SPAULDING REHABILITATION HOSPITAL BOSTON

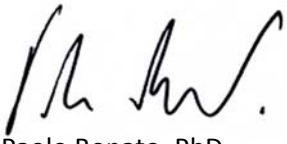
300 First Avenue Charlestown, MA 02129 617.952.5000 www.spauldingnetwork.org

May 24, 2019

To Whom It May Concern

The attached documents relate to the study entitled "Augmenting Back Pain Exercise Therapy Using an Interactive Game-Based Intervention in the Home Setting". The first document is the letter of IRB approval for the last year of the study (i.e., the letter for the period from June 2016 to June 2017). The original approval was obtained in 2015. The second document is the protocol summary (including a description of the planned data analyses). Please notice that the protocol summary was submitted in 2015 to Spaulding Rehabilitation Hospital's IRB and never amended afterwards. Hence, the attached version of the protocol summary is dated July 10th, 2015. Review of the study in 2016 for continuing renewal of the study protocol led to approval of the use of the protocol dated July 10th, 2015 until June 2017, when the study was completed and hence terminated. Although the use of the protocol was approved in 2016 to cover the period from June 2016 to June 2017, it is the policy of Spaulding Rehabilitation Hospital's IRB that the protocol summary would show the date when the latest version of the protocol was submitted rather than when the continuing renewal application was submitted or when the application was approved. We sincerely hope that this policy will not generate any confusion. This letter is to attest that the version of the attached version of the protocol summary is the one that was utilized until completion of the project in 2017. If you have any additional questions, please feel free to contact our IRB administration, Ms. Line J Papin at IRB@partners.org.

Best regards,



Paolo Bonato, PhD
Study PI
pbonato@mgh.harvard.edu

Institutional Review Board

Tel: 617.952.6182

SPAULDING REHABILITATION NETWORK

Spaulding Rehabilitation Network
Research Institute
79/96 Thirteenth Street
Charlestown Navy Yard
Charlestown, MA 02129

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Continuing Review: Notification of IRB Approval/Activation
Protocol #: 2015P000663/SRH

Date: June 29, 2016

To: Paolo Bonato, Ph.D
SRH
Dept of Physical Med and Rehab

From: Spaulding Rehabilitation Network Research Institute
79/96 Thirteenth Street
Charlestown Navy Yard
Charlestown, MA 02129

Title of Protocol:	Augmenting back pain exercise therapy using an interactive game-based intervention in the home setting.
Version Date:	7/10/2015
Sponsor/Funding Support:	Name: Departmental Funds

Study Population:	Adults
Consent/Authorization:	Required
Documentation of Consent:	Written
Informed Consent From:	Adult Subject
Informed Consent By:	Non-Physician Investigator Other Study Staff
IRB Continuing Review #:	1
IRB Review Type:	Full
IRB Approval Date:	6/20/2016
Approval Activation Date:	6/29/2016
IRB Expiration Date:	6/20/2017

This project has been reviewed by SRH IRB #IRB00000817. During the review of this project, the IRB specifically considered (i) the risks and anticipated benefits, if any, to subjects; (ii) the selection of subjects; (iii) the procedures for obtaining and documenting informed consent; (iv) the safety of subjects; and (v) the privacy of subjects and confidentiality of the data.

Please note that if an IRB member had a conflict of interest with regard to the review of this project, consistent with IRB policies and procedures, the member was required to leave the room during the discussion and vote on

this project except to provide information requested by the IRB.

The IRB found that the risks to subjects are minimized and are reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that may reasonably be expected. The selection of subjects is equitable. Informed consent is sought from each prospective subject and is appropriately documented. Adequate provisions are in place for monitoring the data collected to ensure the safety of subjects, protecting the privacy of subjects, and maintaining the confidentiality of the data. The study is approved to continue for (1 year) another year.

Approved Documents:

Protocol Summary - Version Date: June 30th, 2015
Schema
Detailed Protocol - Version Date: June 30th, 2015
Consent Form - Version Date: 7 21 15
Flyer
Phone Screen
Assessment I
Assessment II
Baseline Assessment
Follow-up Assessment
Home-exercise Report
Valedo User Manual
Recruitment Email
At-Home Devices Instruction Manual
Information Sheet
Thank You Letter
Adverse Event Tracking Log

As Principal Investigator, you are responsible for ensuring that this project is conducted in compliance with all applicable federal, state and local laws and regulations, institutional policies, and requirements of the IRB, which include, but are not limited to, the following:

1. Submission of any and all proposed changes to this project (e.g., protocol, recruitment materials, consent form, status of the study, etc.) to the IRB for review and approval prior to initiation of the change(s), except where necessary to eliminate apparent immediate hazards to the subject(s). Changes made to eliminate apparent immediate hazards to subjects must be reported to the IRB as an unanticipated problem.
2. Submission of continuing review submissions for re-approval of the project prior to expiration of IRB approval and a final continuing review submission when the project has been completed.
3. Submission of any and all unanticipated problems, including adverse event(s) in accordance with the IRB's policy on reporting unanticipated problems including adverse events.
4. Obtaining informed consent from subjects or their legally authorized representative prior to initiation of research procedures when and as required by the IRB and, when applicable, documenting informed consent using the current IRB approved consent form(s)with the IRB-approval stamp in the document footer.

5. Informing all investigators and study staff listed on the project of changes and unanticipated problems, including adverse events, involving risks to subjects or others.
6. When investigator financial disclosure forms are required, updating your financial interests in Insight and for informing all site responsible investigators, co-investigators and any other members of the study staff identified by you as being responsible for the design, conduct, or reporting of this research study of their obligation to update their financial interest disclosures in Insight if (a) they have acquired new financial interests related to the study and/or (b) any of their previously reported financial interests related to the study have changed.

The IRB has the authority to terminate projects that are not in compliance with these requirements.

Questions related to this project may be directed to Catherine E Sutherland, CSUTHERLAND1@PARTNERS.ORG, 617-952-6182.

CC: Ryan McIntosh, SRH - Dept of Physical Med and Rehab, Non-Study Staff
Catherine P. Adans-Dester, PT, SRH - Dept of Physical Med and Rehab, Research Assistant

PARTNERS HUMAN RESEARCH COMMITTEE
PROTOCOL SUMMARY

Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR

Paolo Bonato, PhD

PROTOCOL TITLE

Augmenting back pain exercise therapy using an interactive gaming-based intervention in the home setting.

FUNDING

Internal funding

VERSION DATE

July 10th, 2015

SPECIFIC AIMS

Concisely state the objectives of the study and the hypothesis being tested.

Aim: To compare the outcomes of a traditional, exercise-based rehabilitation intervention for chronic low back pain with the outcomes achieved by combining a traditional intervention with adjunct therapy delivered using an interactive gaming-based system for home-based therapy.

BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

1. Background

Chronic low back pain (cLBP) is among the most burdensome health problems in both prevalence and cost of care and it is highly associated with disability, quality of life, emotional changes, and work absenteeism[1-2]. Low back pain (LBP) affects approximately 80% of people at some stage in their lives[3] and 62% of people experiencing their first episode will develop chronic symptoms lasting longer than one year, with 16% of people still sick listed from work at 6 months[4-5].

The aggregate economic burden of this condition is staggering: $8.15 billion in lost productivity (certificated and non-certificated costs included)[6] and in the United States, the total indirect and direct costs due to LBP are estimated to be greater than $100 billion annually[7-8].

Up to one third of acute low back pain cases may become chronic and lead to disability. Around 95% of chronic cases, which presents pain for at least 12 consecutive weeks, are absent findings of well-understood causes, i.e. neoplastic, infectious or inflammatory (including pain attributed to nerve compression) conditions, and are generally designated as "uncomplicated", "non-specific," or "mechanical" LBP[9-10].

Current theories of low back pain chronicity may be divided into cognitive-behavioral, biomechanical, and reflex-spasm types. Factors of each type have been shown to be associated with cLBP, and this has led to a wide acceptance that chronicity is probably maintained by a poorly understood interaction between multiple factors[11].

The known risk factors for cLBP include low socioeconomic status, physical attributes like obesity, general medical health, environmental factors like physical activity status and psychological status like depression, pain-catastrophizing, cognitive style and pain-related fear of movement[12-15].

The management of LBP comprises a range of different intervention strategies including surgery, drug therapy, and non-medical interventions, such as physiotherapy[10]. These subjects are routinely referred to physiotherapy and the treatment can involve a number of different techniques ranging from spinal manipulations, mobilization, advice, general exercises and specifically tailored exercises[16]. Exercise therapy is recommended as an effective treatment to reduce pain intensity and increase functional status when compared to other conservative treatments[10, 17-19].

However, to maximize the decrease in pain and disability a home-based exercise prescription is an essential addition to the supervised and individually-tailored exercise therapy the subject receives with their clinician[18, 20]. The home-based exercises vary greatly in the method of delivery and content[21-23] but different programs appear to have similar effects on subjects[24-25].

The main focus is the subject adherence to this type of intervention since many recurring cases of low back pain may have been avoided if the subjects adhered to their home programs during the first treatment plan[26]. Only a small percentage of the subjects meet the current recommendations of their home exercise program. The combination of exercising and the use of technology associated with enjoyment could be an important factor to help with adherence to home exercise programs[27].

Recent wearable sensor technologies have been developed, opening many possibilities in order to promote benefits in clinic and help in the assessment, monitoring and treatment of subjects[28-29]. Among the main benefits, the wearable sensors showed to be a valid and reliable technology[30-31], portable, low cost, easy to use, and lightweight[31-32].

Many of the body-worn sensors consist of accelerometers, gyroscopes, footswitches, and/or insole pressure sensors, which can quickly and inexpensively provide accurate measures of balance and gait for clinical and/or home environments over extended periods of time[28-32].

An example of such a wearable sensor is the Valedo System® by Hocoma AG (Switzerland) shown in Figure 1. The Valedo System® is a medical back training device aimed to improve compliance and increases motivation by real time augmented feedback based on trunk movements made by the subject. The motion sensors (at the chest and low back), attached to the skin with double side medical tape, communicate with interactive games displayed on an iPad® through Bluetooth and provide a different way to perform therapeutic exercisesinto a motivating game environment and guides the subject through exercises specifically designed for low back pain therapy. To facilitate challenging the subject and achieving efficient training, the exercises can be adjusted according to the subject's specific needs[29, 33-34]. Currently, the Valedo System® is registered as a 510k device by the FDA and has 17 movements incorporated into 45 therapeutic exercises, which are designed to target one or a combination of the following therapeutic goals: mobilization, stabilization, body control, improvement of movement awareness, stretching and balance.

Figure 1:Valedo System (Hocoma AG) for low back pain exercises.

Home-based rehabilitation interventions based on games may help promote physical and cognitive improvements and adherence to physical activity in subjects with Parkinson's Disease[35], children with Cerebral Palsy[36] and older adults[27, 37-39]. By gathering accurate and objective measures of symptoms, it could reduce the duration and costs of treatment required to observe such an effect.

The aim of this study is to observe the benefits of the home-based rehabilitation program using the Valedo system in conjunction with the conventional physiotherapy in subjects with cLBP. We hypothesize that, in the same number of sessions, the subjects who undergo Valedo home-based exercise and clinic based physiotherapy will receive the same benefit of subjects who undergo non-Valedo home-based exercise and clinic based physiotherapy.

2. Significance

Healthcare costs for low back pain (LBP) are increasing. Hence, it is important to provide treatments that are effective and cost-effective. There were inconsistent findings regarding the cost-effectiveness of home-based rehabilitation based on games for people with cLBP. If it becomes clinically relevant for the rehabilitation of these subjects, possibly, the costs and number of physiotherapy sessions will decrease.

RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

A. Sample Size:

50 subjects with non-specific cLBP will be recruited in the study. Following baseline measures, study volunteers will be randomized to either the Usual Care alone group or to the Interactive Home-Based System group. In each group, an endpoint assessment session will be conducted at approximately 4 and 8 weeks post baseline measures.

B. Inclusion/exclusion criteria:

Inclusion criteria**:**

1. English speaking and reading
2. Male or female, from age 18 to 65
3. Back pain subject-rated at $\geq$ 3 on an 11 point VAS scale (0-10), with a duration $\geq$ six months)
4. Able to commit to all study visits.
5. Low back pain attributable to mechanical etiology as opposed to infectious, neoplastic, or inflammatory causes.
6. BMI $\leq$ 40
7. Familiar with tablet use

Exclusion Criteria:

1. Impairment in vision or mobility interfere with required participation in the study
2. Current or anticipated receipt of payments from Worker's Compensation or other insurance for disability attributed to low back pain.
3. Plans to initiate additional treatment for back pain during the period of the study, such as acupuncture.
4. Unresolved musculoskeletal pathology of the lower limbs.
5. Severe radiculopathic pain. (As a predictor that the candidate will require either surgery or epidural analgesia within the next five months)
6. Alcohol or substance abuse
7. Prior discectomy or implantation of rods, screws or plates. (Bulging disc without radicular pain is not exclusionary; hip or shoulder replacement is not exclusionary)
8. Current medication with coumadin or prednisone, chronic use of steroid medications, daily use of narcotic analgesics, or estrogen supplementation, tricyclic anti-depressants (if not on a regular steady dose at least one month prior to enrollment), or any substance that could impair balance.
9. Current diagnosis of:
    a. Balance problems due to vestibular or other neurological impairments.
    b. Osteoporosis (Osteopina is not an exclusionary condition)
    c. Fibromyaligia
    d. Severe or progressive neurological deficits, including neuromotor impairment
    e. Any hypercoagulation condition
    f. Eczema, Psoriasis, or skin infectionsdeep vein thrombosis
    g. Burns or other acute trauma including unhealed bone fractures or open wounds
    h. Psychiatric illness not well controlled, or current episode of exacerbated major depressive disorder.
    i. Rheumatoid arthritis,

10. Any other major medical condition that would impair the subject's ability to complete the study visits.
11. Any other major medical condition that has not been stabilized, or that would impair the subject's ability to complete the activities required by the study.

Briefly describe study procedures. Include any local site restrictions, for example, "Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

SCREENING AND ENROLLEMENT

At the first point of contact (usually a phone call), study staff will administer a phone-screening questionnaire. Phone screening questionnaires will not contain identifiable information unless the subject is eligible and agrees to attend the first visit to give informed consent. Potential subjects will also be given the option to attend the screening in person.

If the subject is found eligible for the study after an in-person screening, he/she will be met by an investigator and guided through consent procedures. A study staff member trained in human subject protection and not involved in subject's clinical care will conduct the informed consent procedures. All subjects will be recruited by IRB approved study staff for this protocol: research assistant, co-investigator or principal investigator.

STUDY PROCEDURES

Assessments sessions:

At baseline, post-treatment I (after 1-month period), post-treatment II (after completion of treatment) sessions will be conducted in the Motion Analysis Laboratory at Spaulding Rehabilitation Hospital (SRH) Charlestown, Massachusetts, USA. SRH is an affiliated hospital of Harvard Medical School. While the 6 months follow-up assessment will be administered either by phone or by email. Details of data collected in these study visits are given below, in the assessment part.

Randomization to intervention:

Following baseline measures, subject will be randomized with equal probability (50/50) and stratified by gender to one of two groups by opening the next in a previously prepared series of envelopes containing randomly determined assignments:

A. Control (Usual Care group):

Subjects will receive a combination of physical therapy and home exercise program during 8 to 12 weeks. Home exercise will be recommended at least two times a week. Usual Care of LBP provided in SRH consists of exercises and manual therapy in various combinations according to the needs of the subject. Subjects will fill out a questionnaire about their pain and how much time they spent doing the home exercises every two weeks.

B. Intervention (Interactive Home-Based System group):

Subjects randomized to this group will receive a combination of physical therapy (during 8 to 12 weeks) and at least two sessions of interactive exercises program at home with the Valedo® System (Hocoma AG). The system will be loaned at no cost

to the subject and a research assistant will explain to the subject how to use the Valedo system safely (including care and storage of the device components). Subjects will fill out a questionnaire about their pain and send us the PDF report from the Valedo system (including time spend exercising and quality of movement) every two weeks during the treatment period.

Concurrent medications and other therapies: Enrolled subjects will continue any existing prescribed medications. They will be asked not to change their prescription medications unless their physician requests it. We will ask them to inform us of any such changes. Enrolled subjects will also be asked not to receive any type of adjunct therapy other than that provided by this study during the period of their participation. However, if a treating clinician decides that additional therapy treatment is necessary for their optimal medical care, it will be allowed.
All changes in medications and/or therapies during the course of the study we will be recorded in the subject file.

Assessments:

Four assessments points:

1. Baseline (before intervention) 2. Post-treatment I (after 1-month period) 3. Post-treatment II (after completion of treatment)	Test Battery I	About 2 hours visit, at the Motion Analysis Laboratory at Spaulding Rehabilitation Hospital (SRH).
4. Follow-up at 6 months	Test Battery II	administered either by phone or by email

TEST BATTERY I:

- Based on **Patient Reported Outcomes Measurements** recommended for cLBP studies[40-41] and include the following:

Instruments	**Sensitivity, Reliability**	**Items**
VAS Pain: *"How bothersome has your low back pain been during the past week"* (Primary outcome)	The most widely accepted type of pain questionnaire, excellent reliability, adequate validity, and sensitive to change in clinical populations.	0-10 cm, anchored from "none" to "highest imaginable."
Pain Frequency: "How many days did you have low back pain during the last week"		0-7 days in the week.
Owestry Low Back Pain Disability Questionnaire	It measures a subject's permanent functional disability	10 disability graduation items
Days disabled: i) days of restricted activity due to	Adapted from the National Health Interview Survey.	Two integer values

back problems ii) number of half days spent in bed, home from work or school or cutting down on usual activity.		
SF-36	Widely used general health status questionnaire. Normed on large and diverse populations, demonstrated validity; reliability coefficients from 0.72-0.93.	36 questions, variously yes/no or Likert scales of from 3 to 6 anchored points.
Global satisfaction with care: "Over the course of treatment for your low back pain in this study, how would you rate your overall medical care?" (Asked at post-treatment I and II)	Recommended by an international group of back pain researchers.	7 point Likert scale, anchored from -3 (extremely dissatisfied) to +3 (extremely satisfied).

- **Standing postural sway parameters computed form force plate data (AMTI®, Watertown, MA)**: Data will be collected from each subject in three stances: two-footed parallel with eyes closed, one-footed balance on left foot with eyes open, one-footed balance on right with eyes open. One-footed tasks will last for 30 seconds, with data recorded from the final 20 secs; two-footed tasks will last 70 seconds, with data recorded continuously for the final 60 seconds. Rest periods will be provided between tasks as necessary. For the sake of reliability, each task will be performed 5 times. Additionally, the subject will wear an accelerometer (Shimmer), the device will be positioned on First Sacrum vertebrae. Finally, opto-kinematic data will be collected using a set of reflective markers attached to the skin using medical double-sided adhesive tape. Markers will be attached to the feet (lateral malleolus) of the subject in order to assess the lateralization movement during the balance task.

Figure 2: Accelerometer sensor (Shimmer)

Raw data will be low-pass filtered to attenuate noise, and computer processed to generate parameters averaged across three trials of each task:

Parameter	**Sensitivity & Reliability**
Average velocity of center of pressure (avgCOPvel)	For one-footed task with eyes open, avg COPvel was significantly higher in severe cLPB/controls (p=0.0003), with ROC=0.54. Change values pre/post rehabilitation therapy were sig different for "poor outcome" versus controls (p=0.04). 1 week test-retest trials were within 95% standard deviation. Similar reliability and sensitivity of avgCOPvel have been

	reported for one-footed stance w/eyes closed.
Root mean square of COP medio-lateral excursion (RMSml)	RMSml significantly differentiated cLBP from controls in 2-footed eyes closed task (p=0.031); the forward lean with eyes closed task showed largest between group differences (p=0.0002). Reliability was ICC = 0.89 for eyes closed; 0.64 for forward lean w/eyes closed.
Mean shear force anterior-posterior (mSFa-p)	Reliability reported at r=0.98

- Only at baseline, anthropometric data (height and weight) cognitive-behavioral factors and psychological morbidity will be assessed and include the following:

Instruments	**Sensitivity, Reliability**	**Items**
Pain Catastrophizing Scale	Validity and reliability established.	13 items, scored on 5 point scales anchored from 0="totally disagree" to 4 "totally agree."
Tampa Scale of Kinesiophobia	Internal consistency in acute LBP varies between alpha - 0.70-0.80, test-retest reliability r=0.78-0.79.	17 items scored on 5 point Likert scales anchored from "strongly disagree to "strongly agree."
Hospital Anxiety and Depression Scale	Validated for detecting mild mood disorders in non-psychiatric outsubjects; excludes physical symptoms to avoid confounding in groups of medical subjects.	14 items; sub-scales for anxiety and for depression; designed to minimize confounding by subjects' somato-sensory symptoms.
Whiteley Index-7	Validated with primary care subjects for identification of somatoform disorders; widely used as a measure of somatization; high internal validity.	7 items; sub-scales for Illness Worrying and Illness Conviction.

At the end of the training period, the research coordinator will collect all the devices lent for the duration of the study to the subject. The devices include: one tablet and the Valedo box containing 2 sensors, 1 USB charging cable, a user manual and quick reference guide. If the subject fails to return the devices or intentionally damage them, the principal investigator will contact them and he/she will be responsible for their cost.

TEST BATTERY II:

This last interview will be administered either by phone call or by email, depending on subject prefrerence. It will be done at 6 months after the baseline assessment and include the following instruments:

Instruments **Sensitivity, Reliability** **Items**

NAS Pain: *"How bothersome has your low back pain been during the past week"* (Primary outcome)	The most widely accepted type of pain questionnaire, excellent reliability, adequate validity, and sensitive to change in clinical populations.	0-10 cm, anchored from "none" to "highest imaginable."
Pain Frequency: "*How many days did you have low back pain during the last week"*		0-7 days in the week.
Owestry Low Back Pain Disability Questionnaire	It measures a subject's permanent functional disability	10 disability graduation items
Days disabled: i) days of restricted activity due to back problems, ii) number of half days spent in bed, home from work or school or cutting down on usual activity.	Adapted from the National Health Interview Survey.	Two integer values

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

Usual care for cLBP may also include oral medication, injection medication, and exercise-based physical therapy. Therapy interventions vary across clinical centers and rely on the experience of the individual physical therapist or prescribing physician. Surveys of the United States have found high rates of complementary therapy use by patients suffering from back (54%) and/or neck (37%) pain, with chiropractic, massage and relaxation techniques being the most common, each of which is readily available in the Boston area [42-43].

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

Minimizing risks:

- In-person and phone-based questionnaires data: on low back related pain and disability, other therapeutic outcomes, and psychological data will be collected by patient-completed instruments that have been widely used in cLBP research and entail no significant risk to patients[44-46]. The risk of discomfort will be minimized by assuring subjects that they may decline to answer any of the questions asked. The risk of public disclosure of their responses will be minimized by using subjects study code and date only, deletion of any personally identifying information from the transcripts, storage of the files in the locked file cabinet and on the lab's secure server.
- Biomechanical data: the conduct of measures sessions will be supervised by Paolo Bonato, PhD, director of MAL, and his research assistants. Subjects will be supervised by trained study staff during all tests and will be monitored for indications of adverse events. Subject may become tired during the test, they will be given regular rest breaks during testing, and between trials if necessary, during which they will be allowed to rest until ready to resume. To minimize the risk that a subject may have an allergic reaction to the adhesive tape used to secure reflective markers to the skin, we will use hypo-allergenic tapes.
- Intervention:

Subjects might become tired or sore due to the exercises prescribed by their therapists for cLBP treatment. Physical therapists will monitor patients for signs of adverse effects during treatment sessions by questioning and visual observation.
To minimize the risk that a subject may have an allergic reaction to the adhesive tape used to secure the Valedo System® to the skin, we will use hypo-allergenic tapes. Research assistant will explain to the subject how to use the Valedo system safely (including care and storage of the device components) and instruct them to stop the session if pain or fatigue occur and get in contact with us. Additionally, research assistants will follow-up by phone every two weeks in ensure compliance and safety.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

Subjects will be screened prior to and during enrollment for the presence of medical conditions that might make their participation in the study unsafe. During their participation, they will be screened and monitored by their physical therapist and experienced study staff for any possible adverse event they might encounter. Experiences study staff will guard subjects while they perform all the procedures. Subjects who begin study participation will be withdrawn from the protocol under the following circumstances:

- If the subject cLBP worsen while undergoing study procedures;
- If the risk-benefit ratio is no longer respected;
- If their treating physician request to stop the Interactive Home-Based program.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

- The collection of demographic, anthropometric, medical history and subject safety data entail no significant risk in themselves. The same is true of qualitative interviews when subjects are permitted to pass on any questions they would rather not answer.
- Therapeutic outcomes and psychological data will be collected entirely by subject-completed questionnaires which have been very widely used in other trials and entail no significant risk.
- Biomechanical data: Procedures for the collection of biomechanical data will follow established procedures with which Motion Analysis Lab (MAL) personnel are familiar and which entail minimal risk. Risks include the low possibility that a subject could fall or trip while walking, that a subject may become tired during a test. The sensors (Shimmer) used in this study are powered by low voltage batteries and are completely isolated from other electrical sources such as power lines. Subjects will be questioned prior to sensors and markers application for past occurrences of fragile skin, or sensitivity to tape or latex. The investigators will use tapes least likely to irritate the skin. For persons with fragile skin, there is a risk of skin irritation from the adhesive that secures the sensor to the skin. The risk is equivalent to wearing a Band-Aid for a few hours and peeling it off. All laboratory equipment meets or exceeds hospital standards for electrical safety.

- Risks and discomforts of interventions:
  Usual Care: exercise or manual therapy may cause transient soreness or pain. Side effects of established pain medications are generally mild to moderate.
  Interactive Home-Based Gaming System: exercise may cause transient soreness or pain. Side effects of established pain medications are generally mild to moderate. They might present some skin irritation due to the adhesive tape used to secure the sensor used in the Valedo System®, we are providing them with hypo-allergenic medical double-sided tape to reduce the risks.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects." Indicate how the results of the study will benefit future subjects with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

Subjects may experience an improvement in the symptoms of their low back pain and/or function, or they may derive no direct benefit. The results of these studies may benefit future patients if the findings of this study show that the Valedo System® improved compliance and symptoms of cLBP. Data obtained from this research may lead to larger, adequately powered studies to test the hypothesized therapeutic impact of Home-Based Therapy with on cLBP, and of the mechanistic factors hypothesized to contribute to that impact.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

Subject with low back pain attributable to infectious, neoplastic, or inflammatory causes will be excluded from the study due to confounding effects of brain development on stroke recovery. The distribution of subjects across gender, ethnic, and racial classes will be determined by exposure to the planned recruitment methods cited above at SRH. No person will be excluded from participation in this study on the basis of gender, ethnic, or racial group.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

Non-English speaking subjects will be excluded from the study because the software of the Valedo System® is English only and we want subject to be able to use the device appropriately for their own safety.

For guidance, refer to the following Partners policy:

Obtaining and Documenting Informed Consent of Subjects who do not Speak English
http://healthcare.partners.org/phsirb/nonengco.htm

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

Potential subjects will be identified by the following sources:
Printed flyers will be given to physical therapy departments of participating hospitals.

1. Referrals from Physical Therapists.
2. Flyers posted in the outpatient clinics, therapy gyms and in public spaces inside and outside of the hospital.
3. The Partners RSVP for health website.
4. Via research recruitment emails, for example Spaulding Rehabilitation Network Research Recruitment emails, and Social Medias.
5. Via contact to the patients listed in the Partners Research Patient Data Registry (RPDR).

Eligible patients will be asked to either contact study staff or give permission to be contacted by study staff to obtain more information about the study and give informed consent.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

Subjects will be compensated based on the procedures undertaken. The amount of compensation will be as follows:

- $50 for the in-person assessment session (up to 3 visits: baseline, post-treatment I, and post-treatment II).
- $10 for each completed Subject's Questionnaire that is received by study staff (up to 4).
- $20 for the follow-up phone/email interview.

Each subject will receive up to $210 for completing the whole study. Additionally, parking fees at the Spaulding Rehabilitation Hospital will be reimbursed ($5).

For guidance, refer to the following Partners policies:
Recruitment of Research Subjects
http://healthcare.partners.org/phsirb/recruit.htm

Guidelines for Advertisements for Recruiting Subjects
http://healthcare.partners.org/phsirb/advert.htm

Remuneration for Research Subjects
http://healthcare.partners.org/phsirb/remun.htm

CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own subjects, describe how the potential for coercion will be avoided.

At the first point of contact (usually a phone call), study staff will administer a phone-screening questionnaire. Phone screening questionnaires will not contain identifiable information unless the subject is eligible and agrees to attend the first visit to give informed consent. Potential subjects will also be given the option to attend the screening in person.

Informed consent will be obtained by the investigators who have completed the Partners Healthcare System's human subject protection educational requirements (i.e. HIPAA), and the CITI Program in Protection of Human Subjects, in compliance with all Federal regulations regarding such training. Study staff from the Motion Analysis Laboratory will clearly explain to the subject the nature of the informed consent process, study purpose and procedures, time commitments, risks, potential benefits, treatment alternatives, rights as research participants, study staff contact information, confidentiality procedures, and arrangements for medical care provided in case of injury during the study. The subject will be given adequate time to consider their decision and encouraged to ask questions, both during the initial interview and throughout the study. A member of the study staff will answer any questions regarding the study at the time consent is given. Enrollment will begin when the subject thoroughly understand and signs the informed consent form. The will be provided with a signed copy of the completed consent and assent form. The subject may pause or terminate his/her enrollment at any time during the study.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:
http://healthcare.partners.org/phsirb/newapp.htm#Newapp

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects
http://healthcare.partners.org/phsirb/infcons.htm

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

Approval of protocol, informed consent procedures, and recruitment will be obtained from the IRB during annual reviews. Quarterly data and procedural reviews by the PI in consultation with study staff will be done to identify and ameliorate any potential safety issues. Any safety concerns about the equipment or protocol will be brought to the immediate attention of Dr. Bonato. Study staff will conduct bimonthly audits to ensure compliance with regulatory standards for study documentation.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

Study staff will report any adverse event promptly to Dr. Bonato. A written report will be submitted to the IRB within 48 hours, and appropriate changes in procedure and protocol will be implemented to prevent reoccurrence. Remedial action to prevent reoccurrence of the event will be instituted prior to resumption of the study treatment.

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

The study coordinator will be responsible for monitoring the completeness of all data and source documents. The Principal Investigator will monitor the informed consent procedures in accordance with the Informed Consent Compliance Checklist of Partners HealthCare Systems HRQIP. The subject's data/protocol adherence will be monitored by the study coordinator at each step in the study.

For guidance, refer to the following Partners policies:
Data and Safety Monitoring Plans and Quality Assurance
http://healthcare.partners.org/phsirb/datasafe.htm

Adverse Event Reporting Guidelines
http://healthcare.partners.org/phsirb/adverse_events.htm

PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

Subjects will be assigned a study number, which will be used for all documentation except for a master list matching subjects' names and study numbers, and forms for which subjects' names must be recorded (e.g. intake interview forms, copies of reimbursement receipts etc). The master list and interview forms will be kept in a secure location in locked offices. No non-study staff will have access to any identifiable subject study data or demographic information. All subjects will be informed of their privacy rights and receive a HIPAA privacy notice booklet. Study staff in the Motion Analysis Laboratory will conduct quarterly audits to ensure compliance with regulatory standards for study documentation.

SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

No personally identifiable data will be sent to or viewed by collaborators outside of SRH.

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

Data will not be stored for future use not described in the protocol.

RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

This study does not involve receiving data or specimens from outside collaborators.

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