Post-stroke Arm Rehabilitation using 5-7 Implanted Microstimulators: Implantation Procedures, Safety and Efficacy.

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Abstract

Seven Participants with post-stroke arm weakness and spasticity were chosen and agreed to have 5-7 Radio-frequency Microstimulators (RFM) implanted on radial nerve branches and then to undergo programmed electrical stimulation to extend the elbow, wrist and fingers. Their stroke had occurred at a mean of 3.9yrs (1.1 to 10.5yr.); 4 males and 3 females, mean age: 49yrs(32-62yrs).

The first subject’s implantation was in April 2005 and the seventh in March 2006. Pre-operatively, implantation sites were identified by needle EMG. Under local anesthesia, using 5mm incisions, the targeted nerve/motor-points (N/MP) were identified using an inserted probe with stimulation, and then an RFM was inserted using an introducer and ejection tools. RFMs with an attached suture could be retrieved during surgery and up to 8 days. Each device receives power and activation commands via a 2 MHz RF inductive link from the 2 externally placed cuff-coils connected to the Control Unit. Initially a total of 41 RFMs (5-7/subject) were implanted. Each surgery session took 3.5 to 6 hrs (av: 4.9 hr). In subject #4, 5 months post-surgery, 2 more RFMs were inserted in the 2 triceps’ sites for elbow extension. Mean thresholds of 2.2 μC/cm2/phase indicate that cathodes were within 1-2mm from their target sites. No RFMs have failed. No infections have occurred.

Introduction

In the USA, 1.69% or 4.6 million people have had strokes, with 1 occurring every minute. 85% of stroke survivors regain the ability to walk but over 80% of those who have arm problems do not regain useful function (Am. Heart Ass.). Typically, there is difficulty reaching with an ineffective grip due to an inability to open the hand and maintain wrist extension during grasping. The aim of this study was to improve recovery of upper limb function by programmed stimulation of individual radial nerve branches using implanted radio-frequency microstimulators (RFM) 1. This study has been on-going and was partially reported at the IFESS 06 meeting.

2. METHODS

2.1. Subjects
Seven subjects have been included with a chronic stroke causing a hemiparesis, with impaired arm and hand function due to poor control and weakness of finger, wrist and elbow extension; and with some voluntary control of finger flexors and proximal arm and shoulder muscles. Their stroke had occurred at a mean of 3.9yrs (1.1 to 10.5yr.) earlier; there were 4 Male and 3 Females, mean age of 49yrs, with a range of 32-62yrs. Subjects have given written informed consent, and the protocol was approved by the Thames Valley multicentre research ethics committee, UK (#04/12/021), and by the Medicines and Healthcare products Regulatory Agency (CI/2004/0027). The study was conducted following guidelines of good clinical practice.

2.2. Microstimulator and Control System
The RF Microstimulator is cylindrical (2.4 mm x 17 mm) with an eyelet attached at the anodal end, to which a dissolvable suture is tied allowing the RFM to be retrieved from the tissues during implantation and up to 7 days post-operatively1,2. The RFM is a single-channel, implantable stimulator that produces capacitively-coupled, charge balanced, asymmetric, biphasic, and constant-current pulses. In each subject, 5 to 7 devices were implanted on nerves/motor-points (N/MP) of radial nerve branches to extend the elbow, wrist and fingers in each subject. For the 7 subjects, a total of 41 devices were inserted; however in subject #4, 2 more RFMs were inserted 5 months later in the medial and lateral triceps’ N/MPs to produce elbow extension.

Once implanted, the devices receive power and stimulation commands via a 2 MHz RF inductive link provided by 2 external cuff-coils, one for the forearm and the other for the upper
arm; both were connected to a Control Unit. The stimulation parameters were set by a laptop based fitting system, and can be programmed to respond to triggers issued by sensors.

2.3. Surgical Implantation Procedure

2.3.1. Target Sites
Each RFM was inserted adjacent to target muscle motor-point/nerve (N/MP) using the surgical insertion tools and techniques developed by the Alfred Mann Foundation (Valencia, CA)\(^1,2\). The upper extremity implantation sites (Table 1) were the N/MPs of each of the medial and lateral triceps muscles (MHT/LHT) for elbow extension, N/MPs of the extensor carpi radialis (ECR) and ulnaris (ECU) for wrist extension, and the posterior interosseous nerve (PIN) which may have 2 branches for finger and thumb extension (ED).

<table>
<thead>
<tr>
<th>Subject #</th>
<th>Upper arm</th>
<th>Forearm</th>
<th>RFMs</th>
<th>Retrieval</th>
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<tr>
<td>1</td>
<td>LHT, MHT,</td>
<td>ECU, ECR, PIN</td>
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<td>0</td>
</tr>
<tr>
<td>2</td>
<td>LHT, MHT,</td>
<td>ECU, ECR, PIN, ED</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>LHT, MHT,</td>
<td>ECU, ECR, PIN, ED</td>
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<tr>
<td>4</td>
<td>LHT, MHT, (R), LHT(R)</td>
<td>ECU, ECR, PIN, ED</td>
<td>7 (+2)</td>
<td>9</td>
</tr>
<tr>
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<td>ECU, ECR, PIN</td>
<td>5</td>
<td>10</td>
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<td></td>
<td></td>
<td></td>
<td>Total: 41(+2R)</td>
<td>29</td>
</tr>
</tbody>
</table>

Table 1

2.3.2. Pre-operative Functions
During the pre-operative week, an EMG study was performed (by C.W.) to identify and mark co-ordinates of the N/MP target sites. At commencement of the implantation procedure, an IV dose of Cefuroxime 1.5 gm was given and an additional dose of 0.75gm was given 6 hours later, before subjects were discharged home. The affected hand, forearm and mid to lower upper arm areas were thoroughly scrubbed with antiseptic solution for 5-7 minutes, then side towels were placed. A plastic drape impregnated with an iodinated antiseptic, was placed over the skin and peripheral sterile towels/drapes.

Prior to implantation, the RFMs were tested, a dissolvable suture was tied to an eyelet attached to the anode, and the devices were stored temporarily in sterile saline solution with antibiotic: colomycin 1,000,000 units in 1 liter.

2.3.3. Insertion Procedure
Local anesthesia was used, 2 subjects required IV Benzodiazepine during the procedure because of discomfort. At 4-7 cm distal on the arm to the target skin marking, a 5mm skin incision was made allowing insertion of a rounded-tip probe (dia: 0.7 mm; Fig.1) which connects with an external pulse generator for stimulating. The target N/MP was identified by which muscle contracts. If correct, the #7Fr. Gauge introducer (outer sheath + dilator; Fig.1) was slid down the probe to be within 2-3 mm from the probe tip.

![Surgical Instruments](image)

Stimulation to the probe was repeated to ensure that the relationship with the N/MP was unchanged. The probe and the dilator were withdrawn; the RFM’s cathode was inserted into the sheath, followed by the ejection tool to gently push the RFM down to where the tip of the cathode protruded from the sheath. The stimulation RF coil was positioned to activate & control the RFM generating a stimulus to the N/MP and contraction of the target muscle. The sheath has small holes in the distal 1/3 of the shaft, when saline/antibiotic solution was injected into the sheath from the ejector tool, the cathodal current from the RFM stimulus can return to its anode inside the sheath. Prior to ejecting the RFM into the tissues, more saline/antibiotic solution was instilled into the sheath and surrounding tissues. The sheath was withdrawn up the shaft of the ejector tool so uncovering the entire length of the RFM in the tissues. Care was taken not to pull on the attached sutures emerging from the skin opening. Further RF coil testing ensured that the muscle response activated the desired movement. If movement was acceptable, the skin incision was pressed down and the sutures were cut-off at skin level, the skin pressure was released and the suture ends were now lying below the subcutaneous tissue, available to be
withdrawn during the next 8 days before encapsulation occurred. If the muscle response was inadequate the emerging sutures were gently pulled while stimulation was maintained; this gave a chance that the muscle response could improve with this retrograde withdrawal. If this manoeuvre was not successful then the probe and RFM was reinserted.

### 2.3.4. RFM Retrievals

Of the 41 RFMs inserted, 5 of the 7 subjects required 29 retrievals of the RFMs by suture withdrawals due to the insertions not producing an adequate target muscle response (Table 1). The most difficult N/MPs to target were for the Triceps muscles, especially the medial head which required 8 retrievals in 5 subjects.

Once devices were inserted in positions that elicited acceptable motor responses, motor thresholds were measured, the incision was irrigated with antibiotic saline, and the skin was closed. Final verification of the device placement was done with the 2 RF cuff-coils positioned over the upper arm and forearm.

### 3. RESULTS

#### 3.1.1. Implant Time

The completed implantations in the 7 subjects took an average of 4.9 hours (3.5 to 6 hrs). The forearm insertions with 3/4 devices/subject averaged 40.7 min/device, while in the upper arm (2 devices / subject) was 50.9 min/device. Subjects were given a prescription for a 10 day supply of Cefalexin 250mg 3/day. Radiological films were taken after each surgery. After surgery, the subjects were followed up at 7 days, then 15, 30, 60 and 90 days post surgery. Stitches were removed at 15 days. During each follow up session, implant sites were examined, operation of each device was verified, and motor threshold was measured.

#### 3.2.1 Adverse Events

With 43 devices implanted, there have been no serious adverse events. No sign of infection or allergic reaction has been observed. Those subjects, who expected, did experience surgical pain on VAS (0-10) ranging from 1.3-7.5 (mean: 4.8 SD+/-2.7). Paracetamol was sufficient to resolve the pain. Minor post-operative adverse events included moderate pain in 2 subjects for 1 week and in 1 subject for 4 weeks.

Three subjects showed signs of swelling in the forearm for 2 weeks after surgery; 2 showed mild tenderness over 1 implant site and 1 showed moderate bruising. One subject had a small amount of bleeding at 1 implant site after 1 week, which required early dressing change. One subject reported digestive problems associated with antibiotics after 1 week.

#### 3.2.2. RFM Thresholds

Forty of the initial 41 implanted RFMs remained stable over the first 90 days, allowing for test–retest repeatability. At 3 months, the mean charge density at threshold was 2.2 µC/cm²/phase, and at the 90th percentile of thresholds had charge density of 7.8 µC/cm²/ph which was 1.1% of the maximum output of the RFMs. In subject #4, at 5 month after the initial implantation, 2 new RFMs were inserted, one on the N/M-P of the MHT and one on the LHT producing satisfactory contractions of the triceps to extend the elbow. The ability to obtain mean thresholds of 2.2µC/cm²/ph indicates, from our sheep studies, that the RFM cathodes were probably within 1-2mm of their target sites.

### 4. CONCLUSION

From this pilot study of 7 post-stroke subjects, it has been possible with pre-operative EMG studies, specially developed insertion tools and local anesthesia, to safely and effectively implant 5-7 RFMs per subject onto targeted branches or motor-points of the radial nerve with no failure of the RFMs. There were only minor temporary post-implantation side effects. Only one RFM moved sufficiently to need a further 2 RFMs inserted to reproduce effective elbow extension. Phase 1 rehabilitation results are presented at this meeting (Burridge et al.).

### References

