# Evolution of Neuroprosthetic Approaches to Restoration of Upper Extremity Function in Spinal Cord Injury

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**Background:** Spinal cord injury (SCI) occurring at the cervical levels can result in significantly impaired arm and hand function. People with cervical-level SCI desire improved use of their arms and hands, anticipating that regained function will result in improved independence and ultimately improved quality of life. Neuroprostheses provide the most promising method for significant gain in hand and arm function for persons with cervical-level SCI. Neuroprostheses utilize small electrical currents to activate peripheral motor nerves, resulting in controlled contraction of paralyzed muscles. **Methods:** A myoelectrically-controlled neuroprosthesis was evaluated in 15 arms in 13 individuals with cervical-level SCI. All individuals had motor level C5 or C6 tetraplegia. **Results:** This study demonstrates that an implanted neuroprosthesis utilizing myoelectric signal (MES)–controlled stimulation allows considerable flexibility in the control algorithms that can be utilized for a variety of arm and hand functions. Improved active range of motion, grip strength, and the ability to pick up and release objects were improved in all arms tested. Adverse events were few and were consistent with the experience with similar active implantable devices. **Conclusion:** For individuals with cervical SCI who are highly motivated, implanted neuroprostheses provide the opportunity to gain arm and hand function that cannot be gained through the use of orthotics or surgical intervention alone. Upper extremity neuroprostheses have been shown to provide increased function and independence for persons with cervical-level SCI. **Key words:** *functional electrical stimulation, myoelectric control, neuroprosthesis, spinal cord injury, upper extremity function*



Spinal cord injury (SCI) occurring at the cervical levels can result in significantly impaired arm and hand function. Traditionally, rehabilitation has focused on restoring function through conservative measures such as strengthening and exercise, splinting and orthotics, and adaptive equipment to facilitate increased independence in performing activities of daily living. After maximizing these conservative interventions, many individuals with tetraplegia seek additional options to improve hand function, such as surgical reconstructive procedures. People with cervical-level SCI desire improved use of their arms and hands, believing that regained function will result in improved quality of life.[1-3] The most common type of reconstructive surgery for restoring upper extremity function in people with tetraplegia is a tendon transfer. A tendon transfer is a surgical procedure in which the tendon insertion of a redundant voluntary muscle is detached and sewn into that of a paralyzed muscle.[4,5] In addition, there has been recent attention to the feasibility of using microsurgical nerve transfers to restore function after cervical SCI, which can potentially complement existing methods for restoring function.[5,6] Despite these surgical alternatives, there is still significant need for improved hand and arm function in SCI.

Neuroprostheses provide the most promising method for significant gain in arm and hand function in persons with cervical-level SCI. Neuroprostheses utilize small electrical currents to activate peripheral motor nerves, resulting in controlled contraction of paralyzed muscles for a desired activity. The fundamental aspects of electrical activation of nerves are well understood, and the safe levels of stimulation for long-term use have been established.[7] Muscle contractions

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can be orchestrated to produce coordinated grasp opening and closing; thumb opening, closing, and positioning; wrist extension/flexion; forearm pronation; and elbow extension for individuals with C5 and C6 neurological level of injury. The individual controls the desired activity through the electrical activation of paralyzed muscle through recorded myoelectric signals from retained voluntary muscle activation. Neuroprostheses can be coupled with tendon transfers in order to maximize function.[8] The objectives of neuroprostheses are to reduce the need of individuals to rely on assistance from others, reduce the need for adaptive equipment, reduce the need to wear braces or other orthotic devices, and reduce the time it takes to perform tasks. Typically, patients use the neuroprosthesis for such tasks as eating, drinking, personal hygiene, writing, and office tasks.

The first upper extremity neuroprosthesis was implanted in a human subject in 1986.[9] Early neuroprostheses required donning external components to operate the system.[10] Results of the first clinical trial have been previously published by Peckham and colleagues.[11-17] A second-generation neuroprosthesis internalized the control source using myoelectric recording electrodes to capture voluntary signals to control opening and closing of the hand.[18-21] In addition to implanting the control source, this system provided four additional channels of stimulation to refine additional functional activities. This article summarizes the results of a clinical study of this second-generation neuroprosthesis and compares the implementation strategy and outcomes with the first-generation system. The results of the first three subjects implanted with the second-generation device were previously published[19] and are included in the complete cohort data presented in this article.

## Methods

### Neuroprosthesis design

The IST-12 neuroprosthesis has the potential to provide grasp and release, forearm control, and elbow extension for individuals with cervical-level SCI. The system consists of an implanted stimulator-telemeter (IST) with the capacity to stimulate 12 paralyzed muscles and to record the myoelectric signals (MES) from two muscles under voluntary control (see ref. 19 for design details). The most novel feature of the IST-12 neuroprosthesis compared to the earlier eight-channel design[11] is the elimination of the external control source. This is achieved through the use of implanted MES recording electrodes and MES processing circuitry in the implanted device. The system is driven from an external power and processing unit, which is connected to a coil that the participant places on the skin over the implanted device.

An important aspect of the myoelectric recording circuit design in the IST-12 is the ability to record MES in the presence of the large stimulus artifacts produced by 12 stimulating electrodes.[22] The stimulation pulses used to activate paralyzed muscle normally will saturate MES amplifiers so that the ability to record a usable signal is lost.[18,20] Therefore, it is necessary to remove the stimulus artifact from the MES recording. This was accomplished by implementing several design features. First, all stimulus pulses are grouped together at the beginning of each stimulus period so that their artifact is not spread throughout the stimulation sequence. Second, during the MES integration window, the stimulating electrode recharge current path is disconnected. Third, the MES integrator is enabled only during the MES window. Fourth, outside the MES window, the variable gain is set to the minimum value. Fifth, during stimulation, the front-end multiplexer entirely disconnects the MES processor from the MES electrodes. In vivo studies in animals demonstrated the ability of this processing to eliminate stimulus artifact even when the recording electrodes are within a few centimeters of the stimulating electrode.[20]

The myoelectric signal is rectified, filtered, and integrated within the IST-12 device. The value of the integrated signal is sampled at the end of the integrating window, and the data are transmitted to the external controller. The IST-12 has four programmable amplifier gains, from 200 to 4000, which can be controlled on a sample by sample basis.

**Participant selection criteria**

Candidates considered for implantation included individuals with cervical SCI. Subjects had International Standards for Neurological Classification of SCI (ISNCSCI) motor score at the C5 or C6 and were classified as American Spinal Injury Association Impairment Scale (AIS) group A or B (motor complete).[23] Based on the International Classification for Surgery of the Hand in Tetraplegia (ICSHT), subjects were classified as group O/Cu:0 through O/Cu:3.[24] Candidates were required to be in generally good health, have minimal upper extremity contractures, be medically stable, have electrically excitable muscles,[25] and have good social support.

**Testing timeframe**

Functional testing was performed at key points in time throughout the study. Baseline measurements were made prior to surgery, generally within a month prior to the surgery date. Testing was repeated at approximately 3 months after surgery, upon completion of rehabilitation period of training in use of the neuroprosthesis.

**Outcome measures**

The goal of this study was to demonstrate that the use of MES-controlled grasp function can be achieved in a fully implanted neuroprosthesis. Outcome measures presented in this paper focused on the domain of body function and structures (BFS) as identified by the World Health Organization's (WHO) International Classification of Function (ICF).[26] Specific outcome measures include grip strength, range of motion, and a basic test of grasp function (the Grasp and Release Test [GRT]).

*Stimulated range of motion*

Range of motion of the hand and arm was measured according to standard occupational therapy techniques using a hand-held goniometer.[27] Finger and thumb range of motion was measured with the wrist splinted in neutral. Finger extension and flexion was measured using stimulation parameters in each subject's palmar grasp pattern. Thumb extension and flexion was measured using stimulation parameters in each subject's lateral grasp pattern.

*Grasp strength*

Grasp strength was measured using a standard B&L (Model PG30; B&L Engineering, Tustin, CA) pinch meter that was modified with an "L"-shaped extension to better accommodate the tetraplegic hand. This extension increased the sensitivity of the device, and measured units are converted based on a calibration factor as a result of the extension.[11] Strength was measured for both lateral and palmar prehension. Measurements were made prior to implantation and approximately 3 months post implantation. Postsurgery measurements were made with the neuroprosthesis turned on and off.

*Grasp and Release Test*

The GRT was developed by the Cleveland FES Center to detect changes in hand function after implantation of an upper extremity neuroprosthesis.[28] This pick-and-place test requires the participant to unilaterally acquire, move, and release six objects varying in weight and size. Three of the objects require use of a lateral grasp; the other three require palmar grasp. The participant completes a pretest to determine how many of the six objects can be successfully grasped, moved, and released. A main test follows to measure number of repetitions achieved in three 30-second trials for each object that was successfully passed in the pretest. The psychometric properties of the GRT were further established by Mulcahey and colleagues.[29] The GRT was administered prior to surgery and 3 months post surgery. Postsurgery tests are conducted with the neuroprosthesis on and off.

**Statistical analyses**

Differences in grasp strength and range of motion were analyzed using paired *t* tests. The proportion of subjects who were able to increase the number of objects they could manipulate in

the GRT was compared to the proportion without the neuroprosthesis using the Wilcoxon rank-sum test.

## Results

Fifteen arms in 12 individuals with motor level C5 or C6 tetraplegia were implanted with the IST-12 device and evaluated, as detailed in **Table 1**. In this cohort, a total of 16 IST-12 devices were implanted, with most individuals receiving one device to provide function in one arm. However, three individuals received bilateral function (a device for each arm) and one individual received two devices to provide function in the upper arm and shoulder as well as the hand. Two of the 12 participants were female. Average age at implantation was 37 years (range, 26-56). Average time from injury to implantation was 5.5 years (range, 1-21).

### Reconstructive procedures

All of the participants except for one had voluntary upper extremity reconstructive procedures to augment function provided by the implanted neuroprosthesis, as shown in **Table 1**. Almost half of these participants underwent surgical reconstruction and postoperative training prior to neuroprosthesis implantation, while the

**Table 1.** Study cohort demographic summary.

| Participant | Sex | COI | Age at implantation, years | Motor level of injury[a] | | Time from injury to implant, years | Prior[b] | Voluntary reconstructive procedures |
|---|---|---|---|---|---|---|---|---|
| | | | | Right | Left | | | |
| A | M | Swimming | 26 | ***C5 (O:0)*** | C4 | 2 | | None |
| B | M | Fall | 39 | ***C5 (O:0)*** | C5 (O:0) | 9 | X | Bi-Tri, Br-ECRB |
| C | M | MVA | 28 | C5 (O:1) | ***C5 (O:1)*** | 2 | | Bi-Tri, Br-ECRB |
| D | M | Diving | 43 | ***C5 (O:1)*** | C5 (O:1) | 21 | | Br-ECRB |
| E[c] | M | MVA | 35 | ***C5 (O:1)*** | C6 (O:1) | 11 | X | PD-Tri, Br-ECRB, FPL split |
| F-R | M | MVA | 27 | ***C5 (O:1)*** | C6 (O:2) | 3 | | PD-Tri, Br-ECRB |
| F-L | M | MVA | 27 | C5 (O:1) | ***C6 (O:2)*** | 3 | | PD-Tri, Br-FPL |
| G | M | MVA | 38 | ***C6 (O:2)*** | C5 (O:1) | 5 | | Br-FPL, FPL split |
| H | M | Surgery | 56 | ***C6 (O:2)*** | C6 (O:2) | 4 | | Bi-Tri, Br-FPL |
| I-R | M | MVA | 37 | ***C6 (O:2)*** | C6 (O:2) | 3 | X | PD-Tri, Br-FPL, FPL split |
| I-L | M | MVA | 38 | C6 (O:2) | ***C6 (O:2)*** | 4 | | PD-Tri |
| J-L | F | MVA | 44 | C6 (O:2) | ***C6 (Cu:2)*** | 1 | | PD-Tri, Br-FPL, FPL split, small finger PIP pinning |
| J-R | F | MVA | 45 | ***C6 (O:2)*** | C6 (Cu:2) | 2 | | PD-Tri, Br-FPL, FPL Split |
| K | F | MVA | 30 | C6 (O:2) | ***C6 (O:3)*** | 2 | X | PD-Tri, Br-FPL, thumb IP fusion |
| L | M | MVA | 42 | C6 (Cu:3) | ***C6 (Cu:3)*** | 10 | X | Wrist fusion, ECRL-FDP, ECRL-FPL, Br-EDC |
| | | **Average** | **37.0** | | | **5.5** | | |

*Note:* Bi-Tri = biceps-triceps (dash indicates tendon transfer); Br-ECRB = brachioradialis (Br)-extensor carpi radialis brevis; Br-EDC= Br-extensor digitorum communis; Br-FPL= Br-flexor pollicis longus (FPL); COI = cause of injury; ECRL-FDP = extensor carpi radialis longus (ECRL)-flexor digitorum profundus; IP = interphalangeal; MVA = motor vehicle accident; PD-Tri = posterior deltoid-Tri; PIP = proximal interphalangeal joint.

[a]Bold italic denotes arm implanted. International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI)[36] motor score listed first, and the International Classification for Surgery of the Hand in Tetraplegia (ICSHT)[24] listed in parentheses.

[b]Procedures performed prior to study entry.

[c]Subject upgraded from a prior Freehand System.

remaining participants underwent the surgical reconstruction in the same procedure as the neuroprosthesis implantation. The most common procedure was a transfer of the posterior deltoid or biceps into triceps to provide elbow extension, followed by brachioradialis (Br) transferred to either extensor carpi radialis brevis (ECRB) or flexor pollicis longus (FPL) for wrist extension or thumb pinch, respectively. The single individual who did not receive voluntary reconstructive procedures was not a candidate for them due to lack of voluntary donor muscles (ISNCSCI C5, ICSHT Group 0).

In order to evaluate the evolution of the extent and types of surgical procedures performed in the 15 IST-12 arms, we compared the procedures performed with the first 15 Freehand subjects implanted at our site. This data are summarized in **Table 2**, and they indicate significant changes over time despite that fact that the distribution in the level of injury is similar between the two groups. In the Freehand cohort, multiple synchronization procedures were performed in the extrinsic finger muscles in an attempt to gain synchronous flexion and extension of the digits, whereas the IST-12 cohort had none of these procedures. Six subjects in the Freehand cohort had a thumb interphalangeal (IP) joint arthrodesis, but this was generally abandoned in favor of an FPL split tendon transfer in which one slip of the distal FPL tendon is transferred to the insertion of the EPL, providing IP joint stability when the FPL muscle is activated while still allowing IP joint flexibility in the passive condition. Other procedures performed to correct finger posture deformities, such as the flexor digitorum superficialis (FDS) Zancolli lasso and the FDS instrinsicplasty procedures, were performed in the Freehand cohort but not in the IST-12 cohort. Finally, transfer of the voluntary (not paralyzed) Br to provide thumb flexion was performed in nearly half of the IST-12 cohort, whereas it had not been performed previously in any of the Freehand cohort.

**Table 2.** Surgical procedure comparison

| Description | Freehand (*n*=15) | IST-12 (*n*=15) | Change (IST – Freehand) |
|---|---|---|---|
| Group 0 | 2 | 2 | 0 |
| Group 1 | 6 | 4 | -2 |
| Group 2 | 6 | 7 | 1 |
| Group 3+ | 1 | 2 | 1 |
| **Total** | **15** | **15** | **0** |
| Finger tendon synchronization | 24 | 0 | -24 |
| Thumb IP arthrodesis | 6 | 1 | -5 |
| FPL split transfer | 4 | 6 | 2 |
| FDS Zancolli lasso | 3 | 0 | -3 |
| FDS intrinsicplasty | 1 | 0 | -1 |
| FES+TT | 12 | 8 | -4 |
| Rotational osteotomy | 2 | 0 | -2 |
| PD->Tri | 11 | 8 | -3 |
| Bi->Tri | 3 | 3 | 0 |
| Br->ECRB | 8 | 5 | -3 |
| BR->FPL | 0 | 7 | 7 |
| **Total** | **74** | **38** | **-36** |

*Note:* IP = interphalangeal joint; FPL = flexor pollicis longus; FDS = flexor digitorum superficialis; FES+TT = functional electrical stimulation of a tendon transferred muscle; PD->Tri = posterior deltoid to triceps tendon transfer; Bi->Tri = biceps to triceps tendon transfer; Br->ECRB = brachioradialis to extensor carpi radialis brevis tendon transfer; Br->FPL = brachioradialis to flexor pollicis longus tendon transfer.

### Electrode placement and movement patterns provided

The eTable (supplemental digital content) shows the muscles that have been implanted with stimulating and recording electrodes. Each system was customized to the participant's physiological characteristics and functional goals. Each implanted device activates 12 muscles and records MES from two voluntary muscles. As such, individuals with one unilateral device have 12 paralyzed muscles activated and use two muscles where voluntary function is retained to control the function of the arm. The bilateral participants have this same distribution in each arm, and the one participant with two devices to activate one arm has 24 paralyzed muscles activated in the hand, arm, and shoulder.

The Freehand System could activate eight muscles, and thus the IST-12 allowed activation

of four additional muscles. In 13/15 arms, two of these additional electrodes were placed in the finger intrinsic muscles to provide improved finger IP extension and metacarpophalangeal (MCP) flexion. The remaining two electrodes were generally placed in muscles that provided specific functions consistent with the goals and physiology of each subject. This allowed the majority (8/15) arms to gain triceps activation and 6/15 arms to gain wrist flexion via the palmaris longus (PL). Additional functions provided included forearm pronation and shoulder stabilization. In 4/15 subjects, multiple electrodes were placed in the extrinsic finger flexors and/or extensors.

### Control

All but one of the IST-12 participants controlled hand opening and closing proportionally through activation of wrist extension. Voluntary wrist extension was achieved through activation of the extensor carpi radialis longus (ECRL) or through tendon transfer of Br to the extensor carpi radialis brevis (ECRB). In the latter case, the recording electrode was placed on the Br muscle. The second recording electrode of each system was typically reserved as a logic source or a way to activate certain features of the system such as change grasp patterns.[19] The muscles most commonly reserved for this function included the platysma and the trapezius. These muscles could also be used for proportional control of grasp if the wrist extensor was too weak to provide a reliable signal. The participant with two implanted devices for unilateral function also had recording electrodes placed on his middle deltoid and biceps for control of arm and trunk function.

### Motor patterns

All IST-12 participants were provided with lateral and palmar hand grasp patterns, as described elsewhere.[30] Additional grasp patterns were provided that were customized to specific functional needs of the user and included a "sandwich" grasp (light palmar pinch with finger IP joints extended), pointer grasp (index finger extension, other fingers flexed), "cashew" (fine index finger and thumb tip pinch), and grasps designed for use of cell phones.

Elbow extension was provided by electrical stimulation of the triceps muscle, often in combination with a tendon transfer (the triceps tendon is *not* disconnected when the tendon transfer is performed). Forearm pronation was provided by stimulation of the pronator quadratus (PQ). Both elbow extension and forearm pronation is controlled through voluntary activation of the antagonist muscles.[31,32] In some cases, separate grasp patterns are provided with these functions (eg, lateral grasp without elbow extension and lateral grasp with elbow extension). Stimulation of pectoralis (Pec), supraspinatus (SS), and rhomboids was performed to provide shoulder stabilization during reaching movements.

### Range of motion

Stimulation produced active extension and flexion for all five digits in all 15 arms studied. As shown in **Figure 1**, the median total range of motion for the fingers varied from 105° for the long finger to 41° for the small finger. The median range of motion for the thumb was 41°, noting that, for most hands, the thumb IP joint range of motion was limited surgically. No subject had any active movement in their fingers or thumb when the stimulation was turned off.

### Grasp strength

There was a significant difference in grasp strength with the neuroprosthesis turned on compared to off for both lateral and palmar grasp for all 15 arms evaluated in this study ($p < .0001$), as shown in **Figure 2**. Additionally, there was a significant difference in postsurgery strength with the neuroprosthesis turned off compared to presurgery measurements for both lateral ($p = .0043$) and palmar ($p = .0094$) grasps. Three arms displayed mildly decreased strength (less than one-half pound) in lateral grasp post surgery with the neuroprosthesis turned off compared to pre surgery. Similarly, three arms showed mildly decreased (less than one-third pound) palmar grasp post surgery.

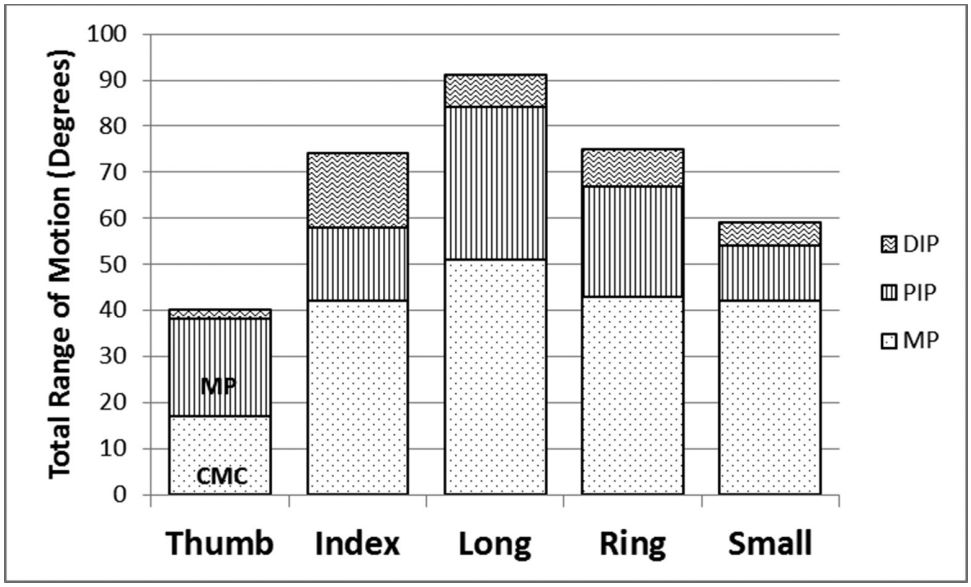


**Figure 1.** Stimulated range of motion for all 15 hands in the study. Each region represents the median joint range of motion obtained in the study. Movement was obtained for the proximal two joints in all digits for all hands. Range was recorded with the wrist splinted in neutral and stimulation of the lateral (thumb range) or palmar (finger range) pinch. CMC = carpometacarpal joint; DIP = distal interphalangeal joint; MP = metacarpal phalangeal joint; PIP = proximal interphalangeal joint.

The strength data from the IST-12 were compared to strength data collected in the clinical trial for the Freehand System.[11] **Figure 2** shows the comparison of strength from 50 arms with the Freehand System and 15 arms with the IST-12 device. The strength due to the stimulated grasp patterns is similar for either generation, whereas the IST-12 cohort had significantly stronger lateral and palmar strength prior to intervention and after surgical intervention with the stimulation turned off.

#### Grasp and Release Test

**Figure 3** shows the number of objects each person in the IST-12 study was able to successfully manipulate or "pass" prior to surgery and 3 months post surgery with the neuroprosthesis turned on and off. Out of 15 arms tested, all but one were able to pass at least two objects (92%) of the six possible prior to surgery, and one subject could pass four of the six objects prior to surgery. Three months post surgery, all participants could pass at least five out of the six possible objects with the neuroprosthesis turned on. Eight participants passed all six objects (62%) and five participants passed five of the six objects (38%). The objects most often failed included the two heaviest objects – the weight (three cases) and the tape (two cases). Most of the participants passed the same number of objects post surgery with the neuroprosthesis off compared to pre surgery. However, three of the 13 participants passed one additional object and one of the 13 participants passed two additional objects. Three of the four participants who made improvements also had a voluntary tendon transfer of Br-FPL between the presurgery and postsurgery testing. The other participant had the same tendon transfer prior to study entry. The number of objects passed when participants used the neuroprosthesis exceeded the number passed by the participants with the Br-FPL transfer.

#### Adverse events

The adverse events experienced in this series of subjects are summarized in **Table 3**. In the single case of the stimulator infection, no outward signs of infection were apparent. The subject was undergoing a surgical procedure to reposition

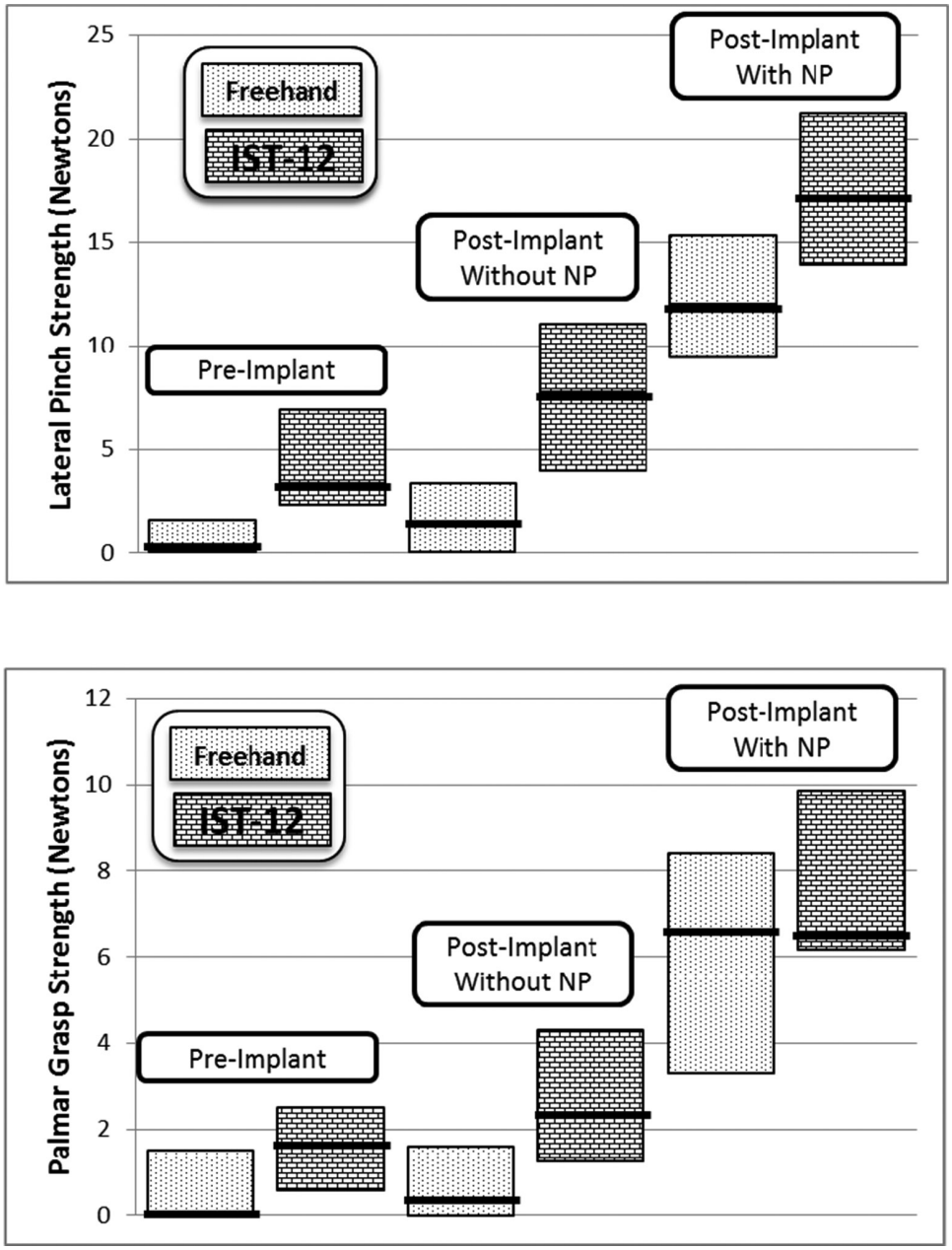


**Figure 2.** Lateral and palmar grasp force obtained for all 15 hands in the IST-12 study, with comparison to the Freehand cohort.[11] Black line indicates the median and the boxes represent the second and third quartiles. Every hand improved in pinch strength with the neuroprosthesis. Pinch strength without the neuroprosthesis is generally due to passive tenodesis grip. NP = neuroprothesis.

the implant. Upon surgical exposure, the tissue capsule around the implant was brownish in color and a culture revealed a low-grade infection. The implant was removed with the proximal portion of the leads distal to the connector site, and the area was allowed to heal. The infection resolved without any further treatment. This subject had experienced a trauma to the implant region secondary to being dropped during a wheelchair transfer on an airplane and experienced significant bruising near the implant. This incident may have contributed to the subsequent infection. The

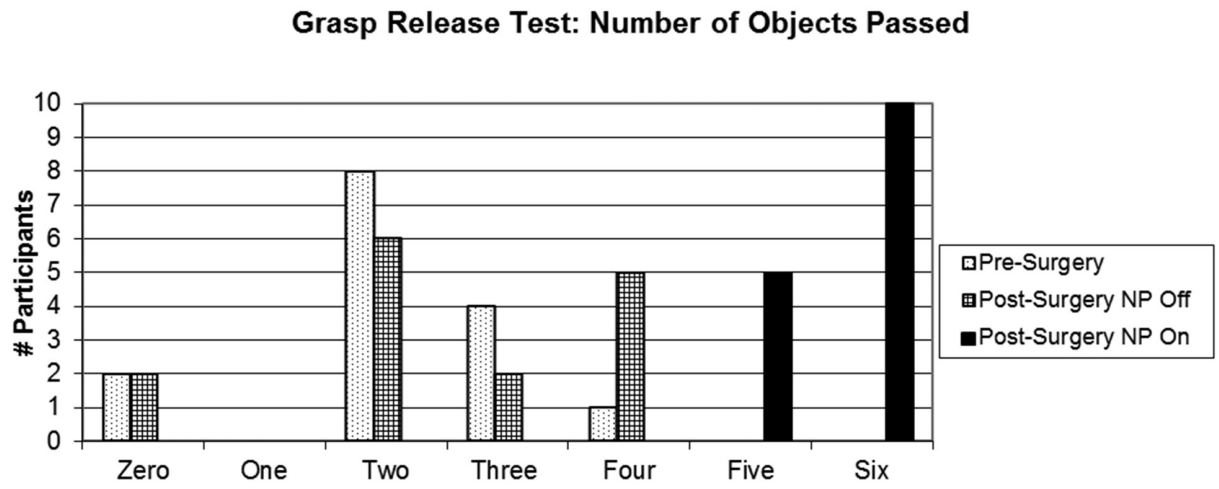


**Figure 3.** Grasp and Release Test results of the 15 IST-12 arms studied. Using the neuroprosthesis (NP), all 15 arms could pass at least five of the six objects, whereas only one hand could pass as many as four objects prior to implantation (or after implantation with the NP turned off).

**Table 3.** Summary of adverse events

| Event | No. of arms |
|---|---|
| Infection requiring device removal | 1 |
| Infection requiring electrode removal | 1 |
| Implant repositioning | 1 |
| Electrode repositioning | 3 |
| Connector repair | 2 |
| Surgical procedure to improve hand posture | 3 |

incident occurred 18 months after the original implantation of the device.

One subject had an episode of cellulitis in his dorsal forearm. The cause for the cellulitis was unknown and, as a precaution, the five electrodes that were positioned in the subject's dorsal forearm were removed, including the leads extending into the upper arm. The infection subsequently resolved. The volar electrodes and implanted stimulator remain implanted in that subject with no further incident. This subject also has an implanted device in the opposite arm, which remained unaffected.

In one subject, the leads exiting the implant appeared to be very superficial as they crossed over the top of the deltoid muscle. Due to concern that one or more of these leads might erode through the skin, a preemptive procedure was performed to re-route the leads more caudally and less superficial. This procedure was performed within 2 months of the initial implant, and no further incident was encountered.

One IST-12 device stopped responding after 3 years. The device has not been removed and the cause of this failure is unknown at this time.

Revision surgeries were performed in eight of the 15 arms, as outlined in **Table 1**. The revision procedures for subjects A, I-R, and J-L have been previously discussed.[19] Three of the eight procedures involved revising either stimulation or recording electrode locations to improve functions, and three involved procedures to refine the passive positioning of the fingers or thumb.

## Discussion

This study confirms the high success rate for neuroprosthetic approaches in the upper extremity. In our cohort of 15 arms across 13 subjects, a useful hand grasp with significantly increased pinch force and range of motion was achieved in every arm with the IST-12 neuroprosthesis. These results match the results obtained with the earlier generation of neuroprosthesis, where 100% of that cohort also achieved increased grip strength.[11] The high success rate is due, in large part, to the fact that subject screening using surface stimulation[25] is a good predictor of functional movements. In addition, the technology has a predictable and well-characterized effect on muscle contraction,

and the coordination of electrical stimulation into purposeful movements is a well-established process.[30] This is in contrast to implanted devices that rely on neuromodulation approaches, where the mechanism of action is not precisely known, such as spinal cord stimulators. These devices tend to have success rates of approximately 50%.[33]

A key improvement in the second-generation neuroprosthesis was the use of an implanted control source, specifically MES. The results of this study demonstrate that implanted MES control in neuroprostheses is a viable and highly desirable option. All subjects were able to control grasp opening and closing proportionally, using one of their MES channels, typically the wrist extensor. It was possible to obtain a usable MES during stimulation in all subjects. Our study also demonstrates that MES can be recorded from implanted recording electrodes during stimulation of nearby muscles. For example, myoelectric signals could be recorded from the ECRL during stimulation of the extensor digitorum communis (EDC) where the stimulating and recording electrodes are within 5 cm of each other.

The use of myoelectric control in neuroprostheses allows considerable flexibility in the control algorithms that can be utilized. In this series of subjects, performance could be improved by customizing the control scheme for each subject. A principal consideration regarding the command control scheme was to make maximal use of muscles with voluntary function. Whenever possible, muscles that are synergists to the function to be provided serve as the control muscle in order to make the control scheme easier to learn. Specifically, in the case of C6 level SCI, the wrist extensors, which are under voluntary control, are direct agonists to grasp closing. Therefore, by using the MES from the wrist extensor to proportionally control grasp closing, a very natural augmentation of the tenodesis function can be achieved. We have previously demonstrated that proportional MES control of grasp provides improved function over other forms of control.[18] All control signals are derived from ipsilateral muscles, thus enabling bilateral function to be provided in the future by implementing the system in the contralateral limb. All three subjects implemented with bilateral systems demonstrated the ability to independently control each arm. These results indicate that implanted myoelectric control is a very desirable option for neuroprostheses. Even if other forms of control can be developed (eg, brain–computer interfaces), MES can provide valuable control options for implanted systems.

The study results indicate that every subject improved significantly in pinch force strength. In all cases, the presurgery pinch force was achieved by passive finger and thumb tone augmented with wrist extension. For most subjects, this pinch force is only useful for acquiring light objects, such as a piece of paper. With the neuroprosthesis turned on, pinch force typically doubled or tripled. Most participants also gained pinch force from a tendon transfer and therefore had stronger pinch force even with the neuroprosthesis off after surgery. A small number of subjects had minor decreases in their postoperative pinch force with the neuroprosthesis off, and this is due to a change in hand posture as a result of exercise from the neuroprosthesis.

As demonstrated by the Freehand study results, stimulation of eight forearm and hand muscles can be sufficient to provide functional grasp patterns. The additional channels provided by the IST-12 system provided enhanced opportunities for function. Pinch force results show a trend toward increased grip strength with the IST-12, but a larger cohort would need to be evaluated to establish this. In some cases, intrinsic muscles have been included to enhance the strength of finger flexion. The addition of elbow extension via triceps stimulation is highly desirable to all subjects. Finally, the opportunity to place multiple electrodes in a single muscle allows for later selection of an electrode that gives the best response, further enhancing the function obtained.

Concomitant surgical interventions are a key component in the implementation of neuroprosthetics for upper extremity function.[8] These include tendon transfers of muscles under voluntary control, providing function even when the neuroprosthesis is off, as well as tendon transfers of paralyzed muscles to enhance the function obtained from the neuroprosthesis. Other surgical procedures are generally targeted to restoring the passive balance of the hand and arm in order to improve grasp function.

The two most common tendons transfers of voluntary muscles are a transfer for elbow extension (using either posterior deltoid [PD] or biceps [Bi]) and transfer of Br to ECRB for subjects with weak or no wrist extension. One of the primary goals of the Freehand trial was to demonstrate the benefit of the neuroprosthesis alone, and therefore subjects in that trial did not receive tendon transfers that would affect finger or thumb function, allowing clear direct assessment of the impact of the neuroprosthesis. However, with this benefit clearly established, we removed this restriction in the IST-12 trial. As a result, in the IST-12 series, 47% of the arms underwent a Br to FPL tendon transfer, which provided a degree of active on pinch even with the neuroprosthesis off. This is demonstrated by the significant increases in pinch force for the IST-12 cohort with the neuroprosthesis off (**Figure 2**). In addition, the voluntary use of the FPL could be coupled with the stimulated grasp, allowing subjects to have finer control of thumb positioning. In these transfers we did not disconnect the FPL tendon and therefore, in most cases, we also placed an electrode on the FPL muscle for stimulation. Thus, the Br was used as a tendon transfer donor in 12 of the 15 arms instrumented.

The most significant change in emphasis with respect to the surgical procedures is the reduction of extrinsic finger tendon synchronizations and procedures to restore passive balance to the intrinsic minus hand. In the Freehand cohort, there were 34 of these procedures performed in the 15 arms, whereas none of these procedures were performed in the IST-12 cohort. With respect to the finger synchronization procedures, the goal was to have all four digits close simultaneously or in a cascade (index first, small last). Performing these procedures at the time of electrode placement often provided less than optimal results. It was difficult to balance the active and passive forces at the time of surgery while also placing electrodes on muscles that were not fully exercised. In addition, the healing process for the tendon transfers complicated the postsurgical electrical stimulation protocol, sometimes resulting in tendon adhesions. In the IST-12 cohort, we opted to place the electrodes without synchronization procedures, conduct a period of conditioning to build muscle strength, enable the subject to use the hand functionally, and then make a determination as to whether a follow-up synchronization procedure was necessary. In practice, such a follow-up procedure was not deemed critical in any of the arms studied. We often focused one of the finger flexor electrodes on the index finger to ensure full flexion of that digit. However, as illustrated by the range of motion data, the IST-12 cohort had less range of motion in the small finger. Thus, if additional channels were available, targeting a muscle such as the abductor digiti minimi might be of benefit.

The additional four electrodes with the IST-12 is one contributing factor to the significant reduction in augmentative procedures. The addition of the finger intrinsic muscle activation reduced the need for procedures such as Zancolli lasso or the FDS intrinsicplasty. These procedures were found to be difficult to properly balance and therefore we proposed that a better approach was to place the electrodes to evaluate the need for any subsequent fine-tuning procedures. In practice, few such procedures were performed and only included a procedure to tighten the extensor slips (ring, small) in one arm and a thumb MP capsulodesis and pinning procedure in another arm.

Joint stabilization procedures have also evolved over time. Based on our experience with earlier percutaneous systems, we found that some form of thumb IP joint stabilization was required in order to achieve strong thumb pinch against small objects. This is primarily due to the strong IP flexion activity of the FPL, which is a key thumb flexor. Force generated by the FPL tends to preferentially produce IP flexion. If the tip of the thumb presses against the lateral aspect of the index finger, this strong IP flexion force will create a gap between the surface of the thumb and the flexed index finger. Small objects placed in such a grip will be relatively unstable as, unless they are placed directly under the thumb tip (generally difficult to maintain), very little of the thumb flexion force is directed through the object. If the IP joint is stabilized in full extension (or slight flexion of ~15 degrees), then the thumb flexion force is transmitted directly through small flat objects and the grip on those objects becomes much more stable. Although it should be, in principle, possible to co-contract the FPL and EPL to balance forces across the IP

joint and maintain the joint in full extension, in practice we found that this could not be reliably achieved with stimulated muscles. Further, such delicate balances of force cannot be maintained throughout the day as muscles fatigue at different rates based on usage and physiological properties. As a result of these considerations, we sought a surgical approach to stabilization of the thumb IP joint. As **Table 2** illustrates, our initial approach was to do a direct thumb IP arthrodesis. This procedure was successful, with no complications in our series, and it was performed routinely. Some subjects were concerned, however, about the loss of movement in that joint. We migrated from this procedure to the FPL split procedure, as described. This has produced the desired results and was performed in 40% of the arms receiving the IST-12 system. In one subject, we subsequently performed an IP arthrodesis because the FPL split transfer stretched out over time and was no longer providing sufficient IP stability. The FPL split is thus a highly recommended procedure for neuroprosthetic upper extremity systems and allows for later IP arthrodesis if necessary.

Infection remains the primary concern with respect to adverse events. Infection requires removal of the infected components. To date, there has not been a case of infection that required removal of the entire system. There was also one case where a revision surgery was performed over concern that a lead was too superficial. These incidents are consistent with the Freehand System experience and with the experience of similar implantable medical devices.[11,34,35]

The durability of the technology was very high. One stimulator stopped working after 3 years. There have been no cases of electrode lead failure in this cohort. Two cases of intermittent connector function were resolved by replacing the connector assembly in a revision procedure.

## Conclusion

Upper extremity neuroprostheses have been shown to provide increased function and independence for cervical level SCI. This study demonstrates that an implanted neuroprosthesis utilizing MES-controlled stimulation allows considerable flexibility in the control algorithms that can be utilized. Improved active range of motion, grip strength, and the ability to pick up and release objects were improved in all arms tested. Adverse events were few and were consistent with the experience with similar active implantable devices. For individuals with cervical SCI who are highly motivated, implanted neuroprostheses provide the opportunity to gain grasp function that cannot be gained through the use of orthotics or surgical intervention alone.

### Conflicts of Interest

The authors declare no conflicts of interest.

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