

A Retrospective Study of High-Voltage, Pulsed Current as an Adjunctive Therapy in Limb Salvage for Chronic Diabetic Wounds of the Lower Extremity

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Abstract

Complex diabetic ulcers of the lower extremity can be slow to heal and may lead to amputation. A retrospective study was conducted to evaluate the effect of a form of electrical stimulation using high-voltage, pulsed current (HVPC) as an adjunct to a multidisciplinary approach to limb salvage for chronic diabetic wounds of the lower extremity. Data from 30 patients with diabetes (17 men, 13 women, mean age 65.8 ± 12.6 years, mean HgbA1c level = 8.2 ± 1.5 , with varying comorbidities) and 45 wounds were reviewed. Mean wound duration before referral and treatment was 25.0 weeks (range 4.0 to 60.0) and the mean wound surface area was 7.8 cm^2 (range 0.6 cm^2 to 62.0 cm^2). The majority (62.2%) of wounds were classified 1C, 2C, or 3D (University of Texas diabetic wound classifications). The mean number of treatments, administered two or three times a week, was 23.0 (range 6.0 to 65.0) and 35 wounds (77.8%) healed after a mean of 14.2 weeks (range 3.4 to 59.0). Of those, 31 remained healed at a mean follow-up of 39.8 weeks (range 11.1 to 84.3) and additional HVPC healed two of the four recurrences. These results suggest that HVPC is a useful addition to a multidisciplinary limb salvage management approach for complex lower extremity wounds. Further study is warranted to elucidate its role in this application.

Key Words: chronic wounds, diabetic wounds, electrical stimulation, lower extremity wounds, wound healing

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Complex diabetic wounds of the lower extremity can be slow to heal and have a significant impact on patient quality of life.^{1,2} Approximately two thirds of patients with lower extremity ulcers exhibit a triad of neuropathy, foot deformity, and minor foot trauma.^{3,4} Diabetic foot complications are the principal cause of nontraumatic lower extremity amputations.⁵ Based on an average of 133,235 limb-loss hospital discharges per year, Goldman et al⁶ estimate the direct annual cost of amputations in the US was \$13 billion in 2004. Previous evidence⁵ suggests that up to 85% of diabetic foot and leg amputations may be prevented with appropriate knowledge of risk factors and application of evidence-based multidisciplinary treatment.

The effects of electrical stimulation on chronic wound healing have been studied since the mid-1960s.^{7,8} Although the mechanism of action is not entirely understood, it has been theorized that the increased blood flow induced by electrical stimulation promotes microcirculation and healing in wounds.^{6,8-10} Others have suggested that electrical stimulation increases the rate of wound healing by attracting and proliferating different cell types to the wound.^{7,10} Electrical stimulation also has been shown to inhibit bacterial activity *in vitro*, which may further enhance wound healing.¹¹ A summary of the studies supporting these theories is beyond the scope of this paper; information has been detailed in several recent reviews and a meta-analysis.^{7,8,12,13}

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Gardner et al's¹³ meta-analysis of 15 studies demonstrated that electrical stimulation therapy increased the rate of chronic wound healing 144% compared to control samples and concluded that electrical therapy is an effective adjunct for chronic wound healing.

In 2002, the Centers for Medicare and Medicaid Services approved payment for electrical stimulation for the treatment of pressure ulcers and lower extremity wounds caused by venous and arterial insufficiency and diabetes that have not responded to at least 30 days of standard wound treatment.^{8,14} A few prospective randomized studies and several retrospective studies documenting successful results with various forms of electrical stimulation in chronic lower extremity wounds have been published.^{1,6,8-10,13,15-17}

Many of the authors' patients with diabetes and chronic foot wounds are referred for care in a final effort to achieve limb salvage and prevent major amputation; a previously unstudied form of high-voltage, pulsed current (HVPC) is used as an adjunct to a multidisciplinary approach to help achieve that goal. This form of HVPC uses higher voltage amplitude than previous methods and causes deep-layered, fused muscle contraction, which may facilitate muscle contraction and relaxation, thereby enhancing blood flow. Because this method of HVPC differs from traditional HVPC used in previously published studies focusing on chronic, lower extremity wounds,^{1,6,9,10,16,17} a retrospective study was conducted to evaluate the effect of this treatment approach on healing for a consecutive series of patients with chronic, full-thickness, diabetic, lower extremity wounds.

Methods and Procedures

Standard management protocol. All patients included in this retrospective cohort were managed by a family physician or referring internist in conjunction with a multidisciplinary wound clinic at a level I trauma center. The multidisciplinary wound team included a plastic surgeon (senior author), vascular surgeon, infectious disease consultants, and podiatrists. As part of diabetic counseling, every effort was made to maintain glycemic control with a glycosylated hemoglobin (High) A1C level <7 and smokers were instructed about the necessity of nicotine cessation. Tissue perfusion was evaluated in all patients using noninvasive Doppler. Patients with ankle-brachial indices <0.7 or biphasic waveforms were seen by vascular surgery for angiography or peripheral vascular intervention as needed. All necrotic tissue was surgically excised to the level of healthy tissue. Wound cultures were obtained from all patients at the beginning of treatment and during treatment as dictated by change in wound status. Persons with bacterial colonization received oral or intravenous antibiotics in accordance with culture results and infectious disease consultation. Bioburden was minimized with appropriate topical antibacterials and weekly local wound debridement. Patients with osteomyelitis were treated with intravenous antibiotics as appropriate, excision of

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Key Points

- Despite diagnostic and treatment advances, managing lower extremity diabetic ulcers and preventing amputations remain considerable challenges.
- Although not completely understood, electrical stimulation has been documented to affect healing of chronic wounds, including diabetic foot ulcers.
- The results of this retrospective study involving 30 patients (45 wounds) suggest that prospective, controlled clinical studies to ascertain the efficacy of electrical stimulation using high-voltage, pulsed current as part of a multidisciplinary limb salvage program are warranted.

necrotic bone, and topical antibacterials. Regular podiatric consultations to maintain appropriate offloading were obtained, and complete offloading with wheelchairs was encouraged for all patients with plantar ulcers.

HVPC therapy was instituted after patients achieved glycemic and bacteriologic control as documented by negative wound cultures and following revascularization procedures if indicated. Treatment was provided two to three times per week for 16 weeks or until wound closure. Treatment three times per week was preferred but if travel was problematic a twice-weekly visit schedule was developed. All treatments were standardized — they were performed in a procedure room where the temperature was controlled at 74° F using the HVPC system (MicroVas Vascular Therapy System, MicroVas Technologies, Inc., Tulsa, OK). The MicroVas treatment system is a patented technology — patent number US 6,745,078, issued June 1, 2004. The MicroVas was pre-programmed at 45 minutes for each treatment. Four emitter pads are placed strategically over the wound and major muscle groups as fol-

Table 1. University of Texas (UT) Wound Classification System^{5,18}

Grade

- 0 Completely epithelialized pre- or postulcerative lesions
- 1 Superficial wounds penetrating through the epidermis only or both the epidermis and dermis
- 2 Wounds penetrating into tendon or capsule, but not bone
- 3 Wounds penetrating to bone or into joint

Stage

- A No infection or ischemia
- B Infection only present
- C Ischemia only present
- D Both infection and ischemia present



Figure 1: Photographs (A-C) demonstrating strategic emitter pad placement for HVPC.

lows: rectangular (5 inch x 8 inch) pads on the anterior and posterior upper thigh; round (4-inch diameter) pads on the anterior compartment and posterior gastrocnemius muscle; smaller rectangular (3 inch x 5 inch) pads just above the ankle, overlying the path of the dorsalis pedis and the posterior tibial arteries; and square (3 inch x 3 inch) pads on the pedal arch on the top and bottom of each foot. Emitter pads were secured with enough pressure to ensure full contact between the pad and the lower extremity without compromising blood flow. In all instances, one emitter pad was placed directly over the wound, which first was covered with saline-soaked gauze. The opposing emitter pad was placed 180° from the wound (see Figure 1a-c). This form of HVPC creates a current that passes through the limb, in many cases creating muscular contraction, and produces a standardized biphasic, symmetric, square pulse wave, with a pulse width of 90- to 100 msec at 55.19 Hz with a cycle width of 18 msec. The duration of the cycle was 1.5 seconds on and 1.5 seconds off. The voltage amplitude is variable to a maximum of 140 volts. The amplitude is individualized so each patient can maximize a fused tetanic contraction but remain below the noxious stimulation threshold. Relative contraindications to HVPC included cardiac pacemakers, malignant ulcers, pregnancy, partial-thickness wounds, or age less than 18 years.

Study methods. After obtaining institutional review board approval, data from a consecutive series of patients with diabetes and chronic, full-thickness wounds of the lower extremity who were treated with HVPC as an adjunctive therapy to standard wound management during a period of 22 months (from October 2005 through August 2007) were reviewed. All patients had previously failed a multidisciplinary wound treatment plan. Data from all patients who returned for scheduled treatments were in-

Table 2: Wound distribution (N=30 patients)

UT Wound Grade	N = 45
UT Grade 1	21 (46.7%)
1A	5 (11.1%)
1B	2 (4.4%)
1C	14 (31.1%)
1D	0 (0.0%)
UT Grade 2	12 (26.7%)
2A	1 (2.2%)
2B	0 (0.0%)
2C	7 (15.6%)
2D	4 (8.9%)
UT Grade 3	12 (26.7%)
3A	0 (0.0%)
3B	2 (4.4%)
3C	3 (6.7%)
3D	7 (15.6%)

cluded. After reviewing a listing of all patients who received HVPC adjunctive therapy, 30 eligible patients (45 wounds) were identified.

Variables. The senior author reviewed patient records to extract patient demographics, social history, comorbidities, previous lower extremity procedures, vascular interventions, High A1C blood levels, and wound variables. Wounds were classified according to initial presentation using the University of Texas (UT) Wound Classification System^{5,18} (see Table 1). A digital planimeter is used to obtain pre-treatment surface area measurements from wound tracings routinely obtained during office examinations; the average of three measurements is recorded. In addition, the number of HVPC treatments performed, the incidence and time to wound healing, length of follow-up, and incidence of wound recurrence were extracted from the records. Healing was considered complete when full epithelialization was present across the wound or when the wound was closed by supplemental skin graft (see Figure 2a-e). Procedure-related complications and additional treatments also were documented. A spreadsheet using Microsoft® Excel 2002 (Microsoft Corporation, Redmond, WA) was created for data entry.

Statistical analysis. Descriptive statistics (mean, me-

dian, standard deviation, frequency, and percentage) were used to describe demographic, diagnostic, treatment, and outcome data. Demographic and outcome variables were compared between the three UT grades. Kruskal-Wallis One Way Analysis of Variance on Ranks was performed to compare non-normally distributed, continuous variables. Chi-square analysis was used to compare categorical data. Additional analyses were conducted comparing demographic and outcome variables between full-thickness skin and subcutaneous tissue wounds and wounds with exposed tendon, muscle, or bone, neuropathic and non-neuropathic wounds, ischemic and nonischemic wounds, and infected and noninfected wounds. Student's *t*-test was used to compare normally distributed, continuous variables; Mann-Whitney Rank Sum Test was used to compare non-normally distributed, continuous data. Fisher Exact Test was used to compare categorical data. Spearman Rank Order Correlation was employed to ascertain a correlation between wound size and the number of treatments. Differences were considered to be statistically significant when the *P* value was <0.05 with a power of at least 0.8. Statistical analyses were performed using SigmaStat® Software, version 2.0 (SPSS, Inc., Chicago, IL).

Results

Patient data. Of the 30 study participants, 17 (56.7%) were men and 13 (43.3%) were women, mean age of 65.8 years (SD = 12.6; median = 67.1; range 33.0 to 90.7 years). The mean High A1C blood level was 8.2 (SD = 1.5; median = 8.1; range 5.4 to 11.6). Diabetes was uncontrolled in eight (26.7%) patients. Other comorbidities included neuropathy (25, 83.3%), peripheral vascular disease (23, 76.7%), cardiac disease (11, 36.7%), infection (10, 33.3%), osteomyelitis (five, 16.7%), and morbid obesity (three, 10.0%). The majority (20, 66.7%) of patients did not have a history of smoking. Nine patients (30.0%) underwent previous amputations due to pre-existing vascular insufficiency or wound complications, five (16.7%) had normal peripheral vascular status, 11 (36.7%) had moderate peripheral vascular disease with biphasic waveforms, and 14 (46.7%) patients were documented as having severe peripheral vascular disease with monophasic waveforms and/or ischemic tissue loss. Ten (33.3%) patients underwent previous vascular interventions and two (6.7%) had unreconstructable peripheral vascular disease.

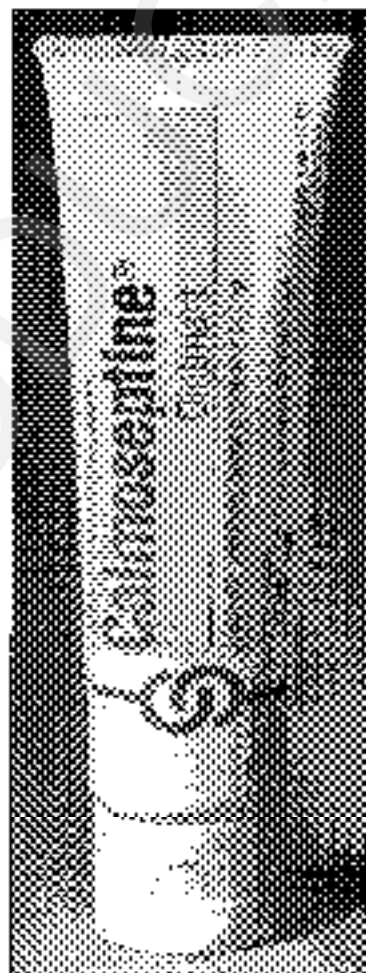
Wound/treatment data. Wounds were located on the forefoot (22, 48.9%), heel (12, 26.7%), anterior/posterior tibia (seven, 15.6%), and ankle (four, 8.9%). Mean wound duration before treatment initiation was 25.0 weeks (SD = 15.6; median = 24.0; range 4.0 to 60.0 weeks).

The study population was split nearly equally between full-thickness skin and subcutaneous tissue wounds (UT Grade 1) and wounds with exposed tendon, muscle, or bone (UT Grades 2 and 3) (see Table 2). The majority of wounds (35, 77.8%) were ischemic, 15 (33.3%) were clinically infected, and 11 (24.4%) were both ischemic and infected. The mean wound surface area before starting electrical stimulation treatment was 7.8 cm² (SD = 12.5; median = 2.4; range 0.6 to 62.0 cm²).

The mean number of HVPC treatments was 23.0 (SD = 10.8; median = 21.0; range 6.0 to 65.0 treatments). Skin grafts were used to close five (16.7%) wounds, all of which remained healed at a mean follow-up of 31.3 weeks. Thirty-five wounds (77.8%) healed in a mean time of 14.2 weeks (SD = 9.8; median = 12.6; range, 3.4 to 59.0 weeks). The patient with the largest wound measurement (62.0 cm²) — a 53.8-year-old man with a history of transmetatarsal amputation who had a neuropathic UT 1C plantar ulcer 16 weeks before treatment initiation — required the highest number of treatments (65) and the longest time to heal (59.0 weeks). The patient initially underwent 35 HVPC treatments in a 5- to 6-month period, at which time his wound was 90% healed before he became noncompliant regarding finishing treatments. When he returned to the physician's office 3 months later, HVPC treatments resumed and the wound completely healed after 30 treatments over 5 months.

Of the 45 wounds, 10 (22.2%) failed to heal (see Figure 3). One patient required a

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Figure 2: A pre-treatment photograph of the foot of a 61.9-year-old man with controlled diabetes, neuropathy, and infection who had a UT 1B forefoot plantar ulcer for approximately 9 months (A). Before beginning HVPC therapy, the patient was discouraged by the ineffectiveness of previous treatment and soaked the wound in extremely hot water containing Epsom salt. After suffering third-degree burns of the foot from the water temperature, the patient developed a UT 1B heel ulcer (B and C). After 25 HVPC treatments, both wounds healed at 8.9 and 12.6 weeks, respectively, and have not recurred at a most recent follow-up of 5 months (D and E).

transmetatarsal amputation (one wound) and below-knee amputation was performed in four patients (five wounds). Of the four remaining wounds, one wound in one patient deteriorated and required further excision of necrotic tendon. Two patients (three wounds) were still undergoing treatment at the time of data collection. Only two of the 10 wounds that failed to heal deteriorated during the course of treatment.

At a mean follow-up of 39.8 weeks (SD = 22.7; median = 36.5; range, 11.1 to 84.3 weeks) after complete healing, equivalent to a mean 56.4 weeks (SD = 23.4; median = 50.4; range 26.1 to 10.7 weeks) from treatment initiation, 31 (88.6%) of the 35 wounds remained healed. Of the four (11.4%) recurrences, additional HVPC was employed and subsequently healed two (5.7%) wounds, below-knee amputation was required in another, and treatment is continuing for the remaining wound. No complications related to the use of HVPC were reported.

Statistical analysis. No statistically significant differences were noted between UT grades and patient demographic or wound outcome variables. Patient demographic, wound duration, wound size, and number of stimulation treatments also did not differ between healed and nonhealed wounds. In addition, no significant differences were noted in patient demographics, number of stimulation treatments, healing time, and wound failure rate between full-thickness skin and subcutaneous tissue wounds (UT Grade 1) and wounds with exposed tendon, muscle, or bone (UT Grades 2 and 3); between neuropathic and non-neuropathic wounds; between ischemic and nonischemic wounds; or between infected and noninfected wounds. No significant relationships were found among the following comparisons: 1) wound duration before treatment or wound size and number of stimulation treatments; 2) wound duration before treatment and healing time; and 3) wound size and number of stimulation treatments.

Discussion

Although not entirely understood, the theoretical effects of electrical stimulation on microcirculation, cell migration, cell

proliferation, and bacterial inhibition suggest that this therapy has the potential to enhance the healing of chronic, diabetic wounds.⁶⁻¹¹ The method of HVPC employed in this study differs from those used in previously published studies focusing on chronic, lower extremity wounds.^{1,6,9,10,16,17} Traditional HVPC therapy involves placement of a few emitter pads on one side of the limb, which causes current penetration into the tissue by only a few centimeters. Typically, therapy is administered offsite using portable units and in many reported studies, the amplitude was set to evoke a sensory response, but was below the level of fused tetanic contraction.^{6,9,10} The HVPC used in this study is administered in clinic and involves the use of multiple emitter pads placed on both sides of the limb. As a result, current penetrates to the major muscle groups. The voltage amplitude is increased until deep-layered, fused muscular contraction is achieved without noxious stimulation. This type of stimulation with a short pulse width of 90- to 100-msec, high-peak current, and a relatively long interpulse interval (55.19 Hz) allows a relatively comfortable stimulation while still effecting skeletal muscle contraction.¹⁹ In addition, it is theorized that this level of stimulation may facilitate sympathetic smooth muscle contraction and relaxation; thereby, improving blood flow at the small arteriolar or venule level.¹⁹

Because treatment is conducted at the clinic and not self-administered, incorrect application is prevented and patient noncompliance greatly reduced. Conducting treatments in a clinic setting also ensures that the stimulation is conducted in a warm room, which has been shown in previous prospective clinical trials^{20,21} to increase skin blood flow and wound healing. Finally, although optimal treatment frequency and duration remain the subject of investigation, HVPC was applied two to three times per week in the current study versus relying on self-administered daily treatment protocols 3 to 7 days per week as reported in previous studies.^{1,6,9,10,17} Although less convenient than home use, administering HVPC in the clinic setting eliminates patient usage errors and reduces patient device use noncompliance, which was reported to be as high as 30%



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in a previous randomized clinical trial.¹⁷

The wounds comprising this study population were complex limb salvage cases — most were ischemic and neuropathic ulcers and occurred in patients with a history of severe diabetes and previous amputation. Despite this complexity, 33 of the 45 wounds (73.3%) healed and no amputations were needed in 66.7% of patients. Furthermore, no infections occurred and routine surveillance cultures taken during the treatment period remained negative, which may suggest a possible bacterial inhibitory effect, as previously demonstrated.²² The results from this study support the use of HVPC as an adjunctive therapy in the management of chronic, full-thickness, diabetic wounds of the lower extremity for which previous conservative management failed.

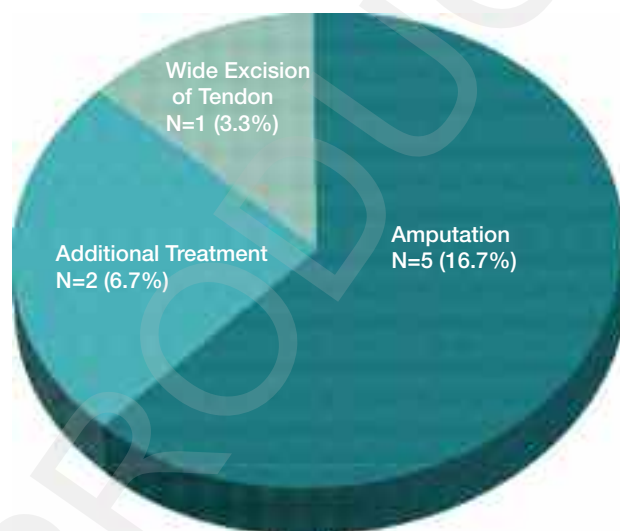
Because no significant differences between wound types and outcome were observed, no conclusions based upon wound types and their responsiveness to HVPC could be made, which may be due to the study population size or be a reflection of the heterogeneity of ischemic wounds and their outcomes.⁶ Although direct comparisons cannot be made, the results of this study correlate with previous studies examining HVPC in chronic diabetic wounds of the lower extremity that report complete healing.^{9,10,17} In Peters et al's¹⁷ randomized, double-blind, placebo-controlled pilot trial of HVPC as an adjunct in diabetic foot ulcers, 65% of wounds undergoing electrical stimulation healed at a mean time to healing of 6.8 weeks compared to a 35% healing rate for wounds receiving placebo at a mean time of 6.9 weeks. Although the proportion of healed ulcers is similar to the current findings, mean time to healing of 14.2 weeks in the current study is higher. However, patients in the Peters et al study received nightly HVPC treatments for 8 hours, 7 days per week, for 12 weeks or until healing was achieved, compared to the current study protocol of two to three times per week for 16 weeks or until healing was achieved.

In a retrospective, observational case series⁹ of six patients with inframalleolar ischemic diabetic wounds treated with HVPC, four (66.7%) wounds healed and two (33.3%) wounds resulted in amputation. Although the proportion of ulcers healed in the current study is similar, patients in the reported case series received more frequent (daily) treatments and wounds took an average of 7.25 months to heal, considerably longer than the current mean treatment duration of 14.2 weeks.

Goldman et al's¹⁰ retrospective, observational, controlled study demonstrated healing of nine out of 10 (90%) inframalleolar ischemic wounds after 1 year of HVPC. The mean duration of treatments for these healed wounds was 3.4 months and the protocol consisted of daily 1-hour treatments, 5 to 7 days per week, until healing. This population achieved a slightly higher incidence of healing with more frequent treatments within a comparable time period, but did include nondiabetic wounds, which may have influenced the overall healing incidence.

Because no control group was involved, the positive re-

Figure 3: Summary of additional procedures required for wounds that failed to heal using HVPC.



sults cannot be generalized to the total population of chronic diabetic lower extremity wounds or said to be the result of HVPC treatment only. However, results of providing good wound care for patients with neuropathic diabetic foot ulcers have been published. Specifically, Margolis et al²² conducted a meta-analysis to determine the percentage of neuropathic diabetic foot ulcers that heal after receiving good wound care, defined as a standard care regimen consisting of debridement, wound care with either saline-moistened gauze or placebo gel and gauze, and explicit instructions to patients about avoiding weight-bearing ambulation. This protocol of care resulted in healing of approximately 31% of diabetic neuropathic ulcers (N = 450) after 20 weeks. The current study also was comprised primarily of neuropathic wounds but had a healing incidence twice as high as the benchmark provided in the Margolis et al²² meta-analysis. The standard wound management protocol used in the current study meets the Margolis et al definition of good care, as it consisted of debridement, wound care with either saline-moistened gauze or placebo gel and gauze, and explicit instructions regarding avoiding weight-bearing ambulation.²² Thus, current results support the management of complex wounds via a multidisciplinary approach, which may include HVPC as an adjunct treatment.

Based on these promising preliminary results, prospective, controlled randomized studies are warranted to elucidate the role of this form of HVPC in multimodal limb salvage and compare outcomes to control as well as other HVPC treatments. The wide range of HVPC protocols utilized in chronic diabetic lower extremity wound studies also illustrates the importance of additional studies examining optimal frequency and duration. Finally, standardized reporting of amplitude, frequency, and duration is needed to assist in comparing re-



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sults between studies.

Conclusion

The encouraging results from this retrospective study suggest that this form of HVPC is a useful addition to a multidisciplinary limb salvage management approach for complex lower extremity diabetic wounds. Although this study is not without weaknesses (ie, retrospective design and lack of a control group), this study serves as a first step in assessing this particular treatment modality and was not designed to address rate of wound healing or tissue perfusion. Further study is warranted to better elucidate HVPC's role in this application. This overall multi-modal limb salvage approach will continue to be used by the senior author, who recommends its use to other clinicians. ■

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