



Epidermal Nerve Fiber Density (ENFD) Testing

Diagnosis and management of Small Fiber Peripheral Neuropathy

Do your patients complain of pain, numbness, tingling, or burning in their toes, feet, or legs?

Your patients could be suffering from small fiber peripheral neuropathy.



One quick in-office procedure can provide a definitive diagnosis, allowing you to determine effective treatment and symptom relief.

Small fiber peripheral neuropathy (SFPN) is a progressive disease that primarily affects the terminal end-branches of peripheral nerves that result in disintegration of the nerve fiber cytoskeleton, and eventually complete nerve loss.

Patients often feel pain, tingling, or numbness in their toes, feet, legs, fingers, and hands in a stocking- glove distribution.

Peripheral neuropathy affects more than 20 million people in the US¹, and small fiber neuropathy is often misdiagnosed with large fiber neuropathy due to its complex array of symptoms. Patients with small fiber neuropathy usually have normal reflexes, muscle strength, NCV, and EMG results.

Epidermal Nerve Fiber Density testing analysis is the best diagnostic tool for early detection and early treatment of small fiber peripheral neuropathy.

¹ "Peripheral Neuropathy Fact Sheet", NINDS, Publication date: August 2018. NIH Publication No. 18-NS-4853

BakoDx ENFD testing is the gold standard for diagnosing SFPN

Obtain an accurate and definitive diagnosis of SFPN for improved patient outcomes

- ✓ The most objective tool for diagnosing, documenting, and monitoring SFPN
- ✓ Accurately assesses degree of SFPN severity (mild, moderate, severe)
- ✓ Quick, in-office procedure with little to no post-procedure care
- ✓ Definitive diagnosis in 5-7 days enabling patient-centered treatment using evidenced-based medicine
- ✓ Reimbursable by most insurance companies

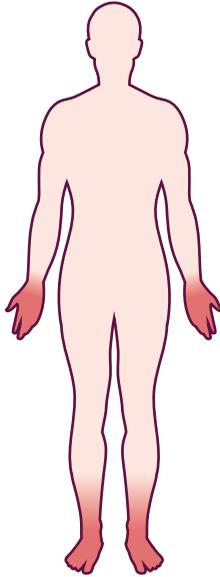


The BakoDx ENFD kit

Minimally invasive, the ENFD method makes it a useful tool, not only in clinical practice, but also for monitoring the progression of neuropathy during neuroprotective treatments.²

² Lauria G, Devigili G. Skin biopsy as a diagnostic tool in peripheral neuropathy. *Nat Clin Pract Neurol.* 2007;3(10):546-557. doi:10.1038/ncpneuro0630

Conditions associated with Small Fiber Peripheral Neuropathy



METABOLIC CAUSES

Diabetes mellitus, metabolic syndrome, hyperlipidemia

INHERITED CAUSES

Fabry's disease, Tangier's disease, familial amyloid polyneuropathy

TOXIC CAUSES

Chemotherapy, alcoholism, solvent exposure

AUTOIMMUNE CAUSES

Sjögren's syndrome, vasculitis/polyarteritis nodosa

AMYLOIDOSIS

Non-inherited forms of amyloidosis, e.g. lymphoma or plasma cell dyscrasias

INFECTIONS

HIV, hepatitis C, Lyme disease

IDIOPATHIC

For a relatively large percentage of cases, there is no identifiable cause of SFPN

“Diabetic neuropathy has some important clinical consequences in a patient’s life. There’s clearly impaired function, a lower quality of life, and increased mortality.”

Dr. Eva L. Feldman, author of ADA’s clinical guidelines for diabetic neuropathy.³

What is ENFD analysis?

The Epidermal Nerve Fiber Density (ENFD) test is the best objective tool for documenting small fiber peripheral neuropathy by quantifying the terminal branches of peripheral nerves within the epidermis.

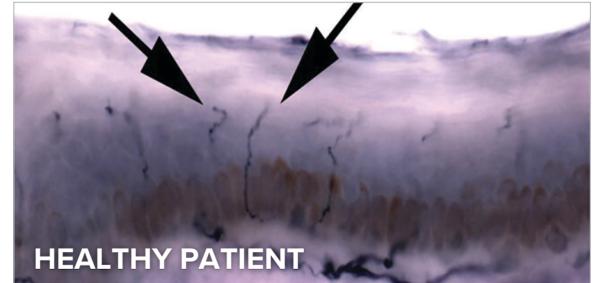
ENFD analysis allows for the direct visualization of small nerve fibers. Small nerve fibers are assessed for structural integrity and counted.

A diminished number of small nerve fibers are indicative of established diseases; the lower the count, the more severe the disease state.

ENFD testing measures degeneration, but can also be used as a predictive tool, and to assess the effectiveness of therapy over time.

What is the specificity and sensitivity of Epidermal Nerve Fiber Density analysis?

The test is highly specific and sensitive. BakoDx's specificity of ENFD is 95%-to-97%; and the sensitivity is approximately 90%.



The BakoDx Difference

BakoDx's ENFD reporting methodology provides an assessment of small fiber peripheral neuropathy's degree of severity.

The ENFD test report also offers treatment recommendations that empower the treating clinician with evidence-based medical information. This leads to better, more timely and cost effective health care for your patients.

ANALYZING ENFD RESULTS

Normative Range	7.1mm fibers & above
Mild Nerve Degeneration	7.1mm - 3.8mm fibers
Moderate Nerve Degeneration	3.8mm - 2.0mm fibers
Severe Nerve Degeneration	2.0mm - 0.0mm fibers



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EPIDERMAL NERVE FIBER DENSITY ANALYSIS

DIAGNOSIS:

A. SKIN, RIGHT CALF, PUNCH BIOPSY:

- INTRA-EPIDERMAL NERVE DENSITY MILDLY DECREASED (5.86 FIBERS/MM).
- MILD MORPHOLOGIC DEGENERATIVE CHANGES ARE SEEN AMONG INTRA-EPIDERMAL NERVE FIBERS.
- SEE COMMENT.

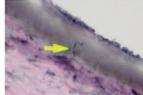
B. SKIN, LEFT CALF, PUNCH BIOPSY:

- INTRA-EPIDERMAL NERVE DENSITY MILDLY DECREASED (6.73 FIBERS/MM).
- MILD MORPHOLOGIC DEGENERATIVE CHANGES ARE SEEN AMONG INTRA-EPIDERMAL NERVE FIBERS.
- SEE COMMENT.

COMMENT, A/B: The nerve fiber density reductions and degenerative changes identified in 50 µm sections on which an anti-PGP 9.5 immunostain was performed, are consistent with a mild (early-evolving) neuropathic process affecting small fibers.

The published normative range for epidermal nerve fiber density at 10 cm proximal to the lateral malleolus is 13.8 +/- 6.7 fibers per millimeter. Values under 7.1 fibers/mm are below the normative range in this location. **Reference:** Mathur J, Stocks EA, Hauer P, Cornblath DR, Griffin JW. Epidermal Nerve Fiber Density. Normative reference range and diagnostic efficiency. Arch Neurol 55:1513-15120, 1998.

Based on the epidermal nerve fiber density analysis in this case, one potential clinical course for this patient could include a dietary supplement containing **Alpha-Lipoic Acid (2600mg daily)** and **Benfotiamine (600mg daily)**. When clinically indicated, such products may be helpful to both diminish the symptoms of neuropathy, and to improve overall epidermal nerve health. Additionally, investigators have shown benefit to using combination therapy that includes L-methylfolate, methylcobalamin (B12) and pyridoxal 5'-phosphate (B6). **References:** Ziegler D. Effect of 4-year antioxidant treatment with alpha-lipoic acid in diabetic polyneuropathy: the NATHAN 1 trial. Diabetes 2007; 56(Suppl 1):A2. Luong KV, et al. The impact of thiamine treatment in diabetes mellitus. J Clin Med Res 2012; 4(3):153-160. Walker M, et al. Improvement of cutaneous sensitivity in diabetic peripheral neuropathy. Rev Neurol Dis 2010; 7(4):132-139.

CLINICAL INFORMATION:

A. Rule out neuropathy; right calf.
B. Rule out neuropathy; left calf.

GROSS DESCRIPTION:

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“My patients have seen a drastic improvement in their quality of life through providing ENFD analysis and subsequent treatment. Your patients will love you for offering this test.”

Lilly Khavari, DPM, DABPM is a board certified, surgically-trained foot and ankle specialist focusing on pediatric and diabetic foot care, sports injuries, as well as acute and chronic conditions of the foot and ankle. She is a physician-owner of Carrollton Foot Center in Carrollton, Texas.



Get started by ordering the BakoDx supplied ENFD kit

We are your trusted lab partner for diagnosis and management of small fiber peripheral neuropathy.

Bako Diagnostics | 855-422-5628 | [BakoDx.com](https://www.BakoDx.com)