

# Robot-assisted gait training versus treadmill training in patients with Parkinson's disease: a kinematic evaluation with gait profile score

Manuela Galli, PhD<sup>a,b</sup>  
Veronica Cimolin, PhD<sup>a</sup>  
Maria Francesca De Pandis, PhD, MD<sup>c</sup>  
Domenica Le Pera, MD<sup>b</sup>  
Ivan Sova, MD<sup>b</sup>  
Giorgio Albertini, MD<sup>b</sup>  
Fabrizio Stocchi, MD<sup>b</sup>  
Marco Franceschini, MD<sup>b,d</sup>

<sup>a</sup> Department of Electronics, Information and Bioengineering, Politecnico di Milano, Milan, Italy

<sup>b</sup> IRCCS San Raffaele Pisana, Tosinvest Sanità, Rome, Italy

<sup>c</sup> San Raffaele Cassino Hospital, Tosinvest Sanità, Rome, Italy

<sup>d</sup> San Raffaele University, Rome, Italy

Correspondence to: Veronica Cimolin  
E-mail: veronica.cimolin@polimi.it

## Summary

**The purpose of this study was to quantitatively compare the effects, on walking performance, of end-effector robotic rehabilitation locomotor training versus intensive training with a treadmill in Parkinson's disease (PD). Fifty patients with PD were randomly divided into two groups: 25 were assigned to the robot-assisted therapy group (RG) and 25 to the intensive treadmill therapy group (IG). They were evaluated with clinical examination and 3D quantitative gait analysis [gait profile score (GPS) and its constituent gait variable scores (GVs) were calculated from gait analysis data] at the beginning (T0) and at the end (T1) of the treatment. In the RG no differences were found in the GPS, but there were significant improvements in some GVVs (Pelvic Obl and Hip Ab-Add). The IG showed no statistically significant changes in either GPS or GVVs. The end-effector robotic rehabilitation locomotor training improved gait kinematics and seems to be effective for rehabilitation in patients with mild PD.**

*KEY WORDS: gait analysis, gait profile score, Parkinson's disease, rehabilitation, robotic rehabilitation, treadmill*

## Introduction

Gait disorders are among the most common and most disabling symptoms of Parkinson's disease (PD) (Tan et al., 2012; Kwakkel et al., 2007; Smania et al., 2010; Toole et al., 2005), and they can manifest themselves as different types of clinical involvement of various body segments: shuffling of the feet, ankle and knee stiffness, flexion of the pelvis and trunk, slowness of movement of the entire lower limbs, and reduction of associated movements (e.g. arm swinging), together with difficulty changing direction or modulating velocity.

Thus, recovery of walking is a crucial aspect of PD rehabilitation, serving to improve the patient's quality of life and level of independence. Pharmacological therapy, with levodopa as the "gold standard", is commonly used to manage the motor symptoms of PD. Many studies have demonstrated the ability of levodopa to increase stride length and walking speed (Morris et al., 2001). However, as the disease progresses, chronic levodopa treatment is associated with the development of motor complications, including wearing-off episodes and dyskinesia (Stocchi et al., 2014; Warren Olanov et al., 2013). Motor complications are the primary reason for surgical interventions in PD (deSouza et al., 2013). It is therefore important to use rehabilitation treatment approaches designed to help patients manage motor complications, and rehabilitation is, indeed, playing an increasingly important role in the treatment and care of subjects with PD. Non-pharmacological treatments, such as exercises (Goodwin et al., 2008) and physiotherapy (Davey et al., 2004; Comella et al., 1994; de Goede et al., 2001), have been shown to be effective on gait impairment in PD. In recent years, electromechanical devices such as treadmill training systems have also been used in patients with PD, and shown to improve cognitive and motor features in these patients (Mehrholtz et al., 2010; Picelli et al., 2016). Recently, robotic assistive devices have been used for gait training in neurological disorders such as stroke, spinal cord injury and multiple sclerosis, giving good results in terms of gait recovery (Sale et al., 2012; Semprini et al., 2009; Mehrholz and Pohl, 2012; Spenko et al., 2006; Lee et al., 2011a,b; Roy et al., 2011; Forrester et al., 2011). The literature now also reports interesting results of the application of robotic assistive devices in PD (Lo et al., 2010; Picelli et al., 2012, 2013; Ustinova et al., 2011; Sale et al., 2013); gait was

found to be improved and freezing episodes were reduced after using robot-assisted gait training. However, most of these analyses were based mainly on clinical evaluations and questionnaires: Unified Parkinson's Disease Rating Scale (UPDRS), 10-meter walking speed, distance walked in 6 minutes, the Freezing of Gait Questionnaire, the Parkinson's Disease Questionnaire-39. Only two studies used some quantitative gait indices, but these were limited to spatiotemporal parameters (Lo et al., 2010; Sale et al., 2013), and there was no investigation of gait kinematics.

The aim of the present study was to investigate the effects, on walking performance, of an end-effector robotic rehabilitation locomotor training program in patients with PD, comparing these patients with PD subjects who underwent intensive treadmill training therapy. In particular, the analysis focused not only on spatiotemporal parameters, already assessed in the literature, but also on gait kinematics of the main lower limb joints.

## Materials and methods

### Participants

In this study, idiopathic PD patients were recruited from rehabilitation centers. They had been on stable

doses of PD medications for at least four weeks prior to the study onset, and they showed a level of endurance that allowed them to maintain an upright position, assisted or unassisted, for at least 20 minutes. A preliminary medical examination included a physical and a neurological test, and a 3D gait analysis (GA).

The inclusion criteria for all groups were: i) a diagnosis of idiopathic PD according to the UK Brain Bank criteria, without any other significant neurological or orthopedic problems; ii) age between 18 and 90 years; iii) ability to walk, unassisted or with little assistance, for a distance of 25 feet.

The following exclusion criteria were applied: i) inability to understand the study instructions (as shown by the Informed Consent Test of Comprehension); ii) primarily wheelchair bound; iii) chronic and ongoing alcohol or drug abuse, active depression, anxiety or psychosis liable to interfere with the use of the equipment or with the testing; iv) diagnosis of atypical parkinsonian syndrome; v) implantation of deep brain stimulation electrodes.

We screened 176 patients, 50 of whom satisfied the inclusion criteria and were randomly assigned to the groups as follows: 25 to the robot-assisted therapy group (RG) and 25 to the intensive therapy group (IG) (Fig. 1).

The random allocation to treatment was concealed; it was performed using a custom computerized system

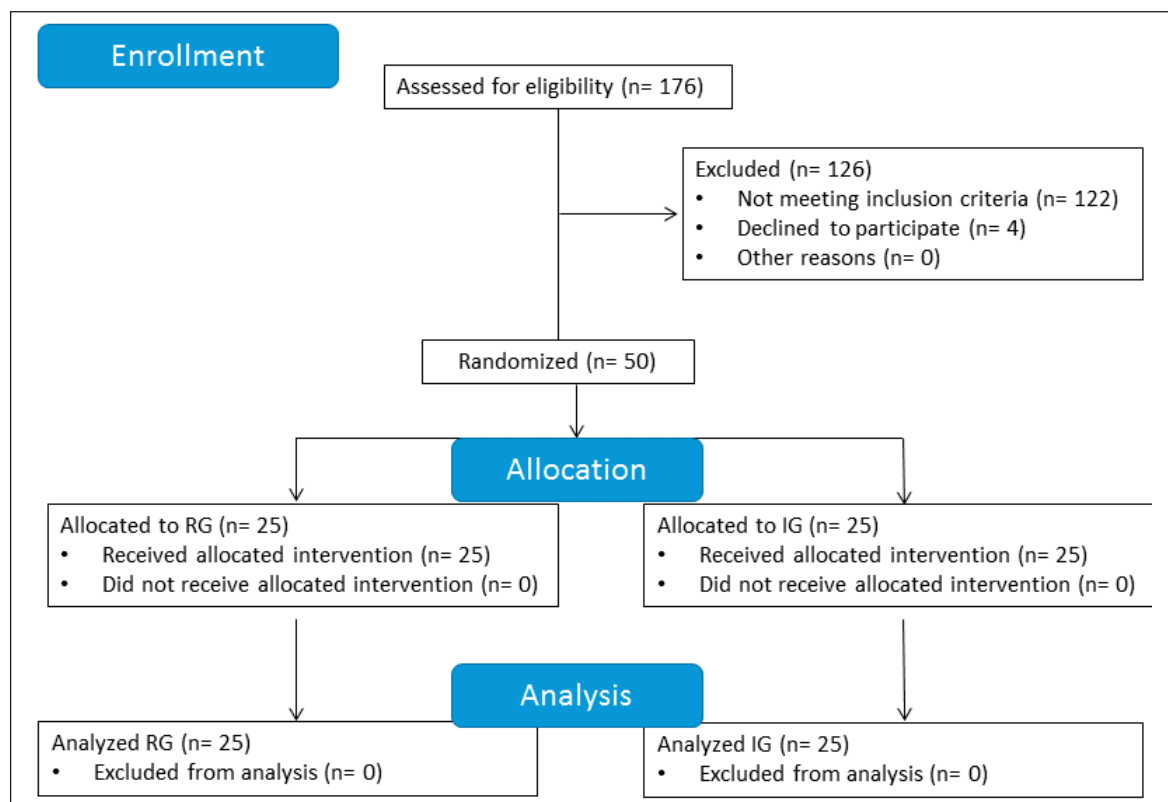


Figure 1 - CONSORT 2010 flow diagram of the study.

with purpose-built software. In order to allow balanced subject allocation into the two groups, the Lehmer algorithm was applied. Therapists were assigned to each group of patients randomly. Blinded assessors conducted clinical assessments at the beginning (T0) and at the end (T1) of the treatment.

This study was performed in accordance with the Declaration of Helsinki and was approved by the ethics committee of IRCCS San Raffaele Pisana. Informed consent was obtained from all the subjects enrolled in the study.

### **Measures**

The clinical assessments included administration of the Hoehn and Yahr scale (Hoehn and Yahr, 1967) and the UPDRS (Song et al., 2009). These assessments and the instrumental evaluations were carried out, respectively, by medical doctors and engineers with the necessary expertise. These practitioners were not directly involved in the research and did not know, at the time of the assessments, which group the patients had been randomized to. All clinical and instrumental examinations were performed an hour and a half after the patients had taken their own usual dosage of levodopa and with the subjects in the "on phase".

### **3D gait analysis**

All the participants were assessed using an optoelectronic system (ELITE2002, BTS, Milan, Italy) with a sampling rate of 100 Hz, two force platforms (Kistler, CH) and a 2 TV camera video system (VideoController, BTS, Italy) synchronized with the optoelectronic system, and the platforms for video-recording. After collection of several anthropometric measures (height, weight, tibial length, distance between the femoral condyles or diameter of the knee, distance between the malleoli or diameter of the ankle, distance between the anterior iliac spines and thickness of the pelvis), passive markers were placed at specific points of reference, directly on the subject's skin, as described by Davis et al. (1991), in order to evaluate the kinematics of each body segment. In particular, they were placed at: C7, the sacrum and bilaterally at the anterior superior iliac spine, greater trochanter, femoral epicondyle, femoral wand, tibial head, tibial wand, lateral malleolus, lateral aspect of the foot at the fifth metatarsal head and at the heel (only for static offset measurements). All the trials were acquired by the same operator to ensure reproducibility of the acquisition technique and to avoid the introduction of errors due to different operators. After the placement of the markers, the participants completed two or more practice trials along a 10-meter walkway where the two force platforms were placed, to ensure that they were comfortable with the experimental procedure. After this familiarization, at least seven trials were acquired asking the participants to walk, barefoot, at their self-selected speed.

### **Therapeutic intervention**

The patients underwent a cycle of outpatient rehabilitation treatment, consisting of at least one daily three-hour cycle, divided as follows: 45 minutes of lower limb treatment using either the robotic device or the treadmill, according to the randomization, followed by an individually tailored occupational therapy intervention for the upper limb, including both dexterity exercises and neuropsychological treatment. The entire treatment was performed under the supervision of a physiotherapist.

#### **Robot-assisted therapy group**

Each RG subject was asked to undergo 20 sessions (5 days a week for 4 weeks) of robot-assisted gait training, using the commercially available G-EO system (end effector system machines G-EO system device) (Reha Technology AG, Olten, Switzerland). From the engineering point of view, the G-EO robot consists of an end effector device with partial body-weight support (BWS) and a footplate placed on a double crank and a rocker gear system, each with three degrees of freedom. This makes it possible to choose the length and the height of the steps. The footplate angles can be used to simulate and repeatedly practice real over-ground gait (Hesse et al., 2010). The trajectories of the footplates and the vertical and horizontal movements of the center of mass are fully programmable, enabling wheelchair-bound subjects to do repetitive practice not only of simulated floor walking, but also of simulated stair use. Heart rate and blood pressure were monitored at the beginning and at the end of each training session, during which the therapist supervised the treatment standing in front of the patient, so as to help if necessary. The treatment parameters (device settings, i.e. footplate trajectories and vertical and horizontal movements of the center of mass) were noted for each session, and the steps taken during the simulated walking were converted into the distance covered, based on the step length previously chosen (Hesse et al., 2012). The session consisted of robot-assisted walking therapy, at variable speeds, for 45 minutes, with BWS. All participants started with 30–40% of BWS and an initial speed of 1.5 km/h; subsequently the speed was increased to between 2.2 and 2.5 km/h, and the initial BWS was decreased. After 45 minutes the session was stopped.

#### **Intensive treadmill therapy group**

Each IG subject received 20 sessions (5 days a week for 4 weeks) of treadmill rehabilitation treatment. All the subjects were asked by the therapist to perform a 45-minute session of treadmill training, setting the treadmill parameters as they wished, at levels they were comfortable with. The patients received video feedback to improve their gait quality. The Gait Trainer™ 3 (Biodex Medical Systems, New York, USA),

equipped with visual biofeedback screen, provided the necessary stimulus for retraining neural pathways, thus improving the patient's gait pattern and allowing assessment of his/her progress. The biofeedback parameters could be set by the therapist according to the patient's specific impairment and the desired goals (i.e. improvement in velocity and/or step length and/or cadence). In particular, the patients could follow a graphical representation of their feet, on the treadmill screen, and simultaneously receive visual feedback on their performance. Heart rate and blood pressure were monitored at the beginning and at the end each session. During the training sessions, the therapist supervised the treatment standing alongside the patient. The treatment parameters were noted for each session.

In both groups, subjects who interrupted the treatment for more than three consecutive days or did not return for post-treatment evaluation were excluded from the study.

### Data analysis

In this analysis, only spatiotemporal parameters and kinematic data were considered. Although ground reaction forces were also acquired during the study, they are not included in the present analysis and are not discussed in this paper.

The following spatiotemporal parameters were analyzed:

- % stance (as a % of the gait cycle): % of the gait cycle that begins with initial contact and ends at toe-off of the same limb;
- mean velocity (m/s): the mean velocity of progression
- step length (mm): longitudinal distance from one foot strike to the next one;
- step width (mm): mediolateral distance between the two feet during double support
- cadence: number of steps in a unit of time (steps/min).

All kinematic graphs obtained from the GA were normalized as a percentage of the gait cycle producing sagittal kinematic plots of the pelvis, hip, knee and ankle for each cycle. Using specific software (BTS EliteClinic, version 3.4.109) data were exported in .txt and .xls files. From these data formats, we computed the gait profile score (GPS), which summarizes the overall deviation of kinematic gait data relative to normative data (Baker et al., 2009). The GPS and Movement Analysis Profile (MAP) method was implemented as described by its authors (Baker et al., 2009) using data relating to a control group of 10 healthy subjects (age: 72.06±4.64). The GA data were then processed to obtain the GPS and MAP according to the published method (Baker et al., 2009).

The GPS represents the root mean square (RMS) difference between a particular gait trial and averaged data from people with no gait pathology. It has an advantage over other indices as it is comprised of a number of gait variable scores (GVSSs) representing an equivalent RMS difference for different kinematic

variables. These can be displayed as a bar chart known as the MAP. The GPS is based on various GVSSs, each of which represents the RMS difference between a specific time-normalized gait variable and the mean data from a reference population calculated across the gait cycle. Thus, if  $x_{i,t}$  is the value of a gait variable, is calculated at a specific point in the gait cycle  $t$ , and is the mean value of that variable at the same point in the gait cycle for the reference population, then the  $i$ th gait variable score is given by:

$$GVS_i = \frac{1}{T} \sum_{t=1}^T (x_{i,t} - \bar{x}_{i,T}^{ref})^2$$

where  $T$  is the number of instants into which the gait cycle has been divided. The GPS is thus the RMS average of the GVS variables:

$$GPS = \frac{1}{N} \sum_{i=1}^N GVS_i^2$$

The overall GPS is based on the following clinically important kinematic variables: Pelvic tilt, pelvic obliquity (Pelvic Obl), pelvic rotation (Pelvic Rot) — one value for each of these variables, corresponding to the average for the left and right sides — and hip flexion (Hip Flex-Ext), hip abduction (Hip Ab-Add), hip rotation (Hip Int-Ext), knee flexion (Knee Flex-Ext), ankle dorsi-plantarflexion (Ankle Dorsi-Plant) and foot progression (Foot Int-Ext), each considered separately for the left and right sides. The overall GPS is thus calculated considering a total of 15 variables. In the present analysis a GPS score for each side was used based on all nine GVSSs for that side. As mentioned, the GPS represents the difference between the patient's data and the average from the reference dataset, and the less physiological the gait pattern the higher the GPS value will be.

### Statistical analysis

All the previously defined parameters were computed for each participant in the two analyzed groups.

The Kolmogorov-Smirnov test was used to verify whether the parameters were normally distributed. Since they were not normally distributed, the median and interquartile range (IQR) of all indices were calculated for each group. The Mann-Whitney U test was used to assess the differences between the groups at baseline (T0) and at the endpoint (T1), and the Wilcoxon paired test between T0 and T1 was computed in order to determine whether a specific treatment introduced statistically significant changes. P-values less than 0.05 were considered significant.

### Results

No dropouts were recorded during the treatment in either group, and all the subjects correctly completed

the protocol (compliant subjects: n=50). The distribution of the study subjects (n=50) by age, gender and main clinical and demographic characteristics did not show significant differences between the RG and the IG (Table I).

At baseline (T0), no statistical difference in age, height, weight, clinical scale scores and biomechanical parameters (spatiotemporal parameters, GPS and GVSs) was found between the RG and the IG (p>0.05).

The median and IQR values of the spatiotemporal parameters and GPS (with its GVSs) for the RG and IG are summarized in table II and in figures 2 and 3. With regard to the spatiotemporal parameters (Table II), the data for the RG showed statistically significant improvements in mean velocity, step length and cadence (p<0.05). Conversely, the IG displayed a significant change only in step length. At T1, velocity, step length and cadence were statistically different between the RG and the IG, with the RG recording higher values for velocity and cadence and a lower value for step length. The kinematic data of the RG (Fig. 2) showed that while no differences were found

globally (GPS 10.6±2.8 degrees at T0 vs 11.4±3.0 degrees at T1, p>0.05), some significant improvements were displayed by GVSs, and in particular by Pelvic Obl and Hip Ab-Add (p<0.05), which were statistically different between the RG and IG at T1, too. The IG showed no statistically significant changes in the GPS or its GVSs (Fig. 3).

**Discussion**

As sequential movements are acquired through a process of implicit learning, becoming automatic with practice (Rochester et al., 2010; Abbruzzese et al., 2009), the use of training programs that focus on task-specific activities has been encouraged as a means of improving walking ability, on the strength of the increased retention of motor skill learning observed in adults with mild PD after task practice (Cakit et al., 2007). On this basis, a wide range of conventional physical therapy approaches has been employed to treat PD, without agreement on the optimal practice in the different phases of the disease (Protas et al.,

Table I – Patients' demographic and clinical features.

	Robot-assisted therapy group		Intensive therapy group	
Subjects (M/F)	25 (14/11)		25 (12/13)	
Height (m)	1.6±0.1		1.6±0.1	
Age (years)	68.8±6.9		66.4±9.7	
Disease duration (years)	9.9		8.1	
Clinical form at onset (A/T)	13/12		13/12	
Levodopa equivalent dose (mg)	650.8±176.2		781.8±321.2	
Hoehn & Yahr stage (range)	1.5–3		2–4	
	T0 session	T1 session	T0 session	T1 session
UPDRS III mean score	37.2	32.9*	47.2	39.4*
median (I/III quartiles)	39 (34/45)	36 (29/38)	50 (43/53)	38 (34/46)

Abbreviations: A=akinesic; T=tremor; UPDRS=Unified Parkinson's Disease Rating Scale; \*p<0.05, T0 vs T1.

Table II - Median values and interquartile range of spatiotemporal parameters in the robot-assisted therapy group and intensive treadmill therapy group.

	Robot-assisted therapy group		Intensive therapy group	
	T0 Median (IQR)	T1 Median (IQR)	T0 Median (IQR)	T1 Median (IQR)
% stance (% gait cycle)	61.5 (3.9)	61.9 (3.9)	62.38 (5.55)	62.56 (5.56)
Mean velocity (m/s)	0.65 (0.21)	0.77 (0.24)*, +	0.64 (0.24)	0.73 (0.29)
Step length (m)	0.29 (0.13)	0.31 (0.15)*, +	0.33 (0.09)	0.43 (0.12)*
Step width (m)	0.15 (0.04)	0.14 (0.02)	0.16 (0.03)	0.16 (0.03)
Cadence (step/min)	98.08 (15.95)	101.24 (12.71)*, +	97.14 (15.47)	99.90 (19.83)

\*=p<0.05, T0 vs T1; += p< 0.05, RG vs IG at T1

2005). Forced use therapy, task-specific therapy, and intensive gait rehabilitation programs based on treadmill training have been reported to effectively improve gait speed, walking distance and stride length in PD (Lo et al., 2010). In addition, robotic gait training has been observed to improve gait speed, walking capacity and stride length and reduce fatigue in patients with PD (Picelli et al., 2012; Sale et al., 2013). However, evidence of its effectiveness on walking impairment in terms of lower limb kinematics is lacking. From a clinical point of view, the evaluation of kinematics, together with spatiotemporal parameters, is helpful in measuring abnormal gait and is essential for the assessment of gait abnormalities and for the quantitative evaluation of treatment outcomes and thus for quanti-

fying improvement resulting from interventions (Perry, 1992). In addition, as postural instability and gait impairment are major determinants of disability in PD, their improvement leads to a more functional gait pattern, which in turn leads to an improved quality of life. Gait disorders are in fact a common and significant cause of reduced quality of life and reduced independence. Thus, the aim of this study was to evaluate whether robotic gait training could be more effective than a conventional treadmill training program in improving walking ability (considering both spatiotemporal parameters and kinematics) in patients with PD. Our data showed significant changes (improved values) in mean velocity, step length and cadence after robotic training, in accordance with previous literature

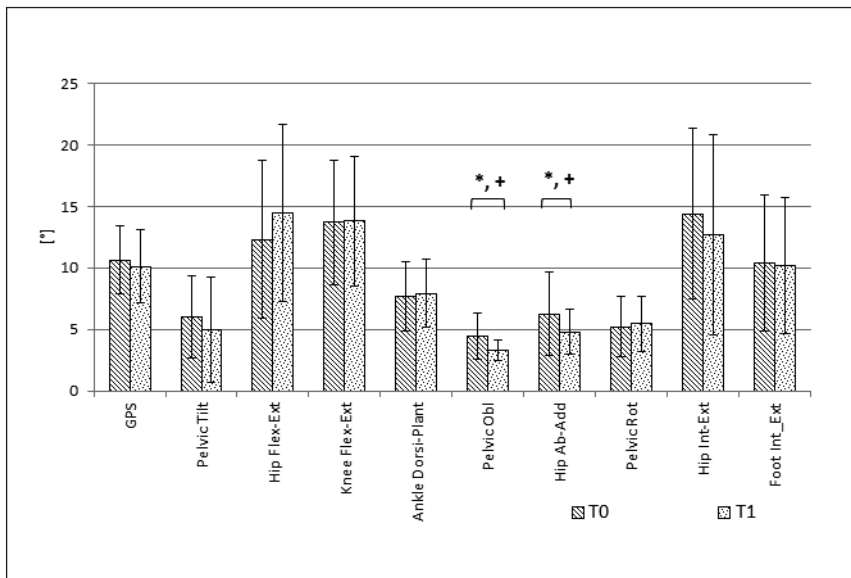


Figure 2 - GPS and GVVs (median and interquartile range) of the robot-assisted therapy group at T0 and T1. \*= $p < 0.05$ , T0 vs T1; +=  $p < 0.05$ , RG vs IG at T1

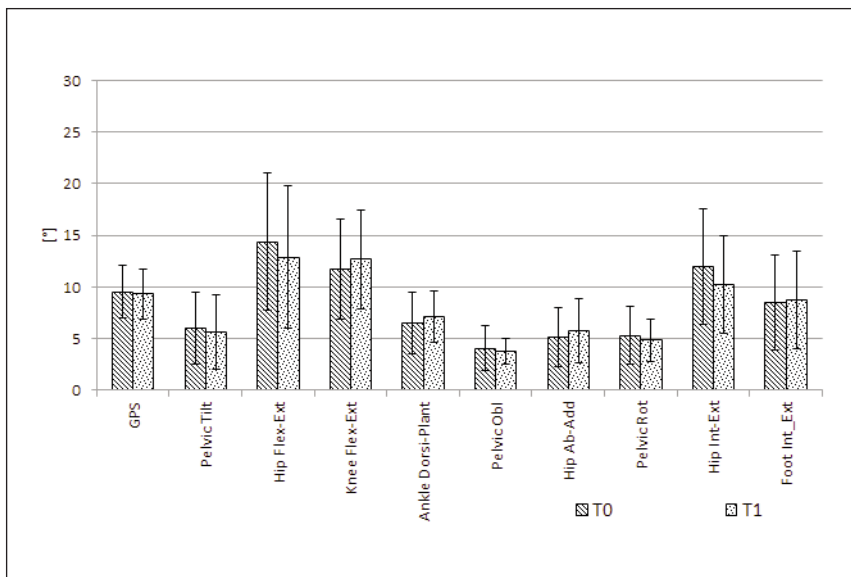


Figure 3 - GPS and GVVs (median and interquartile range) of the intensive therapy group at T0 and T1.

(Sale et al., 2013). As regards the gait kinematics, globally no changes were produced by robot training, as shown by the GPS which remained unchanged, even though we recorded significant improvements in GVSs of the pelvis (Pelvic Obl) and hip (Hip Ab-Add) in the frontal plane. After treadmill training (IG), a significant improvement was found only in step length, which increased, in accordance with the literature (Mehrholtz et al., 2010; Sale et al., 2013). No other changes (in GPS and/or the other GVSs) were observed.

Our study is the first comparative study of robotic training versus treadmill training in PD that considers both spatiotemporal parameters and gait kinematics. The results obtained are interesting from a clinical point of view because they showed that this type of robot-assisted gait training (i.e. the use of an end effector system machine) improved gait pattern not only in terms of spatiotemporal parameters, as already demonstrated in the literature (Sale et al., 2013), but also in terms of gait kinematics and, particularly at proximal level (pelvis and hip joint), in the frontal plane. With the treadmill training, on the other hand, only step length improved; no other changes were found. On the basis of these results, robotic training based on an end effector system seems to be effective for rehabilitation in patients with mild PD. This approach may help to reduce lower limb motor recovery time in PD patients. The fact that this research focuses on gait recovery is a further feature that makes it relevant to clinical practice. Overall, the simplicity of the treatment, the lack of side effects, and the positive results suggest that this treatment should be more widely used. To better investigate the effects of this training approach, further studies should include a larger number of subjects, aim to investigate patients with different levels of pathology (not only mild as in this study), and also include analysis of gait kinematics; in addition, it would be interesting to conduct a long-term follow-up of robotic training in patients with PD.

## References

- Abbruzzese G, Trompetto C, Marinelli L (2009). The rationale for motor learning in Parkinson's disease. *Eur J Phys Rehabil Med* 45:209-214.
- Baker R, McGinley JL, Schwartz MH, et al (2009). The gait profile score and movement analysis profile. *Gait Posture* 30:265-269.
- Cakit BD, Saracoglu M, Genc H, et al (2007). The effects of incremental speed-dependent treadmill training on postural instability and fear of falling in Parkinson's disease. *Clin Rehabil* 21:698-705.
- Comella CL, Stebbins GT, Brown-Toms N, et al (1994). Physical therapy and Parkinson's disease: a controlled clinical trial. *Neurology* 44:376-378.
- Davey C, Wiles R, Ashburn A, et al (2004). Falling in Parkinson's disease: the impact on informal caregivers. *Disabil Rehabil* 26:1360-1366.
- Davis RB, Ounpuu S, Tyburski D, et al (1991). A gait analysis data collection and reduction technique. *Human Movement Science* 10:575-587.
- de Goede CJ, Keus SH, Kwakkel G, et al (2001). The effects of physical therapy in Parkinson's disease: a research synthesis. *Arch Phys Med Rehabil* 82:509-515.
- deSouza RM, Moro E, Lang AE, et al (2013). Timing of deep brain stimulation in Parkinson disease: a need for reappraisal? *Ann Neurol* 73:565-575.
- Forrester LW, Roy A, Krebs HI, et al (2011). Ankle training with a robotic device improves hemiparetic gait after a stroke. *Neurorehabil Neural Repair* 25:369-377.
- Goodwin VA, Richards SH, Taylor RS, et al (2008). The effectiveness of exercise interventions for people with Parkinson's disease: a systematic review and meta-analysis. *Mov Disord* 23:631-640.
- Hesse S, Tomelleri C, Bardeleben A, et al (2012). Robot-assisted practice of gait and stair climbing in nonambulatory stroke patients. *J Rehabil Res Dev* 49:613-622.
- Hesse S, Waldner A, Tomelleri C (2010). Innovative gait robot for the repetitive practice of floor walking and stair climbing up and down in stroke patients. *J Neuroeng Rehabil* 7:30-40.
- Hoehn MM, Yahr MD (1967). Parkinsonism: onset, progression and mortality. *Neurology* 17:427-442.
- Kwakkel G, de Goede CJ, van Wegen EE (2007). Impact of physical therapy for Parkinson's disease: a critical review of the literature. *Parkinsonism Relat Disord* 13 Suppl 3:S478-487.
- Lee H, Ho P, Rastgaar MA, et al (2011a). Multivariable static ankle mechanical impedance with relaxed muscles. *J Biomech* 44:1901-1908.
- Lee H, Patterson T, Ahn J, et al (2011b). Static ankle impedance in stroke and multiple sclerosis: a feasibility study. *Conf Proc IEEE Eng Med Biol Soc* 2011:8523-8526.
- Lo AC, Chang VC, Gianfrancesco MA, et al (2010). Reduction of freezing of gait in Parkinson's disease by repetitive robot-assisted treadmill training: a pilot study. *J Neuroeng Rehabil* 7:51.
- Mehrholtz J, Pohl M (2012). Electromechanical-assisted gait training after stroke: a systematic review comparing end-effector and exoskeleton devices. *J Rehabil Med* 44: 193-199.
- Mehrholtz J, Friis R, Kugler J, et al (2010). Treadmill training for patients with Parkinson's disease. *Cochrane Database Syst Rev* (1):CD007830.
- Morris ME, Huxham F, McGinley J, et al (2001). The biomechanics and motor control of gait in Parkinson disease. *Clin Biomech (Bristol, Avon)* 16:459-470.
- Perry J (1992). *Gait Analysis: Normal and Pathological Function*. Thorofare, NJ, SLACK Inc.
- Picelli A, Varalta V, Melotti C, et al (2016). Effects of treadmill training on cognitive and motor features of patients with mild to moderate Parkinson's disease: a pilot, single-blind, randomized controlled trial. *Funct Neurol* 31:25-31.
- Picelli A, Melotti C, Origano F, et al (2013). Robot-assisted gait training versus equal intensity treadmill training in patients with mild to moderate Parkinson's disease: a randomized controlled trial. *Parkinsonism Relat Disord* 19:605-610.
- Picelli A, Melotti C, Origano F, et al (2012). Robot-assisted gait training in patients with Parkinson disease: a randomized controlled trial. *Neurorehabil Neural Repair* 26:353-361.
- Protas EJ, Mitchell K, Williams A, et al (2005). Gait and step training to reduce falls in Parkinson's disease. *Neuro Rehabilitation* 20:183-190.
- Rochester L, Baker K, Hetherington V, et al (2010). Evidence for motor learning in Parkinson's disease: acquisition, automaticity and retention of cued gait performance after training with external rhythmical cues. *Brain Res* 1319:103-111.

- Roy A, Krebs HI, Bever CT, et al (2011). Measurement of passive ankle stiffness in subjects with chronic hemiparesis using a novel ankle robot. *J Neurophysiol* 105:2132-2149.
- Sale P, De Pandis MF, Le Pera D, et al (2013). Robot-assisted walking training for individuals with Parkinson's disease: a pilot randomized controlled trial. *BMC Neurol* 13:50.
- Sale P, Franceschini M, Waldner A, et al (2012). Use of the robot assisted gait therapy in rehabilitation of patients with stroke and spinal cord injury. *Eur J Phys Rehabil Med* 48:111-121.
- Semprini R, Sale P, Foti C, et al (2009). Gait impairment in neurological disorders: a new technological approach. *Funct Neurol* 24:179-183.
- Smania N, Corato E, Tinazzi M, et al (2010). Effect of balance training on postural instability in patients with idiopathic Parkinson's disease. *Neurorehabil Neural Repair* 24:826-834.
- Song J, Fisher BE, Petzinger G, et al (2009). The relationships between the Unified Parkinson's Disease Rating Scale and lower extremity functional performance persons with early-stage Parkinson's disease. *Neurorehabil Neural Repair* 23:657-661.
- Spenko M, Yu H, Dubowsky S (2006). Robotic personal aids for mobility and monitoring for the elderly. *IEEE Trans Neural Syst Rehabil Eng* 14:344-351.
- Stocchi F, Antonini A, Barone P, et al (2014). Early DEtection of wEaring off in Parkinson disease: the DEEP study. *Parkinsonism Relat Disord* 20:204-211.
- Tan D, Danoudis M, McGinley J, et al (2012). Relationships between motor aspects of gait impairments and activity limitations in people with Parkinson's disease: a systematic review. *Parkinsonism Relat Disord* 18:117-124.
- Toole T, Maitland CG, Warren E, et al (2005). The effects of loading and unloading treadmill walking on balance, gait, fall risk, and daily function in Parkinsonism. *Neuro Rehabilitation* 20:307-322.
- Ustinova K, Chernikova L, Bilimenko A, et al (2011). Effect of robotic locomotor training in an individual with Parkinson's disease: a case report. *Disabil Rehabil Assist Technol* 6:77-85.
- Warren Olanow C, Kieburtz K, Rascol O, et al (2013). Factors predictive of the development of levodopa-induced dyskinesia and wearing-off in Parkinson's disease. *Mov Disord* 28:1064-1071.