Official title: Impact of carbon fiber AFOs on gait and resulting changes in quality of life across time in persons with PD

NCT number: NCT03192046

IRB Approved date: February 15, 2017

The University of Texas Southwestern Medical Center at Dallas
Institutional Review Board

Protocol

Title: Impact of carbon fiber AFOs on gait and resulting changes in quality of life across time in persons with PD

1. Introduction and Purpose:

Parkinson disease (PD) is a progressive neurological disease that results in characteristic gait dysfunction. Gait problems include decreased velocity, decreased stride length, difficulty with initiation of gait, postural stability problems and alteration in joint kinematics.[1] In this typically older patient population, these gait deviations affect their participation in household and community activities. The standard of care is currently focused on therapeutic exercise and cueing of various types (visual, auditory, verbal). Current interventions have not been demonstrated to markedly improve gait kinematics, so there is a need to identify interventions that could improve gait performance in this population. Lower extremity bracing is a common and well-established intervention for gait dysfunction with other populations, including stroke and brain injury. The braces allow for improved stability, sensory feedback, and consistent tactile cues to allow patients to have the best gait mechanics with each step. It is reasonable to hypothesize that appropriate bracing may have the potential to improve gait function and kinematics in PD since these patient often have gastroc-soleus weakness. Data from our early pilot studies indicates that bracing individuals with PD can positively impact their mobility. This includes improvements in velocity, step length, and dynamic balance. Additional data supported an upward trend in quality of life.

The purpose of this study is to investigate the impact of a specifically designed ankle foot orthosis (a custom fabricated carbon fiber brace) on the spatial and temporal gait parameters, kinematics, and walking endurance in individuals with Parkinson's disease. The brace utilized will be chosen according to patient need and presentation. The carbon fiber orthosis is fabricated to allow ankle range of motion while providing external stability and energy storing qualities.

This study has three hypotheses. 1) subjects who are fit with carbon fiber orthoses will demonstrate better spatial and temporal gait parameters compared to controls; 2) subjects who are fit with carbon fiber orthoses will demonstrate improvements in gait kinematics during gait as compared to controls, and 3) as a result of the improvements in their mobility, subjects fit with carbon fiber orthoses will have an overall improvement in their quality of life compared to controls.

2. Background:

Parkinson's disease results in a variety of functional impairments including weakness, gait dysfunction and postural changes. Exercise has been a key tool in the treatment of such limitations, although there is not robust evidence supporting any specific type of intervention in the management of PD.[2] There is some evidence that exercise in general can be beneficial regarding quality of life, strengthening, balance and gait speed but optimum dosing and exact content of the ideal intervention has not been identified.[3] Gait dysfunction is one of the most disabling effects of PD yet clear direction on how to treat this problem is lacking. While there is evidence of brain disturbances leading to gait problems[4] is it also acknowledged that weakness and sensory loss are significant contributors to gait dysfunction in PD.[1]
Orthotic management of gait disturbance in diagnoses such as stroke and brain injury is common as such devices have the potential to address weakness as well as sensory impairment. However, the potential role of bracing in PD has not been explored in the literature. This study is designed to

evaluate the effectiveness of bracing on some of the common manifestations of gait dysfunction in PD.

3. Concise Summary of Project:

This is a randomized, repeated measures, matched group study. There will be two groups of participants, 8 participants per group, 35 participants total from time of initial enrollment in this study. Group one (G1) will receive bilateral custom braces and a standardized home walking/exercise program. Group two will receive the standardized walking/exercise program without any brace or AFO. Subjects will be randomized upon enrollment in the study. At the time of consent, random drawing from concealed envelopes with red, blue or green chips will be done to determine group assignment. Subjects will be recruited through the Clinical Center for Movement Disorders at UT Southwestern Medical Center where patients with PD receive routine evaluation and follow-up. Subjects will be followed for 6 months during this study and outcome measures will be collected 3 times over the course of the study. Subjects will be seen every 3 months for the duration of the study for testing as well as for other visits as noted in the table below. Participants will not need to have insurance benefits for initial physical therapy evaluation and for ankle braces. All subsequent visits to the Crowley gait lab for assessments and brace adjustment will be provided at no cost to the participants.

Outcome measures

Testing Procedures:

6-Minute Walk Test: Each subject will be asked to walk at a self-selected velocity on level surfaces for 6 minutes. They will be allowed to use assistive devices if necessary.

Computerized Gait Analysis: Each subject will be asked to walk on a 12-16 foot long vinyl pad placed on the floor. The mat will record and analyze temporal and spatial gait parameters.

Observational Gait analysis: Gait will be evaluated using the Observational Gait Analysis system during over ground walking. A sample of the gait will be videotaped for detailed analysis.

Three-Dimensional gait analysis: Prior to testing, subjects will be outfitted with small retro-reflective markers secured to anatomical locations with easily removable tape. Once markers have been positioned properly, the subject will then be asked to walk up and down a level 15-foot walkway. Four walking trials will be recorded for averaging purposes.

Four Square Step Test: Balance while stepping in different directions will be assessed using this test. Skills such as stepping over an obstacle and stepping backwards are included in the test.

Falls data: Patients will be asked to fill out a fall log at home.

Short Orientation-Memory-Concentration Test of Cognitive Impairment: Gross cognitive function will be tested using this brief questionnaire.

Daily Activity: Steps per day recorded from a pedometer the patients will wear for the week prior to each testing visit. Daily walking (steps/day) will be recorded throughout the study.

PDQ-39: The PDQ-39 is the most widely used Parkinson's Disease specific measure of health status. It contains thirty nine questions, covering eight aspects of quality of life. The instrument was developed on the basis of interviews with people diagnosed with the disease. It has been widely validated, and translated into over fifty languages.

4. Study Procedures: -

Screening, consent and randomization	Confirm medical diagnosis and medical history, assess sensation and range of motion. Consent process. Appointment made for casting.	60 minutes
Baseline Testing (T1)	Initial outcome measures completed with no	120 minutes

	orthoses and first set of orthoses.	
Visit 1 - 4 Month 1 **Visit 5** – Month 2	Gait training session. Instruct in home walking program.	45 minutes
Testing 2 (T2) – Month 3	All outcome measures completed.	120 minutes
Visit 6 and 7- Month 4 & 5	Gait training session.	45 minutes
Testing 3 (T3) – Month 6	All outcome measure completed	120 minutes

The gait training home program is outlined as follows:

- One to two bouts of focused walking per day. Regardless of the number of walking bouts, the goal is 30 minutes total per day.
- Increase the bouts by 2-5 minutes as tolerated working up to 30 minutes total
- Each subject will receive individualized tape walking protocol based on GAITRite data
- Each subject will receive standard instructions for a home exercise program and will receive handouts

5. Sub-Study Procedures:

There are no sub-studies.

6. Criteria for Inclusion of Subjects:

1. Confirmed diagnosis of Parkinson's Disease according to the UK brain bank criteria.[5]
2. Age between 30 and 85.
3. Measurable decrement in gait velocity (between 35 and 15 percent below age-predicted norms for self-selected walking velocity) as measured by the 6 MWT
4. Hoehn and Yahr stage 2-3.
5. Less than 10 full heel raises in single limb stance bilaterally.

7. Criteria for Exclusion of Subjects:

1. Body mass index greater than 40.
2. Passive dorsiflexion range of motion less than approximately neutral (90 degrees)
3. Any other uncontrolled health condition for which gait training is contraindicated
4. Self-report of > 1 fall/month
5. A score of 11 or less on the Short Orientation-Memory-Concentration Test of Cognitive Impairment

8. Sources of Research Material:

Some data will be extracted from the medical record to provide needed information prior to treatment. This includes: prior medical history, confirmation of Parkinson's diagnosis, medication history and use. The dependent assessments include: The outcome measure for the study include: 1. GAITRite System for temporal and spatial parameters, 2. Kinematics, 3. 6-Minute Walk Test (gait endurance), 4. Four Square Step Test, 5. Video tape of over ground gait analysis, 6. PDQ-39 (Parkinson's Disease Questionnaire 8), 7. Falls data; 8. Daily activity (pedometer).

9. Recruitment Methods and Consenting Process:

Subjects will be recruited through the Clinical Center for Movement Disorders at UT Southwestern Medical Center where patients with PD receive routine evaluation and follow-up. Each participant will be scheduled to attend an initial meeting at the School of Health Professions Gait Disorders Clinic. The research project will be explained by Staci Macklin Shearin using the Subject Consent Form as a guide and participants will be randomized to the groups following consent. If they are candidates. This meeting will take approximately 90 minutes. A second visit will be scheduled for the initial assessments and this will take approximately 120 minutes. The original consent and HIPAA Authorization will be maintained in the research file, and the participant will receive a copy of each.

10. Potential Risks:

There is minimal risk involved in participating in this study. There may be minor skin irritation as the result of the new brace(s) as well as minor skin irritation from the surface electrodes used in the EMG testing. There may be minimal fatigue associated with the walking and testing sessions.

11. Subject Safety and Data Monitoring:

The participant's identity will be kept in a separate locked file cabinet in the David M. Crowley Research and Rehabilitation Lab. The subjects will be closely monitored during treatment and testing.

12. Procedures to Maintain Confidentiality:

Each participant will be assigned a unique identification number once it has been determined that the person meets the inclusion criteria and has signed the consent form and HIPPA authorization form. The unique number will be used to identify all data sets for the individual participant. De-identified information obtained during this study will be released to requesting agencies only with a written release of information from the participant. The results of this research may appear in scientific publications but the participants' names will not be used. All data will be maintained in a research folder in a locked cabinet in the David M. Crowley Research and Rehabilitation Laboratory. The UT Southwestern Institutional Review Board is responsible for assuring that participants' rights are respected. Members of the staff may review records for audit purposes. That review will take place at The Department of Physical Therapy.

13. Potential Benefits:

It is anticipated that the application of this orthosis will result in an immediate improvement in gait parameters (temporal and spatial) as well as long term improvements in activity and gait tolerance as well as balance and strength.

14. Biostatistics:

The proposed design thus consists of two treatment groups ("between" effect) with 8 patients (subjects)/group studied over 3 test sessions ("within" effect). At each data point, nine classes of measures are to be obtained, e.g., the 6-minute walk test, computerized gait analysis, etc. Some of these classes may yield more than one measure. We propose four groups of analyses.

Intent to treat analysis.

Not all patients who initially consent and are randomized may complete the study. We plan to compare (a) those that finish with those who do not finish to see if they differ with respect to any of the dependent variables and (b) the proportions of those who do not finish to see if they are equally divided among the groups. The former will be compared by means of t-tests or its nonparametric

counterpart, the Mann-Whitney U, depending upon how well normality assumptions are met. The latter will be compared by means of chi-square or Fisher exact test depending upon sample size.

Preliminary psychometric analyses.

We feel it important to evaluate the relations among the various classes of dependent variables by intercorrelating them to infer their structure, e.g., how many dimensions do they span and are any sufficiently redundant so they can be combined. This involves standard item analysis and exploratory factor analysis. Similar analyses will be performed on the scores obtained from the inclusion measures and other demographics, e.g., can the Hoehn and Yahr scores be combined with other measures to obtain a composite impairment measures that can serve as a better covariate.

Analysis of observed measures.

If all patients who complete the study do so without missing any of the test sessions, ordinary repeated measures analysis of variance (ANOVA) will be used to evaluate the main effect of groups, the main effect of testing sessions, and their interaction. Planned comparisons will be employed comparing (a) groups G1 and G2 with each other This involves comparing what in effect are two control conditions with each other and their average against the active treatment condition. This will be done as a series of univariate tests.

Next, we will examine the effects of covariates such as age of onset and impairment as inferred through the Hoehn and Yahr scale and other measures, again in a univariate manner.

We will then perform a multivariate analysis of variance (MANOVA) to test the null hypotheses that differences on the three effects of interest (groups, testing session, and their interaction) are all nonsignificant across the set of dependent variables.

It is quite likely that there will be missing data from patients who fail to attend one or more testing sessions. We will deal with this problem in two ways. One is to attempt to impute the missing data (see next subsection). The other is to use a mixed model (random regression) which does not require all data to be present, e.g. can analyze the testing effect using whatever data are present. This allows for the same univariate tests to be conducted, but makes multivariate testing extremely difficult to impossible with the data as obtained.

Analysis of imputed measures.

Assuming there will be missing data, we will attempt to impute the missing data and perform the analyses as listed in the previous section, including the MANOVA, on these imputed data.

References

1. Nallegowda M, Singh U, Handa G, Khanna M, Wadhwa S, Yadav SL, Kumar G, Behari M. Role of sensory input and muscle strength in maintenance of balance, gait, and posture in parkinson's disease: A pilot study. *American journal of physical medicine & rehabilitation / Association of Academic Physiatrists*. 2004;83:898-908
2. Deane KH, Jones D, Ellis-Hill C, Clarke CE, Playford ED, Ben-Shlomo Y. A comparison of physiotherapy techniques for patients with parkinson's disease. *The Cochrane database of systematic reviews*. 2001:CD002815
3. Goodwin VA, Richards SH, Taylor RS, Taylor AH, Campbell JL. The effectiveness of exercise interventions for people with parkinson's disease: A systematic review and meta-analysis. *Movement disorders : official journal of the Movement Disorder Society*. 2008;23:631-640
4. Hanakawa T, Katsumi Y, Fukuyama H, Honda M, Hayashi T, Kimura J, Shibasaki H. Mechanisms underlying gait disturbance in parkinson's disease: A single photon emission computed tomography study. *Brain : a journal of neurology*. 1999;122 (Pt 7):1271-1282
5. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic parkinson's disease: A clinico-pathological study of 100 cases. *Journal of neurology, neurosurgery, and psychiatry*. 1992;55:181-184