NeuroMetrix DPNCheck

DPNCheck Gen 1 Device Training



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Commercial stage neurotechnology company

- Based in Woburn, MA
- Trade on Nasdaq (NURO)
- Over 5M patients served
- Three commercial products
- Extensive IP portfolio
- Fully integrated operations

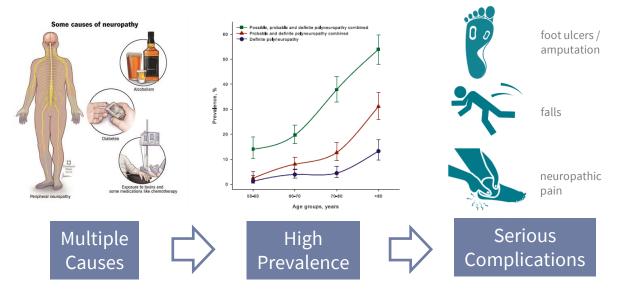


Our mission is to improve patient outcomes and population health by detecting, quantifying, and helping providers to reduce the impact of neurological disorders

Polyneuropathy Background

Polyneuropathy is common and leads to substantial morbidity and mortality Prevalence* 10% in overall population

- Clinical testing has low sensitivity for early-stage disease
- Laboratory testing is expensive, only appropriate for confirmation
- Unmet need for accurate, widely available, screening test for polyneuropathy



Up to 30%+ in Medicare Population

*Mold et al. 2004. Hanewinckel et al. 2016. Singer et al. 2012. Dyck et al. 1993.

Etiology of Peripheral Neuropathies

• Metabolic

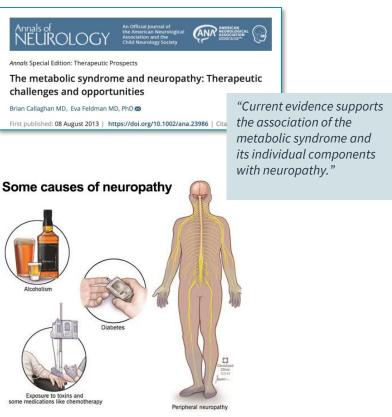
- Diabetes (30% of patients)
- Metabolic syndrome (IGT, hypertension, dyslipidemia, obesity)
- B12 deficiency
- Thyroid disease
- Chronic Hypoxia
 - o Obstructive sleep apnea
 - o COPD

• Toxic

- o Chemotherapy Induced Peripheral Neuropathy (CIPN)
- o Alcoholic neuropathy, uremic neuropathy

• Inflammatory

- o Rheumatoid arthritis
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- o Guillain-Barré syndrome (GBS)
- Infectious
 - o HIV, Lyme disease
- Hereditary
 - Charcot-Marie-Tooth (CMT)

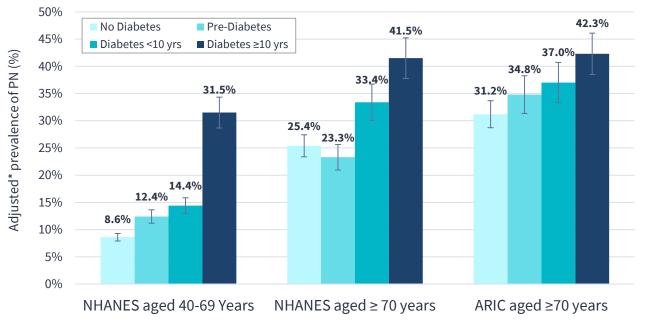


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5

Peripheral neuropathy has a high population prevalence

Hicks et al. Sci Rep, 2021.: https://doi.org/10.1038/s41598-021-98565-w

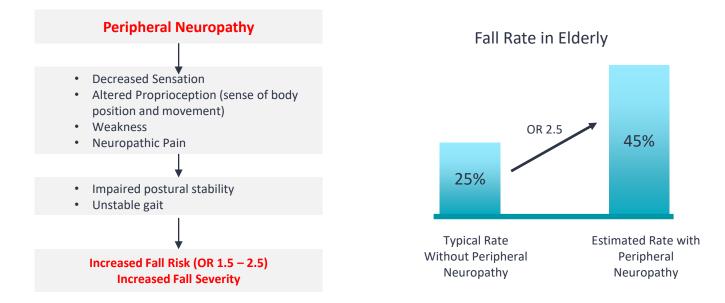


*Age, sex and race-adjusted prevalence of peripheral neuropathy stratified by diabetes status in US adults aged 40-69 and ≥ 70 Years (NHANES, 1999-2004) and ARIC participants aged ≥ 70 years (Visit 6, 2016-2017).

NHANES: 1999–2004 National Health and Nutrition Examination Survey

ARIC: 2016-2017 Atherosclerosis Risk in Communities Study

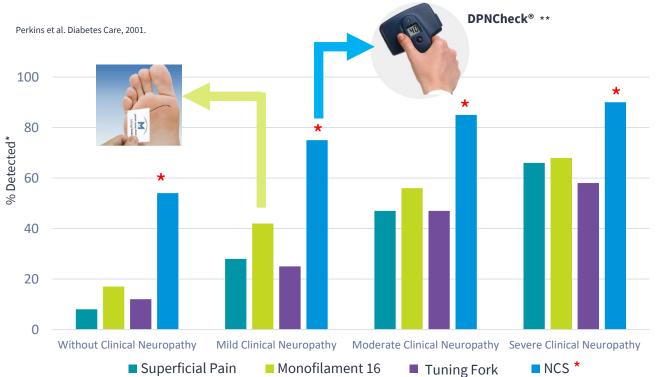
Peripheral neuropathy is an independent risk for falling and fall severity



OR, odds ratio.

References: Richardson and Hurvitz. J Gerontol, 1995. Cheng et al. J Clin Nurs, 2002. Erlandson et al. J Acquir Immune Defic Syndr, 2019. Riskowski et al. J Ournal of Foot and Ankle Research, 2012.

Clinical screening tests have low sensitivity - Monofilament only detects loss of protective sensation



*Corrected for false positive rate.

**Referenced publication utilized traditional NCS. DPNCheck sural nerve conduction demonstrated to have high agreement with traditional NCS.

Kural et al. 2018. Kamiya et al. 2021. Scarr et al. 2018. Lee at al. 2014.

DPNCheck® Overview

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DPNCheck is a standardized and automated sural nerve conduction test



- Performed in minutes by medical assistant
- Gold standard NCS technology
- Device + single-patient use biosensor
- High diagnostic accuracy
- Validated in 30+ peer-reviewed studies
- 2M patients tested over 10 years



device display is simulated

Half of peripheral neuropathy is coded as non-specific, but may have an identifiable etiology

Coded comorbidities that may be causative for peripheral neuropathy*	G6289/ G629 (Unspecified Polyneuropathy)	2019 Claims Data
Rheumatoid Arthritis	Yes	0.71%
Substance Dependence	Yes	0.61%
AIDS/ HIV	Yes	0.03%
Cancer	Yes	0.89%
Unspecified Diabetes	Yes	0.71%
Cirrhosis/ End-Stage Liver	Yes	0.13%
Dialysis	Yes	0.76%
At least one comorbidity	Yes	2.81%
No comorbidity*	Yes	2.58%
	causative for peripheral neuropathy* Rheumatoid Arthritis Substance Dependence AIDS/ HIV Cancer Unspecified Diabetes Cirrhosis/ End-Stage Liver Dialysis	causative for peripheral neuropathy*G6289/ G629 (Unspecified Polyneuropathy)Rheumatoid ArthritisYesSubstance DependenceYesAIDS/ HIVYesCancerYesUnspecified DiabetesYesCirrhosis/ End-Stage LiverYesDialysisYesAt least one comorbidityYes

*Additional potential causes include metabolic

syndrome, hypoxic conditions, nutritional **Total Unspecified/ General**

5.39%



DISCLAIMER: The information contained in this slide is provided as general information only. It is not intended to serve as medical, health, legal or financial advice or as a substitute for professional judgment of a medical coding professional, healthcare consultant, physician or medical professional, or legal counsel.

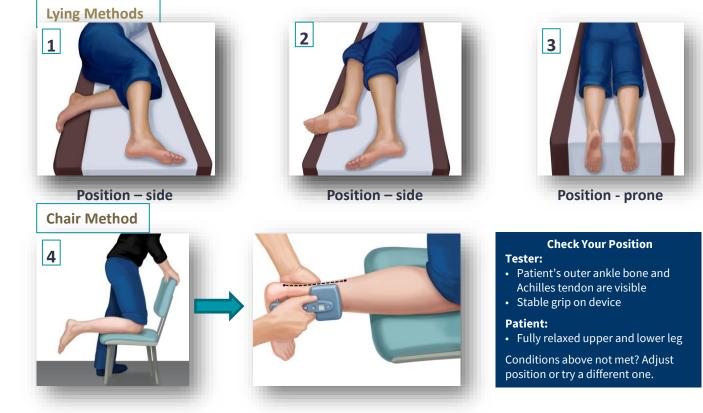
Neuropathy

Device Components



The device is powered by a 3V Panasonic CR123A battery. A USB-mini to USB-A cable is provided for uploading test results to the DPNCheck Reporter PC application.

Patient Positioning Techniques



Anatomical Landmarks

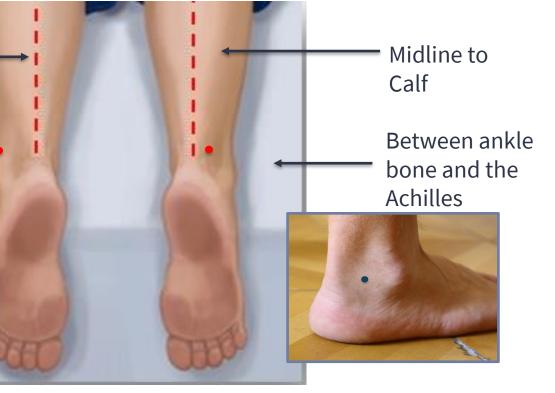
Midline to Calf

Between ankle bone _____ and the Achilles tendon

The patient should be in a **comfortable** position that allows for relaxation of the leg and foot - it is important that the patient remains **relaxed** during the test.

Make sure you have **access** to the outer ankle bone and the calf.

Make sure you can **see the midline** of the calf.



Preview: Device Alignment

The long probe should align with the outer ankle bone and is placed between the ankle bone and the Achilles tendon.

Ensure that the entire device is parallel to the midline.

Ensure that the edge of the biosensor aligns with midline of calf.*

*Refer to previous slide for reference.

Step 1: Skin Preparation



Vigorously scrub (don't rub) the test area with an alcohol prep pad.

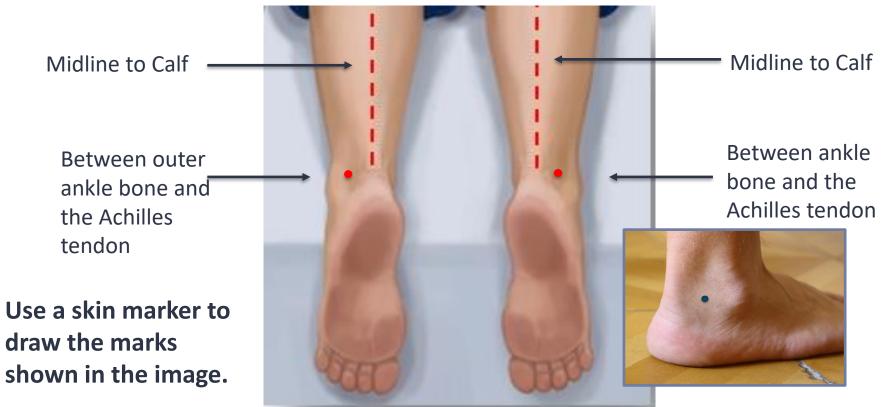
Remove any dirt, lint, moisturizer, etc.





Alcohol prep pad

Step 2: Mark Anatomical Landmarks



<u>Step 3:</u> Power on Device



- Press button to power on device.
 The display will show --.
- The light will turn amber \bigcirc or red \bigcirc if the battery needs to be replaced.

<u>Step 4:</u> Insert Biosensor



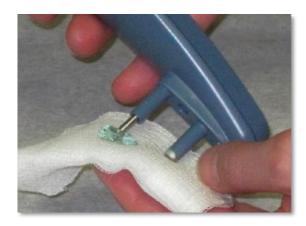
- Fully insert biosensor tail into the port and align to the foam pad on all sides.
- The "REMOVE BACKING" label side faces up.
- The light will turn green once the biosensor has been properly inserted, and the display will show []

<u>Step 5:</u> Set Leg to be Tested



- The display screen will blink with the leg selected (I = left; r = right)
- To switch the leg, hold the button for 1-2 seconds and the selection will change to the opposite leg.
- Be sure to select the correct limb to ensure accurate results.

<u>Step 6:</u> Apply Gel



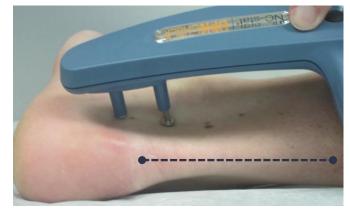
- Apply a small pea-sized amount of <u>conductive gel</u> to each probe. Do not use ultrasound gel.
- The head of the probe should be covered with gel, but make sure extra gel is not smeared between probes.
- Gel can be applied directly from tube onto probes or by using gauze

<u>Step 7:</u> Remove Backing



Remove the backing from the biosensor.

<u>Step 8:</u> Place Probes



Make a mark in the soft spot halfway between the center of the outer ankle bone and the midline of the calf (Achilles tendon), as seen in the dotted line here. Place the long probe on that mark.

Tip: The probes should be behind and not over the ankle bone.

<u>Step 9:</u> Align device on lower calf



- Align the device on the lower calf by pushing down firmly on the foam.
- The device should point towards the back side of the knee with the **inner edge of the biosensor placed next to the midline** (Achilles tendon).
- Ensure that the device is held flat with equal pressure across the biosensor and keep it parallel to the surface of the ankle (do not rock or twist device from side to side).
- Check to see if the biosensor edge is aligned to but does not cross over the midline as shown by the dashed line in the image above.
- Check for good contact on both sides of the foam.

<u>Step 10:</u> Start Test



- Press and release the button to start the test. Do not hold.
- The light will blink with each stimulation.
- Maintain constant pressure equally across device throughout the test.
- Test time may vary per patient but normally lasts for 10-15 seconds.

Step 11: Results



- Test results will display once completed.
- The lower number is most often the **Amplitude.** Look for a dot in the upper right corner to signify Amplitude.
- The higher number is most often the **Conduction Velocity**.
- If a 0 is displayed, this is the Amplitude, and it is the only number that will be displayed.
- If a 0, 2, 3, or 4 is displayed and there is no other value, this is still is a valid result.* -- *<u>Spotlight: Undetectable Result video</u>

Testing Protocol

- The test will provide a nerve conduction result the first time in most patients.
- If the first test does not provide a result, the test should be repeated.
 - Pressing the test button again is usually all that is required.
- If the repeat test does not provide a result, the opposite leg should be tested.
 - $\circ~$ The same biosensor may be used on both legs for the same patient.
- There will be a small percentage of patients on which you will not be able to obtain results.

Examples of Test Results and Actions Required

Display Example	Result	Actions
40	Conduction Velocity – meters/second	Record and interpret result.
ч [.]	Amplitude – microvolts	Record and interpret result.
0.	Undetectable Response; no Conduction Velocity displayed	Record and interpret result.
Pr Sn Ec °C Hd	Test Unsuccessful	Note displayed code and refer to Troubleshooting on back.

Troubleshooting

Display	Light	Description	Possible Causes	Solution		
LЬ	•	Data quality issue	 Incorrect limb setting on device. 	 Ensure that the limb setting on the device is correct. If incorrect, re-select the limb on the device by pressing the button down for 1-2 seconds until correct limb is selected (I = left; r = right). Retest. 		
Pn	•	Data quality issue	 Adequate signal could not be recorded. 	1. Confirm placement and retest.		
Pr	•	Stimulation issue	 Insufficient gel on probes. Poor contact of probes with skin. Inadequate skin preparation in probe contact area. Probe movement during test. Gel smeared between the probes. 	 Re-do skin preparation and device placement. Clean probes and re-apply gel. Vigorously scrub the ankle area. Reposition the device on the patient with firm pressure to both probes and on biosensor. Retest with constant force to limit device movement during test. 		
5n	0	Biosensor disconnected during test	• Biosensor disconnected during test.	 Re-insert biosensor with tail traces facing outward. <u>Entire biosensor tail</u> must be inserted. If problem persists, replace biosensor. 		
5n	•	Data quality issue	 Biosensor backing not removed. Incomplete biosensor contact. Skin in biosensor contact area inadequately prepared. 	 Remove biosensor backing and retest. Check for good contact on <u>both sides</u> of the foam. If problem persists, re-prepare skin and replace with new biosensor. Retest. 		

Troubleshooting (continued)

Display	Light	Description	Possible Causes	Solution
Ес	•	Data quality issue	 Signal contamination due to patient movement or excessive muscle contraction. 	 Confirm that the patient is relaxing leg muscles. Reposition patient if necessary. Retest.
Ec	•	Data quality issue	Biosensor backing not removed.	1. Remove biosensor backing and retest.
0	•	Patient ankle cold	 Temperature detector field of view obstructed. Patient's ankle temperature <23°C. 	 Ensure that tester's hand does not obstruct temperature detector. Warm patient's lower leg by: putting a sock on and elevating the leg. If unsuccessful: instruct the patient to put on their shoes and socks then walk around for 1-2 minutes if able. OR wrap the patient's lower leg and ankle with a blanket or heating pad. OR
Lo	•	Low battery	Battery is low.	1. Replace battery.
Нд	•	Device hardware issue	• Device hardware issue.	1. Contact Customer Service.
ШЬ	•	Excessive biosensor reuse detected. Device is disabled	 Excessive biosensor reuse detected. Excessive repeat testing. 	1. Contact Customer Service.

Using the DPNCheck Reporter Software

Simple Process:

- 1. Connect device to PC via USB cable
- 2. Enter Patient ID, data transfers
- 3. Enter gender, name, DOB, height
- 4. Select Physician & Technician
- 5. Enter interpretation and notes
- 6. Generate Report
- 7. Print PDF
- 8. Select "Complete"

1. Connect Device to the PC via USB Cable

Make sure the DPNCheck device is powered on when you connect it to the PC



2. Enter Patient ID#

DPNCheck Reporter		- 0 ×
File Studies Settings Help		
New Studies Completed Studies Today 12/9/2020		
December(excluding today)	Enter Patient ID	
Prior Months	Enter identifier of the person tested. Then press the Ok button to upload the test data from the DPNCheck	
	Cancel Ok	

3. Enter Name, Gender, DOB and Height

DOB and Height are required to generate an interpretation guide.

DPNCheck Reporter		– 0 ×
File Studies Settings Help		
A New Studies	Patient Report Waveforms	_
• 12/9/2020 8:26 PM, R Fairfield		
✓ Completed Studies	Gender: Female O Male Unspecified	
T oday 12/9/2020	First Name: Robert	
December(excluding today)	Last Name: Fairfield	
Prior Months	Patient ID: 3337654	
_	Birth Date: (M/D/YYYY) 3 v 3 v 1933 v	
	Age: 87	
	Height (ft in): 5 ft 11 in	
	Weight (lb):	
l L		
	Export Datasheet	Report Complete
	LAPORT Datasticet	complete

4. Select Physician & Technician

New Studies	Patient Repo	rt Waveforms			
12/9/2020 8:26 PM, R Fairfield Completed Studies	Date:	12/9/2020 8:26 PM		Interpretation Guide	
T oday 12/9/2020	Physician:	Thomas Kelvin, MD 🔹	32-	•	
December(excluding today) Prior Months	Practice: Address:	Main Street Primary Care	16 -		
- FIOI MOINTS	City, State Zip:	Boston, MA 01234	<u> </u>	Mild Normal	
	Technician:	Sarah Thomas 🔍	(At) aphilide At		
	Amplitude (uV):	Right Leg Normal Limit 26 3	2-		
	Conduction Veloci	ty (m/s): 58 44	1-	Moderate Severe	
			0-1 2b	3b 4b 5b 6b Conduction Velocity (m/s)	70
			Interpretation:		
			Normal Nerve Mild PN Moderate PN	conduction study of the right sural ne	erve is normal.
			Severe PN Other		
					Notes

5. Select Enter Interpretation

Studies	Patient	Report	Waveforms			
2/9/2020 8:26 PM, R Fairfield						
mpleted Studies	Date:		12/9/2020 8:26 PM		Interpretat	tion Guide
Today 12/9/2020	Physician		Thomas Kelvin, MD 🔹	32-		•
December(excluding today)	Practice:		Main Street Primary Care	16-		
Prior Months	Address:		100 Main St			
	City, State	Zip:	Boston, MA 01234	≥ ⁸⁻	Mild	Normal
	Technicia	1:	Sarah Thomas 🔹	(Vit) abnilidmA		
	Amplitud Conducti	on Velocity (m/s): 58 44	1- 0-(- 20	S 30 40	evere 50 60 70 Velocity (m/s)
				Interpretation: Normal Mild PN Moderate PN Severe PN Other	rve conduction stud	y of the right sural nerve is normal.

6. Complete Study

Click the Complete button to finish.

		-	and a second						
New Studies	Patient	Report	Waveforms						
• 12/9/2020 8:26 PM, R Fairfield					In	torprotot	ion Guide		
Completed Studies	Date:		12/9/2020 8:26 PM	33		terpretat	ion duide	_	
🖿 Today 12/9/2020	Physician:		Thomas Kelvin, MD 🔹		-		٠		
December(excluding today)	Practice:		Main Street Primary Care	16	5-				
Prior Months	Address:		100 Main St						
	City, State		Boston, MA 01234	S.	8- M	ld	Normal		
	Techniciar		Sarah Thomas 🔹	Amplitude (µV)					
	Conductio	n Velocity	(m/s): 58 44		1- 20 30	Se 40	derate evere 50 60 Velocity (m/s)	70	
				Interpretation:					
				Mild PN	Nerve cond	uction study	y of the right sural nerve	is normal.	
				Moderate PN					
				Other					
				Other				N-1	
								Note	es

7a. Generate Report

New Studies	Patient Rep	oort Waveforms			
• 12/9/2020 8:26 PM, R Fairfield Completed Studies	Date:	12/9/2020 8:26 PM		Interpretat	ion Guide
	Physician:	Thomas Kelvin, MD 👻	32-1	280	
T oday 12/9/2020	Practice:	Main Street Primary Care			•
December(excluding today)	Address:	100 Main St	16-		
Prior Months	City, State Zip:	Boston, MA 01234	_ 8-	Mild	Normal
	Technician:	Sarah Thomas 💌	Amplitude (VV)		
	Conduction Velo	ucity (m/s): 58 44	1- 0- 20	30 40	svere 50 60 70 Velocity (m/s)
			Interpretation: Normal Mild PN Moderate PN Severe PN Other	ve conduction stud	y of the right sural nerve is normal.
					Notes

7b. Print Report



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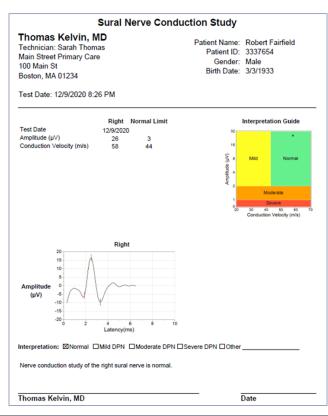
NEURO**Metrix**[®] | **DPN**Check[®]

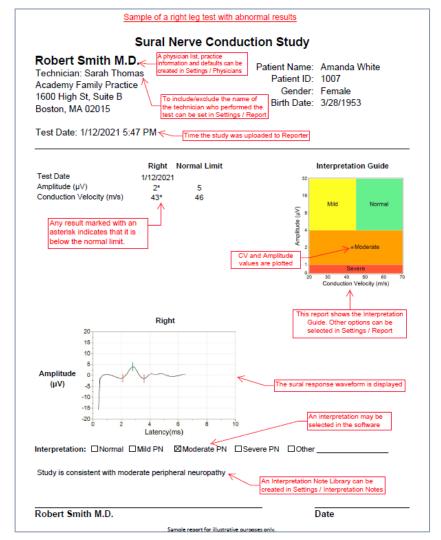
Documentation & Reporting

Reporting Documentation & Interpretation

• Report Generation Software:

- Generate report (PDF, HL7 or XML)
- Automatic comparison to normal limits
- Archive data
- NCS waveforms and values provide detailed documentation of neuropathy status
- Currently relies on manual data entry, development underway for EHR integration capabilities.





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Cleaning/Re-Use

- The biosensor may be used to test other leg on the same patient if needed.
- The biosensor **must** be changed between patients.
- The device probes should be cleaned between patients
 - Clean device by wiping probes straight up with alcohol swab or soft cloth. **Do not twist** while cleaning probes.
 - Wipe away excess gel
 - $\circ~$ Isopropyl Alcohol wipes may be used to clean/disinfect probes
 - $\circ~$ Check temperature lens between probes for gel and wipe away
- The foam does not contact the patient and should not need cleaning unless contaminated. Replace the foam when no longer sticky or when opening a new biosensor kit.
- A soft cloth or wipe with water or isopropyl alcohol may be used to clean the unit exterior as needed; do not use abrasive cleaners or strong solvents.

39

Additional Support Resources

www.dpncheck.com/resources-nc-030/

NEUROMetrix learn about dpncheck risk assessment clinical trial use resources about DPNCheck NC-030 Resources

These resources are provided for the first-generation DPNCheck device (model NC-030).

Click here for documentation and resources for our latest model (DPNCheck 2.0)

Training & Product Resources

- DPNCheck NC-030 Brochure
- DPNCheck Sural Nerve Conduction & Code Interpretation Guide
- DPNCheck NC-030 Reference Guide
 Patient Positioning Guide

DPNCheck NC-030 Device User Manual

DPNCheck Reporter & Communicator Software

DPNCheck Reporter Software Download

DPNCheck Reporter Software User Manual

DPNCheck Communicator Software User Manual (deprecated)

Training Videos:

Instructional Video



Resources

- DPNCheck User Manual (Model NC-030) is available on the website: <u>https://www.dpncheck.com/resources-nc-030/</u>
- The following materials are available on our website, and are also provided with your DPNCheck device:
 - Reference Guide with quick-start instructions
 - Patient Positioning Guide
 - Interpretation Guide (without age/height adjustment)

Contact Information

For immediate help when testing contact: NeuroMetrix Customer Service @ (888) 786-7287

41

Demo

Click to add text



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Practice



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Questions and discussion



Appendix

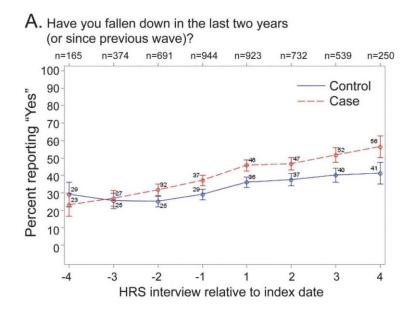
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Elevated risk of falls and pain precede peripheral neuropathy Dx by several years

Callaghan et al. Neurology, 2015: https://doi.org/10.1212/WNL.000000000001714

Figure 1 Comparison of the patient-oriented outcome trajectories between patients with neuropathy and propensity-matched controls



"We found that older adults with neuropathy have more falls and pain and lower self-rated health compared to carefully matched controls without neuropathy. These differences were present 3–5 years prior to a neuropathy diagnosis and persist for several years after diagnosis."

"This finding may be partly explained by a delay in diagnosis in this highly prevalent condition, and also highlights the fact that neuropathy often develops slowly over time. Patients typically report neuropathic symptoms to their physician years after their insidious onset."

DPNCheck[®] has been clinically validated - Published data on thousands of patients

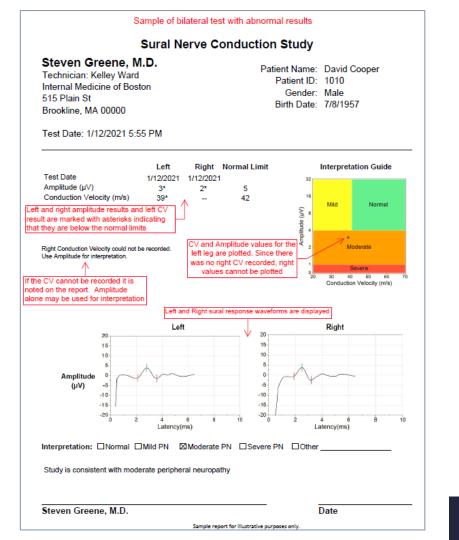
Over 30 peer-reviewed clinical studies and review articles



Study Publication	Type 2	Type 1	No Diabetes	Total	Reference Diagnosis	Sensitivity	Specificity
Binns-Hall et al. 2018	231	5	0	236	Clinical	0.84	0.68
Papanas et al. 2019	0	53	0	53	Clinical	0.96	0.93
Chatzikosma et al. 2016	114	0	46	160	Clinical	0.91	0.86
Hirayasu et al. 2018	92	0	0	92	Clinical	0.85	0.86
Lee et al. 2014	28	16	0	44	NCS	0.95	0.71
Kural et al. 2018	168	0	0	168	NCS	0.82	0.85
Scarr et al. 2018	0	68	71	139	NCS	0.86	0.79
Total	633	142	117	892		0.88*	0.82*

DDNCHECK DETECTS DIABETIC DEDIDHEDAL NELIDODATHY WITH HIGH SENSITIVITY AND SDECIEICITY

9 out of 10 polyneuropathy cases detected



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