Chronic limb ischemia of peripheral vascular disease commonly leads to severe pain and skin ulcerations, eventually resulting in gangrene if untreated. When revascularization procedures are not possible or fail because of poor outflow, the surgeon must consider other means of limb salvage to control the patient’s pain and to preserve the patient’s independence. Spinal cord stimulation (SCS) has long been known to ameliorate chronic intractable pain associated with various pathological conditions, including the rest pain of peripheral vascular disease.

Early investigators using SCS for the control of ischemic pain in peripheral vascular disease noted improved warmth and apparently increased blood flow in limbs with severe vascular disease. Other reports have suggested improved healing of previously intractable limb ulcerations and the return of distal pulses in some patients along with improvement in microcirculation values in ischemic limbs. We have also found that the beneficial effects of SCS seem to extend beyond simple pain control to actual improvements in peripheral blood flow that are measurable using micro- and macrocirculatory values.

This prospective study was designed to assess the efficacy of SCS for the control of pain, the improvement of blood flow parameters, and the salvage of limbs in patients suffering from severe peripheral vascular disease and threatened limb loss.

Clinical Material and Methods

Patient Population

Our series of SCS-implanted patients included 276 patients, of whom 46 received implants to control chronic pain caused by peripheral vascular disease. All patients required narcotic medication for pain relief prior to SCS and all had received other modalities of pain relief, such as physical therapy, acupuncture, nerve blocks, or transcutaneous electrical nerve stimulation, without achieving adequate pain control. A 6-month period of conservative therapy for pain relief was attempted by a multidisciplinary pain clinic in each patient prior to referral for SCS. (All spinal cord implants used in this study were systems manufactured by Medtronic Inc., Minneapolis, MN, in...
Spinal cord stimulation for peripheral vascular disease

including 39 Pisces-Quadripolar electrodes and seven Re-sume electrodes.) All patients had electrodes placed at T9–L1 in a manner previously described. 6,17 Pulse gener-ators used for stimulation (Medtronic Irel II systems) had a cycling mode of 1 minute on/2 minutes off.

Systems were placed internally if patients reported paraesthesia and pain relief in the symptomatic limb; only patients with unilateral lower extremity symptoms were included in this study to reduce variables for analysis and to allow study of the possible bilateral effects of spinal stimulation.

Patients with peripheral vascular disease who were se-llected for SCS therapy were required to meet additional specific clinical and objective criteria, which were formu-lated on the basis of input from vascular and neurological surgeons with previous experience using SCS for pain control.

Inclusion Criteria

Medical Indications. The patients had chronic claudica-tion and rest pain in the lower limbs secondary to occlu-sive vascular disease or vasospastic disorders. Diagnoses included: 1) arteriosclerosis; 2) arteriosclerosis with diabet-es; 3) Buerger’s disease; and 4) Raynaud’s disease. All patients in the current series had arteriosclerosis without elements of vasospasm. In this particular series, no cases of Buerger’s or Raynaud’s disease were enrolled.

Clinical Criteria. There were five clinical selection cri-teria required in addition to one of the aforementioned diagnoses. 1) End-stage lower limb peripheral vascular disease with pain unresponsive to medical therapy. All patients were evaluated by a vascular surgeon, underwent angiography, and were judged unsuitable candidates for revascularization procedures. All patients had previously undergone chemical sympathectomy without lasting benefit. Although peripheral vascular disease is a known generalized disease, patients were selected such that their symptoms were primarily unilateral. The symptomatic limb obviously was the limb with the more advanced pathophysiology. The contralateral limb was used as a control in each patient for the purposes of data tabulation and analysis. 2) Severe, nonreconstructable arteriob-struction. This was demonstrated by an ankle/brachial index that was less than 0.4 (unless arteries were incom-pressible, as with diabetes), or by a great toe pressure less than 30 mm Hg. 3) Foot ulcers, if present, must be less than 2 cm in diameter and could not extend deep into the dermis. 4) Gangrene, if present, must be dry and must sat-isfy the ulcer conditions stated above. 5) Patients with sig-nificant heart failure, pulmonary or renal insufficiency, or unstable angina were also excluded from this study.

General Criteria. Patients were required to meet each of the following criteria: 1) a demonstrable pathology accounted for the pain; 2) conservative therapies had failed or were contraindicated; 3) untreated drug addiction problems did not exist; 4) psychological assessment did not identify major barriers to treatment success; 5) pa-tients were motivated sufficiently to understand and coop-erate with instructions on the use of the device and its adjustment, and were able to return for regular follow-up visits; 6) patients were able to detect paresthesia in the painful area during the trial implantation screening period; 7) patients reported substantial pain relief following trial stimulation; 8) patients had a life expectancy greater than 6 months; and 9) patients were able to give informed con-sent to the treatment.

Methodological Considerations

Before and after entry into the study, objective parame-ters of limb macrocirculation and microcirculation were obtained. Macrocirculation was studied by: 1) Doppler peak blood flow velocities at the common femoral, pop-liteal, and dorsalis pedis arteries, and the digital arteries in the great toe; 2) pulse volume recording at the midthigh, calf, foot, and big toe; 3) ankle/brachial indices; and 4) claudication distance evaluated by walking on a treadmill with no incline at 2 miles/hour. Peak flow velocities were measured and interpreted by a radiologist. Microcircula-tion was quantified by transcutaneous monitoring to mea-sure the transcutaneous partial pressure of oxygen (TcPO2) over the dorsum of the foot with a portable oximeter. Measurements of each patient’s TcPO2, peak flow velocit-ies, and pulse volume recordings were taken in the affected leg as well as in the unaffected limb; this allowed eval-uation of the possible bilateral effects of spinal stimulation on the peripheral vasculature.

Measurements of micro- and macrocirculation indices were obtained immediately before implant placement and repeated on discharge (usually 5–7 days after implantation of the hardware, if performed) with continuing assessment at 2, 3, and 6 months postdischarge and every 6 months thereafter. For purposes of statistical analysis, the values of each parameter obtained at each interval were averaged.

Pain relief was scored by interview with a disinterested third party physician who was not involved in patient care. A modified Visual Analog Scale11 incorporating the per-centage of pain relief on a grading scale was used to quan-tify pain levels before and after SCS. Interviews to assess pain relief were conducted at every 6-month interval of self-stimulation for each patient. The patients were graded according to their pain control as follows: 1) less than 50% relief = poor; 2) 50 to 75% relief = good; and 3) greater than 75% relief = excellent.

Those patients who were given implanted hardware were followed at discharge, 8 weeks and 6 months post-operatively, and every 6 months thereafter. The patients were followed until clinical failure occurred. Endpoints for this study consisted of: 1) failed trial stimulation re-sulting in avoidance of device implantation; 2) amputation indicating failure of therapy; 3) device explantation as a result of poor pain control, uncomfortable paresthesia, infection, malfunction, or other problem with the SCS hardware or stimulation.

Criteria of Success. A case was considered successful if four of the following five criteria were met: 1) greater than 50% pain relief; 2) an improvement of at least twice the baseline claudication distance; 3) an improvement of greater than 50% in TcPO2 from baseline value over the dorsum of the foot; 4) an improvement of at least 25% in mean peak blood flow velocity; and 5) an improvement of at least 25% in pulse volume recording in either the calf or the foot.
**Results**

The original group of 46 patients consisted of 34 men and 12 women with an average age of 70 ± 9 years. Of these 46 patients, 39 (85%) (29 men and 10 women) were given internal SCS devices after a successful trial stimulation period. Thirty (77%) of these 39 patients were considered a success at long-term follow up. Follow-up review ranged from 2 to 36 months (average 21.2 months). All 39 patients had complete measurements of \( TcPO_2 \) and peak flow velocity recorded, but only 28 patients obtained pulse volume recordings. Patients who did not receive implants had their \( TcPO_2 \) measurements recorded at discharge. Statistical analyses, therefore, were performed on 46 patients with \( TcPO_2 \) records, 39 with peak flow velocity records, and 28 with pulse volume recording records.

Treatment in three of 39 patients failed acutely within 2 months of implantation. Two patients stated that pain relief was inadequate and the third found the paresthesia uncomfortable. Six other patients underwent lower limb amputation at an average of 10 ± 4 months after the procedure. Three patients who underwent amputation are continuing to use their stimulators regularly to achieve adequate pain control in the contralateral limb. Pain relief was graded using a modified Visual Analog Scale pain questionnaire with a range of 0% (no pain relief) to 100% (total pain relief) as described by each patient. All patient interviews were conducted by a disinterested third party physician who was not directly involved with the clinical care of the study patients.

Evaluation of changes in pain control in the 39 patients with implants at follow-up evaluation showed that four (10%) reported an increase in pain following SCS, four (10%) reported no change in pain, five (13%) reported less than 50% pain control, and 26 (67%) reported greater than 50% pain relief with 10 of these patients obtaining more than 75% pain relief. Of the eight patients (21%) reporting no improvement or increased pain following SCS, four (50%) had objective improvements in \( TcPO_2 \) and/or peak flow volume. This segmentation of pain and circulatory parameters produced patient subsets too small for statistical analysis.

**Microcirculatory Values.** Measured \( TcPO_2 \) was used as an objective indicator of microcirculatory blood flow changes in response to SCS; \( TcPO_2 \) was measured in both symptomatic and contralateral limbs. Of primary interest is the finding that SCS improves oxygen delivery to distal tissues, implying augmented blood flow in the skin microcirculation. In successful patients with an initial \( TcPO_2 \) of less than 30 mm Hg, there was a significant (p < 0.05) average increase in \( TcPO_2 \) of 45.5 ± 17 mm Hg in the symptomatic leg, with the greatest improvements seen in successful patients with a low baseline \( TcPO_2 \) (Fig. 1). The \( TcPO_2 \) was higher among successful patients (23.8 ±
23.9 mm Hg) than among patients in whom therapy failed (5.2 ± 16.3 mm Hg) (Table 1).

The relationship between preoperative TcPO$_2$ and the change in TcPO$_2$ measured at follow up was significant ($p < 0.05$) in successful patients and is represented in Fig. 2. The positive change in TcPO$_2$ resulting from SCS was greatest when the initial TcPO$_2$ was less than 30 mm Hg. In comparison, successful patients who had a high preoperative TcPO$_2$ typically had a small increase or even a decrease in TcPO$_2$. Table 1 also shows the nonsignificant change in TcPO$_2$ within the control leg. Although TcPO$_2$ in the control leg exhibited the greatest increase in those patients with an initial TcPO$_2$ of less than 30 mm Hg, this result was not significantly different from the change in TcPO$_2$ in the control leg of patients with an initial TcPO$_2$ of more than 30 mm Hg. The control leg also did not show significance in discriminating success from failure based on a change in TcPO$_2$ (Table 1).

Generally, in patients in whom TcPO$_2$ persisted below 10 mm Hg, the clinical endpoint of amputation was reached within the first 3 months of follow up. Trophic ulcers tended to show evidence of healing if TcPO$_2$ rose to

![Graph comparing baseline measurements of TcPO$_2$ obtained preoperatively over the dorsum of the symptomatic foot in patients with peripheral vascular disease with the difference in TcPO$_2$ values from baseline to follow up.](image)

**TABLE 1**

Relationship among initial TcPO$_2$, change in TcPO$_2$, and outcome in all patients who underwent SCS for peripheral vascular disease*

<table>
<thead>
<tr>
<th>Initial TcPO$_2$ (mm Hg)</th>
<th>Total No. of Patients</th>
<th>No. of Patients</th>
<th>Change in TcPO$_2$ (mm Hg)</th>
<th>No. of Patients</th>
<th>Change in TcPO$_2$ (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success</td>
<td></td>
<td></td>
<td>Symptomatic Limb</td>
<td>Asymptomatic Limb</td>
<td>Symptomatic Limb</td>
</tr>
<tr>
<td>&gt;30</td>
<td>22</td>
<td>17</td>
<td>7.2 ± 12.0</td>
<td>0.1 ± 10.4</td>
<td>5</td>
</tr>
<tr>
<td>&lt;30</td>
<td>24</td>
<td>13</td>
<td>45.5 ± 17.0</td>
<td>14.7 ± 17.1</td>
<td>11</td>
</tr>
<tr>
<td>total</td>
<td>46</td>
<td>30</td>
<td>23.8 ± 23.9</td>
<td>6.4 ± 18.9</td>
<td>16</td>
</tr>
</tbody>
</table>

* Post-SCS changes in TcPO$_2$ are expressed as the mean values ± standard deviation. Successfully treated patients with an initial TcPO$_2$ of less than 30 mm Hg showed a significant increase in TcPO$_2$ of 45.5 ± 17.0 mm Hg ($p < 0.05$). Asymptomatic limbs showed a similar, but less impressive response.
greater than 25 mm Hg, with a general ulcer healing rate of about 20%. Ulcers that did not heal tended to exist in patients in whom TcPO\textsubscript{2} failed to increase above 25 mm Hg or in whom the ulcers were accompanied by persistent epicritic pain. There was no linear correlation found between degree of pain relief and change in TcPO\textsubscript{2}.

**Macrocirculatory Values.** Blood flow velocities were measured at the levels of the common femoral, popliteal, and posterior tibial arteries and in the dorsal digital arteries of the great toe. The blood flow velocities at the common femoral artery were considered the most valid in patients with peripheral vascular disease who had undergone previous vascular surgery. Table 2 demonstrates the change in peak blood flow velocity at the level of the common femoral artery. An average increase of $40.4 \pm 40.2$ cm/second was observed.

**TABLE 2**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of Patients</th>
<th>Initial Peak Flow Velocity (cm/second)</th>
<th>Change in Peak Flow Velocity (cm/second)</th>
<th>Post-SCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>success</td>
<td>30</td>
<td>41.9 ± 32.4</td>
<td>40.4 ± 40.2</td>
<td></td>
</tr>
<tr>
<td>failure</td>
<td>9</td>
<td>43.5 ± 54.2</td>
<td>4.5 ± 13.3</td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>39</td>
<td>42.3 ± 40.7</td>
<td>32.1 ± 32.4</td>
<td></td>
</tr>
</tbody>
</table>

*Measurements of peak blood flow velocity were obtained at the level of the common femoral artery in the symptomatic leg. Values are expressed as the mean ± standard deviation. Successfully treated patients showed a significant (p < 0.05) increase in peak blood flow velocity of $40.4 \pm 40.2$ cm/second.

**TABLE 3**

<table>
<thead>
<tr>
<th>Level</th>
<th>Preop Pulse Volume Recording (mm\textsuperscript{3})</th>
<th>Post-SCS Pulse Volume Recording (mm\textsuperscript{3})</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>all patients (28 patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>thigh</td>
<td>21.6 ± 12.3</td>
<td>27.8 ± 15.6</td>
<td>NS</td>
</tr>
<tr>
<td>ankle</td>
<td>12.3 ± 11.1</td>
<td>17.0 ± 12.8</td>
<td>NS</td>
</tr>
<tr>
<td>metatarsal</td>
<td>5.9 ± 4.8</td>
<td>13.4 ± 5.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>great toe</td>
<td>2.5 ± 3.2</td>
<td>7.6 ± 3.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>successful patients (23 patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>thigh</td>
<td>22.8 ± 6.8</td>
<td>30.6 ± 7.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ankle</td>
<td>12.0 ± 10.2</td>
<td>17.3 ± 8.8</td>
<td>NS</td>
</tr>
<tr>
<td>metatarsal</td>
<td>5.6 ± 5.0</td>
<td>13.1 ± 6.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>great toe</td>
<td>2.8 ± 3.0</td>
<td>8.2 ± 4.0</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*Values are expressed as the mean ± standard deviation. Abbreviation: NS = not significant.
cm/second was seen in successful patients as compared to an increase of 4.5 ± 13.3 cm/second in patients in whom therapy failed. This demonstrated a marked and statistically significant (p < 0.05) increase in flow velocity over the follow-up period. The change in peak flow velocity demonstrated a significant relationship to the change in TcPO₂ for all patients with implants, as shown in Fig. 3. This relationship was intact for all patients as both the TcPO₂ and peak flow velocities changed in direct proportion to one another (regression coefficient r = 0.84; p < 0.01).

Pulse volume recording measurements were not performed in all patients; in early cases the equipment was not available. The pulse volume recording values did show significant (p < 0.05 at specific anatomical sites) changes when all patients were considered, as well as when successful patients were considered (Table 3). Figure 4 illustrates individual changes found in successful patients at the level of the great toe, which demonstrated significant increases in pulse volume recording. No relationship could be found between pulse volume recording and TcPO₂ or between pulse volume recording and peak flow velocity.

The improvement in macro- and microcirculation seemed to occur within the first 6 weeks in most patients and tended to plateau at approximately 6 months postdischarge. We observed that if stimulation was terminated because of mechanical failure or noncompliance, parameters of macro- and microcirculation seemed to regress within 1 week. Optimum results were obtained with cycling modes of stimulation with a cycle of 1 minute on/2 minutes off.

An increase in claudication distance on noninclined treadmill testing was found in successful cases, but was not statistically significant. No linear correlation was found between the recorded increase in TcPO₂ and claudication distance. Ankle/brachial indices showed no consistent changes with stimulation.

**Prognostic Factors**

Initial values of TcPO₂, peak flow velocity, and pulse volume recording are not prognostic for the outcome of SCS for peripheral vascular disease. However, values obtained during the trial stimulation of SCS were predictive of success in our series. Two very important relationships that correlate to long-term success were discovered before discharge. The first relationship was the combination of excellent pain relief (> 75% pain relief) and a substantial increase in TcPO₂; this association showed a significant (p = 0.016) correlation to long-term SCS success, as described in Table 4. The second relationship we found was that patients with a substantially larger increase in peak flow velocity at the level of the common femoral artery immediately following implantation displayed a greater long-term success rate (p = 0.031), as outlined in Table 5.

**Discussion**

The initial use of SCS was for the treatment of chronic, intractable pain of various etiologies. As experience with
TABLE 4

<table>
<thead>
<tr>
<th>Early Pain Relief</th>
<th>No. of Patients</th>
<th>Change in TcPO₂ From Preop to Discharge</th>
<th>Long-Term Successes</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;75%</td>
<td>31</td>
<td>11.1 ± 10.4 mm Hg</td>
<td>27</td>
</tr>
<tr>
<td>≤75%</td>
<td>15</td>
<td>3.8 ± 5.9 mm Hg</td>
<td>3</td>
</tr>
</tbody>
</table>

* The TcPO₂ levels were measured over the dorsum of the symptomatic foot. Values representing change in TcPO₂ are expressed as the mean ± standard deviation. The difference between changes in TcPO₂ values for excellent pain relief (>75% pain relief) and less than excellent pain relief has a significance of p = 0.016.

SCS expanded, other physiological effects were recognized. In 1973, Cook and Weinstein⁶ reported improvement in bladder control and mobility in patients with multiple sclerosis after institution of SCS for pain control; they also noted the apparent healing of previously intractable chronic leg ulcers. Several European trials²⁵,¹²,¹³,¹⁹,²⁰ have validated the effects of SCS on the peripheral circulation with success rates of 50 to 60% for the relief of symptoms along with concurrent improvement in objective tests of peripheral circulation. Microcirculation parameters have shown improvement after SCS; these include objective tests such as red blood cell velocity and capillary density,¹²,¹³ sodium fluorescein appearance time,¹ xenon-133 washout time,¹⁰,²⁷ TcPO₂ levels,⁷,²⁵ Doppler flowmetry,² and thermography.¹,² Microcirculatory parameters such as the ankle/brachial index and toe pressures have not been shown to improve with stimulation.²,³,⁸,¹² Functional tests such as claudication distance have shown statistically significant improvements.² A prospective randomized controlled study comparing SCS to analgesic treatment demonstrated significantly less tissue loss and a significantly lower amputation rate in patients without arterial hypertension in the SCS group.¹⁴

Effects on Perfusion

Several parameters of macro- and microcirculation have been investigated for their relationships to long-term success of SCS for peripheral vascular disease. Jacobs and colleagues¹²,¹³ found significant increases in red blood cell velocity in patients responsive to SCS 1 day after SCS. Several authors have speculated on the relationship between good pain relief and increased perfusion values or long-term success.²,³,⁸,¹² Improvement in latency times and rise times have also shown an association with greater pain relief.³ In addition, TcPO₂ measurements have been hypothesized to predict SCS effectiveness during the trial stimulation period.⁷,²⁵ Our results demonstrate two critical relationships between early measurable parameters and long-term success, which may be used as future prognostic factors for the selection of peripheral vascular disease patients for SCS. These are: 1) the combination of pain relief greater than 75% and an increase in TcPO₂ of 10 mm or greater above baseline values; and 2) an increase in peak flow velocity of 10 cm/second or greater at the level of the common femoral artery. These parameters are easily measurable during a period of trial stimulation and should assist in the prediction of SCS success for peripheral vascular disease in the individual patient.

Modes of Action

The clinical benefits of SCS for peripheral vascular disease have become accepted, but the physiological basis for its efficacy is not known. Other explanations for the effects of SCS have been proposed since Melzack and Wall²⁰ originally suggested the gate control theory of pain. The most popular theories suggest that antidromic stimulation of dorsal root afferents causes vasodilation, which may be mediated by prostaglandins.⁵,¹⁰,¹⁸,²⁶ It has also been suggested that pain relief in itself might relieve vasoconstriction, or that cholinergic nerve fibers are directly stimulated by SCS.²⁷ Takahashi, et al.,²⁶ demonstrated in animal models that the rate of blood flow during electrical stimulation of the sciatic nerve varied with the voltage, frequency, and duration of the stimulation, independent of spinal cordotomy and sympathetic block. However, it has been believed that some sympathetic activity remains because of the difficulty of obtaining complete sympathectomy, and if tests to evaluate autonomic function show complete sympathectomy, the normal vasodilatory effect of SCS is lost.¹⁹,²³ Speculation has also centered on the release of vasoactive substances with local and possibly systemic effects, including vasoactive intestinal peptide, substance P, and calcitonin gene–related peptide.¹⁵,²⁴ It may be possible that several mechanisms are active simultaneously, with both inhibition of autonomically mediated vasoconstriction and activation of vasoactive substances participating in the efficacy of SCS.

Conclusions

Our study confirms the beneficial effects of SCS in treatment of peripheral vascular disease through measurement of objective parameters of the micro- and macrocirculation (TcPO₂, peak flow velocity, and pulse volume recording). Trial stimulation parameters of excellent pain relief combined with an increase in TcPO₂ of 10 mm Hg or greater, as well as an increase in peak flow velocity of 10 mm or more, give significant predilection for long-term success of SCS. In summary, SCS seems to be an efficacious treatment for arteriosclerotic peripheral vascular disease in certain patients who respond favorably to trial stimulation.
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References


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