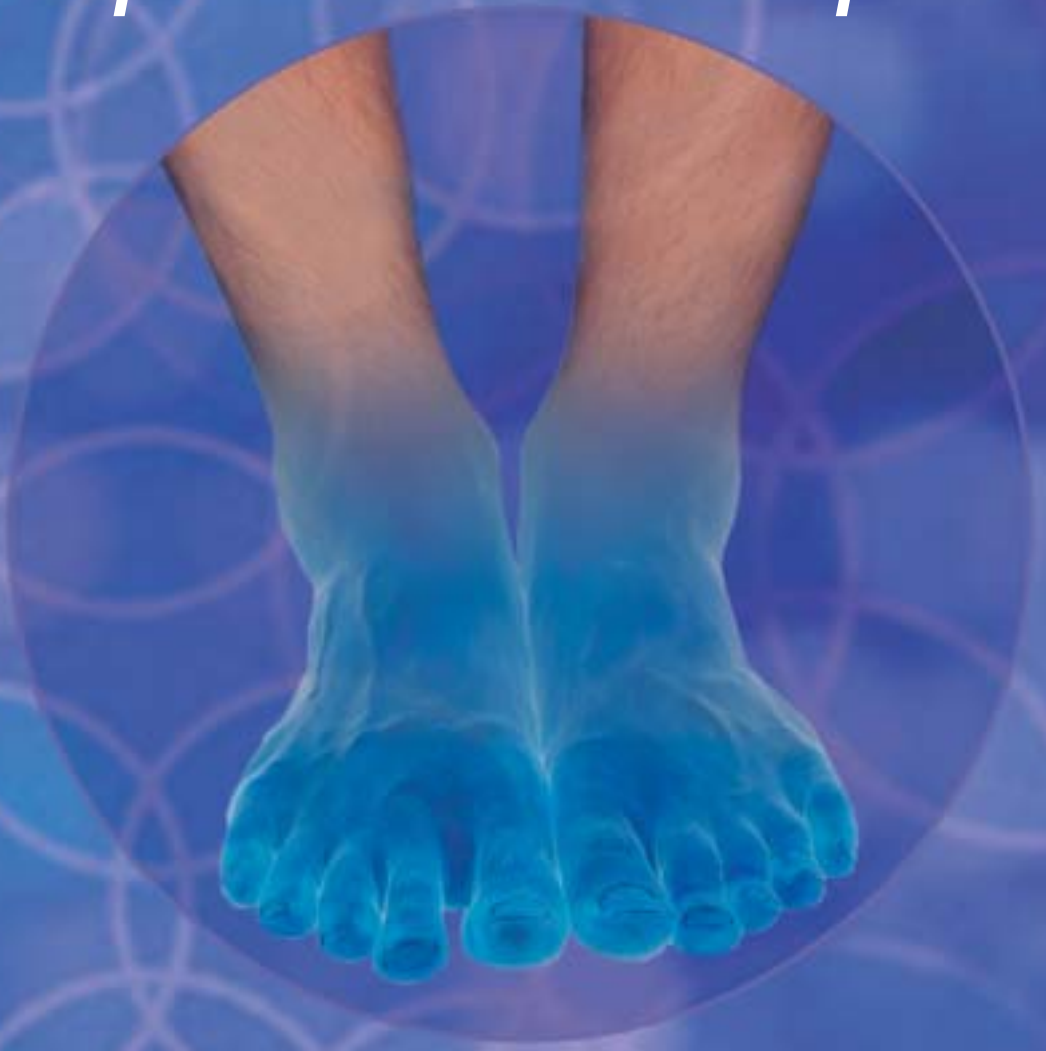
Diabetic and Non-diabetic
Peripheral Neuropathy



Restore Sensation and Eliminate Pain*
Through MicroVascular Therapy

MicroVas
TECHNOLOGIES, INC.

*Not all people benefit from MicroVascular Therapy.
No double blind randomized studies have taken place.

MicroVascular Therapy (MVT)

Most of the possible mechanisms in the pathogenesis of neuropathy result in ischemia, and the resultant hypoxia is, in every case, a major causitive agent in the degredation of axonal structure. The common response in seeking new therapeutic solutions is to search for a pharmacological agent to work on the selected mechanism to achieve an increase in neuronal blood flow and a reduction or elimination of hypoxia.

MVT is a physical medicine modality which addresses the problem from a different perspective: working directly and mechanically to move blood flow through neuromuscular stimulation of the venous muscle pump.

In MVT, a MicroVas Vascular Treatment System generates ionic impulses which pass through the body, or its extremities, using strategically placed carbon emitter pads. The pads are positioned 180° from each other in groups of up to 8 pairs. The ionic impulses pass completely through the limb or body, creating neuromuscular stimulation of the venous muscle pump, and simultaneously upregulating the metabolic process.

While very little information exists concerning the MVT mechanism of action or efficacy, one study of 25 diabetics[1] shows encouraging results (Chart 1).

While the 48% average increase in $TcPO_2$ for patients after one 45 minute treatment is dramatic, the 157% increase in baseline $TcPO_2$ for patient number 4, suggests that the benefits of treatment are cumulative and perhaps long-lasting. It is postulated that this is the result of angiogenesis, or perhaps the reversal of stenosis brought about through the repeated pulsations with increased blood flow and increased hydrostatic pressures.

In terms of limb salvage, patient number 2 may be the single most dramatic example. In week one, with a $TcPO_2$ reading of 0 before treatment and 2 after treatment, he represented an unsalvageable limb. After four weeks of treatment, he still reads only 3 before treatment and 8 after treatment: quite an improvement, but still not a salvagable limb. Following treatment in the eighth week, however, he reached a reading of 35—very likely a salvageable limb!

While data regarding microvascular therapy as applied in peripheral neuropathy are scarce, initial findings show promise (Chart 2, right). Patients were referred to this clinic by neurologists, vascular and orthopedic surgeons as well as family practitioners, all of whom had depleted their pharmacological armamentarium on these patients without results.[2]

Patients were 71% female (40), 29% male (16) and ranged in age from 58 to 80. Both diabetic (88%) and non-diabetic neuropathy (12%, unknown etiology) were represented. (MVT has been used in other studies on chemotherapy-inspired neuropathy).

Not shown in the data, but of significant importance is the patient response to MVT, which included a reduction or elimination of drug use. Patient HS went from a dose of six Tramadols, 1200 milligrams of Neurontin and three to four Hydrocodone daily, to a use of half a Hydrocodone three times daily. Patient

48%
Average tissue oxygen tension improvement in one treatment:

58%
Average tissue oxygen tension improvement in baseline over 4 weeks:

1003%
Largest tissue oxygen tension improvement in one treatment:

157%
Largest tissue oxygen tension improvement in baseline, 8 weeks:

CHART 1

	Day 1		Week 4		Week 8	
Patient	Baseline	End TX	Baseline	End TX	Baseline	End TX
1. RH	3	3	8	-	-	
2. EH	2	3	8	5	35	
3. MM	24	18	29	-	-	
4. VW	36	32	48	54	63	
5. SB	27	-	-	-	-	
6. ED	21	24	36	-	-	
7. JF	46	48	52	-	-	
8. WG	6	2	14	-	-	
9. RG	45	-	-	-	-	
10. BH	56	-	-	48	60	
11. KH	46	-	-	-	-	
12. DH	60	-	-	-	-	
13. RJ	31	-	-	-	-	
14. BK	65	-	-	-	-	
15. JR	21	-	-	-	-	
16. HL	23	-	-	-	-	
17. JM	46	-	-	46	51	
18. RM	32	-	-	-	-	
19. MN	1	-	-	-	-	
20. JN	37	-	-	-	-	
21. AO	34	-	-	-	-	
22. AS	25	-	-	-	-	
23. WT	16	-	-	-	-	
24. DW	47	-	-	-	-	
25. NW	62	-	-	-	-	

$TcPO_2$ readings were taken:
1. At the beginning of treatment
2. After treatment
3. Pre and post treatment at four weeks
4. Pre and post treatment at eight weeks

1. Clinical Study, University of Oklahoma Health Science Center, 1999, unpublished
2. Clinical Study, MicroVas Treatment Center, 2003, unpublished
3. Can VEGF reverse diabetic neuropathy in human subjects? Veves, A. King, G.L. J Clin Invest. 2001 May;107(10):1215-8

THE MICROVASCULAR HYPOTHESIS

DIABETES

LEADS TO

HYPERGLYCEMIA

WHICH LEADS TO

N-6 Fatty Acid Metabolism and/or
DAG ↑PKC Activation and/or
Glycated Products and/or
Oxidative Stress and/or
Activation of Polyol Pathway *

WHICH LEADS TO

↓ Neurotrophic factors
↓ Na^+, K^+, ATPase
Vasoconstriction

WHICH LEADS TO

Reduced Blood Flow and Hypoxia
Reduced Nerve Conduction Velocity

WHICH LEADS TO

Degradation of Axonal Structure

NEUROPATHY

Treatment With

MICROVASCULAR THERAPY

CREATES

Increased Blood Flow and Elevated Tissue Oxygenation

WHICH LEADS TO

↑Neurotrophic factors
↑ Na^+, K^+, ATPase
Vasodilation

WHICH LEADS TO

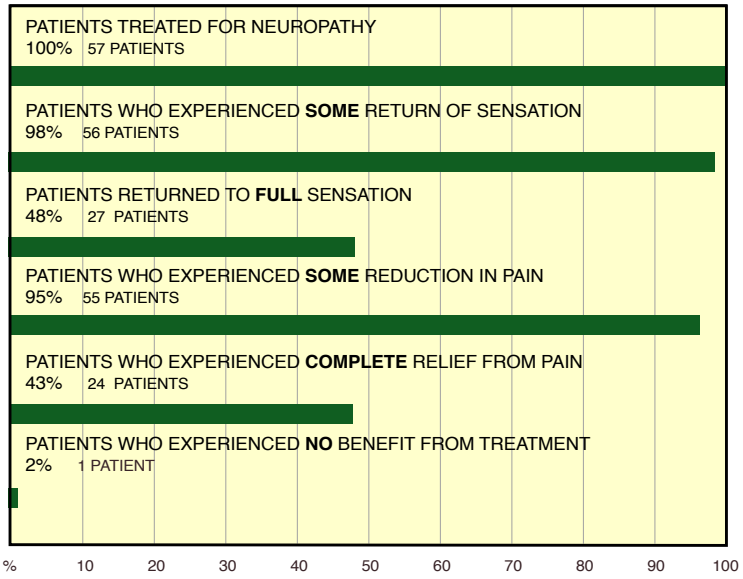
Improved Nerve Conduction Velocity

WHICH LEADS TO

Restoration of Sensation and Amelioration of Pain

VS was taking 4 Tegretol, 3 Norgesic Forte and 16 ibuprofen daily. After six weeks of treatment, the patient has ceased all drug use. Patient JP was taking 3,200 milligrams of Neurontin daily, then went to Methadone twice daily. Today, he is drug-free and pain-free.

CHART 2



There is a need for more studies with precise measuring methods, such as quantitative nerve conduction velocities and amplitudes of evoked responses, which are objective techniques for accurately assessing nerve function, rather than relying on the patient's subjective response.

Can a relatively short regimen of physical medicine actually reverse neuropathy without addressing the underlying causes? (See chart "The MicroVascular Hypothesis" at left) Are the apparent improvements shown in these limited trials transient or long-lasting? There is a need for long-term studies. In a recent article, King and Veves of Harvard Medical School said, "an urgent need exists to develop new therapeutic approaches that will improve nerve function in diabetic patients". Perhaps MVT is that new therapeutic approach.

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* Possible pathogenesis of diabetic neuropathy: Factors implicated in the pathogenesis of diabetic neuropathy include the activation of the polyol pathway, the activation of protein kinase C (PKC), increased oxidative stress, the impaired N-6 fatty acid metabolism, auto-oxidation of glucose, the formation of advanced glycation end products (AGEs), and the reduced bioavailability of neurotrophic factors. All these mechanisms are interrelated and can potentiate each other's detrimental effects. Although the exact mechanisms of their action are not well understood, it is currently believed that these factors lead to reduced Na+, K+ ATPase activity and vasoconstriction, reduced endoneurial blood flow and nerve hypoxia. The latter changes then lead to reduced nerve conduction velocities, axonal loss, axonal demyelination, and nerve dysfunction.

Other physiological changes that accompany the onset of diabetes may also contribute to peripheral neuropathy. In particular, decreased blood flow to these nerves is one of the earliest functional findings in the development or induction of diabetes. The resulting local hypoxia in the peripheral nerves is believed to be a major pathogenic factor, although impaired mitochondrial functions and apoptosis of neurons and Schwann cells also occurs with similar timing and may act independently of hypoxia to induce peripheral nerve dysfunction. In addition, reduction in neurotrophic factors such as nerve growth factor availability (including neurotrophin-3 [NT-3], brain-derived neurotrophic factor, and neurotrophin-4/5 [NT-4/5]) and aberrant phosphorylation of the neurofilaments that are responsible for the structural nerve axon integrity have also been implicated in the pathogenesis of diabetic neuropathy.[3]

PATIENT TESTIMONIALS

Specialists and Drugs Brought No Relief

Now , thanks to MicroVas, I can do whatever I want

John Pearson

My neuropathy came on gradually over a couple of years. But first let me say that my feet have lots of problems. I'm a rancher and my feet have been stomped on by horses many times with lots of broken bones.

When I started getting the neuropathy, I was in a lot of pain and I couldn't feel my feet. When I was driving, I couldn't tell whether I was pushing the accelerator or the brake except by what the truck did.

"Improvement in conduction velocity by improvement in tissue oxygenation suggests that studies of agents which bring about improvements in microvascular blood flow should be urgently considered."

Young, Veves et al. Restoring lower limb blood flow improves conduction velocity. Diabetologia (1995) 38: 1051-1054

I was sent to a specialist, a neurologist, who thought I should have an operation and he sent me to a second specialist who disagreed. By this time I'm taking 800 milligrams of Neurontin four times a day, then they put me on Methadone twice a day. It helped the pain but didn't help with the feeling. I wasn't interested in being a dope head so I cut myself back.

I was living now with pain all the time that was pretty near unbearable, around a ten on the pain scale all day. I was up a lot at night, unable to sleep. After the third or fourth MicroVas treatment, I could tell it was really helping. After about two months of treatment, three times a week, I was pretty much back to normal.

My feet don't hurt any more and I don't take drugs. Now I can haul hay and do most of the things I used to do.

I Just Wanted to Wear Shoes Again!

I had severe, burning pain, diabetic neuropathy and plantar fasciitis.

Helen Stewart

I was originally diagnosed with diabetic neuropathy and then I began having severe pain in my feet and ankles. The diagnosis was modified to include plantar fasciitis.

The pain, which took the form of a burning sensation, originated in my feet and ankles and radiated up my legs to the hips, primarily the right leg. The pain began in January and by the end of June, I suffered excruciating pain trying to wear shoes. The pain eased up at night, but when my feet hit the floor in the morning, it started all over again. On a scale of one to ten, I was living with pain at the ten level, on a more or less constant basis.

My physician tried to deal with these conditions through the use of prescription drugs. On a daily basis, I was taking six Tramadols, twelve hundred milligrams of Neurontin and three to four Hydrocodone. Despite all these drugs, however, the pain was getting worse.

"Reversal of hypoxia halts the progression of diabetic neuropathy"

Akbari et al. Arch Surg 1997; 132: 148-152

Today I am virtually pain free. and no longer take Tramadol or Neurontin, only half a Hydrocodone three times daily. I am having no problems with neuropathy or plantar fasciitis. I recently wore high heels for the first time in months with very little discomfort.

I'm a CNA, and I am now planning on returning to work, which would have been impossible before. MicroVas has given me my life back.

My Life Is Normal And I'm Lovin' It!

I wore sandals in the winter, and couldn't cover my feet in bed.

Vicki Steely

I've had neuropathy for about three years. I tried to deal with it myself for about a year. Finally I went to see my doctor. She said she was sure that it was neuropathy and that it would only get worse, it wouldn't get any better. I suffered along for about another year, usually around a five or six on the pain scale. Then, the last six months or so, I couldn't tell the difference between a wood floor or a cold tile floor on my feet. I could have had a rock in my shoe, and I wouldn't have known it.

I started taking Tegretol, but it seemed to wear off in about eight to twelve weeks. Next I was on Neurontin, taking 600 milligrams twice a day and also taking 16 Ibuprofen and three Norgesic Forte every day.

I was staying home almost all the time so I could go barefoot and keep my feet up. For two years I slept with my feet uncovered and a fan blowing on them After about five treatments I woke up in the middle of the night and my feet were cold and it dawned on me: hey I'm getting better! I was so excited I woke my husband up.

I have taken thirteen treatments so far and am enjoying wearing dress shoes and hose to church as well as wearing tennis shoes with my jeans. Thanks to MicroVas, my life is normal again, and I'm loving it!

MicroVas has been a blessing—an answer to prayer.

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Not all people benefit from MicroVascular Therapy. No double blind randomized studies have taken place.