

# Treating Diabetic Neuropathy Via MicroVas Technology

*This unique electrotherapeutic device has shown positive results.*

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**Disclaimer:** *The author has no financial ties to NeuroVasix and personally does not benefit from its success.*

**D**iabetic neuropathy has been identified as an important risk factor for foot problems in the diabetic patient. The cost of diabetic neuropathy and its consequences to the U.S. healthcare system is approximately \$13.7 billion dollars annually. About 50 to 60 percent of patients with diabetes will develop neuropathy and 15 percent of patients with diabetes will develop an ulcer in their lifetimes. Patients with diabetic neuropathy do not always have pain but for those who do, the Food and Drug Administration (FDA) has approved Duloxetine (Cymbalta, Eli Lilly) and Pregabalin (Lyrica, Pfizer) for the management of painful diabetic neuropathy. These are the only two drugs with an indication to manage this specific type of pain.

However, little is known about the epidemiology and natural history of diabetic neuropathy. Many researchers have spent their entire careers investigating its etiology and have concluded that hyperglycemia is the most important factor leading to the development and severity of neuropathy.

That is not to say that other etiologies play no role. The Rochester Neuropathy Study demonstrated that the cause of the neuropathy in 10 percent of the diabetic patients

was due to etiologies other than diabetes.<sup>1</sup> Deficiency of growth factors, advanced glycosylated end product accumulation, immune mechanisms, glucose auto-oxidation, and PKC-beta inhibition activation are among other etiologies advocated in the medical literature.

However, it is clear that hyperglycemia plays a central role in creating the vascular imbalances that are so unique to the diabetic process. Glucose does not directly cause adverse changes to the vascular system. These changes are accomplished indirectly through the alteration of multiple metabolic pathways. This sequence of events leads to early changes in functional flow and pressure as well as late structural changes that ultimately compromise the ability of the microvasculature, namely the endothelium, to carry out its functions in an ever-changing environment. These disturbances eventually may involve capillary closure, extinction, thrombosis or non-perfusion.

## **Understanding the Impact of Microvascular Diseases in Patients with Diabetes**

Patients with diabetes may present with a spectrum of lower extremity vascular disease in both the macrovasculature and microvasculature, and this spectrum correlates with the duration and degree of diabetes and the presence of co-morbid risk factors, such as dyslipidemia, obesity, hypertension, smoking, family history and

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## **New Concepts and Studies**

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anatomic location (i.e, proximal versus distal).

Microvascular dysfunction is a systemic disease that can lead to progressive and destructive retinopathy, nephropathy, neuropathy, impotence and gastro paresis, all of which can serve as clinical markers of disease severity. This same microvascular dysfunction can occur in the nutritional capillaries of the foot of the diabetic patient, and can affect clinical outcomes even in the absence of overt macrovascular disease. The staging of diabetic microvascular disease in other organs may prove helpful in predicting and explain-

ing prolonged morbidity in patients with diabetic foot disease.

of one or more organ systems. Clinical manifestations of autonomic neuropathy are noticeable in patients with long-standing diabetes and in those with less acute dysfunction occurring within 1-2 years of being diagnosed with the disease.

The pathogenesis of autonomic neuropathy includes theories of metabolic insult to the nerve fibers, neurovascular insufficiency, autoimmune damage and neurohormone growth factor deficiency. The cause of direct neuronal damage and/or the decrease in nerve blood flow is the result of increased glycemic activation leading to sorbitol accumulation. It's also thought that activation of protein kinase C may be the contributing cause of vasoconstriction and reduction in neuronal blood flow. Additionally, increased oxidative stress with increased free radical production may be a cause of vascular endothelial damage, reducing the bioavailability of

nitric oxide.

Nitric oxide is the most potent and abundant vasodilator. Also, the endothelium has the ability to produce vasoactive substances that help control the tone of the microvasculature such as thromboxane and angiotensin. This process is called autoregulation. Nitric oxide also has a role in the modulation of the wound healing process along with another vasodilator, prostacyclin, which is a potent antithrombotic agent which decreases white blood cell adhesion to the endothelium. Research has found a low



level of nitric oxide in patients with diabetes.<sup>2</sup> Therefore, autoregulation is abnormal and poor oxygenated blood diffusion occurs.

### How Does This Relate to the Diabetic Foot?

The Autonomic Nervous System controls microvascular skin flow. In the diabetic population, the rhythmic contraction of small vessels such as arterioles, venules and small arteries is affected. Loss of control of these vessels will increase blood flow in the absence of large vessel peripheral arterial occlusive disease. This is also a consequence of an increase in arteriovenous shunting, and results in a warm foot, with distended dorsal foot veins. According to Low et al., this physiological problem may lead to diabetic neuropathy as well.<sup>3</sup> This problem resembles premature aging. The clinical pedal manifestations of autonomic neuropathy are dry skin, loss of sweating, distended veins, and fissuring which may lead to ulcerations, infection, and gangrene. It has been documented in the medical literature that autonomic neuropathy may increase osteoclastic activity resulting in reduced bone density. Young et al. found in 17 patients with Charcot evidence of reduced bone density in the lower limbs compared with the 10 neuropathic control subjects. Therefore, Charcot arthropathy may reflect the severity of autonomic neuropathy.<sup>4</sup>

Nerve function can be divided into large and small nerve fibers. Tests such as vibration, proprioception, and loss of protective sensation, deep tendon reflexes, muscle strength, two point discrimination, and pinprick are good indicators of

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ing prolonged morbidity in patients with diabetic foot disease.

### Importance of Autonomic Neuropathy

Diabetic Autonomic Neuropathy is noted to be a serious and common complication among the diabetic population. Despite the negative impact on survival and quality of life in people, it is one of the least understood and recognized of diabetic complications. Autonomic neuropathy generally involves the entire autonomic nervous system, which is manifested by dysfunction

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large fiber neuropathy. These patients present with symptoms such as lancinating pain, radiating pain, heaviness, or numbness in the feet and legs. Clinically, the patient demonstrates wasting of the intrinsic muscle of the foot, and with cheiroarthropathy, or ankle equinus. Nerve conduction velocity is rarely indicated for diagnosing diabetic neuropathy, and it is primarily a large fiber test. It represents the transmission of electrical impulses through the largest myelinated fibers. Small fiber nerve functions are perception of heat, cold, and pain sensation. Signs and symptoms of small fiber neuropathy include burning, cold feet, "pins and needles", and hyperalgesia. A practical, diagnostic test for small fiber neuropathy does not exist yet, though there are several tests described in the literature. The QSART machine allows measurements of the sweating function of the foot. However, the variability of the test is not well understood. Although autonomic neuropathy is considered a small fiber neuropathy it is imperative to identify these patients with autonomic neuropathy by questioning specific signs and symptoms that they may experience. Asking the patient for symptoms such as gastroparesis, incontinence, sexual dysfunction, and dizziness with change in position (postural hypotension) may help you identify this patient subset.

Therefore it has been proven that autonomic dysfunction is a complicating factor in the diabetic population. Identifying the patient with diabetic autonomic neuropathy will help the health care professional to assess the spectrum of the disease, and to place this patient in an "at risk" category, knowing that he /she could be at risk for ulcerations, gangrene, or Charcot arthropathy.

### **Rationale for Transcutaneous Electrotherapy, or MicroVas**

Currently there are various medications which may provide symptomatic relief for neuropathy, relief that varies widely among individuals.<sup>5</sup> These antidepressants, opioids, and non-opioid analgesic medications can cause gastrointestinal side effects and excessive sedation and may interact with drugs currently being taken by the diabetic patient.<sup>6,7</sup> Certain electrotherapy, on the other hand, when used to treat diabetic neuropathy, has been noted to improve neuropathic symptoms without any discernable side effects.<sup>8,9</sup> This unique electrical device, MicroVas (by NeuroVasix [www.neurovasix.com](http://www.neurovasix.com); 888-423-1867) stimulates angiogenesis and generation of denser capillary networks in the tissues. This lays the groundwork for new tissue growth and repair in the healing process. The MicroVas technology also raises the metabolic rate in the treated tissues, and thus helps the intimal lining of the arteries to metabolize the excess unused nutrients clogging them. This results in improved blood flow that has been shown to be persistent.<sup>10</sup>

Transcutaneous Electrical Nerve Stimulation produces neurophysiological and chemical effects. These

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effects include an increase in endogenous opioid-like substances (e.g. endorphins, enkephalins) in the central nervous system<sup>11</sup>, a decrease in nerve conduction latency, mechanical pain threshold when applied over a nerve,<sup>12</sup> local vasodilatory effect, enhanced wound healing, influence upon neuronal afferent transmission and conduction velocity, increase in the nociceptive flexion reflex threshold, and changes to the somatosensory evoked potentials.<sup>13,14</sup> MicroVas stimulation of the nerves and the consequent release of nitric oxide in the tissues are felt to be one of

the mechanisms by which increased blood flow and oxygen levels in the tissues occur, therefore rehabilitating the damaged nerves caused by diabetes.

The MicroVas uniquely causes muscle fasciculation and contraction-relaxation cycles in eight separate regions bilaterally, effectively pumping blood through the microcirculation, draining the venous beds and raising the tissue oxygen levels, all of which equates to a 3-mile walk. This, in turn, supplies the oxygen and substrates necessary to accelerate the healing process. In contrast to other technologies on the market that only dilate the capillary beds, MicroVas in-

creases blood flow and raises pressure gradients across the capillary beds. MicroVas has a potent effect on the microcirculation: transcutaneous oxygen probes have demonstrated marked increases in tissue oxygen levels within minutes of initiating treatment. Tissue oxygen levels with successive treatments continue to improve.<sup>10</sup>

### Three Case Studies

#### Case 1

A 56 y/o Hispanic female presented to our institution with history of sharp, dull, constant pain. Her past medical history includes NIDDM for 8 years, hypertension, hyperlipidemia, coronary artery disease, and myocardial infarction in 1995, nephropathy, and retinopathy. Her current medications include metformin, glipizide, enalapril, and metoprolol. She has no history of smoking and denies any alcohol consumption.

Her physical examination reveals an obese lady who is very pleasant and oriented. She demonstrates palpable dorsalis pedis pulse and barely palpable posterior tibial pulse in both feet. Her capillary filling time is less than 3 seconds. She does have absent pedal hair and dry, xerotic skin. She also demonstrates loss of protective sensation to 4/10 sites in both feet. Her deep tendon reflexes, which included Achilles and patellar, were normoflexic. Tuning fork response to the hallux was absent as well to both feet. Musculoskeletal exam was normal to any foot pathology-leading pain. Laboratory evaluation is within normal limits, except A1C of 8.5. The diagnosis of painful neuropathy was made. The Neuropathy Pain Scale (NPS) was used to quantify the type and intensity of her pain (Table 1). The Short-Form McGill Pain questionnaire (SF-MG) was used to measure improve-

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### TABLE 1

#### Pre-Treatment Neuropathy Pain Scale

	CASE 1	CASE 2	CASE 3
Intensity pain	9	6	3
Sharpness pain	7	7	2
Hot pain	5	4	4
Dullness pain	8	5	2
Coldness of pain	4	2	4
Sensitivity of skin	6	3	4
Itchiness of pain	1	1	2
Time quality of pain	all the time	all the time	sometimes
Unpleasantness of pain	9	7	3
Severity of pain			
Deep pain	8	7	2
Surface pain	5	3	3

### TABLE 2

#### Post-Treatment Neuropathy Pain Scale

	CASE 1	CASE 2	CASE 3
Intensity pain	5	2	2
Sharpness pain	4	2	1
Hot pain	4	1	1
Dullness pain	4	2	2
Coldness of pain	4	3	1
Sensitivity of skin	4	4	2
Itchiness of pain	4	1	3
Time quality of pain	sometimes	sometimes	sometimes
Unpleasantness of pain	4	3	2
Severity of pain			
Deep pain	4	6	1
Surface pain	4	5	2

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ment of quality of pain (Table 2). Treatment with MicroVas was three treatments weekly for forty-five minutes each. The patient underwent a total of 17 treatments. Table 1 shows NPS response prior to treatment, and table 2 shows response after treatments. Results show a noticeable improvement in intensity and unpleasantness of her pain. The results of SF-MG are seen in Table 3 before treatment and Table 4 after treatment. Again, improvement in pain rating index, visual analog scale, and overall intensity is noticed.

### Case 2

A 50 y/o Hispanic male presented to our institution with history of sharp, dull, constant pain. His past medical history includes NIDDM for 12 years and coronary artery disease. His current medications include metformin, glipizide, Actos, and low dose aspirin. He has no history of smoking, and denies any alcohol consumption.

Physical examination reveals a very pleasant and oriented man. He demonstrates palpable dorsalis pedis pulse, and posterior tibial pulse in both feet. His capillary filling time is less than 3 seconds; normal pedal hair and skin are noticed. He demonstrates loss of protective sensation to 2/10 sites in both feet. His deep tendon reflexes, which included Achilles and patellar, were hypoflexic. Tuning fork response to the hallux was absent at both great toes. Musculoskeletal exam was normal to any foot pathology-leading pain. Laboratory evaluation is within normal limits, except A1C of 7.0. The diagnosis of painful neuropathy was made. The patient underwent a total of 36 treatments. The results for NPS are in table 1 and table 2. Results show a noticeable improvement in intensity and unpleasantness of his pain. The results of SF-MG are seen in table 3 and table 4 treatments. Again, improvement in pain rating index, visual analog scale, and overall intensity is noticed.

### Case 3

A 52 y/o Caucasian male presented to our institution with a history of lancinating, dull pain, especially at night. His past medical history includes NIDDM for 17 years, coronary artery disease, and hypertension. His current medications include metformin, glipizide, hydrochlorothiazide, and low dose aspirin. He has 35 years history of smoking and 2-3 beers/week of alcohol consumption.

Achilles and patellar, were hypoflexic. Tuning fork response to the both great toes was absent. Musculoskeletal exam was normal to any foot pathology-leading pain. Laboratory evaluation is within normal limits, except A1C of 9.2, and random serum glucose of 168. The diagnosis of painful neuropathy was made. The patient underwent a total of 33 treatments. The results for NPS are in table 1 and table 2. Results show an improvement

**TABLE 3**  
**Pre-Treatment Short-Form McGill Pain Questionnaire**

	CASE 1	CASE 2	CASE 3
Sensory Pain Rating Index	24	12	2
Affective Pain Rating Index	9	2	0
Total Pain Rating Index	33	14	2
Visual Analog Scale	9.7	5.3	0.7
Overall Intensity of Total Pain	4	2	1

**TABLE 4**  
**Post-Treatment Short-Form McGill Pain Questionnaire**

	CASE 1	CASE 2	CASE 3
Sensory Pain Rating Index	15	4	2
Affective Pain Rating Index	4	1	0
Total Pain Rating Index	19	5	2
Visual Analog Scale	6.7	2.3	0.2
Overall Intensity of Total Pain	2	2	2

Physical examination reveals a very pleasant and oriented man. He demonstrates non- palpable dorsalis pedis pulse, and palpable posterior tibial pulses in both feet. His capillary filling time is less than 3 seconds; absent pedal hair and dry skin is noticed. Non-invasive studies were ordered. Findings included left ABI .91, right ABI .88, and left TBI .71, and right TBI .76. Triphasic waveforms to anterior tibial artery and posterior tibial artery were also appreciated. He demonstrates loss of protective sensation to 1/10 sites in both feet. His deep tendon reflexes, which included

in intensity and unpleasantness of his pain. The results of SF-MG are seen in table 3 and table 4 treatments. Again, improvement in pain rating index, visual analog scale, and overall intensity is noticed.

### Conclusion

MicroVas treatments have proven to be a very effective tool in relieving patients of neuropathic pain and even restoring sensation by the process described in this article. With approximately 1,000 devices in the podiatric marketplace,

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physicians have noted that the results are long-lasting and an improvement over the pharmaceutical alternatives, which may have side effects and only treat symptomatology, without causing any metabolic or physiological changes within the body. Additionally, physicians receive insurance reimbursement for this office-based treatment modality. ■

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