic findings from another lesion in the same patient or the clinical, electrodiagnostic, and radiographic findings.

All ultrasound examinations were performed by C.M.Z. using Philips HD11xe or iU22 ultrasound systems with a linear L12-5 or L17-5 transducer. MRI, performed at multiple imaging centers, included multiplanar and multisequence protocols

Table 1 Subjects with diagnosis determined by clinical or electrodiagnostic findings

Patient no.	Clinical findings	Electrodiagnostic findings	MRI	Ultrasound
16	Unilateral hand weakness and remote history of trauma	Brachial plexopathy affecting medial cord or lower trunk	False-negative: normal brachial plexus	True-positive: enlargement of lower trunk
17	Foot drop after knee replacement surgery	Sciatic neuropathy	False-negative: normal sciatic nerve	False-negative: normal peroneal, tibial, and poorly visualized sciatic nerve
21	Bilateral foot drop, right worse than left	Asymmetric axonal peripheral neuropathy, right worse than left	True-negative: no nerve abnormalities; muscle denervation suggestive of peripheral neuropathy	True-negative: no focal nerve abnormalities; slightly reduced nerve size in right compared to left leg possibly from axon loss
23	Acute foot drop and pain after trauma while running	Peroneal neuropathy	True-positive: intramuscular hematoma at fibular neck	True-positive: intramuscular hematoma abutting peroneal nerve at fibular neck
25	Leg pain and weakness	Sciatic neuropathy	True-positive: enlarged, enhancing proximal sciatic nerve	True-positive: enlarged and hyperechoic proximal sciatic nerve
28	Idiopathic unilateral foot drop	Peroneal neuropathy	True-positive: enlargement, edema, and enhancement in peroneal nerve at fibular neck	True-positive: hypoechoic signal and mild enlargement in peroneal nerve at fibular neck
29	Neurofibromatosis Type 1, prior resections of intraneural neurofibromas, complains of axillary mass that when palpated causes dysesthesia in the hand	Not performed	False-negative: normal nerves in the axilla	True-positive: mass in median nerve in axilla
36	Calf weakness	Partial tibial neuropathy	False-negative: normal tibial and sciatic nerve	True-positive: enlarged tibial nerve and tibial portion of sciatic nerve
38	Idiopathic unilateral foot drop and leg weakness	Lumbosacral plexopathy	False-negative: normal plexus and sciatic nerve	True-positive: enlarged, hypoechoic proximal sciatic nerve (gluteal level)
42	Progressive hand numbness in digits 1-3	Proximal median neuropathy	False-negative: normal median nerve	True-positive: enlargement of proximal median nerve
47	Rheumatoid arthritis and enlargement of distal volar forearm, normal strength and sensation	Not performed	True-negative: flexor tenosynovitis	True-negative: flexor tenosynovitis
51	NF1 and progressive unilateral hand weakness and numbness	Cervical radiculopathy	True-positive: cervical radiculopathy with nerve root enlargement	True-positive: cervical nerve root enlargement and multifocal nerve enlargements in median and ulnar nerve
52	Wrist drop and hand numbness after gunshot wound	Radial neuropathy	False-negative: no nerve abnormalities	True-positive: enlargement of radial and median nerves at site of penetrating trauma
53	Hand numbness	Cervical radiculopathy of nerve root 5 or 6	False-negative: normal cervical roots and plexus	True-positive: focal enlargement of C5 root suggestive of peripheral nerve tumor

and most ($n = 36$) included IV contrast. All clinical, surgical, electrodiagnostic, or pathologic evaluations were performed at Washington University in St. Louis. Examiners were not blinded to the clinical findings or results of other diagnostic tests. Neither images nor the reports from the first performed imaging study (MRI or ultrasound) were reviewed prior to acquiring/interpreting the second imaging study (ultrasound or MRI). Tumor size was determined by the largest linear (width, height, or length) measurement from the ultrasound or MRI. For identifying the location of pathology, the popliteal fossa was included with the leg rather than the thigh, and the antecubital fossa was included with the forearm.

The study was approved by the Washington University Institutional Review Board. All results are mean (SD) unless otherwise specified. Normal distributions were assessed using the Kolmogorov-Smirnov test. Continuous variables were compared with a 2-tailed paired t test for parametric or a related sample Wilcoxon signed rank test for nonparametric data and proportions were compared with McNemar test²² using VassarStats.net and PASW statistics version 18.

RESULTS The 53 patients ranged in age from 1 to 78 years. A total of 25 were male. Diagnosis was determined by surgical evaluation in 39 (74%), by clinical and electrodiagnostic examination in 12 (23%), and by clinical examination only in 2 (4%) (table 1). In

patients who underwent surgery, the time interval between imaging and surgery was less for ultrasound than MRI (50 vs 125 days, $p < 0.001$). In patients who did not undergo surgery, the time interval between imaging and the clinical/electrodiagnostic evaluation was similar between ultrasound and MRI (11 vs 29 days, $p = 0.05$). The MRI examination preceded the ultrasound in 30/53 (57%) subjects.

Pathology involving the nerve was diagnosed in 46 patients (87%) and excluded in 7 (13%, figure 1). Diagnoses included peripheral nerve sheath tumors ($n = 18$), traumatic ($n = 10$) or idiopathic ($n = 8$) mononeuropathy/plexopathy, fibrosis ($n = 4$), compression by ganglion/synovial cysts ($n = 4$) or other soft-tissue structures ($n = 3$), non-nerve soft tissue tumor ($n = 3$), intraneural granuloma ($n = 1$), vasculitis ($n = 1$), and foot drop due to asymmetric peripheral neuropathy ($n = 1$). Nerve pathology ($n = 46$) was large (>2 cm) in 34 (74%), small (<1 cm) in 3 (7%), between 1 and 2 cm in 7 (15%), and not measured in 2 (4%). Pathologies (single and multiple) were detected in the brachial plexus/axilla ($n = 7$), arm ($n = 9$) and forearm ($n = 10$), thigh ($n = 9$), and leg ($n = 13$).

Figure 1 Flow diagram of study design and results

US = ultrasound.

Ultrasound detected lesions more frequently than MRI (43/46 vs 31/46; sensitivity 93% vs 67%; $p < 0.001$, 2-tailed McNemar) and excluded nerve pathology equally to MRI (6/7; specificity both 86%). Ultrasound was accurate in more cases (49/53 [93%]) than MRI (37/53 [70%], $p = 0.002$, 2-tailed McNemar) (table 2). In 13 (25%) cases, ultrasound accurately identified pathology that was either not seen, or incorrectly identified, on MRI. Pathology accurately identified on ultrasound but not MRI included enlarged nerves ($n = 8$), peripheral nerve sheath tumor ($n = 3$), compression by anomalous muscle ($n = 1$), and a hemangioma ($n = 1$). The hemangioma was incorrectly identified as being likely intraneural pathology (peripheral nerve sheath tumor) on MRI but was correctly identified as an extraneural soft tissue mass on ultrasound. Pathology accurately identified on ultrasound but not MRI was often (10/13 [77%]) larger than 2 centimeters and in each of these, the long axis

(in plane with the long axis of the nerve) was the largest linear dimension. Pathology missed on MRI but not ultrasound was only occasionally (2/13; 15%) outside the field of view of the MRI study. In the 13 cases with accurate ultrasound but not MRI, there was no difference in the interval from the time of diagnosis to the ultrasound or MRI ($p = 0.08$).

In 11 patients with inaccurate MRI (of 16 total), all false-negative, imaging using a 1.5 T magnet was performed and interpreted at Washington University Medical Center and was available for review. Review resulted in accurately identified nerve pathology in 6 (54%), each of which had an accurate ultrasound. Review of all 4 inaccurate ultrasound images did not result in any revisions.

Multifocal pathology was identified only by ultrasound in 6 cases and by both MRI and ultrasound in one case (table 3). Multifocal pathology identified on ultrasound was outside the field of view of the MRI in most (5/7; 71%) cases.

Table 2 Seventeen patients with inaccurate MRI or ultrasound findings

Patient no.	Neuroimaging findings of peripheral nerve			Surgical evaluation	Lesion size, cm	Location	Nerve
	Ultrasound	MRI	Diagnosis				
3	Normal ^a	Normal ^a	Neuroma	Yes	<1	Distal arm	Medial antebrachial cutaneous
6	Normal ^a	Normal ^a	Postradiation fibrosis	Yes	Not measured	Neck	Brachial plexus
10	Compression by anomalous abductor digit minimi	No mass identified ^{a,b}	Anomalous muscle	Yes	>2	Wrist	Ulnar
16	Enlarged, hypoechoic	Normal ^a	Traumatic neuroma	No	>2	Neck	Lower trunk, brachial plexus
17	Normal ^a	Normal ^a	Traumatic neuropathy	No	Not measured	Proximal leg	Sciatic
24	Disrupted fascicles ^a	Normal	Traumatic plexopathy, no gross abnormality in nerve identified	Yes	Not measured	Proximal arm	Ulnar
29	Defined, focal enlargement consistent with tumor	Normal ^a	Neurofibroma (patient has neurofibromatosis and prior resections of neurofibromas)	No	1-2	Axilla	Median
32	Defined, focal enlargement consistent with tumor	Normal ^a	Neurofibroma	Yes	>2	Axilla	Ulnar/medial cord
36	Enlarged, hypoechoic	Normal ^{a,c}	Idiopathic neuropathy	No	<1	Proximal leg	Tibial
38	Enlarged proximal sciatic nerve	Normal ^a	Idiopathic sciatic/lumbosacral plexopathy	No	>2	Proximal leg	Sciatic
40	Defined area of intraneural fascicular enlargement, tumor	No mass identified ^{a,b}	Intraneural caseating granuloma	Yes	<1	Distal arm	Median
42	Enlarged	Normal ^a	Idiopathic neuropathy	No	>2	Proximal arm	Median
45	Enlarged throughout arm	Entrapment, elbow ^a	Vasculitis	Yes	>2	Proximal and distal arm	Ulnar
48	Enlarged	Normal ^a	Traumatic neuropathy	Yes	>2	Proximal leg	Tibial
49	Soft-tissue mass abutting but not arising from nerves	Nerve sheath tumor ^a	Hemangioma	Yes	>2	Proximal arm	Near ulnar/medial antebrachial cutaneous
52	Enlarged, hypoechoic	Normal ^a	Traumatic neuropathy	No	>2	Proximal arm	Radial
53	Defined, focal enlargement consistent with tumor	Normal ^a	Idiopathic neuropathy	No	>2	Neck	C5 root, upper trunk

^a Inaccurate findings.

^b Outside the field of view of the MRI.

^c Lesion identified by magnetic resonance neurography.

Table 3 Multifocal nerve pathology: Ultrasound and MRI

Patient no.	Lesion location	Nerve	Detected by ultrasound	Detected by MRI	Pathology
12	Distal forearm	Median	Yes	Yes	Schwannoma
	Proximal arm	Ulnar	Yes	No ^a	Schwannoma
15	Proximal arm	Median	Yes	Yes	Schwannoma
	Elbow	Ulnar	Yes	No ^a	Entrapment
	Wrist	Median	Yes	No ^a	Entrapment
37	Proximal arm (right)	Ulnar	Yes	Yes	Fibrotic thickening
	Distal arm (right)	Ulnar	Yes	No ^a	Fibrotic thickening
	Proximal arm (left)	Ulnar	Yes	Yes	Fibrotic thickening
	Distal arm (left)	Median	Yes	No ^a	Fibrotic thickening
41	Proximal/distal arm	Multiple	Yes	Yes	Schwannomatosis
44	Proximal arm	Radial	Yes	Yes	Traumatic neuroma
	Wrist	Median	Yes	No ^a	Entrapment
51	Distal arm	Median	Yes	No ^a	Neurofibroma
	Distal arm	Ulnar	Yes	No ^a	Neurofibroma
	Wrist	Median	Yes	No ^a	Entrapment
	Proximal arm	Ulnar	Yes	No	Neurofibroma
	Axilla	Median	Yes	No	Neurofibroma
	Axilla	Ulnar	Yes	No	Neurofibroma
	Neck	Plexus	Yes	Yes	Neurofibroma
	Proximal arm/axilla	Radial	Yes	No	Traumatic neuroma
52	Proximal arm/axilla	Median	Yes	No	Traumatic neuroma

^a Outside the field of view of the MRI.

DISCUSSION In this retrospective study of patients with mononeuropathies or brachial plexopathies, ultrasound of accessible regions detected neuropathology more frequently ($p < 0.001$) than MRI. Ultrasound was more sensitive (93% vs 67%), similarly specific (86%), and identified more multifocal nerve pathologies than MRI. The greater sensitivity of ultrasound than MRI is not likely due to differences in the timing of the 2 studies. We found no difference in the time intervals between imaging and diagnosis in patients with inaccurate MRI but not ultrasound. A superior or additive sensitivity of ultrasound to MRI is supported by previous reports of positive sonographic imaging identifying peripheral nerve lesions not detected by MRI or electrodiagnostic testing.⁷ The sensitivity of MRI for detection of peripheral nerve tumors in our study (67%) is similar to a prior study (75%).²³ Based on these findings, we recommend ultrasound as opposed to conventional MRI as the preferred initial imaging modality for radiologic evaluation of suspected peripheral nervous system lesions (figure 2).

Nerve pathology can be difficult to read on MRI even at a tertiary care center with experienced examiners. Eleven of the inaccurate MRI studies were

performed at our tertiary care center and read by radiologists with expertise in MRI of the nervous/musculoskeletal system. The nerve pathology found on ultrasound was ultimately identified in over half (54%) of the “false-negative” MRI after re-review with our musculoskeletal radiologist.

Prospective, blinded studies will determine the comparative accuracy, sensitivity, and specificity of ultrasound and MRI in detecting different types of peripheral nerve lesions. Our retrospective study included a high proportion of patients with nerve lesions (87%). This frequency could be due to ascertainment bias and likely does not represent all patients with suspected mononeuropathies/brachial plexopathies. Diagnosis in this study was determined by either surgical confirmation or clinical/electrodiagnostic findings, which may not detect all pathologies. However, the high proportion of patients in this study with nerve lesions and low number of false-positive results from imaging argues against a high rate of unidentified pathology. Although the images and reports of the MRI studies were not reviewed prior to performing or interpreting the ultrasound study, examiners were not blinded to the results of other diagnostic tests. This could have affected the imaging results. Our

Figure 2 Suggested diagnostic pathway for peripheral nerve imaging

study also compares results of several radiologists and imaging techniques/equipment to one neuromuscular sonographer (C.M.Z.) and cannot evaluate the effects of examiner expertise on accuracy of ultrasound. MRI techniques optimized for nerve imaging, such as magnetic resonance neurography and diffusion tractography, and use of higher strength magnets, may improve MRI for evaluation of peripheral nervous system lesions.^{20,24–26} One patient in our study (patient 36) had normal conventional MRI but, following an abnormal ultrasound study, had identification of the lesion using magnetic resonance neurography. Additional studies are required to determine how newer MRI methodologies compare to high-resolution ultrasonography for evaluation of peripheral nerve pathology.

MRI and ultrasound each have unique advantages and limitations for imaging nerve pathology. Advantages

of ultrasound over MRI for detecting peripheral nerve pathology include lower cost, rapidity of examination, higher spatial resolution, imaging of the nerve in continuity (without slicing), and ease of side-to-side comparisons. Ultrasound may better detect subtle changes in nerve caliber. This is important because peripheral nerve pathology is often fusiform in shape and can extend along the length of the nerve without greatly altering its cross-section area. In our study, all pathologies greater than 2 centimeters that were missed with MRI but not ultrasound were largest along the length (long axis) of the nerve. Advantages of MRI over ultrasound include superior contrast between tissues, imaging of structures that are deep or surrounded by bone, and tissue characterization using multisequence analysis and IV contrast. The superior tissue characterization with MRI may affect differential diagnosis. For instance, a prior study of lepromatous neuropathy found that although MRI and ultrasound were equivalent for detecting lesions, MRI was superior in determining which were active.²⁷ Finally, neither ultrasound nor MRI can detect pathology that is outside the field of view. We found that MRI frequently missed multifocal (71%) and occasionally single pathologies identified with ultrasound because lesions fell outside the area visualized by the MRI study. To maximize the advantages and minimize the limitations of each imaging modality, we generally recommend a stepwise approach of ultrasound followed by MRI for evaluating peripheral nerves (figure 2). Exceptions to this rule include evaluation of suspected lesions in areas that are poorly visualized by ultrasound, including nerves that lie very deep or beneath bone (i.e., radiculopathy/root avulsion, subclavicular brachial plexus, proximal sciatic nerve, lumbosacral plexus).

In conclusion, imaging with MRI or ultrasound frequently detects pathology in and informs the differential diagnosis of suspected mononeuropathies and plexopathies. Ultrasound is more accurate than conventional MRI for evaluating suspected peripheral nervous system lesions and identifying multifocal pathology. As ultrasound is less expensive than MRI and can be performed at the bedside, we recommend it for the initial radiographic evaluation of nerves as a routine adjunct to the clinical and electrodiagnostic evaluation. In certain instances, MRI may confer additional diagnostic advantages to ultrasound such as improved tissue characterization and imaging of deep or bone-encased structures. Interpretation of both MRI and ultrasound of peripheral nerves requires availability of clinical differential diagnoses (possible lesion location) and experience in performing studies.

AUTHOR CONTRIBUTIONS

Dr. Zaidman: study concept and design, acquisition of data, interpretation, and critical revision of manuscript. Michael Seelig: acquisition of data, interpretation, and critical revision of manuscript. Dr. Baker: acquisition of data,

interpretation, and critical revision of manuscript. Dr. Mackinnon and Dr. Pestronk: data interpretation and critical revision of manuscript.

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C. Zaidman received salary support (5%) from NIH R01AR060850-01A, provided expert witness testimony, and performs clinical imaging as part of his practice. M. Seelig reports no disclosures relevant to the manuscript. J. Baker is a research consultant for Biomedical Systems, provided expert witness testimony, and performs clinical imaging as part of his practice. S. Mackinnon reports no disclosures relevant to the manuscript. A. Pestronk receives revenue related to antibody patent licenses from Athena; owns stock in Johnson & Johnson; directs the Washington University Neuromuscular Clinical Laboratory, which performs antibody testing; and receives research support from the NIH, Muscular Dystrophy Association, Neuromuscular Research Fund, Inmed, Knopp, Cytokines, Biogen Idec, ISIS, Genzyme, GSK, Ultragenyx, and Sanofi. Go to Neurology.org for full disclosures.

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