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Virtual Rehabilitation of Elbow Flexion Following Nerve Transfer Reconstruction for Brachial Plexus Injuries Using the Single-Joint Hybrid Assisted Limb

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Purpose: The upper limb single-joint hybrid assistive limb (HAL), a wearable robot that can support elbow flexion and extension motions, was originally used to rehabilitate patients with stroke. We report the preliminary outcomes of serial HAL use for rehabilitation following nerve transfer (NT) for elbow flexion reconstruction in brachial plexus injuries.

Methods: Hybrid assistive limb training consisted of virtual and power training courses. Virtual training was started before HAL picked up motor unit potentials (MUPs) from the target muscle through electrodes attached to the skin overlying the original donor muscles. Power training was started after the maturation of MUPs, the stage where the MUPs were strong to be recognized to arise from the target muscles. Hybrid assistive limb assist at this stage was carried out by decreasing the settings in an inversely proportionate manner to the increase in target muscle strength. Fourteen patients underwent HAL training following NT. Eight patients had the intercostal nerve to musculocutaneous nerve (ICN-MCN) transfer, and their postoperative functional outcomes and rehabilitation performance were compared to 50 patients with ICN-MCN transfer who underwent conventional postoperative rehabilitation with electromyographic biofeedback (EMG-BF) techniques.

Results: Comparison of the long-term results following ICN-MCN transfer between EMG-BF and HAL groups showed similar follow-up times, elbow flexion range of motion, or power of elbow flexion assessed using the British Medical Council grade, and quantitative measurement using Kin-Com dynamometer. However, the number of rehabilitation sessions was significantly fewer in the HAL than EMG-BF group.

Conclusion: HAL training accelerated patients' learning to convert the original muscle function into elbow flexion following NT by replicating elbow flexion during the pre-MUP detection stage and shortening the rehabilitation time.

Type of study/level of evidence: Therapeutic IV.

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Nerve transfer (NT), including reinnervation of free functioning muscle flaps, is the pillar technique for elbow flexion reconstruction following brachial plexus injury (BPI).¹ Nerve transfer donors may be obtained from an intraplexal or extraplexal nerve, and the

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donor's nerve affects a different motor function from its original function, such as in the intercostal nerve to musculocutaneous nerve (ICN-MCN) transfer.² The ICN-MCN transfer was the preferred choice for elbow flexion reconstruction in total or C5-8 types of BPI because of limitations in alternative NTs such as phrenic NTs with postoperative pulmonary complications and inconsistent recovery results after contralateral C7 root transfer.³⁻⁶

However, outcomes of ICN-MCN transfer cited in the literature varied considerably.⁷⁻¹² Some patients had poor recovery of voluntary elbow flexion, and the main factors attributed included age, time from injury to operation, and surgical technique.

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Postoperative rehabilitation was also an important factor in long-term recovery.

Motor recovery following NT surgery depends on successful reinnervation of the new target muscle by regenerating axons. Cortical plasticity and motor relearning also play a major role during functional recovery. Successful neuromuscular rehabilitation entails detailed afferent biofeedback (BF) and surface electromyographic (EMG) BF, which have been widely used to rehabilitate peripheral nerve injuries.¹³ Following EMG documentation of target muscle reinnervation, which was usually evident between 3 and 8 months after surgery, EMG-BF rehabilitation was commenced using small portable myotrainers with surface electrodes to train the reinnervated muscles to move the elbow and fingers, as patients had difficulty contracting each muscle effectively.¹⁴ Electromyographic biofeedback has been demonstrated to be helpful in the early stages. However, the patient is required to visualize waveforms and hear the activity on the EMG monitor. The lack of tangible, tactile sensation of muscle contraction through the monitor made it difficult for patients, especially those of advanced age, to synchronize the monitor motor unit potential (MUP) waveforms with muscle contraction.

The upper limb single-joint hybrid assistive limb (HAL) (HAL-FS01, Cyberdyne, Inc) is a wearable robot that can support elbow flexion and extension motion. The advanced features of HAL enable real-time voluntary elbow motion by the wearer using actuators driven by electrical signals converted from muscle action potentials detected by surface electrodes on the overlying skin. The original clinical treatment indication for HAL used its biofeedback techniques to enable elbow flexion training in stroke patients.^{15,16} Isolated case reports of HAL for rehabilitation of upper limb paralysis have been published for cervical radiculopathy and obstetric palsy.^{17,18}

We used HAL to rehabilitate elbow flexion reconstruction following BPI by implementing virtual and muscle power strengthening training. This study aims to report the preliminary outcomes of HAL used in postoperative rehabilitation after NT surgery performed for elbow reconstruction in BPI, and compare

Table 1

Demographics and Long-Term	Outcomes of Patients HAL Training
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the rehabilitation performance between HAL and EMG-BF training groups. We hypothesized that the HAL training group could decrease the number of rehabilitation sessions compared with the EMG-BF group.

Materials and Methods

This was conducted as a preliminary study in a single institution involving patients with BPI who underwent postoperative rehabilitation using a HAL device or conventional EMG-BF training following ICN-MCN transfer. The local hospital institutional review board approved the study, and informed consent was obtained from each patient.

Patients

Between April 2018 and March 2019, postoperative HAL training rehabilitation following NT reconstruction of elbow flexion was used in 14 BPI patients (Table 1). Eight patients in the HAL group who had ICN-MCN transfer were compared with a reference group who had conventional EMG-BF rehabilitation post-ICN-MCN transfer to determine the efficacy of HAL in postoperative rehabilitation following INC-MCN transfer. Of the remaining 6 patients of the HAL group, 5 had free gracilis muscle transfer, of which the donor nerves used were the spinal accessory nerve, and one patient had a partial ulnar NT.

Surgical procedure

The biceps branch proper fasciculus, which was identified by retrograde fascicular dissection of the biceps motor branch proximally into the MCN, was coapted to the third, fourth, and fifth ICN using perineural 10-0 nylon sutures without tension. After surgery, the limb was immobilized in a sling.¹⁹

Since 2005, 58 patients with traumatic total and C5-8 type BPI types who underwent ICN-MCN transfer by a single senior surgeon fulfilled the inclusion criteria and were recruited into the study.

No.	Age at Injury (y)	Sex	Involved Side	BMI Type of Palsy		Flexion	Reinnervation Time of Target Muscle After NT (mo)	HAL Training Final Outcome (sessions)						
								Total	VT	PT	Follow-up Period (mo)	Range of Elbow Flexion (degrees)	Power of Elbow Flexion (Nm)	MRC
1	54	F	L	17	Total	ICN-MCN	7	187	-	187	53	70	2.3	2
2	41	Μ	L	22	Total	SAN-FMT	4	12	8	4	24	75	3.1	2
3	18	Μ	L	24	C5-8	ICN-MCN	3	38	38	-	24	110	4.5	3
4	21	Μ	R	24	Total	SAN-FMT	3	22	4	18	18	100	4.1	3
5	31	Μ	R	24	Total	ICN-MCN	4	6	-	6	30	120	3.2	4
6	57	Μ	R	21	C5-8	SAN-FMT	3	8	-	8	23	95	2.5	3
7	35	Μ	R	31	C5-7	PUN-MCN	3	11	-	11	24	100	8.5	3
8	41	Μ	R	22	Total	SAN-FMT	4	10	-	10	33	80	2.7	3
9	18	F	L	19	Total	ICN-MCN	4	18	18	-	15	110	4.6	4
10	21	Μ	L	28	C5-8	ICN-MCN	4	22	22	-	27	125	13.9	4
11	32	F	L	39	C5-7	ICN-MCN	6	4	-	4	27	130	5.1	3
12	24	Μ	L	22	Total	ICN-MCN	4	64	52	12	23	140	4.6	3
13	45	Μ	L	23	C5-8	ICN-MCN	5	13	13	-	17	115	5.1	3
14	20	Μ	R	24	Total	SAN-FMT	3	44	-	44	29	130	22.3	3
Mean	33			24			4	33	22	33	26	106	6.2	
SD	13			5			1	55	16	56	9	21	5.3	
Total		M: 11 F: 3	L: 8 R: 6		Total: 8 C5-8: 4	ICN-MCN: 8 SAN-FMT: 5 PUN-MCN: 1								M2: 2 M3: 9 M4: 3

L, left; R, right; SAN-FMT, spinal accessory nerve to the motor branch of free muscle transfer; PUN-MCN, partial ulnar to musculocutaneous nerve transfer.

These patients were followed up for at least 18 months after surgery. Among them, 8 patients underwent HAL training between 2015 and 2019, and the remaining 50 patients had conventional postoperative rehabilitation using EMG-BF training. The demographics of both groups are described in Tables 2 and 3. Groups were similar in age, sex, body mass index (BMI), time to operation after injury, and type of nerve palsy.

HAL device

The HAL is a wearable device that assists the wearer's motion and is comprised of 7 components to effect elbow motion (Fig. 1)

Fitting of the device

The electrodes for elbow flexion were attached over the sixth intercostal muscle (Fig. 2) or biceps brachii muscle depending on the training stage (virtual or power) (Fig. 3), and the electrodes for elbow extension were over the triceps brachii muscle. Following free muscle transfer, the electrodes for elbow flexion were attached over the trapezius or the transplanted gracilis muscle.

The HAL unit comprised the upper arm and forearm attachments, power unit, and ring LED and was worn on the upper limb (Fig. 4). The controller screen allowed the user to set the flexion/ extension signal balance, limiting assistance torque and angle range. Each extension and flexion signal balance was adjustable from 0% to 100%, in increments of 5%.

The HAL Cybernic Voluntary Control (CVC)-AutoExt mode detected Bio-Electrical Signals (BES) and converted them into calibrated extension signals for patients with minimal or absent elbow extension power to activate the extension. In the CVC-AutoExt mode, assistant torque was also generated when the extension signal was not detectable. The assist gain and level to flex the elbow started at 90 and 16, respectively, and decreased inversely with increased target muscle strength (Video E2). The torque of joint motion was set to 100°.

When the wearer attempted voluntary movement, signals were transmitted from the brain, via the spine and motor neurons, to reach the muscle to elicit movement. During this transmission, faint BES appear on the skin surface. The HAL detects these signals through the electrodes affixed on the skin surface. In CVC mode, the HAL power unit was activated by the generated BES to assist the wearer in completing the intended motion.

HAL training

Hybrid assistive limb training was divided into 2 courses, virtual training (VT) and power training (PT). Virtual training was started postoperatively before reinnervation to the target muscle could be detected on the EMG. The electrodes were attached to the original

 Table 2

 Patients' Demographics of HAL and EMG Biofeedback Groups*

donor nerve muscles, for example, the sixth intercostal muscles in ICN transfer (Fig.3). The mode of flexion-extension was selected as auto-extension, and the counter electrodes were always attached to the triceps brachii muscle. After assembly, the patient would attempt to activate the original donor nerve-muscle function, for example, exhalation action for intercostal muscle, and the HAL would automatically induce elbow flexion (Fig. 4, Video E1). Hybrid assistive limb-VT could be performed by setting a low level of HAL to assist, consisting of assist gain 60 and level 1.

After maturation of the target muscle MUP to a stage where it was strong enough to be recognized by the electrodes, the training was converted to the PT course. The electrodes were switched to be placed over the recipient muscle of the NT, such as the biceps or transferred functioning muscle. The HAL standard-setting started at an assist level of 1440 and was gradually decreased to assist level 60, depending on the actual power of elbow flexion (Fig.5, Video E2). This course was continued daily with 3 sets of 30 times of flexion exercises until the patient could actively flex to greater than 45° without the HAL device.

EMG-BF technique

Following EMG documentation of reinnervation of the transferred muscle, usually detected at 3 to 8 months after surgery, EMG-BF technique using small portable myotrainers with surface electrodes, MYO ANALYZER, MA-230 (MINATO), was commenced to train the target muscle to move the elbow (Fig 5), as patients usually had difficulty contracting each muscle effectively. Surface electrodes were placed on the overlying skin of the biceps, or the donor nerve innervated muscle. The myotrainer, or myomonitor, allowed the patient, or therapist, to see the muscle activity waveforms and thereby learn better control. Initially, the biceps muscle, which was reinnervated by the third to fifth ICNs, was trained by activating maximal expiration or inspiration. Electromyographic biofeedback was helpful in the early stages by allowing the patient to visualize and hear the activity.¹⁴

Statistics

Data were presented as mean and standard deviations for normal distribution and median (interquartile ranges, IQR) for non-normal distribution. Based on the data normality, either the Student's *t* test or Mann-Whitney U test was used to compare 2 independent levels. The threshold for significance was set at P < .05.

Results

Fourteen patients underwent HAL-PT, among which 7 had VT. The mean number of VT sessions was 22 ± 16 . Target muscle EMG reinnervation activity was detected at 4.1 ± 1.2 months after NT,

	EMG Biofeedback	HAL	Test	P Value	Power
n	50	8			
Age, y	29.0 (21.3-44.8)	27.5 (20.3-35.3)	M-W test	.874	0.057
Sex					
Male	45	5	χ^2 test	.123	0.555
Female	5	3			
BMI	23.0 ± 3.7	24.6 ± 6.1	t test	.348	0.137
Time to Op after injury (mo)	5.0 (4.0-6.0)	4.5 (3.8-6.0)	M-W test	.971	0.053
Type of palsy					
Total	28	4	χ^2 test	.947	0.072
C5-8	22	4			

Op, ICN-MCN transfer operation; M-W, Mann-Whitney U test.

^{*} Normal distribution, mean \pm SD; non-normal distribution, median (interquartile range).

Table 3

Outcomes of Both Electromyographic Biofeedback and HAL Groups

	EMG	HAL	Test	P Value	Power
Follow-up (months)	27.0 (18.0–36.0)	25.5 (21.8-27.8)	M-W test	.647	0.095
Elbow flexion range (degrees)	110 (90-130)	118 (110-126)	M-W test	.449	0.141
Power of elbow flexion					
≦MRC 3	33	7	χ^2 test	.419	0.232
\geq MRC 2	17	1			
Quantitative power (Nm)	5.9 ± 3.2	5.4 ± 3.6	M-W test	.425	0.065
Rehabilitation					
Period (d)	72 (52–96)	50 (39-84)	M-W test	.287	0.05
Times	52 (35-64)	20 (11-45)	M-W test	.04	0.123

M-W test, Mann-Whitney U test.



Figure 1. Product components of HAL-single-joint for elbow motion. ①, Electrodes; ②,Upper arm attachment; ③, Ring LED; ④, Forearm attachment; ⑤, Power unit; ⑥, Control box storage bag; ⑦, Controller.



Figure 3. The electrode attachment for PT. The electrodes are attached to the surface skin over the biceps brachii muscle (③) and the triceps brachii muscles (③). ③ denotes the reference electrode.

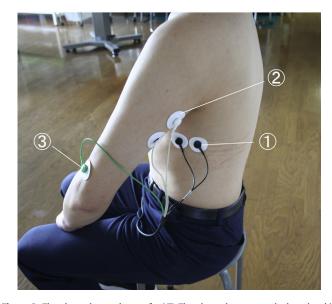


Figure 2. The electrode attachment for VT. The electrodes are attached to the skin surface over the sixth intercostal muscle (O) and the triceps brachii muscle (O). O denotes the reference electrode.

and HAL-PT was started at a mean of 6.6 \pm 8.2 months after EMG reinnervation, which corresponded to when HAL electrodes recognized activity as useful signals. The mean number of PT sessions was 33 \pm 55. Four patients with ICN-MCN transfer and HAL-VT did not participate in postoperative rehabilitation after HAL-VT (Table 1).



Figure 4. Wearing and Fitting of HAL-single-joint. ①, Electrodes; ②, Upper arm attachment; ③, Ring LED; ④, Forearm attachment; ⑤, Power unit; ⑥, Control box storage bag; ⑦, Controller.

A comparison of long-term results following ICN-MCN transfer between EMG-BF and HAL groups was listed in Table 3. Groups were similar in follow-up duration, elbow flexion range of motion, or power of elbow flexion assessed by the British Medical Council grade (MRC) and quantitative measurement using Kin-Com dynamometer between HAL and EMG-BF groups. However, the number of rehabilitation sessions was significantly fewer in the HAL (median, 20 times [IQR, 11–45]) than EMG-BF (median, 52 times [IQR, 35–64]) group (P = .04).

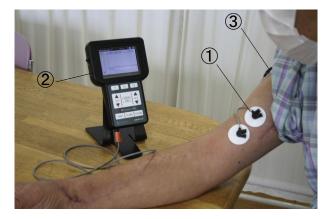


Figure 5. Electromyographic biofeedback technique. Skin surface electrodes (①) are placed over the biceps brachii muscle, and the patients look at the myomonitor (@) to visualize the EMG patterns generated and, thereby, learn better contraction and control. (③) A ground plate.

Case studies

Case 1 (case no. 3)

An 18-year-old man sustained left C5-8 type BPI and underwent third, fourth, and fifth ICN-MCN transfer for elbow flexion. He started HAL-VT 4 months after surgery, when EMG documented biceps muscle innervation, but prior to HAL detecting BES. The electrodes were attached over the left sixth intercostal and triceps muscles. Virtual training was performed over 33 sessions, and he mastered how to contract to reproduce elbow flexion. He returned home before clinical recovery of elbow flexion and continued self-training without HAL. At 22 months after surgery, he obtained 110° elbow flexion with a strength of 4.45 Nm, which was 11% of the contralateral limb. This case showed that it was unnecessary to attend sessions at the postoperative rehabilitation center following NT because the patient could master the technique to reproduce the desired elbow flexion action after VT training (Video E1).

Case 2 (case no. 13)

A 24-year-old man sustained left total type BPI and underwent third, fourth, and fifth ICN-MCN transfer for elbow flexion. He completed 52 VT sessions and 12 PT sessions. Power training started at 1440 Nm of assist-torque within one week after EMG documentation to biceps and was gradually decreased to 60 Nm at week 22. He obtained 100° elbow flexion with 5 Nm power. This case illustrated that a shortened period of post-reinnervation rehabilitation was required when HAL was used (Video E2).

Case 3 (case no. 1)

A 54-year-old woman with left total type BPI underwent ICN-MCN transfer. Electromyographic documentation of biceps brachii reinnervation was delayed until the eighth postoperative month, and she was unable to flex the elbow even at 26 months after surgery. With the initiation of HAL-PT, she obtained 70° of elbow flexion with 2.3 Nm power (8% of uninvolved side power) 2 years after HAL-PT. This case suggested the usefulness of HAL-PT for older patients with delayed recovery (Video E3).

Discussion

The functional recovery of NT following BPI depends on the successful reinnervation of the targets in the periphery and the motor relearning process that entails cortical plasticity. The former is affected by factors such as patients' age, time from injury to operation, donor nerves, and surgical skillfulness. The latter is

mainly affected by preoperative and postoperative rehabilitation. While there are an increasing number of methods to improve rehabilitation, routine implementation in a clinical setting remains a challenge because of complexity and long duration.^{13,14,20–22}

Initial reinnervation motor activity can be detected via EMG before clinical recovery is evident. Multimodal biofeedback is used during this rehabilitation phase to relearn motor function. This is especially critical after NT, as muscle activation patterns change because of the altered neural connection.

As neural pathways are altered after NT, patients cannot be treated with standard postoperative therapy protocols otherwise used after direct nerve repair.¹³ ICN-MCN transfer in brachial plexus reconstructive surgery is the most extensively studied NT for changes in brain plasticity after transfer. When donor axons grow into the new target, they take on a motor function they did not previously have, while still being cortically connected to their original function. In the ICN-MCN transfer used to restore elbow flexion after total type of BPI, despite successful reinnervation, these fascicles from the ICN were still cortically connected to their previous function of respiration.⁹ On a functional level, this implies that during the early phase of rehabilitation, the patient needs to focus on the previous nerve function (inspiration or expiration) to activate and strengthen the recipient muscle (biceps contraction). This approach is also known as the "donor activation focused rehabilitation approach."23

At the beginning of recovery, patients who have undergone this NT generally exhibit involuntary biceps contraction that is linked to breathing. After a short period, patients develop voluntary biceps contraction with sustained inspiration or expiration. Later, contraction (and the maintenance of elbow flexion) ultimately become independent of respiration.²⁴ Hybrid assistive limb can more easily achieve this shift in cortical activity between the donor and recipient than EMG-BF training.²⁵ The potential for plasticity should be considered by surgeons when planning surgical strategy and postoperative rehabilitation because it influences results.^{13,23,24,26}

Although we found that VT using the HAL device may be useful for rehabilitation following NT, there is still no evidence that VT may improve outcomes better than traditional therapy because of the multifactorial nature of recovery. In case 1, although the patient with only VT did not attend rehabilitation after reinnervation, he could flex the elbow subsequently through self-training. In case 2, the patient obtained good elbow flexion by virtual and a short period of PT. Virtual training may not need consecutive PT rehabilitation.

The conventional visual—audio EMG-BF therapy assisted the patient's learning of how to contract the reinnervated muscle by visualizing or listening to the EMG monitor. However, no elbow flexion was elicited when the power of elbow flexion was MRC 1. The HAL device had the advantage of flexing the elbow when electrodes were attached to MRC 1 power strength biceps. Through the electrical amplifier circuit, the patient experienced the full recovery of elbow flexion even in the early stages of rehabilitation. Furthermore, patients could easily train and strengthen their muscle power when the HAL assist mode was employed in a gradually decreasing manner.

In patients with MRC 1 power strength, visual input from HAL augmented elbow flexion possibly stimulated the proprioceptors in the muscle spindle (deep sensibility) and re-established actual muscle contraction earlier after surgery with the repetitive joint motion training. This was in contrast to the traditional EMG-BF method, which provided presumed elbow flexion without experiencing the actual elbow flexion during the early rehabilitation stage. This difference between actual and presumed elbow flexion for each intervention course was non-negligible.

Power training with the upper limb HAL may accelerate the achievement of voluntary motion to an equivalent of MRC grade 3 by stimulating changes in neural plasticity within the central nervous system following ICN-MCN transfer. Hybrid assistive limb training is an example of virtual reality in rehabilitation, which is defined as the "use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real-world objects and events."²⁷ Several studies are suggesting that virtual reality training is motivating and enjoyable, with some studies finding the intervention to be more engaging than conventional therapeutic exercises in stroke.^{28–31}

Functional conversion from the original respiratory function into elbow flexion might be simpler in young patients, while for older patients to relearn, the functional conversion into the subconscious can seem impossible to synchronize. The VT and PT of HAL might potentially stimulate instinctive functional conversion from the original function (respiration) into a targeted function (elbow flexion) in older patients. The patient in case 3 had rehabilitation using EMG-BF before HAL training intervention yet could not obtain M2 power strength of elbow flexion. However, the result of HAL training was impressive because the patient experienced full elbow flexion on the first day of HAL intervention.

Anastakis et al³² recommended a minimum training program of 2 years with strengthening exercises starting after initial motor movement. In our country, postoperative rehabilitation for BPI is covered by medical insurance for 2 to 3 years after surgery. Hybrid assistive limb-VT and PT in the early postoperative phase could shorten the rehabilitation duration to master reconstructed elbow flexion.

We concluded that HAL training contributed to patients' accelerated learning in converting its original function into elbow flexion following NT, replicating elbow flexion during the pre-MUP detection stage, and hence shortening the rehabilitation time.

Acknowledgments

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