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TITLE: Longitudinal Observation of Myoelectric Upper-Limb Orthosis Use among Veterans with Upper-Limb Impairment

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CONTRACTING ORGANIZATION: Northwestern University, Evanston, IL

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14. ABSTRACT The objective of this observational study was to document longitudinal outcomes in Veterans and non-Veterans using the myoelectric upper limb orthosis with powered elbow and grasp using both patient-centric performance and patient-reported outcome measures. Longitudinal observation allowed us to document therapeutic and neuroplastic effects, as well as functional outcomes of orthosis use. This was a prospective, observational, longitudinal outcomes study wherein subjects acted as their own control. The study required 29 visits over 22 weeks and was divided into four parts: enrollment, orthotic fitting, therapy/training, and home use. We recruited 16 subjects, 13 of whom completed the study. For the entire cohort, statistically significant changes were observed for all measures at both time points, with the exception of CHART, which assesses participation, where a significant change did not occur until the end of the Home phase. Device repetitions during the Home phase were significantly greater for the TBI cohort at the elbow. No adverse events occurred.						
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INTRODUCTION

Upper limb deficits are common after traumatic brain injury (TBI) and stroke, and recovery is often limited even after therapy. Adjuvant treatments that enhance motor learning-based therapy may improve outcome. The MyoPro® is a myoelectrically controlled upper limb orthosis that harnesses the user's muscle signals and assists the user to move the weak arm. The purpose of this project was to assess the feasibility of delivering combination motor learning-based therapy and MyoPro® in chronic stroke by assessing longitudinal outcomes in Veterans using both patient-centric performance and patient-reported outcome measures. The study required 29 visits over 22 weeks and was divided into four parts: enrollment, orthotic fitting, in-clinic therapy/training, and home use.

KEYWORDS

Traumatic brain injury, stroke, rehabilitation, motor learning-based therapy, upper extremity, robotics, myoelectric orthosis, orthotic devices, MyoPro.

ACCOMPLISHMENTS

Major goals of the project

Major Task 1: Institutional Review Board (IRB) Approvals			
	Louis Stokes Cleveland VA Medical Center (LSCVAMC-IRB)	Northwestern University (NU-IRB)	Human Research Protections Office (HRPO)
Initial submission approved	8/11/16	8/26/16	10/5/16
Modification approved	11/10/16 12/23/16 6/8/17	12/21/17 2/17/17 6/16/17	n/a n/a n/a
Continuing Review approved	7/13/17	7/20/17	7/28/17
Continuing Review and modification approved	5/10/18	6/27/18	5/25/18 (LSCVAMC) 7/12/18 (NU)
Continuing Review and modification approved	4/18/19	6/13/19	5/8/19 (LSCVAMC) 6/24/19 (NU)
Notification to halt research due to COVID-19	3/20/20	3/31/20	4/2/20
Continuing Review approved	4/9/20	6/4/20	4/21/20 (LSCVAMC) 6/10/20 (NU)
Major Task 2: Coordinate Project Meetings			
Y1 Meetings	Y2 Meetings	Y3 Meetings	Y4 Meetings
11/1/16	10/20/17	11/16/19	10/16/19
12/15/16	12/7/17	1/11/19	12/1/19
2/3/17	3/1/18	3/29/19	3/24/20
4/7/17	4/6/18	6/16/19	7/7/20
6/21/17	6/26/18	9/6/19	8/13/20
9/1/17	8/31/18		
Major Task 3: Recruit, Screen and Enroll Subjects			
In total we discussed the study with 73 individuals, screened 28 individuals in person, and enrolled 16.			

Y1	Y2	Y3		
s2801 enrolled on 12/5/16. Subject completed study on 12/8/17.	s2804 enrolled on 11/30/17. Subject completed study on - 7/3/18.	s2809 enrolled on 12/10/18. Subject completed study on 8/9/19.		
s2802 enrolled on 6/1/17. Subject completed study on 12/14/17.	s2805 enrolled on 5/24/18. Subject completed study on 9/6/19.	s2810 enrolled on 2/15/19. Subject completed study on 9/30/19.		
s2803 enrolled on 7/11/17. Subject completed study on 2/20/18.	s2806 enrolled on 6/28/18. Subject completed study on 11/27/18.	s2811 enrolled on 1/11/19. Subject completed study on 11/21/19.		
S5 enrolled on 5/12/17. Subject withdrew on 5/13/2017.	s2807 enrolled on 8/28/18. Subject completed study on 9/10/19.	s2812 enrolled on 8/26/19. Subject completed study on 5/20/20.		
	s2808 enrolled on 9/17/18. Subject completed study on 6/10/19.	s2813 enrolled on 6/25/19. Subject withdrawn on 10/21/19.		
		s2814 enrolled on 8/26/19. Subject completed study on 5/4/20.		
		s2815 enrolled on 12/13/2019. Subject withdrawn on 6/3/20.		
Major Task 4: Cast and Fit Myoelectric Orthosis				
We cast and fit 11 myoelectric orthoses (MyoPro®, Myomo, Inc., Cambridge, MA) for the study. Subjects s2801 and s2806 were recruited for the study at the time they received their own MyoPro® devices through the VA.				
Major Task 5: Evaluate Therapeutic and Functional Effects of Myoelectric Upper Limb Orthosis				
Thirteen subjects completed both phases of the study. Three subjects withdrew from the study. Two subjects enrolled but withdrew before fabrication of the orthosis occurred (one withdrew because of concerns about keeping study schedule/unwillingness to forego Botox and the other had an unrelated acute medical issue and when re-assessed after it resolved, subject no longer met study inclusion criteria for enrollment). The final subject who withdrew had begun the in-clinic phase, however due to COVID-19 we had to stop his participation.				
Major Task 6: Aggregate and Analyze Data				
See below "Accomplishments under these goals".				
Major Task 7: Technical Reporting				
	Y1	Y2	Y3	Y4
Q1 Report	1/13/17	1/14/18	1/14/19	1/14/20
Q2 Report	4/13/17	4/14/18	4/14/19	4/14/20
Q3 Report	7/12/17	7/14/18	7/14/19	7/14/20
Annual Report	9/30/17	9/30/18	10/30/19	1/27/20 (final)

Accomplishments under these goals

Succinct description of methodology

Participants were recruited from among Veterans at the Cleveland VA and civilians from surrounding hospitals. Participants were included in the study if they were over 18 years of age and a minimum 6 months since injury; had full passive range of motion at the elbow, forearm, wrist, and hand; had active shoulder flexion of at least 30 degrees and active shoulder abduction of at least 20 degrees; had a minimum of 1/5 on manual muscle test of elbow flexion and extension (biceps and triceps) and forearm flexors and extensors; had the ability to generate volitional, consistent, and detectable electromyography (EMG) signals from the upper arm and forearm sensor sites with wrist in neutral or flexed positions as detected by the MyoPro® Motion-G software; had a Modified Ashworth Scale (MAS) score ≤ 3 for the biceps, triceps, supinators and pronators of the impaired arm; were able to

read and comprehend the English language; had cognitive abilities sufficient to perform testing and training protocols; were able to tolerate functional tasks for 60 minutes without excessive fatigue; were medically and psychologically stable; and had at-home support from a family member or care giver if needed.

After custom fabrication and fitting of the MyoPro®, subjects participated in an In-clinic phase consisting of motor learning-based therapy paired with MyoPro® (twice weekly for 9 weeks) followed by a Home Use phase (9 weeks) (Figure 1). Motor learning-based therapy consisted of part and full task practice and MyoPro® training included device assisted movement of the hand and elbow. Please refer to Pundik et al.¹ in Appendices for a more detailed description of the training provided. Subjects took the MyoPro® home to complete a home exercise program (HEP) mirroring in-clinic training. During the Home Use phase, participants used their HEP consisting of exercises with and without MyoPro®. The HEP was re-evaluated weekly.

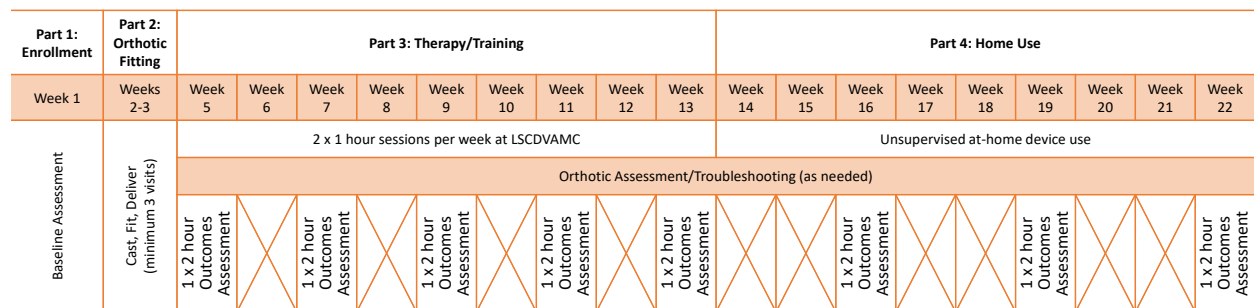


Figure 1 Flow chart illustrating subject participation in each part of the study.

Outcome measures (Table 1) included Fugl-Meyer Assessment for upper limb (FM), Chedoke Arm and Hand Activity Inventory (CAHAI), modified Ashworth scale (MAS) calculated as the sum of 9 arm muscles, Arm Motor Ability Test (AMAT), Craig Handicap Assessment and Reporting Technique (CHART), Orthotic and Prosthetic Users' Survey (OPUS) satisfaction module (OPUS-Sat), passive joint range of motion (ROM), H-Reflex, and Transcranial Magnetic Stimulation (TMS). Purposeful movement cycles were logged by the MyoPro® motors (defined as an electromyography (EMG) signal followed by 30 degrees of motion and 1 second of no motion).

Table 1 Schedule of Assessments

Assessment	Part 1: Enrollment		Part 3: In-Clinic Therapy/Training					Part 4: Home Use		
	Screen	Week 1 (Baseline)	Week 5	Week 7	Week 9	Week 11	Week 13	Week 16	Week 19	Week 22
X assessed without orthosis; O assessed with orthosis										
Passive ROM	X	X	X	X	X	X	X	X	X	X
Active shoulder ROM	X		X	X	X	X	X	X	X	X
MMT	X		X				X	X	X	X
EMG signal	X		X				X	X	X	X
MAS	X	X	X	X	X	X	X	X	X	X
Shoulder subluxation, pain, dislocation	X	Ongoing monitoring for safety. Development of shoulder pain or additional subluxation would result in subject withdrawal from the study if modifications such as adding a shoulder harness was insufficient to overcome shoulder stability issues.								
Skin rash/open wounds	X									
Monofilament	X	X	X	X	X	X	X	X	X	X

Assessment	Part 1: Enrollment		Part 3: In-Clinic Therapy/Training					Part 4: Home Use		
	Screen	Week 1 (Baseline)	Week 5	Week 7	Week 9	Week 11	Week 13	Week 16	Week 19	Week 22
Performance-Based Measures										
Wrist Position Sense Test		X	X	X	X	X	X	X	X	X
Fugl-Meyer (FM)		X	XO	XO	XO	XO	XO	XO	XO	XO
BBT		X	XO	XO	XO	XO	XO	XO	XO	XO
CAHAI		X	XO	XO	XO	XO	XO	XO	XO	XO
AMAT			X				X			X
Patient-Reported Measures										
OPUS-UEFS		X					X			X
OPUS-Sat		X					X			X
CHART		X					X			X
Neuroplasticity measures (for subset of suitable subjects)										
MRI			X				X			
TMS Measure			X		X		X			X
H-reflex			X		X		X			X

ROM: range of motion; MMT: manual muscle test; EMG: electromyography; MAS: Modified Ashworth Scale; BBT: Box and Blocks Test; CAHAI: Chedoke Arm and Hand Activity Inventory; AMAT: Arm Motor Ability Test; OPUS: Orthotic and Prosthetic Users' Survey; UEFS: upper extremity functional status; SAT: satisfaction; CHART: Craig Handicap Assessment and Reporting Technique; MRI: magnetic resonance imaging; TMS: transcranial magnetic stimulation.

We first examined all variables and outcomes univariately for association with diagnostic group. Continuous variables were evaluated using a standard student's t-test; categorical variables were evaluated using a chi-square test. Then we fit longitudinal linear mixed effects models to model the change of outcomes at time points from baseline. Two-sided significance level was set at 0.05. Models included fixed effects for time (post In-clinic phase, post Home Use phase), adjusted for baseline status and diagnostic group, and random effects for subjects to account for within-subject correlation.

Significant results and key outcomes

Recruitment occurred between December 2016 and December 2019. Sixteen subjects were enrolled in the study with 13 subjects (7 stroke, 8 females, 50.6±19.9 years of age, 99.3±116.8 months post-injury) completing participation. The 3 subjects who did not complete the study withdrew for various reasons, including lack of willingness to forgo Botox injections, medical issue that altered eligibility, and COVID-19. Baseline characteristics for the cohort that completed the study are shown in Table 2. Subjects with TBI were significantly younger than stroke subjects (p<0.0001) with a higher baseline CAHAI score (p=0.012).

Table 2 Participant Characteristics (p-value signifies difference between cohorts)

		Total (n=13)	TBI (n=6)	Stroke (n=7)	P
Gender (n (%))	female	8 (61.5)	3 (50.0)	5 (71.4)	0.59
	male	5 (38.5)	3 (50.0)	2 (28.6)	
Age (years, Mean (SD))		50.62 (19.91)	33.33 (11.47)	65.43 (11.36)	<0.0001
Affected side (n (%))	left	9 (69.2)	5 (83.3)	4 (57.1)	0.56
	right	4 (30.8)	1 (16.7)	3 (42.9)	

Dominant hand (n left right (%))	2 (15.4) 11 (84.6)	1 (16.7) 5 (83.3)	1 (14.3) 6 (85.7)	1.00
Time post injury (months, Mean (SD))	99.31 (116.80)	163.67 (147.65)	44.14 (37.76)	0.06
Baseline (Mean(SD))	Total (n=13)	TBI (n=6)	Stroke (n=7)	P
FM	29.23 (9.95)	35.00 (11.31)	24.29 (5.44)	0.05
CAHAI	29.61 (16.17)	40.83 (17.49)	20.00 (5.86)	0.012
MAS	8.58 (3.02)	8.67 (3.43)	8.50 (2.90)	0.926
AMAT Total	44.62 (16.91)	21.39 (7.04)	51.26 (11.91)	0.013
AMAT Functional	1.69 (0.79)	2.78 (0.55)	1.38 (0.52)	0.013
AMAT Quality	1.55 (0.80)	2.72 (0.70)	1.21 (0.44)	0.006
CHART	338.86 (98.52)	358.82 (109.74)	321.76 (92.94)	0.52
OPUS-Sat	51.00 (19.32)	41.67 (16.13)	62.20 (17.89)	0.076
	Total (n=12)	TBI (n=5)	Stroke (n=7)	P
Active ROM* elbow extension	57.09 (32.67)	75.92 (31.29)	43.64 (28.26)	0.091
elbow flexion	56.80 (32.31)	75.23 (30.75)	43.64 (28.26)	0.095
shoulder abduction	78.33 (24.26)	91.33 (16.45)	69.05 (25.63)	0.12
shoulder flexion	59.00 (22.36)	75.53 (22.03)	47.20 (14.25)	0.022
wrist extension	23.20 (26.46)	51.56 (18.37)	6.99 (12.48)	0.001
wrist flexion	23.83 (27.36)	53.28 (19.13)	6.99 (12.48)	0.001
	Total (n=12)	TBI (n=5)	Stroke (n=7)	P
H-Reflex involved	0.41 (0.31)	0.47 (0.39)	0.37 (0.26)	0.62
uninvolved	0.10 (0.13)	0.16 (0.20)	0.07 (0.06)	0.32
	Total (n=5)	TBI (n=1)	Stroke (n=4)	P
TMS involved side flexion	0.59 (0.71)	1.62 (n/a)	0.33 (0.47)	0.091
involved side extension	1.06 (1.42)	3.08 (n/a)	0.39 (0.56)	0.052
uninvolved side flexion	4.70 (2.79)	2.57 (n/a)	5.23 (2.91)	0.48
uninvolved side extension	4.22 (2.69)	1.77 (n/a)	5.45 (2.32)	0.42

*Active range of motion expressed as a percent of the passive range of motion.

Bold P-value indicates significant difference between cohorts at 0.05.

FM: Fugl-Meyer Assessment; CAHAI: Chedoke Arm and Hand Activity Inventory; MAS: Modified Ashworth Scale; AMAT: Arm Motor Ability Test; CHART: Craig Handicap Assessment and Reporting Technique; OPUS: Orthotic and Prosthetic Users' Survey; SAT: satisfaction; ROM: range of motion; TMS: transcranial magnetic stimulation.

Changes in response to combined treatment and controlling for baseline characteristics are shown in Table 3. Statistically significant changes were observed for FM, MAS, CAHAI and OPUS-Sat in both phases, but not for CHART until the end of the Home Use phase. No adverse events occurred.

Table 3 Changes in response to combined treatment (N.S. – not significant)

	Total (n=13)	TBI (n=6)	Stroke (n=7)
Baseline to end of in-clinic phase (Mean(SE))			
FM	7.32 (1.10) (p<0.0001)	8.67 (1.46) (p<0.0001)	6.00 (1.26) (p<0.0001)
CAHAI	7.46 (1.34) (p<0.0001)	9.50 (2.15) (p=0.0013)	5.71 (1.63) (p=0.0043)
MAS	2.54 (0.31) (p<0.0001)	3.00 (0.51) (p<0.0001)	2.09 (0.44) (p<0.0001)

CHART	N.S.	N.S.	N.S.
OPUS-Sat	25.0 (4.87) (p=0.0004)	32.7 (8.68) (p=0.013)	15.8 (4.63) (p=0.027)
Baseline to end of home use phase (Mean(SE))			
FM	7.55 (1.10) (p<0.0001)	8.33 (1.46) (p<0.0001)	6.71 (1.26) (p<0.0001)
CAHAI	8.85 (1.34) (p<0.0001)	9.67 (2.15) (p=0.0012)	8.14 (1.63) (p=0.0003)
MAS	2.31 (0.31) (p<0.0001)	2.83 (0.51) (p<0.0001)	1.79 (0.46) (p=0.0004)
CHART	34.9 (13.6) (p=0.025)	N.S.	55.5 (14.5) (p=0.0086)
OPUS-Sat	26.7 (4.87) (p=0.0003)	36.3 (8.68) (p=0.0086)	15.2 (4.63) (p=0.030)

FM: Fugl-Meyer Assessment; CAHAI: Chedoke Arm and Hand Activity Inventory; MAS: Modified Ashworth Scale; AMAT: Arm Motor Ability Test; CHART: Craig Handicap Assessment and Reporting Technique; OPUS: Orthotic and Prosthetic Users' Survey; SAT: satisfaction.

Device repetitions during the Home Use phase were significantly greater for the TBI cohort at the elbow (Table 4).

Table 4 Movement cycles with MyoPro® (p-value signifies difference between cohorts)

Home Use Phase	Total (n=13)	TBI (n=6)	Stroke (n=7)	p
Total elbow cycles	5401.62 (6283.41)	9563.40 (7586.92)	2428.93 (3043.79)	0.046
Total hand cycles	11141.29 (9974.43)	16618.50 (11542.16)	7229.00 (7122.20)	0.11

Combined therapy of 27 hours in clinic resulted in impairment changes (FM) that were close to those reported with 150 hours of in-person motor learning-based therapy alone.² While most outcomes improved during the in-clinic phase and were maintained during the home use phase, participation as assessed by CHART improved through both phases.

The results for the entire cohort are described in greater detail in the submitted manuscript. Included in the Appendices are two abstracts accepted for presentation at 2021 conferences that summarize findings for different cohorts.

As part of this study, we had 8 individuals with **severe** chronic motor deficits (6 post-stroke and 2 post-TBI). The results for these subjects showed that arm performance gains made during the In-clinic phase were maintained during the Home Use phase.

There was a statistically significant improvement in both arm motor impairment and function according to the following measures: FM, active range of motion (active ROM), Arm Motor Ability Test Function scale (AMAT-F) and CAHAI. FM increased from 22.8±4.5 by 7.4±4 points (p=0.002) at the end of the home phase, which is above the Minimally Clinically Important Difference (MCID) for FM of 5.25 points.³ These gains are greater than what has been reported in other studies that used motor learning-based therapy for severely impaired stroke survivors where following 150 hours of in-clinic therapy FM improved by only 4.7.² Active ROM, measured as a percent of passive ROM, increased by 15.7±12.4% for wrist flexors (p=0.04), 20±15% for wrist extensors (p=0.04), 20.7±26% for elbow flexors (p=0.1) and 20±26% for elbow extensors (p=0.1). AMAT-F improved by 0.35±0.16 points, which is within the MCID range (0.29-0.44).⁴ CAHAI improved from 19.6±5.9 by 5.3±3.8 (p=0.01) at the end of the in-clinic phase, a value close to the MCID of 6.3.⁵ Muscle tone, assessed using the modified Ashworth Scale (MAS) improved and was maintained in these severely impaired subjects. MAS was calculated as a sum of the nine arm muscles tested (shoulder internal rotators, elbow extensors, elbow flexors, forearm pronators, forearm supinators, wrist flexors, wrist extensors, digit flexors, and digit extensors). MAS decreased from 13.5±8.8 by 2.4±1.9 points (p=0.007), which is similar to what was achieved in a different study following 300 hours of therapy.⁶ Overall, these

results suggest that training with a MyoPro® may produce better results with less face-to-face therapy.

The above results for severely impaired individuals formed the basis of two recent grant applications to the VA (single site trial) and DOD (multi-center trial) with the primary objective of conducting a randomized controlled trial to investigate the efficacy of combining MyoPro® with motor learning-based therapy for individuals with post-stroke chronic (>6 months post) severe upper limb motor deficits (FM≤30) compared with a similar dose of motor learning based rehabilitation alone. Secondary objectives included evaluating neuroplasticity mechanisms, identifying biomarkers of greater response to the intervention, and exploring cost-effectiveness.

Grant Applications Submitted

“Exoskeleton Research: Myoelectric orthosis for rehab of severe chronic arm motor deficits.” Submitted to VA Merit Review on June 10, 2020. Principal Investigator: Svetlana Pundik, MD, MS. Co-Investigator: Stefania Fatone, PhD. Resubmitted December 8th, 2020.

“Myoelectric orthosis for rehabilitation of severe chronic arm motor deficits: randomized control trial.” Submitted to CDMRP OPORP 2020 on July 29, 2020. Principal Investigators: Stefania Fatone, PhD, and Svetlana Pundik, MD, MS. Not recommended for funding.

Opportunities for training and professional development provided by the project

While the project was not intended to provide training and professional development, during Y3 of the project, Dr. Svetlana Pundik (site PI at LSCVAMC) recruited post-doctoral fellow, Dr. Ahlam Salameh, to work on the project. Dr. Salameh was trained in the motor learning-based therapy methods administered to subjects, application of the MyoPro® technology to therapy, and data collection/analysis. As a result of these experiences, Dr. Salameh went on to submit an application in a related topic and, in 2020 procured a Career Development Award (CDA1-grant #11K1RX003554) from the Department of Veterans Affairs to study application of the MyoPro® in the acute severe stroke population. CDA1 Award is an important step in establishing a research career at the VA. The award will support Dr. Salameh’s research effort for the next two years while she continues to improve her neurorehabilitation research skills with the goal of building an independent scientific career at the VA.

Dissemination of results to communities of interest

Nothing to Report.

Plans for next reporting period

Nothing to Report.

IMPACT

Impact on the development of the principal discipline of the project

The effects of stroke and TBI are often severely debilitating with many long-standing individuals demonstrating arm motor deficits. Persistent arm motor deficits result in decreased function, increased dependence on caregivers for assistance with everyday activities, increased caregiver burden, and decreased life participation. When severe impairments result, few current rehabilitation methods help restore arm function. Although strongly recommended as part of clinical practice, there is still much to learn about the most effective method of delivering motor learning-based therapy.

Prior research has shown that the burden on caregivers is directly related to severity of arm disability.⁷ Rehabilitation that leads to improved function could help ease this burden. Motor learning-based therapy can improve function but requires many hours of therapy time to be effective (e.g. 150-300 hours).² In this study, clinically meaningful improvements on Fugl-Meyer upper limb Motor Assessment (FM) were achieved when the MyoPro® was paired with motor learning-based therapy.

Our results for FM approached those achieved in prior work with 300 hours of in-person therapy delivered using a group training paradigm (3 patients:1 therapist).^{2, 8} In our study, subjects received 27 hours (1 patient:1 therapist) and improved with 1/10 of the face-to-face training time. This result may have tremendous implications for clinical practice. It is important for future research to examine whether this improvement is attributable to the addition of the MyoPro® to therapy.

The MyoPro® can be used at home, so should further research efforts confirm that it substantively shortens the in-person therapy time needed to achieve meaningful improvements in arm impairments, it would make motor learning-based therapy more feasible to provide to patients. This would support the next critical step of implementation of the training paradigm into the clinical practice setting. Since there is already utilization of the MyoPro® in clinical care,⁹ our study results offer insights into the underlying principles of application of the MyoPro® that can impact how it is utilized.

Severity of upper limb impairment has been strongly associated with decreased health-related quality-of-life (HRQL),¹⁰ however there is a paucity of interventions that can functionally impact the severely impaired upper limb.¹¹ Most interventions have focused on compensation and protection of the limb as opposed to functional restoration.¹¹ The few interventions that have shown efficacy,^{8, 12, 13} have not yet translated into clinical practice. It is likely that these interventions are too costly and labor intensive to implement in the clinic. As interventions for the severely impaired are developed, the issue of translation to clinical practice should be considered in parallel.¹⁴

One issue confounding clinical translation is the belief that individuals with severe deficits after stroke or TBI cannot make meaningful gains, though emerging evidence supports otherwise.¹⁵ It is critical to develop upper limb rehabilitation methods for those with severe chronic stroke deficits to maximize function and improve HRQL. Therapies that are clinically deployable, such as the combined therapy that was the focus of this study, will serve to advance care and promote further functional recovery and independence. Specifically for those with chronic severe motor deficits (i.e., Fugl-Meyer upper limb Motor Assessment < 30) our study results showed that combined therapy increased Fugl-Meyer upper limb Motor Assessment score significantly by 7.4±4 points (p=0.002). These gains are clinically important and greater than what has been reported in other studies that used motor learning-based therapy for severely impaired stroke survivors where following 150 hours of in-clinic therapy Fugl-Meyer upper limb Motor Assessment score improved by only 4.7 points.²

In summary, our results can impact the clinical care of those with arm impairments due to TBI and stroke because they provide insights into how to use the MyoPro® as part of therapy effectively, that doing so can potentially reduce face-to-face treatment required to achieve clinically meaningful reductions in arm impairment, and that it appears to work even for those with severe chronic arm impairment who haven't responded well to other interventions.

Impact on other disciplines

Nothing to Report.

Impact on technology transfer

Nothing to Report.

Impact on society beyond science and technology

Nothing to Report.

CHANGES/PROBLEMS

Nothing to Report. All changes/problems were previously reported in writing.

Changes in approach and reasons for change

Nothing to Report. All changes/problems were previously reported in writing.

Actual problems or delays and actions taken to resolve them

Nothing to Report. All changes/problems were previously reported in writing.

Changes that had a significant impact on expenditures

Nothing to Report. All changes/problems were previously reported in writing.

Significant changes in use or care of human subjects

Nothing to Report. All changes/problems were previously reported in writing.

PRODUCTS**Publications, conference papers, and presentations**Journal publications

Citation	Status	Acknowledgement of federal support
Pundik S, McCabe J, Kesner S, Fatone S (2020) Use of a myoelectric upper limb orthosis for rehabilitation of the upper limb in traumatic brain injury: A case report. Journal of Rehabilitation and Assistive Technologies Engineering 2020; 7: 2055668320921067. https://journals.sagepub.com/doi/full/10.1177/2055668320921067 PMID: 32612847. (included in appendices)	Published, open access	Yes
Pundik S, McCabe J, Skelly M, Salameh A, Naft J, Chen Z, Tatsuoka C, Fatone S. Myoelectric upper limb orthosis combined with motor learning-based therapy in chronic stroke and traumatic brain injury: a longitudinal feasibility study.	Draft in process	Yes

Books or other non-periodical, one-time publications

Nothing to Report.

Other publications, conference papers, and presentations

Pundik S (chair), McCabe J, Cabell M and Wengerd L. (2018) Myoelectric Upper-Limb Orthosis: Debating the Merits of Function and Therapeutic Utility of a Myoelectric Wearable Upper-Limb Orthosis. Invited symposium presented at the American Academy of Orthotists and Prosthetists Annual Meeting, February 14-17, New Orleans, LA.

McCabe J, Skelly M, Salameh A, Fatone S, Chen Z, Pundik S (accepted) Combining myoelectric upper limb orthosis use with motor learning-based therapy in Chronic TBI. CSM 2021, American Physical Therapy Association, February 24-27, 2021, Orlando, FL. Abstract and poster attached.

Fatone S, McCabe J, Skelly M, Naft J, Salameh A, Chen Z, Tatsuoka C, Pundik S (accepted) Combining myoelectric upper limb orthosis use with motor learning-based therapy in chronic stroke and TBI. American Academy of Orthotists and Prosthetists Annual Meeting and Scientific Symposium, May 4-7, 2021, New Orleans, LA. Abstract attached.

Website(s) or other Internet site(s)

Study registered on clinicaltrials.gov on 7/3/17:

<https://clinicaltrials.gov/ct2/show/NCT03215771?term=myoelectric+orthosis&rank=1>

Project page on the Northwestern University Prosthetics and Orthotics Center website:

http://www.nupoc.northwestern.edu/research/projects/orthotics/myomo_longitudinal-dod.html

Technologies or techniques

Nothing to Report.

Inventions, patent applications, and/or licenses

Nothing to Report.

Other Products

Nothing to Report.

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Individuals who have worked on the project

Name:	Stefania Fatone, PhD, BPO(Hons)
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	0000-0002-5802-035X
Nearest person month worked:	1
Contribution to Project:	Dr. Fatone led the project by coordinating and submitting IRB approvals and technical reports, coordinating and conducting regular team teleconferences, and registering the clinical trial. She contributed intellectually to all aspects of the project including publications and presentations.

Name:	Svetlana Pundik, MD, MSc
Project Role:	LSCVAMC Principal Investigator
Researcher Identifier (e.g. ORCID ID):	orcid.org/0000-0002-7262-458X
Nearest person month worked:	1
Contribution to Project:	Dr. Pundik oversaw all aspects of the project at the LSCVAMC, including IRB approvals, subject recruitment and testing. She contributed intellectually to all aspects of the project including publications and presentations.
Funding Support:	No cost to project. VA position supports research activities.

Name:	Samuel Kesner, PhD
Project Role:	Myomo Principal Investigator (until May 2019)
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	1
Contribution to Project:	Dr. Kesner oversaw all aspects of the project at Myomo until May 2019 when he left Myomo.

Name:	Jessica McCabe
Project Role:	LSCVAMC Study Therapist
Researcher Identifier (e.g. ORCID ID):	000-0002-0736-2798
Nearest person month worked:	7
Contribution to Project:	Ms. McCabe was responsible for subject recruitment, screening and enrollment. She scheduled study visits, provided therapy and training, conducted outcome assessments, and maintained study records. She contributed intellectually to all aspects of the project, including publications and presentations.

Name:	Margaret Skelly, PhD
Project Role:	LSCVAMC Study Engineer
Researcher Identifier (e.g. ORCID ID):	0000-0002-7680-7922
Nearest person month worked:	1
Contribution to Project:	Ms. Skelly has been responsible for lab maintenance and data collection and processing. She contributed intellectually to all aspects of the project, including publications and presentations.

Name:	Ahlam Salameh, PhD
Project Role:	LSCVAMC Post-Doctoral Fellow
Researcher Identifier (e.g. ORCID ID):	0000-0003-1687-6093
Nearest person month worked:	3
Contribution to Project:	Since joining the project in Y3, Dr. Salameh has been responsible for subject recruitment, screening and enrollment. She has scheduled study visits, provided therapy and training, conducted outcome assessments, and maintained study records.

Name:	Jon Naft, CPO
Project Role:	Myomo Orthotist Myomo Principal Investigator (from May 2019)
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	1
Contribution to Project:	Mr. Naft was responsible for training LSCVAMC staff with the orthosis, and assisting with fabrication, fitting and tuning of devices to subjects. As of May 2019, Mr. Naft assumed the role of Site PI at Myomo. Since that time, he has overseen all aspects of the project at Myomo, including facilitating device availability and contributing intellectually to all aspects of the project, including publications and presentations.

Name:	Curtis Tatsuoka, PhD
Project Role:	Statistician
Researcher Identifier (e.g. ORCID ID):	0000-0001-9991-4440
Nearest person month worked:	1
Contribution to Project:	Dr. Tatsuoka oversaw all aspects of statistical analysis of the study data.

Name:	Zhengyi Chen, PhD
Project Role:	Statistician
Researcher Identifier (e.g. ORCID ID):	0000-0002-2745-4454
Nearest person month worked:	1
Contribution to Project:	Dr. Chen contributed to statistical analysis of the study data.

Change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period

Permission to reduce Dr. Fatone's effort was requested on 1/22/2020 and approved. Effort was reduced from 10% to 3% during the no cost extension period beginning September 30, 2019. During the no cost extension period, the remaining funds were used to support the sub-sites work as well as support the reduced effort for Dr. Fatone. The change did not affect Dr. Fatone's engagement in this project nor the project scope.

Other organizations involved as partners

Organization Name:	Louis Stokes Cleveland VA Medical Center
Location of Organization:	Cleveland OH
Partner's contribution to the project (identify one or more)	<ul style="list-style-type: none">• In-kind support of project staff• Collaboration

Organization Name:	Myomo Inc.
Location of Organization:	Cambridge MA
Partner's contribution to the project (identify one or more)	<ul style="list-style-type: none">• In-kind support of devices• Collaboration

SPECIAL REPORTING REQUIREMENTS

See attached Quad Chart.

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1. Pundik S, McCabe J, Kesner S, Skelly M, Fatone S. Use of a myoelectric upper limb orthosis for rehabilitation of the upper limb in traumatic brain injury: A case report. *J Rehabil Assist Tech Eng* 2020;7:2055668320921067.
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APPENDICES

Documents are attached in the following order:

1. Pundik S, McCabe J, Kesner S, Fatone S (2020) Use of a myoelectric upper limb orthosis for rehabilitation of the upper limb in traumatic brain injury: A case report. *Journal of Rehabilitation and Assistive Technologies Engineering* 2020; 7: 2055668320921067. <https://journals.sagepub.com/doi/full/10.1177/2055668320921067> PMID: 32612847.
2. McCabe J, Skelly M, Salameh A, Fatone S, Chen Z, Pundik S (accepted abstract and poster) Combining myoelectric upper limb orthosis use with motor learning-based therapy in Chronic TBI. CSM 2021, American Physical Therapy Association, Feb. 24-27, 2021, Orlando, Florida.
3. Fatone S, McCabe J, Skelly M, Naft J, Salameh A, Chen Z, Tatsuoka C, Pundik S (accepted abstract) Combining myoelectric upper limb orthosis use with motor learning-based therapy in chronic stroke and TBI. American Academy of Orthotists and Prosthetists Annual Meeting and Scientific Symposium, May 4-7, 2021, New Orleans, Louisiana.
4. Quad Chart

Use of a myoelectric upper limb orthosis for rehabilitation of the upper limb in traumatic brain injury: A case report

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Svetlana Pundik^{1,2} , Jessica McCabe¹, Samuel Kesner³, Margaret Skelly¹ and Stefania Fatone⁴

Abstract

Background: Upper limb motor deficits following traumatic brain injury are prevalent and effective therapies are needed. The purpose of this case report was to illustrate response to a novel therapy using a myoelectric orthosis in a person with TBI.

Case description: A 42-year-old female, 29.5 years post-traumatic brain injury with diminished motor control/coordination, and learned nonuse of the right arm. She also had cognitive deficits and did not spontaneously use her right arm functionally.

Intervention: Study included three phases: baseline data collection/device fabrication (five weeks); in-clinic training (2×/week for nine weeks); and home-use phase (nine weeks). The orthosis was incorporated into motor learning-based therapy.

Outcomes: During in-clinic training, active range of motion, tone, muscle power, Fugl-Meyer, box and blocks test, and Chedoke assessment score improved. During the home-use phase, decrease in tone was maintained and all other outcomes declined but were still better upon study completion than baseline. The participant trained with the orthosis 70.12 h, logging over 13,000 repetitions of elbow flexion/extension and hand open/close.

Discussion: Despite long-standing traumatic brain injury, meaningful improvements in motor function were observed and were likely the results of high repetition practice of functional movement delivered over a long duration. Further assessment in a larger cohort is warranted.

Keywords

Traumatic brain injury, rehabilitation, motor learning-based therapy, upper extremity, robotics, myoelectric orthosis, orthotic devices

Date received: 9 August 2019; accepted: 20 March 2020

Introduction

Traumatic brain injury (TBI) affects 1.7 million people in the general US population annually¹ and is one of the most common neurologic disorders causing disability.² Motor deficits are present in 30% of TBI survivors with arm and hand problems occurring in about 17%,³ limiting the ability to perform activities of daily living (ADL). However, there is less research on motor recovery in patients with TBI compared with other neurologic diseases involving the brain, such as stroke.²

Activity-based interventions hope to maximize rehabilitation outcomes and enhance adaptive neural plasticity;³ however, optimal doses and schedules of

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training have not been adequately established. Repetition is one parameter important for activity-dependent neural plasticity. Studies assessing US rehabilitation found that stroke and TBI survivors receive an average of 32–50 repetitions of upper extremity active and passive movement per therapy session, significantly less than the 400–600 repetitions achieved in animal studies.³ Although persons with TBI benefit from traditional therapy,⁴ it is clear that more is needed to attain full recovery, especially with severely affected individuals.

Consistent with this idea, Krebs and Volpe⁵ argued that the basis of all assistive and therapeutic devices should be to induce the intent to move followed by that movement actually happening, referred to as “intent-driven rehabilitation”. One way this can be accomplished is through myoelectric control wherein a weak electromyography (EMG) signal from the muscle of an impaired limb is detected, processed, and used to activate a motor within the orthosis. The motor then assists the user in producing the desired movement. The patient-directed “intentional” action of the device promotes patient engagement as the orthosis will only reward the patient with movement when they use the correct muscles to complete a task. Previous studies of myoelectric driven lab-based robotic interventions⁶ showed improved Fugl-Meyer motor control scores of the upper extremity⁷ and reduced spasticity as assessed by the modified Ashworth scale (MAS).⁸ While demonstrating a benefit of “intent-driven rehabilitation”, in-lab robotic intervention restricted the amount of practice because training was restricted to the short lab sessions only and no home practice was possible.⁶

While myoelectrically-driven orthotic technology has been in development for many years,^{9–11} recent advances have made it more accessible and clinically deployable for rehabilitation. However, initial research has focused on persons with stroke^{12–18} and not TBI. The ability of severely hemiplegic stroke survivors to activate a powered elbow orthosis using myoelectric control has been reported,¹³ along with increased elbow range of motion with orthosis use.¹⁸ Kim et al.¹⁵ reported that after a combined period of training and at home-use of an elbow-only myoelectric orthosis, a statistically significant three-point change in Fugl-Meyer motor control score was found in the upper extremity of nine persons post-stroke. We have recently reported a case series of chronic stroke survivors who used a myoelectric upper limb orthosis over a period of several months and achieved a 9.0 ± 4.8 point improvement in Fugl-Meyer.¹⁹ Since upper limb motor deficits in TBI are a problem that can lead to decreased independence in ADLs and given that there is a lack of effective therapies and supportive devices for upper

limb impairment, the purpose of this case report was to illustrate the response to therapy combined with a myoelectric elbow–wrist–hand orthosis in a person with longstanding TBI.

Case description

The protocol described in this case report complies with standards of the Declaration of Helsinki and was approved by the Institutional Review Boards of participating institutions (IRB #16039-H29 and STU00203728) and met the Health Insurance Portability and Accountability Act (HIPAA) requirements for disclosure of protected health information. Written informed consent for participation was obtained from the patient’s legal guardian.

The participant was a 42-year-old female who sustained a TBI from being struck by a motor vehicle at age 12. At study entry, she was 29.5 years post injury, dependent on caregivers for most ADL/instrumental activities of daily living (IADLs), used a manual wheelchair for mobility, resided in a group home setting, and required assistance from caregivers to help her make decisions. She attended an adult workshop where she would perform general fitness/mobility activities along with interacting with peers socially, and had done so for several years. As a result of her injury, she had abnormal tone, weakness and dysmetria/ataxia leading to decreased motor control and coordination of the right upper limb. She has avoided using her right (dominant) arm, which has led to learned nonuse of the right arm and overuse of the left arm. Furthermore, she had cognitive, short-term memory, and perceptual deficits. Right visual processing deficits made it difficult for her to read and distinguish color. Her mini mental state exam (MMSE) score at baseline was 15 out of 30. Due to these impairments, she did not spontaneously use her right upper limb functionally. Over the years since her injury, interventions including traditional physical and occupational therapy (functional mobility training, upper limb task practice, aquatic therapy provided by licensed therapists) have been implemented with limited success to increase the use of her right upper limb.

Intervention

The participant underwent casting and a myoelectric elbow–wrist–hand orthosis (MyoPro Motion-G, Myomo Inc., Cambridge, MA) was custom fabricated by a certified and licensed orthotist. The orthosis is intended to help individuals with a weakened or paralyzed arm to complete patient-initiated movements and enhance function (Figure 1).

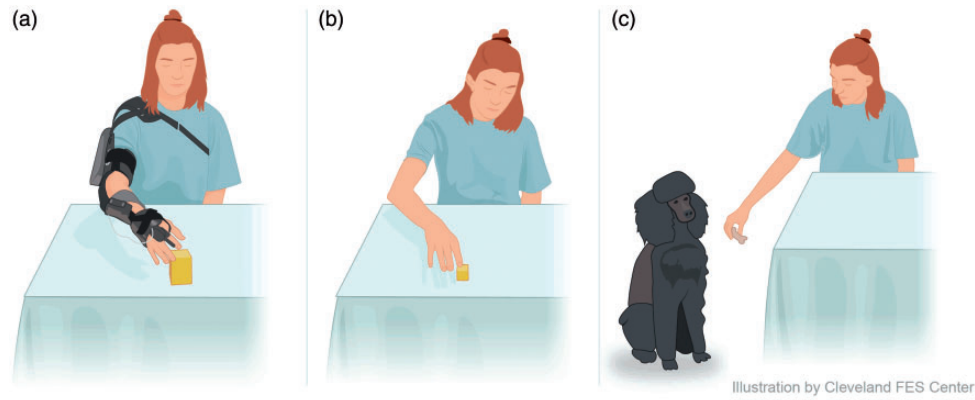


Figure 1. Functional task practice example. (a) Myoelectric elbow–wrist–hand orthosis custom fabricated to fit the participant using MyoPro Motion G components (Myomo Inc.). When the user tries to move the elbow or grasp objects, sensors in the orthosis detect the myoelectric signal generated by the user’s volitional effort, to activate the motor and move the elbow/hand in the desired direction, assisting the user to complete the desired movement. (b) Functional task practice without the orthosis donned to reinforce training. (c) Demonstration of return of functional use showing the participant spontaneously using her impaired limb to feed her pet treats.

Table 1. Types of practice/training and hierarchy of motor control challenge that can be employed with the orthosis.

Less challenging	a. Single-joint movement practice <ul style="list-style-type: none"> • BICEP • TRICEP • hand OPEN • hand CLOSE
↓	b. Agonist/antagonist coordination across a single joint (DUAL-mode single-joint practice) <ul style="list-style-type: none"> • BICEP+TRICEP • hand OPEN+hand CLOSE
	c. Individual movement practice across contiguous joints <ul style="list-style-type: none"> • BICEP+hand CLOSE • BICEP+hand OPEN • TRICEP+hand CLOSE • TRICEP+hand OPEN
More challenging	d. Agonist/antagonist coordination across contiguous joints <ul style="list-style-type: none"> • DUAL-mode elbow+hand CLOSE • DUAL-mode elbow+hand OPEN • TRICEP+DUAL-mode hand • BICEP+DUAL-mode hand • DUAL-mode elbow+DUAL-mode hand

The participant was seen for follow-up to ensure proper orthosis fit and her caregivers were trained in donning/doffing and operation of the orthosis. Study interventions were provided by a licensed physical therapist trained in the use of the orthosis and experienced in the implementation of motor learning-based interventions for individuals with neurological disorders.

Study participation was divided into three phases: (1) baseline assessments (week 1 and week 5) and orthosis fitting/fabrication (weeks 1–5), (2) in-clinic training (weeks 5–13), and (3) home-use (weeks 14–22). All study related visits were conducted in the research clinic of the medical center. During the

in-clinic training phase, the participant attended two training sessions per week lasting 1.5 h each, for a total of 18 sessions. Additionally, the participant was instructed to complete a customized home exercise program that incorporated the principles from the in-clinic training sessions and was encouraged to use the orthosis to complete functional tasks at home.

Training progression followed a movement hierarchy previously described.²⁰ An adaptation of this hierarchy in use is illustrated in Table 1. The orthosis was used to train a variety of movements across a hierarchy of motor control difficulty as follows: starting with single-joint movement practice, advancing to agonist/

antagonist coordination practice across a single joint, then to individual movement practice across contiguous joints, and finally, working on agonist/antagonist coordination across contiguous joints. Motor learning-based therapy in the device was complemented by part and whole task practice without the device with an emphasis on volitional movement as close to normal as possible. High repetition of quality movements were encouraged both within sessions, during home exercise practice, and throughout the home-use phase. The participant was asked to use the device not only for home exercise practice but also during functional task performance. Training was tailored to meet the specific needs of the participant and exercises both with and without the device were selected to address her particular deficits. Detail regarding progression of training employed can be found in Table 2.

Outcome measures were administered longitudinally by the same assessor across the three phases of the study. There were two baseline assessments (weeks 1 and 5), four assessments during in-clinic training (weeks 7, 9, 11, and 13), and three assessments during the home-use phase (weeks 16, 19, and 22).

Impairment was assessed using the following measures. Passive and active range of motion (ROM) of the shoulder, elbow, and wrist were assessed using a goniometer. The MAS, using a 0–5 point ordinal scale, was used to assess muscle tone and spasticity⁸ of the finger flexors/extensors, wrist flexors/extensors, forearm pronators/supinators, elbow flexors/extensors, and shoulder internal rotators. MAS has been widely used to quantify muscle tone following brain injury. Interrater reliability of MAS for arm assessments has been reported as kappa=0.92 or percent of agreement=97.4%.²¹ Individual muscle tone ratings were then summed to give an overall MAS score. Manual muscle testing (MMT), using a 12-point grading scale (0, 1, 2–, 2, 2+, 3–, 3, 3+, 4–, 4, 4+, 5), was used to assess muscle power.²² Numerical values were then assigned to the grades (i.e. 2+=2.33; 3–=2.66; and so on) and the overall MMT score was the sum of individual muscle values. The Fugl-Meyer Assessment of Motor Recovery (FM) upper limb subsection is one of the most widely used quantitative measures of motor impairment.²³ The upper limb subsection includes 33 items measuring movement, coordination, and reflex action about the shoulder, elbow, forearm, and wrist with a three-point scale from zero (unable to perform) to two (able to perform) used to score each item for a total score of 66. It has good interrater reliability for use with TBI patients (ICC=0.97).²⁴

Functional task performance without the orthosis was assessed using the following measures. The box and blocks test (BBT) is a standardized assessment of unilateral gross manual dexterity. The participant was

seated at a table, facing a rectangular box that was divided into two square compartments of equal dimension by means of a partition. One hundred and fifty colored, wooden 2.5 cm blocks were placed in one of the compartments. The BBT was scored by counting the number of blocks carried over the partition during a one-minute trial. Higher scores on this test indicate better gross manual dexterity. Psychometric properties such as validity and reliability have been well-established in numerous populations including TBI.²⁴ Performance of ADLs was assessed using the Chedoke Arm and Hand Activity Inventory, which is suitable for populations with upper limb paresis²⁵ and consists of 13 functional tasks. It is not designed to measure the participant's ability to complete the task using only their unaffected hand, but rather to encourage bilateral function.

Orthosis utilization (i.e. time of use and number of repetitions of elbow flexion/extension and hand open/close) was recorded by the built-in orthosis software while the participant wore the orthosis for in-clinic training and home-use phase. The orthosis software records the time the orthosis is powered on and off, computing the elapsed time for each activation session. It counts a repetition when the motor activates, generating movement greater than 30° at the elbow or greater than 30% of the preset range of motion at the hand followed by 1 s rest or change in direction of motion. Subthreshold movements are not counted, hence unequal values of flexion/extension and open/close can be generated. Data were downloaded from the orthosis periodically during the in-clinic training phase and at each assessment visit conducted during the home-use phase. Caregivers were also asked to record the time the participant spent at home practicing specific exercises from the home program and to report any changes in her function, which were recorded as functional milestones by study staff.

Outcomes

There was a stability of performance on clinical measures between the two baseline assessments. The study protocol was well tolerated, with no adverse or unanticipated events, and the training schedule was appropriately followed with the subject attending all scheduled training and testing sessions.

During the in-clinic training phase, active ROM improved for shoulder, elbow, and wrist, while passive ROM remained essentially unchanged (Figure 2(a)). There was a two-point improvement in summed MAS, while summed MMT increased by 13.98 points (Figure 2(b)). FM improved by 16 points, BBT improved by 5 blocks, and Chedoke improved by 10 points (Figure 2(b)). During the home-use phase,

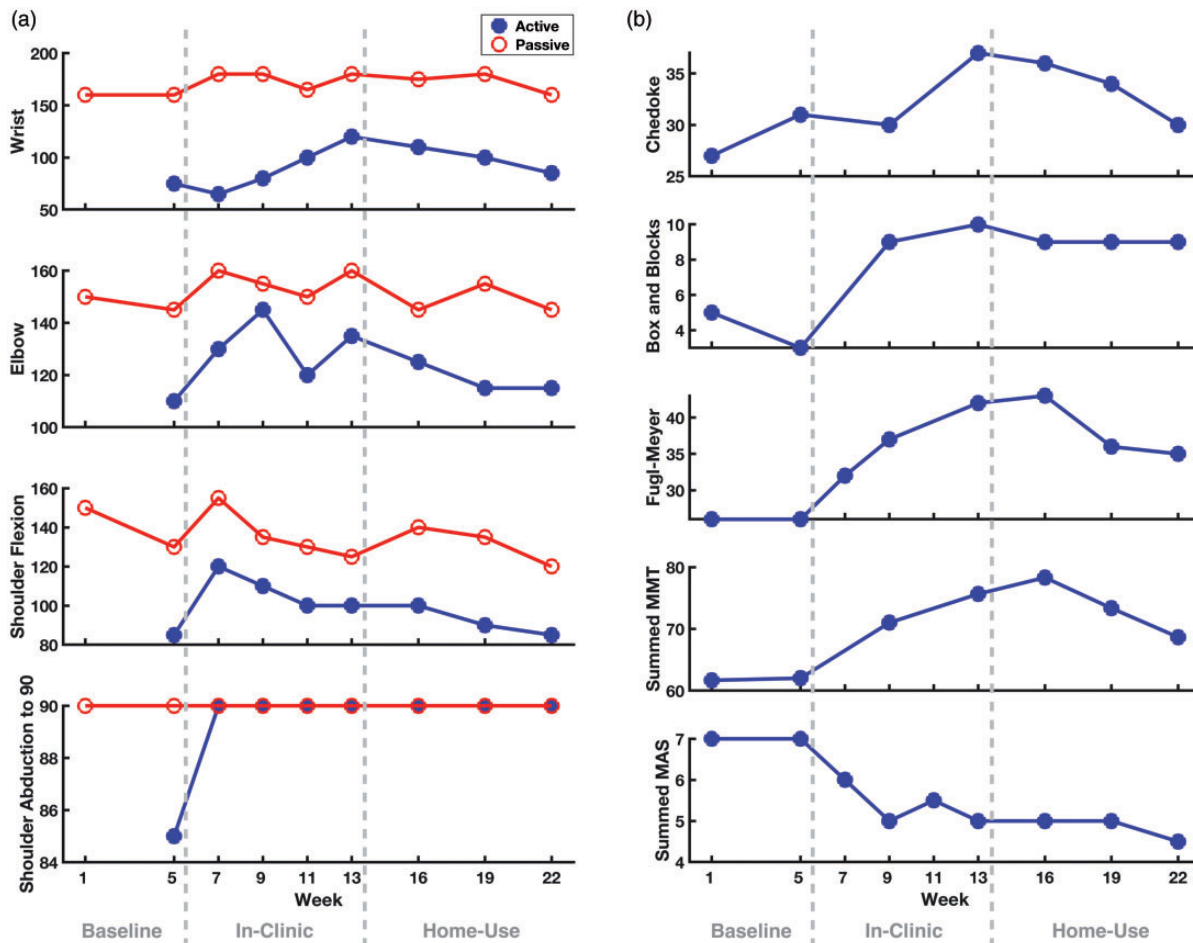


Figure 2. Change in outcome measures over the study duration: (a) passive and active range of motion at the shoulder, elbow, and wrist; and (b) impairment measures (summed modified Ashworth scale (MAS), summed manual muscle test (MMT), Fugl-Meyer assessment of motor recovery) and functional measures (box and blocks test and Chedoke Arm and Hand Activity Inventory).

passive and active ROM returned to baseline values with the exception of shoulder abductors (Figure 2 (a)) but a summated MAS decrease of two points was maintained (Figure 2(b)).

Over the course of the study, MAS improvements were observed in shoulder internal rotators (from 2 to 1.5), elbow flexors (2 to 1.5), and wrist flexors (from 2 to 1). All other clinical measures retained a gain at the end of study participation, although a decline in some assessments was noted during the home-use phase. For example, there was a seven-point decline in FM score during the home-use phase, but the final assessment was still nine points higher than at baseline. There was a one block decline in the BBT during the home-use phase, but the final assessment was still five blocks higher than at baseline. There was a seven-point decline in Chedoke during the home-use phase, but the final assessment was still three points higher than at baseline (Figure 2(b)).

Over the course of both in-clinic training and home-use phases, the participant trained with the orthosis a

total of 70.12 h and, in total, logged 15,849 repetitions of elbow flexion, 16,859 repetitions of elbow extension, 13,397 repetitions of hand closing, and 13,520 repetitions of hand opening with the orthosis (Figure 3). Through self-report using logs to record home practice time during the in-clinic training and home-use phases, the participant demonstrated consistent practice with assigned exercises/tasks.

Functional milestones were reported by the participant's caregivers (Table 3). Overall, more spontaneous functional use of the right arm was observed during the in-clinic training phase and continued during the home-use phase. After one month of training, the participant began incorporating her right arm into ADLs, including spontaneously using her right hand for feeding, brushing teeth and manipulating small objects. She also began to incorporate her right arm into bimanual tasks such as maneuvering her wheelchair, which reduced the need to readjust direction when propelling herself independently.

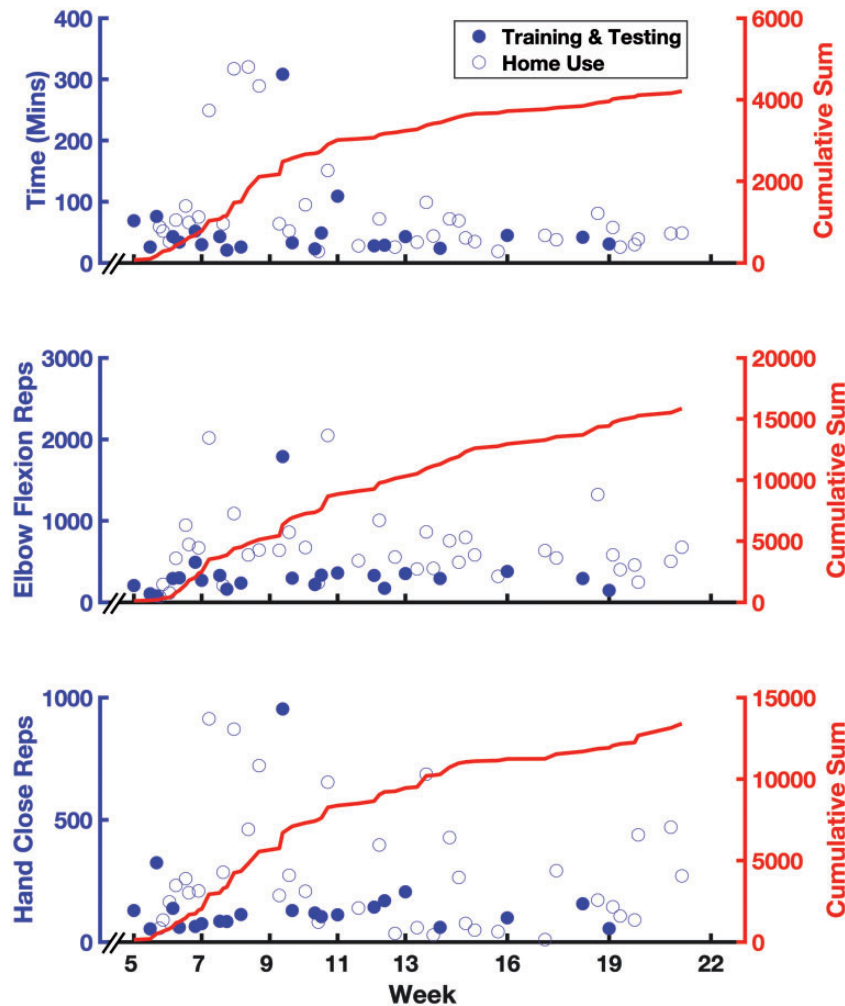


Figure 3. Orthosis utilization was recorded while the participant used the device for in-clinic training, home-use and during functional task performance assessment. The orthosis software recorded the date/time the device was worn and number of repetitions of elbow flexion/extension and hand opening/closing. The number of repetitions includes full and partial completion of movement.

Table 3. Self-reported and observed functional milestones.

Week 9	Increased use of right upper limb for ADLs with occasional cuing (i.e. brushing teeth, eating with utensil, answering phone, feeding dog treats with precision pinch).
Week 10	More independent initiation of functional tasks with right upper limb (i.e. picking up toothbrush; feeding herself finger foods spontaneously); participant manipulated object into a functional position in her hand during testing.
Week 11	Initiated self-feeding with utensil without cuing (i.e. was “eating macaroni salad at a picnic” using a spoon in the right hand).
Week 12	Eating finger foods with her right hand without cuing; increased precision with pincer grasp when feeding the dog or picking up small objects; ate a small pastry with her right hand in therapy; stacked three checkers during therapy.
Week 13	Increased awareness of the right upper limb, states she has been “using her left hand too much in the past and needs to use her right hand more”. Caregivers note she can reach out further in front of her to use her right upper limb.
Week 14	Able to pick up very small pieces of dog treat with the device and feed them to her dog.
Week 15	Using right upper extremity more evenly during wheelchair mobility. Able to maneuver her wheelchair in her home without having to readjust/reposition as often.
Week 19	Continues to use her right upper extremity more spontaneously and maneuvers her wheelchair more independently.

Discussion

This case report demonstrates the potential benefit of using a myoelectric elbow–wrist–hand orthosis in motor learning-based rehabilitation of upper limb deficits in an individual with chronic severe brain injury. The participant demonstrated gains on measures of motor impairment and function, and caregivers reported functional improvement in her home setting in response to the intervention. Importantly, meaningful changes in motor performance were observed 30 years after initial neurological injury suggesting that patients with chronic severe TBI have the potential to improve in response to training.

The use of myoelectric orthoses may have a therapeutic effect in addition to previously demonstrated orthotic effect.²⁶ Therapeutic effect refers to improvements in impairment, defined by the International Classification of Functioning, Disability and Health (ICF) framework as changes related to “problems in body function and structure”.²⁷ Orthotic effect refers to functional improvements that are possible while wearing the orthosis that increase activity and participation. Activity and participation are defined by the ICF as “execution of a task or action” and “involvement in life situations”, respectively.²⁷ We observed a therapeutic effect according to several measures of both impairment (MAS, MMT, FM) and function (Chedoke, BBT) of upper limb motor performance. The basis for a therapeutic benefit of the intent-triggered myoelectric devices likely rests in the encouragement and reinforcement of coordinated volitional practice of motor control⁵ and the ability to gradually progress the training. Use of the device motivates practice and allows appropriate progression of therapy as the EMG threshold that triggers mechanical motion is gradually increased requiring the user to elicit greater volitional muscle activation and reciprocal agonist/antagonist activity. Thus, myoelectric orthoses provide the opportunity to engage and build on small residual volitional muscle activation, and through the application of motor-learning principles can be used to treat upper limb motor impairment for individuals with brain injury.

The design and implementation of efficacious training methods for individuals with neurological dysfunction is challenging. Treatment approaches based on motor learning theory are currently the prevailing choice in neurorehabilitation²⁸ and have been shown to improve impairment, function and quality of life in the setting of chronic neurological disease.^{20,29–31} Common across motor-learning based approaches are the application of critical motor learning principles. These principles include high repetition of functionally relevant movement performed as close to normal as

possible; feedback on performance (i.e. knowledge of results or knowledge of performance); part versus whole task practice; massed versus distributed practice; and practice variability to ensure transfer to novel tasks.³² However, the current healthcare environment does not support implementation of these time-intensive yet critical motor learning principles in the traditional rehabilitation clinic. First, treatment duration is considerably short and patients have limited access to skilled care. In a recent study of outpatient therapy utilization 1–3 months post-stroke, patients attended on average only 24 outpatient therapy sessions in the first year, which equates to less than one therapy session every two weeks.³³ In chronic stages after brain injury, there is even more limited or no access to rehabilitation services. Second, typical outpatient upper limb rehabilitation provides insufficient repetition of arm movement that is an order of magnitude below numbers needed for effective neuroplasticity.³⁴ Individuals perform an average of 32–50 repetitions of upper extremity practice per therapy session while animal studies report 400–600 repetitions per session are required to induce neuroplasticity.³ Even though high dose has been identified as a crucial ingredient to induce neuroplasticity, it is not being accomplished adequately in the clinical setting. Third, there is a need to ensure high quality practice of adequately challenging patient-driven functional movement. When under the skilled supervision of a therapist, motor performance can be closely monitored and progressed incrementally with clinically significant results.^{19,20,31} However, in-clinic training needs to be supplemented with home practice. Unfortunately, in-home practice usually lacks quality, capacity to progress and sufficient adherence.³⁵ Therefore, portable devices that are used in both clinical and home settings have the potential to allow for this critical repetition of quality practice to occur. The biofeedback technology employed by myoelectric orthoses such as the Myopro, ensures that training is patient-driven in that the patient must activate the correct muscle(s) in order to experience the desired movement. Training complexity can be progressed from single joint to multijoint movement and, very early on in training, functionally relevant tasks can be practiced.

In our case, the participant practiced an array of exercises and functional tasks that were progressed during the in-clinic training sessions and reinforced in the assigned home practice. Indeed, utilization data reported for this participant supports that much of the training occurred in her home setting. She performed several thousands of volitional muscle activations at home over the course of study participation. Early in treatment, functional task performance both with and without the orthosis was encouraged and

assigned as part of her home practice. For example, since our study participant enjoyed the companionship of her pet, she was highly motivated to practice the functional activity of “feeding treats to her pet,” thus reinforcing use of her impaired right upper limb. This motivation resulted in adherence to high quality repeated practice.

It is compelling that meaningful changes in motor performance were achieved in response to training many years after injury, and after demonstration of a stable baseline. According to her caregivers, the participant had many opportunities following her injury to rehabilitate use of her right arm; however, success was limited. From initial assessment, it was apparent that although she had motor impairments that affected her right arm, they were not sufficiently severe to preclude movement of the arm. She had weakness of her right upper limb but was able to move against gravity; increased tone but was still able to move her joints through partial range; decreased coordination but had the ability to move out of stereotypical synergy patterns. Despite this, she avoided using her right arm and did not attempt to incorporate it into everyday function. Working with the myoelectric orthosis allowed her to overcome the barrier of decreased attention to her right arm as the orthosis produced large arm movements in response to her activating the appropriate muscle. By focusing the training on the right upper limb through both volitional and orthosis-driven exercises, the patient was being guided to use the right limb in a coordinated way. High repetition and the introduction of meaningful functional task performance further reinforced use of her right arm. Minimal clinically important difference (MCID) and minimal detectable change values (MDC) of the measures used in this study have not been established for TBI; however, values have been reported for chronic stroke. When considering these values, the effects of training produced robust improvement on the FM (16-point increase during in-clinic phase; nine points increase overall at conclusion of home phase) exceeding the MCID range of 4.25–7.25 for chronic moderate stroke.³⁶ The score for box and block test improved by 5, a result that is close to the MDC reported for chronic stroke population (5.5–6 blocks/min).³⁷ For the Chedoke Arm and Hand Activity Inventory, she exceeded the 6.3-point MDC for chronic stroke (10-point increase after the in-clinic phase; three points at conclusion of the home phase).^{38,39}

In conclusion, for this case of an individual with long-standing TBI and motor deficits of the right upper limb, motor function improvements were observed in response to training with a myoelectric elbow–wrist–hand orthosis combined with motor learning-based therapy. Meaningful improvements on

study measures and self-reported function were observed 30 years after initial injury. It may be that the combination of motor learning and the reinforced use of an impaired limb through high repetition practice of functional movement that was delivered over a long duration led to these results. Further assessment in a larger cohort of TBI patients is warranted.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: SK is an employee of the manufacturer of the myoelectric orthosis used in this case report. Other authors have no conflicts of interest to declare. All authors are co-investigators on the following grant which funded this work. The U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick MD 21702-5014 is the awarding and administering acquisition office. Opinions, interpretations, conclusions, and recommendations are those of the author and are not necessarily endorsed by the Department of Defense.

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Guarantor

SP.

Contributorship

SF, SP, and SK researched literature and conceived the study. SF, SK, JM, and MS were involved in protocol development, gaining ethical approval, patient recruitment, and data analysis. SF wrote the first draft of the article. All authors reviewed and edited the article and approved the final version of the article.

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Title: Combining myoelectric upper limb orthosis use with motor learning-based therapy in Chronic TBI

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Purpose/Hypothesis: Individuals with traumatic brain injury (TBI) often present with chronic upper limb motor deficits. Consensus on the best treatment methods is lacking. Motor learning-based therapy is often applied; yet restoration of normal function is not always achieved. Adjuvant treatments that support motor learning-based therapy may improve outcomes. The MyoPro® is a myoelectrically controlled upper limb orthosis that harnesses the user's EMG signal and supports movement of the weak arm. The purpose of this study was to assess feasibility of pairing motor learning-based therapy with MyoPro for chronic upper limb motor deficits after TBI.

Subjects: n=6 (50% male; 13.6±11.2 years post).

Materials/Methods: After custom fitting with a MyoPro, subjects participated in an In-clinic phase consisting of motor learning-based therapy paired with MyoPro (2x/wk for 9 weeks) followed by a Home phase (9 weeks). Motor learning-based therapy consisted of part/full task practice and MyoPro training included device assisted movement of the hand and elbow joint. Subjects took the MyoPro home to complete a home exercise program (HEP) mirroring in-clinic training. During the Home phase, participants used their HEP consisting of exercises with and without MyoPro. The HEP was re-evaluated weekly. Outcomes included Fugl-Meyer for upper limb (FM), modified Ashworth scale calculated as sum of 9 arm muscles (MAS), Chedoke Arm and Hand Activity Inventory (CAHAI), Craig Handicap Assessment and Reporting Technique (CHART), and OPUS satisfaction survey (OPUSsat). Outcomes were collected at baseline, after In-clinic Phase and after the Home Phase. Statistical analyses included descriptive statistics (Mean(SE)) and longitudinal linear mixed effect models including fixed effects for timepoints (post In-clinic phase, post-Home phase), and random effects of subjects to account for within-subject correlation.

Results: Baseline characteristics (mean(SE)) were as follows: FM= 35(1.04) , MAS= 8.7(0.43), CAHAI= 40.8(1.96), CHART 358.8(9.86) and OPUSsat= 41.67(6.4). Subjects performed 21093.6(4755.8) hand reps and 11173.8(3607.0) elbow reps. Using mixed models, statistically significant changes in response to treatment and controlling for baseline were observed for FM, MAS, CAHAI and OPUSsat, but not for CHART. Significant changes(SE) from baseline to end of In-clinic phase and baseline to end of Home phase were as follows: 1) FM improvement of 8.67(1.42) (p=0.0001) and 8.33(1.42) (p=0.0002); 2) MAS improvement of 3.00(0.57) (p=0.0004) and 2.80(0.57) (p=0.0006), 3) CAHAI improvement of 9.50(2.15) (p=0.0013) and 9.67(2.15) (p=0.0012) and 4) OPUSsat improvement of 32.67(6.68) (p=0.0006) and 36.30(6.68) (p=0.0003). No adverse events occurred.

Conclusions: It was feasible and safe to deliver the combination therapy. Improvement in impairment (FM, MAS), function (CAHAI) and satisfaction (OPUSsat) were observed. Individuals responded to the intervention regardless of baseline impairment (FM).

Clinical Relevance: MyoPro paired with motor learning-based therapy may allow high quality practice of movement both in the clinic and during home practice after TBI.



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PURPOSE/HYPOTHESIS:

Individuals with traumatic brain injury (TBI) often present with chronic upper limb motor deficits. Consensus on the best treatment methods is lacking. Motor learning-based therapy is often applied; yet restoration of normal function is not always achieved. Adjuvant treatments that support motor learning-based therapy may improve outcomes. The MyoPro® is a myoelectrically controlled upper limb orthosis that harnesses the user's EMG signal and supports movement of the weak arm. The purpose of this study was to assess feasibility of pairing motor learning-based therapy with MyoPro for chronic upper limb motor deficits after TBI.

METHODS:

- ♦ **Subjects:** 6 chronic TBI survivors (50% male; 13.6 ± 11.2 years post) with upper limb impairment participated in a 22-week program.
- ♦ **Intervention:** Motor learning-based upper limb therapy combined with MyoPro. Subjects participated in orthosis fitting (week 1-5); an In-clinic phase (2x/week for 9 weeks; week 5-13) followed by a Home-use phase (9 weeks; week 13-22)
- ♦ **Outcomes:** 1) Baseline (week 5), 2) End of In-clinic phase (week 13), 3) End of Home-use Phase (week 22).
 - ♦ Fugl Meyer for Upper limb (FM); (clinically significant change = 5.25 points)
 - ♦ Modified Ashworth Scale (MAS)
 - ♦ Chedoke Arm and Hand Activity Inventory (CAHAI)
 - ♦ Craig Handicap and Reporting Technique (CHART)
 - ♦ Orthotics and Prosthetics User Survey satisfaction (OPUSsat)
- ♦ **Statistical analysis:** Descriptive statistics (Mean (SE)) and longitudinal linear mixed effect models including fixed effects for timepoints (post In-clinic phase, post Home-use phase), and random effects of subjects to account for within-subject correlation.

RESULTS:

Subjects' Characteristics

Subject	Age	Gender	Months Post TBI	Affected Side	Injury Type
1	24	male	41	left	MVA
2	25	male	89	left	GSW
3	52	female	344	left	MVA
4	43	female	354	right	MVA
5	29	male	29	left	GSW
6	27	female	125	left	GSW

MVA: motor vehicle accident; GSW: gunshot wound

Baseline Functional Measures

Subject	Fugl-Meyer	MAS	CAHAI	CHART	OPUSsat
1	18	13.5	16	292	60
2	37	11	33	293	45
3	47	8	61	500	22
4	26	7	31	216	28
5	46	3.5	59	394	35
6	36	9	45	458	60

Measurement Changes* over time and 95% confidence intervals

	Change from Week 5 to 13	p	Adjusted p**	Change from Week 5 to 22	p	Adjusted p**
FM	8.7 (5.5, 11.8)	0.0001	0.0002	8.3 (5.2, 11.5)	0.0002	0.0004
MAS	-3.0 (-4.3, -1.7)	0.0004	0.0008	-2.8 (-4.1, -1.6)	0.0006	0.0012
CAHAI	9.5 (4.7, 14.3)	0.0013	0.0026	9.7 (4.9, 14.5)	0.0012	0.0024
OPUSsat	32.7 (17.8, 47.5)	0.0006	0.0012	36.3 (21.5, 51.2)	0.0003	0.0006

	Change from Week 1 to 13	p	Adjusted p**	Change from Week 1 to 22	p	Adjusted p**
CHART	6.0 (-16.0, 28.0)	0.56	1.00	13.0 (-9.0, 35.0)	0.22	0.44

*Results from longitudinal mixed model adjusting baseline score
 ** Using Holm-Bonferroni correction

Figure 1 Illustration of MyoPro use and implementation in motor learning. A) The appropriate user's muscle electromyography (EMG) signals control the two motors on MyoPro; one for elbow flexion and extension and a second for hand opening and closing. B) Task practice without the device does not achieve coordinated movement. In the device, the user is able to produce the desired movement.

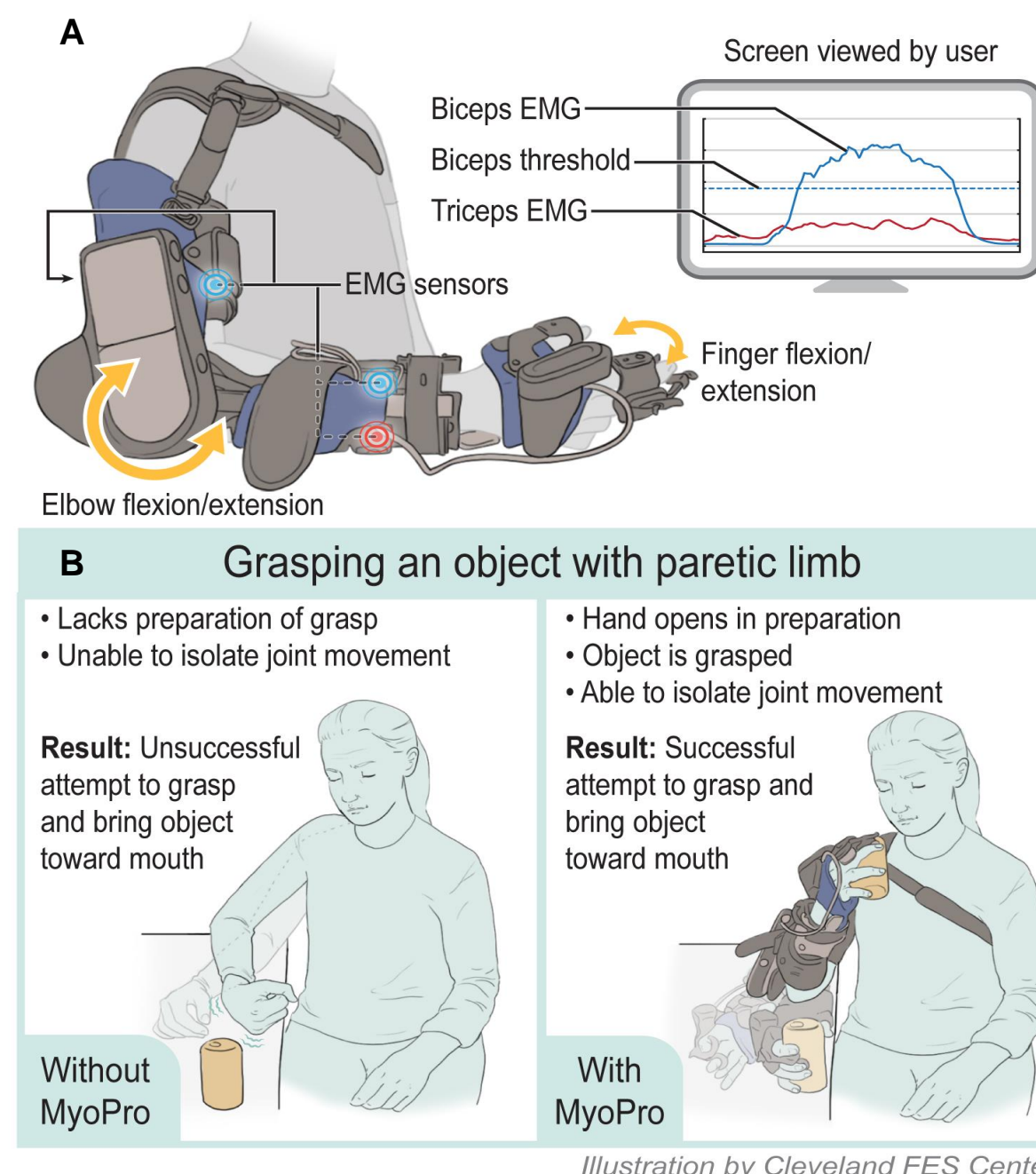


Illustration by Cleveland FES Center

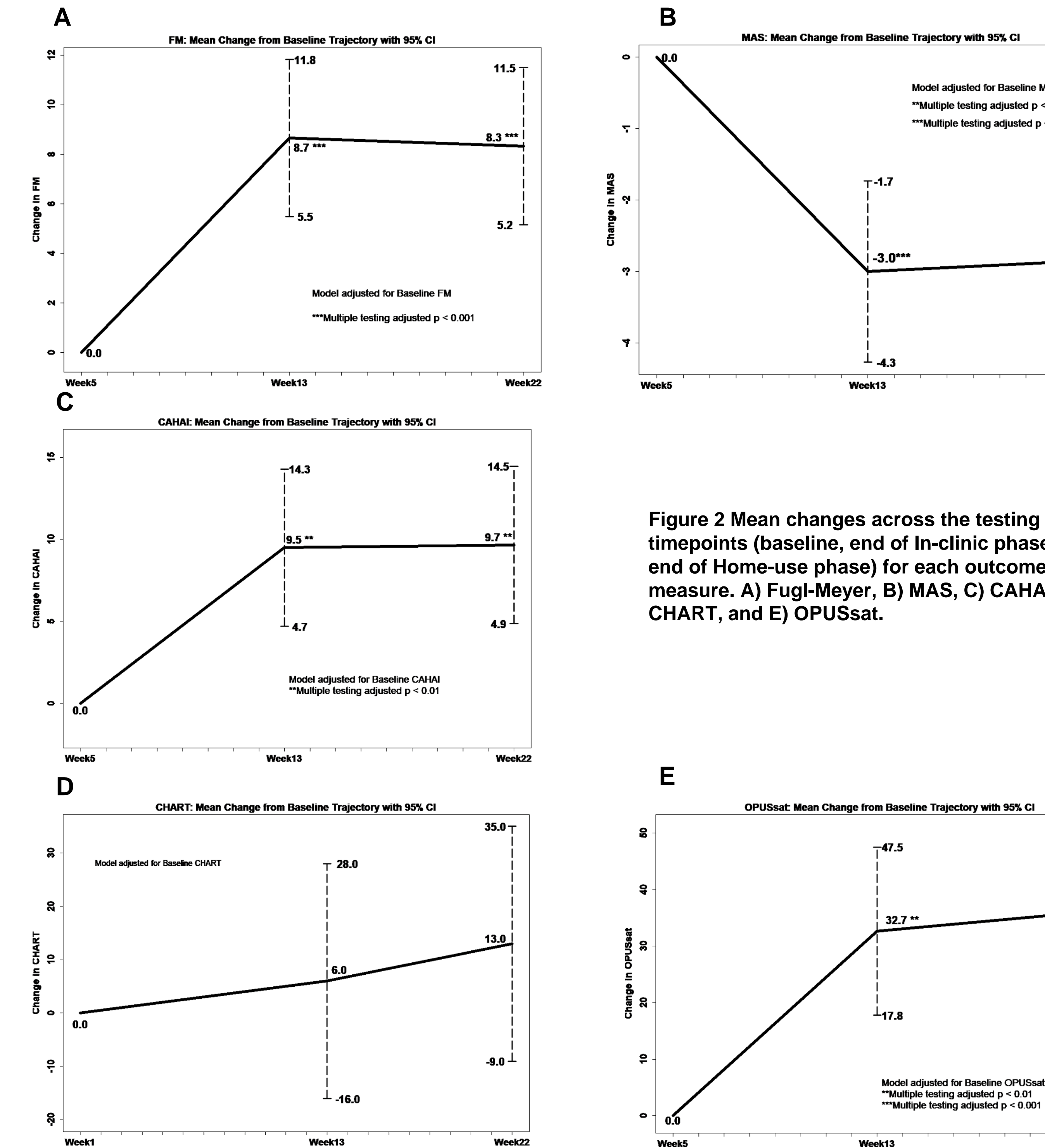


Figure 2 Mean changes across the testing timepoints (baseline, end of In-clinic phase, end of Home-use phase) for each outcome measure. A) Fugl-Meyer, B) MAS, C) CAHAI, CHART, and E) OPUSsat.

CONCLUSIONS:

- ♦ It was feasible and safe to combine MyoPro with upper limb motor learning-based therapy. Improvement in impairment (FM, MAS), function (CAHAI) and satisfaction (OPUSsat) were observed. Individuals responded to intervention regardless of baseline impairment (FM).
- ♦ After TBI, MyoPro paired with motor learning-based therapy may allow high quality practice of movement both in the clinic and during home practice.

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COMBINING MYOELECTRIC UPPER LIMB ORTHOSIS USE WITH MOTOR LEARNING-BASED THERAPY IN CHRONIC STROKE AND TBI

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INTRODUCTION

Upper limb deficits are common after stroke and traumatic brain injury (TBI) with recovery often limited even after therapy. Adjuvant treatments that enhance motor learning-based (MLB) therapy may improve outcomes. The MyoPro® is a myoelectrically-controlled elbow-wrist-hand orthosis that harnesses the user's electromyography (EMG) signal to assist motion of the impaired arm. The purpose of this pilot clinical trial was to assess the feasibility of delivering combination MLB therapy and MyoPro® in a mixed cohort of persons with chronic stroke and TBI.

METHOD

Subjects: With IRB approval and informed consent, 13 subjects (7 stroke, 8 females, 50.6±19.9 years of age, 99.3±116.8 months post-injury) participated.

Outcome Measures: Fugl-Meyer for upper limb (FM), modified Ashworth scale calculated as sum of 9 arm muscles (MAS), Chedoke Arm and Hand Activity Inventory (CAHAI), Orthotic and Prosthetic Users' Survey satisfaction module (OPUS_SAT), Craig Handicap Assessment and Reporting Technique (CHART). All measures were administered without the MyoPro®. Purposeful movement cycles were logged by the MyoPro® motors (defined as an EMG signal followed by 30° of motion and 1s of no motion).

Procedures: After custom fabrication and fitting of the MyoPro®, subjects participated in an In-clinic phase consisting of MLB therapy paired with MyoPro® (1.5 hours twice weekly for 9 weeks) followed by a Home phase (9 weeks). MLB therapy consisted of part and full task practice and MyoPro® training included device assisted movement of the hand and elbow. Subjects took the MyoPro® home to complete a home exercise program (HEP) consisting of exercises performed with and without the MyoPro®. The HEP was re-evaluated weekly.

Data Analysis: We first examined all variables and outcomes univariately for association with diagnostic group. Continuous variables were evaluated using a standard student's t-test; categorical variables were evaluated using a chi-square test. We then fit longitudinal linear mixed effects models to model the change of outcomes at time points from baseline. Models included fixed effects for time (post In-clinic phase, post-Home phase), adjusted for baseline status and diagnostic group, and random effects for subjects to account for within-subject correlation. Two-sided significance was set at 0.05.

RESULTS

At baseline (Table 1), TBI subjects were significantly younger than stroke subjects (p<0.0001) with higher

baseline CAHAI (p=0.012) scores. Despite these differences, diagnostic group and baseline status did not influence the model (except for MAS and Satisfaction) but assessment time did. For the entire cohort, statistically significant changes were observed for all measures at both time points, with the exception of CHART, which assesses participation, where a significant change did not occur until the end of the Home phase (Table 2). Device repetitions during the Home phase were significantly greater for the TBI cohort at the elbow (Table 3). No adverse events occurred.

	Total	TBI	Stroke	p
Gender	f 8 (61.5)	3 (50.0)	5 (71.4)	0.59
	m 5 (38.5)	3 (50.0)	2 (28.6)	
Age	50.6 (19.9)	33.3 (11.5)	65.4 (11.4)	<0.0001
Months post Injury	99.3 (116.8)	163.7 (147.7)	44.1 (37.8)	0.06
Baseline (Mean (SE))				
FM	29.23 (9.95)	35.00 (11.31)	24.29 (5.44)	0.05
MAS	8.58 (3.02)	8.67 (3.43)	8.50 (2.90)	0.926
CAHAI	29.61 (16.17)	40.83 (17.49)	20.00 (5.86)	0.012
OPUS_SAT	51.00 (19.32)	41.67 (16.13)	62.20 (17.89)	0.076
CHART	338.86 (98.52)	358.82 (109.74)	321.76 (92.94)	0.52

Table 1. Baseline characteristics. Bold values are significant.

n=13	Baseline to end of in-clinic phase (Mean(SE))	Baseline to end of home phase (Mean(SE))
FM	7.32 (1.10) (p<0.0001)	7.55 (1.10) (p<0.0001)
MAS	-2.54 (0.31) (p<0.0001)	-2.31 (0.31) (p<0.0001)
CAHAI	7.42 (1.27) (p<0.0001)	8.80 (1.27) (p<0.0001)
OPUS_SAT	25.00 (4.87) (p=0.0004)	26.73 (4.87) (p=0.0003)
CHART	14.22 (13.60) (p=0.3162)	34.91 (13.60) (p=0.0247)

Home Phase	Total (n=13)	TBI (n=6)	Stroke (n=7)	p
Total elbow cycles	5401.62 (6283.41)	9563.40 (7586.92)	2428.93 (3043.79)	0.046
Total hand cycles	11141.29 (9974.43)	16618.50 (11542.16)	7229.00 (7122.20)	0.11

Table 3 Cycles logged by device motors. Bold values are significant.

DISCUSSION

Combined therapy of 27 hours in clinic resulted in impairment changes (FM) that were close to those reported with 150 hours of in-person MLB therapy alone (Daly et al. 2019). While most outcomes improved during the in clinic phase and were maintained during the home phase, participation as assessed by CHART improved through both phases.

CONCLUSION

It was feasible and safe to deliver the combination therapy.

CLINICAL APPLICATIONS

Combined therapy may allow high quality practice of movement in clinic and at home after stroke and TBI.

REFERENCES

Daly et al. Neurorehabil Neural Repair 2019; 33(7):1545968319846120.

Longitudinal Observation of Myoelectric Upper Limb Orthosis Use Among Veterans with Upper Limb Impairment



OP150074

PI: Stefania Fatone, PhD, BPO(Hons) Org: Northwestern University

Award Amount: \$500,000

Study/Product Aim(s)

The objective of this observational study was to document longitudinal outcomes in Veterans using the myoelectric upper limb orthosis with powered elbow and grasp (Figure 1) using both patient-centric performance and patient-reported outcome measures. Longitudinal observation allowed us to detect both the initial therapeutic effects as well as the later functional outcomes of orthosis use.

Approach

We recruited 16 Veterans from the Cleveland VA who had Traumatic Brain Injury (TBI) or stroke and upper limb impairment. The study required 29 visits over 22 weeks and is divided into four parts: enrollment, orthotic fitting, therapy/training (9 weeks), and home use (9 weeks). Therapeutic and functional benefits were evaluated every 2- to 3-weeks over 18 weeks using simple, short clinical tests.

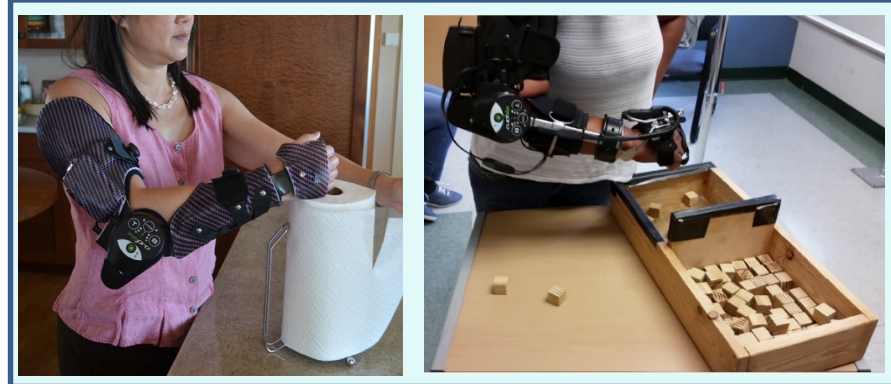


Figure 1 (left) MyoPro powered elbow only and (right) function with added powered grasp unit (MyoPro Motion-G).

Timeline and Cost

Activities	CY	16-17	17-18	18-19
Aim 1: Evaluate therapeutic effects of myoelectric upper limb orthosis.		[Bar spanning 16-17, 17-18, and 18-19]		
Aim 2: Evaluate functional effects of myoelectric upper limb orthosis.		[Bar spanning 17-18 and 18-19]		
Data analysis and dissemination				[Bar in 18-19]
Estimated Budget (\$K)		\$171	\$162	\$166

Expenditure to Date: \$496 633

Updated: 1/4/2021

Goals/Milestones

CY16 Goal – Subject Recruitment, Training and Testing

- Recruit 5 Veterans with TBI and upper limb impairment
- Evaluate therapeutic effects of myoelectric upper limb orthosis
- Evaluate functional effects of myoelectric upper limb orthosis

CY17 Goal – Subject Recruitment, Training and Testing

- Recruit 5 Veterans with TBI and upper limb impairment
- Evaluate therapeutic effects of myoelectric upper limb orthosis
- Evaluate functional effects of myoelectric upper limb orthosis

CY18 Goal – Subject Recruitment, Training and Testing

- Recruit 5 Veterans with TBI and upper limb impairment
- Evaluate therapeutic effects of myoelectric upper limb orthosis
- Evaluate functional effects of myoelectric upper limb orthosis
- Data analysis and dissemination