PARTNERS HUMAN RESEARCH COMMITTEE
DETAILED PROTOCOL

PRINCIPAL/OVERALL INVESTIGATOR
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PROTOCOL TITLE
A Mobile Tai Chi Platform for Fall Prevention in Older Adults – Phase II

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I. BACKGROUND AND SIGNIFICANCE

TC is a multi-component mind–body exercise that is growing in popularity worldwide, especially among older adults. TC integrates training in balance, flexibility, and neuromuscular coordination with a number of cognitive components including heightened body awareness, focused mental attention, and multi-tasking, which together may result in benefits to postural control, beyond conventional exercise [1,2]. Meta-analyses support that TC reduces falls by 20-45% [3]. A recent Cochrane review concluded that TC is among the most effective available exercise options for fall prevention in ambulatory older adults [4]. TC appears to reduce falls by positively impacting multiple fall-related risk factors including: lower extremity strength and flexibility, proprioception and postural awareness, neuromuscular coordination, executive function, and fear of falling [5].

While research is beginning to provide guidelines regarding targeted applications of TC-based therapies for specific medical conditions and populations, methodological challenges limit the conclusions that can be drawn from this research [6]. One important challenge inherent in the study of multi-component mind-body interventions is objectively quantifying measures of adherence and proficiency. Because variability in proficiency of practice can significantly alter physiological responses to a training session, simple measures of class attendance or logged practice time are unlikely to capture practice components needed to objectively evaluate the impact of TC-based interventions on clinical outcomes of interest. The development of objective, non-invasive measures that can accurately record and verify practice of specific TC intervention components, along with measures of practice duration, would represent a significant advance in the field.

During phase I of the SBIR NIH grant, we developed algorithms based on information gathered from wearable sensors to estimate adherence, proficiency, and safety metrics. During the non-clinical stages of phase II, we developed a complete beta-version of the Tele-TC platform. The Tele-TC system consists of a set of 5 wearable sensors and an app installed on a commercially available tablet.

As a preliminary step toward designing a future study to assess the clinical benefits of the Tele-TC platform as a training system, we herein propose to assess:

• If the system enables monitoring longitudinally of adherence, proficiency, and safety;

• If the system is acceptable and user-friendly for its intended use in the home setting;

• As an exploratory aim, if a 12-week training program using the Tele-TC platform leads to improvements in balance, physical activity, self-efficacy, health-related quality of life, and gait.

If this preliminary study leads to positive results, we will embark on a follow-up study to assess the potential clinical benefits of using the technology as part of a clinical intervention on balance, physical activity, self-efficacy, health-related quality of life, and gait.

II. SPECIFIC AIMS

The overall goal of the study is to test the delivery of a novel Tele-Tai Chi (TC) intervention in a single-arm feasibility study for community-dwelling TC-naïve older adults (N=30 total). We will assess feasibility and acceptability measures of the Tele-TC intervention and its specific components through both qualitative and quantitative feedback, as well as the systematic tracking of adherence data to inform future trials and potential clinical use of the Tele-TC system. We will also explore changes in clinically relevant outcome measures including physical activity, self-efficacy, quality of life, balance, gait, and evaluate changes in TC proficiency.

Figure 1: Study system.

We will pursue the following specific aims:

Primary aims

Aim 1: *To evaluate the feasibility, acceptability, and safety of a novel home-based Tele-TC intervention by tracking recruitment, retention, adherence, and adverse events.*

Hypothesis 1: We will be able to recruit 30 older adults and limit withdrawals to 20% or less.

Hypothesis 2: Participants will complete >60% of recommended Tele-TC sessions.

Hypothesis 3: Protocols for assessing safety can be developed and reliably administered, and preliminary evidence will support Tele-TC can be delivered safely.

Exploratory aims

Aim 2: *To evaluate changes in the level of proficiency of TC during a 12-week simplified TC program using the Tele-TC platform at home.*

Hypothesis 1: We will be able to collect reliable data on TC proficiency during Tele-TC use by study participants.

Hypothesis 2: Proficiency scores will improve over 12 weeks of training using the Tele-TC program.

Aim 3: *To gather feedback from end-users on ease of use of the Tele-TC platform*. We plan to collect feedback from elderly subjects to assess if the system is user-friendly enough to envision its use in a clinical setting.

Hypothesis 1: We will be able to collect reliable data on ease of use of the platform using qualitative and quantitative measures.

Aim 4*: To explore changes in clinically relevant outcome measures including physical activity, self-efficacy, quality of life, balance, and gait.*

Hypothesis 1: We will be able to collect reliable outcomes data at each testing visit.

Hypothesis 2: We will see clinically relevant changes in outcomes measures at 12 weeks.

III. SUBJECT SELECTION

As a preliminary test of our platform's suitability as a home-based TC program, we will recruit a convenience sample of 30 community-dwelling TC-naïve older adults into a single-arm longitudinal study of home-based TC learning, combined with remote and/or in-person data collections. In-person data collection will take place at the Spaulding Rehabilitation Hospital Motion Analysis Laboratory.

Inclusion criteria:

Eligibility criteria are purposefully broad to maximize generalizability of the study results. To be eligible to participate in the study, individuals will have to meet the following criteria:

- Men and women between 60 and 85 years old
- TC naïve (never practiced TC)
- Self-reported ability to walk continuously for 15 minutes without an assistive device
- Working email address
- Prior experience with and current access to a computer, smart phone or tablet device

Exclusion criteria:

Individuals will not be eligible to participate in the study if they exhibit any of the following:

- Chronic neuromuscular conditions (e.g. Parkinson's disease, multiple sclerosis, stroke)
- Acute medical conditions requiring hospitalization within the past 6 months or that could interfere with the safely participation in the study
- Active cancer
- Significant musculoskeletal conditions requiring chronic use of pain medication
- Cognitive impairment (Diagnosed with dementia (self-reported), or Montreal Cognitive Assessment (MoCA)-Blind score < 18)

All subjects will be recruited by IRB approved study staff for this protocol. Recruitment strategies will include the use of the following sources:

1. Physicians and therapists may refer interested patients to the study (we will provide physicians and therapists with study flyers and brochure to inform clinicians of the study details).

2. Flyers posted in outpatient clinics, therapy gyms, and public spaces both inside and outside the hospital campus.
3. PowerPoint presentation to inform clinicians and prospective participant about the study.
4. Contacts at local senior and community centers.
5. Recruitment letters sent to patients within the Partners network who have previously expressed interest for participating in research studies.
6. Via letters to prospective subjects co-signed by their physician and study PI.
7. Via contacts with patients who have consented to be directly contacted in the Partners Research Patient Data Registry (RPDR) or RSVP for Health.
8. Via the Partners Clinical Trials (Rally) website.
9. Via newsletters or community boards such as the Osher Center for Integrative Medicine newsletter.

The study procedures will be carried out remotely using a Zoom Enterprise Partners account or in person in the Motion Analysis Lab (MAL). Prior to the first visit, we will perform a phone screening to determine eligibility of prospective study volunteers. Individuals will be informed that identifiable information may be recorded during the phone screening. If a subject is deemed eligible, identifiable information (e.g. name, contact info) will be collected, and an informed consent form will be emailed to subjects for review. Baseline testing at a future date will be scheduled.

Eligible subjects will undergo the informed consent process via phone or on Zoom Enterprise with a trained research assistant at the beginning of baseline testing visit. The subjects will be provided with a signed copy of the consent form. The subjects may decide to pause or terminate their participation in the study at any time during the study.

IV. SUBJECT ENROLLMENT

When subjects first contact the study team, a member of the study team will provide them with a detailed description of the study over the phone or in person. If interested and deemed potentially eligible, a member of the study team will offer to send the informed consent form to the subject. Subjects will be encouraged to call study staff with any questions or concerns they might have prior to their first study visit. Consent will be obtained remotely using the eConsent process on REDcap by a trained research staff member designated by the Principal Investigator as adequately knowledgeable of the risks/benefits of the study and the vulnerability of the study population and capable to critically assess the subject's awareness of these factors. The subject will be encouraged to continue to ask questions and express concerns - if any - to study staff throughout their participation in the study. Enrollment will begin when it is clear that the subject thoroughly understands and e-signs the informed consent form. Testing will only take place once the informed consent form is signed.

V. STUDY PROCEDURES

The study procedures will be carried out remotely using a Zoom Enterprise Partners account or in person.

Eligible subjects will undergo the informed consent process in person, by phone or on Zoom Enterprise with a trained research assistant at the beginning of the baseline testing visit. Once consented, subjects will undergo baseline assessments (visit #1) in person or remotely using Zoom Enterprise and REDcap Survey. After baseline testing, subjects will participate in the Tele-TC intervention, with recommended training sessions at least three times a week, along with two or more supplementary one-on-one live sessions (lasting upwards to 45 minutes) with TC instructors. TC proficiency using wearable sensors will be assessed at visit #1 baseline, at two follow-up assessments (visit #2 and visit #3) at approximately 4 and 8 weeks, and at a final assessment (visit #4) at 12 weeks. A semi-structured qualitative interview will also be performed at visit #1 and #4.

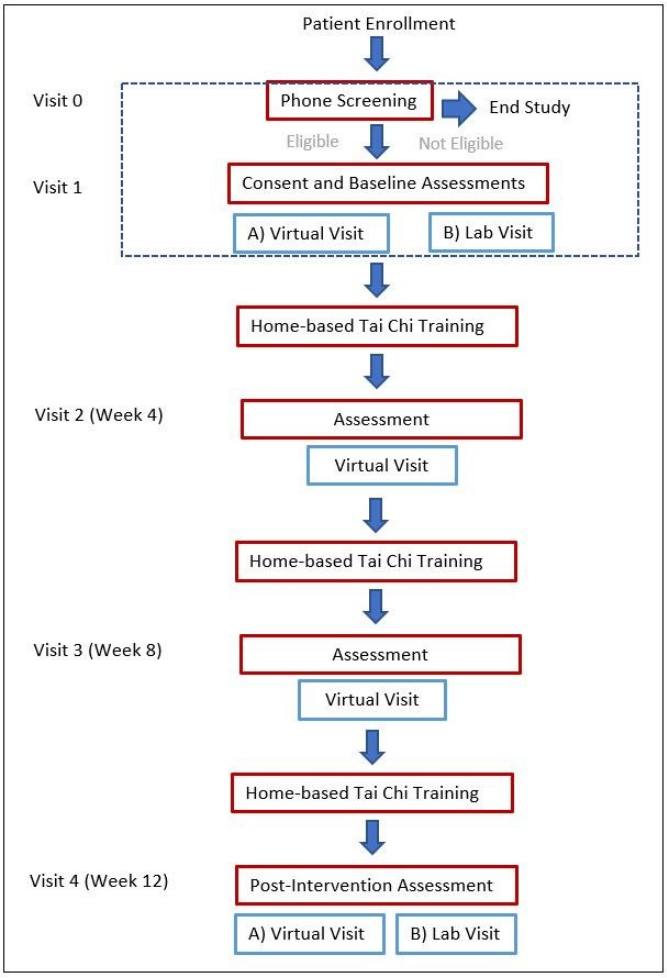

Figure 2: *Flow Chart of the study.*

Below, we provide a detailed description of the study procedures.

1. *Remote Screening and Informed Consent (Visit #1A)*

Prior to beginning the consent process, study staff will ensure subjects' eligibility using a brief questionnaire. This, in addition to the phone screening done as part of the recruitment process prior to the first visit, will ensure the eligibility of prospective study volunteers. The phone screening is not only undertaken to allow researchers to confirm the subjects' eligibility, but it is also an opportunity for the volunteer to ask any additional questions they might have regarding the study.

Informed consent will be obtained by trained study staff in person, over the phone or by using Zoom Enterprise and eConsent on REDcap. Study staff will explain all the study procedures, equipment, and the risks associated with them as outlined in the informed consent form (ICF).

The devices will be sent or provided to the subjects after consent. Subjects will be provided among others with two mobile devices and requisite chargers, a tablet travel stand, tripod, two GeneActiv watches, 5 wearable sensors, each of them with elastic bands and with chargers and wires. Of the two mobile devices, one will be used to interact with the developed TC app and the other will be used an extra mobile device and stand for virtual visits and video recording.

2. Remote Assessments (Visits #1B, #2, #3 and #4)

At *Visit #1B*, subjects will be instructed in how to use the tablet-based Tele-TC program. The mobile devices and the sensors will be provided to each participant and will be preprogramed will all required software. It is worth emphasizing that, as part of the consent process, all subjects will be asked permission to be videorecorded during the assessments via Zoom Enterprise.

Visits will be divided into two components: 1) clinical assessments and 2) instrumented monitoring of TC performance,

The following clinical assessments will be performed during *Visits #1B and #4*.

The following questionnaires will be provided to the subjects through REDcap Survey with an email link. It will take around 45 minutes to complete all of the questionnaires.

- *Activities Specific Balance Confidence (ABC):* 16-item self-report measure in which patients rate their balance confidence for performing activities.
- *PROMIS® (Patient-Reported Outcomes Measurement Information System) 29 (PROMIS-29)* instrument: 29-item questionnaire assessing each of the following domains: anxiety, depression, fatigue, physical function, pain interference, pain intensity, sleep disturbance, and ability to participate in social roles and activities. The instrument contains four items from each primary domain plus a single pain intensity rating.
- *Physical Activity Scale for the Elderly (PASE):* self-reported level of physical activity in individuals aged 65 years or older during the previous 7 days.
- *Exercise Self-efficacy Questionnaire (SEE):* A 9-item questionnaire that focuses on the self-efficacy expectations for exercise for older adults; specifically, the ability to continue to exercise despite barriers.

Clinical assessments which take around 15 minutes will include tests such as:

- *Camera recorded Trail Making Test A/B:* Executive function will be assessed using the Trail Making Test. Participants will be timed while sequentially connecting a series of

numbered circles (part A), as well as connecting an alternating series of numbers and letters (part B). The adjusted trail making score (i.e., part B minus A, sec) is sensitive to changes in executive function and frontal lobe pathology in older adults.

- *Instrumented and camera-recorded monitoring of balance in each leg separately.*
- *Instrumented and camera-recorded Timed-Up-and-Go:* Subjects will be asked to stand up from a chair, walk at their normal speed around a cone, turn around, and come back to sit in the chair.
- *Instrumented and camera-recorded Timed-Up-and-Go dual task:* Subjects will be asked to complete the previous task while counting backwards by three.
- *Instrumented and camera-recorded Sit-to-Stand:* Subjects will be asked to stand up from a chair while keeping their arms crossed across their chest during 30 seconds.
- *Instrumented and camera-recorded monitoring of balance in both legs* with feet shoulder-width apart and as close as possible without touching.
- *Instrumented and camera-recorded monitoring of gait.*

Instrumented and camera-recorded monitoring of TC performance will be performed during Visits #1B, #2, #3 and #4:

- Participants will be instrumented with 5 sensors (one on each limb and one on the trunk) and they will be following the instructions from the Tele-TC platform.

Study staff will use Zoom to communicate with subjects during these visits if done remotely. We hypothesize that data collected over 4 sequential visits will show that the sensor-based estimates of the metrics of adherence, proficiency, and safety developed in Phase I are sensitive to longitudinal changes that take place in response to the interventions. The performance of TC exercises will also be videorecorded and scored using the proficiency metric described in our preliminary studies section to provide a gold standard.

Subjects will be asked to don one Smart GeneActiv watch by ActivInsights* in their wrist to monitor activity during approximately a week after visits *#1B* and a week before visit *#4.*

We will ask the participants to send the GeneActiv back to the lab after wearing it. We will be sending another GeneActiv about two weeks before visit #4.

3. *TC Training Sessions the Tele-TC Platform (12 weeks)*

Study volunteers will participate in a 12-week simplified TC program that we have used in multiple prior clinical studies. In this pilot study, the intervention will be delivered via our platform-based application. All participants will be provided with a tablet with the Tele-TC software installed. The structured intervention, designed for older adults, emphasizes essential TC movements that are easily comprehensible and can be performed repetitively in a flowing manner. The protocol includes up to six core TC movements based on the traditional Cheng Man-Ch'ing's Yang-style short form. Additionally, a complementary set of traditional TC warm-up exercises that focus on loosening the physical body, incorporating mindfulness and imagery into movement, promoting overall relaxation, and coordinating breathing awareness are included. Chairs are used in the

protocol for a subset of seated warm-up exercises, as well as for stability and rest as needed. Participants will be asked to practice the protocol (45-60 min) at home for at least 3 days a week for 12 weeks. In addition to data on practice frequency, duration, protocol adherence and training proficiency being automatically collected through our platform, a weekly REDcap survey will be used to monitor adverse events. The TC program will also include 2 or more live instructional sessions via Zoom with a TC instructor.

4. *Remote Monitoring of Falls and Other Adverse Events*

We will monitor falls during the subject's participation in the intervention study. Falls will be defined as any event in which the participant unintentionally comes to rest on the ground or other lower level, not as a result of a major intrinsic event or an overwhelmingly external hazard. Falls will be systematically monitored in two ways. As part of our safety and adverse events (AE) monitoring, participants will be asked to complete a weekly REDcap adverse events survey about their TC practice and activities of daily living. Study staff will follow-up by phone with participants as necessary. During study visits #1b-#4, study personnel will inquire about and record characteristics and details of falls and other adverse events.

5. *Feedback from the Subjects*

During the last visit (visit #4), we will conduct a semi-structured qualitative interview to gather feedback from the subjects regarding the feasibility and acceptability of the study overall, and more specifically the usability of the Tele-TC platform. We will ask them to provide us with feedback regarding general characteristics of the platform, possible improvements of the system, and whether they would consider using the system on a daily basis at home. The qualitative interview will be audiorecorded. In addition, at the end of the study, we will use an adapted version of the System Usability Scale (SUS).

6. In Lab Assessments (Visits #1b and #4)

Subjects will be asked if they are willing to perform a lab testing at baseline and post-intervention visits (#1 and #4) in the Motion Analysis Laboratory (MAL) at Spaulding Rehabilitation Hospital (SRH). Lab visits will include the same battery of assessments utilized in the remote visits, as well as the Mini Balance Evaluation System (Mini BEST) Test. The lab visits will include instrumented monitoring of TC performance as well. The miniBEST is a shortened version of the Balance Evaluation System Test (BESTest). It is a 14-item test scored on a 3-level ordinal scale. It aims to target and identify different balance control systems. The sessions will be videotaped, and the miniBEST test may be instrumented.

7. Return of devices

The subjects will be asked to return the devices (mobile devices, sensors, tablet stands) in a prepaid and addressed box by mail after the completion of the study. The final payment for the study ($50) will be contingent on the return of the study equipment. Those that come into the lab for their final testing visit will be asked to return the devices in person.

VI. BIOSTATISTICAL ANALYSIS

The primary outcomes of the study are the retention and the protocol adherence during the study, and the System Usability Scale collected post-intervention.

The exploratory outcomes will include the following:

- The ease of use of the Tele-Tai Chi platform measure with the qualitative interview collected post intervention.
- The changes in outcomes collected at baseline and post-intervention: the Activities-specific Balance Confidence (ABC) scores, PROMIS 29 scores, the Physical Activity Scale for the Elderly (PASE), the Trail Making Test A/B scores, Self-Efficacy Exercise (SEE) scores, the Timed-Up-and-Go, the Timed-Up-and-Go dual task single leg stance, the Sit-to-Stand performance, the balance on both legs with feet shoulder-width apart, the balance on both legs with feet close to each other, the normalized-to-height stride length and stride time variability, the activity level, and the Mini-Balance Evaluation Systems Test (MiniBEST) collected only in individuals who are willing to be tested in the MAL
- The changes in The Tai Chi proficiency scores collected at baseline, 4 weeks, 8 weeks, and pos-intervention.

Descriptive statistics will be derived for all the above-described clinical assessment outcomes and correlations will be sought with the sensor-based estimates of the metrics of adherence, proficiency and safety derived using the previously developed algorithms. Exploratory statistical analyses will be performed to power future clinical studies aimed to test the relationship between the proposed metrics of adherence and proficiency and the clinical outcomes of the intervention. Whereas conclusive statistical analyses to explore such correlations are beyond the scope of the proposed project, the data collected in this pilot study are expected to provide justification for a future trial aimed to assess the efficacy of the Tele-TC Platform as a training system.

VII. RISKS AND DISCOMFORTS

TC is likely to be safe, as there have been no reports of serious adverse impacts in the TC literature. We experienced no serious adverse events in our pilot studies with COPD, heart failure, vestibulopathy, and osteopenic populations. However, there may be some potential expected risks to participants including the following:

1. TC and other motor tasks included in the clinical evaluations of balance and gait may cause some muscle soreness in highly deconditioned individuals. This soreness is likely to only last a short time. In addition, shortness of breath, dizziness, or falls are possible. However, these risks are unlikely and will be discussed in both the protocol and consent form.
2. Possible discomforts associated with using the sensors are the same as those experienced when wearing other wearable devices such as bracelets, watches and heart monitor straps. Prolonged use of the sensors may cause sweating and skin irritation.

There is a possibility that subjects could fall or trip during the experimental procedures, or that they may experience an allergic reaction or minor skin irritation to the band used to attach the

sensors to the body. There is also a possibility that subjects may become fatigued or experience muscle soreness.

The risk of falling during the TC exercises and balance tests will be minimized by excluding subjects with balance impairments and risk of falls based on medical history, self-reported previous falls, and some clinical tests to assess potential balance impairments in study participants, whose outcome will be used by a rehabilitation specialist to determine if the subject can safely perform the TC exercises. If a subject falls during remote visits or TC practice, they will be referred to their physician or to urgent care as needed.

Fatigue and muscle soreness will be minimized by allowing subjects to rest at any point during the experimental procedures.

Subjects will be encouraged to contact MAL staff with any questions or concerns they may have at any time during the study or after its completion.

Overall, the potential risks to participants are modest and are likely to be viewed as reasonable in relation to the anticipated benefits to subjects and others.

Safety

When - according to a rehabilitation specialist during in-person testing, or research staff during virtual testing - subjects are unable to safely perform the TC exercises that are part of the experimental procedures, the experiment will end. Subjects will be told why the experiment must stop and will be advised to seek medical care if appropriate.

Subjects will be told that the study procedures may be associated with discomfort due to wearing the sensors and by fatigue/muscle soreness. In case subjects experience discomfort or excessive fatigue, they will be free to remove the sensors and end their participation in the study.

Foreseeable Risks and Discomfort

Unintentional loss/disclosure of Protected Health Information may occur and is considered a minimal risk due to the security measures enforced at SRH. Confidential information will be kept in a locked filing cabinet, on REDcap, and on password-protected computers in the MAL.

VIII. POTENTIAL BENEFITS

Study participants are not expected to directly benefit from their participation, but it is possible that subjects will experience some positive impact on physical and mental health as a result of their performing TC exercises, as has been shown in prior TC studies. Information gained during the study is expected to contribute to the development of systems to facilitate the deployment of TC-based interventions.

IX. MONITORING AND QUALITY ASSURANCE

Because this study's procedures pose minimal risk to the subjects, bimonthly data and procedural reviews by the PI in consultation with study staff will be sufficient to identify and ameliorate any

potential safety issues. Any safety concerns about the equipment or testing protocol will be brought to the immediate attention of Dr. Bonato. Study staff will conduct bimonthly audits to ensure compliance with regulatory requirements for study documentation.

Approval of protocol, informed consent procedures, and recruitment will be obtained from the IRB during annual reviews.

Adverse event reporting will be done according to Partners Human Research Policy. Remedial action to prevent reoccurrence of the event will be instituted prior to the resumption of study procedures.

Study staff will conduct quarterly audits to ensure compliance with regulatory standards for study documentation.

The MAL will assign each new subject an alphanumeric identifier, which will henceforth be the sole means of identification connected to their data. All data will be collected under this identifier and will be kept isolated from any personal health information. All data will be stored on REDcap. Information shared with individuals outside of Partners will be labeled using an alphanumeric identifier and will be devoid of personal health information.

Video and audio recordings and photos will be stored securely in the MAL; only investigators listed on the study will have access to them. The video recordings will be destroyed in compliance with Partners Record Retention Policy. Patients will be given the choice to have video/photo material used for academic articles and presentations.

X. REFERENCES

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