Development of a Multifunctional Rehabilitation Device for Persons With Parkinson's Disease

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Development of a Multifunctional Rehabilitation Standing and Stepping Device for persons with Parkinson's disease

BACKGROUND

Mobility, cognitive problems and common medical comorbidities in PwP: Postural instability and gait disturbances (PIGD) are a common (falls 37.2%, freezing of gait 16%) i and a significant cause of disability and reduced quality of life in PwP (1-3). Quality of life is further compromised by fear of falling resulting in reduced physical activity and increasing sedentariness (4). Although PT can be very effective, economic (healthcare costs) or patient (therapy adherence) barriers undermine long-term outcomes (5). A Cochrane review showed that effects of PT quickly faded within 1-3 months in PwP (6). Fortunately, **new trends emphasize the importance of post-rehabilitation in-home interventions that have the potential for long-term adherence and sustained benefits** (7-9). Cognitive impairment is another major source of disability and lower quality of life in PwP with point prevalence of MCI of 40% (10) and a major risk factor for dementia in PwP. **Importantly, there are shared pathophysiologies between mobility disturbance and cognitive impairment, where PIGD motor features are a major risk factor for development of dementia in PwP (11)**. Mechanistically, the overlap between mobility disturbance and cognitive impairment can be explained because sensorimotor integration to maintain postural control is heavily dependent on sufficient allocation of attentional resources (12-14). **Therefore, neural pathways subserving attention are critical for effective postural control and gait functions** (15, 16), For example, safe ambulation and navigation functions require a combination of afferent information processing, automatic movement processes, and situations-specific corrections or adjustments (17). Consequently, the development of mobility problems reflects an increased need for cognitive control of previously automated actions (18, 19). Apart from cognitive impairment, common medical comorbidities (esp. metabolic syndrome/diabetes, frailty/sarcopenia and age-associated vestibular dysfunction) further aggravate PIGD motor features in PwP. Therefore, successful and effective rehabilitation interventions need to target each of these mechanistic factors when present in a PwP.

Critical knowledge gap: Although PT may improve mobility functions in PwP in the short-term, there are currently no cost effective and sustainable approaches to ensure long-term success.

Problem to be solved: Novel approaches are needed to ensure sustainable long-term outcomes of PIGD programs in PwP by targeting the current dilemmas of intermittent series of PT: (i) healthcare costs of PT; (ii) limited sustained long-term adherence of patients to post-PT physical activity instructions, (iii) lack of emphasis on sedentariness, and (iv) lack of routine PT to integrate walking therapy with cognitive-motor dual tasks.

Specific Aim: To develop and clinically test a Multifunctional Rehabilitation Standing and Stepping Device (MRSSD) prototype. We will develop a multidirectional MRSSD system based on a rotary motor propulsion system to enable multidirectional stepping therapy integrated with desktop activities requiring cognitive attention. Data from initial user acceptance studies will provide design feedback for optimized use in the PwP target population. Preliminary motor and cognitive effectiveness will be tested in a 12-week (plus or minus one week) randomized controlled in-home pilot clinical trial comparing the MRSSD to a static desk & control groups to provide preliminary data to power a large-scale clinical trial in phase II.

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Methods

Human Subjects, Recruitment, and Informed Consent:

Eligibility criteria: PwP (n=45, *as close to equal number of females/males as possible*); age 50 years and over). Diagnosis of PwP is based the UK Parkinson's Disease Society Brain Bank Research Center (UKPDSBRC) criteria (20) with evidence of at least one of the following PIGD motor features (slow gait, imbalance, falls, freezing of gait) and/or MCI (21). Medical comorbidities of metabolic changes, DM, frailty/sarcopenia or age-associated vestibular changes are allowed (22-24).

Exclusion criteria:

1. PD dementia (based on the Emre et al. diagnostic criteria (25) - cognitive and instrumental activities of daily living assessment);
2. Parkinsonism plus syndromes;
3. Inability to stand, step or walk without an assistive device;
4. History of symptoms in stance that preclude safe and comfortable participation, such as severe dizziness and lightheadedness, severe orthostasis, severe symptomatic leg or back musculoskeletal pain, painful neuropathy, significant ankle edema or medication side effects;
5. History of symptomatic cardiovascular or pulmonary disease interfering with stance;
6. History of active rheumatic arthritis;
7. History of uncontrolled chronic pain syndrome;
8. Any other history of medical or psychiatric comorbidity precluding safe participation in the project;
9. Venous stasis or severe varicosities.

Subject Recruitment: Prior to any research procedures, written informed consent will be obtained from each subject followed by initial study eligibility email
. PwP subjects will be recruited from the University of Michigan Functional Neuroimaging, Cognitive & Mobility Laboratory and from Dr. Richardson's clinical practice in Physical Medicine & Rehabilitation. Our laboratory has already collected a waiting list of volunteers who have expressed interest in this or similar studies. Additional recruitment strategies are detailed in the Recruitment & Retention clinical form.

Test Sites:
There will be two test sites where these studies can be conducted: in participant's home offices and the Functional Neuroimaging, Cognitive, and Mobility Laboratory (fNiCoMo) at Domino's Farms.

Research Design and Methods:

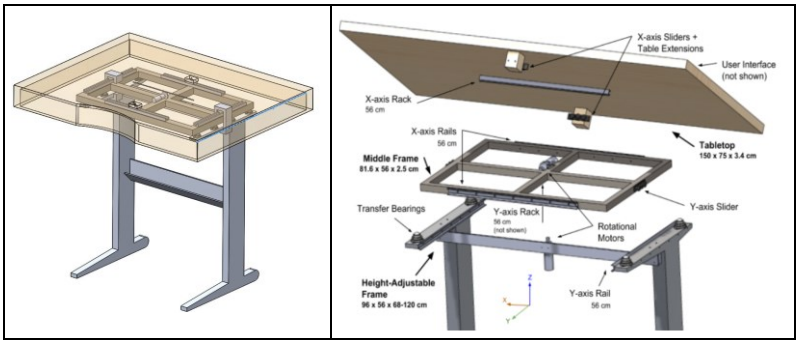

Figure 1. Design concept of the new MRSSD prototype reflecting a glass-view of propulsion system (left) and exploded view of the tabletop propulsion system (right).

The main aims of this STTR are (i) to develop the new multifunctional rehabilitation desk (MRSSD); (ii) perform a clinical acceptance study in the target population, and (iii) collect preliminary motor and cognitive effectiveness data in a randomized MRSSD vs. regular static standing desk in a 4-month in-home pilot clinical trial in PwP.

MRSSD Design: We have developed a concept design for an MRSSD prototype that will form the basis for further development (Figure 1). Several design criteria have been identified that the MRSSD will need to meet (Table 1). The motion of the tabletop is created by a system of motors and gears. The rotational motors have a gear screwed onto their shafts and will spin along with the motor shaft rotation. The teeth of the gear interlocks with a gear rack to propel the gear rack (and everything it is attached

to) in a linear but adjustable direction. The transfer bearings, clamps, and slider assemblies support the weight of the table while also allowing the tabletop to move in a safe and confined path. The middle frame is used to spatially separate the X-axis motion from the Y-axis motion while also connecting them to allow tabletop movement in diagonal, circular, and square patterns. We will adhere to ISO (14971) and IEC (60601) International Standards to ensure safety, reliability, and quality use.

Table 1. Overview of critical user needs, requirements, and specification for MRSSD prototype development during Phase I.

User need	**Requirement**	**Specification**
Stepping movements	Prompts multi-directional motion.	• Drives user movement in left-right, forward-backward, combined and non-linear pattern directions. Users take > 3 steps per minute at ~2.5 mm/s.
Safety	Device is level, does not vibrate, and does not tip or fall.	• Device does not tip with 50 kg load at edge of tabletop at 25 cm excursion distance. Vibration on tabletop surface < 0.1m/s^2 during use.
	Device is electrically safe.	Device functions in range of conditions as described by IEC 60601-1-11
Integration with home activities	Device is large enough to facilitate a variety of activities.	Dimensions: Height: 66 cm to 130 cm Width: 67 cm to 104 cm Length: 48 cm to 84 cm
	Device is able to bear a variety of loads throughout use.	Device can function with 0–50 kg load at center of tabletop during excursion.
Low noise level	Sound produced by device is not distracting in home setting.	< 35 dB directly above device surface.
Long duration continuous use	Device cycle time > 4 hours.	No overheating (>60°C) or stress beyond 50% of functioning capacity.

Human User Acceptance Sub-Study #1

Aim: The main aim of the PwP user acceptance study is to identify an average of 80% acceptability of a number of specific MRSSD settings and user response derived from 18 PwP across a range of imbalance, slow gait, cognitive impairment, physical frailty, fear of falling and medical comorbidities (metabolic changes, DM, or age-associated vestibular changes. This will enable identification of MRSSD settings that are feasible for the majority of PwP. However, these settings can be adjusted up or downward when mandated by the subject's specific condition and individualized therapy goals. The functional use and duration of utilization of the MRSSD will be assessed in a laboratory-based environment at the University of Michigan by on-site interaction with the STTR team. This will allow for close monitoring of safe use of the MRSSD, avoid estimated time-of-use bias when relying on self-reporting in the home environment, and discuss immediate user feedback that will inform the development of a monitoring and biofeedback driven interface device in Phase II of this STTR.

Study entry screening session: University of Michigan Institution Review Board (IRBMED) approved written informed consent will be obtained from each subject prior to any research procedures. After consenting, participants will complete a screening and neurological examination using the UK diagnostic UK Parkinson's Disease Society Brain Bank Research Center (UKPDSBRC) criteria (44) with evidence of at least one of the following PIGD motor features (slow gait, imbalance, falls, freezing of gait) and/or MCI (21). Medical comorbidities of metabolic changes, DM, frailty/sarcopenia or age-associated vestibular changes are allowed (22-24). PwP with dementia will be excluded (49). More and detailed exclusion criteria are provided in ("Protection of Human Subjects). Males and females will be studied as equally as possible, though more men are diagnosed with Parkinson's than females by a ratio of 2:1 (78) (Biological variables, NIH Rigor statement).

Subjects will also complete the Montreal Cognitive Assessment Scale which will serve as a measure of general cognitive status (75).

Participants will have 2 study visits about a week apart with goal of shown ability to operative and use the desk for a minimum of 1 hour at the time of the 2nd visit. We will use the User Acceptance Study Questionnaire and SUS instrument on each day. Responses on the 2nd day after 1 hour of use will serve as the main primary acceptance outcome. An activity monitor (ActivPAL) will be worn during each of the sessions to measure overall movement. Total movement for each session will be defined as the number of 'counts' per minute – a unit of activity measurements that is the result of summing post-filtered accelerometer values into epochs (i.e., the higher the number of counts, the greater the amount of activity). We will obtain additional measures to determine optimal directionality, including the extent of musculoskeletal muscle fatigue using visual analogue scales and user feedback on preferred directional movements (7). Optional measurements of weight, height, pulse and blood pressure, feet and ankle measurements may be taken. We will also use a System Usability Scale (SUS) at each study visit.

Human User Acceptance Sub-study #2

Aims:
In-lab supervised feasibility study of repeated standing MRSSD sessions in PwP (n=8) after initial user acceptance study to assess:
(i) multi-session safety and tolerance of 2 hr/d for 5d/2 wks of MRSSD use,
(ii) successful ability of cognitive/motor dual-task desktop activities,
(iii) sensitivity of the proposed outcome parameters to be used in the in-home clinical trial &
(iv) to directly allow the investigators to observe how participants learn the interact with the desk across multiple sessions.

Study entry screening session: University of Michigan Institutional Review Board (IRBMED) approved written informed consent will be obtained from each subject prior to any research procedures. After consenting, participants will complete a screening and neurological examination using the UK diagnostic UK Parkinson's Disease Society Brain Bank Research Center (UKPDSBRC) criteria (44) with evidence of at least one of the following PIGD motor features (slow gait, imbalance, falls, freezing of gait) and/or MCI (21). Medical comorbidities of metabolic changes, DM, frailty/sarcopenia or age-associated vestibular changes are allowed (22-24). PwP with dementia will be excluded (49). More and detailed exclusion criteria are provided in ("Protection of Human Subjects). Males and females will be studied as equally as possible, though more men are diagnosed with Parkinson's than females by a ratio of 2:1 (78) (Biological variables, NIH Rigor statement). Subjects will also complete the Montreal Cognitive Assessment Scale which will serve as a measure of general cognitive status (75).

In-lab supervised feasibility study of repeated MRSSD standing sessions in PwP:
All subjects will complete a baseline clinical test battery and assessment of 3-day physical activity prior to the 2-week in-lab supervised feasibility study of repeated MRSSD standing sessions in PwP. The clinical test battery and assessment of 3-day physical activity will be completed after the 2-week intervention study (see Table 1 below). Optional measurements of weight, height, pulse and blood pressure, feet and ankle measurements may be taken. Additionally, optional measures of grip strength with a handheld dynamometer and optional measures of trunk strength with a lateral plank may be completed (79). Optionally, a microFET3 handheld dynamometer will be used to assess hip abduction strength (80).

Table 1: Clinical test battery measures pre/post the 2-week intervention:

Outcome measures	Tests	Function	Validity
Primary motor:	Timed Up and Go (TUG) test (26) and	Integrated postural control & gait measure	Mobility measure; Predictor of falls

	Romberg Balance Test (81) with instrumented sensor assessment (iTUG, Mobility Lab, APDM, Inc., Portland, OR); figure 2.		
Primary cognitive-motor dual task:	Stroop Color Word stepping test (27); figure 3.	Complex stepping test requiring inhibitory control	Fall risk: Predictor anticipation of and/or in response to environmental hazards
Primary cognitive:	Stroop Color Word Interference test (28, 29)	Interference susceptibility (inhibitory control)	Executive function measure (cognition)
Exploratory motor (muscle strength/frailty/sarcopenia)::	Muscle strength hip abductors & adductors (microFET3 handheld dynamometer, (optional) (80)); grip strength with handheld dynamometer (optional), hip/oblique strength with timed lateral plank (optional) (79)	Quantitative muscle strength mediolateral leg adductors & abductors	Predictor of falls, postural stability (30) & proxy measures of frailty
Exploratory cognitive:	WAIS-III: Digit Symbol-Coding (31), Delis-Kaplan Trail Making Test (32), Eriksen Flanker test (33)	Information processing speed, concept shifting & visual attention	Daily functional performance; fall risk
Exploratory cognitive-motor dual task(s)	Clinical reaction time grasping falling computerized stick (34, 35)	Cognitive-motor response inhibition	Predictor of falls
Exploratory measures:	Actigraphy (activPAL™, Glasgow, UK)	Carry-over effects of desk use on daily physical activity	Physical activity (inversely correlated to fear of falling)
Exploratory measures:	Continuous glucose monitoring (Dexcom G6 Pro, San Diego, CA)	Average glucose level	Metabolic parameter
Exploratory measures:	VO_2 energy expenditure (Cosmed K4b2 gas analyzer Cosmed, Rome, Italy).	VO_2	Energy expenditure measure
Exploratory measures:	Time behind table	Desk utilization	Adherence to intervention

In-lab intervention: There will be 5 sessions (2 hr per sessions; 5 sessions in a two week period) of in-lab supervised feasibility study of repeated MRSSD standing sessions in PwP

Subjects will be asked to use the standup desk *ad libitum* with the choice to alternate between sitting down and standing if desired or needed. Subjects will be able to choose the directionality of the desk (mediolateral, anteroposterior or oblique) and adjust the speed and amplitude as per instructions. A set of specific instructions

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that will be given to our participants: "*You will be asked to stand behind the raised table until you develop discomfort, such as back or leg pain for which you normally would sit down. At that point, you will lower the table and remain seated until the discomfort has resolved and you feel you are able to stand again* ".

Subjects will stand on an anti-fatigue mat. Subjects will be asked to perform all the office routines behind the stand-up desk as they normally would. Except when completing specific assessment tests, subjects can perform their preferred desktop activities, including use of computer, games, videos/movies, listening to music or reading. Specific elected activities will be tracked. The total time spent in upright standing compared to sitting will be tracked. Total time to take breaks will be recorded. Each session will not exceed 2 hours. As many rest breaks will be provided to the subject as needed. Participants will be supervised by trained research staff under the supervision of a physical therapist. (see below). User Acceptance Study Questionnaire and SUS instrument will be administered during the visits. Optional instrumented ADPM sensors (Mobility Lab, APDM, Inc., Portland, OR) can be used during the standing sessions to track movement and center of mass (76).

Individualized interventions. The study PT will provide individualized targeting of specific morbidities in PwP, such as imbalance (emphasis on mediolateral excursions), gait turning (emphasis on rotatory excursions), metabolic syndrome and sarcopenia (emphasis on higher intensity and large excursions), vestibular changes (emphasis on anterior-posterior and rotatory excursions), and cognitive impairment (emphasis on cognitive-motor dual tasking desktop activities).

The following assessment swill be made during the 2-week trial:

- Cumulative number of adverse events as categorized by the University of Michigan IRBMED classification (mild, moderate, severe; related/unrelated)
- Daily and cumulative musculoskeletal discomfort
- Percentage of participants able to complete specific cognitive desktop activity (reading task, typing performance, web search task).

Physical therapy instructions: Physical activity studies have shown that individualized instructions and supervision during a study are of paramount importance. Instructions on proper body positioning at the table, individual adjustment of table height, proper positioning of upper extremities, use of anti-fatigue mat, and optimal monitor height will be performed by trained research staff under the supervision of a physical therapist.. They will also monitor the subject and provide feedback about best standing practices, including pelvis and lumbar spine positions. Additionally, they will monitor each subject throughout the study and will guide the mobility assessments in this study.

Sub-study #3: Randomized controlled and examiner-blinded MRSSD vs. regular static standing desk vs. non-desk control group in a 12-week in-home pilot clinical trial in PwP

Aim: The main aim of the pilot randomized controlled clinical trials is to collect preliminary motor and cognitive effectiveness data in a randomized controlled and examiner-blinded MRSSD vs. regular static standing desk vs. usual care non-desk control group (n=6 per group; to account for attrition, n=25) in a 12-week in-home pilot clinical trial in PwP. We hypothesize that PwP in the MRSSD group will have better motor and cognitive-motor dual task performance compared to the static standing desk and usual control group. To accommodate participants' schedules, the in-home portion of the study will be 12 weeks plus or minus one week. This will allow for some flexibility if participants are out of town or unable to schedule their post-intervention visit at exactly 12 weeks.

Study entry screening session: University of Michigan Institutional Review Board (IRBMED) approved written informed consent will be obtained from each subject prior to any research procedures. After consenting, participants will complete a screening and neurological examination using the UK diagnostic UK Parkinson's Disease Society Brain Bank Research Center (UKPDSBRC) criteria (44) with evidence of at least one of the following PIGD motor features (slow gait, imbalance, falls, freezing of gait) and/or MCI (21). Medical comorbidities of metabolic changes, DM, frailty/sarcopenia or age-associated vestibular changes are allowed (22-24). PwP with dementia will be excluded (49). More and detailed exclusion criteria are provided in

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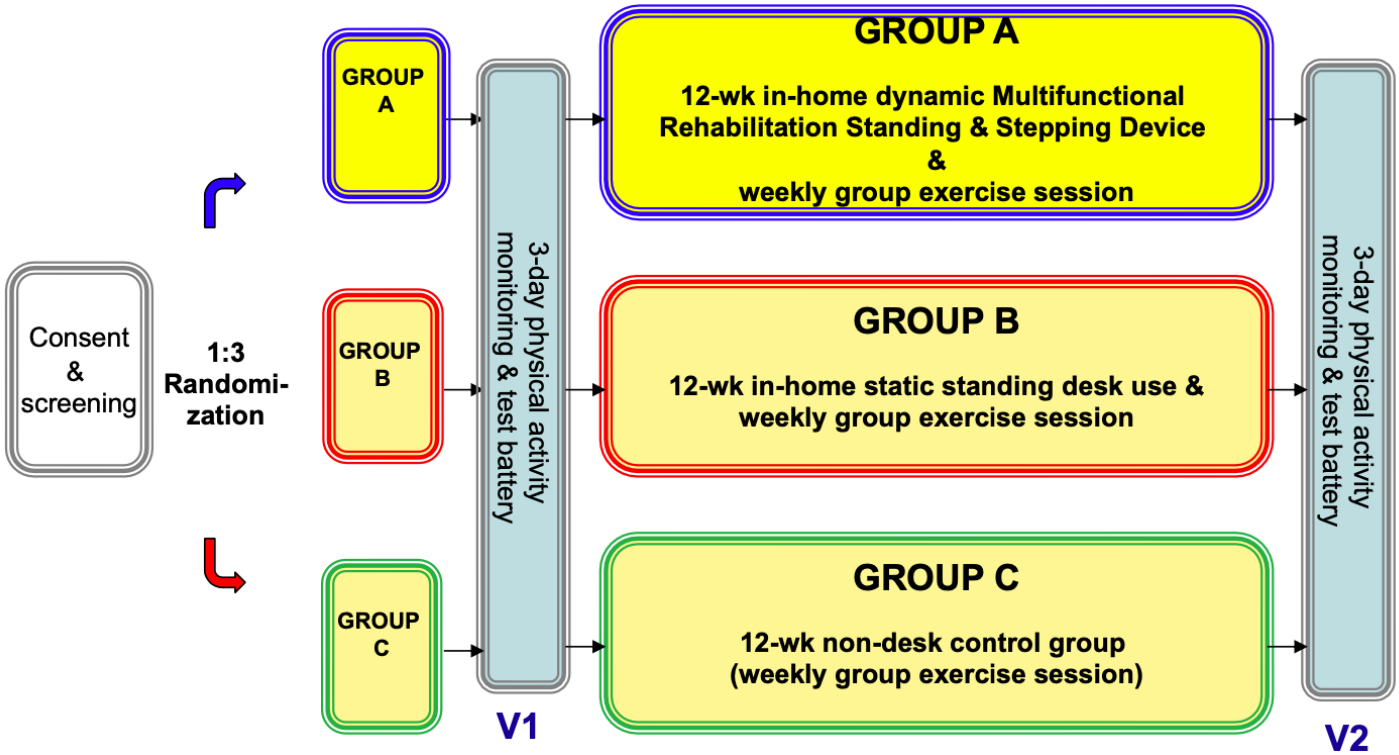
("Protection of Human Subjects). Males and females will be studied as equally as possible, though more men are diagnosed with Parkinson's than females by a ratio of 2:1 (78) (Biological variables, NIH Rigor statement). Subjects will also complete the Montreal Cognitive Assessment Scale which will serve as a measure of general cognitive status (75).

Design: Randomized, controlled examiner-blinded clinical pilot trial.

All subjects will complete a baseline clinical test battery and assessment of 3-day physical activity prior to the 12-week in-home use of the MRSSD vs. static standing desk vs. usual care control group. The clinical trial design and details are shown in figure 2 below. For participants who received a desk, they will have the option to participate in an open label extension of using the table. Participants can decide if they would like to keep the desk in their home for an additional 1-2 years. During this time, they will have the option to provide user feedback. This will enable participants who feel they are receiving a personal benefit of being more active to continue to use the device. The study team may ask participants about discomfort they experience while using the device and ease of use.

A clinical test battery and actigraphy will be administered prior to (V1) and at the end (V2) of the 12-week (plus or minus 1 week) intervention period (V1= visit 1; V2 = visit 2). Study randomization will be semi-random based on age (±7 yr) and the number of males and females will be matched in each group.

Figure 2: Outline of in-home randomized controlled clinical pilot trial of MRSSD vs. static standing desk use vs. usal care control group (all three having a weekly exercise group) in 18 PwP (n=6 per group). Trained research staff under the supervision of a physical therapist will make biweekly (i.e. every other week) phone calls during the study to provide monitoring of the participants and identify and remedy any issues that may occur. If participants do not answer phone call on specified date or establish that they prefer emailing to calling, the study team may email the participant to satisfy the monitoring requirements. These monitoring calls/emails will occur every two weeks plus or minus 3 days.



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In-home therapy table/standing desk instructions: As in-home therapy desk use will be unsupervised, trained research staff under the supervision of a physical therapist will perform an initial in-home safety assessment to ensure safety of the dynamic stepping desk set-up. The table cut-out side will be situated to optimize safety (based on PT and research staff judgement). Instructions on proper body positioning at the table, individual adjustment of table height, proper positioning of upper extremities, use of anti-fatigue mat, and optimal monitor height (if using a PC) will be given. The table also as a 'red button' emergency stop button. The tabletops have a cut-out that partially encircles the user. This construction will provide a gentle tactile cue to move and take a step and at the same time provide safety given the partial surround. OHSU "neutral body positioning" guidelines will be explained to the participant. The therapist will instruct the subjects to use the table for an average of 2 hours per day for at least 5 days per week. The therapist will review with the subject a wide range of computer and non-computer desktop activities and advise on properly performing these tasks on the desk. The therapist will instruct in proper use and adjustment of the table and of the table-use monitoring system. Unlike typical more rigid standing instructions for a static standing desk more frequent stepping and postural adjustments are encouraged for users of the dynamic stepping desk, including transient leaning if desired.

Individualized interventions in PwP with PGD motor features, MCI, frailty and associated common medical comorbidities (metabolic changes, DM, frailty/sarcopenia or age-associated vestibular changes). Based on the V1 assessment the study PT will prescribe individualized targeting of specific morbidities in PwP, such as imbalance (emphasis on mediolateral excursions), gait turning (emphasis on rotatory excursions), metabolic syndrome and sarcopenia (emphasis on higher intensity and large excursions), vestibular changes (emphasis on anterior-posterior and rotatory excursions), and cognitive impairment (emphasis on cognitive-motor dual tasking desktop activities). These settings will be practiced during initial 1-2 supervision sessions (in-home, in-lab). These practice sessions will apply to participants in groups A & B.

Outcome measures & scientific rigor: The scientific rigor of our proposal is strengthened by the high reproducibility and clinical relevance of our primary outcome measure, the randomized trial design of the study, and blinding of examiners who administer the clinical test battery but are not part of the daily operations of the study.

Primary outcome measures: Timed Up and Go (TUG) Test. The primary outcome measure will be the TUG test (total time) (26). The TUG is the most frequently used test to assess functional mobility (36). Functional mobility is a person's ability to move to accomplish activities of daily living; it bridges the concepts of mobility and functional ability. Functional mobility is commonly lost in PD. The TUG has also been shown to have good prediction to distinguish elderly fallers from non-fallers (37). Stroop Color Word Stepping Test, a cognitive motor dual-task requiring inhibitory control, is a prime example of an attention and cognitive processing-dependent motor stepping test where PwP perform less well compared to healthy control persons (38). Impaired inhibitory control contributes to stepping errors, impairs gait adaptability and may increase fall risk in people with PD (39). Optional measurements of weight, height, pulse and blood pressure, feet and ankle measurements may be taken.

Regarding exploratory measures, an optional vertical jump test may be performed to measure power, only after a bone density scan is performed or a trained clinician evaluates the subject for any evidence of bone weakness (77). APDM sensors would be used during the administration of this test to track the position of different joints. Additionally, optional measures of grip strength with a handheld dynamometer and optional measures of hip and oblique strength with a lateral plank may be completed (79). Optionally, a microFET3 handheld dynamometer will be used to assess hip abduction strength (80).

Exploratory outcome measures are listed in table 2 below:

Table 2: Pilot clinical trial outcome measures

Outcome measures	**Tests**	**Function**	**Validity**
Primary motor:	Motor assessment, MiniBest (55), Timed Up	Integrated postural control & gait measure	Mobility measure; Predictor of falls

	and Go (TUG) test (26) ISAW and ISWAY (56-58) with instrumented sensor assessment (iTUG, Mobility Lab, APDM, Inc., Portland, OR); figure 2. MDS-UPDRS examination (parts 1-4) (67-68), Modified H&Y (69-72)		
Primary cognitive-motor dual task:	Stroop Color Word stepping test (27); figure 3.	Complex stepping test requiring inhibitory control	Fall risk: Predictor anticipation of and/or in response to environmental hazards
Primary cognitive:	Stroop Color Word Interference test (28, 29)	Interference susceptibility (inhibitory control)	Executive function measure (cognition)
Exploratory motor (muscle strength/frailty/sarcopenia):	Muscle strength hip abductors & adductors (microFET3 handheld dynamometer, (optional) (80)); Whole body DXA scan (Hologic); Vertical Jump Test (optional) (77), grip strength with handheld dynamometer (optional), hip/oblique strength with timed lateral plank (optional) (79).	Quantitative muscle strength mediolateral leg adductors & abductors & lean muscular mass lower body	Predictor of falls, postural stability (30) & Proxy measures of frailty
Exploratory cognitive:	WAIS-III: Digit Symbol-Coding (31), Delis-Kaplan Trail Making Test (32), Eriksen Flanker test (33)	Information processing speed, concept shifting & visual attention	Daily functional performance; fall risk
Exploratory cognitive-motor dual task(s)	Clinical reaction time grasping falling computerized stick (34, 35)	Cognitive-motor response inhibition	Predictor of falls
Exploratory Questionaries	Fatigue Severity Scale (62), Activity Questionnaire (73), Short Falls Efficacy Scale (65), The Short Activities-specific Balance Confidence Scale (64), PDQ39 (61), Mayo Sleep Questionnaire (60), Epworth (59), Insomnia Severity Index (63), Instruments of Daily Living (66), Modified Numeric Rating Scale(74), and	Neurobehavioral assessment	Quality of Life, Sleep energy benefit ADL Pain level

	User Acceptance Study Questionnaire (53) and SUS instrument scales (54)		
Exploratory measures:	Actigraphy (activPAL™, Glasgow, UK or Actigraph by ActiLife)	Carry-over effects of desk use on daily physical activity	Physical activity (inversely correlated to fear of falling)
Exploratory measures:	Continuous glucose monitoring (Dexcom G6 Pro, San Diego, CA)	Average glucose level	Metabolic parameter
Exploratory measures:	VO_2 energy expenditure the (Cosmed K4b2 gas analyzer Cosmed, Rome, Italy).	VO_2	Energy expenditure measure
Exploratory measures:	Time behind table	Desk utilization	Adherence to intervention

Figure 2: APDM Mobility Lab iTUG: design of test & placement of Opal sensors (iTUG, Mobility Lab, APDM, Inc., Portland, OR)

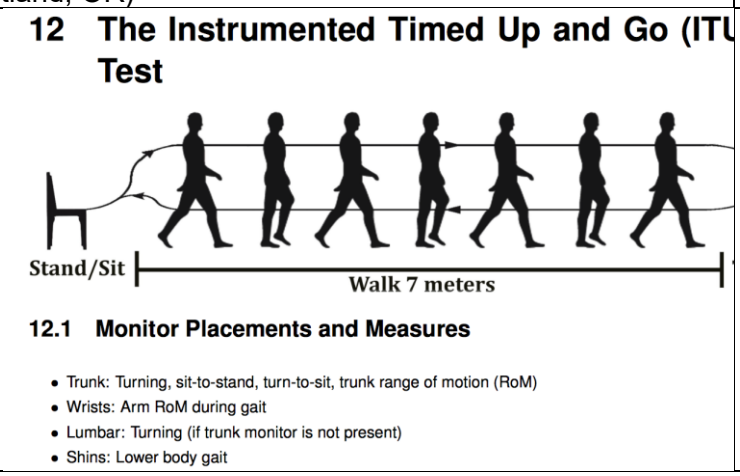
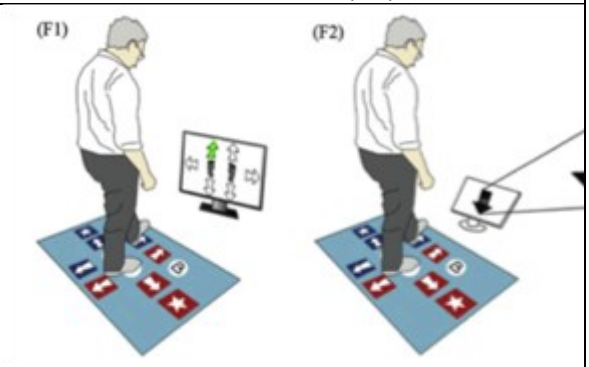


Figure 3: Stroop stepping test Participants step according to the word and not the arrow orientation, incongruent stimulus (27)



Actigraphy: Subjects will first wear a physical activity monitor (activPAL™; PAL Technologies Ltd, Glasgow, United Kingdom or Actigraph by ActiLife) for 3 days for overall physical activity monitoring. The 3-day physical activity monitoring and the clinical testing will be repeated immediately following the completion of the 12 week in-home clinical trial (see also **Figure 1).** This monitoring period will be for a minimum of 3 days, however, if there is a scheduling conflict (i.e. holiday, inclement weather), the monitoring period may need to be extended. The visits will be scheduled for the next possible business day.

Potential pitfalls and alternative strategies:

Tolerability and safety of MRSSD in target population of PwP. We have designed the human user acceptance study such that we will set the primary MRSSD utility functions (range and speed of directional movements, ability to write/type or read on moving desktop, and absence of subjective head sensation of dizziness/headache and musculoskeletal discomfort) to be acceptable in at least 80% of the target population while using the desk for a minimum of 1 hour. Although this may result in initial lower range or slower speed settings we anticipate that with continued use settings can be adjusted while having therapeutic gains.
The project also includes an in-lab supervised feasibility study (see sub-study #2) of repeated standing sessions in PwP (n=6) after initial user acceptance study to assess (i) safety and tolerance of 2 hr/d for 5d/ 2 wks of

MRSSD use, (ii) successful ability to cognitive/motor dual-task desktop activities; (iii) sensitivity of the proposed outcome parameters before starting this pilot RCT in-home clinical trial and (iv) to directly allow the investigators to observe how participants learn the interact with the desk.

Division of work: The technical development (hardware and electrical engineering) of the MRSSD will take place at Tulip Make Me Move Desk, LLC and will be performed by the Principal Engineer, Mr. Warren VanHout, BSEE, RN. The user acceptance testing will take place at the University of Michigan's Functional Neuroimaging, Cognitive & Mobility laboratory under supervision of Dr. Richardson.

Timeline: The timeline of the study is shown in the table below.

Timeline	**Mo 1**	**Mo 2-3**	**Mo 4-11**	**Mo 12**
Building initial MRSSD test prototype	X			
IRB approval, subject recruitment	X			
User feedback and acceptance study (study 1)		X		
Supervised in-lab safety and tolerance study (study 2)		X	X	
MRSSD design & user interface adjustments (study 3)		X	X	X
In-home pilot clinical trial			X	
Statistical analysis		X (study 1)	X (study 2)	X (study 3_

The following **milestones** need to be achieved: (i) build an MRSSD prototype using cost-effective components, including low noise level and rotational motors (company task), month 1. Initial prototype device completion, testing are scheduled to be complete within 120 days (end of month 3); (ii) University of Michigan IRB approval for MRSSD human user studies (academic partner tasks, month 1); (iii) user acceptance study showing proof of principle that 80% or more of older adults with PwP (including those who are more frail or have cognitive complaints) can independently operate the MRSSD and are able to stand behind the desk for at least 1-2 hour(s), months 2-3; *completion of in-lab sub-study by 6-months*. *Benchmark of success*: completed testing of 9 subjects by end of month 2; (iv) complete randomized controlled clinical pilot trial (*study 3*) during months 4-11; *benchmark of success*: completed testing of 8 subjects prior to month 8; (v) statistical analysis and final MRSSD design upgrades (month 12). If these milestone criteria are met, we will consider the novel MRSSD prototype suitable for further development and the company will apply for Phase II funding. Based on movement biofeedback that will be collected during testing we will also create a concept design for the interface device.

Potential pitfalls and alternative strategies: The most significant problem that may arise is the inability to meet the design specifications as laid out in Table 1. The proposed design concept (Figure 4) is the lead design based on preliminary design feasibility research by our engineer. The engineering challenges associated with the MRSSD arise from the requirement to make noise, vibration and surface movement '***insensible***' to the desktop user (at least at default speed of 3 mm/sec). Therefore, the single most important cost-effective component is to have a low-cost drive system that also meets a **low noise level requirement** (<35 dB directly above device surface). Alternative activity-surface suspensions, drive systems, controllers and noise/vibration management and suppression techniques are under evaluation. Alternative designs (e.g., hydraulics) and alternative power sources of non-linear actuation, will be further developed, if needed.

Attrition: Our net recruitment goals for the user acceptance study will be 18 PwP and 18 for the pilot clinical trial (6 per group). Our recruitment goals for the repeated standing study will be 8 PwP. Due to possible diagnostic screen failures and attrition we will recruit up to a maximum of 40 participants for the whole phase I project.

Adherence with actigraphy use: We have preliminary data from our pilot studies showing that PD patients have 100% compliance without missing data with a 3-day actigraphy protocol at home. The ActivPal is adherent to the thigh and can be worn 24 hours/day and is more convenient than typical actigraphy. The actigraph can adhere to clothing and can be worn 24 hours/day. Participants will also use daily logs to track usage.

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Variations in time-behind-table utilization: Our Parkinson study data showed that patients were able to use the dynamic standing desk for an average 2.2±0.4 hours per day for at least five days per week without a drop in daily use in the later stages of the trial (excellent sustained 4-mo adherence rate). It is possible that some participants may deviate from this average. Therefore, we will tract the time behind the table use in upright as well as sitting mode and use this as a covariate in the analysis in a sensitivity analysis (see also section on compliance and monitoring of table use below).

Compliance and monitoring of table use ('time-behind-table'): To monitor compliance with the dynamic standing table protocol video surveillance will be performed as developed by our collaborator Lauro Ojeda (82). A frame will be recorded during the waking times when the participant stands in front of the desk. This camera is motion activated and will record 60 second clips. This technique will provide information regarding protocol compliance, but also provide table use durations. Since only the participant is permitted to use the desk in the dynamic setting during the in-home portion of the table, this will also allow us to distinguish between anyone who may be using the desk in the static setting (i.e. spouse, other family members).

Adherence with actigraphy use in the PD patients: We have preliminary data from our pilot studies that PD patients (n=4) have 100% compliance without missing data with a 3-day actigraphy protocol at home. The ActivPal is adherent to the thigh and can be worn 24 hours and is more convenient than typical actigraphy.

Tolerability of MRSSD in target population of older adults with PwP. We have designed the human user acceptance study in such a way that the default MRSSD utility settings and functions (range and speed of directional movements, ability to write/type or read on moving desktop, and tolerance of musculoskeletal discomfort to be acceptable in at least 80% of the PwP target population while using the desk for a minimum of 1 hour. Although this may result in initial lower displacement range or slower speed settings we anticipate that with continued use settings will be adjusted upward due to therapeutic gains. Furthermore, a more simple dynamic stepping desk desk model was very well tolerated in PwP.

In-home safety of MRSSD: There were no serious adverse events or falls during desk use in our 4-month in-home study using the dynamic stepping desk prototype in PwP. However, safety measures will be in place, using a desk cut-out wherein the participant can stand and can hold on to the desk when needed, a 'red' button alarm stop button, handles to each side of the desk cut-out, positioning of the MRSSD close to the wall and individual-specific RFID on/off control (RFID control worn at the user's wrist with deactivation when stepping away from desk).

Assessment of use over 4 months may not accurately represent long-term user acceptance but will be further evaluated in **Phase II** of this application (see below). We also anticipate that a user feedback system will increase long-term adherence.

Plans for Phase II: If milestones for Phase I have been met, we plan to submit a proposal for Phase II funding with the focus in Phase II on two major goals. The first aim for Phase II is to perform a large scale randomized controlled clinical trial to assess the clinical mobility (including fall risk), cognitive-motor dual-tasking, functional ability, quality of life effects and long-term utilization of MRSSD use in older adults with PwP. The larger number of participants in this phase II clinical trial will allow sensitivity analyses to assess relative effectiveness of the MRSSD on the major clinical components of the PwP syndrome: slow walking, balance, cognition, fall risk, and frailty and to assess differential mechanistic effects of directional use, range and speed of excursion, type of (cognitive) desktop activity. For example, mediolateral excursion may strengthen hip abductors and adductor important for dynamic balance, rotatory movements for fall risk reduction, higher intensity settings for frailty and more engaging cognitive desktop activities for cognitive impairment. The second aim is to optimize a monitoring and feedback-driven human interface device to control the MRSSD that is optimized for the PwP target population. Example of basic specifications are listed in Table 2. We will also further develop the product to meet commercial and marketable preferences such as affordability ($2000 for device, comparable to Medicare cap for PT), device reliability, and an aesthetically pleasing device.

Table 2. Overview of critical user needs, requirements, and specification for MRSSD feedback-driven human interface device during Phase 1.

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User Need	Requirement	Specification
Ease of use	Simple user interface	• < 20 minutes to learn • Large interface buttons
	User interface is reachable by person with decreased mobility	User interface < 90 cm from user's shoulder when standing at center of tabletop.
Personalizable	Speed can be varied	1 to 5 mm/sec
	Excursion distance can be varied	25 cm to 1 m.

Subject Compensation:
The subjects will receive $50 per clinical assessment and screening session completed and $10 per physical therapy and exercise session attended. The maximum total for sub-study 1 (screening visit, 2 standing session), sub-study 2 (7 visits), and sub-study 3 (2 visits, 12 exercise classes) would be up to $720. Subjects will be paid after their last study visit or, in case they decide to withdraw from the study, they will be paid for the portions that they have completed. Since each sub-study consists of a separate consent, subjects will be paid after their last study visit for a given sub-study.

Overnight accommodations may be provided depending on personal circumstances or if you live far away. We will discuss with you the need for these accommodations as the research appointment(s) are being arranged. If eligible, overnight lodging can be arranged through the UMHS Patient and Visitor Accommodations Program either by a study team member or by you. However, you may decide to make alternative arrangements. In that case, please discuss with the study team first if you are eligible for reimbursement prior to making any reservations. We can only reimburse for expenses that have been approved in advance by the study team. You will need to provide receipts to the study team before expenses can be reimbursed. We will reimburse to a maximum of $200 for lodging. You will receive a voucher for valet parking at the University Hospital. Parking at Domino's Farms is free.

Transportation: Recognizing that some interested individuals may lack reliable means of transportation, we have developed detailed transportation protocols that include using UM fleet vehicles and UM shuttle services as well as low- or no-cost cabs and shuttles available to seniors in the counties immediately surrounding Ann Arbor. We have developed a sound transportation plan and have budgeted a travel allowance for participants who require transportation or lodging services.

Data Analysis/Interpretation:

Statistical analysis: The user acceptance study will consist of open-label assessment and reporting of success rates of independent completion of the acceptance criteria for a minimum 1-hr desk utilization target time on the 2nd day of acceptance testing in ≥ 80% of PwP subjects (study 1). For study 2 ratings of adverse events, discomfort, and percentage of participants able to complete cognitive desktop activity (reading task, typing performance, web search task), 5-session sustained acceptance testing in n ≥ 80% of PwP subjects, and to assess sensitivity of change of proposed outcome parameters for the subsequent in-home clinical trial. For study 3, ANOVA/mixed linear modeling will be used to determine if the change in the main outcome parameters between pre- and post-trial performance is different between the three groups. The effects of **gender** and **age** will be included as an important biological variable in both analyses.

Potential Risks

Confidentiality of Research Information: The research data to be collected from subjects will consist of confidential clinical screening information and behavioral observation data relating to musculoskeletal discomfort. These research data are not intended for entry into subjects' clinical medical records. However, the data remain potentially discoverable. This may lead to violation of privacy and embarrassment of the subject. We will employ stringent safeguards against unintended and inappropriate discovery and dissemination of

personal medical and research data in our subjects by a multilayered approach. All data bearing potential subject identifiers will reside solely in locked files in the offices of the study investigator. Original data collection documents will be maintained in secure files under the control of the investigators. Entries regarding details of the research project and its results will not be submitted to clinical medical databases. Electronic databases in the project will employ subject codes that cannot be linked directly to participants without a "key", possessed only by the study investigators in a secure location, and maintained separately from the databases. Databases will not be housed on systems with internet access, preventing unauthorized intrusions. Personal information that would directly identify study subjects will not be used in any publications or presentations resulting from this research study, unless separate written permission is given by the subject (or proxy). Any superfluous records will be shredded.

Musculoskeletal discomfort: There is a risk of musculoskeletal discomfort with prolonged standing. The *ad libitum* sit-stand design of the study will allow the subject to sit down at any time. Subjects are also allowed to lean on the tabletop if desired.

Standing: Subjects will be standing upright behind a table making small steps. This is not different from normal standing conditions that can be encountered during normal daily routines. Nonetheless, there is a rare risk of falling, comparable to the risks of everyday life. Subjects will be standing close to a wall and rest breaks will be provided when needed. The total duration of up to 4 hours per condition may cause some musculoskeletal discomfort. The electronic sensors to measure movement and balance are about the size of a watch and will be worn around the ankles and wrists affixed with ankle- and wristbands, or around the waist. Subjects will be provided as many rest breaks as needed and they will also stand on anti-fatigue mats. Each condition will be performed on a different test day. Subjects will also be advised that they have the option to completely stop testing if they feel too uncomfortable. The overall study looks at normal standing and taking small steps and sitting, which are all normal activities of daily life. Therefore, the risks are deemed comparable to the risks of everyday life. There is also an infrequent risk of lightheadedness, dizziness, a decrease in blood pressure, feeling disoriented, or feeling off balance. People with Parkinson's disease often experience lightheadedness and dizziness as a symptom of underlying disease. These risks can be mitigated by sitting down, drinking water, or having a snack. Subjects may stop standing if they feel too uncomfortable.

Falling: There is a small risk of falling with the MRSSD use. For this reason, the device will be positioned about 0.5 meters from a wall ensuring positioning of subjects closely to the wall to minimize this risk. Overall, risk of falling is very small as subjects can lean on the table and the table moves very slowly. There were no falls in our study of the 14-week post-PT extension of in-home use of dynamic standing desk in patients with Parkinson's disease.

Test Anxiety: There is a rare risk that subjects may experience some minor anxiety ('test anxiety'), become worried, or have an anxiety reaction in response to any of the tests and procedures. For example, subjects may suddenly experience anxious feelings or become worried about their health. Trained research staff will conduct all tests and procedures. The staff will be prepared to respond to anxiety, concerns, and behavioral changes, by temporarily suspending testing, breaking up testing or answering questions.

Varices and venous stasis: There is a risk of worsening or developing varices with upright postures. Participants will be screened for lower extremity venous stasis and/or excessive varicosis. However, the risk of varicosis is greater for static than dynamic standing as the lymphatic pump function of calf musculature is less effective with static standing. Subjects with mild varicosis are commended to wear low-pressure support stocks in the range of 20-30 mm Hg to reduce the possible risk of varicosis during the study.

Risk of foot swelling: Paul *et al*. compared foot swelling in users of sit-stand adjustable furniture to non-adjustable sitting workstations and actually found significantly less foot swelling in the adjustable stand workstation users compared to the sitting condition (40). There is also a reduced risk of deep venous thrombosis with standing compared to sitting (41).

Balance/gait assessments: There is a very rare risk that the sensors to measure overall movement and balance gait may become detached and that subjects may trip, or that a subject may trip while walking. The sensors will be checked regularly for appropriate attachment quality. Many of the tests are comparable to normal standing and walking conditions that you may experience in everyday life. Nonetheless, there is an infrequent risk of falling or near-falling during these tests which may result in fall-related injuries. Trained research staff will remain in close proximity to you at all times and observe ('spot') you to prevent you from falling.

Actigraphy: There is a very rare risk of the movement monitoring device (activPAL or actigraph) detaching, which may result in a trip during the at home monitoring of movement. It should be noted that the device only measures overall movement. It does not record your geographical location or specific activities that subjects were performing, neither can this be derived from the data that is stored in the device. Subjects will receive instruction for proper attachment of the activity monitoring device.

Continuous glucose monitoring: The CGM system is FDA approved. The FDA safety information includes the following contraindications and potential adverse effects. Contraindications: 1) Sensor and transmitters need to be removed before Magnetic Resonance Imaging, Computed Tomography scan, or diathermy treatment. It is unlikely that our participants will have to do any of those tests for personal reasons. If so, during the recruitment phase we will schedule them to participate in the study during different days than the tests. We will also remind the participants regularly about this contraindication. 2) Taking medications with acetaminophen while wearing the sensor may falsely raise their glucose readings. This is not a contraindication for our non-diabetic participants since it is not critical for them to monitor their glucose levels. However, it can introduce bias in our analysis. We will remind them to avoid acetaminophen during the study and use alternative painkillers if needed. The following events are possible adverse device effects of inserting a sensor and wearing the adhesive patch: local infection, inflammation, pain or discomfort, bleeding at the glucose sensor insertion site, bruising, itching, scarring or skin discoloration, hematoma, tape irritation, sensor or needle fracture during insertion, wear or removal. All these adverse events are considered minor and easy to resolve. We will train the participants in the insertion of the sensors and we will ask the participants to communicate us immediately in the event of any adverse effect.

iv) Adequacy of Protection against Risks:

Older adults with PwP who are interested to participate in this study will be scheduled for the research procedures at which time the nature and risks of the procedures will again be reviewed with the subjects and a written informed consent form will be obtained by one of the study investigators. One copy of the signed consent form will be given to the subject, one will be placed in the patient's medical record and a third will be kept in the patient's study binder kept at the patient's research site.

Confidentiality of research information: We will employ stringent safeguards against unintended and inappropriate discovery and dissemination of personal medical and research data in our subjects by a multilayered approach. All data bearing potential subject identifiers will reside solely in locked files in the offices of the study investigator. Original data collection documents will be maintained in secure files under the control of the investigators. Entries regarding details of the research project and its results will not be submitted to clinical medical databases. Electronic databases in the project will employ subject codes that cannot be linked directly to participants without a 'key', possessed only by the study investigators in a secure location, and maintained separately from the databases. Databases will not be housed on systems with internet access, preventing unauthorized intrusions. Personal information that would directly identify study subjects will not be used in any publications or presentations resulting from this research study, unless separate written permission is given by the subject (or proxy). Any superfluous records will be shredded.

Physical discomfort and side effects of standing: Subjects will be advised to return to a seated position if they experience physical discomfort from using the stand-up desk. Subject will be standing on anti-fatigue mats to prevent musculoskeletal discomfort. Participants will be screened for lower extremity venous stasis and/or excessive varicosis. However, the risk of varicosis is greater for static than dynamic standing as the lymphatic pump function of calf musculature is less effective with static standing. Subjects with mild varicosis are commended to wear low-pressure support stocks in the range of 20-30 mm Hg to reduce the possible risk of

varicosis during the study. There is a reduced risk of deep venous thrombosis with standing compared to sitting. Subjects will also be advised that they have the option to completely stop the study if they feel too uncomfortable with the dynamic standing desk.

Test anxiety: Trained research staff will conduct all tests and procedures. The staff will be prepared to respond to anxiety, concerns, and behavioral changes, by temporarily suspending testing, breaking up testing or answering questions.

Frailty assessment: A popular approach to the assessment of geriatric frailty encompasses the assessment of five dimensions that are hypothesized to reflect systems whose impaired regulation underlies the syndrome. These five dimensions are:

(a) unintentional weight loss,
(b) exhaustion,
(c) muscle weakness (using grip strength dynameter),
(d) slowness while walking, and
(e) low levels of activity.

Those who meet at least three of the criteria are defined as frail (42). We will also determine muscle mass using a whole body DXA scan to assess for sarcopenia (see below).

Dual-energy X-ray absorptiometry (DXA): A whole body DXA scan will be performed to evaluate total body composition, fat content and lean muscular mass (for assessment of frailty). Hip and spine scans will also be taken to assess bone mineral density. The DXA scan will be performed on a Discovery-W DXA system (Hologic) at the UM Functional Neuroimaging, Cognitive, and Mobility Laboratory. The scan time is approximately six minutes for the whole body scan and less than one minute each for the hip and spine scans.

The biological effect of radiation in humans is measured in terms of Sieverts (Sv) or mSv (1/1000 Sv), which is a unit of uniform whole body exposure. Radiation to which a subject will be exposed from this research project will be approximately 0.0159 mSv for a DXA scan. The effects on the body of this radiation exposure will be added to the subject's overall lifetime radiation risk. The US Federal Government requires that the annual amount of radiation exposure of radiation workers does not exceed 50 mSv per year; the radiation to which the subject will be exposed with the DXA scan is less than 0.1% of this amount.

Actigraphy: Subjects will receive instruction for proper attachment of the activPAL™ or actigraphy device.

Continuous glucose monitor: The continuous glucose monitor can be worn at the lower abdomen. The continuous glucose monitor will be inserted using an automatic applicator. The inserted sensor filament will be covered by a water-resistant cover what users can take a bath, shower or swim. The sensor is contained in a bandaid and can be removed the same way as removing a regular bandaid.

v) Potential Benefits of the Proposed Research to the Subjects and Others:

PwP may benefit from this repeated session or in-home intervention. Furthermore, in the course of this study PwP will receive clinical evaluations including limited clinical, mobility, and cognitive testing. No direct immediate benefit of these studies is anticipated. Although generally the results of these examinations will not be made available to their treating physician, if a significant, unexpected abnormality is detected this will be reported to the patient and his/her physician.

vi) Importance of the knowledge to be gained

Data obtained from this research will be important for the development of a novel rehabilitation device to improve balance, gait, frailty and possibly cognition in older adults with PwP. Positive outcomes in Phase I of this study would provide the basis for larger controlled clinical trials of this rehabilitation device in Phase II of the STTR. Positive findings in this study may allow expanded indications and research in mobility disorders other than PwP.

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DATA SAFETY MONITORING PLAN

Drs. Pongmala and Richardson will serve as chairs for the DSMP for this study. They will review outcomes with the PI on a semi-annual basis. The DSMP will be asked to review the cumulative safety data up to the date identified to make a determination if the study is safe to proceed unchanged or to provide recommendations to the sponsor as to how to proceed.

Review of study procedures and adverse effects will be performed on a monthly basis. Drs. Pongmala and/or Dr. Richardson be responsible for the day-to-day monitoring any potential breach of confidentiality and for reporting any adverse events (AE) following University of Michigan IRB guidelines.

For purposes of this study, an AE is defined as any unfavorable or unintended change in structure, function, signs, or symptoms temporally associated with participation in this study, whether or not a causal relationship with the study has been established.

Breaches of confidentiality will be considered related to the research whenever they occur and will be reported. Withdrawals from the study and the reason for these withdrawals will also be reported. The PI will be in daily contact with the PT and study research staff. The research staff will test the participants, score and enter the data and will monitor their procedures to ensure that confidentiality is maintained. Research staff will be responsible for reporting any significant events to the PI. The PI will ensure that the IRB is notified of any adverse event following the IRB guidelines.

Expected and unexpected serious (including fatal) adverse reactions and major unresolved disputes between the research investigator(s) and the research participant or between research investigator(s) will be expeditiously reported to the IRB of the University of Michigan. At the time of renewal, the IRB will be provided with a summary indicating the frequency of the monitoring, cumulative adverse event data, information regarding participant safety or ethics changes, confidentiality issues, benefit-to-risk changes and recommendations on continuing, changing or terminating the study.

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RECRUITMENT AND RETENTION PLAN

Recruitment: PwP subjects will be recruited from the University of Michigan Functional Neuroimaging, Cognitive & Mobility Laboratory . Our laboratory also has a high throughput of volunteers for our regular clinical and imaging studies and many have provided informed consent to be enrolled for a registry for possible future studies. Our laboratory has already collected a waiting list of volunteers who have expressed interest in this or similar studies.

We will leverage a number of resources to ensure we meet (or surpass) our targeted recruitment goals, including women and minorities:

i) UM Functional Neuroimaging, Cognitive & Mobility Laboratory*:* PwP subjects will be recruited from the University of Michigan Functional Neuroimaging, Cognitive & Mobility Laboratory. Our laboratory has already collected a waiting list of volunteers who have expressed interest in this or similar studies. Our laboratory also has a website with our current studies for potential participants to come across.

ii) ***PMR clinic Dr. Richardson***: PwP subjects will also be recruited from Dr. Richardson's busy clinical practice in Physical Medicine & Rehabilitation.

iii) ***Ann Arbor Parkinson's Support Group*** **(**PT Miriam van Emde Boas leads a weekly exercise group) will also provide recruitment opportunities.

iv) ***UMHealth Research:*** UMHealth Research is a free, secure password protected database available to all University of Michigan researchers. The study team will access this UM established subject pool.

v) ***ClinicalTrials.gov Recruitment:*** Since this project is considered an Applicable Clinical Trial (ACT), the study team will be required to post the study on the ClinicalTrials.gov website. This also provide another broad avenue for recruitment.

vi) We have prior successful experience with **posting radio, TV or newspapers ads**, including the Detroit area, as an additional strategy to boost recruitment of women or minorities when needed.

Retention**:** Retention of our study participants is of utmost importance for the successful completion of the project. For the human user acceptance study participants will be in daily direct contact with the research team for the two testing days. For the pilot clinical trial, our therapist will make biweekly phone calls during the study to provide monitoring of the participants and identify and remedy any issues that may discourage continued study participation.

RESOURCE SHARING PLAN

The investigators are committed to resource and data sharing with the clinical research community. Optimally effective data sharing is carefully planned. The specific contents and strategy for creating and sharing a public use dataset will be established at the beginning of the study, rather than at the end. The primary results of the study will be disseminated by publication in the peer reviewed medical literature. In accordance with the NIH Public Access Policy, the investigators will submit an electronic version of their final, peer-reviewed manuscripts (directly or through the publisher) to the National Library of Medicine's PubMed Central, no later than 12 months after the official date of publication. After completion of the study and dissemination of primary study results, we plan to make the data publicly available in accordance with approval and regulations of e policies and guidelines established by the NIH with respect to sharing research resources, in particular as laid out in section 8.2.3 (Sharing Research Resources) of the NIH Grants Policy Statement and the recent new NIA guidance https://www.nia.nih.gov/research/grants-funding/nia-specific-funding-policies#datasharing . In accordance with these policies, we intend to release and share final research data and materials from NIH-supported studies for use by other researchers in a timely manner.

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Subject to UM IRBMED approval, de-identified data will be made available to all requesting investigators with the following considerations:

(i) The location of study data repository will be arranged with University of Michigan (UM), e.g. storing it at UM's deep blue repository: https://deepblue.lib.umich.edu/data .

(ii) The timeline of submission of the public use dataset will comply with all relevant repository guidelines but in general we plan to submit data to the repository approximately one year after the primary manuscript of the trial is accepted for publication. During that year, the investigators will have opportunities to digest the study results and generate further hypotheses, and submit manuscript proposals, if so desired. The rationale for the timelines is to ensure that there is sufficient time to properly prepare the data, to provide priority to the study investigators in manuscript development, but with incentives to do so in an efficient and rapid manner, and to release the data to external investigators early.

(iii) Restrictions on sharing:

* An investigator requesting data must submit a formal written request stating the specific data required and its intended scientific use.
* Upon approval of the request, a data use agreement or material transfer agreement will be created between the University of Michigan and the receiving institute.
* They must agree to refrain from secondary dissemination of the data to other investigators; requests from others must be made to this program.
* All manuscripts, abstracts and press releases using the study data must acknowledge the investigators and the study sponsor with the relevant grant numbers. The requesting investigator(s) attest to the scope of their intended use of the data, and that they will acknowledge the NIH and this program in the reporting of any results.
* The investigator may not propose an intended analysis that competes with a stated hypothesis or aim of the study until that analysis has been completed and reported in the literature. Thereafter, there will be no restriction on the nature of the intended data use, as long as there is a plausible scientific value to the request.
    * No commercial use of the data
    * Only qualified users may access the data,
    * No attempt to reveal personal or private information may be made.
    * Investigators may also set different levels of access, for example, for expert users and novice users.

(iv) Given the involvement of human subjects the following restrictions will apply:

*The public use dataset will be stripped of any and all personal identifiers and will undergo a de-identification process.

DISSEMINATION PLAN

For Phase I direct communication to caregivers, patients and therapists by means of an information session on the outcome of this project will be organized in our laboratory. This will provide participants the opportunity to be informed about the results of the study, discuss them with the researchers, and have an opportunity to participate in the phase II study.

The data will also be output to *clinicaltrials.gov* for widespread public dissemination.

Phase II study clinical trials findings will be published in peer-reviewed journals and presented at scientific meetings.

FDA STATUS

The study device will be administered under a non-significant risk FDA exempt status and monitored following the University of Michigan IRB approval and regulatory process.

INCLUSION OF INDIVIDUALS ACROSS THE LIFESPAN

No children, young or middle-aged adults will be included in this study. PwP is an age-associated disorder of older age starting from middle age and increases with increasing older age. Therefore, the research topic to be studied is not relevant to children, young or middle-aged adults. Further development of the MRSSD, however, may lead to new indications of MRSSD (or simplified prototypes) use such as possible use in schools for children and office workers of any age.

INCLUSION OF WOMEN AND MINORITIES

Inclusion of Women: Women will be included in this research project and will be given equal priority in recruitment as men. The PI will monitor the recruitment of women for this project throughout the study, and institute procedures to enhance the enrollment of women, if numbers are not adequate.

Inclusion of Minorities: Enrollment targets of minorities are based on population estimates of the 2010 US census for the State of Michigan. Estimates are 14.2% for African Americans, 2.4% for Asian Americans, 0.6% for American Indians and Alaska Natives, <0.1% for Native Hawaiians or Pacific Islanders, 1.5% identify by another race, and 2.3% identify themselves by two or more races. Minorities will be given equal priority in recruitment. The PI will monitor the recruitment of minorities for this project throughout the study, and institute procedures to enhance the enrollment of women, if numbers are not adequate. See also the Targeted/Planned Enrollment Table.

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OVERALL STRUCTURE OF STUDY TEAM

STUDY DESIGN & SETTING

Single site open-label single group intervention trial at the University of Michigan

Administrative sites: University of Michigan

Data coordinating sites: n/a (not a multi-center trial)

Enrollment/participating sites: University of Michigan

Separate laboratory or testing centers: n/a (single site)

PERSONNEL (University of Michigan study team)

James Richardson, MD, PD/PI**:** Dr. Richardson is Professor of Physical Medicine & Rehabilitation at the University of Michigan. He will be in charge of the scientific aspects of the grant, manage project operations, provide regulatory oversight and reporting, and supervise personnel. He will also be the supervisor of the physical therapist. Will not be blinded.

Fay Pongmala, PhD., Co-Investigator: Dr. Pongmala wrote her PhD thesis on postural deviations in Parkinson's Disease and is now the lead of the Functional, Neuroimaging, Cognitive and Mobily Lab Kinesiology team. She will take on the role of the blinded rater for the participants in the clinical trial portion of this study.

Lauro Ojeda, MSc, Co-investigator**:** Mr. Ojeda is Associate Research Scientist, Department of Mechanical Engineering, University of Michigan. Mr. Ojeda is a mechanical engineer with specialty expertise in the use of IMU sensor and signal detection technology. He will analyze the collected sensor data and will assist with the processing of the RFID unique desk user data to provide the specific quantitative table use and other mobility outcome measures for this study. Will not be blinded.

Miriam van Emde Boas, DPT, Physical Therapist: Miriam van Emde Boas is a Doctor of Physical Therapy and will assist Drs. Richardson with the three sub-studies. In particular, she will continuously evaluate subject's physical performance and safety during standing sessions and evaluate for musculoskeletal discomfort. Will not be blinded.

Simon David BSc: Mr. David is working on his masters for medical engineering. For this study he will be responsible for building and maintaining the study devices. Will not be blinded.

Alexis Griggs BSc: Ms. Griggs is a Lab Specialist Intermediate at the Functional Neuroimaging, Cognitive and Mobility Lab. She will assist the physical therapist during sub-study 3 when setting up the study device in participant homes. She will coordinate the table deliveries and assist the PT. Will not be blinded.

Abbey Biddix, BSc, Research Technician Associate: Ms. Biddix is a Research Technician Associate at the U of M Functional Neuroimaging, Cognitive and Mobility Laboratory. Ms. Biddix will coordinate the study visits, perform clinical testing, and obtain informed consent. Since some testing will be done pre and post intervention, Ms. Biddix will be blinded to prevent bias.

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