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The Effect of Robot-assisted Locomotor Training on Walking Speed

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***Abstract*—This study was to quantify the effects of Lokomat training on ambulation capacity of patients with incomplete spinal cord injury (SCI), and to examine the potential assistance of anti-spasticity medication on training. Twenty-nine SCI subjects with spastic hypertonia at their ankle participated in a 12-session Lokomat training regimen, with half receiving Lokomat only (LOKO) and half receiving Lokomat combined with tizanidine (LOKO+TIZ). Walking capacity was evaluated in terms of the 10-meter walking (10MW) speed—a major clinical evaluation of SCI rehabilitation—four times (at the baseline, 1-, 2- and 4-weeks after training). Growth Mixture Model (GMM) was used to classify the walking speed into recovery patterns. Two latent classes were found for each treatment group, corresponding to low speed and high speed. Walking speed increased with training for high-walking-capacity subjects in the LOKO group, and for both high- and low-capacity subjects in the LOKO+TIZ group. Improvement magnitude between pre- and post-test varied among latent classes. Within each class, the baseline measure had a significant effect on walking speed improvement. This study shows that the Lokomat training improves walking speed for patients with SCI, and anti-spasticity medication, such as tizanidine, can improve the efficacy of Lokomat training, particularly for patients with low walking capacity.**

Keywords— **spinal cord injury, Lokomat, tizanidine, Growth Mixture Model, Random Coefficient Regression**

I. INTRODUCTION

Impaired voluntary motor coordination is one of the major consequences of spinal cord injury (SCI). Advanced locomotor training such as provided by the Lokomat (a robot-assisted body-weight support treadmill training system) has been widely used in neurorehabilitation to promote ambulation capacity [1]. The effectiveness of Lokomat training is routinely evaluated by clinical evaluations, such as overground walking speed. Since a pre- *vs.* post-treatment analysis usually neglects the time progression of the recovery pattern during treatment, and the use of group averaging techniques neglects the substantial variation among SCI patients, a thorough investigation of the impact of the Lokomat training, with a comprehensive statistical analysis recognizing recovery pattern, is essential to accurately characterize therapy outcomes and to establish recovery prognosis for individual patient.

It has been shown that pharmacological interventions such as tizanidine (an α2-adrenergic agonist, TIZ) are able to suppress spasticity and increase range of motion (ROM) [2, 3], which potentially can also improve the functional efficiency of the Lokomat training. Since the outcomes of the Lokomat training coupled with pharmacological treatment have been seldom reported, we plan to evaluate and compare the effects of the Lokomat training (LOKO) and the Lokomat training combined with tizanidine (LOKO+TIZ) on ambulation capacity.

In one of our previous studies with Lokomat training for patients with SCI [4], the results did not agree with the findings reported in other Lokomat training studies that walking speed improved significantly after the Lokomat training [5]. We believe that the small number of participants reduced the sensitivity of the statistical analysis; in addition, the effect of the baseline measurement was not taken into account in the regression analysis.

Accordingly, this paper inspected the effect of baseline measure as a covariate in the Random Coefficient Regression (RCR) modeling with more subjects in both treatment groups, and also performed pre-test and post-test comparisons. We were interested in whether the subjects with SCI showed improvement during the treatments, and whether the time progression of the recovery pattern during treatment could be presented by regression modeling.

II. EXPERIMENTAL PROTOCOL

A. Experimental Procedure

As part of our current ongoing research study, two groups of subjects were selected based on the objectives specified in this paper: 14 subjects received the Lokomat training alone (LOKO) (Fig. 1), and 15 subjects received the combined intervention of the Lokomat training and tizanidine (LOKO+TIZ). All subjects exhibited hypertonia spasticity in their lower extremity. All participants were recruited from the outpatient clinics of the Rehabilitation Institute of Chicago. Each subject gave informed consent according to the policies of the Institutional Review Board of Northwestern University.

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Subjects received a 1-hour Lokomat training 3 times a week for 4 weeks. The training speed was increased up to 3.4 km/hr over the twelve training sessions based on the subject's improvement. In each session, the guidance force was decreased gradually from full assistance of the robot, until the subject was no longer able to maintain the set speed. The first Lokomat training occurred after the baseline measurement was taken. Subjects in the LOKO group did not take any muscle relaxant medication (e.g., baclofen or tizanidine) during the training period; subjects in the LOKO+TIZ group started taking tizanidine before the first experiment (baseline) to maintain a consistent condition for the neuromuscular properties during training.

Subjects were evaluated 4 times: at the baseline, and 1-, 2- and 4-weeks after training. All participants were ambulatory and could complete 10-Meter-Walking (10MW) test. This test assesses walking speed by measuring the time it takes to walk a straight 10-meter course (T_{10MW}) [6].

B. Analytical Procedure

The Growth Mixture Model (GMM) [7] was used to characterize the growth patterns of T_{10MW} over the 4-week training period. The analysis was performed separately for the Lokomat training (LOKO) and Lokomat+Tizanidine (LOKO+TIZ) treatment groups.

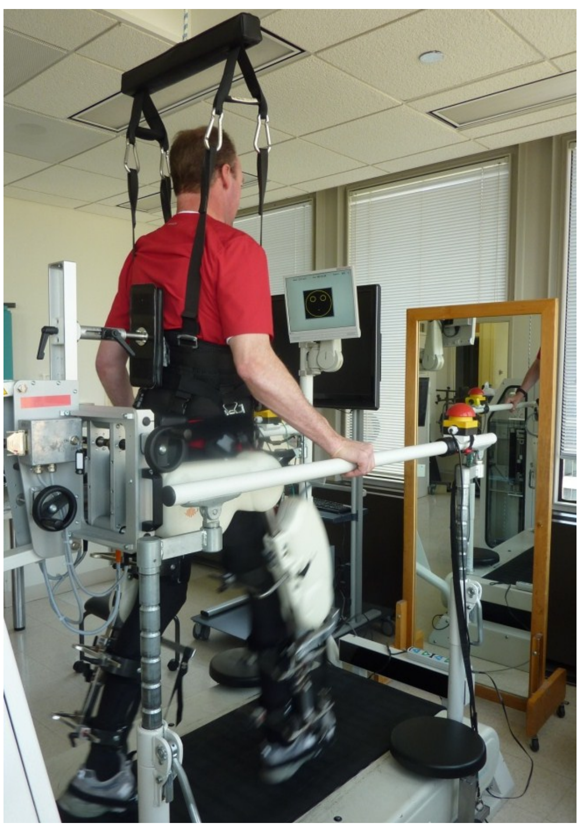

Figure 1. LOKOMAT, a robot-assisted walking training system, consists of the robotic gait orthosis, body weight support and treadmill.

The GMM has been widely used in psychological and educational research to capture heterogeneity in developmental pathways. It assumes that the population can be divided into a finite number of latent classes (homogeneous inter-subject subpopulations) by inspecting the intra-subject difference in growth pattern, with the assumption that individuals within each latent class share the same structural relationships, such as the same recovery pattern. The quality of the resulting classification will be evaluated by the posterior probabilities of class membership among subjects. The number of latent classes and the model fit are determined by the Bayesian Information Criterion (BIC) [7]. Subject was assigned to the latent class in which he/she had the highest posterior membership probability.

To inspect monotonic changes of overground walking speed along time during training, the RCR modeling [8] was applied in each latent class to define the growth pattern, with the baseline measure considered as a covariate. Such a model allows for individual difference in the response function to accommodate inter-subject variability.

$$y_{ijk}=[\beta_{00k}+\beta_{10k}t_j]+[\alpha_{ik}y_{i0k}]+[\mu_{0jk}+\mu_{1jk}t_j+e_{ijk}] \quad (1)$$

where i denotes subject number, j is for time (week), k corresponds to the latent class number, and e_{ijk} is the random residual of the model. Parameters β_{00k} and β_{10k} were held constant for all subjects in subclass k, while parameters μ_{0jk} and μ_{1jk} vary with subject k and time point j.

The components of (1) in the first bracket are the fixed effect, the component in the second bracket represents the baseline effect, and the components in the third bracket are the random effect for the current growth model.

Due to the small sample size, non-parametric statistics were used to perform the comparison within and across latent classes. Within each latent class, the pre-test and post-test measures were inspected by using the Wilcoxon signed rank test. Across latent classes, the improvement percentages of post-test measures with respect to the pre-test (baseline) were examined by the Kruskal–Wallis one-way ANOVA.

Thus, both models provide a flexible and accurate analytical framework by classifying the individuals into several subclasses, each of which contains only subjects with homogenous measures.

The standard level of significance was 0.05 during the statistical tests.

III. RESULTS

A. Growth patterns of 10MW test

Using the Growth Mixed Model, two distinct latent classes for the 10MW test, corresponding to low speed (Class 1) and high speed (Class 2), were found for each of the treatment groups (LOKO and LOKO+TIZ). RCR was

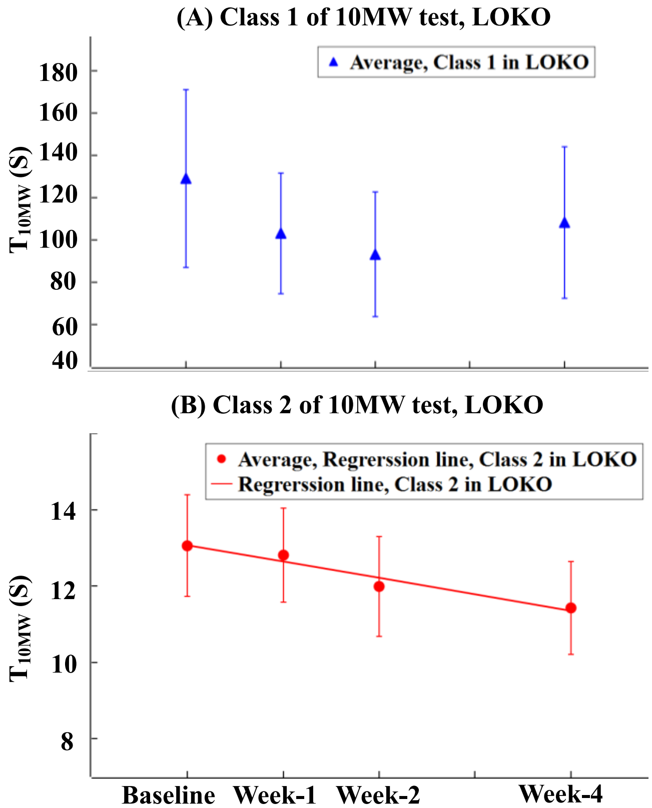

Figure 2. T_{10MW} as a function of time (week) for subjects in group of LOKO. Averages across all subjects in each latent class, corresponding standard error, and the linear regression line obtained from RCR are shown for Class 2. Note that the ordinate scales are different among subplots.

used to examine the relationship between T_{10MW} and time (weeks) in each latent class.

In the LOKO group (Fig. 2(A) and 2(B)), there was significant improvement for subjects in Class 2 (*P*=0.028), with a rate of -0.43 s/week. No significant improvement was observed for subjects in Class 1 (*P*=0.332).

In the LOKO+TIZ group (Fig. 3(A) and 3(B).), there was significant improvement for subjects in Class 1 with a rate of -1.38 s/week (*P*=0.013) and in Class 2 with a rate of -0.35 s/week (*P*=0.049).

It was found that the baseline measurement was a significant regression covariate for each latent class ($P<0.001$).

Linear Mixed Model analysis was used to compare the slopes of T_{10MW} over the 4-week period among the latent classes that showed significant improvement. It was found the slope magnitude of Class 1 in group of LOKO+TIZ was larger than Class 2 in LOKO and Class 2 in LOKO+TIZ treatment group (*P*=0.002 and 0.001 separately), while the slope magnitudes of Class 2 in the two intervention groups of LOKO and LOKO+TIZ were the same (*P*=0.774). This implies that participants in the LOKO+TIZ group that had a low baseline walking capacity could achieve higher improvement in walking speed than subjects who had high baseline walking capacity in both LOKO and LOKO+TIZ groups. On the other hand, subjects with high baseline walking capacity did not show a difference in improvement in their walking speeds between the LOKO and LOKO+TIZ groups.

B. Pre-test and post-test comparison of 10MW test

In the LOKO group, subjects in Class 2 showed significant improvement in the pre- *vs.* post-treatment comparison (*P*=0.008, median percentage improvement= 10.1%). Subjects in Class 1 did not improve significantly (*P*=0.125), although they had the highest post-test improvement magnitude (median of 15.5s) and percentage (median of 19.5%) among all latent classes (TABLE I). We found that one subject gained large improvement in the first two tests (about 40% improvement in walking speed after two weeks of training) but decreased his walking speed in his last test. We are getting more subjects in this treatment group to increase the statistical power.

For the LOKO+TIZ group, subjects in each latent class showed significant improvement in the pre- *vs.* post-treatment comparison (*P*=0.031, median percentage improvement= 13.2% in Class 1; *P*=0.047, median of percent improvement= 9.8% in Class 2) (TABLE I).

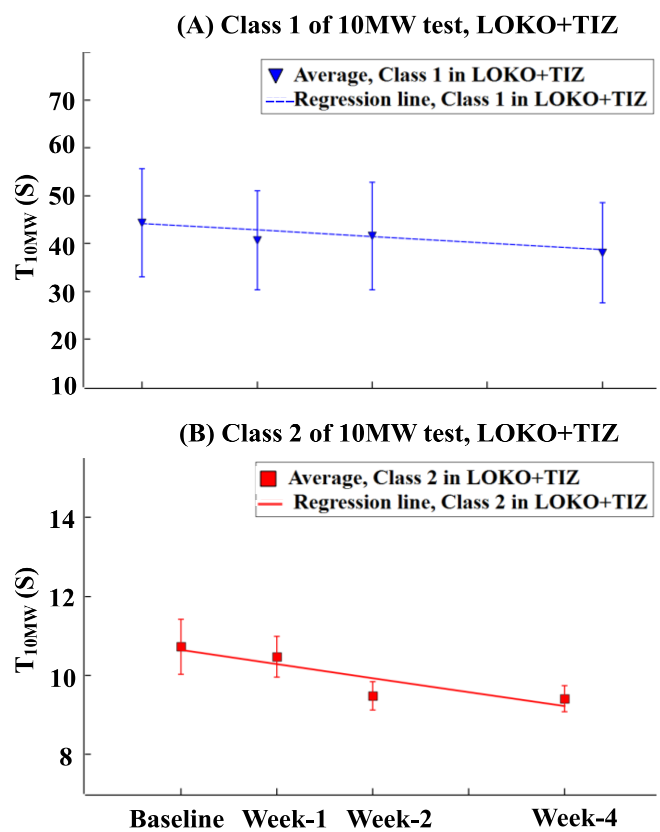

Figure 3. T_{10MW} as a function of time (week) for subjects in group of LOKO+TIZ. Averages across all subjects in each latent class, corresponding standard error, and the linear regression lines obtained from RCR are shown for both classes. Note that the ordinate scales are different among subplots.

The between-group comparison of the post-test improvement magnitude was performed over Class 2 in the LOKO group and Class 1 and Class 2 in the LOKO+TIZ group using the Kruskal-Wallis test. It showed that Class 1 in LOKO+TIZ had the largest improvement (*P*=0.007). Similarly, the between-group comparison of the percentage improvement of the post-test measurement was also performed among the above latent classes. It was found the percentage improvement of post-test was not different among Class 2 in the LOKO group, and Class 1 and Class 2 in the LOKO+TIZ group (*P*=0.660).

TABLE I. Median of improvement between pre-test and post-test, median of percentage improvement between pre-test and post-test, pre-test and post-test nonparametric comparison, and RCR model for each latent class. Note: asterisk symbol * means significant statistical results from both pre-post comparison and RCR model in the specific latent class.

Latent classes	**Median of pre-post improvement**	**Median percentage improvement**	**Pre-post comparison, *P*-value**	**RCR, *P*-value**
Lokomat training				
Class 1	15.5 s	19.5%	0.125	0.332
Class 2 *	1.22 s	10.1%	0.008	0.028
Lokomat+Tizanidine				
Class 1 *	6.29 s	13.2%	0.031	0.013
Class 2 *	0.97 s	9.8%	0.047	0.049

V. Discussion and Conclusions

We used the GMM to classify the 10-meter walking test for SCI patients. Two distinct latent classes, which corresponded to low speed and high walking speed in the 10-meter walking test, were observed for both LOKO and LOKO+TIZ groups (Fig. 2 and Fig. 3). The improvement magnitude between pre- and post-test measures varied among latent classes, while the percentage of improvement with respect to pre-test did not show difference among latent classes and treatment groups (TABLE I).

This study found that individuals respond differently to the Lokomat training based on their individual characteristics, such as baseline measurements. The GMM analysis provides a way to identify the differential effect of the Lokomat training on ambulation capacity.

The monotonic pattern of walking speed improvement over time during the training period was defined by the RCR modeling for each latent class, and the comparison between the pre-test and post-test measures was further examined by the Wilcoxon signed ranks test. Results from the two statistical approaches were consistent. Participants with a high 10-meter walking speed at baseline showed significant improvement for both intervention groups, while subjects with low walking speed in the LOKO+TIZ group improved significantly. These findings reveal that patients with incomplete SCI benefited from ongoing Lokomat training, with a consistent pattern of improvements to their ambulation. It implies that the recovery pattern can be modeled for the patients with SCI who receive the Lokomat training.

The improvement between pre- and post-test varied among latent classes. For example, subjects with a low baseline walking capacity in the LOKO+TIZ group achieved larger absolute improvement (6.29 s) than subjects with a high walking capacity in both treatment groups, while the percentage of improvement with respect to pre-test (baseline) measurements did not vary significantly among latent classes. On the other hand, within each latent class, the relationship between baseline measure and the improvement in walking speed was also found to be significant, i.e., subjects with a larger baseline value of 10MW had higher improvement. Such a significant baseline effect on walking improvement—both between and within latent classes—suggests that the baseline measures of individuals should be taken into account during the clinical evaluations. This will consequently help to individualize the prognosis and tailor the therapy program to the specific needs of the SCI individual.

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References

[1] Wirz M, Zemon DH, Rupp R, Scheel A, Colombo G, Dietz V, Hornby TG. Effectiveness of automated locomotor training in patients with chronic incomplete spinal cord injury: a multicenter trial. Arch Phys Med Rehabil. 2005 Apr;86(4):672-80.
[2] Nance PW, Bugaresti J, Shellenberger K, Sheremata W, Martinez-Arizala A. Efficacy and safety of tizanidine in the treatment of spasticity in patients with spinal cord injury. North American Tizanidine Study Group. Neurology. 1994 Nov;44(11 Suppl 9):S44-51; discussion S-2.
[3] Taricco M, Pagliacci MC, Telaro E, Adone R. Pharmacological interventions for spasticity following spinal cord injury: results of a Cochrane systematic review. Eura Medicophys. 2006 Mar;42(1):5-15.
[4] Niu X, Patel C, Varoqui D, Mirbagheri MM. The Effect of Robot-assisted Lokomotor Training on Gait Recovery: A Multivariate Analysis. 2011 Annual International Conference of the Ieee Engineering in Medicine and Biology Society (Embc). 2011:3542-5.
[5] Field-Fote EC, Lindley SD, Sherman AL. Locomotor training approaches for individuals with spinal cord injury: a preliminary report of walking-related outcomes. J Neurol Phys Ther. 2005 Sep;29(3):127-37.
[6] van Hedel HJ, Wirz M, Dietz V. Assessing walking ability in subjects with spinal cord injury: validity and reliability of 3 walking tests. Arch Phys Med Rehabil. 2005 Feb;86(2):190-6.
[7] Jung T, Wickrama KAS. An introduction to latent class growth analysis and growth mixture modeling. Social and Personality Psychology Compass. 2008 Jan;2(1):302-17.
[8] Bliese PD, Ployhart RE. Growth modeling using random coefficient models: Model building, testing, and illustration. Organizational Research Methods. 2002 Oct;5(4):362-87.