EKSO GT™ CLINICAL RESEARCH

SUMMARY OF FINDINGS

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Ekso Robotic Exoskeleton Research Synopsis

Research with Ekso is expanding internationally, and data is amassing quickly. Currently, 44 studies have been completed or are ongoing: 28 are completed, 16 are ongoing; 19 in North America and 25 in Europe, Middle East, and Asia (EMEA); and 4 are multi-center. These studies include the following diagnoses: spinal cord injury (SCI) (28), stroke (10), multiple sclerosis (2), cerebral palsy (1), and multiple diagnoses (4). Total target enrollment is over 1,000 participants, with over 450 completed to date. Several trials are scheduled to start in 2017. Six SCI studies and one stroke study have been published with several more in both diagnoses expected in 2017. Ekso has been included in five published review articles[1-5] and one book chapter.[6]

Spinal Cord Injury

Of the 27 studies with SCI, 17 are completed (n=202); 10 are ongoing (target n=384); 14 in North America and 13 in EMEA. Several early studies demonstrated the feasibility of Ekso, reporting on its positive progression in amount of walking (n=86), good safety (n=76), and learning curve (n=7).[2,7-14] Notably, the PanEuro study found significant increases in "Up time," "Walk time," and number of steps in participants with acute and chronic paraplegia or tetraplegia following a training protocol of 3x/wk for 8 weeks (n=52).[7] They noted skin irritation as a safety issue. Kozlowski et al. found that 6 of 7 participants with a variety of SCIs could perform sit to stand and walk with minimal assist in a median of 8 sessions, and 5 of 7 could walk with contact guard assist or close supervision in a median of 15 sessions while training 1-2x/wk for up to 2 hours each session.[11] The cardiorespiratory effort of walking in Ekso is reported to be that of light exercise (25-40% peak VO_2, n=11)[10,15] at 2.6 METS (n=8),[16] equivalent to a person without SCI walking at 2.0 mph. On the other hand, the user may also be challenged by reduced assistance from Ekso, thereby increasing muscle activity (n=5)[17] and increasing HR and VO_2 (n=10).[18] Baunsgaard et al. studied cardiovascular measures and verified increased circulation while walking in Ekso.[15] Based on users' reports, standing in Ekso required only slight effort and walking in Ekso required only light or very light effort (n=8).[15] Thus, users can reap the benefits of walking with reduced fatigue.

Six trials reported gait outcomes as measured while walking in Ekso, mostly for those with *complete* SCI.[8,10,11,19-21] They showed increased gait speed (n=21)[8,10,11,14,19,20] and timed walking distance (n=23),[8,10,11,19,21] as well as improved balance (n=14)[8,19] during walking in Ekso. Gait parameters have been studied showing significantly increased cadence and bilateral step lengths in Ekso after 20 sessions, 3-4x/wk (n=3).[19] Ramanujam et al. determined that increased step and stride lengths and decreased stance time were highly correlated to increased gait speed in exoskeletons (n=7).[20] These researchers tracked the center of mass of participants with SCI during walking in the Ekso (n=5), showing closer and more symmetric stability around midline, as well as more efficient weight shifts after high dosage training (avg of 87 hrs).[20] Ekso is able to activate trunk musculature below the level of injury in those with complete SCI (n=6),[22] adding to their postural control of weight shifts in Ekso. EMG data from the lower extremities (n=7)[20] and trunk (n=6)[22] showed that those with more volitional activity have faster speeds while walking in Ekso. In those with *incomplete* SCI, Ekso targets muscle activation of proximal lower extremity muscles (n=10).[18] Gait speed in this group measured outside of the device pre-post training has also been shown to significantly increase (n=29);[17,23,24] specifically, Bonatti et al. reported a significant average increase from 0.26m/s to 0.40m/s in 20 people with sub-acute to early chronic incomplete paraplegia after 18 sessions with Ekso GT.[23] This speed is nearly 3 times faster than the average speed from 3 earlier studies that used Ekso 1.1 (0.14 m/s) (n=17).[1] Bonatti's group's speed approximates the threshold for limited community walking for SCI (0.44 m/s) and surpasses the minimal clinically important difference (MCID) for slow walkers with SCI (0.15 m/s).[25] Significant improvements in timed walking distance (n=24)[23,24] and functional balance (n=4)[24] have also been shown.

Ekso has been reported to ameliorate a myriad of secondary complications following SCI and increase quality of life. Two studies have shown significantly increased muscle volume and reduced intramuscular fat in chronic SCI (n=13).[17,26] Lower extremity strength (n=5+)[17,21,27] and bone density (n=6)[26,27] have also been shown to improve. Participants have reported significantly reduced pain (n=18)[10,11,19,27,28] and pain medication use (n=2)[11,27] and reduced spasticity (n=32),[9,11,12,21,28] with some having trained 1-3x/wk for 5-20 sessions, but about half having only walked in Ekso for one session. Participants have also reported improved bowel and bladder function (n=15)[11,12,21,27] and improved sleep (n=5).[10,11] Participants have reported improved mood and motivation with Ekso training (n=6)[21] and satisfaction with using Ekso (n=35).[11,16,23] Notably, participants have reported significantly improved quality of life after 18 sessions (n=20).[23] Through interviews, Stearns-Yodel et al. gave a voice to veterans with SCI using Ekso (n=8), extolling the psychological benefits of being upright and walking: appreciation of upright interactions with others, reduced anxiety and anger, and feelings of control, accomplishment, and hope.[29]

Stroke

Of the 10 studies with stroke, 7 have been completed (n=323); 3 are ongoing (target n=129); 4 have been or are being conducted in North America and 6 in EMEA. Several studies have shown the feasibility, safety, and positive progression in Ekso in the acute and chronic stroke populations (n=127).[30-32] Nolan et al. showed that participants in inpatient rehabilitation had a 150-200% increase in dosage (average distance walked) during Ekso training sessions (550-620 ft) compared to standard PT sessions in historical matched controls (n=15)[30] or compared to their own standard PT sessions (n=29)[31] (~215ft). The most notable difference in dosage came at the first sessions (431 ft in Ekso vs. 7 ft in standard PT).[31] When compared to gait training in standard PT, training in Ekso also allowed for more normal stepping via improvements in gait parameters:[31,33] increased stride lengths (n=11), single stance time (n=5), and swing time (n=5) with decreased double stance time (n=11) and step width (n=5) on both affected and unaffected legs. Motion capture showed weight shifts to be more centered with better symmetry of steps, while EMG showed more normal, distinctive lower extremity muscle bursts from the user (n=5).[31] An extensive EMG study by Molteni et al. stated that Ekso can modulate the timing and intensity of the muscle activity during walking in both acute and chronic stroke groups (although their use of highly constrained trajectories allowed participants to walk with greatly reduced muscle activity) (n=51).[34] A case study has shown improved midline alignment of center of pressure and improved bilateral lower extremity strength over 4 weeks of training (n=1).[35] This more normal gait pattern, more centered static and dynamic postures, enhanced strength, and higher dosage may enhance functional outcomes. Participants from both Nolan et al. studies (n=44)[30,31] had an average admission FIM score of about 27; however, those 15 participants who trained in Ekso had a significantly greater increase from admission to discharge scores of 27 points when compared to the historical controls' increase of 22 points (n=15).[30]

Ekso has been shown to increase gait speed (n=42)[32,33,35,36] and walking distance (n=35)[32] in people with acute and chronic stroke. Researchers presented preliminary data comparing Ekso training (n=12) and standard PT gait training (n=8) in participants with chronic stroke 2-3x/wk for 26 sessions.[32] They found that those using Ekso increased their gait speed by 0.07 m/s to 0.24 m/s when walking outside Ekso at their self-selected speed compared to an increase of 0.06 m/s to 0.20 m/s for those in standard PT.[32] Both groups met the "substantial meaningful change" MCID of 0.14 m/s for stroke.[37] However, when asked to walk as fast as possible, those using Ekso significantly increased their speed by 0.11 m/s to 0.32 m/s, compared to an increase of 0.04 m/s to 0.23 m/s for those in standard PT.[32] The endurance of those using Ekso was only improved by 14.5 m to 91.4 m during walking over 6 minutes, compared to an increase of 43.8 m to 110 m for those in standard PT.[32] Notably, the PT performing the training stated that they trained in short spurts in Ekso, not long distances. Both groups improved their balance scores similarly, but remained at increased risk for falls.[32] However, those using Ekso were more confident that they could complete daily tasks without falling.[32] Participants with stroke have also reported they were more positive and motivated about their recovery when using Ekso (n=4).[38] Finally, a new study published online in January, 2017 has added to the positive outcomes in people with sub-acute (n=12) and chronic (n=11) stroke after a training protocol of 3x/wk for 4 weeks in Ekso.[36] Statistically significant improvements were found in gait speed, walking distance, lower extremity strength, and ambulatory function for both groups, but not spasticity.[38] Moreover, statistically significant improvements were found in trunk control and home/community ambulation in the sub-acute group.[36]

Future Directions

The immediate future of Ekso research is to determine the effectiveness of a training protocol (3x/wk for 12 weeks) on gait, secondary complications, and PT burden as compared to standard physical therapy for those with incomplete SCI. The company-sponsored, multi-center, RCT WISE trial began in 2016. Pilot studies have already begun for a similar study to be conducted in stroke this year. We also plan to optimize its use in clinics by determining the most efficient dose and how to integrate it into therapy. A collaborating site in Canada has created a software algorithm to determine how best to use their gait training technology.[39] When they incorporated Ekso with their standard interventions, they saw "improved walking ability in patients previously thought to have plateaued."[40]

Combining therapies often results in improved outcomes. Researchers at UCLA combined transcutaneous spinal cord stimulation (tSCS) with Ekso gait training for 5 sessions in one person with complete SCI to successfully evoke volitional lower extremity movement (even outside of the device), perspiration, and cardiovascular control.[41] Brain stimulation before or during Ekso training via transcranial direct current (tDCS) or magnetic field (TMS) may be another way to augment outcomes. Despite the intervention, assessments of brain activity (EEG) and/or muscle activity/motor control (EMG) will be critical to future studies to show neuroplastic changes in the brain and spinal cord. We must understand these mechanisms underlying functional changes and relate them to participant characteristics of responders and non-responders to optimize Ekso's use in neurorehabilitation.

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