NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of functional electrical stimulation for drop foot of central neurological origin

Drop foot is the inability to lift the foot and toes when walking. It can result from conditions such as stroke, multiple sclerosis or spinal cord injury. In functional electrical stimulation electrodes are placed on the surface of the skin above the peripheral nerves that supply the paralysed muscle. The electrodes can also be implanted in the peripheral nerves themselves. Electrical impulses are delivered that stimulate the nerves to produce contractions of the paralysed muscles. The aim is to restore muscular function.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in April 2008

Procedure name

Functional electrical stimulation for spasticity of the foot

Specialty societies

- Association of Chartered Physiotherapists with an Interest in Neurology
- British Society of Rehabilitation Medicine
- Institute of Physics and Engineering in Medicine
- Society for Research in Rehabilitation
- Society of British Neurological Surgeons.

Description

Indications and current treatment

Drop foot is a neurological deficit of central neurological origin. It arises from an upper motor neuron lesion, that is, an injury to the corticospinal tracts in the brain or spinal cord.

This occurs in patients with conditions such as stroke, cerebral palsy, multiple sclerosis and spinal cord injury.

Symptoms of an upper motor lesion include muscle weakness in a pyramidal distribution (an imbalance causing arm flexion and leg extension), hypertonicity, exaggerated reflexes, clonus and an extensor plantar response.

The pyramidal pattern of an upper motor lesion causes hip, knee and ankle straightening resulting in the foot dragging when walking. Patients often compensate for this by exaggerating the motion of the hip by swinging their stiff leg outward so that the foot can clear the ground (known as ‘circumduction’). The result is an abnormal, slow, tiring and sometimes unsafe gait.

Treatments for drop foot include physiotherapy, orthotic devices, medical therapy, electrical stimulation of the affected nerves and surgery. These options can be used alone or in combination with one another.

First-line treatment is usually physiotherapy or the use of an ankle foot orthosis (AFO). An AFO is a device, usually made of plastic, which is worn on the lower part of the leg and on the foot. It is used to align the lower leg correctly and control the motion of the ankle and foot, to provide stability and improve gait.

Medical therapy includes orally administered drugs such as baclofen, dantrolene or tizanidine. More recently, botulinum toxin type A (Botox) injections into the most affected muscles have been used to treat spasticity. Surgery includes selective tendon release of these muscles, selective dorsal rhizotomy and intrathecal delivery of baclofen (also called Baclofen pump).

Surgery is rarely indicated and is usually reserved for the most refractory cases.

What the procedure involves

Function electrical stimulation (FES) involves the application of electrical pulses to the common peroneal nerve. The pulses are produced by a stimulator unit worn externally and delivered via skin surface or implanted electrodes. The aim is to produce muscle contractions that mimic normal voluntary movement lifting the foot so that it does not drag on the ground and so improve gait.

FES delivered via skin surface electrodes does not require anaesthesia and can be performed on an outpatient basis. Skin surface electrodes are typically placed over the nerve where it passes over the head of the fibula and the motor point of tibialis anterior. Leads connect the electrodes to the stimulator unit and a foot switch located under the heel.

Skin surface electrodes must be repositioned each time the stimulator unit is used. Teaching the technique to patients requires several sessions during the first few months and regular review.

FES can also be delivered via implanted electrodes. This procedure requires general anaesthesia. The electrodes are usually inserted into the epineurum of the superficial and the deep branch of the common peroneal nerve. Radiowaves or leads passed through the skin are used to connect to the stimulator and foot switch as with the surface electrodes.

The advantage of this procedure is that the electrodes do not need to be positioned by the patient.

Various devices can be used for this procedure.

Efficacy

A meta-analysis of three studies on skin surface-applied FES found that it increased gait speed by a mean difference of 0.18 metres /second (95% CI 0.08 to 0.28) in stroke patients (n = 36) compared with conventional therapy (n = 35) (absolute numbers not given). When evidence was considered from all studies (three controlled trials and two non-controlled trials) the mean effect size ranged from - 0.11 to 1.43[1].

In a case series of 140 patients undergoing skin surface FES, stroke patients (n = 111) showed an increase in walking speed of 12% (0.07metres/second) and a decrease in effort of 18% (-0.16 beats/metre) (measured by a physiological cost index) when using the stimulator (orthotic effect) compared with baseline. At 4.5-month follow-up there was a 14% (0.08 metres/second) increase in walking speed and a 19% (-0.17 metres/second) reduction in effort. In patients with multiple sclerosis (n = 21) there was a 16% (0.08 metres/second) increase in walking speed and a 24% (-0.20 beats/metre) decrease in effort. However, when not using the stimulator the patients reported a 7% (-0.03 metres/second) decrease in walking speed and a 16% (0.13 beats/metre) increase in effort[2].

Two randomised controlled trials reported on efficacy outcomes following implantation of electrodes[6, 4]. In the first trial FES was compared with conventional therapy in 29 patients. FES resulted in a 23% improvement in walking speed measured with the six-minute walking test (6MWT), compared with an improvement in the control group of 3% (p = 0.010).Comfortable

walking speed measured on a 10-metre walkway was also significantly improved in the FES group ($p = 0.038$)[6].

In the second randomised controlled trial no significant differences in the 6MWT were found between the group with implanted electrodes (post-treatment mean/median walking distance 252.2 metres) and the control group who received physiotherapy training (post-treatment mean/median walking distance 165.9 metres; $p = 0.184$). The primary outcome measure in this study was gait component execution according to the Tinetti gait scale, a 12-point scale assessing gait components such as gait initiations, walking path and trunk alignment. The FES group had a statistically significant greater gain versus the control group for gait component execution ($p = 0.003$; parameter estimate 2.9, 95% CI 1.2 to 4.6). Around 50% of the control group had no gains, whereas 14% of the FES group had no gains[4].

Both groups subjectively reported gains in walking endurance and functional milestones. Functional milestones were reported in 11 instances (such as prepared dinner', 'walked outside') for the control group and 53 instances for the FES group. Milestones of greater motor complexity were demonstrated more frequently in the FES group than in the control group[4].

Safety

Few studies reported safety outcomes following FES..

Three studies reported safety outcomes following the implantation of electrodes. In a randomised controlled trial of 29 patients with chronic stroke, 14 of whom received FES, four instances of skin erythema were reported[4]. In a case series of 17 patients, 14 instances of skin erythema in 6 patients were reported, with 1 patient requiring electrode removal[5]. Two patients developed wound infection following electrode implantation in a case series of 15 patients[11].

One instance of device malfunction was reported after 10 weeks in a randomised controlled trial of 29 patients, 14 of whom had implanted electrodes[6].

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to function electrical stimulation. Searches were conducted via the following databases, covering the period from their commencement to 5th March 2008, and updated to 7th August 2008: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See appendix C for details of search strategy.)

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with presenting with drop foot as a result of an upper motor neuron lesion
Intervention/test	Functional electrical stimulation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on one meta-analysis of five studies, three randomised trials and three case series studies (this is around 230 patients who have had the procedure) [1, 6, 4, 5, 2,11].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Existing assessments of this procedure

A Cochrane review titled 'Electrostimulation for promoting recovering of movement or function ability after stroke' has been published[8].

This review includes studies reporting on both functional electrical stimulation (FES) and transcutaneous electrical stimulation, looking at outcomes for both upper and lower limbs.

The results of this review have not been extracted in this overview.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

IP overview: functional electrical stimulation for spasticity of the foot

Interventional procedures

Selective dorsal rhizotomy for spasticity in cerebral palsy. NICE interventional procedures guidance 195 (2006). Available from www.nice.org.uk/IPG195

Clinical guidelines

- A clinical guideline on the diagnosis and acute management of stroke and transient ischaemic attacks is in development; however, this does not include reference to functional electrical stimulation.

Table 2 Summary of key efficacy and safety findings on function electrical stimulation for for drop foot of central neurological origin

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; M/S – metres per second; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation

Study details	Key efficacy findings	Key safety findings	Comments
Kottink (2007) [6] **Study type: randomised controlled trial** Country: Netherlands Study period: not stated Study population: patients with chronic hemiplegia after stroke. Mean time after stroke was 9 years in the FNS group and 6 years in the control group. **n = 29:** • **14 functional neuromuscular stimulation) – implanted (FNS-IM)** • **15 control group (conventional walking device, consisting of an ankle foot orthosis, orthopedic shoes or no device)** Age: mean 55.2 years (FNS); 52.9 years (control). Range not stated. Sex: 71% (10/14) male (FNS); 67% (10/15) male (control) Inclusion criteria: drop foot identified by inability to achieve a normal heel strike during walking; first hemiplegia of at least 6 months in duration as a result of a CVA with a stable neurology, subject	***Six-minute walk test (6MWT) (participants were allowed to use walking aid)*** A significant difference between groups was found when all assessments were taken into the linear mixed model (p = 0.010) showing a positive effect of FES on the performance of the 6MWT. At the first follow-up both the intervention and control groups showed an improvement from baseline. At 26 weeks, the intervention group continued to show improvements whereas the control group exhibited some deterioration – walking speed at 26 weeks relative to baseline now differed significantly between groups (p = 0.049). The authors note in the abstract that FNS-IM resulted in a 23% improvement in walking speed compared with the control group 3% (p = 0.10). This is not contained in the text of the article and the results are presented as graphs. **Walking speed (10 metres)** Walking speed remained constant over time within the control group (p = 0.572). The intervention group showed a small deterioration in walking speed immediately after starting FNS treatment followed by an improvement in walking speed when FNS was used for a longer period. Overall, when baseline was compared with the last follow-up assessment, the change in walking speed in the intervention group was statistically significant (p = 0.010). The authors note in the abstract that comfortable walking speed measured on a 10-metre walkway was also	Authors did not report on safety. It was noted that one implant failed after functioning properly for about 10 weeks.	Random allocation was performed in blocks of two subjects and was carried out by an independent person. All patients were allowed to continue their usual PT sessions. Prior to entering the study, seven patients in the FNS group used a plastic AFO, three wore orthopaedic shoes and four did not use a walking aid. In the control group all patients wore a plastic AFO. All measurements were performed by the same examiners. Blinding was not possible. An intention- to-treat analysis was undertaken. Four subjects dropped out of the study: one woman in the FNS group (implant failed) and three men in the control group (unrelated reasons). Activ PAL is an accelerometer-based measurement device used to record subjects' primary physical activities (stepping,

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; M/S – metres per second; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
is an outdoor walker, able to give informed consent. Technique: implantable 2-channel peroneal nerve stimulator. Under general or spinal anesthesia, electrode surgically positioned under the epineurium of the superficial peroneal nerve and another under the epineurium of the deep peroneal nerve. **Follow-up: 26 weeks** Conflict of interest: research was supported by the European Eureka Program, the Department of Dutch Ministry of Economic Affairs in the Hague.	significantly improved for the FNS group ($p = 0.038$). This is not contained in the text of the article and the results are presented as graphs. **Assessment of activity level (activPAL)** Time spent stepping decreased by 3% and 0.8% in the intervention and control groups ($p = 0.13$). Time spent standing declined by around 3% in the FNS group but improved by 2% in the control group ($p = 0.06$). Time spent sitting/lying increased by 6% in the FNS group whereas it decreased by 1% in the control group ($p = 0.04$)		standing, sitting). Only two systems were available and so 10/15 and 11/14 patients were randomly selected to be monitored over a 5-day period. Authors note that patient group had a relatively good walking function at the start of the trial. Outcomes are presented as graphs; absolute numbers are not given in the text of the study.

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; M/S – metres per second; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Daly (2006)[4]
Study type: randomised controlled trial
Country: USA
Study period: September 1999–June 2004
Study population: Chronic stroke patients

n = 29:
• 14 functional neuromuscular stimulation – implanted (FNS-IM)
• 15 no functional neuromuscular stimulation (FNS); coordination exercises

Age: mean 57.7 years (FNS); 63.6 years (no FNS). Range not stated.

Sex: 79% (11/14) male, 21% (3/14) female (FNS-IM); 73% (11/15) male, 27% (4/15) female (no FNS)

Inclusion criteria: more than 12 months after a single stroke; inability to clear the floor normally in the sagittal plane; hyperflexion or hyperextension of knee during stance; walking without human assistance; passive joint range of motion of hip, knee, and ankle equal to normal excursion needs for walking; normal corrected distance vision; and not participating in rehabilitation.</td>
<td>Tinetti gait (TG)
12-point scale assessing the following coordinated gait components: gait initiations; walking path; trunk alignment; swing-phase limb trajectory; step continuity; step symmetry and swing floor clearance and forward swing limb excursion.
<table>
<tr><th></th><th>Baseline (mean; range)</th><th>Post treatment (mean; range)</th><th>p (compare groups)</th></tr>
<tr><td>FNS-IM</td><td>6.5 (3-10)</td><td>9 (6-12)</td><td>p = 0.003</td></tr>
<tr><td>No FNS</td><td>6 (3-10)</td><td>7 (3-10)</td><td></td></tr>
</table>
Authors note that in the FNS-IM group, 64% had gains of 2–6 points whereas only 13% of no-FNS patients had gains ≥ 2 points. Around 50% of the no-FNS group had no gains whereas only 14% of FNS-IM patients had no gains.

Fugl-Meyer lower extremity coordination (FMLE)
34-point scale: 0–19 severe; 20–28 moderate; > 29 mild
<table>
<tr><th></th><th>Baseline (mean; range)</th><th>Post treatment (mean; range)</th><th>p (compare groups)</th></tr>
<tr><td>FNS- M</td><td>22 (16-28)</td><td>28 (19-32)</td><td>p = 0.182</td></tr>
<tr><td>No FNS</td><td>20 (11-28)</td><td>23 (13-29)</td><td></td></tr>
</table>
</td>
<td>FNS-IM group
4 patients reported erythema on the skin surface at lead exit sites.</td>
<td>Selection: 58 candidates were screened; 26 did not meet inclusion criteria and 5 declined to participate after screening.
Prior to treatment 2 patients in the FNS group and 1 in the no-FNS group dropped out .
Authors note that sample size was limited by time constraints.

Randomisation: two independent individuals were involved in either treatment or allocation. Treatment was allocated based on a cross-matching of enrollment date with the treatment allocation sequence (open-list methods). Patients were stratified according to severity and blocking was used to ensure balance between the groups.

Authors stated that there were no baseline differences between the groups.

Blinding: outcomes were assessed by clinicians masked to treatment groups.

Primary outcome measure was gait component execution

A 2-point gain in Tinetti gait can indicate a reduced frequency of</td>
</tr>
</table>

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; M/S – metres per second; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Technique: all patients were treated for 1.5 hours per session, 4 sessions per week, for 12 weeks including 0.5 hours coordination exercises, 0.5 hours body weight supported treadmill training (BWSTT) and 0.5 hours overground walking (OG).
Treatment was identical for both groups except that FNS was used for all treated aspects. Eight muscles were provided with electrodes.
Follow-up: 26 weeks

Conflict of interest: not stated.</td>
<td>
Fugl-Meyer knee flexion coordination(FMKnFX)
6-point ordinal measure
<table>
<tr><th></th><th>Baseline (mean; range)</th><th>Post treatment (mean; range)</th><th>p (compare groups)</th></tr>
<tr><td>FNS-IM</td><td>4 (1-5)</td><td>5 (2-6)</td><td>p = 0.049</td></tr>
<tr><td>No FNS</td><td>3 (0-5)</td><td>4 (1-2)</td><td></td></tr>
</table>
Tinetti balance (TB)
16-point ordinal scale assessing balance
<table>
<tr><th></th><th>Baseline (mean; range)</th><th>Post treatment (mean; range)</th><th>p (compare groups)</th></tr>
<tr><td>FNS-IM</td><td>13.5 (10-15)</td><td>15 (12-16)</td><td>p = 0.133</td></tr>
<tr><td>No FNS</td><td>10 (6-14)</td><td>13 (8-16)</td><td></td></tr>
</table>
Six-minute walking test (6MWT)
Measured walking distance within 6 minutes
<table>
<tr><th></th><th>Baseline (mean; range)</th><th>Post treatment (mean; range)</th><th>p (compare groups)</th></tr>
<tr><td>FNS-IM</td><td>186.6 m (75.6–309.7)</td><td>252.2m (111.6–407.8)</td><td>p = 0.184</td></tr>
<tr><td>No FNS</td><td>128.3 m (14.6–285.9)</td><td>165.9m (29.9–299.3)</td><td></td></tr>
</table>
</td>
<td></td>
<td>falls.

Details of the operative procedure were not described.</td>
</tr>
</table>

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; M/S – metres per second; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
	Functional milestones Patients were queried bimonthly regarding milestones that had been achieved in the previous 2 weeks. Authors report that both groups subjectively reported gains in walking endurance and functional milestones. Functional milestones, such as 'prepared dinner', 'walked outside', were reported in 11 instances in the control group and 53 instances in the FNS-IM group. Milestones of greater motor complexity were demonstrated more frequently for FNS-IM versus no-FNS.		

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; M/S – metres per second; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Burridge (2007)[11]

Study type: case series
Country: Denmark
Study period: not stated

Study population: stroke patients

n = 15 (13 evaluable)

Age: mean 56 years (range 46–68 years)

Sex: 73% (11/15) male

Inclusion criteria: Had a drop foot following a stroke at least 6 months prior to recruitment. All participants had at least 30 degrees of passive ankle movement and were able to stand upright s with heels touching the floor when the hip and knee were in a neutral position
Technique: Spinal anaesthesia was used to place the electrodes/nerve cuff. The common peroneal nerve was exposed through a longitudinal incision.

Follow-up:11.6 months (range 6-15 months)

Conflict of interest: not stated</td>
<td>4 patients experienced problems with the implantable device (nerve cuff was too large). It was modified and 3 patients underwent re-implantation (the remaining patients was awaiting re-implantation surgery at the time of writing).

Distance walked in 4min with and without stimulation

Baseline: 117.3m (range 34-184m)
<table>
<tr><th></th><th>90 days</th><th>Final assessment (15 months)</th></tr>
<tr><td>Non - stimulated</td><td>115.4 metres (range 40-189m)</td><td>131 metres (range 43-203m)</td></tr>
<tr><td>Stimulated</td><td>124.9 metres (range 54-194m)</td><td>142.9 metres (range 59-199m)</td></tr>
</table>
Orthortic effect of stimulation: (final)
Distance walked 11.46m 95% CI (-0.12,23.04) p=0.052
Long-term therapeutic effects of stimulation (final-baseline)
Distance walked 4.77m 95% CI (-8.42,17.96) p=0.446
Long-term effects of stimulation (final-baseline)
Distance walked 16.23m 95% CI (2.03,30.43) p=0.028</td>
<td>Authors report that no adverse events were reported during surgery.

In 2 patients minor wound infections required treatment with antibiotics and in one patients wound healing was delayed.
No serious device related adverse events were reported.

There were no changes in nerve conduction velocity related to the nerve cuff.</td>
<td>This paper was included as it aimed to evaluate FES in terms of safety (nerve conduction velocity and adverse events)

Consecutive sample of participants were recruited from3 stroke centres.

Patients who could walk faster than 1.2 meters/second were excluded.

Patients were tested with and without stimulation

Authors note that during the course of the study it was found that the nerve cuff was too large for some patients, and that there were problems with the wireless communication. Both problems were resolved with device modification.</td>
</tr>
</table>

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; M/S – metres per second; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation

Study details	Key efficacy findings	Key safety findings	Comments
	Maximum walking speed over one complete circuit (20m) **Baseline 0.50 m/sec (range 0.15-0.80m/sec)**		

	90 days	**Final assessment (15 months)**
Non-stimulated	0.51m/s (range 0.19-0.83)	0.58m/s (range 0.18-0.87)
Stimulated	0.55 m/s (range 0.25-0.83)	0.66m/s (range 0.25-0.87)

Orthortic effect of stimulation: (final)

Maximum speed 0.07m/s 95% CI (0.02, 0.11) p=0.011

Long-term therapeutic effects of stimulation (final-baseline)

Maximum speed 0.04m/s 95% CI (-0.04,0.11) p=0.282

Long-term effects of stimulation (final-baseline)

Maximum speed 0.10m/s 95% CI (0.03,0.17) p=0.008

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; M/S – metres per second; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation

Study details	Key efficacy findings	Key safety findings	Comments

Daly (2001)[5]

Study type*:* case series

Country: USA

Study period: not stated

Study population: stroke patients

n = 17 (124 electrodes)

Age: mean 62.5 years (range 48–82 years)

Sex: 82% (14/17) male

Inclusion criteria: not stated

Technique: local anaesthesia was used to place the electrodes (up to 8 electrodes per person). All electrode leads exited in the same region.

Follow-up: range 6–24 months

Conflict of interest*:* not stated

This paper is included to present information on safety.

No of electrodes producing a comfortable stimulus

Number patients	Number of electrodes	Number of electrodes painful sensation	Number of electrodes comfortable sensation
Chronic 9	69	3	66
Acute 8	55	0	55
Total	124	3	121

Physiological factors of electrode performance

Patients	Number of infections	Instances of skin site erythema	Number of electrodes removed following erythema
Chronic	0	14	1
Acute	0	0	0
Total	0	14	1

65% of patients had no instance of skin erythema. Four patients had one instance and two patients had four and six instances. The authors state that these patients had erythema for known reasons (scrubbing and irritating the skin around the lead wires and uncleanliness).

Biocompatibility of electrode fragments

Patients	No of fragments in body	Fragments months	No of infections/ other symptoms
Chronic	51	3,667.6	0
Acute	39	624.7	0
Total	90	4,292.3	0

The paper describes the design and first use of a system specifically designed to be implanted.

Limited clinical outcomes have been described.

Six electrodes exhibited high impedance and assumed breakage. However five of these six failed electrodes were in the same patient who was first to enter the trial..

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Robbins (2006)[1]
Study type: meta-analysis
Country: Canada
Literature search period: January 1966–March 2005
Study population: stroke patients included in prospective trials
n = 8 studies (5 FES, 3 TENS – only the studies reporting on FES will be included here)
Controlled trials
Alon and Ring[9] n = 19
Bogataj et al.[10] n = 20
Burridge et al.[11] n = 32
Non-controlled trials
Burridge et al. {275) n = 18
Granata et al. {387} n =18
Age: not stated (not applicable)
Sex: not stated (not applicable)
Inclusion criteria: prospective studies that used the treatment of FES or TENS with surface electrodes; studies with subjects who had sustained a stroke; used gait speed as an outcome measure and assessed without electric stimulation and were written in English.
Technique: skin surface electrodes</td>
<td>
<table>
<tr><th></th><th>Baseline gait speed</th><th>Final gait speed</th><th>Change (%)</th></tr>
<tr><td>Alon and Ring</td><td>m/s</td><td>m/s</td><td>Mean effect size d =1.34</td></tr>
<tr><td>Control</td><td>0.76</td><td>0.75</td><td>-0.01 (-1.32%)</td></tr>
<tr><td>Intervention</td><td>0.88</td><td>1.20</td><td>0.32 (36.36%)</td></tr>
<tr><td>Bogatai</td><td></td><td></td><td>Mean effect size d =1.43</td></tr>
<tr><td>Control</td><td>0.23</td><td>0.26</td><td>0.03 (13.04%)</td></tr>
<tr><td>Intervention</td><td>0.19</td><td>0.41</td><td>0.22 (115.8%)</td></tr>
<tr><td>Burridge</td><td></td><td></td><td>Mean effect size d =-0.11</td></tr>
<tr><td>Control</td><td>0.48</td><td>0.51</td><td>0.03 (6.25%)</td></tr>
<tr><td>Intervention</td><td>0.64</td><td>0.63</td><td>-0.01 (-1.56%)</td></tr>
<tr><td>Burridge</td><td></td><td></td><td>Mean effect size d =0.37</td></tr>
<tr><td>Intervention</td><td>0.63</td><td>0.74</td><td>0.11 (17.46%)</td></tr>
<tr><td>Granata</td><td></td><td></td><td>Mean effect size d =0.02</td></tr>
<tr><td>intervention</td><td>0.94</td><td>0.95</td><td>0.01 (1.06%)</td></tr>
</table>
A total of 36 subjects were in the treatment group and 35 subjects were in the control group. The studies were not heterogeneous (x2 test = 4.80, p = 0.09).
The fixed-effects model produced a mean difference and 95% CI (mean 0.18, 955 CI, 0.08-0.28) that were significant (z = 3.65, p<0.01) for the effectiveness of FES treatment.
The study examining FES using subjects in the acute or subacute stages of recovery from a stroke (onset < 6 months) had a larger effect size (d =1.43) than the mean effect size (d =0.400) of the studies examining
</td>
<td>The authors do not report on safety outcomes</td>
<td>This paper reports on the therapeutic effect of FES (carry – on effect FES has on gait)
The authors comment that the three controlled trials examining FES differed in methodology and treatment.
In the controlled trials, the control groups received PT or conventional gait training (not placebo).
The methods and amount of exposure to FES varied between the studies (single vs multichannel).
Some of the studies included both acute and chronic stroke patients.
One study included patients in the subacute phase (Bogatai), that is, 6 months from stroke onset.
In addition, compliance was not measured in most of the studies in which subjects used the FES devices at home.</td>
</tr>
</table>

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation

Study details	Key efficacy findings	Key safety findings	Comments
Follow-up: range 1 month–12 weeks Conflict of interest*:* not stated	FES using subjects in the chronic stage of recovery (onset > 6 months). The mean effect size (d =1.38) of the studies using multichannel FES was larger than the mean effect size (d = 0.09) of the studies examining single-channel FES.		
Taylor (1999)[2] **Study type*:* case series** Country: UK Study period: not stated Study population: patients with a dropped foot resulting from an upper motor neuron lesion **n = 140:** • **111 stroke** • **21 multiple sclerosis** • **8 incomplete spinal cord injury** Age: mean age 55.4 years (stroke); 55.8 years (multiple sclerosis); 42.1 years (spinal cord injury). Range not stated. Sex: not stated. Inclusion criteria: unilateral dropped foot that was caused by an upper motor neuron lesion and was corrected by electrical stimulation. Patients were able to move from sitting to standing unaided and able to walk at least 10 metres with appropriate aids. Technique: two appointments were made to the fit the Oddstock Drop Foot Stimulator (ODFS – a single-channel	**Outcomes measured: walking speed as measured by physiogical cost index (PCI) over a 10-metre course** **Patients (stroke)** The stroke patients showed a statistically significant improvement in all measurement parameters. A carryover (therapeutic) effect, both in an increase in walking speed of 0.08metres/sec (14%) and a reduction in PCI of 0.17 beats/metre (19%) was found at 4.5-month follow-up. The immediate effect of using the stimulator was also shown to be statically significant, with an increase in walking speed of 12% and a decrease in effort of 18%, with a similar effect recorded at follow-up. **Patients (multiple sclerosis)** These patients showed a 7% (0.03metres/sec) decrease in walking speed and a 16% (0.13beats/metre) increase in the effort of walking when not using the ODFS, 4.5 months after starting to use the stimulator. At the initial visit the patients walked slightly faster (0.03metres/sec) and with less effort (0.09beats/metre) with the stimulator than without it. However, the ODFS was of significant orthotic benefit to these patients, reducing PCI by 24% and increasing walking speed by 16% when the ODFS was used at the third assessment. **Patients (spinal cord injury)** While a trend towards a carryover effect was seen, this	The authors do not report on safety.	The data in this study were obtained retrospectively from patient records. The average time since stroke was 5.4 years (range 1 month–24 years); The average time since first diagnosis of multiple sclerosis was 14.6 years. For patients with spinal cord injury the average time since the injury was 10.9 years. The walking speed and PCI were also recorded for a group of normal, age-matched subjects and were collected in a similar manner to that used in the study. Eleven subjects who started using the ODFS discontinued its used before the assessment at 4.5months and 9 stroke patients stopped using the device between 4.5 months and the next assessment 6 months later. The procedure has been assessed in terms of both therapeutic and orthotic effects.

Abbreviations used: 6MWT, six minute walk test; AFO, ankle foot orthosis; CVA, cerebrovascular accident; FES, functional electrical stimulation; FNS, functional neuromuscular stimulation; IM, implantable; PCI, physiological cost index; PT, physiotherapy; TES, threshold electrical stimulation			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
stimulator) **Follow-up: 4.5 months** Conflict of interest: Medical Device Agency funding the initial trial	was not significant. Orthotic benefit was recorded at the first assessment and at the final assessment in terms of speed. The total orthotic effect of using the stimulator for this group of patients was an increase in walking speed of 19% (0.10m/sec).		

Validity and generalisability of the studies

- There is significant variation in the way the procedure is carried out, including the length of treatment stimulation (exposure), use of single–channel or multichannel devices and whether electrodes are placed on the skin surface or implanted.
- Patient characteristics varied across the studies, which included acute and chronic stroke patients, patients with multiple sclerosis and patients with cerebral palsy. The majority of evidence relates to chronic stroke patients.
- In the randomised controlled trials FES was compared with placebo and conventional rehabilitation treatment such as physiotherapy. It is possible that results may vary depending upon the comparator.
- Efficacy outcomes varied across the studies: while most studies reported on walking speed some studies reported on other outcomes such as peak torque.
- Improvements in physiological outcome may be poor predictors of functional improvement. Conversely, a small improvement in a physiological measurement may have a disproportionately large impact on disability or caring requirements.
- There is limited evidence about quality of life and impact of the procedure on disability, for either patients or carers/family members.
- FES can be assessed in terms of either its orthotic benefit (immediate effect during stimulation) or its therapeutic effect (carryover effect when stimulation is not applied).
- Few studies reported absolute numbers.

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Dr Jane Burridge, Ms Geraldine Mann (Association of Chartered Physiotherapists with an Interest in Neurology), Professor Rushton (British Society of Rehabilitation Medicine), Richard Caley, Professor Swain (Institute of Physics and Engineering in Medicine), Dr Rosie Jones, Dr Duncan Wood (Society for Research in Rehabilitation) Mr Paul Eldridge (Society of British Neurological Surgeons).

- Established procedure and no longer new.

- Implanted device is considered novel.
- The system is disadvantaged because of the need to use surface stimulation technology – patients must receive adequate training and adhere to the instructions so that they maintain adequate muscle development for the system to remain effective.
- Training is important for patients and for clinical staff
- FES is widely regarded as being useful but patient selection and treatment application are important.
- Not all patients with spasticity of the foot will benefit from this procedure.
- Treatment has to be long term in many cases.
- Most commonly used for stroke patients, less widely used in other conditions but still beneficial.
- Role of the implanted device is still unclear.
- Implanted device should be viewed as a minor variation.
- Implanted device can be more convenient for some patients and overcomes a number of problems with skin reaction and electrode placement.
- From the literature it appears that there is considerable variation in treatment regimes and protocols. This is because FES is widely used in the research environment and hence a large number of papers are concerned with research rather than clinical provision.
- Diffusion of the procedure is currently limited by staff training and willingness of primary care trusts to fund the procedure.

Issues for consideration by IPAC

- The title was debated at the scope stage. Several suggestions have been made: functional electrical stimulation (FES) for foot drop of central neurological origin; functional electrical stimulation (FES) for the treatment of spastic drop-foot; functional electrical stimulation (FES) for disorders of gait associated with lesions of the central nervous system.

- FES is not a new procedure. There is a considerable body of evidence published over a 30-year period (particularly on patients with chronic stroke) and several Specialist Advisers consider the skin surface application of FES to be established.
- FES is included in the Royal College of Physicians Guideline on Stroke (see appendix C
- Studies including acute stroke patients were excluded from the main data extraction table so as to control for the effect of spontaneous recovery. These have been included in appendix A.
- A major 5-year trial comparing FES with the use of an AFO for dropped foot is being conducted in the USA with around 170 patients. There are also other ongoing trials on FES.

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2. Taylor PN, Burridge JH, Dunkerley AL et al. (1999) Clinical use of the Odstock dropped foot stimulator: its effect on the speed and effort of walking. Archives of Physical Medicine & Rehabilitation 80: 1577–1583.
3.
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5. Daly JJ, Kollar K, Debogorski AA et al. (2001) Performance of an intramuscular electrode during functional neuromuscular stimulation for gait training post stroke. Journal of Rehabilitation Research & Development 38: 513–526.
6. Kottink AI, Hermens HJ, Nene AV et al. (2007) A randomized controlled trial of an implantable 2-channel peroneal nerve stimulator on walking speed and activity in poststroke hemiplegia. Archives of Physical Medicine & Rehabilitation 88: 971–978.
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8. Alon G. (2003) Gait and hand function enhancement following training with a multi-segment hybrid-orthosis stimulation system in stroke patients. Journal of Stroke and Cerebrovascular Diseases 12: 209–216.
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10. Burridge JH, Taylor PN, Hagan SA et al. (1997) The effects of common peroneal stimulation on the effort and speed of walking: a randomized controlled trial with chronic hemiplegic patients. Clinical Rehabilitation 11: 201–210.
11. Burridge JH, Haugland M, Larsen B et al. (2007) Phase II trial to evaluate the ActiGait implanted drop-foot stimulator in established hemiplegia. Journal of Rehabilitation Medicine 39: 212-218.

Appendix A: Additional papers on functional electrical stimulation for drop foot of central neurological origin not included in summary table 2

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Bogataj U, Gros N, Kljajic M et al. (1995) The rehabilitation of gait in patients with hemiplegia: a comparison between conventional therapy and multichannel functional electrical stimulation therapy. Physical Therapy 75: 490–502.	n = 20 Follow-up =6 weeks	There was improved performance of the subjects during FES combined with conventional therapy as compared with conventional therapy alone.	Included in the systematic review in table 2
Cozean CD, Pease WS, Hubbell SL. (1988) Biofeedback and functional electric stimulation in stroke rehabilitation. Archives of Physical Medicine & Rehabilitation 69: 401–405.	n = 36 Follow-up = 4 weeks after treatment	Combined therapy with biofeedback and FES resulted in improvements	Larger studies included in table 2
Johnston TE, Betz RR, Smith BT et al. (2003) Implanted functional electrical stimulation: an alternative for standing and walking in pediatric spinal cord injury. Spinal Cord 41: 144–152.	n=9 (implanted) Follow-up= not stated	Participants completed four activities faster ($p<0.02$) and five activities more independtly ($p<0.025$) with FES compared to long leg braces.	Larger study included in Table 2
Kottink AI, Oostendorp LJ, Buurke JH et al. (2004) The orthotic effect of functional electrical stimulation on the improvement of walking in stroke patients with a dropped foot: a systematic review. [Review] [50 refs]. Artificial Organs 28: 577–586.	Systematic review 8 studies	Review suggests a positional orthortic effect of FES on walking speed.	Meta-analysis included in table 2 (controlled studies).

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Kottink A, Hermens H, Nene A et al (2008). Therapeutic effect of an implantable peroneal nerve stimulator in subjects with chronic stroke and footdrop: a randomized controlled trial. Physical Therapy 88 (4) 437-448.	n = 29 RCT: FES vs ankle-foot arthosis. Follow-up: 7 months	No functionally therapeutic affect of FES was found (no change in walking speed when the stimulator was used). There was a significantly higher voluntary muscle output of the tibialis anterior and gastrocnemius muscles after using FES.	Larger study included in Table 2
Ng MF, Tong RK, and Li LS. (2008) A pilot study of randomized clinical controlled trial of gait training in subacute stroke patients with partial body-weight support electromechanical gait trainer and functional electrical stimulation: six-month follow-up. Stroke 39: 154–160.	n = 54 patients Follow-up = 6 months	Patients who trained on the gait trainer with body-weight support with or without FES had a faster gait than those not using gait training. This was sustained through to the 6-month follow-up.	Patients were included within 6 weeks after stroke. Chronic patients included in table 2. Purpose of the study was to study the effectiveness of a gait trainer (with or without FES).
Paul L, Rafferty D, Young S et al (2008) The effect of functional electrical stimulation on the physiological cost of gait in people with multiple sclerosis. Multiple sclerosis 14:954-61.	n = 12 (+ 12 healthy matched controls) Follow-up: not stated	Significant improvement in walking speed and significant reduction in the physiological cost of gait with FES.	Larger study included in Table 2
Taylor PN, Burridge JH, Dunkerley AL et al. (1999) Patients' perceptions of the Odstock Dropped Foot Stimulator (ODFS). Clinical Rehabilitation 13: 439–446.	n = 79 patients	Principal reason cited for using equipment was a reduction in the effort of walking. Principal reasons identified for discontinuing were an improvement in mobility, electrode positioning difficulties and deteriorating mobility. There were some problems with reliability of equipment	Doesn't report clinical outcomes; some information present from the perspective of the patients.
Taylor P, Burridge J, Dunkerley A et al. (1999) Clinical audit of 5 years provision of the Odstock dropped foot stimulator. Artificial Organs 23: 440–442.	n = 132 Follow-up = 4.5 months	After follow-up, stroke patients (n = 111) showed a mean increase in walking speed of 27%; multiple sclerosis patients gained similar orthortic benefit but no carryover.	Retrospective study of a registry. Study by authors included in table 2 on the same population.
Tong RK, Ng MF, Li LS. (2006)	n = 50 patients	Patients who trained on	Patients were

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Effectiveness of gait training using an electromechanical gait trainer, with and without functional electric stimulation, in subacute stroke: a randomized controlled trial. Archives of Physical Medicine & Rehabilitation 87: 1298–1304.	(assigned to 1 of 3 groups). Follow-up = 4 weeks	the gait trainer with body-weight support with or without FES had a faster gait than those not using a gait trainer.	included within 6 weeks after stroke. Chronic patients included in table 2. Purpose of the study was to study the effectivenes of a gait trainer (with or without FES).
van der Linden M, Hazlewood M, Hillman S et al (2008) Functional electrical stimulation to the dorsiflexors and quadriceps in children with cerebral palsy. Pediatric Physical Therapy 20: 23-29	n = 14 children with cerebral palsy (RCT) Follow-up: not stated	2 weeks of neuromuscular electrical stimulation followed by 8 weeks of FES. FES of the ankle dorsiflexors resulted in a significant improvement in gait kinematics. However, no long-term treatment effect of using FES for 8 weeks was found	Larger study included in Table 2
Yan T, Hui-Chan CW, and Li LS. (2005) Functional electrical stimulation improves motor recovery of the lower extremity and walking ability of subjects with first acute stroke: a randomized placebo-controlled trial.[see comment]. Stroke 36: 80–85.	N = 46 (assigned to 1 of 3 groups) Follow-up = 8 weeks	FES+ standard rehabilitation improved their motor and walking ability to the degree that more subjects were able to return home.	Acute stroke (9 days after stroke). Chronic patients included in table 2

Appendix B: Related NICE guidance for functional electrical stimulation for for drop foot of central neurological origin

Guidance	Recommendation
Interventional procedures	**Selective dorsal rhizotomy for spasticity in cerebral palsy. NICE interventional procedures guidance 195 (2006).** 1.1 Current evidence on the safety of selective dorsal rhizotomy (SDR) for spasticity in cerebral palsy appears adequate; however, there is evidence of only limited efficacy. Therefore, the procedure should not be used without special arrangements for consent and for audit or research. 1.2 Clinicians wishing to undertake SDR for spasticity in cerebral palsy should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients or their parents/carers understand the uncertainty about the efficacy of this procedure, that it is irreversible and that there is a risk of serious complications. They should also be counselled on the extensive physiotherapy and rehabilitation required after this procedure and clinicians should provide them with clear written information. Use of the Institute's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG195publicinfo). • Audit and review clinical outcomes of all patients having SDR for spasticity in cerebral palsy (see section 3.1). 1.3 Patient selection should be carried out in the context of a multidisciplinary team with specialist

	expertise in various treatment options for spasticity in patients with cerebral palsy. This should normally include a physiotherapist, a paediatrician, an orthopaedic surgeon and a neurosurgeon. 1.4 Further evidence on the efficacy outcomes of the procedure will be useful. The Institute may review the procedure upon publication of further evidence.

Appendix C: Related guidelines for functional electrical stimulation for drop foot of central neurological origin

National clinical guidelines for stroke (Royal College of Physicians) (2004)

http://www.rcplondon.ac.uk/pubs/books/stroke/

4.4.3 Improving motor control: functional electrical stimulation
Functional electrical stimulation (FES) is the use of direct electrical stimulation of muscle or peripheral nerves to cause movement. It has been proposed both as a means of improving muscle function (ie as treatment), and also as a way of replacing or augmenting weakened muscle function.

Recommendations
a Functional electrical stimulation should not be used on a routine basis (A)
b Individual patients should be considered for FES as an orthosis in certain circumstances, such as improving arm movement, ankle dorsiflexion and gait performance (A)

Evidence (Table 4.4.3)
a Glanz et al 1996; Ada & Foongchomcheay 2002 (Ia); De Kroon et al 2002 (Ia)
b Burridge et al 1997; Popovic et al 2002 (Ib) 63

National clinical guidelines for stroke: second edition
Local guidelines
When considering the use of FES as an orthosis, local teams may wish to specify:
1 which patients are considered suitable;
2 how its benefit is to be judged for any patient trying it.

Please note the evidence for this incorporates studies on both upper and lower limbs.

Appendix D: Literature search for functional electrical stimulation for drop foot of central neurological origin

IP 657: functional electrical stimulation (FES) for spasticity of the foot		
Database	Date searched	Version searched
Cochrane Library	05/03/2008	Issue 1, 2008
CRD databases (DARE & HTA)	29/02/2008	Jan/Feb 2008
Embase	05/03/2008	1980 to February Week 9
Medline	05/03/2008	1950 to February Week 3 2008
Premedline	29/02/2008	March 04, 2008
CINAHL	05/03/2008	1982 to February Week 4 2008
British Library Inside Conferences	05/03/2008	-
NRR	05/03/2008	-
Controlled Trials Registry	05/03/2008	-

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in other databases.

The search strategy was adapted for use in the databases above

1. Electric Stimulation Therapy/
2. Electric Stimulation/
3. Transcutaneous Electric Nerve Stimulation/
4. ((function$ or neuromuscul$ or peripheral$ or transcutan$ or electric$) adj3 stimulat$).tw.
5. (FES or TENS or NMES or FNS).tw.
6. or/1-5
7. exp Gait Disorders, Neurologic/
8. exp Gait/

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9. gait$.tw.
10. (foot adj3 drop$).tw.
11. (foot adj3 spastic$).tw.
12. or/7-11
13. 7 and 12
14. Animals
15. Humans
16. 14 not (14 and 15)
17. 13 not 16