Research Square

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Nerve Ultrasound Detects Segmental Peripheral Nerve Variability in Friedreich Ataxia

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Abstract

Introduction/Aims: Friedreich's ataxia (FRDA) is the most common inherited ataxia and is caused by GAA repeat expansions in the *FXN* gene. With the emergence of disease-modifying therapy, structural biomarkers are increasingly needed. This study aimed to assess peripheral nerve cross-sectional area (CSA) in FRDA using high-resolution ultrasound to replicate and further characterize previously described ultrasonographic abnormalities.

Methods: Ten FRDA patients underwent clinical evaluation with established scales (mFARS, FA-ADL, FARS-staging), nerve conduction studies, and standardized ultrasound of the median, ulnar, tibial, fibular, and sural nerves bilaterally.

Results: Among 10 patients, ultrasound abnormalities were present in all (100%). Nerve enlargement was observed in every patient, occurring exclusively in the upper limbs (median and ulnar nerves), predominantly involving the median nerve at the upper arm (90%) and axilla (90%). Reduced CSA consistent with focal atrophy was identified in 50% of patients and was restricted to the upper limbs, most commonly at the forearm level of the median and ulnar nerves (20% each). Lower-limb nerves showed no significant CSA changes. Coexistence of enlargement and atrophy at different segments occurred in 50% of patients.

Discussion: Peripheral nerve ultrasound detects segmental peripheral nerve size abnormalities in FRDA, characterized by the coexistence of focal enlargement and atrophy across different nerve segments. Further longitudinal studies are needed to clarify its potential role in disease characterization and monitoring.

1. INTRODUCTION

Friedreich's ataxia (FRDA) is an autosomal recessive, multisystemic degenerative hereditary disorder that represents the most prevalent inherited ataxia in the world.[1,2] The recent approval of omaveloxolone represents a breakthrough in the pharmacological management of FRDA, offering the first disease-modifying therapy for this condition.[3] In this context, the investigation of biomarkers in FRDA has become vital for insights into disease activity and progression.[4,5]

Peripheral nerve ultrasound has gained attention as a non-invasive imaging modality capable of characterizing nerve involvement in hereditary ataxias.[6–10] Previous studies revealed variable degrees of peripheral nerve enlargement in FRDA[7,8,11] and, more recently, evidence of nerve atrophy,[9] with inconsistent associations between structural findings and clinical severity.[7–9] Current evidence remains limited to a small number of cohorts, and external replication across geographically diverse populations is still lacking. The aim of this study was to evaluate peripheral nerve morphology in FRDA using high-resolution ultrasound, with particular emphasis on segmental patterns of nerve enlargement and atrophy, to replicate and expand upon previously reported[7–9] findings in a Brazilian cohort.

2. METHODS

2.1 Participants

This prospective observational cohort study included 10 patients with FRDA evaluated between January and August 2025. Inclusion criteria included a confirmed genetic diagnosis, completion of standardized clinical scales, nerve ultrasound, nerve conduction studies (NCS) protocol, and no age restriction. Exclusion criteria included coexisting conditions potentially confounding peripheral nerve size, such as known inflammatory neuropathy, prior upper-limb entrapment surgery, or incomplete assessments. The clinical assessment included the collection of demographic data and a comprehensive neurological examination. Neurological severity was assessed using the modified Friedreich's Ataxia Rating Scale (mFARS)[12], which provides a total score ranging from 0 (no ataxia) to 93 (severe ataxia). In this study, we used the Activities of Daily Living part of the Friedreich Ataxia Rating Scale (FARS-ADL)[13], which is a patient-reported outcome measure (PROM) that assesses impairment in daily activities with scores ranging from 0 (normal function) to 36 (severe functional disability). Global disease stage was determined according to the Friedreich's Ataxia Staging (FA-Stage)[14], system, which classifies patients into stages based on ambulatory capacity, ranging from stage 0 (no neurological symptoms) to stage 6 (total disability and dependence). All participants gave informed consent. The study was approved by the Ethics Committee of the Federal University of Ceará under protocol number 6.945.762.

2.2 Genetics

FXN gene analysis was performed using polymerase chain reaction (PCR) and capillary electrophoresis to investigate the trinucleotide repeat region at Mendelics Genomic Analysis (São Paulo, Brazil), a clinical laboratory improvement amendments (CLIA)-certified laboratory. This method allows the detection of expanded alleles with an approximate variability of ± 1 repeat.

2.3 Ultrasound and Electrophysiology

A nerve ultrasound protocol evaluating peripheral nerve was used as previously published in our group.[10] In summary, ultrasound was performed by a single operator (A.E.C.) with experience in neuromuscular ultrasound with a high-resolution probe (6–15 MHz linear probe, LOGIQ 9 GE Healthcare, Chicago, IL, USA) of easily accessible peripheral nerves on both sides. Each nerve was systematically evaluated along its entire course bilaterally, and CSA measurements were obtained at predefined landmarks[8,10] in the median nerve at the wrist, midforearm, cubital fossa, mid-humerus, and axilla, ulnar nerve at midforearm, mid-humerus, and axilla, sural nerve at the distal calf, fibular nerve at the fibular head, and tibial nerve at the popliteal fossa. Additionally, FRDA patients underwent NCS performed under standard conditions using a Litebox workstation (Neurosoft, Ivanovo, Russia), including motor (median, ulnar, fibular, and tibial) and antidromic sensory (median, ulnar, superficial radial, superficial fibular, and sural) conduction studies.

2.4 Statistics

Due to the small sample size and the exploratory nature of this study, formal statistical analyses were not conducted. Instead, the data were summarized using descriptive statistics, with individual values presented for each participant. CSA were compared with reference values and classified as pathologically small if they were below the reported lower bound of the 95% confidence interval.[9,15–19] .

3. RESULTS

Ten patients with FRDA were included in this study (clinical characteristics summarized in Table 1). Late-onset Friedreich's ataxia (LOFA) (onset >25 years) was identified in 2 patients (20%). The median age at the time of evaluation was 27.5 years (IQR, 22.5–46.75), with a predominance of males (male: female ratio, 7:3). The median disease duration was 14 years (IQR 8–28), while the median diagnostic delay was 7 years (IQR 6–13.5). Disease severity was most classified as FA stage 4 (moderate disability; n = 4), followed by stage 2 (n = 2), stage 3 (n = 2), stage 5 (n = 1), and stage 6 (n = 1). None of the included patients were undergoing disease-specific treatment at the time of evaluation.

Electrophysiological findings are presented in Table 2. Reduced or absent sensory nerve action potentials were found in all patients. In contrast, motor nerve conduction parameters were largely preserved.

Table 1. Clinical data in patients with Friedreich's ataxia.

Patient	Sex	Age (y)	Disease Onset (y)	Sensory neuropathy	mFARS	FA Stage	FA-ADL	Other system involvement
1	M	60	32	Yes	55	4	24	DMT2, CM
2	F	52	12	Yes	76.5	5	24	Optic Nerve atrophy, DMT2, CM
3	M	22	14	Yes	35	2	5	None
4	M	31	15	Yes	43.5	3	6	None
5	F	29	14	Yes	45.5	3	7	None
6	M	22	14	Yes	44.5	4	20	None
7	M	26	15	Yes	50	4	18	None
8	F	24	10	Yes	51	4	19	None
9	M	17	10	Yes	26.5	2	6	None
10	M	68	30	Yes	89	6	35	DMT2, Stroke

Abbreviations: CM, cardiomyopathy; DMT2, type 2 diabetes mellitus; F, female; FA-ADL, Friedreich Ataxia Rating Scale–Activities of Daily Living; FA-Stage, Friedreich Ataxia Stage; M, male; mFARS, modified Friedreich Ataxia Rating Scale.

Structural nerve size abnormalities were identified in all patients (Table 3). Nerve enlargement at one or more anatomical sites was observed in every patient (100%), most frequently involving the median nerve at the upper arm (9/10) and axilla (9/10). Nerve atrophy was identified in five patients and coexisted with enlargement at other anatomical sites. Reduced CSA was most common at the forearm level of the median (2/10) and ulnar nerves (2/10) and was accompanied by qualitative hypoechogenicity of the affected segments (Figure 1). Notably, Patient 3 exhibited segmental asymmetry of the ulnar nerve at the forearm, with atrophy on the right and enlargement on the left at the same anatomical level (Figure 1). No significant CSA changes were observed in the lower extremities, including the tibial, fibular, or sural nerves.

Table 2. Nerve conduction study findings in patients with Friedreich ataxia.

		1	2	3	4	5	6	7	8	9	
Motor Conduction Studies:	Median (R/L)	3.3/3.4 8.1/11.7	3.8/3.3 6.6/6.0	3.0/3.1 10.9/12.5	3.3/3.8 16.1/15.4	3.8/3.7 7.1/6.2	3.8/3.9 21.3/17.7	3.5/3.1 9.7/14.5	3.1/3.3 13.3/14.5	3.2/3.5	3 7
DL;		54.1/59.3	55.8/54.3	55.6/55.3	56.3/51.8	52.9/57.1	59.6/56.6	56.3/55.9	58.8/55.3	7.9/10.7	5
CMAP amplitude;										59.8/56.0	
MNCV;	Ulnar (R/L)	2.7/2.8 10.1/6.2	2.8/2.7 9.1/8.3	2.9/2.9 15.9/12.1	2.9/3.2 15.3/11.8	2.8/2.8 16.5/15.3	3.0/3.2 12.1/14.1	2.9/3.0 14.9/15.1	2.3/2.4 11.8/10.5	2.9/3.2	3 1
		56.8/54.4	54.1/52.5	58.4/56.0	54.1/53.5	63.2/60.1	55.1/58.1	53.7/59.3	61.1/57.1	12.6/12.0	5
										55.6/59.3	
	Tibial (R/L)	4.1/4.2 8.4/10.6	4.2/4.0 23.7/26.7	4.2/3.8 26.1/16.6	5.6/4.2 33.5/24.7	3.2/3.6 17.4/30.6	4.4/4.1 19.5/15.8	4.4/4.9 29.7/27.6	4.1/4.2 26.4/28.6	3.4/3.9 24.4/15.4	3 1
		43.3/47.3	43.3/47.3	44.8/48.8	46.9/49.7	49.3/45.3	45.3/45.9	46.9/45.3	44.8/48.0	45.7/47.6	4
F-wave (min latency)	Ulnar (R/L)	29.5/29.2	27.7/27.2	28.9/29.2	28.4/28.8	26.7/25.9	27.7/28.1	28.8/28.9	24.6/25.4	26.1/27.5	3
	Tibial (R/L)	52.8/51.6	49.6/49.2	49.8/50.8	50.1/51.1	48.9/47.5	50.1/50.4	50.3/50.9	48.4/49.1	50.1/51.2	5
Sensory Conduction Studies:	Median (R/L)	**8.8/10.6** 51.9/55.6	**4.6/6.2** 50.1/56.1	**5.0/4.4** 60.1/58.8	**2.5/2.8** 51.5/50.2	**2.2/5.5** 55.9/49.5	**10.1/9.0** 54.8/52.2	**5.0/3.1** 51.6/50.6	**11.3/9.8** 60.6/59.0	- / -	-
SNAP amplitude;	Ulnar (R/L)	**4.7/2.3** 50.4/52.7	**2.7/2.2** 54.6/52.7	- / -	- / -	**4.6/2.8** 54.6/52.8	**5.3/3.4** 51.2/49.6	- / -	**5.0/5.5** 55.3/55.0	- / -	-
SNCV	S. Radial (R/L)	**9.5/4.7** 61.0/59.1	**4.5/2.4** 55.4/56.0	**2.7/1.7** 56.1/54.0	**3.4/1.9** 55.6/51.1	**5.4/2.1** 54.6/52.8	**3.5/4.7** 55.7/51.4	**-/1.3** -/51.1	**11.7/6.5** 59.7/58.6	- / -	-
	Sural (R/L)	**4.3/3.4** 51.0/49.8	**- / -**	- / -	- / -	- / -	**2.3/2.4** 42.7/48.5	- / -	**5.7/5.9** 53.8/53.4	- / -	-
	S. Fibular (R/L)	- / -	- / -	- / -	- / -	- / -	**3.4/3.2** 49.0/45.0	- / -	- / -	- / -	-

Abbreviations: DL (Distal Latency), CMAP (Compound Muscle Action Potential, millivolts), MNCV (Motor Nerve Conduction Velocity, meters per second), S (Superficial), SNAP (Sensory Nerve Action Potential, microvolts), and SNCV (Sensory Nerve Conduction Velocity, meters per second). "-": No potential evoked. Bold numbers indicate abnormalities

Table 3. Peripheral Nerve Ultrasound Findings in Patients with Friedreich's Ataxia

Nerve CSA (mm^2) (Ref)	Pt. 1	Pt. 2	Pt. 3	Pt. 4	Pt. 5	Pt. 6	Pt. 7	Pt. 8	Pt. 9	Pt. 10
MN wrist (4.5-10)	8.2 / 8.1	6.6 / 5.3	8.6 / 8.6	5.2 / 7.6	7.3 / 5.4	7.5 / 5.4	5.7 / 5.7	6 / 5.3	6.5 / 5.4	4.7/ 2.1*
MN forearm (5.9-10)	**11.1** / 9.9	7.2 / 5.8*	9.9 / 9.9	9.2 / 8.7	6.7 / 9.8	**10.5** / 8.8	7.4 / 7.1	7.3 / 5.9	9.5 / 10	6.3 / 4.8*
MN Cf (8-12.5)	12.4 / **21.5**	10.6 / 11.5	11.4 / 10.6	11.1 / **14.7**	**12.6** / 10.9	**13.2 / 17.5**	**13.9 / 15.9**	11.3 / **13.2**	**15.7 / 13.9**	8.7 / **14.7**
MN upper arm (7.5-12)	**18.3 / 16.2**	9.8 / **12.1**	**25.8 / 35.2**	**15.5 / 13.2**	10.3 / 11.6	**15.6 / 13.2**	**13.7 / 13.1**	10.5 / **16.4**	**16.6 / 16**	**14.9** / 8.4
MN axilla (5.3-10.1)	**16.5** / **13.9**	**11.3 / 12.1**	**18.4 / 26.9**	**14.5 / 19.8**	**15.2** / **12.4**	**11.3** / **10.4**	**14.3 / 11.3**	6 / 8.2	**13.1 / 12.4**	**11.4** / 7.7
UN forearm (4.8-8.5)	8.4 / 6.6	6.8 / 6.5	4.7* **/ 10.2**	6.8 / 6.2	7.5 / **9.9**	6.9 / 5.8	3.8* / 6.5	5.1 / 6.8	8.4 / **9.4**	5.5 / 5.2
UN upper arm (5.1-9.5)	**12.9 / 13**	5.2 / 5.3	**19.1 / 18**	5.2 / 9.1	9.3 / **11.1**	**18.5 / 10.3**	**10.8** / 9.1	6 / 4.8*	**14.7 / 12.4**	7.8 / 7.7
UN axilla (3.8-8.6)	**10 / 10.7**	6.7 / 7.6	**12.1 / 19.9**	**13.8 / 12.9**	**9.8** / **12.2**	7.7 **/ 8.8**	6.7 / 6.2	6.7 / 5.2	**9.3** / **14.6**	6.8 / 6.2
TN popliteal (17.5-33f, 17.5-36m)	23.9 / 24.5	18 / 28.6	18 / 28.6	20.6 / 28.1	21.1 / 20.4	21.9 / 21.1	24.5 / 23.6	26.6 / 19.5	26.5 / 21.1	27.6 / 32.7
FN Fh (6.6-11.5)	8.7 / 7.1	7.4 / 7.8	7.4 / 7.8	7.1 / 8.5	6.7 / 8.4	9.7 / 7.9	8.8 / 9.7	6.6 / 6.7	8.2 / 8.3	6.9 / 7.8
SN (1.7-3.5)	1.6 */ 1.8	2 / 1.5*	2 / 1.5*	2 / 2.1	2.1 / 2.2	2.1 / 1.5*	2 / 2	2.3 / 2	1.9 / 1.8	1.6 */ 1.9

Note: Abnormal nerve enlargement is highlighted in bold; abnormal nerve atrophy is marked with an asterisk (*). Abbreviations: CSA, cross-sectional area; CF, cubital fossa; Fh, fibular head; FN, fibular nerve; MN, median nerve; SN, sural nerve; TN, tibial nerve; UN, ulnar nerve; f, female; m, male; n, number.

4. DISCUSSION

This study showed consistent structural abnormalities of peripheral nerves in individuals with FRDA. Nerve enlargement was the predominant finding, primarily affecting upper-limb nerves, with the median nerve at the upper arm and axilla being the most frequently involved segments. In contrast, no significant nerve enlargement was detected in the lower extremities, including the tibial, fibular, and sural nerves. In addition to nerve enlargement, reduced CSA consistent with focal nerve atrophy was identified in a subset of patients (50%) involving the median and/or ulnar nerves in the upper limbs, particularly at the forearm and wrist levels. Notably, a heterogeneous pattern of involvement was observed, including isolated nerve enlargement in 50% and combined nerve enlargement and atrophy in 50%. Isolated nerve atrophy was not observed.

Our findings replicate the abnormalities previously described by Grimm et al.[9], reinforcing the concept of a pleomorphic sonographic pattern in FRDA.[7] In addition, our study provides novel observations of reduced CSA of the median nerve at the wrist, anatomical sites that have not been systematically analyzed previously.[7-9] A notable finding was the segmental asymmetry of atrophic changes. None of the six nerves demonstrating significant atrophy showed contralateral involvement at the same level. In one patient (Pt3), atrophy and enlargement affected the same ulnar nerve segment at the forearm on opposite sides (Figure 1). This observation highlights the importance of systematic bilateral assessment, as unilateral evaluation may underestimate structural heterogeneity in FRDA.

The biological basis of this variable pattern remains incompletely understood. Proposed mechanisms include frataxin-related myelin instability[20] and possible Schwann cell involvement, potentially leading to structural remodeling through de- and remyelination[21]. Grimm et al. suggested that cycles of degeneration and attempted regeneration across different nerve segments may account for the coexistence of nerve enlargement and atrophy in FRDA.[9] Somatic mosaicism in FRDA could hypothetically also contribute to segmental or asymmetric patterns of involvement; however, this remains speculative.[21,22]

This study has some limitations. The small sample size reduces statistical power, limiting the ability to explore associations between nerve CSA and clinical severity. In our cohort, FRDA was confirmed by PCR-based detection of GAA repeat expansion; however, repeat length was not quantified. Consequently, direct comparison with large international series—where median GAA expansions frequently exceed 500–700 repeats[23]. —is not feasible. An additional limitation is the variability of lower reference limits for CSA across populations, anatomical sites, and methodologies, which may affect the definition of nerve atrophy. [9,15,16]

In this study, nerve ultrasound shows consistent peripheral nerve morphological abnormalities in patients with FRDA, predominantly characterized by enlargement of the median and ulnar nerves in the upper limbs, with coexisting segmental nerve atrophy in a subset of patients. Larger prospective longitudinal studies are needed to clarify the clinical significance of nerve ultrasound in FRDA and to determine whether it reflects a structural correlate of disease pathology or a dynamic indicator of disease progression.

Declarations

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Author contributions:

A.E.C.F. and P.L.G.S.B.L. contributed to study conception and design, data collection, data analysis, and drafted the initial manuscript. R.F.R. and O.R.M contributed to data collection, material preparation, and data analysis. D.M.R., P.C.A.A.P.M., and N.M.M.M. contributed to data collection and clinical evaluation. A.F.F, M.V.R.S., and D.S.M. contributed to the interpretation of biomarker data. A.P. contributed to study design and critical revision of the manuscript. P.R.N. and P.B.-N. contributed to study conception and design, supervision of the project, and critical revision of the manuscript. All authors reviewed previous versions of the manuscript, provided important intellectual content, and approved the final version for submission.

Competing interests:

The authors declare no conflict of interest for this publication.

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Ethics Approval:

The study was approved by the Ethics Committee at The Universidade Federal do Ceará under protocol number 6.945.762. Written informed consent was obtained from all participants.

Clinical trial number: not applicable.

Data availability: All data produced is included in the manuscript.

Abbreviations

ADL – activities of daily living

CLIA – Clinical Laboratory Improvement Amendments

CSA – cross-sectional area

FA-Stage – Friedreich's Ataxia Staging system

FARS-ADL – Friedreich Ataxia Rating Scale, Activities of Daily Living

FRDA – Friedreich's ataxia

FXN – frataxin gene

IADL – instrumental activities of daily living

IQR – interquartile range

MRI – magnetic resonance imaging

mFARS – modified Friedreich's Ataxia Rating Scale

NCS – nerve conduction studies

PCR – polymerase chain reaction

PROM – patient-reported outcome measure

SNAPs – sensory nerve action potentials

References

1. Buesch K, Zhang R. A systematic review of disease prevalence, health-related quality of life, and economic outcomes associated with Friedreich's Ataxia. *Curr Med Res Opin*. 2022 Oct 3;38(10):1739–49.
2. Camelo-Filho AE, da Rosa RF, Lima PLGSB, Gomes GRF, de Assis Pereira Matos PCA, Rangel DM, et al. Autosomal Recessive Ataxias in Northeast Brazil: A Regional Multicenter Case Series. *The Cerebellum*. 2025 Mar 12;24(3):59.
3. Subramony SH, Lynch DL. A Milestone in the Treatment of Ataxias: Approval of Omaveloxolone for Friedreich Ataxia. Vol. 23, *Cerebellum.* Springer; 2024. p. 775–7.

4. Rummey C, Thomas-Black G, Garcia-Moreno H, Lynch DR, Abeti R, Arisoy H, et al. Increase of Plasma Biomarkers in Friedreich's Ataxia: Potential Insights into Disease Pathology. *Movement Disorders*. 2025;
5. Frempong B, Wilson RB, Schadt K, Lynch DR. The Role of Serum Levels of Neurofilament Light (NfL) Chain as a Biomarker in Friedreich Ataxia. *Front Neurosci*. 2021 Mar 2;15.
6. Leadbetter R, Weatherall M, Pelosi L. Nerve ultrasound as a diagnostic tool for sensory neuronopathy in spinocerebellar ataxia syndrome. *Clinical Neurophysiology*. 2019 Apr 1;130(4):568–72.
7. Mulroy E, Pelosi L, Leadbetter R, Joshi P, Rodrigues M, Mossman S, et al. Peripheral nerve ultrasound in Friedreich ataxia. *Muscle Nerve.* 2018 May 1;57(5):852–6.
8. Di Pietro G, Cioffi E, Falco P, Galosi E, De Stefano G, Di Stefano G, et al. Nerve ultrasound in Friedreich's Ataxia: enlarged nerves as a biomarker of disease severity. *Clinical Neurophysiology*. 2024 Mar 1;159:75–80.
9. Kneer K, Stahl JH, Winter N, Wittlinger J, Männlin S, Gasimli T, et al. Nerve Ultrasound in Patients With Friedreich Ataxia. *Muscle Nerve*. 2025 Mar 1.
10. Camelo-Filho AE, Lima PLGSB, da Rosa RF, Soares TBS, Pessoa ALS, Nóbrega PR, et al. Nerve Ultrasound Detects Nerve Atrophy in Patients With Ataxia-Telangiectasia: A Pilot Study. *Muscle Nerve*. 2025 Jun 14;71(6):1091–5.
11. Salvalaggio A, Cacciavillani M, Lucchetta M, Manara R, Gasparotti R, Briani C. Unexpected nerve neuroimaging findings in Friedreich's ataxia. *Clinical Neurophysiology*. 2015. p. 1058–61.
12. Rummey C, Corben LA, Delatycki MB, Subramony SH, Bushara K, Gomez CM, et al. Psychometric properties of the Friedreich Ataxia Rating Scale. *Neurol Genet*. 2019 Dec;5(6).
13. Subramony SH, May W, Lynch D, Gomez C, Fischbeck K, Hallett M, et al. Measuring Friedreich ataxia: Interrater reliability of a neurologic rating scale. *Neurology*. 2005 Apr 12;64(7):1261–2.
14. Georgiou-Karistianis N, Corben LA, Reetz K, Adanyeguh IM, Corti M, Deelchand DK, et al. A natural history study to track brain and spinal cord changes in individuals with Friedreich's ataxia: TRACK-FA study protocol. *PLoS One*. 2022 Nov 21;17(11):e0269649.
15. Fisse AL, Katsanos AH, Gold R, Pitarokoili K, Krogias C. Cross-sectional area reference values for peripheral nerve ultrasound in adults: a systematic review and meta-analysis—Part I: Upper extremity nerves. *Eur J Neurol*. 2021 May 23;28(5):1684–91.
16. Fisse AL, Katsanos AH, Gold R, Krogias C, Pitarokoili K. Cross-sectional area reference values for peripheral nerve ultrasound in adults: A systematic review and meta-analysis—Part II: Lower extremity nerves. *Eur J Neurol*. 2021 Jul 7;28(7):2313–8.
17. Niu J, Li Y, Zhang L, Ding Q, Cui L, Liu M. Cross-sectional area reference values for sonography of nerves in the upper extremities. *Muscle Nerve*. 2020;61(3):338-346.
18. Cartwright MS, Shin HW, Passmore LV, Walker FO. Ultrasonographic findings of the normal ulnar nerve in adults. *Arch Phys Med Rehabil*. 2007;88(3):394-396.
19. Ng AJT, Chandrasekaran R, Prakash A, Mogali SR. Normative reference values of the median nerve cross-sectional area using ultrasonography in healthy individuals: a systematic review. *Sci Rep*. 2022;12(1):1-10.
20. Lu C, Schoenfeld R, Shan Y, Tsai HJ, Hammock B, Cortopassi G. Frataxin deficiency induces Schwann cell inflammation and death. *Biochim Biophys Acta Mol Basis Dis*. 2009;1792(11):1052-1061.
21. Barreira AA, Marques W, Sweeney MG, Davis MB, Chimelli L, Paçó-Larson ML, et al. A family with Friedreich ataxia and onion-bulb formations at sural nerve biopsy. *Ann N Y Acad Sci*. 1999;883:466-468.
22. Machkhas H, Bidichandani SI, Patel PI, Harati Y. A mild case of Friedreich ataxia: lymphocyte and sural nerve analysis for GAA repeat length reveals somatic mosaicism. *Muscle Nerve*. 1998;21(3):390-393.
23. Mateo I, Llorca J, Volpini V, Corral J, Berciano J, Combarros O. Expanded GAA repeats and clinical variation in Friedreich ataxia. *Acta Neurol Scand*. 2004;109(1):75-78.

Figures

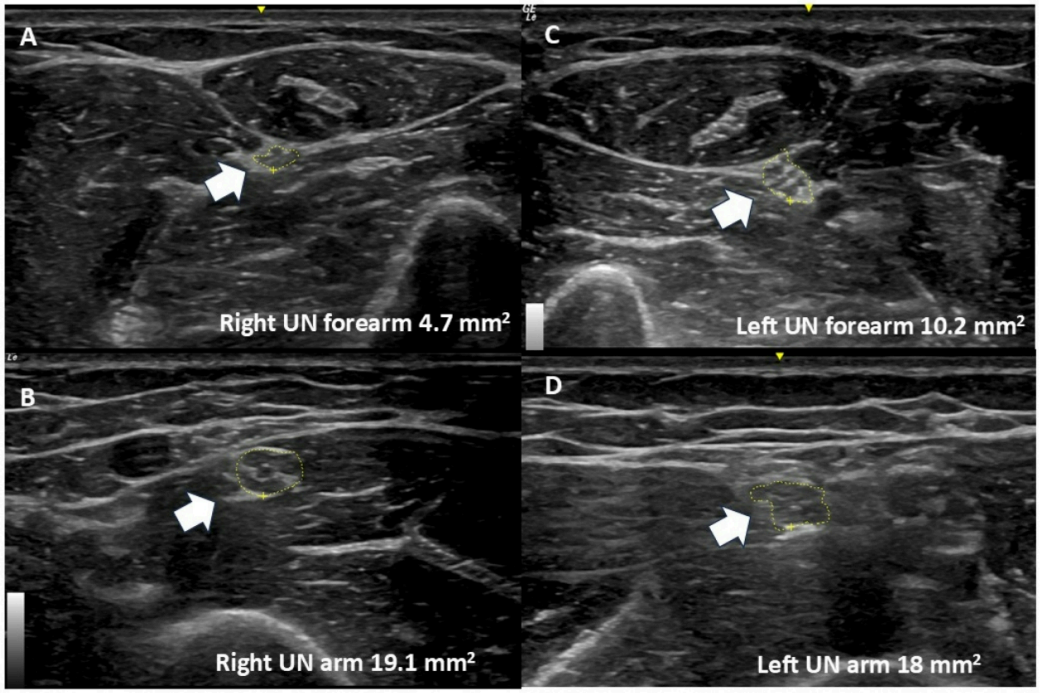


Figure 1

Segmental nerve enlargement and atrophy in Friedreich ataxia.

Nerve ultrasound images of the ulnar nerve (UN) at the forearm (A, C) and upper arm (B, D) in the same patient. The nerve is outlined by a dotted contour; arrows indicate the nerve. Abbreviations: CSA, cross-sectional area; UN, ulnar nerve.