Author’s response to reviews

Title: Exoskeleton-assisted Gait Training to Improve Gait in Individuals with Spinal Cord Injury: A Pilot Randomized Study

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Author’s response to reviews:

We would like to thank the reviewers for providing thoughtful comments and suggestions. We have made our best effort to incorporate reviewers’ suggestions and address the practical issues for better future study designs. Please see attached the detailed point by point response to the generous comments.

Reviewer Comments

Abstract

1. Please change the aim to one of feasibility (delete effect which is for testing in main trial) and add some specific feasibility objectives ie. ‘This pilot study investigated the feasibility of offering exoskeleton-assisted gait training (EGT) in addition to conventional physical therapy (CPT) on gait performance in individuals with incomplete spinal cord injury (iSCI) in preparation for a Phase III RCT. The objectives were to ….’ (these should include potential efficacy)

Response: As suggested by the reviewer we have modified the content in the abstract.
2. In the methods include how many people were screened and eligible before saying how many consented and were randomised.

Response: The screening and consent information has been added. Please see page 2.

3. In the results please delete ‘and unpaired t-tests were used for inter-group differences’. The results on such a small sample are better presented as mean difference estimates with 95% confidence intervals (for paired and unpaired data as appropriate). Please point out the baseline imbalance due to small numbers.

Response: As suggested by the reviewer we have deleted the phrase ‘and unpaired t-tests were used for inter-group differences’ and reported the results as mean difference estimated with 95% confidence intervals. We have only reported the mean difference estimated of the within group comparison. Inter-group comparison was not performed due to the modest sample-size.

4. Please put some of the feasibility findings in the conclusion. What were the lessons learned?

Response: The feasibility findings have been added. Please see page 2.

Main text

Methods

5. Page 4/5 please state the aims and objectives clearly as a coherent whole starting with the primary feasibility objectives (assessing patient eligibility, baseline assessment, randomization process, treatment reliability and post assessments) and then potential efficacy as a secondary outcome.

Response: As suggested by the reviewer, we have rewritten the aims and objectives focusing on the feasibility as the primary objective and potential efficacy as the secondary objective. Please see page 4.

6. There is detail missing from the methods – please see CONSORT extension and add more detail.

For example:
Page 5 where were individuals recruited from and how? Setting, dates etc. How and who consented them?

Response: As suggested by the reviewer, we have added the screening and consent information under the sub-section titled “Design, Setting and subjects” page 5.

7. No methods are given for how the feasibility objectives will be carried out. Please add.

Response: As suggested by the reviewer we have added a sub-section on feasibility objective in the methods and explained how they would be performed. Please see page 7.

8. Please insert a separate subsection describing the randomisation process (who did it, how it was done etc) before the Training Protocol section. Blinding etc.

Response: As suggested by the reviewer we have modified the heading of the sub-section “Training protocol” to “Randomization and training protocol” and added the description of the randomization process. Please see page 6.

9. Page 6 what do ‘don’ and ‘doff’ mean?

Response: Don means to put on and doff mean to take off. In the text it refers to the subjects putting on the device and taking it off with the assistance of the physical therapist.

10. Please give a sample size rationale before the statistical analysis section in the methods.

Response: As suggested by the reviewer we have added the sample size rationale in the sub-section statistical analysis. Please see page 8.

11. Hypothesis tests are not recommended in the CONSORT extension. Please use confidence interval estimation in presenting results. If hypothesis tests are also to be used then please give a rationale as to why. Were baseline imbalances adjusted for? The numbers are too small to give much credibility to hypothesis testing.

Response: As suggested by the reviewer we have reported the mean difference estimates with 95% confidence intervals. We have removed the paired and un-paired t-test results. Please see page 8.
Results

12. Please start with giving the number recruited, eligible, consenting etc. and then address the feasibility objectives before the measurements.

Response: As suggested by the reviewer we have begun the results section by stating the number of subjects recruited, eligible and who consented. Please see page 9. Also, we have added the information on the feasibility objectives before reporting the measurements. Please see page 9.

13. Please put 95% CIs in the tables rather than p-values. P-values are not needed or should be used with caution (with a cautionary caveat).

Response: As suggested by the reviewer we have modified the tables and reported 95% CIs. P-values have been removed.


Response: We have modified the subheading from ASIA LEMS to LEMS but added the ASIA (written in full) in the description of the sub-section. Please see page 7.

15. Results should be presented with the randomised groups as the columns.

Response: As suggested by the reviewer all tables have been modified with randomized groups as columns. Please see Table 1, 2 and 3.

16. What does PD in Table 2 mean? Footnote.

Response: PD is the percentage difference. However, we have removed the PD as it not being used in the confidence interval calculation.

Discussion

17. Please start with a full discussion of the feasibility objectives and whether they were successful. Please see CONSORT extension. These are not limitations but the main focus of the study.
Response: As suggested by the reviewer we have included a discussion on the feasibility objectives. Please see page 12-13.

18. There are many exclusion criteria how has this affected your recruitment results? Do these need amending for a main study?

The current exclusion criteria is mainly for subject safety consideration and seems appropriate and may not need amendment as they have not considerably affected our recruitment results. However, we have highlighted a few areas that could be modified to potentially increase the recruitment criteria.

1. For our protocol, the SCI patients were supposed to have an injury at or above T12 level and be classified as AIS C or D. However, for a SCI patient to be classified as AIS C or D the injury level may not necessarily always be at or above T12, therefore this could be modified to include patients with AIS C or D regardless of the level of injury as long as the upper limb function is sufficient to use assistive device during walking.

2. The subjects were excluded if they received any physical therapy intervention within 3 months, as a wash-out period, prior to enrollment in the study. This criteria may be relaxed to reduce the time to one or two month rather than 3 months.

3. In the EGT protocol, gait training with exoskeleton requires adequate upper body strength to use crutches or walker for balance support and safety. As the training is done in a clinical environment, the use of body weight support system for gait training could help replace the use of walker or crutches. This could potential relax the inclusion criteria, i.e. individuals with reduced upper body strength could also be recruited.

19. Please check all grammar thoroughly – the following were found in the introduction.

Page 3 line 26 ‘in the nervous system’ (grammar).

Line 33 ‘One of the most commonly seen examples of task specific training’. Please correct grammar.

Line 38 ‘a large number’.
Line 42 ‘have been suggested to’.

Line 44 ‘A study by..’.

Page 4 line 3 ‘…principles, over ground gait training with body weight support features from exoskeleton robotic devices should be considered.’

Line 16 ‘joints’.

Line 23 ‘of walking with wearable exoskeleton devices…’

Line 32 ‘engages’

Line 41 ‘potential efficacy’ (insert potential)

Line 50 ‘populations’

Line 54 ‘that lead’

Line 56 ‘who were’

Response: The suggested changes in the grammar have been made and highlighted in blue.