# Reversal of Diabetic Peripheral Neuropathy and New Wound Incidence: The Role of MIRE

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## ABSTRACT

**OBJECTIVE: To determine if improved foot sensitivity to the Semmes-Weinstein 10-g (5.07) monofilament, originally impaired because of diabetic peripheral neuropathy, might be associated with a reduced incidence of new diabetic foot wounds.**

**DESIGN: Retrospective cohort study using a health status questionnaire.**

**SUBJECTS: Sixty-eight individuals over age 64 with diabetes, diabetic peripheral neuropathy, and loss of protective sensation who had clinically demonstrable increases in foot sensation to the Semmes-Weinstein monofilament after treatment with monochromatic near infrared photo energy.**

**MAIN RESULTS: After reversal of diabetic peripheral neuropathy following treatment with monochromatic near infrared photo energy, only 1 of 68 patients developed a new diabetic foot wound, for an incidence of 1.5%. Comparatively, the incidence previously reported in the Medicare-aged population with diabetes was 7.3%.**

**CONCLUSIONS: Improved foot sensitivity to the Semmes-Weinstein monofilament in patients previously suffering from loss of protective sensation due to diabetic neuropathy appears to be associated with a lower incidence of new diabetic foot ulcers when compared with the expected incidence in the Medicare-aged population with diabetes.**

**CLINICAL RELEVANCE: Therapeutic interventions that effectively improve foot sensitivity that has been previously diminished due to diabetic peripheral neuropathy may substantially reduce the incidence of new foot wounds in the Medicare-aged population with diabetes.**


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Of the more than 18 million individuals in the United States who have diabetes, 15% are over age 65.[1] Health care costs in this age-group are often borne by Medicare. The direct cost of diabetes was estimated at $78 billion in 1997,[2] growing to $91 billion in 2002.[3] Over 51% of that $91 billion was spent on patients older than age 65.[3] Treatment for one of the complications of diabetes—lower extremity ulcers—cost Medicare $1.5 billion in 1995.[1] By 2001, the cost for treatment of diabetic foot ulceration and associated amputations had climbed to an estimated $10.9 billion.[4]

Fifteen percent or more of people with diabetes sustain 1 or more foot wounds during their lifetime,[5] and they are 15 times more likely to suffer a nontraumatic lower extremity amputation than people without diabetes.[6] As a result, reduction in the incidence of foot wounds and nontraumatic amputations among people with diabetes is an objective of Healthy People 2010.

Diabetic peripheral neuropathy (DPN), or sensory nerve dysfunction, is typically determined in a clinical setting by diminished sensation to the Semmes-Weinstein 10-g (5.07) monofilament (SWM) or by diminished vibration perception threshold (VPT) in the foot. DPN is widely considered a significant risk factor for diabetic foot wounds.[7] Patients with diabetes who show sensitivity to the SWM rarely develop these wounds.[8] As the severity of DPN progresses toward loss of protective sensation (LOPS), including insensitivity to the

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SWM, so does the risk of foot ulceration.[9]

DPN has been documented in more than 80% of patients who have 1 or more diabetic foot ulcers[10]; it is also a factor in more than 80% of all nontraumatic, lower extremity amputations performed on patients with diabetes.[11] DPN can be identified in the intact, contralateral limb in more than 97% of lower extremity amputees.[12] Although abnormal sensory nerve function has been detected in the contralateral limb of diabetic amputees, it is not present in age-matched amputees without diabetes.[13]

In a study examining the effectiveness of therapeutic shoes in preventing reulceration in patients with diabetes, Reiber et al[14] reported that more than 93% of all foot wounds that developed during the study were found in patients who were insensitive to the SWM. The inability to detect the SWM and a VPT of 25 volts (V) or more—indicators of sensory nerve dysfunction—have been shown to have similar sensitivity[15] and a high correlation to each another.[15] They have also been found to be predictive of diabetic foot wounds.[16] Young et al[16] reported that in a group of patients with no prior foot ulcers, fewer than 4% of patients with a VPT less than 25 V developed a foot wound, compared with almost 19% of those with a VPT of 25 V or more; this represents a five-fold increase in incidence. No recurrent ulcers were seen in the group with a VPT of less than 25 V; however, 30 recurrent foot wounds were noted in patients with a VPT of 25 V or more.

Several studies have discussed the incidence of diabetic foot wounds, with the most exhaustive examination by Harrington et al.[1] They analyzed Medicare claims data from the 1995 and 1996 Standard Analytic Files (SAF) 5%, which is a scalable database containing the complete claims representative of 5% of the Medicare population. Based on the analysis, Harrington et al[1] determined that the incidence rate of wounds in patients over age 65 was 7.3%. Abbott et al[17] reported a 7.2% incidence rate over 1 year in a sample of 1035 patients with diabetes (average age 60; range 23 to 70). Pham et al[18] found an incidence of 11.6% in a group of 248 high-risk patients with diabetes (age 58 ± 12) who exhibited, among other risk factors, sensory nerve dysfunction based on both SWM and VPT testing.

For the present study, it was estimated that the expected annual incidence rate of new diabetic foot wounds among a Medicare-aged population would be 7.3%. This value was used to compare the results of the patient cohort in the present study.

With the incidence of diabetic wounds so closely associated with DPN, increasing foot sensitivity to the SWM in such patients should theoretically reduce the incidence of diabetic foot wounds. The lack of treatment to improve foot sensation in patients with DPN, as measured by either sensitivity to the SWM or VPT, however, has prevented evaluation of such a hypothesis.

Two recent studies [19,20] suggest that temporary increases in foot sensitivity to the SWM are possible through the application of monochromatic near infrared photo energy (MIRE) to patients with diabetes who presented to their health care professional with an already significant LOPS associated with DPN. To date, no long-term evaluation has been conducted to determine any changes (increase or decrease) in the incidence of new foot wounds in patients who had clinically demonstrable evidence of improved sensory nerve function following application of this noninvasive modality.

The present study details outcomes in 68 patients who showed increased sensitivity to the SWM after being treated with MIRE. Between 10 and 15 months after sensation had improved, patients were queried about the incidence of new diabetic foot wounds. These patients were questioned about other outcomes as well, including number of falls, fear of falling, and activities of daily living. Responses to questions concerning these other functional outcomes, however, are outside the objectives of this report.

## METHODS

Insurance records of the only 2 durable medical equipment suppliers offering the MIRE device (Anodyne Therapy System; Anodyne Therapy LLC, Tampa, FL) were reviewed to obtain a list of patients to whom a health status questionnaire would later be administered. Only patients with diabetes and LOPS, whose insurance claims reflected a diagnosis of both diabetes (ICD-9 codes 250.61 or 250.62) and peripheral neuropathy (ICD-9 code 357.2), and who received therapy with the MIRE device between January 1, 2002, and May 31, 2002, were eligible for the study. Prior to providing information to the authors, all patient identifiers were removed by the suppliers; patients had authorized the release of medical information relative to their diagnosis and the therapeutic benefits resulting from MIRE treatment. Medical records for each patient, including written physician orders and treatment notes, were reviewed to confirm the initial diagnosis of DPN with LOPS and subsequent improvement of their sensory nerve dysfunction, as measured by improved sensitivity to the SWM after treatment with MIRE.

Patients who already had a diabetic foot ulcer when they first started using the MIRE device were excluded from the study. This would permit an analysis of the development of new foot ulcers over the next year (mean 12.5 months) of treatment with the MIRE device at home. Patients age 64 or younger were excluded to permit analysis of Medicare-aged patients only.

**Table 1.**
**POST SURVEILLANCE QUESTIONNAIRE**

1. **Prior to using Anodyne:**
   a. Did you ever experience a wound on your foot? *(Yes, No)*
   b. If so, did the wound heal in less than 8 weeks? *(Yes, No)*
   c. Did you ever have a lower extremity amputation? *(Yes, No)*
   d. Did you feel off balance to the extent that you feared falling when you walked? *(Yes, No)*
   e. How many times did you fall during the 12 months prior to the time you started using Anodyne? *(None, 1 time, or 2 or more times)*
2. **Since using Anodyne:**
   a. Have you experienced a wound on your foot? *(Yes, No)*
   b. If yes, did the wound or wounds heal in less than 8 weeks? *(Yes, No)*
   c. Have you had a lower extremity amputation? *(None, Toe(s), Partial Foot, Total Foot, Below Knee, Above Knee)*
   d. Do you feel that your balance has improved and that you now have less fear of falling when you walk? *(Yes, No)*
   e. How many times have you fallen since beginning to use Anodyne? *(None, 1 time, or 2 or more times)*
   f. Compared to what you were able to do most days before using Anodyne, how would you compare what you are now able to do most days? *(A lot less, a little less, about the same, a little more, a lot more)*

Of the original pool of eligible patients, 119 patients qualified for the study, having met the criteria of (1) DPN and LOPS but no current lower extremity ulcers, (2) age 65 or older, and (3) improved foot sensation after use of the MIRE device. An 11-question post-treatment health status surveillance questionnaire was sent to these patients. The questionnaire asked about foot wounds, amputations, fall history, fear of falling, and activities of daily living before and after increased foot sensitivity (Table 1). The prevalence of foot wounds preceding improved sensitivity to the SWM was determined by patient responses to question 1a. Responses to question 2a established the incidence of new ulcers after increased sensitivity to the SWM.

Three interviewers attempted to contact each of the 119 patients at least 3 times to elicit responses to the health status questionnaire. Of the 119 community-dwelling patients, who had been using the MIRE at home for an average of 12.5 months, 68 (57%) agreed to answer the questionnaire.

The 68 patients had been treated by 51 physicians. Before providing the MIRE device to these patients, the durable medical equipment suppliers had received signed certificates of medical necessity from the attending physicians certifying a diagnosis of DPN and LOPS and the fact that these conditions can be reversed with regular use of MIRE.

The MIRE device used by these patients consists of a power unit connected to several therapy pads, each containing 60 luminous diodes that emit monochromatic near infrared (890 nanometers) photo energy.[21] Physicians had instructed their patients to place the MIRE therapy pads in direct contact with the skin on the bottom of the feet for 30 to 40 minutes per day for 2 months. After 2 months, the attending physicians reevaluated their patients to determine whether objective improvement in foot sensation was noted. If so (and if the patient desired ongoing access to the MIRE device for home treatment), the physicians signed a second certificate of medical necessity for lifetime use. The second certificate of medical necessity certified that foot sensation had substantially improved after treatment with the MIRE device. This was accompanied by chart notes documenting the clinical improvement in foot sensation. Patients were instructed to treat themselves at home for 30 to 40 minutes per day, 2 to 7 days a week.

### Statistical analysis

Results were analyzed by a paired 2-tailed *t* test with a null hypothesis that improvement in sensory nerve dysfunction, as measured by increased sensitivity to the SWM, would not decrease the incidence of new foot wounds below a rate of 7.3%. Patients served as their own controls. The 2-tailed *t* test was used because no assumption was made a priori as to whether the incidence of new foot wounds would be higher or lower. A 2-tailed *t* test is more conservative than a 1-tailed *t* test. Significance was accepted when $P < .05$. All values are expressed as mean ± 1 standard deviation.

## RESULTS

Mean age of the 68 diabetic respondents (37 male, 31 female) was 76.6 years (range 64 to 92; Table 2). Twenty-two patients were 80 years or older. The mean duration since the improvement in the sensory nerve function of these community dwellers, as certified by their attending physicians, averaged 12.5 months (range 10.5 to 15 months). These patients had ongoing access to the MIRE device at home during this time.

In the years before obtaining increased foot sensitivity, 19% of patients (13 of 68) had experienced a foot wound (Table 3). This finding is similar to the expected prevalence among individuals with diabetes, which has been reported to be 15%.[1] Patients stated that only 15% of those wounds healed within 8 weeks. Accordingly, the study population was considered to represent the diabetic population in terms of prevalence of diabetic foot wounds and time to wound healing, as reported by Harrington et al.[1]

Only 1 foot wound developed in the study population after

**Table 2.**
**PATIENT DEMOGRAPHICS**

| | |
|---|---|
| Patients contacted by phone | 119 |
| Patients who answered questionnaire | 68 |
| Response rate | 57% |
| Males | 37 |
| Females | 31 |
| Age (years)[a] | 76.6 ± 6.3 |
| Average months after reversal of DPN | 12.5 ± 1.3 |

a = mean ± SD; DPN = diabetic peripheral neuropathy

these patients experienced increased foot sensitivity. The wound occurrence was considered typical because of risk factors associated with sensory nerve dysfunction. This incidence rate is less than 1.5% (1 in 68 patients). A higher rate, 7.3%, is more common, according to the literature.[1]

Another patient reported a topical burn to the dorsal aspect of the foot after he fell asleep for several hours while self-treating with the MIRE device. Such extended use while sleeping is inconsistent with the manufacturer's written warnings.

## DISCUSSION

Sensory nerve dysfunction, as documented by either the SWM or the VPT test, is considered a late consequence of progressively compromised blood flow to the nerves of the lower extremities of individuals with diabetes. Studies have shown that however measured, sensory nerve dysfunction is a major contributory factor to foot wounds[8] and amputations[11,22] in this population. The findings of the present study corroborate those that document a high prevalence of wounds in patients with diabetes who have DPN and LOPS.

In addition, the survey results suggest that improvement of sensory nerve dysfunction, as measured by increased sensitivity to the SWM, may be accompanied by a reduced incidence of new diabetic foot ulcers. In the 68 patients who responded to this survey, the reported number of new diabetes-related wounds was less than 1.5% per year. Clinically published data suggest that an incidence rate of 7.3% should be expected when patients have DPN or LOPS.

Young et al[16] reported that strategies to improve foot sensation in patients with diabetes, who initially had diminished protective sensation, might reduce the incidence of diabetic foot wounds in those without significant sensory nerve dysfunction (VPT of less than 25 V) to under 4%. This outcome could significantly impact the costs associated with treating diabetic foot wounds, as reported by Shearer et al,[5] who concluded, "If all individuals with reduced vibration detection were identified and a new preventative strategy could reduce their risk of ulceration and amputations to levels experienced by those with normal vibration detection, US health payers could save up to $11.8 billion and save 333,000 life-years and 428,000 quality adjusted life-years (discounted) over the next 10 years."[5] These conclusions were based on discounting the cost and benefits to present values at a rate of 3%.

Interestingly, data from the present study indicate that before DPN was reversed, only 15% of wounds had healed in less than 8 weeks. After reversal of DPN, the diabetic foot ulcer and the topical burn discussed above healed within 8 weeks. This time to healing compares favorably with reported times for wound closure among patients with diabetes.[1] No conclusions can be drawn about this observation; it is both outside the objective of the present study and is not sufficiently supported by the sample size and study methodology. However, it may encourage future investigation.

The study has certain limitations. The sample size of 68 patients is less than the number included in the several studies that were used to benchmark these results.[17,18] Improved sensory nerve function was substantiated through analysis of written physician orders and supporting treatment notes. However, both the prevalence of diabetic foot wounds before treatment and the incidence of new diabetic foot wounds after improvement in sensory nerve function are based solely on patient response to the questionnaire. Similar methodology has been used in other studies related to falls[23, 24] or wounds.[25] It is possible that patient recall of a wound may be inaccurate or that an interviewer may have introduced bias in soliciting answers to questions. However, patients should have been able to accurately answer questions that formed the basis of the inquiry about old and new wounds. An attempt to minimize interviewer bias was made by using 8 separate interviewers.

Sensory nerve dysfunction is only 1 risk factor associated with diabetic foot wounds; no multivariate analysis of known comorbid risks for wounds was undertaken. Therefore, it is possible that some of the reported reduction in wound incidence resulted from other variables. Finally, no control group was used in this evaluation. The purpose of this study was to document changes in the incidence of diabetic foot wounds among patients whose sensory nerve function improved and compare them with an already extensive research database; this database served as a historical control.

This study shows an association between improved foot sensation in patients with LOPS due to DPN and a subsequently reduced incidence of foot wounds. Significant conclusions, however, about the relationship between these 2 variables can be derived only through an additional well-designed, randomized, controlled trial that addresses the acknowledged limita-

**Table 3.**
**WOUND INCIDENCE BEFORE AND AFTER REVERSAL OF DPN WITH MIRE**

| | 1 year Prior to DPN Reversal | 1 Year After DPN Reversal | Improvement % | *P* Value |
|---|---|---|---|---|
| **Wounds** | | | | |
| Prevalence | 19%[1] | | | |
| Healed in 8 weeks | 15% | 100% | 667% | |
| Incidence | 7.3% [2] | 1.5% | 79% | <.0001 |

1 Prevalence was measured during the entire period prior to reversal of DPN. Actual prevalence was higher because patients with existing wounds at the time the MIRE device was ordered were excluded from analysis.
2 Historical incidence in the Medicare population as reported by Harrington et al.[1]

tions of the present study, including size of the study population. A future investigation should include an examination of any cost savings related to reduced incidence of new wounds, which would allow a cost benefit analysis of the method used to obtain improved foot sensitivity.

A larger population of patients with diabetes, treated with MIRE for several months to years, has been identified. Medicare carriers will be asked to assist with access to the relevant data in the Centers for Medicare and Medicaid Services Common Working File as part of a new analysis.

## CONCLUSION

Increased sensory nerve function in patients previously diagnosed with DPN and LOPS, based on use of the SWM after continued access to the MIRE device in the home, seems closely related to a significant reduction in the expected incidence of new diabetic foot wounds. The actual reported incidence rate during continued MIRE use appears to be quite low and may be equal to or less than that previously reported for patients who have yet to experience disease-related sensory nerve dysfunction. These results support the conclusions reached by Shearer et al[5] that improvement in sensory nerve function in patients previously diagnosed with DPN and LOPS may have major socioeconomic and quality of life benefits for those with diabetes. This may offer potentially significant cost savings to the Medicare system and other health care organizations. ●

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