A clinical study using implantable microstimulators to facilitate recovery of upper limb function in hemiparesis: preliminary therapeutic outcomes


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Abstract
Patients with post-stroke hemiparesis may have impaired upper limb function related to loss of motor control, weakness and spasticity. Surface electrical stimulation has been shown to improve function but implanted systems may provide finer control over functional movement. In this feasibility study, between five and seven microstimulators were implanted into the arms and forearms of seven chronic state post-stroke participants, who then underwent 12 weeks of exercise with stimulation. A voluntary controlled system was then designed and participants used this for a further 12 weeks unsupervised at home. Results are presented for the first 12 weeks (N=7) in terms of mean (SD) and % changes in ARAT 4.9 (7.89) 21% and Target tracking 57.3 (48.65) 70%. A detailed case study of one participant over the whole study is presented and reasons for variation in response among participants are discussed.

1. INTRODUCTION
The percentage of people in England aged over 65 will increase from 16% in 2003 to 23% in 2031 creating an increased burden on health care and rehabilitation resources. The cost of stroke care in Europe for example is predicted to rise in real terms by 30% between 1991 and 2010. Similar changes are occurring throughout the western world. This rate of increase assumes that dependency rates, patterns of care and current funding arrangements remain unchanged. If the capacity of health services is to meet future demand we need to develop novel approaches to rehabilitation. Embracing rehabilitation technologies aimed at improving recovery of upper limb motor control and function that allow rehabilitation to be undertaken at home with minimal supervision has the potential not only to reduce cost but also to add benefit, both by increasing the intensity of therapy and by shifting the emphasis of responsibility for good health from healthcare care professional to patient.

Approximately 75% of middle cerebral artery infarcts result in a motor deficit, particularly of the upper limb and 24% of patients have residual upper limb motor loss at three months post-stroke. Various longitudinal studies have investigated the long-term outcome following stroke: Kwakkel in his review quotes that for 30 to 60% of patients, the paretic arm remains without function and Wade that half of all acute stroke patients starting rehabilitation will have a marked impairment of function of one arm, of whom only about 14% will regain useful upper limb function. Upper limb function is clearly a major problem and the objective of this project is to develop a system that enables stroke patients to practise functional activities intensively at home using implanted radio-frequency controlled microstimulators (RFMs), that remove some of the problems associated with surface stimulation, such as accurate placement of electrodes, and may provide finer control of muscle activation and thus more functional movement. This paper presents the results of the first phase of the study. A detailed case study of one patient is presented and reasons for variation in response are discussed.

2. METHODS
2.1 Study Design
The study was in three phases: during the first phase we implanted between five and seven devices in the arms of seven post-stroke...
hemiparetic participants to facilitate elbow, wrist, finger and thumb extension, and thumb abduction. We designed open-loop function-based programmes that participants used at home for approximately two hours per day.

2.2 The microstimulator
The RF microstimulators (RFMs), (Figure 1) used in the study were developed by the Alfred Mann Foundation. They are injectable cylindrical microstimulators. RFMs are implanted through a small incision (5mm) under local anaesthesia using specially designed insertion tools. Devices are positioned either adjacent to a peripheral nerve or close to a motor point within a muscle. Risks associated with open surgical procedures and the presence of leads within the body is thus reduced. Each device is individually addressed, allowing control over timing, rise and fall times, amplitude and pulse width of stimulation. RFMs receive power supply and control signals from a control unit via an inductance coil. Stimulation parameters, set by a PC-based fitting system, respond to triggers issued by sensors.

2.3 Implantation and control
Two devices were implanted close to radial nerve branches to the medial and lateral heads of triceps (MHT and LHT) for elbow extension and either one or two devices close to the posterior interosseous nerve (PIN) to open the thumb and fingers. Wrist extension was activated by two devices close to the motor points of extensor carpi ulnaris and extensor carpi radialis longus (ECU and ECRL).

Following implantation, participants used the Phase 1 open loop system (Figure 2). Individualised programmes were set up in the laboratory using custom made software developed with input from the clinical team. Specific functional tasks were identified for each participant and the therapist determined which devices were activated, the required stimulation parameters and timing of each. A series of activity sequences was thus linked to form a functional programme. Once satisfactory programmes were established, participants were able to take the system home and practise between one and two hours per day. Phase 1 lasted for 12 weeks.

During Phase 2 a system for allowing voluntary control of stimulation was designed for each participant, using a force sensor embedded in a mat, a goniometer at the elbow and a ‘push-button’ to initiate the programme. During Phase 3 the system was used independently at home without support from the research team.

2.4 Outcome measures
The main functional outcome measure was the Action Research Arm Test (ARAT). Impairment measures included the Fugl-Meyer (FM) (upper limb section) and measures recorded in a validated instrumented wrist rig which included response to sinusoidal passive stretch at 1.5Hz through 60 degrees – Stretch Index (SI) and ability to track a target moving horizontally at 0.5Hz - tracking Index (TI). Outcome measures were applied at two pre-implantation baseline assessments, at the end of phase 1 (12 weeks post-implantation) and before and after Phase 3 (when the voluntary activated system was used at home).

3. RESULTS
All seven participants, accepted into the study, underwent implantation. Mean age was 50 years and ranged from 32 to 67 years. Three were females and four were males. All participants had suffered an ischaemic stroke ranging from 1.1 to 10.5 years, mean 3.9 years, prior to recruitment to the study; three had a left hemiparesis and four a right. Table1 shows the Normal (SD) values and mean (SD) values for the primary function (Action Research Arm Test [ARAT]) and impairment (Motor control measured by the Tracking Index [TI]) measures at baseline and 12 weeks. Changes are presented in absolute and percentage terms.
Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Normal (SD)</th>
<th>Baseline (SD)</th>
<th>12 weeks (SD)</th>
<th>Change (SD) [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARAT</td>
<td>57 (0)</td>
<td>23.0 (12.7)</td>
<td>27.9 (12.4)</td>
<td>4.9 (7.9)</td>
</tr>
<tr>
<td>TI</td>
<td>192.6 (10.9)</td>
<td>82.0 (49.2)</td>
<td>14.4 - 161.0</td>
<td>57.3 (48.7)</td>
</tr>
</tbody>
</table>

Table 2 shows the results for participant #2 in more detail. This participant has completed all phases of the study and at the end of phase 1 was the second-best responder in the sample. This participant was a male aged 58 with a right sided hemiparesis that occurred 1.4 years prior to recruitment.

Table 2. Values for outcome measures at each stage of the study

<table>
<thead>
<tr>
<th></th>
<th>Baseline 1</th>
<th>Baseline 2</th>
<th>End Phase 1</th>
<th>Start Phase 3</th>
<th>End Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARAT</td>
<td>9</td>
<td>8</td>
<td>17</td>
<td>27</td>
<td>38</td>
</tr>
<tr>
<td>FM*</td>
<td>27</td>
<td>29</td>
<td>37</td>
<td>36</td>
<td>42</td>
</tr>
<tr>
<td>TI</td>
<td>26.0</td>
<td>61.5</td>
<td>146.3</td>
<td>129.5</td>
<td>171.9</td>
</tr>
<tr>
<td>SI**</td>
<td>3.03</td>
<td>9.01</td>
<td>0.37</td>
<td>1.03</td>
<td>2.31</td>
</tr>
</tbody>
</table>

*FM = Fugl-Meyer (upper limb section) **SI = Stretch index (higher values = increased stretch response, Normal value = 0.36 [SD 0.4]).

4. DISCUSSION AND CONCLUSIONS

The potential advantage of the Phase 3 system is that it not only allows voluntary activation of stimulation, so that it is activated on demand by the user, but also allows a greater functionality by responding without further intervention by the user to the speed of the activity.

Although there was a mean improvement in all outcome measures and all participants made some improvement, response was very varied. With such a small sample it is not possible to make generalisations, but participants #2, #3 and #6 who were the only participants who were < 2 years post-stroke, (1.4 and 1.1 and 1.7 years respectively) all had above average improvement in ARAT at 12 weeks (9, 19 and 10 points respectively). There is also a possibility that, in lower functioning participants, impairment may improve without concomitant improvement in function. Participant #7 who had the lowest baseline Tracking Index (14.1) and ARAT score (7) had no improvement in ARAT at 12 weeks, yet had the greatest improvement in TI to 124.1, representing an increase of 109.7.

Based on these preliminary findings we suggest that the use of microstimulators may be an effective and acceptable technology for recovery of upper limb function following stroke. Further investigation is needed to identify which patients are most likely to benefit, but early intervention may be a factor. The single case of a good responder showed enhanced improvement in function during Phase 3 when the system included voluntary activation and control.

References

(2) Truelson et al. Stroke in Europe: Estimating the current and future stroke burden. 14th European Stroke Conference. 1-5-2005. Ref Type: Journal (Full)

Acknowledgements

The Alfred Mann Foundation who supported this work, the patients who are involved in the study and colleagues at the University of Southampton who have provided engineering and technical support, especially Martin Warner and Dr Scott Notley.