Author's response to reviews

Title: Pilot study of locomotion improvement using Hybrid Assistive Limb in chronic stroke patients

Authors:

Hiroaki Kawamoto (kawamoto@iit.tsukuba.ac.jp)
Kiyotaka Kamibayashi (kamibayashi@iit.tsukuba.ac.jp)
Yoshio Nakata (kamibayashi@iit.tsukuba.ac.jp)
Kanako Yamawaki (yamawaki.kanako.ge@u.tsukuba.ac.jp)
Ryohei Ariyasu (ariyasu@ccr.tsukuba.ac.jp)
Yoshiyuki Sankai (sankai@kz.tsukuba.ac.jp)
Masataka Sakane (sakane-m@md.tsukuba.ac.jp)
Kiyoshi Eguchi (kyeguchi@md.tsukuba.ac.jp)
Naoyuki Ochiai (ochiainaoyuki@ob.md.tsukuba.ac.jp)

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Author's response to reviews: see over
Prof Timothy Shipley  
Executive Editor,  
BMC Neurology  
BioMed Central  
236 Gray's Inn Road  
London WC1X 8HB  
United Kingdom  

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Pilot study of locomotion improvement using Hybrid Assistive Limb in chronic stroke patients  

Dear Prof Shipley  

Thank you for your email dated September 21, 2013 regarding our manuscript as well as the valuable comments of the editor and the two reviewers. Enclosed please find our revised manuscript, as well as point-by-point responses to the editor’s and the reviewers’ comments. The responses consist of the following,  

1) RESPONSE TO EDITORIAL COMMENTS (regarding informed consent)  
2) RESPONSE TO REVIEWER 1  
3) RESPONSE TO REVIEWER 2  

Moreover, because of substantial progress in this study since we submitted the manuscript on 10 August 2012, we have unified and added patients and further enriched the results. Further, we have changed the title to “Pilot study for locomotion improvement using Hybrid Assistive Limb in chronic stroke patients” in order to better emphasize the focus of the study, which is the improvement of locomotion function due to HAL.  

We feel that the revised manuscript is a suitable response to the reviewers’ comments and is significantly improved over the initial submission. We trust that it is now suitable for publication in the BMC Neurology.  

Thank you in advance for your kind consideration of this paper.  

Sincerely yours,  

Kiyoshi Eguchi, MD  
Department of Rehabilitation Medicine, Faculty of Medicine  
University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8575, Japan  
Tel: +81-29853-3795 Fax: +81-29853-7047  
E-mail address: kyeguchi@md.tsukuba.ac.jp
RESPONSE TO EDITORIAL COMMENTS:

Thank you for your insightful comments. Text that has changed or been added in accordance with your comments have been highlighted in yellow within the revised manuscript.

Comment 1: After assessing your manuscript, we note that you have presented individual clinical details in table 1. In your revised manuscript you must clarify whether patients provided written informed consent for the publication of individual clinical details.

Response: We appreciate the editorial comment on this point. All patients provided written informed consent for the publication of their individual clinical details before participating in the study, which was approved by the institutional review board of the University of Tsukuba.

To make this point clearer, we have changed the following text in the Introduction from (line 160–163):

“All patients provided informed consent before participating in the study, which was approved by the institutional review board at the University of Tsukuba.”

to

“All patients provided written informed consent, including allowing the publication of individual clinical details, before participating in the study, which was approved by the institutional review board at the University of Tsukuba.”

Comment 2: If this consent was not obtained, then all individual data must be removed from your manuscript, Please note that we will not be able to proceed further with your manuscript until this point has been fully addressed.

Response: This point is not applicable to our trials because the consent was obtained.

Thank you for your valuable comments.
RESPONSE TO REVIEWER 1

Thank you for your insightful comments, which have helped us significantly improve the paper. Text that has changed or been added in accordance with your comments have been highlighted in yellow within the revised manuscript. We have unified and added patients and enriched the results according to the comments of Reviewer 2, who suggested that we focus on uniform groups of patients. Further, we have achieved substantial progress in this study since we submitted the manuscript on 10 August 2012. Text changed or added because of the enriched results is highlighted in blue. Moreover, we have changed the title to “Pilot study for locomotion improvement using Hybrid Assistive Limb in chronic stroke patients” in order to better emphasize the focus of the study, which is the improvement of locomotion function due to HAL.

Comment: This study aims to investigate the effects on gait recovery of patients with chronic study using an ambulatory exoskeleton (HAL) during rehabilitation. The main problem of this study is the absence of a control group of patients performing conventional therapy for the same amount of time of the experimental group. I would suggest to the authors to include a control group, train it with conventional therapy focused on walking recovery for 8 weeks, 2 days at week, and then re-submit the study. Due to the high heterogeneity of experimental group (ischemia, haemorragia, moyamoya...), control group should at least roughly match the features of experimental one. There are problems also with statistics and the application of the protocol (8 weeks?) is unclear. So, despite I judge positive the work using HAL, there are many issued that should be faced:

1) ADD CONTROLS
2) CHANGE STATISTICS USING NON PARAMETRIC TESTS
3) EXPLAIN INCONGRUENCES BETWEEN METHODS AND RESULTS

Response:
We appreciate your interest in adding controls to this study. However, because this study aimed to investigate the feasibility of locomotor training with HAL and obtain the preliminary data needed before controlled trials could be conducted, we consider that the inclusion of controls unnecessary at this point; therefore, we wish to retain the original study design.

To make this point clearer, we have changed the following text in the Introduction from (line 125–126):

“Therefore, we conducted a pilot clinical trial to examine the effectiveness of locomotor training with the HAL in chronic stroke patients.”
"We conducted a pilot clinical trial to investigate the feasibility of locomotor training with the HAL in chronic stroke patients."

Similarly, we have changed the following text in the Abstract from (line 32–34):

“We performed a pilot clinical trial to evaluate the effectiveness of locomotor training using the HAL in chronic stroke patients.”

to

“We performed a pilot clinical trial to investigate the feasibility of locomotor training using the HAL in chronic stroke patients.”

Moreover, in accordance with your comment on statistics, we have used Wilcoxon’s test.

Accordingly, we have changed the following text from (lines 240–242):

“To determine the effects of locomotor training with the HAL, the outcome measures were compared between pre- and post-training using paired Student’s t-tests.”

to

“To evaluate the feasibility of locomotor training using the HAL, the outcome measures were compared between pre- and post-training using a paired Wilcoxon’s test.”

Further, we agree with the reviewer that the application of the protocol is unclear. In this study, locomotor training with HAL consisted of 16 sessions. However, the weekly sessions were tolerated by the patients at a frequency of 2 days/week for 8 weeks. Thus, the locomotor training for some patients was not completed by 8 weeks’ time for personal reasons or pain (all of the patients completed all 16 sessions.)

Therefore, we have changed the following text in the Methods from (lines 166–167):

“All patients underwent 16 sessions of locomotor training using the HAL over 8 weeks.”

to
“All patients underwent 16 locomotor training sessions using the HAL within 2 days/week as tolerated by each patient.”

Similarly, we have changed the following text in the Abstract from (lines 38–39):

“All patients were trained with the HAL in 16 sessions (20–30 min/day on 2 days/week for 8 weeks).”

to

“All patients were trained with the HAL over 16 sessions (20–30 min/day within 2 days/week).”

Further, since we focused on patients with hemiplegia and have increased the number of patients, we have changed the following text in the Results from (line 254):

“The mean duration of the intervention period was 10.6 ± 4.3 weeks in all patients.”

to

“The mean duration of the intervention period was 10.8 ± 3.5 weeks in all patients.”

**Special Comment 1:** This sentence “Patients with impaired walking ability caused by lower-limb paralysis often become dependent on a wheelchair or may even be bedridden.” needs a reference. For example Paolucci et al. 2008.

**Response:** Thank you for this comment. We have added the following reference and have cited it in this sentence (line 65).


**Special Comment 2:** In the Introduction, authors differentiated between exoskeleton and end-effector and between treadmill needing the assistance of 1-2 therapists vs. robots needing less assistance. However, in my opinion, it is important also to introduce the differentiation between ambulatory vs. non ambulatory robots. HAL system is an ambulatory robots allowing patients to walk overground or in more natural environment than devices such as Lokomat or Gait Trainer that performed a simulated walking on a treadmill and in place (not moving around). In this, HAL seems to be closer to physiological gait, and authors should highlight it.
Response: We strongly appreciate your comment on this point.

One of the major differences between other exoskeleton and the HAL is use in an actual ambulatory environment such as a flat floor because the HAL is a wearable system.

Therefore, we have added the following text as one of the differences of HAL (lines 115–119):

“In addition, the other exoskeletons are designed for walking on a treadmill; therefore, they provide a simulated gait that differs from that of walking on a flat floor. In contrast, as a wearable system, the HAL delivers locomotor training in an actual ambulatory environment.”

Special Comment 3: Being the scores of clinical scales ordinal and not continuous, non-parametric statistics should be used (also for the small sample size). So Wilcoxon’s test should be used instead of Student’s t-test.

Response: As mentioned above, we have used a paired Wilcoxon’s test.

Accordingly, we have changed the following text from (lines 240–242):

“To determine the effects of locomotor training with the HAL, the outcome measures were compared between pre- and post-training using paired Student’s t-tests.”

to

“To evaluate the feasibility of locomotor training using the HAL, the outcome measures were compared between pre- and post-training using a paired Wilcoxon’s test.”

Special Comment 4: It is unclear the sentence “The mean duration of the intervention period was 10.6 ± 4.3 weeks in all patients” when in Methods section it has been declared that the protocol lasted 8 weeks. In general it seems from Results that each rehabilitative pathway has been tailored also in length on patient’s needs and not planned before.

Response: The reviewer's comment is correct. In this study, locomotor training with HAL consisted of 16 sessions. However, the schedule of 2 days/week for 8 weeks was tolerated by most patients. As a result, the locomotor training for some patients was not completed at 8 weeks because of personal reason or pain (all of the patients completed all 16 sessions.)
Therefore, we have changed the following text in the Methods from (lines 166–167):

“All patients underwent 16 sessions of locomotor training using the HAL over 8 weeks.”

to

“All patients underwent 16 sessions of locomotor training sessions using the HAL within 2 days/week as tolerated by each patient.”

Similarly, we have changed the following text in the Abstract from (lines 38–39):

“All patients were trained with the HAL in 16 sessions (20–30 min/day on 2 days/week for 8 weeks).”

to

“All patients were trained with the HAL over 16 sessions (20–30 min/day within 2 days/week).”

Further, since we have focused on patients with hemiplegia and increased the number of patients, we have changed the following text in the Results from (line 254):

“The mean duration of the intervention period was 10.6 ± 4.3 weeks in all patients.”

to

“The mean duration of the intervention period was 10.8 ± 3.5 weeks in all patients.”

**Special Comment 5:** In discussion authors introduced the problem of passive vs. active robotic rehabilitation, relating it to motor learning. Discussion would benefit from introducing the concept of bottom up vs. top down rehabilitative approaches.

**Response:** We wish to express our deep appreciation for your insightful comment on this point.

We agree that introducing the concept of bottom up vs. top down as the reviewer suggested would be valuable. Accordingly, we have revised the following text from (line 311–327):
“This study mainly focused on locomotor training. The effectiveness of voluntary drive has been demonstrated in motor learning studies [29, 30]. Comparisons between active training with voluntary drive and passive training without voluntary drive have been reported. For example, Lotze et al. [30] evaluated changes in motion performance and activation in the motor cortex after active or passive training for wrist movements in healthy individuals. Active training led to a greater improvement in performance and greater activation compared with passive training. Training programs based on motor learning principles, such as repetitive task-specific training, are now being applied to rehabilitation. Considering the benefit of voluntary drive on motor learning, it seems likely that active training is more effective than passive training for rehabilitation.”

to

“In recent years, a top-down down approach has emerged as a new rehabilitative methodology. Belda-Lois et al. defined this approach as rehabilitation therapies based on the state of the brain instead of the bottom-up approach, which acts on the physical level [40]. The top-down approach is considered highly promising from the viewpoint of neurorehabilitation because it promotes neuroplasticity. This approach is mainly applied in functional electrical stimulation, assistive robotic devices, and brain–computer interfaces that use myoelectric or brain activity during the patient’s volitional control. Locomotor training using the HAL is based on the top-down approach. The HAL assists motion by myoelectric activity on the basis of the patient’s voluntary drive. The voluntary drive and thus the motion normalized by the assistance provided by the external device forms the foundation for a proprioceptive feedback loop for patients with lesions involving the sensory pathways. The neural activity associated with voluntary drive and normalized motion while repeatedly and intensively executing specific tasks promotes learning [41] and then leads to the reinstatement or restructuring of appropriate proprioceptive feedback. This mechanism explains the therapeutic effect of locomotor training using HAL as one of these top-down approaches.”

We have also added the following reference.


Thank you again for your valuable comments.
RESPONSE TO REVIEWER

We wish to express our appreciation to you for your insightful comments, which have helped us significantly improve our paper. Texts changed or added in accordance with your comments is highlighted in yellow in the revised manuscript. Moreover, we have unified and added patients and enriched the results in accordance with the reviewer who suggested focusing on uniform groups of patients, and we have achieved substantial progress in this study since we submitted the manuscript on 10 August 2012. Text changed or added because of the enriched results has been highlighted in blue. Moreover, we have changed the title to “Pilot study of locomotion improvement using Hybrid Assistive Limb in chronic stroke patients” in order to describe the improvement of locomotion function due to HAL in this study.

Major Compulsory Revisions

Comment 1: “Locomotor training based on gait motion has been suggested for task-specific training programs aimed at restoring walking ability [3-5]”. These references are too old, there are few more recent papers about task-specific motor learning.

Response: We wish to thank the Reviewer for this comment. We have changed the old references from:


To


Comment 2: “Indeed, body weight-supported treadmill training is widely used in clinical practice”. Please add references
Response: We regret this oversight. Accordingly, we have changed the following text in the Methods from (lines 72–73):

“Indeed, body weight-supported treadmill training is widely used in clinical practice.”

to

“Indeed, body weight-supported treadmill training is widely used in clinical research.”

Moreover, in accordance with your comment, we have added the following reference (lines 72–73).


Comment 3: Please try to clarify which are the differences between the still available exoskeleton and HAL.

Response: We appreciate your comment on this point.

HAL significantly differs from other exoskeletons in its voluntary drive and ambulatory performance.

Therefore, we have added the following text to explain the differences between other exoskeletons and HAL (lines 109–119):

“HAL has advantages of voluntary drive and ambulatory performance. The other exoskeletons use autonomously generated predefined motion for users. In contrast, HAL generates motion according to the wearer’s voluntary drive. The wearer operates the HAL by adjusting his/her muscle activities. Therefore, the HAL is able to conduct locomotor training by providing motion support in response to user’s voluntary drive. This assistance mechanism is completely different from those of the other exoskeletons. In addition, the other exoskeletons are designed for walking on a treadmill; therefore, they provide a simulated gait that differs from that of walking on a flat floor. In contrast, as a wearable system,
the HAL delivers locomotor training in an actual ambulatory environment.”

**Comment 4:** Reference 22 refers to paraplegic patient. Please try to justify the rationale behind the hypothesis that HAL could be also useful for stroke subjects

**Response:** We appreciate the reviewer’s comment on this point. In our previous study, we investigated the feasibility of rehabilitation training using the HAL for patients with limited mobility including chronic stroke [31]. The results showed significantly improved gait speed after HAL training in nine stroke patients. Consequently, we hypothesized that HAL could be useful for rehabilitation training in patients with chronic stroke.

Therefore, we have added the following text to the Background (lines 119-121):

“Kubot et al. reported that for patients with limited mobility including chronic stroke, gait speed increased after gait training with the HAL [31]. In this study, gait speed increases were significantly for 9 patients with chronic stroke.”

Moreover, we have changed the following text in the Background section for consistency around the sentences (lines 122–123):

“However, it is still uncertain how effective HAL based training is in terms of improving walking ability or balance,”

to

“However, the feasibility of HAL-based training for improving walking ability or balance, and its benefits for patients with chronic stroke are unclear;”

Further, we have also added the following reference.


**Comment 5:** in the background authors declare 10 stroke patients, while in this paragraph “Eight patients had hemiplegia, one had quadriplegia, and one had ataxia.”. This is not a uniform group.

**Response:** In accordance with your comment, we have focused on hemiplegia patients. We also increased the number of
patients with hemiplegia because the study has been promoted while reviewing the paper.

Therefore, we changed the following text in the Methods from (lines 131–132):

“Ten stroke patients (8 men and 2 women) participated in the study (Table 1). ”

to

“Sixteen stroke patients with hemiplegia (12 men and four women) participated in this study (Table 1). ”

Moreover, we have changed the following text in the Abstract from (lines 38):

“Ten stroke patients with the chronic phase participated in this study”

to

“Sixteen stroke patients in the chronic stage participated in this study”

Finally, we have deleted the item "Paralysis type" from Table 1 and added “Side of paralysis”, and indicated L (Left) or R (Right) for each patient as appropriate.

Comment 6: Inclusion criteria are not well specified

Response: We agree that this point requires clarification, and have added the following text to the Methods (lines 152–156):

“The inclusion criteria were as follows: requirement of physical assistance or assistive devices for standing up, sitting down, and/or walking; understanding an explanation of the study protocol and expressing voluntary consent; a body shape that could fit in the robotic suit HAL (height, 150-180 cm; weight ≤80 kg); and concurrent use of physical and occupational therapies.”

Moreover, we have deleted the following text from the revised manuscript since we realized there was a small typo in the minimum and maximum patient height:

“Because of the design of the HAL, only patients with a height of 145–185 cm could participate.”
Comment 7: Table 1: please add some informations about clinical features of each patient such as Barthel Index and about Trunk control and sitting balance, by using Trunk Control Test. Furthermore, if the objective is to evaluate gait performances, it is useful to classify patients according to a validated clinical scale used for stroke subjects, such as Functional Activity Ambulation (FAC). Also data about the degree of pain, the degree of muscle activity, such as Manual Muscle Test, or the degree of spasticity, by means of Modified Ashworth Scale, are not reported.

Response: We agree that additional information (Barthel Index [BI] and Functional Ambulation Category [FAC]) on each patient’s clinical features would be valuable. Regrettably, however, because Trunk control, sitting balance, the pain, degree, and spasticity degree were not measured, we are unable to show these clinical features. However, we have added the BI and FAC to Table 1, and deleted "Ambulatory status" from Table 1, replacing with FAC.

Comment 8: Last paragraph: How do you quantify the “limiting the range of motion of the lower limb, and severe spasticity.”? Which is the threshold value for range of motion and for spasticity? Do you use some clinical scales, such as Ashworth?

Response: We set the threshold value for range of motion and spasticity using some clinical scales. For severe contractures limiting range of motion, loss of hip or knee extension of >20°, or severe spasticity, the Modified Ashworth Scale is >3.

Accordingly, we have changed the following text from (lines 158–160):

“severe contractures limiting the range of motion of the lower limb, and severe spasticity.”

to

“severe contractures limiting the range of motion of the lower limb (loss of hip or knee extension >20°), and severe spasticity (Modified Ashworth Scale score >3).”

Comment 9: As concerns body weight, the body weight reduction was different between patients? The phrase “the patient's body weight was partially unloaded using the suspension system” indicate different level of suspension.

Response: Thank you for this pertinent comment.
The amount of body weight support was independently adjusted for each patient. Therefore, different levels of suspension were provided depending on each patients’ gait condition. As a guide, we increased the level of suspension as tolerated without excessive knee flexion during the stance phase or toe dragging during the swing phase.

In accordance with your comment, we have changed the following text from (lines 172–174):

“When excessive knee flexion during the stance phase or toe dragging during the swing phase was observed, the patient’s body weight was partially unloaded using the suspension system.”

to

“The level of suspension was independently adjusted for each patient and increased as tolerated without excessive knee flexion during the stance phase or toe dragging during the swing phase.”

Comment 10: Please clarify if patients underwent other rehabilitation therapies or not.

Response: All patients, except for Cases 7, 8, and 15 underwent conventional rehabilitation or exercise instruction before this study.

In accordance with your comment, we have added the following text from (lines 143–145):

“All patients, except for Cases 7, 8, and 15 underwent conventional rehabilitation or exercise instruction before this study.”

Comment 11: “When excessive knee flexion during the stance phase or toe dragging during the swing phase was observed, the patient’s body weight was partially unloaded using the suspension system.” In table are reported in detail for the 10 patients data about body weight unloading during training sessions. According to the literature body weight unloading is a key point for the effectiveness of rehabilitation, such as the “walking speed and distance” that are modified for each subject according to “patient’s tolerance”. Also these data are missing.

Response: Thank you for this comment.

We agree with you that the body weight unloading would be one of the important parameters influencing the effectiveness of body weight-support treadmill training.
In many studies, the amount of weight support was provided in a wide range. This parameter was mainly determined on an individual condition to provide as much body weight support as needed to optimize the walking pattern, enable or comfortable walking, or used as tolerated without substantial knee bucking or toe dragging. Therefore, modifications to vary among studies and across patients within individual studies,

In this study, we used tolerance without excessive knee flexion or toe dragging as a strategy to adjust body weight unloading, although we are not able to show the data quantitatively (lines 172–174).

Moreover, in this study, we investigated the feasibility of locomotor training with the assistive robot device that provides the motion assistance while a patient voluntary operates it. We will investigate the relationship between HAL training and the amount of weight support and intend to report it in a later paper.

**Comment 12:** “Blood pressure and heart rate were measured at the start and end of each training session, and during the rest periods. At the end of each session, the patients stated their fatigue level after training and their level of satisfaction with the robotic assistance during movement.” How these parameters are quantified? No results are reported also for the level of satisfaction.

**Response:** The patients’ fatigue level after training as well as their level of satisfaction were quantified using the visual analog scale. We measured these parameters, including blood pressure and heart rate, to assess the physical condition of patients and safely conduct the training. Therefore, we did not report these parameters in the Results section since they were not related to the outcome measures.

In accordance with the reviewer's comment, we have changed the following text from (lines 188–191):

“At the end of each session, the patients stated their fatigue level after training and their level of satisfaction with the robotic assistance during movement.”

to

“At the end of each session, the patients stated their fatigue level after the training as well as their level of satisfaction with the robotic assistance during movement using visual analog scales.”

**Comment 13:** Please add some clinical scales such as FAC, 6 Minute Walking Test, some data about Physiological Cost Index, the level of Mood, Motivation, Satisfaction
Response: We agree that the addition of the clinical scale information would be valuable and show the effectiveness and methodology of HAL. However, this study aims to investigate the feasibility of locomotor training with HAL because it is still uncertain whether HAL based training improves the locomotor performance of patients with chronic stroke. Therefore, first of all, as a clinical scale of walking ability in this feasibility study, we selected walking speed, an important indicator of function that is related to function and quality of life following stroke, and evaluated the number of steps and cadence, the factors that determine speed. Moreover, we evaluated BBS and TUG (which also include walking speed and other multiple factors), which are often used to evaluate balance ability. Regrettably, FAC, gait endurance (6 Minute Walking Test and Physiological Cost Index) and subjective estimate (levels of mood, motivation, and satisfaction) were not measured at this clinical study (feasibility) stage. We will evaluate these suggested scales at the next clinical study stage to investigate the effectiveness of HAL training.

Comment 14: No distribution data analysis have been performed, but it has to be done according to the population enrolled into the study. No patients for the control group have been enrolled.

Response: We strongly appreciate your comment on this point.

Accordingly, we performed a distribution data analysis. The following figure shows a frequency distribution of baseline walking speed data for the patients (n = 15). Our findings indicate that the enrolled population cannot be presumed to be normally distributed. Therefore, in this study, the outcome measures have been compared between pre- and post-training using Wilcoxon’s test. Moreover, this study intended to investigate the feasibility of locomotor training using the HAL with chronic stroke. Therefore, we wish to retain the original study design that does not include control group.

Comment 15–1: According to my opinion, results section is too much poor, due to the reduced number of parameters/data collected. No crucial clinical scales have been used, as reported above. Furthermore a goal of the study is to define the improvement of balance performances, but besides BBS, no instrumental assessment, such as stabilometry,
has been used. In line with these missing data, also discussion section is without an high degree of consistency.

Response: We appreciate your comment on this point. As stated above, this study was designed to investigate the feasibility of locomotor training with HAL. We evaluated waking speed, cadence, and number of steps as powerful indicators of walking ability. Moreover, as clinical scales of balance ability in the feasibility study, we have evaluated BBS and TUG (which also include walking speed and other multiple factors). In this study, we showed significant difference of BBS score between before and after the HAL training. We would need to further investigate the factor of balance ability using stabilometry. In this feasibility study, we believe that a detailed balance evaluation using stabilometry is not necessary; therefore, we wish to retain the original evaluation design (BBS and TUG).

Comment 15–2: Furthermore, without a control group, even if patients have chronic lesion is not possible to conclude “walking ability may be improved by the HAL”.

Response: Your comment is correct. We have conducted this study as a feasibility study.

Accordingly, we changed the following text in the Abstract from (lines 32–34):

“We performed a pilot clinical trial to evaluate the effectiveness of locomotor training using the HAL in chronic stroke patients.”

to

“We performed a pilot clinical trial to investigate the feasibility of locomotor training using the HAL in chronic stroke patients.”

Similarly, we changed the following text in the Abstract from (lines 55–56):

“This pilot study showed that the locomotor training with the HAL improves walking ability of chronic stroke patients.”

to

“This pilot study showed that the locomotor training using the HAL is feasible for chronic stroke patients.”

Additionally, we changed the following text in the Introduction from (lines 125–126):

“Therefore, we conducted a pilot clinical trial to examine the effectiveness of locomotor training with the HAL in chronic stroke patients.”
“We conducted a pilot clinical trial to investigate the feasibility of locomotor training with the HAL in chronic stroke patients,”

Moreover, we changed the following text in the Discussion from (lines 280–281):

“The aim of the present study was to investigate whether locomotor training using the HAL would improve walking ability and balance function in chronic stroke patients.”

to

“The aim of the present study was to investigate the feasibility of locomotor training using the HAL for improving walking ability and balance in chronic stroke patients.”

Similarly, we have changed the following text in the Discussion from (lines 342-343):

“As a result, the walking ability might be improved through the HAL training.”

to

“As a result, the locomotor performance differed significantly before and after the HAL training.”

Further, we changed the following text in the Conclusion from (lines 356-357):

“In this study, we observed significant improvements in the walking ability of chronic stroke patients following HAL-assisted locomotor training which provides the motion controlled by the user’s voluntary drive.”

to

“In this study, we confirmed the feasibility of HAL-assisted locomotor training for chronic stroke patients.”

Comment 15–3: Furthermore the sentence “…HAL generates torque that is varied according to the bioelectrical signal generated when the wearer exerts force. The HAL user controls the voluntary drive to accomplish walking motion. This control is performed by a perceptual feedback based on visual and/or proprioceptive sense” is not discussed and it’s not
clear how the user can voluntary drive the HAL. Also the concept of visual and/or proprioceptive feedback is not clearly discussed.

Response: To make this point clearer, we have changed the following text in the Discussion from (line 332–339):

“By contrast, the HAL generates torque that is varied according to the bioelectrical signal generated when the wearer exerts force. The HAL user controls the voluntary drive to accomplish walking motion. This control is performed by a perceptual feedback based on visual and/or proprioceptive sense.”

to

“In contrast, HAL generates assistive torque according to the amount of the bioelectric signals generated the user’s voluntary muscle activities. The user obtains motion assistance while simultaneously operating HAL on the basis of the user’s voluntary drive [32]. Therefore, the user is able to control the amount of assistance provided by HAL by voluntarily adjusting their myoelectric activities. As mentioned above, this mechanism forms a proprioceptive feedback loop. A visual feedback loop would be also formed because the patient are able to directly observe the supported motion.”

Minor Essential Revisions

Comment 16: 1° paragraph “is a major cause of paralysis and other physical or cognitive disabilities, ...” please add more references

Response: In accordance with the Reviewer’s comment, we have added these references.


Comment 17: 3° paragraph “Robots are better able to provide cyclic support of the patient’s leg motion compared with therapists.” Please add some papers in order to justify these phrase

Response: Accordingly, we added this reference.

Moreover, to make this point clearer, we added the following text (lines 81–83):

“Compared with therapists, robots are better able to provide cyclic support for a patient’s leg motion: in therapists, excessive fatigue is imposed because of repeated manual support that demands a significant amount of energy [13]”

Comment 18: Please clarify if patients underwent other rehabilitation therapies or not.

Response: All patients, except for Cases 7, 8, and 15, underwent conventional rehabilitation or exercise instruction before this study.

In accordance with your comment, we have added the following text from (lines 143–145):

“All patients, except for Cases 7, 8, and 15 underwent conventional rehabilitation or exercise instruction before this study.”

Comment 19: Protocol is not clear: “Early training sessions for individuals with severe gait impairment involved simple flexion/extension movements of the lower limb and dynamic postural tasks (i.e., sit-to-stand task) with HAL assistance”. Which is the progression of the treatment?

Response: We appreciate your comment on this point.

These exercises were conducted in manner by which the practices with severe gait deficiencies could become familiar with voluntarily operating HAL and receiving its assistance.

Accordingly, we have changed the following text from (lines 179–182):

“Early training sessions for individuals with severe gait impairment involved simple flexion/extension movements of the lower limb and dynamic postural tasks (i.e., sit-to-stand task) with HAL assistance.”

to
“Early training sessions for individuals with severe gait impairment involved simple flexion/extension movements of
the lower limb and dynamic postural tasks (i.e., sit-to-stand task) with HAL assistance to become familiar with operating
HAL and receiving its assistance before progressing to walking training with it.”

**Comment 20:** *Please clarify when all the measurements have been collected*

**Response:** We collected all the measurements for each participant before and after locomotor training with the HAL. In
accordance with the Reviewer’s comment, we have added the following text (lines 211–212):

> “Outcome measures were collected for each participant before and after the HAL locomotor training.”

**Comment 21:** *“The best time of the two trials was used in the analysis.” Please justify these sentence according to some references.*

**Response:** We cited the following references for use of the best time of the two trials of 10MWT for analysis

rehabilitation training with a newly developed wearable robot for patients with limited mobility: Archives of

We also have added the reference regarding the use of the best time of the two trials of TUG for analysis.


Thank you for your valuable comments.