ActiGait implantable drop foot stimulator in multiple sclerosis: a new indication

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OBJECTIVE Direct stimulation of the peroneal nerve by the ActiGait implantable drop foot stimulator is a potent therapy that was described previously for stroke-related drop foot. The authors report here successful long-term application of the ActiGait implantable drop foot stimulator in patients with multiple sclerosis (MS).

METHODS Six patients with MS and 2 years of persisting central leg paresis received an implantable ActiGait drop foot stimulator after successful surface test stimulation. Ten weeks and 1 year after surgery, their gait speed, endurance, and safety were evaluated. Patient satisfaction was assessed with a questionnaire.

RESULTS In the 20-m gait test, stimulation with the ActiGait stimulator significantly reduced the time needed, on average, by approximately 23.6% 10 weeks after surgery, and the time improved further by 36.3% after 1 year. The median distance covered by patients with the stimulator after 6 minutes of walking increased significantly from 217 m to 321 m and remained stable for 1 year; the distance covered by patients after surface stimulation was 264 m. Patients with an implanted ActiGait stimulator noticed pronounced improvement in their mobility, social participation, and quality of life.

CONCLUSIONS The ActiGait implantable drop foot stimulator improved gait speed, endurance, and quality of life in all patients over a period of 1 year. It may serve as a new therapeutic option for patients with MS-related drop foot.

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KEY WORDS ActiGait; multiple sclerosis; neuromodulation; peripheral nerve; drop foot; functional neurosurgery

MULTIPLE sclerosis (MS) is the most frequent chronic inflammatory disorder of the central nervous system. During the later phases of the disease, it may result in central paresis of the lower limbs with a drop foot, which can lead to an increased risk of falls,⁸ limited mobility, and a reduction in social participation and quality of life. Until now, using an ankle foot orthosis and surface stimulation of the peroneal nerve have been the only therapeutic options. However, increased walking speed and improved ankle and knee kinematics that led to improved quality of life¹ were described recently after surface stimulation of the peroneal nerve.^{11,12,15,17} In 12 months of follow-up, this therapeutic effect was reported

to be significant,¹⁶ and there is evidence that chronic use of the surface stimulator strengthens activation of the motor cortex and the descending connections.⁵ This might lead to an improvement in gait after long-term use,⁵ even when the stimulator is off.

Direct stimulation of the peroneal nerve by an implantable device was described recently as a new therapeutic option for patients with stroke-related drop foot, and it resulted in improved ankle joint kinematics and increased walking speed.^{2–4,10} The advantage of this system is the more specific stimulation.³ Patients who used this device also reported a better therapeutic effect and easier operability than patients who underwent surface stimulation.³

ABBREVIATIONS MS = multiple sclerosis.

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In addition, direct 4-channel nerve stimulation in 2 patients with MS-dependent drop foot was reported to result in improvements in walking speed in a follow-up time of 3 months.⁶ Although in patients after stroke and patients with MS, the resulting drop foot is caused by a central lesion, the therapeutic effects of nerve stimulation can differ over time, because MS may be progressive. In contrast, patients with MS tend to be younger and suffer less morbidity than patients after stroke, and they might experience a greater benefit from nerve stimulation and improvement in their quality of life.

In this study, we report the first, to our knowledge, successful long-term benefit of the ActiGait (Neurodan) implantable drop foot stimulator in 6 patients with MS-related drop foot.

Methods

Patient Screening

Six patients with at least 1 year of stable MS and 2 years of persisting spastic paresis of the leg with a drop foot were offered a new therapeutic option via an implantable drop foot stimulator (patient characteristics are listed in Table 1). The drop foot was diagnosed according to features described by Perry et al.,¹³ including a dragging foot during the swing phase. The possible benefit of an implantable stimulator was tested preoperatively by external functional surface stimulation of the peroneal nerve (CE-FAR Step II [Compex Scandinavia AB], SN 2005–312, output 60 mA, frequency 20–100 Hz) with dorsiflexion of the ankle. This observational study was approved by the Technical University of Dresden ethics committee. The trial did not involve experimental medication, surgical products, or techniques.

Gait Tests

To evaluate possible changes in walking speed, patients were asked to walk 20 m, and the time needed was documented. This test was performed preoperatively without walking aids, with an ankle orthosis, and with a surface stimulator and 10 weeks and 1 year after implantation of the ActiGait system. In each case, the patient was asked to perform the test at normal walking speed (“pleasant” gait) and as fast as possible (“maximal” gait). In addition, walking endurance was tested by having the patient walk for 6 minutes continuously before and after surgery. Finally, to assess the risk of falls, the time needed to stand up from a chair, walk 3 m, and go back and be seated again was measured (Timed Up and Go test).¹⁴ All 3 tests were performed without any medical aids, with an ankle foot orthosis (tested only in the 20-m gait test), and with surface stimulation before the operation and with the activated ActiGait stimulator 10 weeks and 1 year after the operation. In addition, patient satisfaction was assessed with a subjective quality-of-life questionnaire (Table 2).

Surgery

For this study, the patients underwent implantation of the ActiGait system, which consists of an implantable 4-channel drop foot stimulator, an external control unit, a footswitch, and a clinical station^{2–4,9,10} (Fig. 1). MRI of

TABLE 1. Patient characteristics and stimulation parameters of 6 patients with MS who underwent implantation of an ActiGait drop foot stimulator

20-m Gait Test/Walking																
Pt No.	Sex	Side of Hemiplegia	Age (yrs)	Duration of Drop Foot (yrs)	Muscle Strength of Foot Elevation*	Speed (sec)			6-min Walking Test (m)			Timed Up & Go Test (sec)			Stimulation Parameters	
						w/o Stimulation	w/ Stimulation		w/o Stimulation	w/ Stimulation		w/o Stimulation	w/ Stimulation			
							Stimulation	After 10 wks		After 1 yr	Stimulation		After 10 wks	After 1 yr		Stimulation
1	M	Lt	65	10	2/5	20.2	16.7	16.5	224	310	320	9.4	8.1	7.9	Channels 1 & 4 active; 1 mA; 30 Hz; optimal impulse duration 70 µsec; heel switch, ipsilat	
2	F	Rt	62	7	2/5	28.7	21.6	20.7	231	324	330	12.6	10.4	9.6	Channel 1 active; 1 mA; 20 Hz; optimal impulse duration 70 µsec; heel switch, ipsilat	
3	F	Lt	47	6	1/5	28.6	22.0	22.0	196	330	340	25.5	15.2	14.8	Channel 4 active; 1 mA; 20 Hz; optimal impulse duration 70 µsec; heel switch, ipsilat	
4	M	Rt	34	15	2/5	27.4	21.4	19.9	220	315	325	14.9	9.8	9.7	Channel 4 active; 20 Hz; optimal impulse duration 60 µsec; heel switch, ipsilat	
5	F	Rt	48	5	2/5	28.3	21.8	20.1	225	310	320	13.8	9.1	9.0	Channels 1 and 4 active; 25 Hz; optimal impulse duration 65 µsec; heel switch, ipsilat	
6	F	Lt	54	9	2/5	28.0	22.3	20.4	195	305	320	16.7	11.2	10.5	Channel 4 active; 25 Hz; optimal impulse duration 70 µsec; heel switch, ipsilat	

Pt = patient.

* Scores based on the Janda Classification.⁷

TABLE 2. Subjective quality-of-life survey from 6 patients with MS 1 year after implantation of an ActiGait drop foot stimulator

Pt No.	Have You Noticed Changes in Mobility in Daily Living? (go for a walk, shopping, public transit)*	Have You Noticed Changes in Interpersonal Contacts & Social Participation?†	Would You Recommend the Operation?‡	Have You Noticed Changes in Your Quality Of Life?§
1	3	3	1	2
2	3	2	1	3
3	2	3	1	2
4	3	2	1	3
5	2	3	1	3
6	3	3	1	3

* -1 = worsening; 0 = no changes; 1 = only minor improvement; 2 = marked improvement; 3 = pronounced improvement, complete return to normal (life).

† -1 = less social interaction; 0 = no changes; 1 = only minor improvement; 2 = marked improvement; 3 = pronounced improvement, complete return to normal (life).

‡ -1 = no; 0 = unsure; 1 = yes.

§ -1 = worsening; 0 = no changes; 1 = only minor improvement; 2 = marked improvement; 3 = pronounced improvement, complete return to normal (life).

the leg was performed preoperatively to determine the anatomical localization of the bifurcation of the sensible branch of the common peroneal nerve for proper electrode positioning. The operation was performed with the patient under general anesthesia, as described by Martin et al.⁹ In brief, the common peroneal nerve was exposed above the knee for 4 cm, and dorsiflexion was tested using a nerve stimulator (GN 015). Afterward, the electrode cuff was closed around the nerve, and the stimulator body was fixed to the lateral femoral fascia. Finally, the correct positions of the cuff and the stimulator were controlled visually in maximal flexion and extension of the knee to ensure free gliding of the cuff.

Postoperative Care and Programming of the Stimulator

For the first 4 weeks after surgery, the patients had to restrict the movement of the leg on which surgery was performed to a maximal knee flexion of 30°. To avoid contractures during this time period, the Achilles tendon was stretched passively. Afterward, every channel was tested for the best dorsiflexion, and the stimulator was activated with 1 mA, 20–30 Hz, and an optimal impulse duration of 70 μ sec (Table 1). Patients were able to readjust the impulse intensity with a programmer. Gait evaluation was performed after 10 weeks to measure gait speed and walking endurance, and the Timed Up and Go test was repeated. In addition, a subjective quality-of-life survey was given. All tests were repeated 1 year after surgery.

Statistics

The results of the gait tests are expressed as mean $\pm$ SEM. The significance level was calculated with a Mann-Whitney U-test in Excel 2010 software.

Results

Surgery and Postoperative Care

Implantation of the ActiGait system in 6 patients with MS resulted in no technical or surgical complications. The implantable device did not appear bulky but was palpable in every patient. Programming of the ActiGait stimulator, as described above, was uncomplicated for all 6 patients. The programming time demand ranged between 45 and

60 minutes. Each patient described the handling of the ActiGait system in daily living as being uncomplicated and easy.

Walking Speed (20-m Gait Test)

The mean time to walk 20 m at normal walking speed was significantly ($p = 0.003$) decreased from 25.9 (± 4.4) seconds preoperatively without walking aids to 19.8 (± 2.9) seconds with ActiGait stimulation 10 weeks after sur-

FIG. 1. Schematic illustration of the implantable and nonimplantable components of the ActiGait drop foot stimulator. The system consists of an external control unit (1) with a transmission coil (antenna) (2), which receives signals from the external footswitch (5) via a wireless radiofrequency signal. It enables precise activation depending on the gait cycle and allows for the adjustment of the stimulation parameters. The subcutaneously implanted stimulator (3) is connected to the 4-channel cuff (4), which is placed around the peroneal nerve. The stimulator communicates via a wireless radio frequency signal with the antenna and transmits the stimulation signals. Copyright Klaus Daniel Martin. Published with permission.

FIG. 2. Evaluation of mean walking speeds in the 20-m gait test at pleasant and maximal walking speeds preoperatively and 10 weeks and 1 year after ActiGait implantation in 6 patients with MS. * $p < 0.05$ compared with no stimulation; # $p < 0.05$ compared with use of ankle orthosis; § $p < 0.05$ compared with surface stimulation.

gery and decreased further to $16.5 (\pm 2)$ seconds 1 year after implantation. Surface stimulation also resulted in a significant ($p < 0.05$) reduction in the mean time needed (to 21.4 ± 2.3 seconds). Ten weeks after surgery, there were no significant differences between ActiGait stimulation and surface stimulation. However, after 1 year, the ActiGait stimulator resulted in significant improvement over surface stimulation ($p < 0.05$). In contrast, the use of an ankle orthosis resulted in no significant change in walking speed over that with no walking aids. Similar results were observed under maximal gait-speed conditions (Fig. 2). Video 1 exemplarily shows Patient 2 without walking aids and with ActiGait stimulation 1 year after surgery.

VIDEO 1. Clip showing walking speed of a patient with an activated ActiGait drop foot stimulator and no walking aids 1 year after surgery. Copyright Klaus Daniel Martin. Published with permission. [Click here to view.](#)

6-Minute Walking Test

Gait endurance was examined by measuring the distances that the patients walked within 6 minutes. Before stimulation, the patients walked, on average, 215 ± 15.6 m in 6 minutes. With surface stimulation, the mean distance increased significantly ($p < 0.05$) to 261 ± 16 m. After the patients underwent ActiGait implantation, their mean covered distance increased even further to 315 ± 9.5 m 10 weeks after surgery and remained stable at 325 ± 8 m 1 year after implantation (Fig. 3). This result, compared with those for patients without walking aids ($p < 0.05$) and with surface stimulation ($p < 0.05$), is significant.

Timed Up and Go Test

To assess activation time and the risk of falls, the Timed Up and Go test was performed without walking aids, with surface stimulation, and with ActiGait stimulation. The time needed for the test without walking aids was 19.5 ± 6.8 seconds, which indicates mild mobility impairment (> 10 seconds needed). After surface stimulation, the time was reduced significantly to 13.2 ± 3.3 seconds. ActiGait stimulation 10 weeks after implantation led to a further

reduction of the time needed to 9.29 ± 1.2 seconds, which was significant compared with surface stimulation, and a slight increase to 10.25 ± 2.4 seconds 1 year after surgery (Fig. 4).

Subjective Quality-of-Life Survey

For subjective changes in daily living after implantation of the ActiGait stimulator, the patients were asked to answer a short quality-of-life survey (Table 2). Four patients noticed an improvement in their mobility in daily living up to normal, in quality of life, and in social participation; 2 patients stated that they had a marked improvement. All of the patients said that they would recommend the surgical procedure.

Discussion

The aim of this study was to elucidate whether the ActiGait implantable drop foot stimulator can provide long-term improvements in gait speed and endurance and re-

FIG. 3. Mean covered distances after 6 minutes of walking by 6 patients with MS with an ActiGait drop foot stimulator 10 weeks and 1 year after implantation. * $p < 0.05$ compared with no stimulation; # $p < 0.05$ compared with surface stimulation.

FIG. 4. Mean times needed to complete the Timed Up and Go tests by 6 patients with MS 10 weeks and 1 year after implantation of an ActiGait drop foot stimulator. * $p < 0.05$ compared with no stimulation; # $p < 0.05$ compared with surface stimulation.

duce the risk of falls in patients with MS-related drop foot, because its efficacy and superiority over surface stimulation in patients after stroke were reported recently.^{10,16} In this study, no adverse events were observed. Until now, only rare complications, such as hematoma and lymphedema (both in 1 of 5 patients),¹⁶ wound-healing deficit (1 of 15 patients) and infections (2 of 15 patients),³ and injury to the peroneal nerve (2 of 27 patients),¹⁰ have been reported. The surgery and postoperative care were easy and uncomplicated. The patients had no problems using the ActiGait stimulator in daily living. In addition, recent reports have shown that the implantable device is easier to use than the surface stimulator.³

Gait evaluations revealed that walking speed was increased significantly by 30.8% 10 weeks after using the ActiGait system and increased more significantly by 57.0% 1 year after surgery. These results are comparable with recent findings in patients after stroke, in which ActiGait stimulation resulted in improvements of 19%⁴ and 25%¹⁰ in a 10-m gait test and 47%¹⁰ in a 20-m gait test. In our study, the implantable stimulator was superior to an ankle foot orthosis ($p = 0.0173$) and to surface stimulation after 10 weeks, but the difference was not significant ($p = 0.07672$). However, after 1 year, a significant improvement in gait over that with surface stimulation ($p = 0.0027$) and with the foot orthosis ($p = 0.00042$) was found.

In addition, gait endurance was improved significantly by 47% 10 weeks after surgery and increased further to 52% improvement after 1 year. Compared with surface stimulation, which had already improved gait endurance, ActiGait stimulation resulted in a pronounced and significant increase in the distance covered by our patients in the 6-minute walking test, and the therapeutic effect was stable over a period of 1 year. This result confirms the superiority of the implantable stimulator over surface stimulation. These findings might be explained by the fact that

an implantable stimulator provides more specific stimulation with finer adjustability of stimulation parameters than does surface stimulation, and it produces a considerable orthotic effect with more physiological kinematics in the lower limb.¹⁶

Furthermore, in the Timed Up and Go test 10 weeks after surgery, a nonsignificant improvement of 47% was measured for patients with the ActiGait stimulator as a result of a safer gait. One year after implantation, this effect decreased to 43% but remained higher than the improvement with surface stimulation (29% improvement compared with no walking aids). In this test, a normal gait without increased risk of falls is determined by a time needed of less than 10 seconds.¹⁴ Only with ActiGait stimulation was this criterion reached, with $9.3 (\pm 0.9)$ seconds needed to finish the test.

Finally, all 6 patients noticed at least a marked improvement of mobility in daily living, in quality of life, and in social participation, and they had no regrets about the implantation.

Conclusions

The ActiGait implantable drop foot stimulator is a safe and simple device for drop foot caused by a lesion of the central nervous system. It improved gait speed and endurance and quality of life and reduced the risk of falls in all 6 patients with MS. In addition, these results were stable and even improved further over a period of 1 year. These results are comparable with recent reported improvements in patients after stroke.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Martin, Polanski. Acquisition of data: Martin, Polanski, Schulz. Analysis and interpretation of data: Martin, Polanski, Schulz, Jöbges. Drafting the article: Martin, Polanski, Sobottka. Critically revising the article: Polanski, Ziemssen, Schackert, Pinzer, Sobottka, Jöbges. Reviewed submitted version of manuscript: Martin, Polanski, Schackert, Pinzer. Approved the final version of the manuscript on behalf of all authors: Martin. Statistical analysis: Polanski. Administrative/technical/material support: Martin, Ziemssen, Schackert. Study supervision: Sobottka.

Supplemental Information

Videos

Video 1. <https://vimeo.com/165306345>.

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