DPNCheck Gen 1 Device Training

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

DPNCheck®

ADVANCE®

Quell®

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

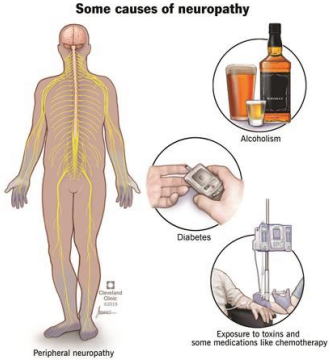
Polyneuropathy is common and leads to substantial morbidity and mortality

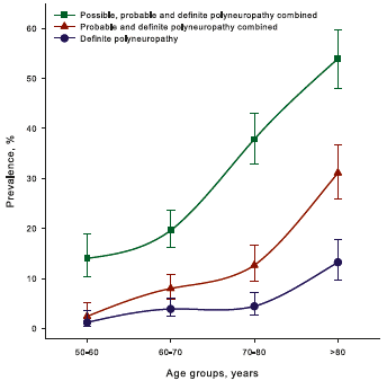
- Clinical testing has low sensitivity for early-stage disease
- Laboratory testing is expensive, only appropriate for confirmation
- Unmet need for accurate, widely available, screening test for polyneuropathy

Prevalence*

10% in overall population

Up to 30%+ in Medicare Population





foot ulcers / amputation

falls

neuropathic pain

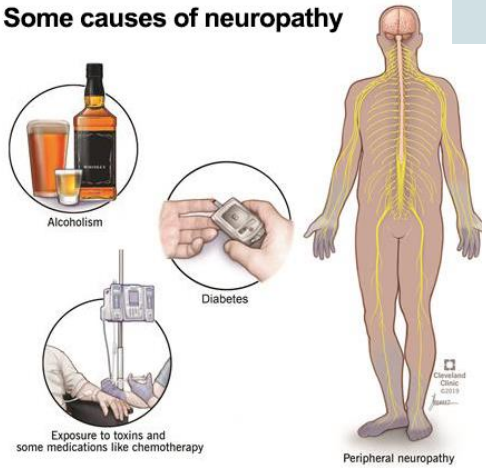
Multiple Causes → High Prevalence → Serious Complications

*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**
  - Obstructive sleep apnea
  - COPD
- **Toxic**
  - Chemotherapy Induced Peripheral Neuropathy (CIPN)
  - Alcoholic neuropathy, uremic neuropathy
- **Inflammatory**
  - Rheumatoid arthritis
  - Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
  - Guillain-Barré syndrome (GBS)
- **Infectious**
  - HIV, Lyme disease
- **Hereditary**
  - Charcot-Marie-Tooth (CMT)

"Current evidence supports the association of the metabolic syndrome and its individual components with neuropathy."

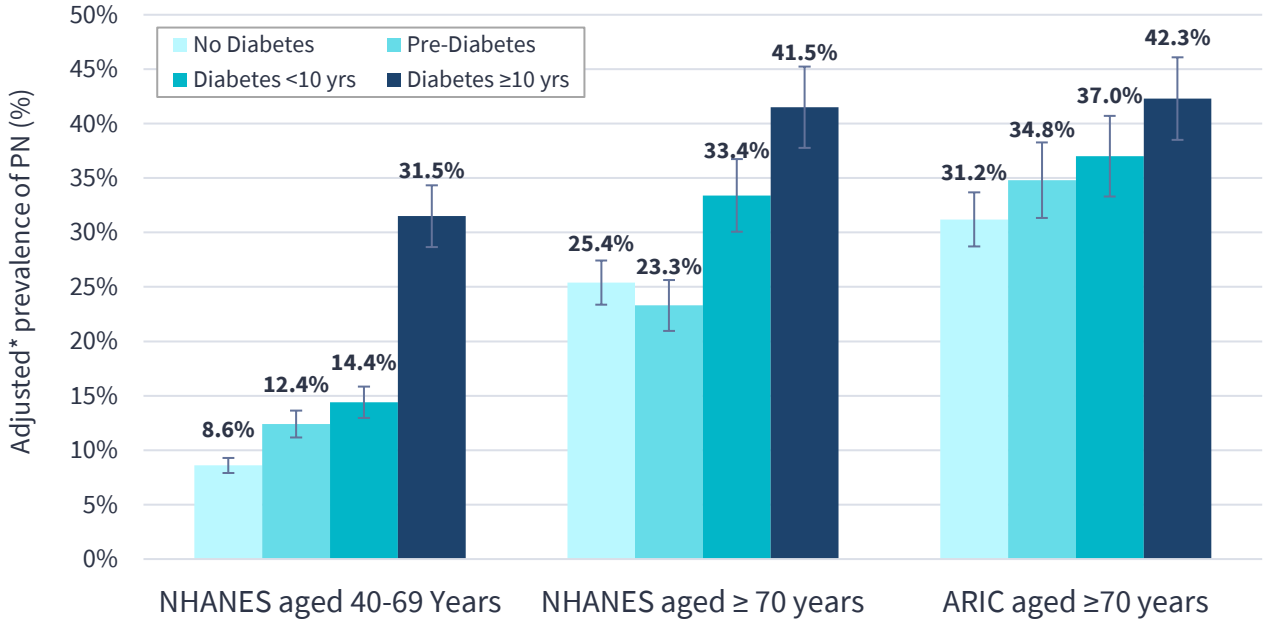


Peripheral neuropathy has a high population prevalence

NHANES: 1999–2004 National Health and Nutrition Examination Survey

ARIC: 2016-2017 Atherosclerosis Risk in Communities Study

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).

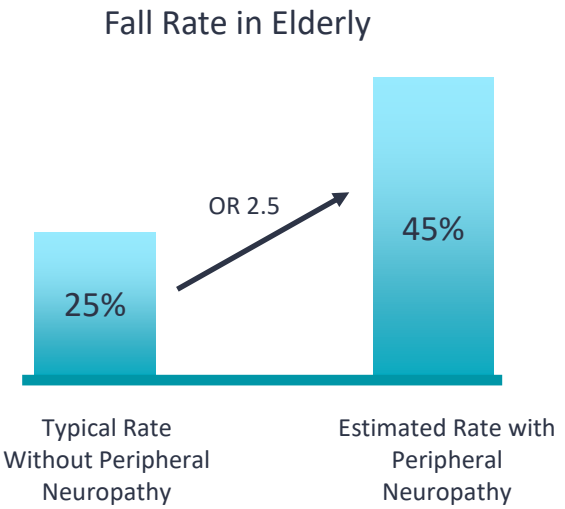
Peripheral neuropathy is an independent risk for falling and fall severity

Peripheral Neuropathy

- Decreased Sensation
- Altered Proprioception (sense of body position and movement)
- Weakness
- Neuropathic Pain

- Impaired postural stability
- Unstable gait

Increased Fall Risk (OR 1.5 – 2.5)
Increased Fall Severity



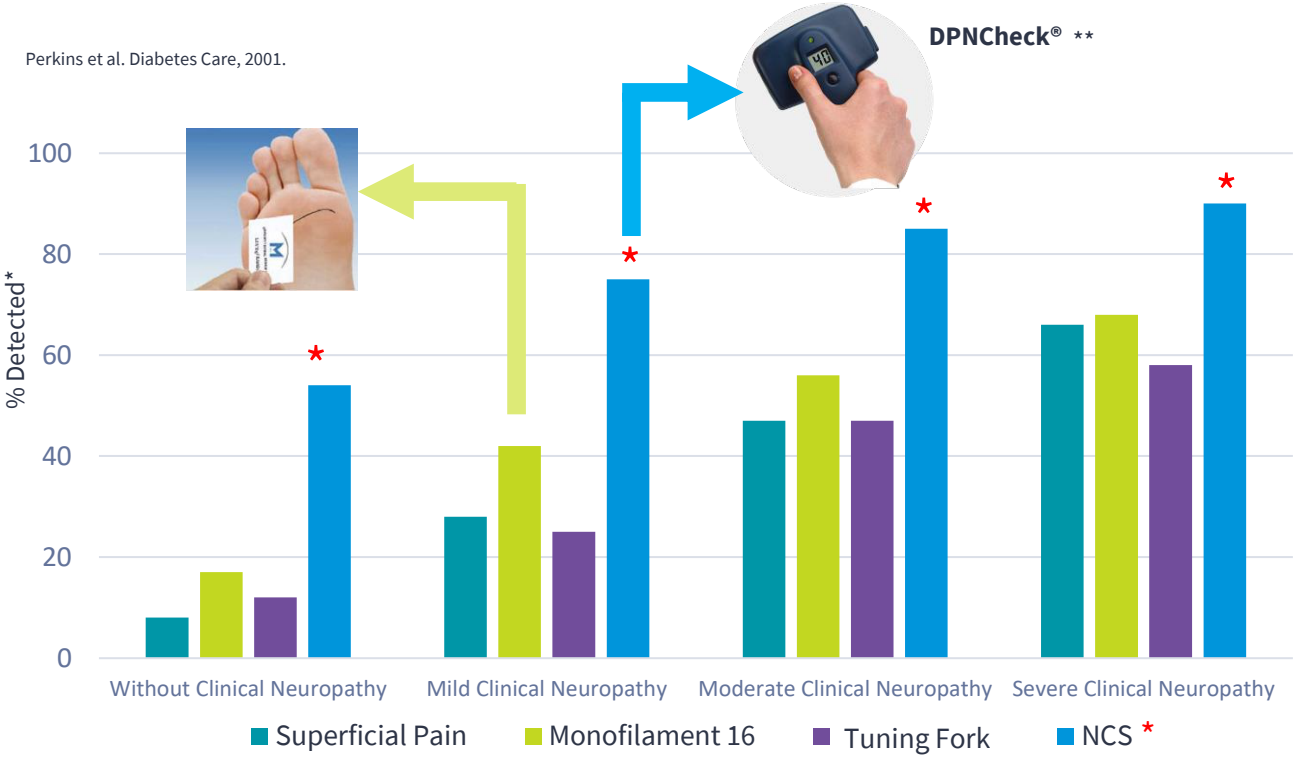
OR, odds ratio.

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. Journal of Foot and Ankle Research, 2012.

Clinical screening tests have low sensitivity

- Monofilament only detects loss of protective sensation

Perkins et al. Diabetes Care, 2001.



*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

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

HCC075	Coded comorbidities that may be causative for peripheral neuropathy*	G6289/ G629 (Unspecified Polyneuropathy)	2019 Claims Data
No	Rheumatoid Arthritis	Yes	0.71%
No	Substance Dependence	Yes	0.61%
No	AIDS/ HIV	Yes	0.03%
No	Cancer	Yes	0.89%
No	Unspecified Diabetes	Yes	0.71%
No	Cirrhosis/ End-Stage Liver	Yes	0.13%
No	Dialysis	Yes	0.76%
Possible Yes	**At least one comorbidity**	**Yes**	**2.81%**
No	**No comorbidity***	**Yes**	**2.58%**

*Additional potential causes include metabolic syndrome, hypoxic conditions, nutritional deficiencies

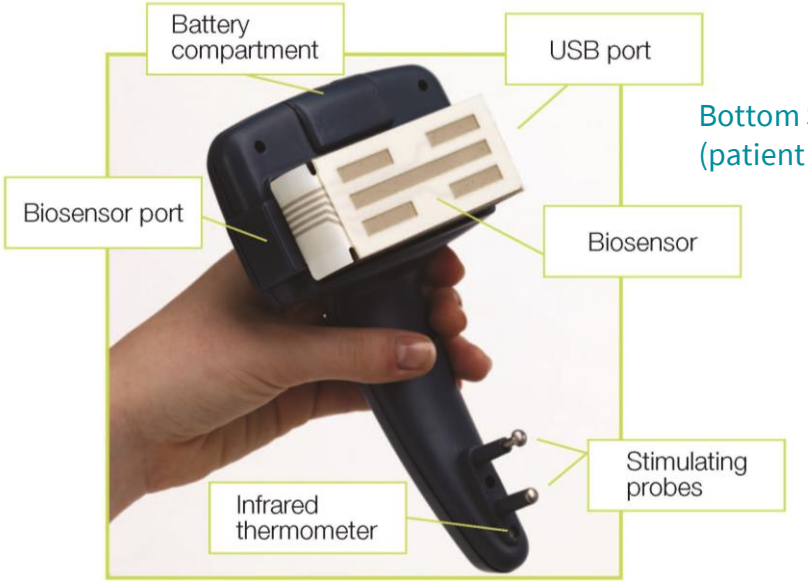
Total Unspecified/ General Neuropathy **5.39%**

ghg

Source: Gorman Health Group analysis, 2021

Device Components

Top Side
(tester facing)

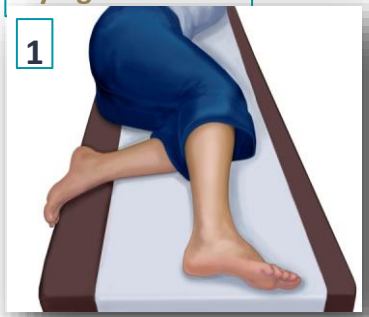


Bottom Side
(patient facing)

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

Lying Methods

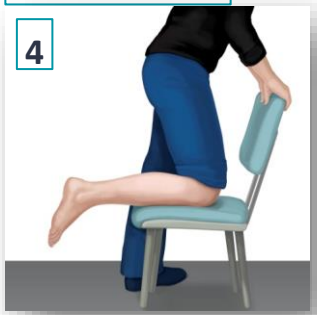


Position – side

Position – side

Position - prone

Chair Method



Check Your Position

Tester:

- Patient's outer ankle bone and Achilles tendon are visible
- Stable grip on device

Patient:

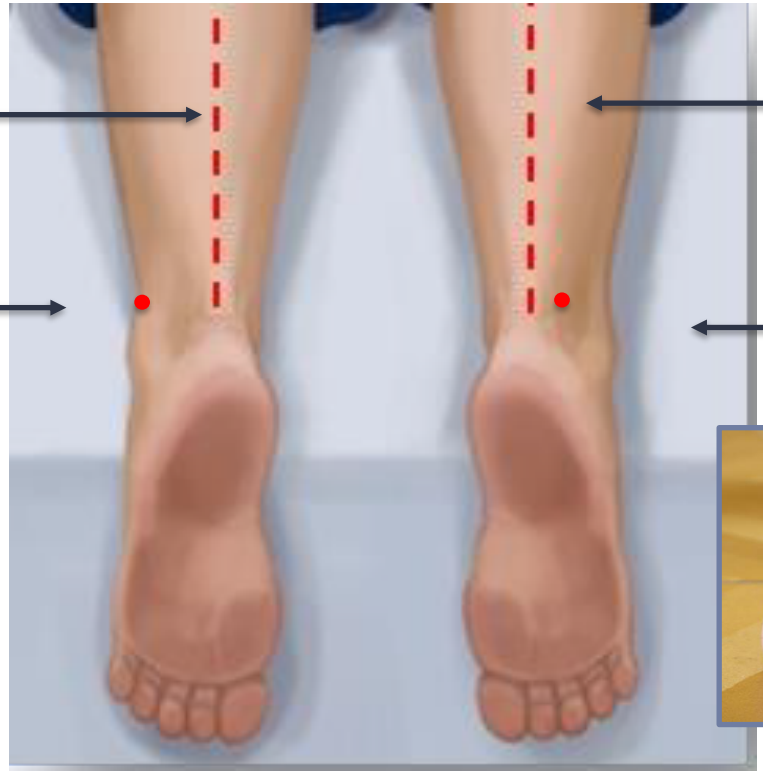
- Fully relaxed upper and lower leg

Conditions above not met? Adjust position or try a different one.

Anatomical Landmarks

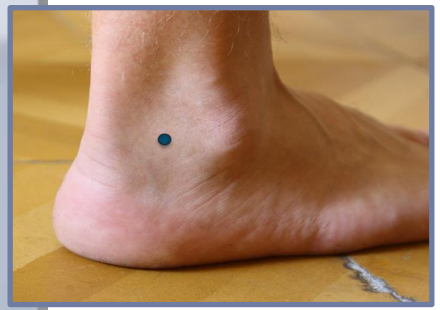
Midline to Calf

Between ankle bone and the Achilles tendon



Midline to Calf

Between ankle bone and the Achilles

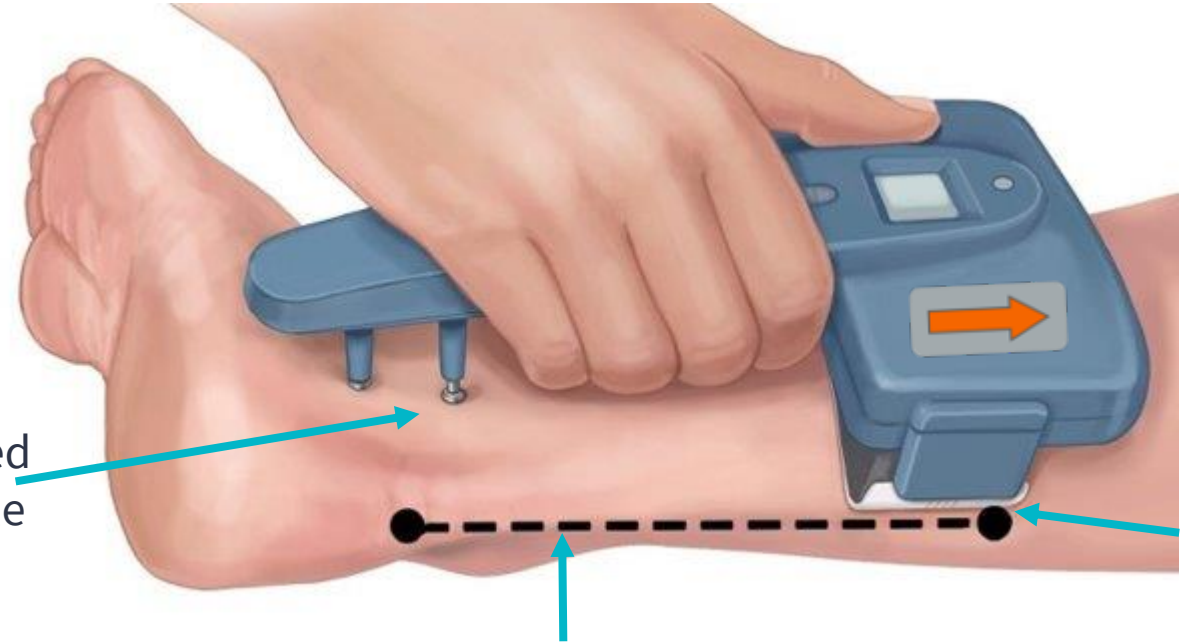


The patient should be in a **comfortable** position that allows for relaxation of the leg and foot - it is important that the patient remains **relaxed** during the test.

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.

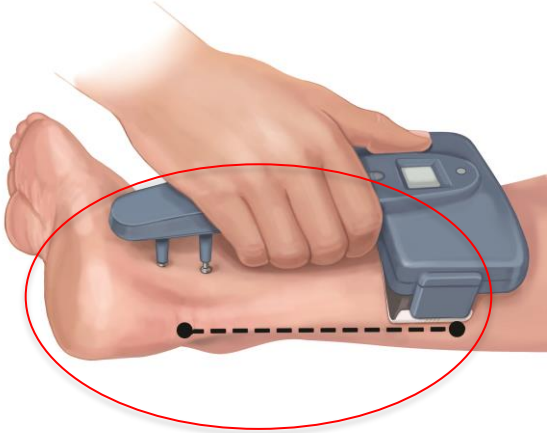
Ensure that the edge of the biosensor aligns with midline of calf.*

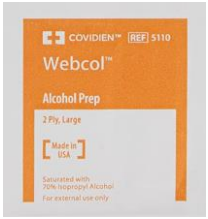
*Refer to previous slide for reference.

Step 1: Skin Preparation

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

Remove any dirt, lint, moisturizer, etc.





Alcohol prep pad

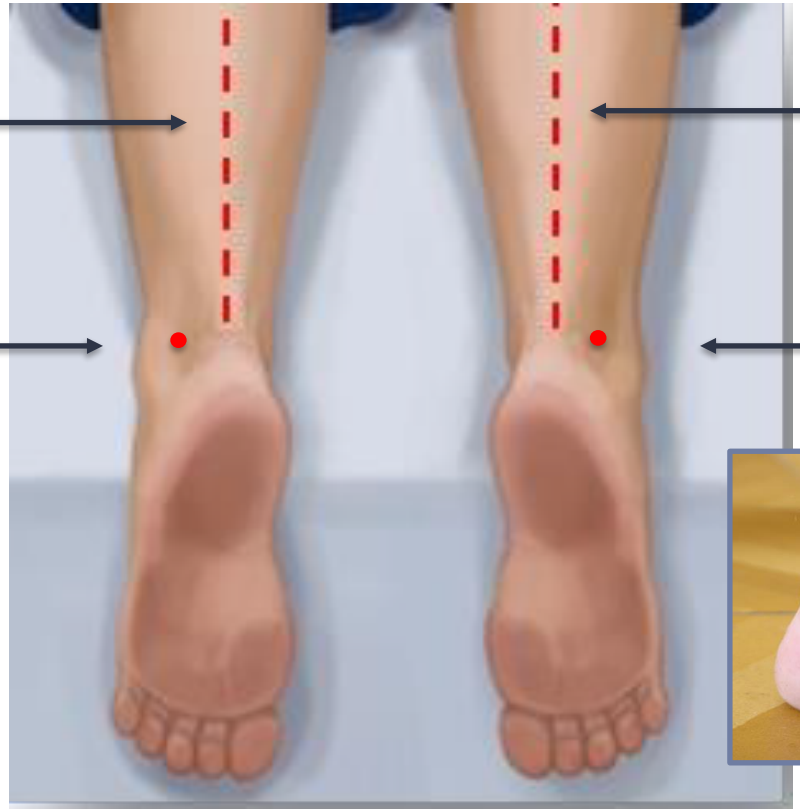
Step 2: Mark Anatomical Landmarks

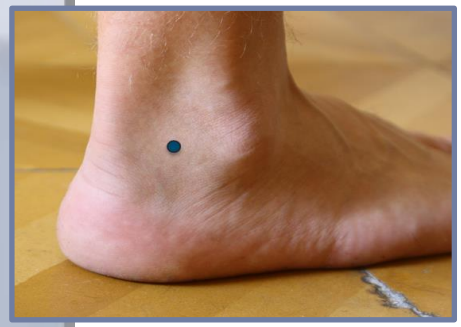
Midline to Calf

Midline to Calf

Between outer ankle bone and the Achilles tendon

Between ankle bone and the Achilles tendon





Use a skin marker to draw the marks shown in the image.

Step 3:
Power on Device

- Press button to power on device. The display will show [--].
- The light will turn amber 🟡 or red 🔴 if the battery needs to be replaced.

Step 4:
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 [1.5]

Step 5:
Set Leg to be Tested

- The display screen will blink with the leg selected (l = 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.

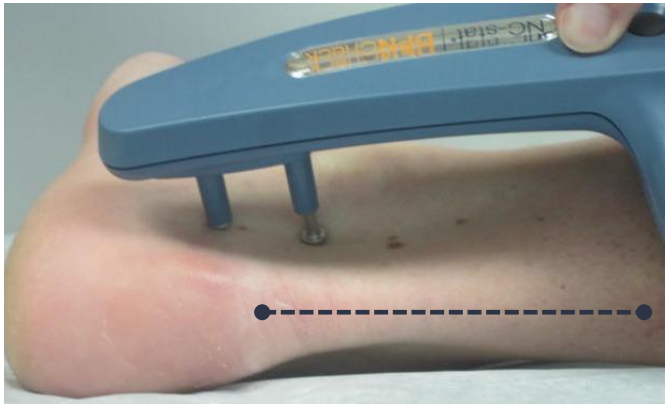
Step 6:
Apply Gel

- Apply a small pea-sized amount of conductive gel 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

Step 7:
Remove Backing

Remove the backing from the biosensor.

Step 8:
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.

Step 9:

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.

Step 10:
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.* [--]

*Spotlight: Undetectable Result video

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.
  - 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.
4.	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
Lb	●	Data quality issue	• Incorrect limb setting on device.	1. Ensure that the limb setting on the device is correct. 2. If incorrect, re-select the limb on the device by pressing the button down for 1-2 seconds until correct limb is selected (l = left; r = right). 3. 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.	1. 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. 2. Retest with constant force to limit device movement during test.
Sn	○	Biosensor disconnected during test	• Biosensor disconnected during test.	1. Re-insert biosensor with tail traces facing outward. • Entire biosensor tail must be inserted. 2. If problem persists, replace biosensor.
Sn	●	Data quality issue	• Biosensor backing not removed. • Incomplete biosensor contact. • Skin in biosensor contact area inadequately prepared.	1. Remove biosensor backing and retest. • Check for good contact on both sides of the foam. 2. If problem persists, re-prepare skin and replace with new biosensor. 3. Retest.

Troubleshooting (continued)

Display	Light	Description	Possible Causes	Solution
Ec	●	Data quality issue	• Signal contamination due to patient movement or excessive muscle contraction.	1. Confirm that the patient is relaxing leg muscles. 2. Reposition patient if necessary. 3. Retest.
Ec	●	Data quality issue	• Biosensor backing not removed.	1. Remove biosensor backing and retest.
oC	●	Patient ankle cold	• Temperature detector field of view obstructed. • Patient's ankle temperature <23°C.	1. Ensure that tester's hand does not obstruct temperature detector. 2. 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 ◦ briskly rub the patient's lower ankle. (Note: Although it is not an ideal approach, this technique can be used if the tester is in a hurry.) 3. Retest.
Lo	●	Low battery	• Battery is low.	1. Replace battery.
Hd	●	Device hardware issue	• Device hardware issue.	1. Contact Customer Service.
Ub	●	Excessive biosensor reuse detected. Device is disabled	• Excessive biosensor reuse detected. • Excessive repeat testing.	1. Contact Customer Service.

Using the DPNCheck Reporter Software

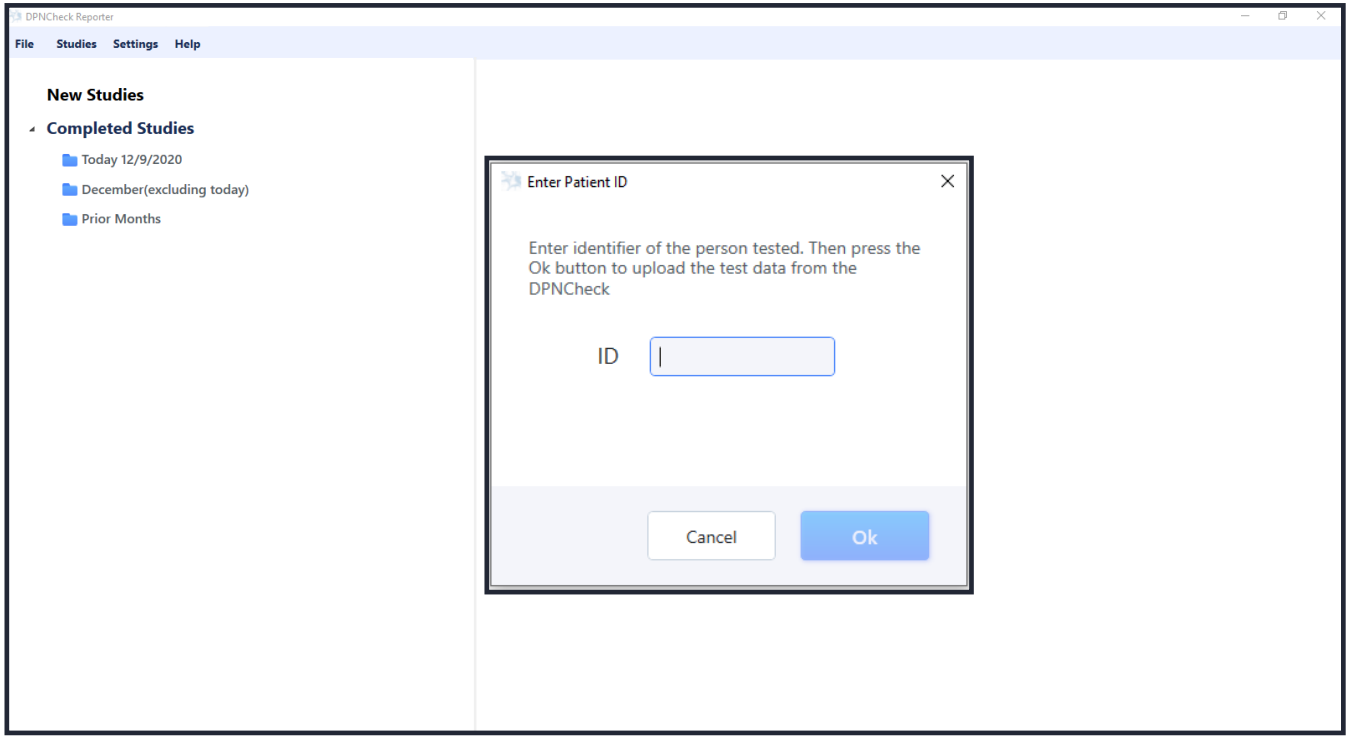
Simple Process:

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

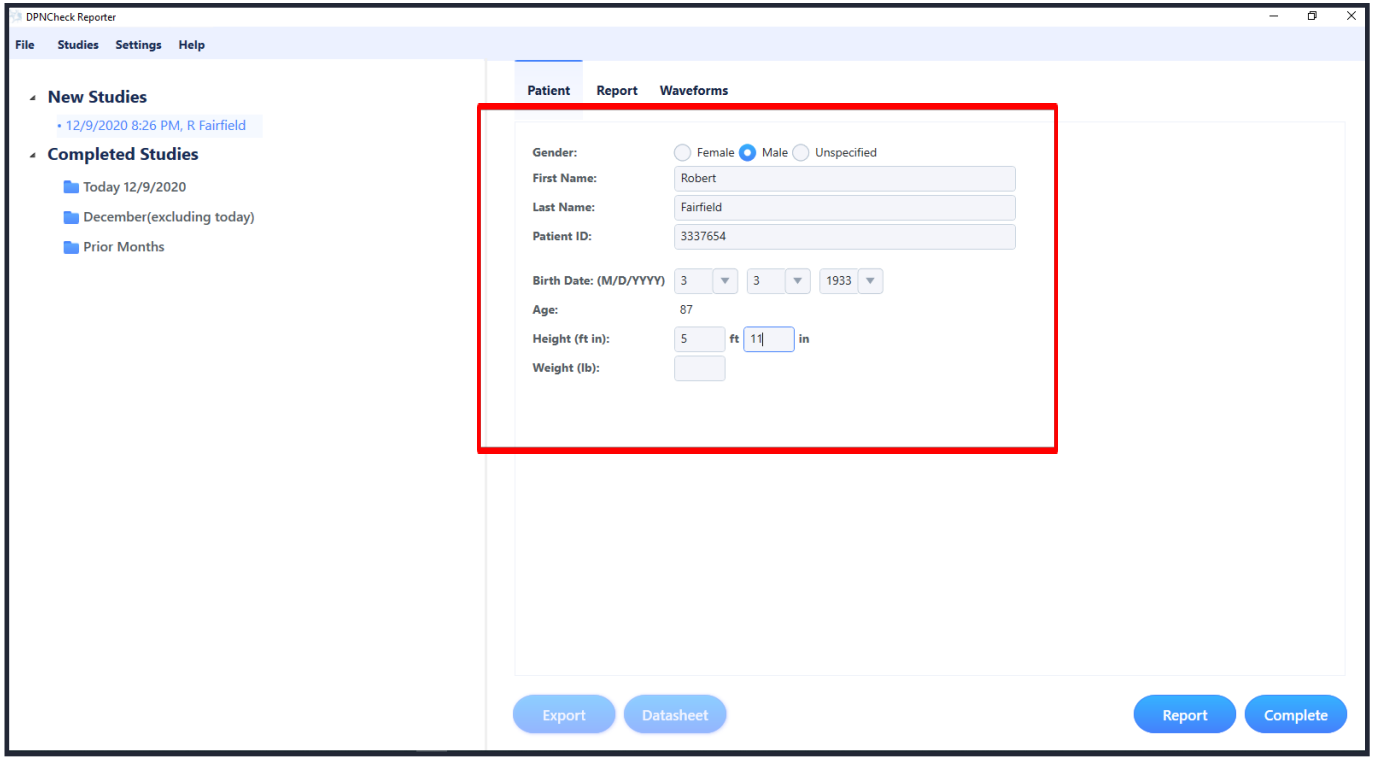
Make sure the DPNCheck device is powered on when you connect it to the PC

2. Enter Patient ID#

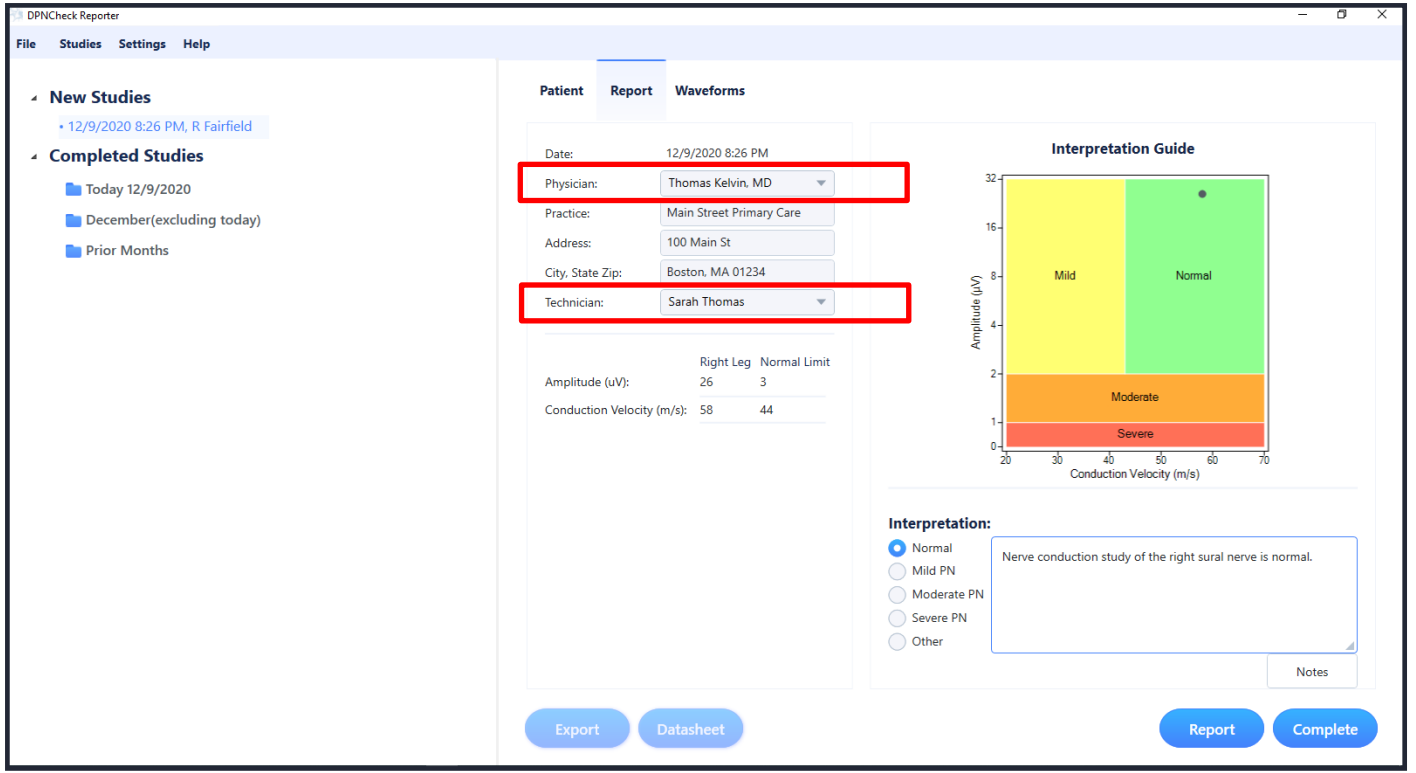


3. Enter Name, Gender, DOB and Height

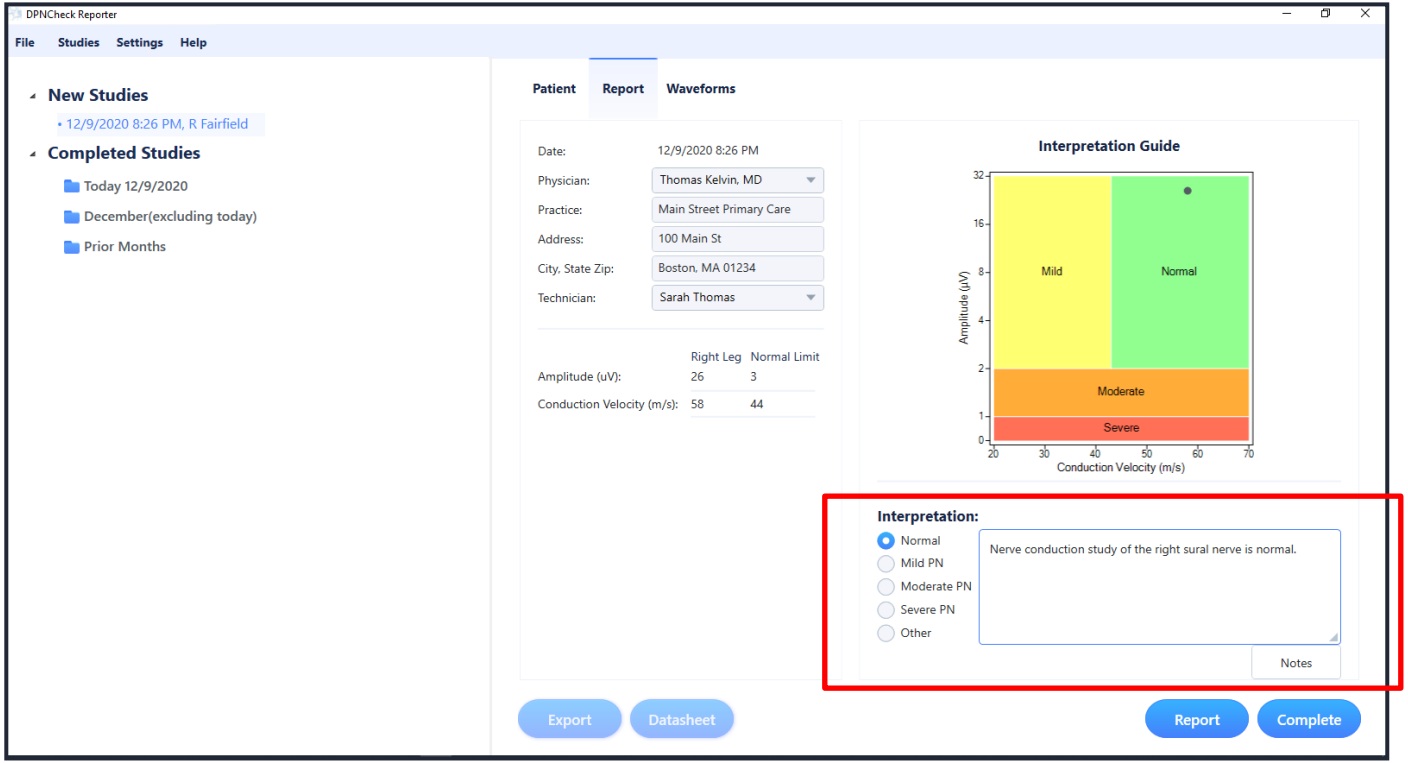
DOB and Height are required to generate an interpretation guide.



4. Select Physician & Technician

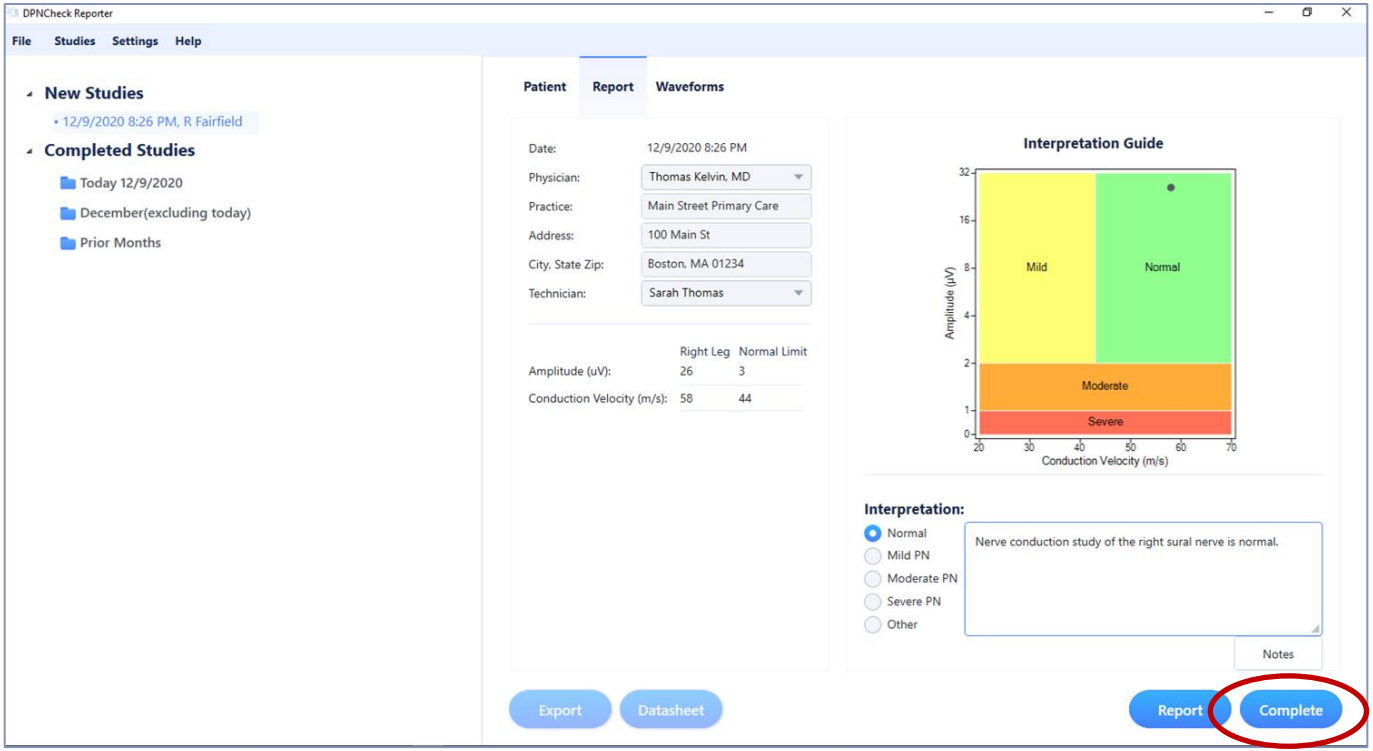


5. Select Enter Interpretation

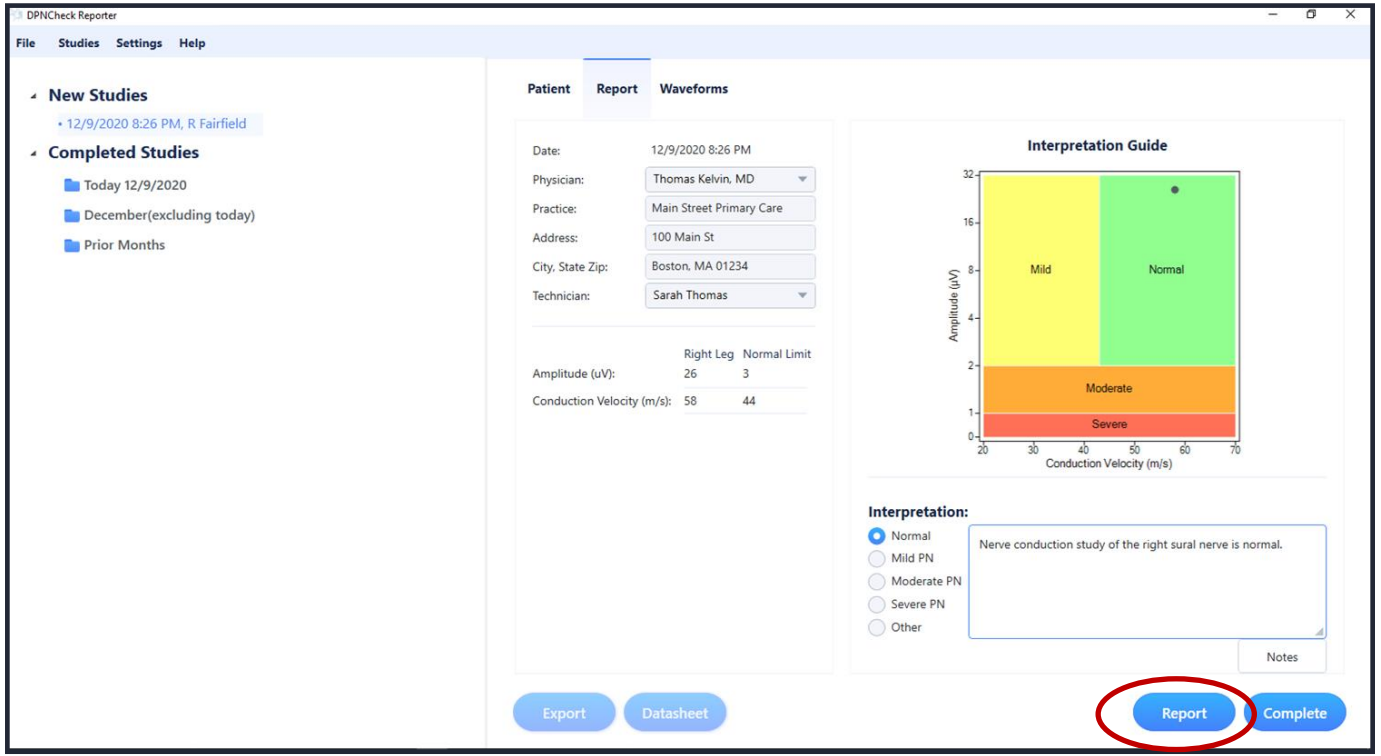


6. Complete Study

Click the Complete button to finish.



7a. Generate Report



7b. Print Report

Sural Nerve Conduction Study

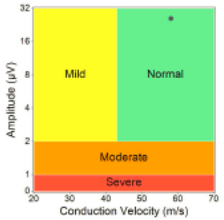
Thomas Kelvin, MD
Technician: Sarah Thomas
Main Street Primary Care
100 Main St
Boston, MA 01234

Patient Name: Robert Fairfield
Patient ID: 3337654
Gender: Male
Birth Date: 3/3/1933

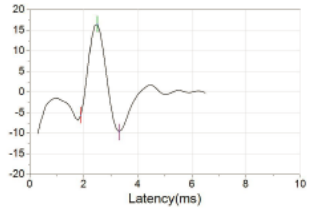
Test Date: 12/9/2020 8:26 PM

	Right	Normal Limit
Test Date	12/9/2020	
Amplitude (µV)	26	3
Conduction Velocity (m/s)	58	44

Interpretation Guide



Right



Interpretation: ☒Normal ☐Mild DPN ☐Moderate DPN ☐Severe DPN ☐Other _____

Nerve conduction study of the right sural nerve is normal.

_____ _____
Thomas Kelvin, MD **Date**

DPNCheck®

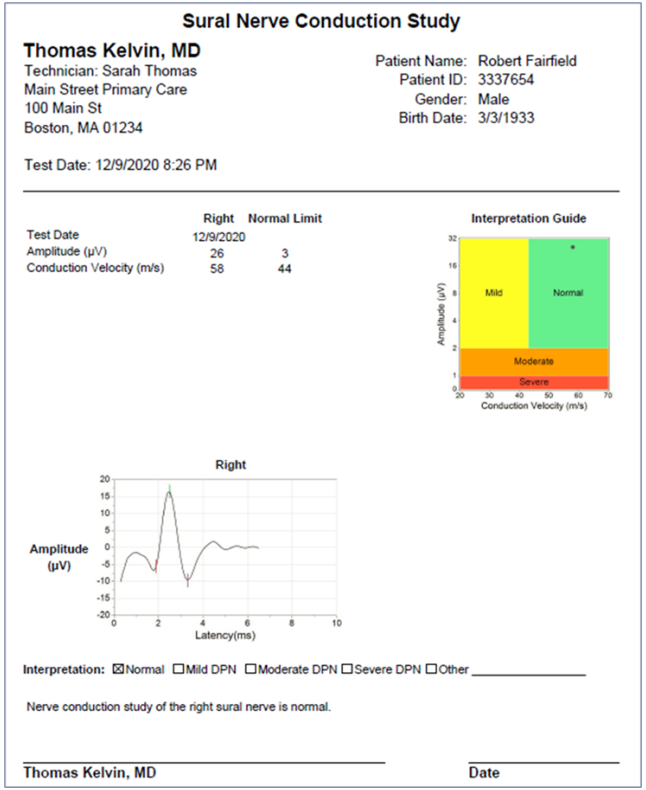
Documentation & Reporting

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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Test Date	12/9/2020	
Amplitude (μV)	26	3
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Interpretation Guide

Right

Interpretation: ☒Normal ☐Mild DPN ☐Moderate DPN ☐Severe DPN ☐Other _____

Nerve conduction study of the right sural nerve is normal.

Thomas Kelvin, MD

Date

Sample of a right leg test with abnormal results

Sural Nerve Conduction Study

Robert Smith M.D.
Technician: Sarah Thomas
Academy Family Practice
1600 High St, Suite B
Boston, MA 02015

A physician list, practice information and defaults can be created in Settings / Physicians

To include/exclude the name of the technician who performed the test can be set in Settings / Report

Patient Name: Amanda White
Patient ID: 1007
Gender: Female
Birth Date: 3/28/1953

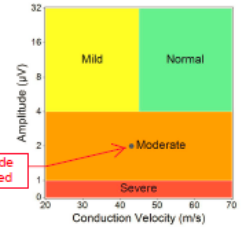
Test Date: 1/12/2021 5:47 PM

Time the study was uploaded to Reporter

	Right	Normal Limit
Test Date	1/12/2021	
Amplitude (μV)	2*	5
Conduction Velocity (m/s)	43*	46

Any result marked with an asterisk indicates that it is below the normal limit.

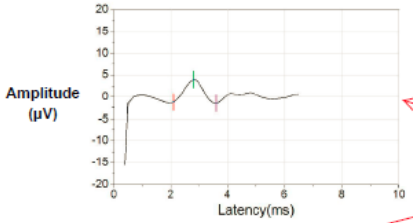
Interpretation Guide



CV and Amplitude values are plotted

This report shows the Interpretation Guide. Other options can be selected in Settings / Report

Right



The sural response waveform is displayed

An interpretation may be selected in the software

Interpretation: ☐Normal ☐Mild PN ☒Moderate PN ☐Severe PN ☐Other _____

Study is consistent with moderate peripheral neuropathy

An Interpretation Note Library can be created in Settings / Interpretation Notes

Robert Smith M.D. **Date**

Sample report for illustrative purposes only.

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
  - Isopropyl Alcohol wipes may be used to clean/disinfect probes
  - 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.

Additional Support Resources

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

NEUROMetrix

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

Demo

Click to add text

Practice

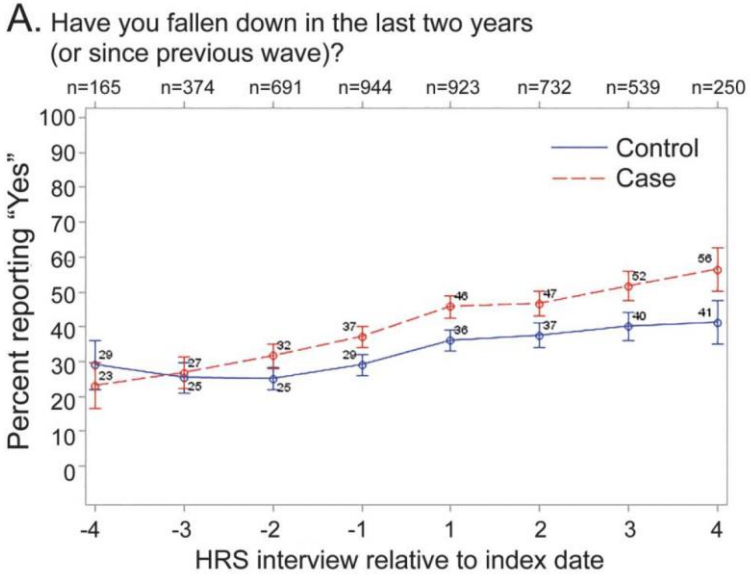
Questions and discussion

Appendix

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

Callaghan et al. Neurology, 2015: https://doi.org/10.1212/WNL.0000000000001714

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

DPNCHECK DETECTS DIABETIC PERIPHERAL NEUROPATHY WITH HIGH SENSITIVITY AND SPECIFICITY

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***

*Summary sensitivity and specificity determined by bivariate meta-analysis.

9 out of 10 polyneuropathy cases detected

Sample of bilateral test with abnormal results

Sural Nerve Conduction Study

Steven Greene, M.D.
Technician: Kelley Ward
Internal Medicine of Boston
515 Plain St
Brookline, MA 00000

Patient Name: David Cooper
Patient ID: 1010
Gender: Male
Birth Date: 7/8/1957

Test Date: 1/12/2021 5:55 PM

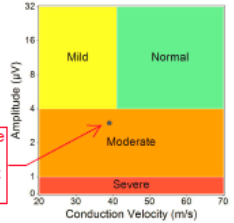
	Left	Right	Normal Limit
Test Date	1/12/2021	1/12/2021	
Amplitude (µV)	3*	2*	5
Conduction Velocity (m/s)	39*	--	42

Left and right amplitude results and left CV result are marked with asterisks indicating that they are below the normal limits

Right Conduction Velocity could not be recorded. Use Amplitude for interpretation.

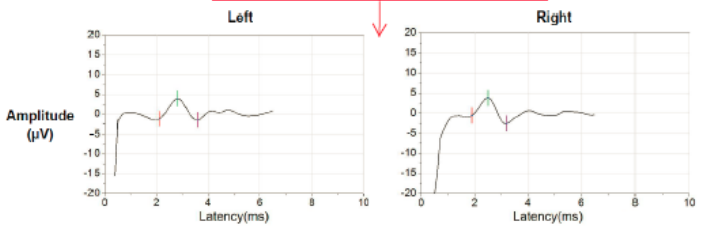
If the CV cannot be recorded it is noted on the report. Amplitude alone may be used for interpretation

Interpretation Guide



CV and Amplitude values for the left leg are plotted. Since there was no right CV recorded, right values cannot be plotted

Left and Right sural response waveforms are displayed



Interpretation: ☐Normal ☐Mild PN ☒Moderate PN ☐Severe PN ☐Other _____

Study is consistent with moderate peripheral neuropathy

Steven Greene, M.D. Date

Sample report for illustrative purposes only.