

**Pathology report by BAKO PATHOLOGY SERVICES**

**EPIDERMAL NERVE FIBER DENSITY ANALYSIS OF PATIENT "EE"**

**Patient Information:** 83-year-old female

Physician: Kevin F Sunshein, DPM  
Neurogenx NerveCenter of Centerville  
6474 Centerville Business Pkwy  
Centerville, OH 45459-2633

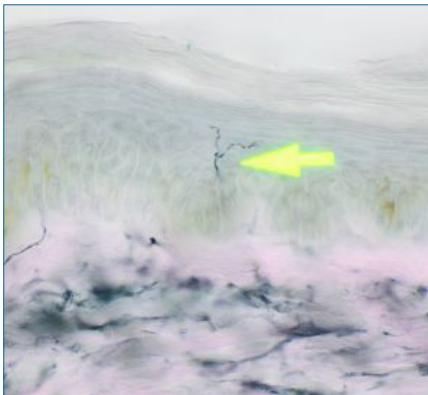
**Post-Treatment Result:**

**68% increase in nerve fiber density**

**Before Neurogenx Treatment - 02/02/16**

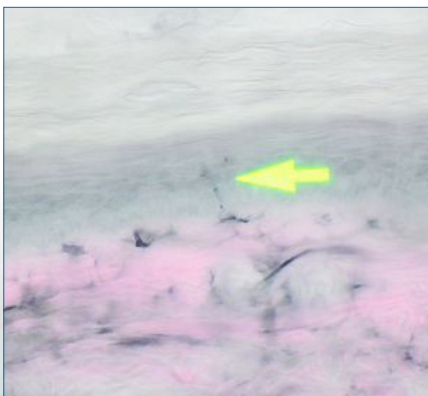
**A. SKIN, RIGHT CALF, PUNCH BIOPSY:**

- Intra-epidermal nerve counts in normative range (**10.30 Fibers/mm**).
- Mild morphologic degenerative changes are seen among intra-epidermal nerve fibers. (See Comment 1).



**B. SKIN, LEFT CALF, PUNCH BIOPSY:**

- Intra-epidermal nerve fiber density is borderline low (**7.97 Fibers/mm**).
- Papillary dermal nerve fibers atretic and slightly diminished. (See Comment 2).

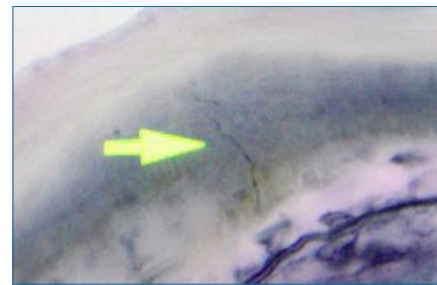


Final Diagnosis performed by Wayne L. Bakotic D.O. Electronically signed 2/8/2016

**After Neurogenx Treatment - 09/09/16**

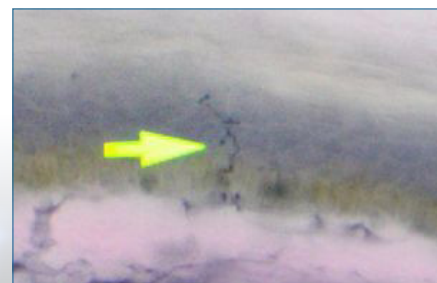
**A. SKIN, RIGHT CALF, PUNCH BIOPSY:**

- Intra-epidermal nerve counts in normative range (**17.31 Fibers/mm**).
- This study demonstrates an increase in epidermal nerve fiber density relative to this patient's previous study. (See comment 3).



**B. SKIN, LEFT CALF, PUNCH BIOPSY:**

- Intra-epidermal nerve counts in normative range (**13.93 Fibers/mm**).
- This study demonstrates an increase in epidermal nerve fiber density relative to this patients previous study. (See Comment 3).



Final Diagnosis performed by Wayne L. Bakotic D.O. Electronically signed 9/15/2016

**Pathology report by BAKO PATHOLOGY SERVICES**

## EPIDERMAL NERVE FIBER DENSITY ANALYSIS OF PATIENT "EE"

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**Patient Information:** 83-year-old femalePhysician: Kevin F Sunshein, DPM  
Neurogenx NerveCenter of Centerville  
6474 Centerville Business Pkwy  
Centerville, OH 45459-2633**Post-Treatment Result:****68% increase in nerve fiber density**

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COMMENT 1: Immunohistochemical studies using anti-PGP 9.5 antibodies; and subsequent morphometric analysis, disclose a density of epidermal nerve fibers that is well within the published normative range. This finding militates strongly against established small fiber neuropathy (sensitivity approaching 90%). This biopsy does, however, disclose degenerative changes within epidermal nerves. These changes are not entirely specific and may be seen in some normal subjects; however, these findings are often predictive of the future development of clinical neuropathy. Because there is no definitive evidence of established small fiber peripheral neuropathy in the current biopsy, but significant degenerative changes are seen, should symptoms persist, an additional biopsy in 6-12 months could be beneficial to assess for disease progression.

COMMENT 2: Immunohistochemical studies and morphometric analysis disclose a low-normal number of all small myelinated (A-delta) and unmyelinated (C) nerve fibers within the epidermis. In addition, fibers within the papillary dermis are atretic and slightly diminished. The depressed number of fibers following immunohistochemical analysis using anti-PGP 9.5 antibodies could be indicative of early-evolving small fiber neuropathy. The published specificity below the fifth percentile, (less than 3.8 fibers/mm), is 97% (in the context of an appropriately fixated post-biopsy specimen). Reference: Ebenezer GJ, P Hauer, C Gibbons, et al. J Neuropathol Exp Neurol 66(12):1059-1073, 2007.

COMMENT 3: Immunohistochemical studies and morphometric analysis disclose a density of small myelinated (A-delta) and unmyelinated (C) nerve fibers that is within the published normative range. The presence a normal intra-epidermal nerve fiber density following immunohistochemical analysis using anti-PGP 9.5 antibodies militates strongly against advanced small fiber neuropathy; however, such cannot be entirely excluded (sensitivity 70-90%). Reference: Ebenezer GJ, P Hauer, C Gibbons, JC McArthur, M Polydefkis. Assessment of epidermal nerve fibers: a new diagnostic and predictive tool for peripheral neuropathy. J Neuropathol Exp Neurol 66(12):1059-1073, 2007.

\*\*\*Original report is available upon request.

**Pathology report by BAKO PATHOLOGY SERVICES**

**EPIDERMAL NERVE FIBER DENSITY ANALYSIS OF PATIENT "RS"**

**Patient Information:** 79-year-old male

Physician: Kevin F Sunshein, DPM  
Neurogenx NerveCenter of Centerville  
6474 Centerville Business Pkwy  
Centerville, OH 45459-2633

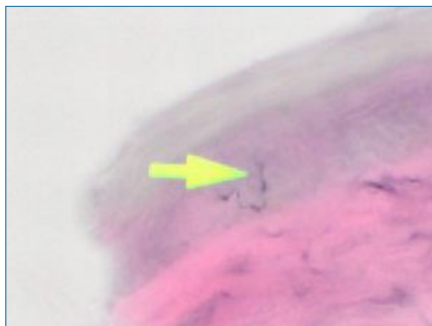
**Post-Treatment Result:**

**An average increase of 496.63% in nerve fiber density.**

**Before Neurogenx Treatment - 12/03/15**

**A. SKIN, RIGHT CALF, PUNCH BIOPSY:**

- Intra-epidermal nerve fiber density is moderately decreased (**2.24 Fibers/mm**).
- Papillary dermal nerve fibers atretic and diminished. (See Comment 1).



**B. SKIN, LEFT CALF, PUNCH BIOPSY:**

- Intra-epidermal nerve fiber density severely decreased (epidermis essentially devoid of fibers: **1.19 Fibers/mm**).
- Papillary dermal nerve fibers profoundly diminished. (See Comment 2).

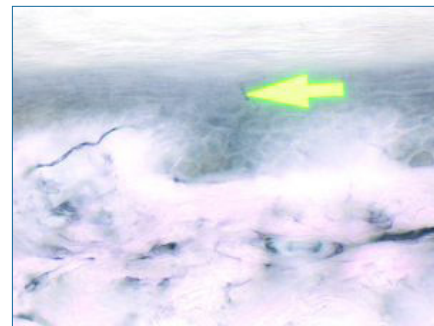


Final Diagnosis performed by Wayne L. Bakotic D.O. Electronically signed 12/15/2015

**After Neurogenx Treatment - 12/12/16**

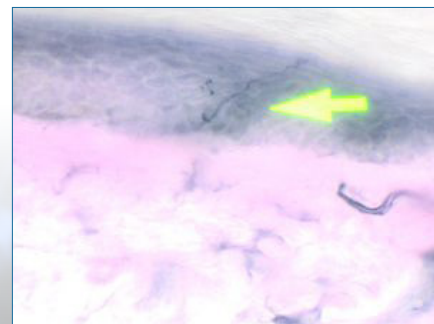
**A. SKIN, RIGHT CALF, PUNCH BIOPSY:**

- Intra-epidermal nerve density low-normal/borderline (**7.51 Fibers/mm**).
- Mild morphologic degenerative changes are seen among intra-epidermal nerve fibers. (See Comment 3).
- **2.24 to 7.51 is an increase of 235.27%**



**B. SKIN, LEFT CALF, PUNCH BIOPSY:**

- Intra-epidermal nerve density within the normative range (**10.21 Fibers/mm**).
- Mild morphologic degenerative changes are seen among intra-epidermal nerve fibers. (See Comment 4).
- **1.19 to 10.21 is an increase of 757.98%**



Final Diagnosis performed by Wayne L. Bakotic D.O. Electronically signed 12/16/2016



**Pathology report by BAKO PATHOLOGY SERVICES**

## EPIDERMAL NERVE FIBER DENSITY ANALYSIS OF PATIENT "RS"

**Patient Information:** 79-year-old malePhysician: Kevin F Sunshein, DPM  
Neurogenx NerveCenter of Centerville  
6474 Centerville Business Pkwy  
Centerville, OH 45459-2633**Post-Treatment Result:****An average increase of 496.63% in nerve fiber density.**

COMMENT 1: Immunohistochemical studies and morphometric analysis disclose a moderate decreased in the number of small myelinated (A-delta) and unmyelinated (C) nerve fibers within the epidermis. In addition, fibers within the papillary dermis are atretic and diminished in number. The depressed number of fibers following immunohistochemical analysis using anti-PGP 9.5 antibodies is indicative of established small fiber neuropathy\*\*. The published specificity below the fifth percentile, (less than 3.8 fibers/mm), is 97% (in the context of an appropriately fixated post-biopsy specimen). Reference: Ebenezer GJ, P Hauer, C Gibbons, et al. J Neuropathol Exp Neurol 66(12):1059-1073, 2007.

COMMENT 2: Immunohistochemical studies and morphometric analysis disclose a severe loss of small myelinated (A-delta) and unmyelinated (C) nerve fibers within the epidermis. In addition, fibers within the papillary dermis are atretic and greatly diminished. The utter absence of fibers following immunohistochemical analysis using anti-PGP 9.5 antibodies is indicative of advanced small fiber neuropathy\*\*. The published specificity below the fifth percentile, (less than 3.8 fibers/mm), is 97% (in the context of an appropriately fixated post-biopsy specimen). Reference: Ebenezer GJ, P Hauer, C Gibbons, et al. J Neuropathol Exp Neurol 66(12):1059-1073, 2007.

COMMENT 3: Immunohistochemical studies using anti-PGP 9.5 antibodies; and subsequent morphometric analysis, disclose a density of epidermal nerve fibers that is within the normative range for this anatomic location; however, it scarcely reaches that threshold (7.1 fibers/mm is the lower limit of normal range). In light of the clinical history in this case, this test suggests significant improvement from the patient's prior small fiber density status. We have found the persistence of degenerative changes in cases such as these to be commonplace. Their significance has not been adequately studied; however, could be a reflection of the patients overall medical status.

COMMENT 4: Immunohistochemical studies using anti-PGP 9.5 antibodies; and subsequent morphometric analysis, disclose a density of epidermal nerve fibers that is within the normative range for this anatomic location (counts reach the threshold of 7.1 fibers/mm. The density in the current biopsy militates against the presence of established small fiber neuropathy (sensitivity approaching 90%) at this point in time. In light of the clinical history in this case, this analysis suggests significant improvement from the patient's prior small fiber density status. We have found the persistence of degenerative changes in cases such as these to be commonplace. Their significance has not been adequately studied; however, could be a reflection of the patients overall medical status.

\*\*\*Original report is available upon request.

**Pathology report by Advanced Laboratory Services**

**EPIDERMAL NERVE FIBER DENSITY ANALYSIS OF PATIENT "JM"**

**Patient Information:** Name: JM

Physician: Steven Weinschel, MD, JD  
Neurogenx NerveCenter of St. Petersburg  
3500 38th Avenue North  
St. Petersburg, FL 33713

**Post-Treatment Result:**

**66% increase in nerve fiber density**

**Before Neurogenx Treatment - 10/21/15**

A. SPECIMEN PUNCH SITE LEFT DISTAL LEG:

- The epidermal nerve fiber density estimate is **2.5 fibers/mm** (normal > 2.1 fibers/mm).



**After Neurogenx Treatment - 6/21/16**

A. SPECIMEN PUNCH SITE LEFT DISTAL LEG:

- The epidermal nerve fiber density estimate is **4.14 fibers/mm** (abnormal < 2.5 fibers/mm; low normal value range = 2.5 - 4.1).



\*\*\*Original report is available upon request.

**Pathology report by Advanced Laboratory Services**

**EPIDERMAL NERVE FIBER DENSITY ANALYSIS OF PATIENT "LR"**

**Patient Information:** 69-year old male

Physician: Baker-Belscher, Carol, ARNP  
Neurogenx NerveCenter of St. Petersburg  
3500 38th Avenue North  
St. Petersburg, FL 33713

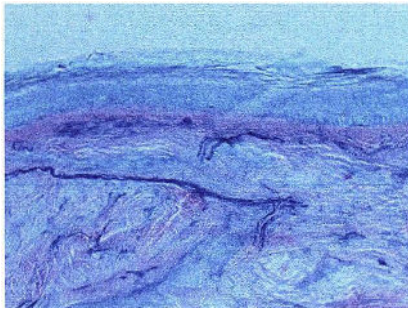
**Post-Treatment Result:**

**Overall average increase in nerve fiber density of 712.44%**

**Before Neurogenx Treatment - 02/22/16**

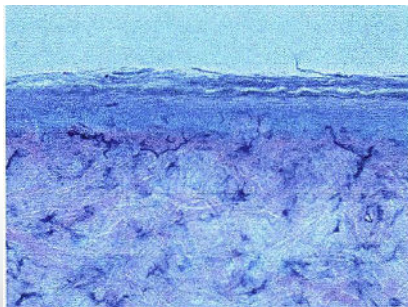
A. SPECIMEN PUNCH SITE RIGHT DISTAL LEG:

- The epidermal nerve fiber density estimate is **0.1 fibers/mm** (normal > 2.8 fibers/mm).



B. SPECIMEN PUNCH SITE RIGHT DISTAL THIGH:

- The epidermal nerve fiber density estimate is **1.8 fibers/mm** (normal > 7.0 fibers/mm).

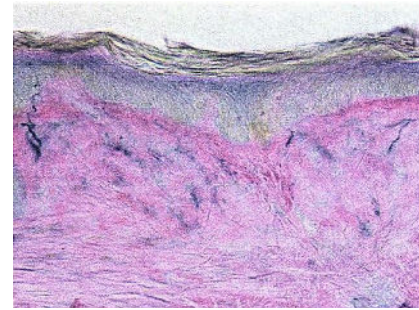


Case reviewed with generated report by Michael Stanton, MD at the University of Rochester  
601 Elmwood Ave. Rochester, NY 14642

**After Neurogenx Treatment - 01/16/17**

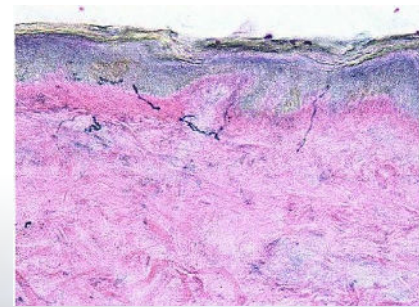
A. SPECIMEN PUNCH SITE RIGHT DISTAL LEG:

- The epidermal nerve fiber density estimate is **6.73 fibers/mm** (abnormal < 2.7 fibers/mm; low normal value range = 2.7 - 4.2).
- 0.1 to 6.73 is an increase of 6630%**



B. SPECIMEN PUNCH SITE RIGHT DISTAL THIGH:

- The epidermal nerve fiber density estimate is **2.69 fibers/mm** (abnormal < 6.2 fibers/mm; low normal value range = 6.2 - 6.8).
- 1.8 to 2.69 is an increase of 49.44%**



Case reviewed with generated report by Charles Shao, MD at Therapath Neuropathology  
545 West 45th Street, New York, NY 10036

\*\*\*Original report is available upon request.



**Pathology report by Advanced Laboratory Services**

**EPIDERMAL NERVE FIBER DENSITY ANALYSIS OF PATIENT "SM"**

**Patient Information:** 73-year-old male

Physician: Steven Weinschel, MD, JD

Neurogenx NerveCenter of St. Petersburg

3500 38th Avenue North

St. Petersburg, FL 33713

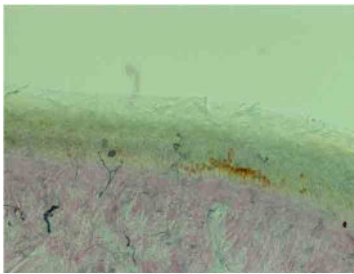
**Post-Treatment Result:**

**Overall average increase in nerve fiber density = 42.45%**

**Before Neurogenx Treatment - 02/23/16**

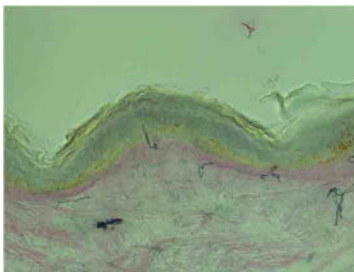
**A. RIGHT DISTAL LEG:**

- The epidermal nerve fiber density estimate is **0.0 fibers/mm** (normal > 2.1 fibers/mm).



**B. RIGHT DISTAL THIGH**

- The epidermal nerve fiber density estimate is **4.0 fibers/mm** (normal > 7.0 fibers/mm).

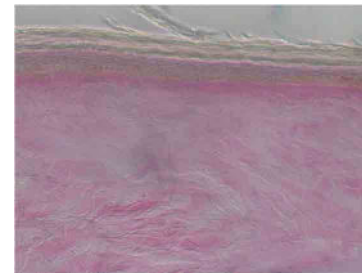


Case reviewed with generated report by David Herrmann, MD at the University of Rochester 601 Elmwood Ave. Rochester, New York 14642.

**After Neurogenx Treatment - 08/15/16**

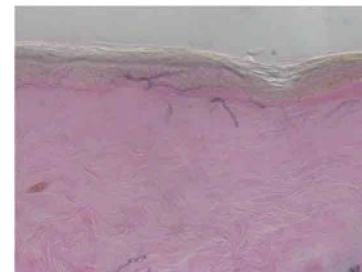
**A. RIGHT DISTAL LEG:**

- The epidermal nerve fiber density estimate is **0.34 fibers/mm** (abnormal < 2.5 fibers/mm; low normal value range = 2.5 - 4.1). **33.9% increase in nerve fiber density.**



**B. RIGHT DISTAL THIGH:**

- The epidermal nerve fiber density estimate is **6.04 fibers/mm** (abnormal < 6.2 fibers/mm; low normal value range = 6.2 - 6.8). **51% increase in nerve fiber density.**



Case reviewed with generated report by Codrin Lacob, MD at Therapath Neuropathology, 545 West 45th Street, New York, NY 10036.

**Pathology report by Advanced Laboratory Services**

**EPIDERMAL NERVE FIBER DENSITY ANALYSIS OF PATIENT "SM"**

**Patient Information:** 73-year-old male

Physician: Steven Weinschel, MD, JD

**Post-Treatment Result:**

**Overall average increase in nerve fiber density = 42.45%**

Neurogenx NerveCenter of St. Petersburg  
3500 38th Avenue North  
St. Petersburg, FL 33713

**Before Neurogenx Treatment - 02/23/16**

**DIAGNOSIS: (A, B) SKIN, RIGHT DISTAL LEG AND RIGHT DISTAL THIGH, BIOPSIES (PROCEDURE DATE 2/23/2016): CONSISTENT IN THE APPROPRIATE CLINICAL SETTING WITH A SEVERE LENGTH-DEPENDENT NEUROPATHY AFFECTING UNMYELINATED SENSORY FIBERS.**

**CLINICAL HISTORY:** Burning/tingling sensations

**GROSS DESCRIPTION:**

A Specimen received in cryoprotectant following Zamboni's fixation. Received in one vial labeled "Right Distal Leg". It consists of a soft tan punch biopsy of skin measuring 3 mm in diameter by 3 mm.

B. Specimen received in cryoprotectant following Zamboni's fixation. Received in one vial labeled "Right Distal Thigh". It consists of a soft tan punch biopsy of skin measuring 3 mm in diameter by 3 mm.

**MICROSCOPIC DESCRIPTION:**

A) Right Distal Leg: Epidermal nerve fibers (PGP 9.5 immunostaining) are almost absent in these sections. The epidermal nerve fiber density estimate is 0.0 fibers/mm (normal > 2.1 fibers/mm).

Morphologic analysis shows excessively segmented immunoreactivity of some remaining sub-epidermal nerve fibers.

B) Right Distal Thigh: Epidermal nerve fiber density (PGP 9.5 immunostaining) is reduced. The epidermal nerve fiber density estimate is 4.0 fibers/mm (normal > 7.0 fibers/mm).

Morphologic analysis shows a focal area of large axonal swellings. Positive controls for IHC were evaluated and are adequate for diagnosis.

**After Neurogenx Treatment - 08/15/16**

**DIAGNOSIS: A. RT DISTAL LEG, SKIN BIOPSY: SKIN WITH SIGNIFICANTLY REDUCED EPIDERMAL NERVE FIBER DENSITY, CONSISTENT WITH SMALL FIBER NEUROPATHY. B. RT DISTAL THIGH, SKIN BIOPSY: COUNT ONLY. SEE COMMENT. C. RT PROXIMAL THIGH, SKIN BIOPSY: SKIN WITH SIGNIFICANTLY REDUCED EPIDERMAL NERVE FIBER DENSITY, CONSISTENT WITH SMALL FIBER NEUROPATHY.**

**CLINICAL HISTORY:** Numbness/paresthesias

**GROSS DESCRIPTION:** A. Specimen received in cryoprotectant following Zamboni's fixation. Received in one vial labeled "Right Distal Leg". It consists of a soft tan punch biopsy of skin measuring 3 mm in diameter by 1.5 mm.

B. Specimen received in cryoprotectant following Zamboni's fixation. Received in one vial labeled "Right Distal Thigh". It consists of a soft tan punch biopsy of skin measuring 3 mm in diameter by 2 mm.

C. Specimen received in cryoprotectant following Zamboni's fixation. Received in one vial labeled "Right Proximal Thigh". It consists of a soft tan punch biopsy of skin measuring 3 mm in diameter by 3 mm.

**MICROSCOPIC DESCRIPTION:** A. Right Distal Leg: From the samples that have been tested, there is no evidence of vasculitis or other histological abnormalities based on the H&E stain. Many disorders, including vasculitis, are focal and this analysis does not exclude the diagnosis. There is almost complete depletion of nerve fibers in the subepithelial neural plexus.

B. Right Distal Thigh: From the samples that have been tested, there is no evidence of vasculitis or other histological abnormalities based on the H&E stain. Many disorders, including vasculitis, are focal and this analysis does not exclude the diagnosis. There is almost complete depletion of nerve fibers in the subepithelial neural plexus.

C. Right Proximal Thigh: From the samples that have been tested, there is no evidence of vasculitis or other histological abnormalities based on the H&E stain. Many disorders, including vasculitis, are focal and this analysis does not exclude the diagnosis.

\*\*\*Original report is available upon request.