



EKSOGT™ CLINICAL RESEARCH

SUMMARY OF FINDINGS

May 2019



Spinal Cord Injury Studies

2019

1. **Cardiometabolic challenges provided by variable assisted exoskeletal versus overground walking in chronic motor-incomplete paraplegia: a case series**

Kressler J, Domingo A. San Diego State University, School of Exercise and Nutritional Sciences, San Diego, CA. *J Neurol Phys Ther.* 2019 Apr;43(2):128-135. doi: 10.1097/NPT.0000000000000262.

This case series consisted of two participants with chronic, motor incomplete paraplegia due to a spinal cord injury and who underwent cardiometabolic testing while walking overground with and without the EksoGT using the variable assist feature.

The two participants (male and female) were assessed for walking capacity utilizing the 10MWT and 6MWT. Heart rate, oxygen consumption, energy expenditure and substrate utilization patterns during both EksoGT walking and overground walking were measured for 6 minutes (each). The female, who had a lower functional walking capacity, had greater cardiorespiratory responses during the EksoGT walking compared to overground walking. The male participant, who had a greater walking capacity compared to the female, had lower cardiorespiratory responses during the EksoGT walking sessions. The authors noted that the female with the lower capacity walking was also able to walk for longer periods of time with the EksoGT compared to overground and that for her, overground bionic ambulation was superior to overground walking in terms of the cardiometabolic conditioning. For the male participant with the higher walking capacity, overground bionic ambulation did not provide better cardiometabolic training compared to overground walking. The authors concluded that the cardiometabolic response to overground bionic ambulation depends on the baseline functional capacity of the patient and the EksoGT programs and settings used.

2. **Feasibility of integrating robotic exoskeleton gait training in inpatient rehabilitation**

Swank C, Sikka S, Driver S, Bennett M, Callender L. Baylor, Scott and White Rehabilitation Institute, Dallas, TX. *Disabil Rehabil Assist Technol.* 2019 Mar 19:1-9. doi: 10.1080/17483107.2019.1587014. [Epub ahead of print].

This case series enrolled participants who were inpatients at a rehabilitation institute due to either a spinal cord injury or weakness due to a brain tumor or stroke. In addition, the physical therapists who were trained to use the EksoGT were asked to provide valuable feedback.

A total of 25 participants completed between 1 and 13 sessions (average of 4.5 sessions) walking in the EksoGT during an average 38.5-day stay as inpatients in a rehabilitation hospital. Sessions in the EksoGT focused on both gait mechanics and overall endurance. Clinical testing, including FIM, MAS and MMT, was performed on all participants. The participants with SCI also completed WSCI II and SCIM testing while the patients with stroke completed STREAM testing.. The therapists' focus group feedback session recording was evaluated by three investigators with exoskeleton experience. Therapists expressed some patient measurement difficulties and limited treatment time that they thought had influenced the effectiveness of the therapy, though this improved after 6 months of continued use. No participant complications or adverse events were reported. All outcomes significantly improved from admission to discharge, except MAS, where average baseline scores were <1 for each muscle group. The authors concluded that integrating EksoGT gait training into inpatient clinical practice was feasible and that inpatient participants enjoyed walking and felt secure in the EksoGT.

3. Overground walking with a robotic exoskeleton elicits trunk muscle activity in people with high-thoracic motor-complete spinal cord injury

Alamro RA Chisholm AE, Williams AMM, Carpenter MG, Lam T. School of Kinesiology, University of British Columbia, Vancouver, Canada. Published in the *Journal of Neuroengineering and Rehabilitation* 2018;15:109 with preliminary results presented at ASNR 2016.

Eight participants with chronic, motor-complete SCI ranging from C7 to T6 performed one session each using the Lokomat, the EksoGT overground, and the EksoGT on a treadmill. EMG measurements recorded their trunk muscle activation in supine and during walking. Comparisons were made between training environments and with eight control (able-bodied) participants.

This study compared the activation of trunk muscles while using two different robotic gait trainers used in rehabilitation therapy after a spinal cord injury: the EksoGT and the Lokomat. The objective of this study was to “characterize and compare” this trunk muscle activation using EMG measurements in people with high thoracic, chronic, motor-complete SCI as they walked in the three different environments described above. Results showed greater trunk muscle activation while walking in the EksoGT compared to using Lokomat, and these differences were not attributable to the use of hand-held assistive devices. Moreover, EMG showed trunk muscle activation below the level of injury when using the EksoGT, even though the injuries had been classified as complete. In addition, the level of trunk activation seen during Lokomat walking was similar to that recorded in a relaxed supine position. The authors concluded that the lateral and forward weight-shifting required for Ekso-assisted walking could promote this postural muscle activation.

4. An overground robotic exoskeleton gait training in complete spinal cord injured patients.

Mazzoleni S, Battini E, Rustici A, Stampacchia G. The Biokinetics Institute, Pisa, Italy. Presented at the International Conference on Neurorehabilitation, October 2018, Pisa, Italy.

Sixteen individuals with complete SCI injuries participated in this study of the EksoGT. Results showed significant improvements in walking ability in the device.

Baseline measurements included multiple quantitative and qualitative tests prior to starting the 20-session training which occurred three times a week. After the first week, patients were allowed to progress from assisted step initiation to the active self-initiated stepping mode. Post-training, significant improvement was shown in the 6MWT, 10MWT, TUG, and number of steps during the session. Inter-session analyses showed that at least seven sessions were required to reach significant improvement in step count whereas at least ten sessions were required to show significant improvement in walking time. The researchers pointed out that the testing normally used for ambulatory patients with incomplete SCI can also be used appropriately for patients with complete SCI when using EksoGT. No adverse events occurred.

5. Novel psychological outcomes with Ekso Bionics technology

Stearns-Yoder KA, - Department of Veterans Affairs; Poster presented at the ACRM 2018, Dallas, TX.

This is a continuation of the study by Brenner et al. that was presented as a poster at ACRM in 2016.

Twenty veterans with an age range of 18-65 years and with lower extremity weakness or paralysis due to neurological pathology were enrolled in this study of the psychosocial effects of using the EksoGT for rehabilitation and gait training. Interviews were conducted to gather qualitative data. Results showed that following training with Ekso, there was lower stress, improvement in mood, and improved self-satisfaction. The authors concluded that the use of the EksoGT has psychosocial benefits in this population.



6. Exoskeleton-assisted gait training to improve gait in individuals with spinal cord injury: a pilot randomized study

Chang SH, Afzal T, Berliner J, Francisco GE. Neurorecovery Research Center, TIRR Hermann Memorial, Houston, Texas. Published in *Pilot and Feasibility Studies* 2018;4:62.

This randomized controlled pilot study described results after a 3-week gait training program, in preparation for a larger RCT for people with chronic, motor incomplete SCI.

Seven participants with chronic, motor iSCI (AIS C or D) were randomized to 1-hour training sessions, 5x/week for 3 weeks, with either the Ekso (n=4) or conventional physical therapy (n=3). Two of the original nine participants were unable to complete the study. Despite the randomization, the two groups were functionally different regarding pre-training walking - the conventional PT group was much faster (averaged at a limited community speed) with better balance and could walk much farther than the Ekso group. Due to these inequities and the small sample size in each group, inter-group outcomes were not statistically compared. All participants were assessed pre-post training using ISNCSCI, LEMS, 10MWT, 6MWT, TUG, and spatiotemporal gait characteristics. Only intra-group means and test results were presented. Both groups improved in gait speed, distance, and balance, but the Ekso group showed significant improvement in the 6MWT, and the conventional PT group showed significant improvement in the TUG, even though the actual change was only 1 second.. Both groups showed improvement in right step length, but the Ekso group also improved in stride length. When looking at relative improvement, however, the Ekso group made far greater gains than the conventional PT in each of these areas, as they were much lower functioning pre-training. The investigators concluded that the Ekso therapy should be used for individuals with motor iSCI as a way to facilitate gait recovery. They encourage larger sample sizes for future studies and studying the effects of combining therapies.

7. The effect of robotic walking and activity-based rehabilitation on secondary complications & psychological well-being in individuals with spinal cord injury (SCI)

Shackleton C, Evans R, West S, Rauch L, Bantjes J, Swartz L, Derman W, Albertus Y. Walking with Brandon Foundation, Orthopaedic and Neurological Department, Sport Science Institute of South Africa, Newlands, Cape Town, South Africa. Presented at the 2018 Southern African Spinal Cord Association (SASCA) conference in Johannesburg, Gauteng, South Africa, August 23-25, 2018.

In this study, participants with chronic, motor incomplete SCI were randomized to either activity-based therapy (ABT) or the robotic locomotive training (RLT) using the EksoGT.

Sixteen participants with incomplete cervical injuries > 1 year participated in 60-minute sessions, 3 times a week for 6 months. Each group (ABT and RLT) was composed of 8 participants. Full assessments were performed at baseline, 6, 12 and 24 weeks with partial (intra) assessments every 4 weeks. The outcomes of interest were body composition, bone density (DEXA), spasticity (Modified Ashworth Scale), pain (International SCI Basic Data Set for pain), and quality of life (International SCI Basic Data Set for quality of life). RLT demonstrated benefits related to secondary complications including pain, but these were not significant. The ABT group showed greater loss of peripheral fat, but also a greater decrease in bone mineral density, whereas the RLT group showed some loss of fat and no decrease in bone mineral density. The longer the RLT group used the EksoGT, the greater the gain in muscle tissue. Both groups improved in quality of life measures but the largest gains were between 12 and 24 weeks. There were no significant changes in pain or spasticity found in either group. The authors concluded that the EksoGT may be "protective" of further bone loss and that both groups had improved quality of life.



8. The effect of robotic walking and exercise activity-based rehabilitation on muscle activity, health-related benefits, functional capacity and psychological well-being in persons with spinal cord injury (SCI)

Evans R , Shackleton C , West S , Rauch L , Bantjes J , Swartz L , Derman W , Albertus Y. Walking with Brandon Foundation, Orthopaedic and Neurological Department, Sport Science Institute of South Africa, Newlands, Cape Town. Presented at the 2018 Southern African Spinal Cord Association (SASCA) conference in Johannesburg, Gauteng, South Africa, August 23-25, 2018.

This is the second of two abstracts regarding the South African RCT conducted in participants with incomplete cervical injuries.

In the sample in the study described above (Shackleton et al.), thirteen participants had 6 week data collected on cardiovascular outcomes (heart rate variability, blood pressure), quality of life, and pain. After 6 weeks, both groups had obtained significant reduction in brachial systolic blood pressure and pain. The RLT group had a significant increase in the high frequency spectrum of heart rate variability, whereas there was a significant decrease in the ABT group. The authors concluded that that RLT may improve the high frequency power of the heart during exercise, which in turn may improve vagal nerve modulation.

9. Oxygen consumption and substrate utilization during bionic ambulation with functional electrical stimulation for SCI.

Glasheen E, Kressler J, Domingo A. San Diego State University, San Diego, CA. Poster presented at the ACRM 94th Annual Conference, Progress in Rehabilitation Research, September 30-October 3, 2018 Dallas, TX.

Energy demands were measured and compared across Ekso ambulation in different assist modes, Ekso combined with functional electrical stimulation (FES), and FES cycling.

Four participants with chronic (4-15 years post), incomplete SCI ranging in age from 26 to 45 years old performed three 6MWT sessions as follows: 1 with FES and EksoGT in the Adaptive mode, 1 without FES with EksoGT in the Adaptive mode, and 1 with Ekso in the Fixed mode. These sessions were followed by 6 minutes of FES cycling. Before and after each session, the participants were seated quietly for 5 and 10 minutes respectively. Heart rate and expired gases were measured continuously during the session. Post exercise, RPE and BP were taken in the standing and seated position (to mimic FES cycling position). Exercise and post-exercise measurements were taken for $\dot{V}O_2$, excess post exercise oxygen consumption, fat and carbohydrate metabolism, and estimated caloric expenditure. The authors concluded that FES with EksoGT in Adaptive mode elicited the greatest cardiorespiratory demand compared to FES cycling and Ekso alone. Moreover, 3 of 4 participants' $\dot{V}O_2$ while walking in Ekso nearly met or surpassed the threshold for moderate to vigorous physical activity (46%) with a range of 40-88% across all 3 Ekso testing environments. RPEs ranged from 4-7 on a 0-10 Borg Scale. FES cycling $\dot{V}O_2$ ranged between 19-34% and RPE were 0.5-3. The authors concluded the level of exercise allowed by Ekso modes, including with FES, may lead to improvements in cardiovascular health and secondary complications.

10. Exoskeleton gait training after spinal cord injury: An exploratory study on secondary health conditions

Baunsgaard C, Nissen UV, Brust AK, Frotzler A, Ribeill C, Kalke YB, León N, Gómez B, Samuelsson K, Antepohl W, Holmström U, Marklund N, Glott T, Opheim A, Penalva JB, Murillo N, Nachtegaal J, Faber W, Biering-Sørensen F.. University of Copenhagen, Denmark. *Journal of Rehabilitation Medicine*. 2018;50. Epub ahead of print.

This is the second paper from the Pan-Euro Study with results of training on secondary conditions, such as pain, spasticity, range of motion, urinary and bowel function, independence, and quality of life in participants with sub-acute or chronic, complete or incomplete spinal cord injuries at various levels who trained in the Ekso1.1 or EksoGT for 3x a week over 8 weeks.

Researchers recorded baseline values of pain, spasticity (MAS), joint range of motion, urinary function, bowel function, self-care and mobility function (SCIM III), and quality of life before training in the Ekso1.1 or EksoGT for 24 one-hour sessions (3 times a week for 8 weeks). Tests were performed at baseline, midpoint, endpoint, and 4 weeks following the completion of training. About half of the participants reported pain before the training, but only 17% reported pain during single training sessions. Pain was reduced over time, but not significantly. There was a reduction in MAS scores immediately after single training sessions, but again not significantly over time. The recently injured participants (n=25) within that group showed significant improvements in overall and sub-scale SCIM III scores, while the chronically injured group (n=27) showed significant improvement in overall SCIM III score and the "Respiration and Sphincter Management" sub-scale. Both groups showed the largest improvement on the "Use of Toilet" item in that sub-scale. Six of 25 people in the recently injured group reported improved "awareness of the need to defecate". The chronically injured group showed significant improvement in "satisfaction with life as a whole." The authors concluded that the training was well-tolerated, did not induce new pain, and that both recently and chronically injured people with SCI could benefit from the training. Note that data was not analyzed by severity of injury (i.e. motor complete vs. motor incomplete SCI).

11. Cardiorespiratory demand and rate of perceived exertion during overground walking with a robotic exoskeleton in long-term manual wheelchair users with chronic spinal cord injury: A cross-sectional study

Escalona MJ, Brosseau R, Vermette M, Comtois AS, Duclos C, Aubertin-Leheudre M, Gagnon DH. University of Montreal. Published in *Ann Phys Rehabil Med* 2018 Jan 31. pii: S1877-0657(18)30005-8. doi: 10.1016/j.rehab.2017.12.008.

This study investigated the cardiorespiratory demands of people with chronic, motor complete SCI and long-term wheelchair use engaged in a walking program using Ekso. The aim was to determine exercise intensity, and if walking in Ekso could potentially help avoid the negative effects of prolonged sitting.

Thirteen long-term wheelchair users who had sustained a motor complete spinal cord injury participated in a walking program using the EksoGT. The researchers measured cardiorespiratory changes and the perceived exertion (RPE) using a portable gas analyzer system. The tests were conducted during sitting, standing, and 10MWT using the EksoGT. The participants showed an increase of 9-35% in cardiorespiratory measures just moving from a sitting to a standing position. When progressing from standing to walking in the Ekso, cardiorespiratory measures increased by 22-52%. RPE on the 10-point Borg ranged from 2-5. The authors concluded that this group of long-term wheelchair users could attain health benefits due to the moderate level of exercise that can be achieved during standing and walking in the Ekso.

12. Training for mobility with exoskeleton robot in person with spinal cord injury: a pilot study.

Sale P, Russo EF, Scarton A, Calabrò RS, Masiero S, Filoni S. Department of Neurorehabilitation, Hospital Via Alberoni, Venice, Italy. Published online in the *European Journal of Physical and Rehabilitation Medicine* 2018 Mar 7. doi: 10.23736/S1973-9087.18.04819-0 and later in *Eur J Phys Rehabil Med*. 2018 Oct;54(5):745-751.

This study investigated the change in gait patterns and quality of life in patients with chronic SCI who undergo adaptive training with the EksoGT.

Eight persons with chronic paraplegia (n=7 AIS A or B SCI, n=1 AIS C SCI) underwent 3D Gait Analysis at baseline and after 20 training sessions that took place over 5 to 6 weeks. The 6MWT, 10MWT, TUG (all tested *in the device*), VAS for pain and for fatigue, Borg Scale for RPE, and a satisfaction questionnaire, and assessed the physical and qualitative changes that occurred after training. All participants showed significant improvements in the 10MWT, 6MWT, and TUG while using the device, and ($p=0.008$). Average gait speed increased from 0.17 m/s to 0.31 m/s, surpassing the MCID. Non-significant improvement occurred in the VAS for pain and the Borg RPE was around 1.6 out of 10. For 10 questions regarding user satisfaction with 3 = somewhat agree and 5 = strongly agree, the average response increased from 3.88 to 4.47 after training. The authors concluded that walking in the Ekso is safe and feasible in a heterogeneous group of SCI participants, and that spatiotemporal and kinematic parameters improved while using the device, demonstrating improved human-robot interaction with training.

13. Respiratory, cardiovascular and metabolic responses during different modes of overground bionic ambulation in persons with motor-incomplete spinal cord injury: a case series

Kressler J et al; San Diego State University, San Diego, CA; Published in the *Journal of Rehabilitation Medicine* (2018);50: 173–180. doi: 10.2340/16501977-2281

Participants with varying levels of chronic, motor incomplete spinal cord injuries were tested for cardiorespiratory and metabolic responses using different modes of Ekso for overground ambulation

Four participants with chronic, motor incomplete SCI ranging in age from 24 to 48 years used the EksoGT in Maximal, Adaptive, and Fixed (set at minimal tolerated for each individual) assist modes. There was a wide variation in cardiorespiratory and metabolic responses based on the modes, participants' level of injury and residual function. The lowest %VO₂ achieved was 24% in the highest functioning participant, and the highest was 124% in the lowest functioning participant. In general, walking in Ekso's Fixed (minimal tolerated) mode induced the highest responses and was thought to be the optimal mode for cardiometabolic health benefits and overall improvements in fitness. The authors note that the other two modes can be used to achieve higher number of steps in the session and/or for lower functioning/endurance patients.

14. Locomotor training using an over ground robotic exoskeleton in long-term manual wheelchair users with a chronic spinal cord injury living in the community: lessons learned from a feasibility study in terms of recruitment, attendance, learnability, performance, and safety.

Gagnon DH et al. University of Montreal; Published in *Journal of Neuroengineering and Rehabilitation*, 2018;15:12

Outcomes in this study were rate of recruitment, attendance and completion as well as the ability to walk in the device (progression) and safety.

Approximately 28% of the people with SCI who showed interest in the study were enrolled and of the 14 individuals with chronic, motor complete SCI who started the program, 13 completed the 6 to 8-week program. Over the 18 sessions, standing, walking, and number of steps increased approximately 45%, 102%, and 249% respectively. Approximately 86% required only one therapist to assist them during walking and reached an average walking speed of 0.25 m/sec. In terms of safety, one participant sustained bilateral calcaneus fractures and was removed from the study. This participant's SCI was over 8 years post and all were long-term wheelchair users. Five participants reported pain and/or stiffness in the upper extremities, four of which had pre-existing upper extremity conditions. The authors concluded that use of Ekso in patients with motor complete SCI is safe and feasible, but that larger studies are required. The authors also recommend pre-training to increase recruitment and better clinical guidelines to reduce the potential of fractures in those who use exoskeletons in the presence of motor complete SCI.

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15. Overground vs. treadmill-based robotic gait training to improve seated balance in people with motor-complete spinal cord injury: a case report

Chisholm AE, Alamro RA, Williams AMM, Lam T. Published in the *Journal of NeuroEngineering and Rehabilitation* 2017;14:27.

Three individuals with chronic, motor complete spinal cord injuries (18-25 years post), ranging from C7 to T4 (AIS A and B) with no voluntary motor function below chest level, were randomized to train with either Ekso-Lokomat-Ekso (n=2) or Lokomat-Ekso-Lokomat (n=1) programs for a total of 30 sessions (10/10/10).

Each 45-minute session (3 to 4 times per week for 10 sessions each phase) was conducted according to the randomization assignment with perceived effort (Borg-10) and EMG recordings taken during walking in each intervention. Testing of static and dynamic sitting balance was performed using center of pressure movement while sitting on a force plate and two dynamic seated functional tasks at baseline (two times, each one week apart) and again within one week of the end of each 10-session phase. There was no period of washout between training phases. Results showed that the Ekso training phases had a greater positive effect on both static and dynamic sitting balance than the Lokomat training phases. Lokomat walking appeared to produce little change in trunk muscle activity compared to resting supine, whereas Ekso walking produced higher trunk muscle activity. Despite the SCIs' classifications of motor-complete at T4 or above and being very chronic, walking in Ekso appeared to activate trunk muscle control below the level of injury. The researchers suggest the lateral and forward weight-shifting required when walking with Ekso elicited the trunk muscle activity, thereby contributing to the improved seated balance.



16. Satisfaction and perceptions of long-term manual wheelchair users with a spinal cord injury upon completion of a locomotor training program with an overground robotic exoskeleton

Gagnon DH et al. University of Montreal. Published in *Disabil Rehabil Assist Technol*. 2017 Dec 19:1-8. doi: 10.1080/17483107.2017.1413145.

This study sought to quantify satisfaction and perception of the participants who engaged in an exoskeleton training program for 6-8 weeks.

Fourteen participants with chronic, motor complete SCI enrolled in a locomotor training program for 18 sessions, then completed an electronic questionnaire encompassing 41 statements about satisfaction, learnability, perceived health benefits and risks, as well as motivation to engage in physical activity. Each statement used a visual analog scale of 0 to 100. The mean satisfaction with the Ekso training program exceeded 95% and the positive feedback about the Ekso alone was around 82%. Attributes of the program were rated high (~85%) and ability to learn sit-to-stand and walking activities were rated close to 80%. Health benefits were perceived by 68%. The respondents (91%) also expressed motivation to engage in physical activity.

17. Weight-bearing overground stepping in an exoskeleton with non-invasive spinal cord neuromodulation after motor complete paraplegia

Gad P et al. University of California, Los Angeles. Published in *Frontiers in Neuroscience* June 2017:Volume 11, Article 333.

This is one of the first reports of spinal cord stimulation combined with the use of the EksoGT exoskeleton.

Transcutaneous electrical stimulation, buspirone, and Ekso stepping were used in combination in an individual who had been completely paralyzed for more than 4 years. The study consisted of four phases: baseline, drug only, stimulation only, and drug plus stimulation. All phases were accomplished while using the EksoGT for stepping practice. Three important points regarding the EksoGT were made: 1) The Ekso provided weight-bearing walking with the assistance of only one person, 2) individuals use muscles in their arms, upper body, and trunk while walking, and 3) the patient has to actively use muscles for balance while walking. In addition, the authors found that long-term training resulted in improved synaptic connections that had long been dormant.

18. Gait training after spinal cord injury: safety, feasibility and gait function following 8 weeks of training with the exoskeletons from Ekso Bionics (Pan-Euro Study)

Baunsgaard C et al. University of Copenhagen, Denmark. Published in *Spinal Cord* online at <https://doi.org/10.1038/s41393-017-0013-7>

The Pan-Euro Study was conducted at 9 European Centers and measured safety, efficacy and quality of life in participants with complete or incomplete spinal cord injuries (recently injured or chronic) who trained in the Ekso or EksoGT for 3x a week over 8 weeks.

Fifty-two participants (mean age 35.8 yrs.) who sustained varying levels of acute or chronic injury to the spinal cord (AIS A through D) completed training and follow-up in this multicenter study. Walk modes used included Max, Fixed, and Adapt while training in the Ekso or EksoGT for 24 one-hour sessions (3 times a week for 8 weeks). Heart rate, blood pressure, and the Rate of Perceived Exertion (RPE/Borg test) were measured at each training session. Though the median number of completed sessions was 21 (mean of 2.6 sessions per week), training was considered “complete” if participants walked for a minimum of 16 sessions. Results showed a significant increase in heart rate during the sessions with no significant change in blood pressure. RPE was significantly lower over time. Total up time, walk time, and number of steps increased

significantly from the first training session to the last training session ($p < 0.001$) within all subgroups which included recently and chronically injured, paraplegia and tetraplegia and incomplete and complete injury. There was a significant increase in the number of participants who could walk at baseline vs. at 12 weeks. There were significant improvements in gait speed, balance, and strength (10MWT, TUG, Berg, and LEMS) for those injured < 1 year, and significant improvements in balance (TUG and Berg) for those injured > 1 year. There were no falls and no serious adverse events.

19. Exoskeleton training may improve level of physical activity after spinal cord injury: a case series.

Gorgey AS et al. The Spinal Cord Injury & Disorders Center of Excellence, Hunter Holmes McGuire Veterans Health Administration; Virginia Commonwealth University, United States. Published in *Top Spinal Cord Inj Rehabil*. 2017 Summer;23(3):245-255. doi: 10.1310/sci16-00025. Epub 2017 May 4.

This study examined whether exoskeleton training could improve levels of physical activity by increasing numbers of steps and walking time after SCI.

The study explored whether exoskeleton training once a week for 10-15 weeks could improve levels of physical activity as determined by the duration of exoskeleton walking in persons with SCI. The main outcome measurements were walking time, standing time, ratio of walking to stand-up time and number of steps. Three men with chronic complete and one with incomplete SCI participated in the study. Walking time, stand-up time, number of steps, and ratio of walking to stand-up time increased in all participants. The maximum walking time increased from 12 to 57 minutes and the number of steps increased from 59 to 2,284 steps. By the conclusion of the study, all 4 participants were able to exercise for 26 to 59 minutes. The authors concluded that exoskeleton training for SCI persons may improve physical activity by increasing the number of steps and walking time, as well as possibly increasing energy expenditure and improving body composition.

20. Effect of short-term exoskeleton rehabilitation programme on central blood pressure and arterial wave reflection in patients with spinal cord injury.

Cook, K. et al. Hobbs Rehabilitation, United Kingdom. Presented at the ISCOS Meeting in Dublin, Ireland, 24-26 October, 2017.

SCI patients have been shown to have greater risk of cardiac disease. This study focused on the changes in cardiovascular markers after short-term (5 day) training in the EksoGT.

Six participants (age 30 ± 13 yrs.) with various ASIA classifications and time since injury of 0.5 to 4.5 years underwent 60 minutes of standard physiotherapy before training in the EksoGT for 90 minutes a day over 5 consecutive days. Prior to and after training, Pulse Wave Analysis was used to detect resting BP, arterial stiffness, and heart rate. The authors found that the training in EksoGT reduced arterial stiffness and that larger, randomized trials are warranted due to the higher risk profile of the SCI patient.

21. Effectiveness of exoskeleton training in SCI: preliminary study on metabolic and cardiac responses.

Corbianco, S. et al.: Pisa, Italy. Presented at the ISCOS Meeting in Dublin, Ireland, 24-26 October 2017.

This study explored the metabolic and cardiac effects of SCI participants walking in the Ekso exoskeleton 3 times a week for a total of 20 sessions.

Four participants engaged in the walking program where physiological changes in metabolic and cardiac markers were assessed at baseline and again at the end of training. Measurements included VO_2 , HR, and MET (energy cost of physical activity). Gait speed and performance task load increased over time, but there was no significant change in VO_2 or metabolic activity. The authors concluded that these four SCI participants increased their speed and performance in the Ekso, without significantly increased metabolic demand.

22. Bowel and bladder functions during and after robotic exoskeleton assisted walking overground training in SCI persons.
Stampacchia, G. et al.: Pisa, Italy. Presented at the ISCOS Meeting in Dublin, Ireland, 24-26 October 2017,

In this study of four participants (two paraplegic and two tetraplegic), bowel and bladder functions were assessed before and after walking in the Ekso exoskeleton.

This study focused on visceral improvement in the four participants with ASIA classification A, B, or C (subacute and chronic) who walked in the Ekso exoskeleton for 20 sessions and were tested again 3 months after the last session. All participants improved in neurogenic bowel function between baseline and end of study but most importantly, involuntary bladder leakage was reduced due to the reduction in bladder infections. The authors found the participants expressed an improved quality of life with improvements in pain and spasticity.

23. Increased serum high-density lipoprotein after 36 exoskeleton-assisted walking sessions

Knezevic S, Hong, E, Asselin P, Cornfield S, Cirmigliaro CM, Gorman P, Forrest G, Bauman WA, Spungen AM of the James J. Peters VA Medical Center in Bronx, NY. Published in *Journal of Spinal Cord Medicine* 2017;40(5) - ASCIP 2017 Conference Abstracts published 30 July 2017

SCI patients have been shown to have lower high-density lipoprotein levels and are, therefore, at increased risk of cardiovascular disease. This study centered around the use of exoskeletons as a means to provide high-intensity exercise and measure the impact on HDL-c levels.

Fifteen participants trained for 36 one-hour sessions over 12 weeks using either EksoGT or ReWalk. Serum HDL-c levels were measured at baseline and after training. A minimally clinically important difference (MCID) was considered to be a >2.0 mg/dl change in fasting serum levels. Results showed that more than half reached the MCID level and notably, those that did walked over 10,000 steps more than those participants who did not reach the MCID level. The authors concluded that walking with exoskeletons for 36 sessions may lead to a favorable change in HDL-c levels.

24. Patient-reported bladder management improvements after exoskeletal-assisted walking

Hong E of the James J. Peters VA Medical Center in Bronx, NY. Published in *Journal of Spinal Cord Medicine* 2017;40(5) - ASCIP 2017 Conference Abstracts published 30 July 2017

This on-going study is a randomized, crossover design involving SCI patients that participated in exoskeleton walking sessions and usual activity sessions.

This interim analysis included ASIA A through D participants who were injured at least 6 months prior to enrollment. Bladder management was self-reported at baseline and after 12 weeks of usual activity and after 36 sessions of exoskeleton-assisted walking (EAW) using both the EksoGT and ReWalk devices. The two groups either started with usual care followed by EAW or started with EAW followed by usual care. Results in 14 participants with a mean age of 42 years showed that 50% of the group showed clinical improvement after EAW vs. 14% after usual activity. In fact, 50% of the group showed negative changes after usual activity. The changes were statistically different between groups. After 36 sessions of exoskeleton walking, bladder management improved during sleep and created less concern for the participants.



25. Exoskeleton assisted walking (EAW) in acute rehab following spinal cord injury

McIntosh K and Ho C of the Alberta Health Services, Alberta, Canada. Published in *Journal of Spinal Cord Medicine* 2017;40(5) ASCIP 2017 Conference Abstracts published 30 July 2017

This on-going Canadian Study is a single-arm study involving acute-injury SCI patients who participate in hour-long EksoGT walking sessions 3x a week for up to 25 sessions.

The primary endpoint of this study is the change in vital signs. Safety endpoints include the number of falls and skin integrity issues, pain, and spasticity issues. Secondary endpoints related to efficacy include the 10MWT, 6 Min Walk Test and the Borg rating of perceived exertion. Data involving 8 participants with an average age of 37 and average time since injury of only 10.6 weeks demonstrated the safety and feasibility of exoskeleton walking after an acute spinal cord injury. Early data show that blood pressure trends were not inhibiting participation and there were no falls. Gait-related outcomes show dramatic improvement in all subjects who completed 13 or more sessions.

26. Neuromechanical adaptations during a robotic powered exoskeleton assisted walking session

Ramanujam A, Cirnigliaro CM, Garbarini E, Asselin P, Pilkar R, Forrest GF of the Kessler Foundation, West Orange, NJ. Published online for *Journal of Spinal Cord Medicine*, 2017, and in *Journal of Spinal Cord Medicine*.2018;41(5):518-528.DOI:10.1080/10790268.2017.1314900

This study analyzed the gait parameters and neuromuscular profiles in both able-bodied and SCI participants.

Four participants who had sustained a spinal cord injury (SCI) were compared to four able-bodied (AB) participants in this single-session, cross-sectional study using the Ekso exoskeleton under Max Assist settings. Data collected included temporal-spatial parameters, kinematics, walking velocity and electromyography results. As expected, AB individuals showed a significant reduction in walking velocity ($P < 0.05$) compared to their normal walk speed outside of the Ekso. However, when the AB individuals voluntarily assisted the Ekso, velocity increased to a "slow walk" speed. SCI individuals demonstrated a higher mean percent stance time, and their walking velocity was consistently lower than the AB group ($P < 0.05$). Muscle activation in the SCI group was demonstrated in several lower limb muscles. AB participants demonstrated some differences in phasing amplitudes of EMGs of lower limb muscle activation, primarily greater temporal-spatial response and neuromuscular phasic adaptations. Similarly, neuromuscular phasic adaptations while walking in the Ekso were shown in the SCI group and these were inconsistent to gait muscle activation outside of the Ekso.



27. Effect on body composition and bone mineral density of walking with a robotic exoskeleton in adults with chronic spinal cord injury

Karelis A, Carvalho LP, Castillo MJ, Gagnon DH, and Aubertin-Leheudre M. University of Quebec at Montreal. Published in the *Journal of Rehabilitation Medicine* 2017; 49: 84–87.

This pilot study examined the physiological changes that occurred while training in the Ekso 3 times per week over a 6-week training period.

Five adults with chronic and complete SCI participated in the study. Baseline body composition was measured via dual energy X-ray absorptiometry and peripheral quantitative computed tomography. After 18 sessions of Ekso training (3 times a week for 6 weeks), participants were again measured using the same modalities. Investigators report a significant increase in lean leg and appendicular mass and a corresponding reduction in fat mass. Calf muscle diameter also increased significantly. Bone mineral density of the tibia increased by 14.5% and was considered to be clinically significant. The authors concluded that training with the exoskeleton appears to be associated with improvements in body composition and possibly bone health as well.

2016

28. Training response to longitudinal powered exoskeleton training for SCI

Ramanujam A, Spungen A, Asselin P, Garbarini E, Augustine J, Canton S., Barrance P., Forrest GF of the Kessler Foundation, West Orange, NJ, Published in a book chapter in Springer series titled "Wearable Robotics: Challenges and Trends", 2016, pp 361-366. - https://link.springer.com/chapter/10.1007/978-3-319-46532-6_59

This study examined how exoskeleton training for 5 hours per week for 20 weeks changed gait parameters in chronic SCI participants.

Five SCI participants and two able-bodied controls trained in either the EksoGT or the ReWalk exoskeleton for 5 hours per week over 20 weeks. The outcomes included gait parameters such as Center of Mass excursions, walking velocity, initial double stance time, single stance time, terminal double stance time, and swing time. Outcomes for spatial parameters included step length, step width and stride length. Exoskeleton training was shown to have a significant effect on walking velocity and increased stability. The authors concluded that the study supports the rationale for the increase in robotic exoskeleton velocity for SCI participants who completed their training.

29. Neurorehabilitation in paraplegic patients with an active powered exoskeleton (Ekso)

Milia P, De Salvo F, Caserio M, Cope T, Weber P, Santella C, Fiorini S, Baldoni G, Bruschi R, Bigazzi B, Cencetti S, Da Campo M, Bigazzi P, and Bigazzi M. Neurorehabilitation and Robotic Area, Prosperius Institute, University of Perugia, Umbertide, Italy. Published in *Digit Med* 2016;2:163-8.

This study looked at both the physical and psychological improvements after training in Ekso 5 times per week over a 4-week training period

Thirteen men and women who had suffered either a complete (N=7) or incomplete (N=6) SCI participated in this study. Training was accomplished in all patients during a daily session lasting 45 to 60 minutes, 5 days a week for 4 weeks. The outcome measures included the 6 min walking test (6MWT), the Ashworth scale for spasticity, and various psychological tests (Beck Depression Inventory and Body Uneasiness Test-A). The incomplete SCI patients showed a statistically significant improvement in distance walked on the 6MWT $P < 0.05$. There were no statistically significant changes in the Ashworth Scale scores, but all patients showed improvement in mood and body perception. The authors concluded that the exoskeleton shows promise in both motor and psychological recovery.

30. Development of a clinical decision support system to improve locomotor outcomes in persons with spinal cord injury

Marrocco S, Aman S, Cornell S, Hsieh J, Fielding M, Wolfe D. Parkwood Institute, Western University, Canada; presented at the ISCoS Meeting in September 2016.

This study determined that taking a systematic, integrated approach to rehabilitation with robotic exoskeletons improved quality of care and provided an optimal research methodology to measure improved walking abilities in SCI patients.

The study explored ways to achieve optimal mobility outcomes through development and implementation of a clinical decision support and data management system that integrates key locomotor training principles to better meet individual patient needs. By proceeding systematically through the steps of examining the literature, collaborating internally, trying in practice, collecting data, studying and assessing – clinicians noticed improved walking ability in patients previously thought to have plateaued.

31. Optimizing mobility outcomes across locomotor training modalities: clinical reflection during development of the PRIME algorithm – a case series

Cornell S, Hsieh J, Fielding M, Marrocco S, Wolfe D. Parkwood Institute, Canada; presented at the ISCoS Meeting in September 2016.

This study explored an algorithmic approach to integrate optimal use of locomotor modalities including robotic exoskeletons.

The study explored and developed the Parkwood Program for Rehabilitation Innovation in Movement Enhancement (PRIME) system which is an algorithmic approach to the integrated, optimal use of available therapeutic modalities for locomotor training customized to patient's situations and needs. Three participants who had previously plateaued were staged according to the Canadian SCI Standing and Walking Assessment tool (C-SWAT). An evolving clinical decision-making protocol was formed based on constant reassessment and participants underwent 8 months or more of outpatient therapy guided by the protocol. The protocol involved one or more robotic therapy tools. In all cases, participants used the EksoGT at some point during their rehabilitation, and each improved in their C-SWAT stage.



32. Locomotor training with exoskeleton EKSO-GT in patients with motor incomplete spinal cord injury in a hospital setting- preliminary results

Bonatti E, Baroncini I, Nalon, C, Giovannini T, Falcone R, Mazzoli N, Bonavita J; Montecatone Rehabilitation Institute, Imola, Italy; presented at the ISCoS Meeting in September 2016.

This study explored whether EksoGT may assist in improvement of motor function and evaluated patient satisfaction.

The study explored how patients respond to rehabilitation training with EksoGT. Twenty participants with motor incomplete SCI had rehabilitation cycles using EksoGT, in addition to conventional treatment. Data was recorded at the beginning of the training, on the 12th session and on the 18th session. The 10-meter, 6-minutes, WISCI-II and SCIM-III tests were used to assess gait speed, mobility, kinetics, and endurance in the lower limb. The study also evaluated the degree of safety and tolerability of treatment, and reduction of pain and/or spasticity. Preliminary data showed significant improvement in SCIM Mobility, WISCI II, walking speed, endurance, and quality of life. In addition, the training proved safe and well tolerated, and all patients said they would recommend the use of Ekso in similar situations.

33. Powered exoskeletons and their implementation into the therapeutic approach of German SCI centers

Bergner U. BGU Murnau, Germany; presented at the ISCoS Meeting in September 2016.

This study explored trends in German SCI centers using powered exoskeletons.

The study explored how powered exoskeletons are implemented in physiotherapy treatment settings of German SCI centers. In April 2016, a questionnaire was sent to 24 facilities using exoskeletons in German SCI acute care and rehab centers. The questionnaire surveyed clinical usage and therapy approaches to mobility training. Out of 22 hospitals that returned the survey, 8 of them have exoskeletons and treat an average of 13.5 patients with a powered exoskeleton per year.

34. Effects of overground gait training using the robotic-exoskeleton Ekso™ and assessment of gait parameters using the GAITRite®system: a pilot study.

Arnell M, Svensson P, Nilsson H, Elmgren Frykberg G. Uppsala University Hospital; presented at ISCoS Meeting in September 2016.

This study explored how the Ekso Bionics exoskeleton may be useful in improving patient gait speed, step length and double limb support.

This study explored the effects of robotic gait training with EksoGT on spatiotemporal gait parameters in spinal cord injured persons with gait disorders. The GAITRite® system, a portable gait analysis system was used to measure step length, gait speed, cadence, and double limb support. Two individuals with incomplete tetraplegia received overground gait training using EksoGT for 8 weeks. Assessments were performed before and after the intervention and in a four week follow up with the GAITRite® system. Both participants showed improvement in gait speed, step length and double limb support.



35. A study exploring the clinical effects of a short-duration exoskeleton rehabilitation programme on key physiological markers in spinal cord injury

Luard K, Martinelli L, Hobbs H, Faulkner J. Hobbs Rehabilitation Center, University of Winchester, United Kingdom; presented at the ISCoS Meeting in September 2016.

This study explored the use of the robotic Ekso Bionic exoskeleton in rehabilitation in patients with SCI.

This study explored the effect of a short duration Ekso Bionic exoskeleton rehabilitation program on several physiological outcomes. Four individuals with SCI and ASIA classifications A-C took part in a 5-day training program. Training consisted of daily 1 hour physiotherapy sessions, followed by 1.5 hours of gait training in the exoskeleton. Settings were used to progress the participants from passive (therapist activated) to active gait patterns. Prior to and following the training program, bladder and bowel function, ankle swelling, spasticity, gait parameters and vascular health were measured. All participants increased their walk time over the week, and improvements in bladder and bowel function along with a decrease in peripheral and central systolic blood pressure were observed.

36. Walking with a powered robotic exoskeleton: subjective experience, spasticity and pain in spinal cord injured persons

Stampacchia G, Rustici A, Bigazzi S, Gerini A, Tombini T, Mazzoleni S. The Center for Spinal Cord Injured Persons, Pisa University Hospital, Pisa, Italy; Published in *Neurorehabilitation* 2016 DOI.10.3233/NRE-161358

This study explored the effects of walking with the Ekso exoskeleton on the reduction of pain and spasticity in spinal cord injured persons.

This study included 21 SCI participants who participated in a walking session assisted by a powered robotic exoskeleton. Prior to and after walking, pain and spasticity were assessed using a Numeric Rating Scale (NRS), the Modified Ashworth scale and the Penn scale. Positive and negative sensations were also evaluated using a questionnaire. The patient's global impression of change (PGIC) scale was administered as well. The post-walking assessment showed a significant decrease in muscle spasticity and pain intensity. Questionnaires indicated a good acceptability of the robot-assisted walking. The authors concluded that "overground robot-assisted walking is well accepted by SCI persons and has positive effects in terms of spasticity and pain reduction."

37. Energy expenditure and cardiovascular drift effect During extended bionic walking

Baunsgaard CB, Maher JL, Gerven JV, Palermo A, McMillian DW, Irwin RW, Biering-Sørensen F, Nash MS. The Miami Project to Cure Paralysis, and ²Department of Neurological Surgery and ³Rehabilitation Medicine, University of Miami Miller School of Medicine, Miami, FL; Presented at the American Spinal Injury Association (ASIA) annual conference 2016.

This pilot study observed changes in circulation during acute extended bionic walking with Ekso.

This study included 8 males with traumatic SCI and 5 non-injured controls. Testing was performed for 45 minutes under each of the following conditions; seated rest, standing, and indoor/outdoor bionic walking. VO_2 for all subjects was collected using a portable spirometer, perceived exertion rated (RPE) using the Borg 0-10 categorical-ratio scale, and the following obtained using wireless transthoracic impedance cardiograph (ZCG): Heart rate (HR), stroke volume (SV), and cardiac output (Q). $\% \text{VO}_{2\text{peak}}$ was computed for all timepoints (timepoints 0-1 min, 14-15 min, 29-30 min, 44-45 min). Comparable percentages of work were observed in subjects with SCI and CON when expressed as % of peak capacity. Increase in Q during bionic walking is explained by increased HR. SV decreased during standing in the exoskeleton, probably due to stasis venous pooling, although bionic walking maintains stable SV during extended walking.



38. Exploring the psychosocial impact of Ekso Bionics technology

Brenner L. Rocky Mountain Mental Illness Research, Education, and Clinical Center, Denver, CO. Published in *Archives of Physical Medicine and Rehabilitation*, Vol. 97, Issue 10, e113. Presented at IBIA 2016.

Stearns- Yoder K, Dorsey-Holliman BA, Penzenik M E, Hadidi DA, Lange SM, Hebert JR, Brenner LA. Rocky Mountain Mental Illness Research, Education, and Clinical Center, Denver, CO. Presented at the ACRM Annual Conference, 2016. (Study update.)

This is the first study in the United States that examines the psychosocial impact of walking in the EksoGT.

Nine Veterans (mean age=47 yrs) with lower extremity weakness or paralysis and various levels of function participated in interviews about their daily activities and psychosocial status before and after walking in the EksoGT. A total of 33 questions were asked and related to (1) change in function; (2) burdensomeness; (3) feasibility; and (4) psychosocial benefits. Preliminary results showed that walking in Ekso was meaningful and had benefits related to standing, walking, exercising and remaining eye-level with others with increasing levels of excitement and confidence expressed.

39. Effects on mobility training and de-adaptations in subjects with spinal cord injury due to a wearable robot: a preliminary report

Sale P, Russo EF, Russo M, Masiero S, Piccione F, Calabrò RS, Filoni S. Department of Neurorehabilitation, Hospital Via Alberoni, Venice, Italy; Published in *BMC Neurology* 2016;16:12.

This is a pilot study examining the feasibility and acceptability of robot training for patients with spinal cord injury.

This pre-post design study enrolled three subjects with SCI and gait disorders. All subjects received walking sessions for 45 minutes 3 to 4 times a week for 20 sessions. All subjects showed improvement in gait based on spatiotemporal indexes, including velocity, step length, step width, and the six minute walk test. Participants also completed satisfaction questionnaires. Subjects expressed positive feelings during the training process and felt safe and comfortable with the robot at the end of the training period.

40. Spinal cord injury to learn to use a powered exoskeleton for assisted walking

Kozlowski A, Bryce TN, Dijkers MP. Department of Rehabilitation Medicine, Icahn School of Medicine, Mount Sinai, NY. Published in *Top Spinal Cord Inj Rehabil* 2015;21(2):110–121. doi: 10.1310/sci2102-110

In this study, researchers explored whether individuals with motor complete and incomplete cervical injuries could learn to walk in an Ekso exoskeleton with little or no assistance and observed their perceptions of effort.

The goal of this study was to quantify the time and effort required by persons with SCI to learn to use the first-generation Ekso powered exoskeleton to walk. Participants were given up to 24 weekly sessions of instruction while collecting data on level of assistance, distance and speed, heart rate, perceived exertion, and adverse events. Using the number of sessions required for participants to stand up, walk for 30 minutes, and sit down, initially with minimal and subsequently with contact guard assistance, time and effort was calculated. Of the 7 participants (2 with tetraplegia and 5 with motor-complete injuries), 5 could stand, walk, and sit with contact guard or close supervision assistance, and 2 required minimal to moderate assistance. Walk times ranged from 28 to 94 minutes with average speeds ranging from 0.11 to 0.21 m/s. For all participants, heart rate changes and reported perceived exertion were consistent with light to moderate exercise. This study provides preliminary evidence that persons with neurological weakness due to SCI can learn to walk with little or no assistance and light to somewhat hard perceived exertion using a powered exoskeleton. Persons with different severities of injury, including those with motor complete C7 tetraplegia and motor incomplete C4 tetraplegia, may be able to learn to use this device.

41. Improving gait performance after spinal cord injury: a comparison between conventional physical therapy and therapy using exoskeletons

Kern M, Chang SH, Jennings J, Davis M, Francisco G. TIRR SCI Clinical Exoskeleton Group, Memorial Hermann, University of Texas Health. Presented at the ASIA 2015 and ISCoS 2015 annual conference.

This group of authors presents four case studies to compare the differences between conventional physical therapy and therapy using the exoskeleton.

Two groups of subjects (2 per group) with chronic incomplete spinal cord injury were randomly assigned to either conventional physical therapy (CPT) or robotic exoskeleton therapy (RET) with CPT. All subjects demonstrated improved outcomes in three measures. However, the RET/CPT demonstrated a greater degree of improvement over the CPT alone group.

42. Iron 'ElectriRx' man: overground stepping in an exoskeleton combined with noninvasive spinal cord stimulation after paralysis.

Gad PN, Gerasimenko YP, Zdunowski S, Sayenko D, Haakana P, Turner A, Lu D, Roy RR, Edgerton VR. Published in *Conf Proc IEEE Eng Med Biol Soc*. 2015 Aug;2015:1124-7. doi: 10.1109/EMBC.2015.7318563.

This case study report was one of the first accounts of transcutaneous neural stimulation combined with overground bionic stepping.

An individual who had been paralyzed for < 4 years received spinal stimulation combined with walking using in the Ekso. Spinal cord stimulation assisted in the stepping effort and coordination of the lower limb muscles was improved. This combination produced a continuous smooth stepping motion, an increased cardiac response, and visible effort (sweating). The authors concluded that there was “considerable potential for positive synergistic effects after complete paralysis by combining the overground stepping in an exoskeleton, a novel transcutaneous spinal cord stimulation paradigm, and daily training.”



2014

43. Lower limb bionic exoskeleton for rehabilitation, exercise or mobility. Exploratory case series in persons with chronic, complete spinal cord injury.

Kressler J Thomas CK, Field-Fote EC, Sanchez J, Widerström-Noga E, Cilien DC, Gant K, Ginnety K, Gonzalez H, Martinez A, Anderson KD, Nash MS. The Miami Project to Cure Paralysis, University of Miami, Miami, FL. Presented at the ASIA annual conference, San Antonio, TX, May 2014; published in *Archives of Physical Medicine and Rehabilitation* 2014, Oct;95(10):1878-1887.

This study explored reduction in pain and other responses to overground bionic ambulation in persons with complete spinal cord injury.

Four participants between the ages of 26-38 years with complete SCI (AIS A) between the levels of T1-T10 for less than a year experienced over-ground bionic ambulation (OBA) three days a week for six weeks. Outcome measures were walking speeds and distances, energy expenditure, exercise conditioning effects, neuromuscular cortical activity patterns, and pain severity. Participants reported an average reduction in pain severity over the study period ranging between -1.3 and 1.7 on a 0 to 6 numerical rating scale. Significant changes in exercise conditioning, neuromuscular and cortical activities were not deemed significant. No adverse events were reported.

2013

44. Evaluation of the clinical criteria for safe and efficient use of exoskeletons in individuals with SCI

Jayaraman A. Center for Bionic Medicine and Department of Physical Medicine and Rehabilitation at the Rehabilitation Institute of Chicago, Chicago, IL. Presented at the American Spinal Injury Association (ASIA) conference, 2013

12 patients were enrolled at the time of this presentation in a 12 week study, two visits per week. Some participants walked faster but seemed to have less balance; others walked slower but demonstrated better balance. Six-weeks of training seemed to be a stable point where training leveled off. Larger numbers were deemed needed to predict proficiency which includes different levels of injury, ROM, patient reported and performance-balanced tests.

45. Safety and feasibility of using the Ekso™ Bionic exoskeleton to aid ambulation after spinal cord injury

Kolakowsky-Hayner SA, Crew J, Moran S, Shah A. Santa Clara Valley Medical Center, San Jose, CA. Presented at the Paralyzed Veterans of America conference and at the annual scientific meeting of the International Spinal Cord Society in London, Aug. 2012. Published in *Spine* (2013) S4:003

This was a feasibility study wherein researchers evaluated the safety of the Ekso Bionics 1.0 prototype.

Eight patients with complete T1 SCI or below, within two years of injury were included in this study of safety and feasibility. Patients participated in six weekly sessions with increasing time and decreasing assistance walking in the device. Blood pressure, pain level, spasticity, amount of assistance for don, doff, and transfer, time ambulating, walking time, and skin effects, among other measures were evaluated. Walking in Ekso was found safe for those with complete thoracic SCI in a controlled environment, in the presence of experts, and may eventually enhance mobility in those without volitional lower extremity function. There appeared to be a training effect in the device but further trials were deemed needed. Future studies of bionic exoskeletons as gait training devices are seen as warranted. Future studies of bionic exoskeletons as a clinical tool to alleviate secondary complications should be considered.



2012

46. The potential of the Ekso exoskeleton for affecting long-term health and well-being in the SCI population

Forrest G. Kessler Foundation, presented at the Academy of Spinal Cord Injury Professionals (ASCIP), Sept. 2012

This early study examined the feasibility of using Ekso in a variety of individuals with spinal cord injuries.

An evaluation of 13 patients (12 paraplegia, 1 tetraplegia) participated in the trials to determine the feasibility of innovative applications of technological advances for mobility after spinal cord injury. Dr. Forrest reported that walking and standing in Ekso is feasible for people with a range of spinal cord disorders, reporting it took a bit longer for higher injuries to learn how to use it. There were improvements in function with training using Ekso: Walking speed and distance, fluidity, gait, and balance all demonstrated improvements. Two individuals were evaluated for the potential benefits for heart, lungs, and circulation. Comparing an experienced walker (30 sessions) with a novice, there was evidence of training effects: the experienced user's oxygen consumption, ventilation, and pulse returned to baseline resting values faster. There was also noted increased muscle firing in lower leg muscles, and it was suggested this will need to be studied further.

2018

1. Electromyography assessment during gait in a robotic exoskeleton for acute stroke

Andrewis GJ, Pilkar R, Ramanujam A, Nolan KJ. Human Performance and Engineering Research, Kessler Foundation, West Orange, NJ. Published in *Frontiers in Neurology* 2018 Aug 7;9:630. doi: 10.3389/fneur.2018.00630.

In this study, EMG analysis, including the new technique of Burst Duration Similarity Index (BDSI) were used to measure lower-limb muscle activation when walking with and without the EksoGT.

Traditional and novel techniques for the analysis of bilateral surface EMG data were used in five participants with hemiplegia following an acute stroke. BDSI is a score based on the coordination of on/off timing of the muscle activity when compared with non-injured norms. EMG from single sessions each of traditional inpatient overground gait training and Ekso gait training, showed neuromuscular changes, such as correctly timed amplitude and temporal adaptations during the EksoGT gait training. The affected side showed more closely matched activation patterns when compared to healthy gait, significantly so in the knee extensors of the affected side. In this small study, the authors state that the data suggest that the EksoGT “provides an effective gait training environment” in the acute stroke population.

2. Exoskeleton locomotion training of patients with stroke: our protocol and experience

Foteinopoulos G, Badani E, Mpakogianni S, Fragkaki M, Saramourtsi K. Animus Rehabilitation Center, Rehabilitation, Larissa, Greece. Poster presentation at the ISPRM meeting in Paris, France in July 2018.

This ongoing trial reports early results on 10 patients with stroke ranging in age from 27 to 65 years.

Patients with hemorrhagic and ischemic stroke are participating in exoskeleton walking 2 times per week for 8 weeks. As of the date of this presentation, the average number of sessions per patient is 18. Measurements include standing and walking time, number of steps, the Modified Ashworth Scale for spasticity, and the Oxford scale for strength. Although this study is small thus far, the authors reported improved balance and perception, decreasing spasticity, and enhanced health.

3. The effects of exoskeleton-assisted overground gait training in chronic stroke - a pilot study

Shröder J, Kenis S, Goos K, Truijen S, Saeys W. REVALution Rehabilitation Center, St. Elisabeth Hospital, Herentals, Belgium. Presented at the International Conference on Neurorehabilitation meeting in PISA, October 2018.

This feasibility study examined the effects of 16 additional hours of either robotic exoskeleton training or conventional training in patients with chronic stroke.

Seven ambulatory participants with chronic stroke (average FAC of 4) were allocated to either the EksoGT group or conventional rehabilitation therapy for their additional 16 hours of training during this feasibility study. The EksoGT group (n=3) received 1 hour of training twice a week for 8 weeks, whereas the conventional therapy group (n=4) extended their training for the same period of time in an effort to “dose-match” time in rehabilitation. Measurements of efficacy consisted of walking speed, distance, and symmetry as well as feasibility measurements of motivation, drop-outs, and adverse events. There were no drop-outs or adverse events during the study. Two out of 3 in the EksoGT group met the minimal clinically important difference (MCID) for “small meaningful change” of 0.5 m/s for the 10MWT versus two out of four in the conventional therapy group. All three in the EksoGT group showed improvement in the 6MWT that surpassed the MCID for “small meaningful change” of 20 versus one out of four in the conventional therapy group. Results of the endurance testing was statistically significant (p=0.034) between groups in favor of the EksoGT. No changes were seen in gait symmetry. The authors note that more walking time per session was found in the EksoGT group, which they hypothesize led to the greater improvements in walking speed and distance. They also state that the lack of change in gait symmetry (determined only by

the ratio in L/R step lengths) suggests that these improvements are due to strengthening compensatory strategies. However, these high level participants step length ratios were already close to 1.0 at baseline in both groups.

4. Feasibility of integrating robotic exoskeleton gait training in inpatient rehabilitation

Arnold D, Sikka S, Swank C, Callendar L, Driver S. Baylor, Scott and White Institute for Rehabilitation, Dallas, Texas. Podium presentation at the ASCIP meeting in New Orleans, LA, September 2-5, 2018.

This cross-sectional feasibility study looked at the process, resources, management, and scientific merit of inpatient exoskeleton gait training using the EksoGT.

This study enrolled 16 patients with stroke, but also included 7 patients with SCI and 5 clinicians. Both patients and clinicians were surveyed using qualitative measures. In addition, the patients' electronic medical records were used to extract outcomes data during inpatient hospitalization. Clinician feedback relating to process, resources, management, and scientific merit of EksoGT use improved when comparing the 6 month responses to baseline. Patient survey responses were also highly positive with up to 95% of the patients agreeing that their time was well spent in the EksoGT. The authors recommended that future studies compare the EksoGT to conventional therapy, explore the optimal dosage, and possibly combine Ekso gait training with FES.

5. Shaping neuroplasticity by using powered exoskeletons in patients with stroke: a randomized clinical trial.

Calabrò RS, Naro A, Russo M, Bramanti P, Caroti L, Ballea T, Buda A, Manuli A, Filoni S, Bramanti A. IRCCS Centro Neurolesi "Bonino-Pulejo", Messina, Italy. Published in *Journal of NeuroEngineering and Rehabilitation*. 2018 Apr 25;15(1):35.

This randomized controlled trial compared the effects of robotic exoskeletons versus overground training alone in improving specific gait functions related to the brain's neuroplasticity in chronic stroke patients.

Forty participants aged 55 or older who had experience a first-time ischemic supra-tentorial stroke (avg 10-11 months post) were enrolled in this randomized, prospective study that tested baseline and post training performance in gait speed, walking balance, and daily function, as well as in the following areas related to neuroplasticity: muscle activation pattern, frontoparietal effective connectivity, corticospinal tract excitability, and sensory-motor integration. All participants received 60 minutes of conventional physiotherapy in addition to their assigned gait training. Participants were allocated to 45 minutes of either overground gait training only (OG, n=20) or Ekso gait training (Ekso, n=20).. All participants were trained 5 days a week for 8 weeks. The data at 8 weeks showed that Ekso participants not only met the minimal clinically important difference (MCID) of all the performance measures (compared to the overground group only meeting or approaching the minimal detectable difference – MDD), they showed significantly greater improvements than the overground group in the assessments for neuroplasticity. These results led to the conclusion that combining Ekso gait training with conventional physiotherapy can promote improved mobility and favorable neuroplastic changes in patients with chronic stroke.

6. Automatic setting procedure for exoskeleton-assisted overground gait: proof of concept on stroke population.

Gandolla M, Guanziroli E, D'Angelo A, Cannaviello G, Molteni F, Pedrocchi A. Villa Beretta Rehabilitation Center, (Costa Masnaga, LC) Italy; Published in *Front Neurobot*. 2018 Mar 19;12:10. doi: 10.3389/fnbot.2018.00010.

This study focused on how to customize the gait rehabilitation of individual patients with stroke by defining muscle activation patterns and fine-tuning the Ekso to optimize the patient's gait pattern

Twenty participants (13 patients with stroke and 7 non-impaired controls) were recruited to study the normal vs. abnormal timing and intensity of the lower limbs during walking. Muscle activation was seen as the key factor in reducing maladaptive neuroplasticity and leading to recovery of a more normal gait pattern. The Ekso was fine-tuned based on the function of the

individual. EMG activity from various muscles was collected in both the neurologically impaired individuals and the non-impaired controls. The non-impaired controls served as the reference muscular activation pattern. Using a Gait Metric Index for each walking trial, gait parameters and settings on the Ekso could be changed to more closely match the gait patterns of the non-impaired controls.

2017

7. Wearable robotic exoskeleton for over-ground gait training in sub-acute and chronic hemiparetic stroke patients: preliminary results.

Molteni F, Gasperini G, Gaffuri M, Colombo M, Giovanzana C, Lorenzon C, Farina N, Cannaviello G, Scarano S, Proserpio D, Liberali D, Guanziroli E. Villa Beretta Rehabilitation Center, Valduce Hospital (Costa Masnaga, LC) Italy; Published in *Eur J Phys Rehabil Med* (2017) Oct;53(5):676-684.; doi: 10.23736/S1973-9087.17.04591-9.

This pre-post pilot study enrolled both sub-acute and chronic stroke patients to test the clinical effects of exoskeleton use during rehabilitation training.

Walking rehabilitation training using the EskoGT was conducted in 23 stroke patients, 12 of which were sub-acute and 11 were chronic. Training consisted of 12 one-hour sessions over 4 weeks. Clinical evaluations using the Ashworth Scale, Motricity Index, Trunk Control Test, Functional Ambulation Scale (FAC), 10-Meter Walk Test (10MWT), 6 Minute Walk Test (6MWT), and Walking Handicap Scale were performed at baseline, after the 6th session, and after the 12th session. Statistically significant improvements were demonstrated in both groups, specifically in the Motricity Index, FAC, 10MWT, and 6MWT. Neither group showed a significant change between baseline and 12 weeks in the Ashworth scale. The sub-acute patients showed statistically significant improvement in the Walking Handicap Scale and Trunk Control Test from baseline to 12 weeks. The authors concluded that in both sub-acute and chronic stroke patients, improvement in ambulatory function can be shown after 12 sessions of gait-training with the Ekso exoskeleton.

8. Use of the Ekso Bionics exoskeleton robotic assisted mobility device with acute rehabilitation patients: preliminary results.

Flaherty V, Anderson C, Ball K, Furman K, Brady S; Marionjoy Rehabilitation Hospital, Wheaton, IL. Presented at the AMRPA in Chicago, IL, October 2017.

This prospective, non-randomized study utilized a pre-post design to evaluate functional changes in acute rehabilitation patients who used the EksoGT.

Thirty-one participants qualified for this study due to paralysis or lower extremity weakness. Though SCI and TBI patients were included, the largest number of participants had experience a stroke (n=22). The mean number of treatments was 5.2 (range 3-11) over a time period ranging from 5 to 64 days. The 10 Meter Walk Test pre/post changes were significantly better (p=0.001) and participants showed improved FIM scores (transfer and locomotion, p≤0.001). With the significantly positive functional changes shown during this acute rehabilitation period, the authors concluded that the “up-time” and increased steps afforded by the use of the device had value in neuroplastic training and neuroplastic changes leading to ambulation recovery.



9. Is a structured exoskeleton overground gait training program superior to traditional care in individuals affected by chronic, severe stroke?

Hohl K, Deems-Dluhy S, Mummidisetty CK, Jayaraman A. Rehabilitation Institute of Chicago, Chicago, IL; Poster presented at AAP 2017.

This study examines whether a high dose regimen in an exoskeleton produced better outcomes in stroke patients when compared to traditional gait therapy.

Twenty-two chronic, severe stroke patients were divided into two parallel training groups that were matched based on gait speed at screening and gender. Twelve participants used the EksoGT for overground gait training and ten performed standard overground gait training (SOC). Each group trained for one hour, three times a week for six weeks, then two times a week for a period of four weeks. The Ekso group was approximately 8 years older on average, and chronicity was 50% longer compared to the SOC group. The authors noted that the first 9 visits (3 weeks) produced the greatest changes in outcomes. Both groups improved significantly in walking speed and balance. When the Ekso group was stratified based on low number of steps vs. high number of steps, there was no difference in outcomes. The authors concluded that walking in the exoskeleton can improve mobility in those chronically and severely impaired patients who have suffered a stroke.

2016

10. Gait training with Ekso in ischemic chronic stroke patients: effects on the timing of muscle activation and metabolic activation of the prefrontal cortex

Simbolotti C, Molteni F, Guanziroli E, Iacovelli C, Padua L, Cicetti S, Caloi M, Caliendo P. Valduce Hospital, Villa Beretta Rehabilitation Center, Costa Masnaga, Italy. Published in *Gait & Posture* 2016;49(1): S27-S28.

Twenty-three chronic stroke participants walked with and without Ekso while measurements of metabolic activity and sEMG were analyzed.

In this study, participants walked 18 meters with and 18 meters without the EksoGT. Muscle activation during spontaneous gait was used to set the EksoGT parameters. After all sessions were conducted, the authors concluded that Ekso induced improved timing of muscle activation in all but a few cases. Those few cases that did not improve were thought to either require improved settings of the EksoGT or that there was an inability of the CNS to activate the affected limb muscles. Prefrontal cortex activation was found to be unrelated to muscle timing.

11. Neuromuscular pattern of the lower limbs of hemiparetic stroke patients during overground gait training: acute changes induced by a wearable exoskeleton

Molteni F. Villa Beretta Rehabilitation Center, Valduce Hospital (Costa Masnaga, LC) Italy; Presented at the Congregazione Delle Suore Infermiere Dell'Addolorata Ospedale Valduce 2016.

This study looks at the neuromuscular patterns and the changes that take place in acute and chronic stroke patients when they use an exoskeleton for overground training.

Fifty-one stroke patients (50% acute) were enrolled. The Oxfordshire Community Stroke Project (OCSP) Classification for cerebral infarction and Knutson's Classification for neuromuscular patterns were used to classify each patient. A sEMG of muscles rectus femoris, hamstrings, tibialis anterior and soleus of both limbs was collected during over-ground walking both in standard condition and with Ekso; results of these tests are categorized and presented in this poster. The aggregate results show that using Ekso overground affects the time and intensity of the neuromuscular patterns in both acute and chronic stroke patients.



2015-2016

12. Benefits of Ekso as a gait training device for post stroke patients during inpatient rehabilitation

Nolan K. Kessler Institute for Rehabilitation, West Orange, NJ; Presented at AAP 2015.

Utilization of a robotic exoskeleton to provide increased mass practice for gait training and its impact on discharge destination for individuals with acute stroke

Russo A, Endersby K, Perret M, Kesten A, King M, Chervin K, Nolan KJ. Kessler Institute for Rehabilitation, West Orange, NJ; Presented at International Stroke Conference 2016

This exploratory investigation of the use of the robotic exoskeleton to provide increased dosing of gait training.

Fifteen participants with acute stroke underwent gait training with Ekso during inpatient rehabilitation in conjunction with traditional therapy. Participants ambulated over level surfaces with PT assistance. A matched sample of participants (n=15) was selected from a hospital database (matching criteria: length of stay, admission motor FIM, age, gender and affected side). The data was analyzed using independent sample and paired sample t-tests. Participants in the RE group walked an average distance of 212 feet in traditional PT where gait training was provided and 551 feet in RE sessions ($p=.033$). Discharge destination for the RE group: 10 home; 3 subacute; 2 nursing facility and for the matched sample: 13 home; 2 subacute. Motor FIM scores significantly increased from admission to discharge: RE group ($p\leq.001$) and matched group ($p\leq.001$). Motor FIM gain at discharge in the RE group significantly increased compared to the matched sample, 26.4 ± 6.4 vs. 21.6 ± 5.9 , ($p=0.044$).

2014

13. Quantifying gait outcomes in chronic stroke using robotic training protocols

Angacian G; Presented as a Burke Summer Student Poster - 2014

This early feasibility study examined the effects of combining upper and lower extremity robotic training.

6 chronic stroke subjects (4 Ischemic and 2 Hemorrhagic, age range 53 to 83 years old) that presented some degree of gait dysfunction were allocated into one of two intervention groups: 1) combined therapy consisting of 1.5 hours of intensive repetitive exercise using the Ekso™ followed by 1 hour of upper arm robotic therapy, or 2) 1.5 hours of intensive repetitive exercise using the Ekso. Participants received robotic training 3 times per week for a total of 4-weeks. Outcome measures were recorded at baseline and post the 4 week training intervention. Both groups improved in all gait parameters tested, and there were statistically significant differences in two of the gait parameters: an increase in both stride length ($p=0.03$) and walking velocity while using the Ekso™ ($p=0.04$), as well as a positive trend in overground gait velocity and a decrease in double support phase percentage that were also noteworthy

Meta-Analysis and Review Papers

1. Heinemann AW, Jayaraman A, Mummidisetty CK, Spraggins J, Pinto D, Charlifue S, Tefertiller C, Taylor HB, Chang SH, Stampas A, Furbish CL, Field-Fote EC. **Experience of robotic exoskeleton at four spinal cord injury model systems centers.** *J Neurol Phys Ther.* 2018 Oct;42(4):256-267. doi: 10.1097/NPT.0000000000000235.

Thirty clinicians from four spinal cord injury centers took part in focus groups with a court reporter recording the discussions. In summary, they reported that they use exoskeletons in outpatient and wellness settings most of the time though one of the four used them in an inpatient setting. In general, they used two staff members for each of 20 to 30 sessions. Standardized assessments are used for the measurements of standing, stepping and gait training. They reported improvement in gait parameters, physiological, psychosocial, and social benefits with few potential risks. The group expressed that there is an urgent need to increase the clinical evidence that would guide clinicians and patients in the use and integration of robotic exoskeletons into the rehabilitation setting..

2. Gorgey AS. **Robotic exoskeletons: the current pros and cons.** *World J Orthop.* 2018 Sep 18;9(9):112-119. doi: 10.5312/wjo.v9.i9.112. eCollection 2018 Sep 18.

This review paper discussed the benefits and limitations of robotic exoskeletons, as well as the need for additional clinical evidence. In addition, Dr. Gorgey expanded the discussion to include several emerging technologies that may help to address some of the current limitations. He cited 28 ongoing clinical trials of exoskeleton use in patients with SCI and how these trials are designed to address the current limitations and maximize the benefits of robotic exoskeletons.

3. Jayaraman A, Burt S, Rymer W. **Use of Lower-Limb Robotics to Enhance Practice and Participation in Individuals With Neurological Conditions.** Published in *Pediatric Physical Therapy* 2017, 29 S48-S56.

The authors of this review paper discussed the currently available technology with a focus on wearable robots, exoskeletons, and treadmill-based training devices. They stated that preliminary data shows that some patients may experience benefits of robotic training, specifically when used with conventional therapy, and these could result in improved function of the lower limbs, as well as a more normal gait. Unfortunately, the data at this time are limited but they believe that the technology will become more prevalent.

4. Onose G, Cârdei V, Craciunoiu S, Avramescu V, Opris I, Lebedev M, Constantinescu M. **Mechatronic wearable exoskeletons for bionic bipedal standing and walking: A new synthetic approach.** Published in *Front. Neurosci.*, 29 September 2016 | <https://doi.org/10.3389/fnins.2016.00343>.

This article reviewed the robotic wearable exoskeletons from the viewpoint of the health professionals, manufacturers, and consumers. In reviewing the current literature, they highlighted the improvements needed in the technology and use of exoskeletons, and noted that a multitude of smaller studies and case series exist, but more data are needed. They cited several important points about exoskeletons including the requirement that the system must be safe, wearable, psychologically acceptable, and able to be used for a long time so that people can use it in the community. It should produce very little noise, be affordable, and cost effective. The article then described the available exoskeletons on the market and cited the literature devoted to some of the studies using the various brands. Further, they presented recommendations for future development, including miniaturization, wearability beneath clothing, and optimization of actuators and sensors.

5. Molteni F, Gasperini G, Cannaviello G, Guanziroli E. **Exoskeleton and end-effector robots for upper and lower limbs rehabilitation: narrative review.** Published in *PM&R* 2018;10(9):S174-S188. DOI: <https://doi.org/10.1016/j.pmrj.2018.06.005>

This article describes end-effector and exoskeleton devices for both upper and lower limb rehabilitation. The article includes a literature search of the meta-analysis papers and randomized, controlled trials (RCTs) that include both stroke and SCI participants. In stroke patients, the results regarding the efficacy of overground powered exoskeletons were sparse and included few patients. However, a notable statement regarding a Cochrane Review by Merholz et al. is as follows: "People in the first 3 months after stroke and those who were not able to walk seemed to benefit most from robotic intervention." In regards to the SCI trials, Nam et al. stated that the data on acute and sub-acute (<6 months) injuries showed improvements in distance, strength, mobility, and independence when robotic gait training was compared to conventional gait training. This present article progresses to a discussion of "fine-tuning and tailored treatments," then moves to a description of how the devices aid neuroplasticity and body perception. They describe how the engagement of the user during robotic sessions leads to an "intensity of intention" and state that, "Psychological states such as intention, motivation, and engagement are known to be critical for the success of rehabilitation." The authors recommend that, "Robotic treatment should be considered a rehabilitation tool useful to generate a more complex, controlled multisensory stimulation of the patient and to modify the plasticity of neural connections through the experience of movement." The authors conclude that it is time to engage in "large and innovative research programs."

6. Palermo A, Maher JL, Baunsgaard CB, Nash MS. **Clinician-focused overview of bionic exoskeleton use after spinal cord injury.** Published in *Top Spinal Cord Inj Rehabil*. 2017 Summer;23(3):234-244. doi: 10.1310/sci2303-234.

This review paper discusses the current availability of various devices, as well as the clinical evidence regarding the benefits and limitations of robotic exoskeletons. In particular, the paper focuses on the patient who has sustained an incomplete spinal cord injury and the potential benefits of early intervention. The authors note that there were few adverse events reported across 14 studies and that manufacturers' limitations and recommendations for assistive devices vary widely making it difficult to streamline the inclusion/exclusion criteria in clinical studies. Due to the variations between devices, the authors recommended that studies conducted in the future employ techniques and designs such as randomization and controlled crossover and consider a narrower inclusion/exclusion criteria. They acknowledged that overground bionic stepping with upper body support has been achieved in SCI and concluded that "early evidence points to improvements over earlier braces and walking systems when testing the energy needed to ambulate."

7. Holanda LJ, Silva PMM, Amorim TC, Lacerda MO, Simão CR, Morya E. **Robotic assisted gait as a tool for rehabilitation of individuals with spinal cord injury: a systematic review.** Published in *Journal of NeuroEngineering and Rehabilitation* (2017);14:126.

The authors of this systematic review compared all available robotic exoskeletons for lower limb ambulation. After agreeing to the inclusion criteria, two reviewers chose 39 articles describing 12 robotic systems with published results up through October 2017. After compiling and reviewing these articles, they concluded that walking in a robotic exoskeleton provides benefits to cardiorespiratory, musculoskeletal, intestinal, sensory, neural, urinary, and psychological functions and systems. They specifically mention the promotion of neuroplasticity and reduction of secondary complications and conclude that robotic assisted gait training is an "innovative and effective therapy for the rehabilitation of individuals with SCI".

8. He Y, Eguren D, Luu TP, Contreras-Vidal JL. **Risk management and regulations for lower limb medical exoskeletons: a review.** Published in *Med Devices* (Auckl). 2017 May 9;10:89-107. doi: 10.2147/MDER.S107134.

This narrative review of the “state of the art” discusses the FDA-cleared exoskeleton devices and the challenge of both the developing regulatory science and industry standards. The authors searched PubMed, Clinicaltrials.gov, and the MAUDE database to look for adverse events as well as the prevailing inclusion and exclusion criteria for the various studies. Both the inclusion/exclusion criteria and the adverse event reports were found to be very diverse. The authors then compared current regulations, regulatory procedures and standards for the medical device applications in the U.S., Europe and Japan. The authors advised increased awareness of the probable risks and the development of standards and regulations.

9. Esquenazi A, Talati M, Jayaraman A. **Powered exoskeletons for walking assistance in persons with central nervous system injuries, a narrative review.** Published in *PM&R* (2017); 9(1): 46–62; [http://www.pmrjournal.org/article/S1934-1482\(16\)30879-6/abstract](http://www.pmrjournal.org/article/S1934-1482(16)30879-6/abstract).

This literature review provides a comparison of different exoskeletons (ReWalk, Indego, Ekso, Exo-H2, REX, HAL/HAL-3, ROBIN, Mina, WPAL, MindWalker) and discusses their development, key features, and functionality. The authors describe how variable assist software allows the therapist to adjust the level of assistance that the device provides to accommodate the requirements of the user. In addition, the authors point out that in recent conferences, data presented indicate improved walking speed, distance, gait, and balance of individuals with spinal cord injury. The authors discuss their personal experiences with the exoskeletons and predict their widespread use in the future after more long-term studies are completed.

10. Miller LE, Zimmerman AK, Herbert WG. **Clinical effectiveness and safety of powered exoskeleton-assisted walking in patients with spinal cord injury: systematic review with meta-analysis.** Published in *Medical Devices: Evidence and Research* (2016);9:455–466.

A review of 14 studies (8 using ReWalk™, 3 using Ekso™, 2 using Indego®, and one unspecified exoskeleton) amassing data in 111 patients were included. Training programs were set up three times a week for 60–120 minutes per session during a period of 1–24 weeks. The majority of studies used flat ground for training. Upon completion of training, 76% of patients were able to ambulate with no physical assistance. The weighted mean distance for the 6-minute walk test was 98 m and physiologic demand of powered exoskeleton-assisted walking was 3.3 metabolic equivalents. The perceived exertion was 10 on the Borg 6–20 scale which is comparable to self-reported exertion of an able-bodied person walking at 3 miles per hour. Improvement in spasticity was reported in 38% and improvement in the regularity of bowel movements was reported in 61% of patients. There were no serious adverse events reported. The incidence of fall at any time during training (tethered) was 4.4%, and did not result in injury. Bone fractures during training occurred at a rate of 3.4%. Risks have since been mitigated with later generation exoskeletons and changes to patient eligibility criteria. The authors concluded that “exoskeletons allow patients with SCI to safely ambulate in real-world settings at a physical activity intensity conducive to prolonged use and known to yield health benefits.”

11. Contreras-Vidal JL, Bhagat NA, Brantley J, Cruz-Garza JG, He Y, Manley Q, Nakagome S, Nathan K, Tan SH, Zhu F, Pons JL. **Powered exoskeletons for bipedal locomotion after spinal cord injury.** Published in *J. Neural Eng* 13 (2016) 031001; <http://iopscience.iop.org/article/10.1088/1741-2560/13/3/031001/pdf>.

This systematic review of 8 powered exoskeletons (Bionic Leg, EksoGT, HAL, Indego, Kinesis, ReWalk, WalkTrainer, WPAL) cited 22 studies that were analyzed based on their protocol design, subject demographics, study duration, and primary/secondary outcome measures for assessing the exoskeleton's performance in SCI subjects. The results showed that the level of injury varies across studies, with T10 injuries being represented in 45.4% of the studies. Outcome measures



varied across studies, and none had measures spanning every category, making comparisons difficult. However, there was an emphasis on ambulatory-related primary outcome measures. The authors predict that the use of the exoskeleton in rehabilitation centers and at home will result in significant growth of the worldwide market.

12. Louie DR, Eng JJ, Lam T and Spinal Cord Injury Research Evidence (SCIRE) Research Team. **Gait speed using powered robotic exoskeletons after spinal cord injury: a systematic review and correlational study.** Published in the *Journal of NeuroEngineering and Rehabilitation* (2015;12:82).

Published abstract: Powered robotic exoskeletons are an emerging technology of wearable orthoses that can be used as an assistive device to enable non-ambulatory individuals with spinal cord injury (SCI) to walk, or as a rehabilitation tool to improve walking ability in ambulatory individuals with SCI. No studies to date have systematically reviewed the literature on the efficacy of powered exoskeletons on restoring walking function. Our objective was to systematically review the literature to determine the gait speed attained by individuals with SCI when using a powered exoskeleton to walk, factors influencing this speed, and characteristics of studies involving a powered exoskeleton (e.g. inclusion criteria, screening, and training processes). A systematic search in computerized databases was conducted to identify articles that reported on walking outcomes when using a powered exoskeleton. Individual gait speed data from each study was extracted. Pearson correlations were performed between gait speed and 1) age, 2) years post-injury, 3) injury level, and 4) number of training sessions. Fifteen articles met inclusion criteria, 14 of which investigated the powered exoskeleton as an assistive device for non-ambulatory individuals and one which used it as a training intervention for ambulatory individuals with SCI. The mean gait speed attained by non-ambulatory participants ($n = 84$) while wearing a powered exoskeleton was 0.26 m/s, with the majority having a thoracic-level motor-complete injury. Twelve articles reported individual data for the non-ambulatory participants, from which a positive correlation was found between gait speed and 1) age ($r = 0.27$, 95 % CI 0.02–0.48, $p = 0.03$, 63 participants), 2) injury level ($r = 0.27$, 95 % CI 0.02–0.48, $p = 0.03$, 63 participants), and 3) training sessions ($r = 0.41$, 95 % CI 0.16–0.61, $p = 0.002$, 55 participants). In conclusion, powered exoskeletons can provide non-ambulatory individuals with thoracic-level motor-complete SCI the ability to walk at modest speeds. This speed is related to level of injury as well as training time.

13. Jayaraman A, Burt S, Rymer WZ. **Using robotic exoskeletons for over-ground locomotor training**, a chapter in *Neurorehabilitation Technology*, Springer 2016: 493-511.

This chapter compares the current exoskeletons on the market, specifically Ekso, ReWalk, HAL, Honda Stride Management Assist, NASA-IHMC Mina, and REX. Notably, prolonged use in the complete-SCI population showed potential therapeutic benefits including the return of sensory and motor function in some study participants. The research on FES combined with Ekso is also discussed.

14. Gorgey A, Abdelrehim Z. **Exoskeletons and rehabilitation after spinal cord injury**, presented at the ISCoS Meeting in Vienna, Austria. September 2016.

This presentation provided a comparison of 4 exoskeletons' (Ekso, ReWalk, Indego, Rex) key features, their functioning, their maximum speed, and other variables. The study explored how the wearable robotic exoskeletons available for persons with SCI differ. PubMed, Medline, Google scholar and Wikipedia were reviewed to identify published and unpublished materials about exoskeletons. The study determined that each exoskeleton offers a variety of features for SCI users and can accommodate different levels of injuries.



15. Federici S, Meloni F, Bracalenti M, De Filippis ML. **The effectiveness of powered, active lower limb exoskeletons in neurorehabilitation: a systematic review.** Published in *NeuroRehabilitation* 37 (2015) 321-340.

The authors of this early systematic review that examined published articles from 2001 through 2014 concluded that the studies conducted to date were primarily an evaluation of safety of the devices and investigations into the physical and cognitive effort required to use the devices. In addition, the studies usually focused on the learning curve and gait enhancement. The authors stated that the studies confirmed the safety of HAL, Tibion Bionic Technologies, and Ekso devices when used in controlled environments. Due to the 2014 cutoff of this systematic review, it included details from earlier Ekso Bionics technologies such as the Human Universal Load Carrier (HULC) and eLegs, followed by a reference to one published clinical study (Kolakowsky-Hayner, 2013).

Many studies are too small to show statistical significance. Ekso Bionics™ does not make any claims about the potential benefits of the use of Ekso. ©2016 Ekso Bionics. All rights reserved. 0614BCRSU