STUDY PROTOCOL

PROTOCOL TITLE:
Outpatient and Home Advanced Rehabilitation Therapeutics Using Jintronix Virtual Reality Telerehabilitation System

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1. BACKGROUND AND RATIONALE

1.1. General Introduction

With First World health system and aging population in Singapore, patients who survived and suffered from chronic disability after conditions like stroke, spinal cord injury, traumatic brain injury and degenerative joint diseases are getting more prevalent. Such patients faced the long term challenges of maintaining and living well with a chronic condition.

After receiving intensive inpatient care, patients faced multiple challenges in accessing intensive therapy inputs. This may be due to several factors, for examples, accessibility issues to outpatient, community and home rehabilitation services due to logistical, financial and other personal issues; lack of trained rehabilitation professionals and therapists in certain community service sectors; and reduced compliance, motivation and interest due to delayed or limited professional inputs. As a result, gains made by patients in time-limited inpatient/outpatient rehabilitation may be lost or not built upon as monitoring of their level of participation and progress is reduced.

1.2. Rationale and justification for the Study

a. Rationale for the Study Purpose

With the emphasis on improving population health, reducing the need for hospital care, and promoting self-management, it will be beneficial to make good use of current available technologies to complement centre-based therapy with cost effectiveness and efficiency.

One mode of such care delivery to a patient's home is through a telerehabilitation system that enables remote monitoring of patients' participation and performance in individualised home exercises. In addition, timely review and adjustments in the home programs to cater to progress or changes in patients' performance can be carried out by therapists remotely.

In the recent years, there has been an increased utilisation of virtual reality applications in physical rehabilitation for specific training objectives, such as, movement retraining, balance control and strength training. Virtual reality exercises when prescribed with defined training objectives and duration can potentially be valuable to increase patients' training intensity in the comfort of their own homes.

b. Rationale for Device (Jintronix System) Selected

The Jintronix Virtual Reality Platform (Figure 1) was developed by a Canadian based team consisting of a group of therapists and IT specialists. It is an online system with a series of therapeutic games meant to rehabilitate patients depending on their individual needs and

physical deficits. This system, that has been approved by the FDA, is in contrast to commercially off-the-shelves gaming systems (such as Wii, Kinect, Playstation) that most patients find challenging in playing the games due to complexity and speed of the games.

Figure 1: Training with the Jintronix System in Sitting and Standing Positions

Another advantage of using Jintronix is that it provides immediate feedback to users and allows for performance charting over time. New games are also added on a regular basis to allow for more training options and to sustain interest. In a study conducted by Archambault et al (2014), more than 80% of subjects found training with the Jintronix to be user-friendly and enjoyable, with all subjects having the ability to progress in the virtual reality- based training sessions. In addition, there are currently ongoing trials in a few States of U.S.A. using the Jintronix Virtual Reality Platform.

In terms of affordability, as long as the user owns a laptop and a HDMI TV, the user is just required to purchase a $300 Kinect Camera and pay a monthly subscription of $50 for the licence. The licence also allows access to regular updates to the suite of games.

Hence, the purpose of our device innovation trial is to develop a telerehabilitation service utilising the Jintronix Virtual Reality Platform to complement current outpatient services for intensifying home exercise participation in a cost effective and efficient manner and also to improve patients' clinical and functional outcomes.

c. Rationale for Study Population

Patients who have completed their acute to subacute inpatient rehabilitation will be considered. The majority of patients receiving outpatient and home based rehabilitation at TTSH Rehabilitation Centre and Centre for Advanced Rehabilitation Therapeutics are patients who have had a stroke. Hence this group of outpatients that are at least 3 months post-stroke will be recruited. They will benefit from increased intensity of upper limb, balance and/or gait rehabilitation with Jintronix telerehabilitation system that facilitates them to further exercise at home and not just at the clinic.

d. Rationale for Study Design

The study is designed to evaluate the feasibility of a novel telerehabilitation service based on the Jintronix Virtual Reality Platform to complement existing outpatient therapy services of TTSH

Rehabilitation Centre (including its outpatient service arm at Centre for Advanced Rehabilitation Therapeutics).

2. HYPOTHESIS AND OBJECTIVES

2.1. Hypothesis

The primary hypothesis is that Jintronix telerehabilitation system is a clinically feasible service to be used for outpatient and home based rehabilitation at TTSH Rehabilitation Centre and Centre for Advanced Rehabilitation Therapeutics.

2.2. Primary Objectives

The primary objective is to evaluate if Jintronix telerehabilitation system is a clinically feasible service to be used for outpatient and home based rehabilitation at TTSH Rehabilitation Centre and Centre for Advanced Rehabilitation Therapeutics.

2.3. Secondary Objectives

Short Term:
a. To explore a more cost-effective method of increasing intensity of rehabilitation without the need for additional therapist manpower.

b. To assess virtual reality exergames potential adverse side effects.

Long Term:
a. To develop best practice guidelines/protocols for physical rehab virtual reality rehabilitation that are easily reproducible, validated and effective.

b. To develop home-based virtual reality exergames with tele-health capabilities to facilitate continual rehabilitation with remote biofeedback mechanisms.

c. To pioneer new knowledge in the field of rehabilitation therapeutics using advanced serious game technologies.

d. To improve quality of life of patients by optimizing their functional potential using enhanced therapeutic systems.

2.4. Potential Risks and benefits:

a. End Points – Efficacy

(1) Inability to activate or achieve complete movement trajectory or slowness to adapt to training environment.
(2) Computer-related eye or visual complaints due to prolonged concentration to the screen.
(3) Mild leg fatigue or discomfort related to repetitive standing and ambulating if needed
(4) Rare risk of seizures due to prolonged visual feedback.

(5) Low risk of falls (will be under close supervision by therapist/carer)

b. End Points – Safety

A. Benefits to Patients
(i) increased home exercise intensity with improved compliance
(ii) improved patient therapy outcomes
(iii) cost-savings due to reduction in clinic visits
(iv) high level of acceptance/satisfaction with a telerehabilitation service

B. Benefits to Outpatient Rehabilitation Service/Staff
(i) optimisation of healthcare resources (manpower, clinic resources)
(ii) successful work re-organisation to run a telerehabilitation service

3. STUDY POPULATION

3.1. List the number of subjects to be enrolled.

The number of subjects to be enrolled for this study will be 35.

3.2. Criteria for Recruitment

Based on inclusion criteria and exclusion criteria as stated below, suitable patients will be recruited for the study.

3.3. Inclusion Criteria

1. Patient with motor deficit(s) due to stroke as diagnosed by CT or MRI, who are attending outpatient rehabilitation services at TTSH Rehabilitation Centre and Centre for Advanced Rehabilitation Therapeutics.
2. Post stroke of at least 3 months with stable neurological status.
3. Age 21 to 75 years old inclusive.
4. Able to perform at minimal level of assistance (i.e. carer provides only up to 25% of physical support to subject) for sitting, standing and/or walking tasks.
5. Has a primary carer that must be present with subject in all trial sessions.
6. Able to understand and participate in a 15 minutes trial Jintronix session during screening.

3.4. Exclusion Criteria

1. Patient with severe cognitive, perceptual (include hemi-neglect), and/or emotional-behavioural issues that preclude from participation.
2. Experiencing moderate to severe levels of pain (Visual Analogue Scale > 5).
3. Has previous seizure episodes.
4. Has unstable medical conditions which may affect participation (e.g. unresolved sepsis, postural hypotension, end stage renal failure) or anticipated life expectancy of <1 year due to malignancy or neurodegenerative disorder.
5. Has known poor cardiac ejection fraction (<30%) or lung function(FEV1<30%).
6. Is non-weight bearing for either of the lower limbs.
7. Is Pregnant or breast feeding.
8. The competency of the carer: in which the potential participant will not be recruited if

his/her carer is unable to pass the competency check by the study team.

3.5. Withdrawal Criteria

Criteria for stopping research are dependent on the following factors:

(1) Completion of recruitment of all subjects.

(2) Permanent software failure of the Jintronix Telehrehabilitation System which cannot be repaired.

(3) Premature cessation of funds from grant or sponsor.

(4) Serious adverse events deemed to be related to research study: E.g. serious injury, falls, severe increase in pain, >30% above baseline scores).

(5) New medical problems unrelated to study intervention.

3.6. Subject Replacement

Subjects who drop out will not be replaced.

4. TRIAL SCHEDULE

Each recruited participant will undergo the following program:

Outcomes Evaluation at 4 time points: week 0 (pre-Phase 1), week 3 (post-Phase 1), week 7 (post-Phase 2) and 1 month-Phase 2.

Phase 1 Training at Outpatient Clinic Service : 9 sessions (3x per week) over 3 weeks training with Jintronix Virtual Reality Platform in-clinic with therapist. Carer training and competency evaluation will be conducted before starting Phase 2.

Phase 2 Training at Home with Telerehabilitation : 20 sessions (5x per week) over 4 weeks training with Jintronix Virtual Reality Platform at home with trained carer and remote monitoring by therapist.

5. STUDY DESIGN

5.1. Summary of Study Design

Exercise Training Protocol

i. Therapist's Prescription

The therapist will prescribe and pre-program exercises individualised to the needs of the subject. Based on results of screening (with the inclusion/exclusion criteria) and the first outcome evaluation (i.e. week 0 assessment), the therapist will prescribe accordingly the choice and challenge level of exercises including the required posture (i.e. in sitting or standing).

This prescription of exercises will be further modified by the therapist as needed as the subject goes through subsequent training sessions so as to provide an appropriate level of physical workout for the participant. The therapist will also ensure that rest breaks will be adequately embedded in the 45-minutes long session based on subject's performance.

For both Phase 1 and Phase 2 training, only the therapist will be able to prescribe and make changes; subject will not be able to access the controls needed to make these changes.

The prescription list can include 3 different components available on the system:

(a) "assessments" - standardized measurements of the user's abilities (for example, see Figure 2)

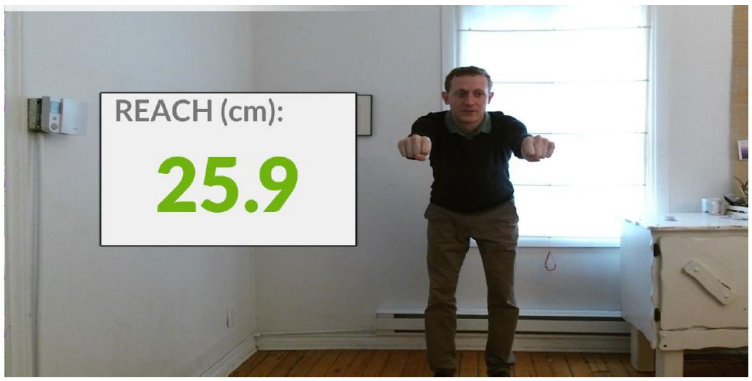

Figure 2. Jintronix "Assessment" for Functional Reach

(b) "exercises" - movement training with guidance from a virtual exercise coach (for example, shoulder movements as shown in Figure 3)

Figure 3. Jintronix "Exercise" for Shoulder Movements

(c) “activities”- games-based exercises (for examples, see Figures 4, 5 and 6)

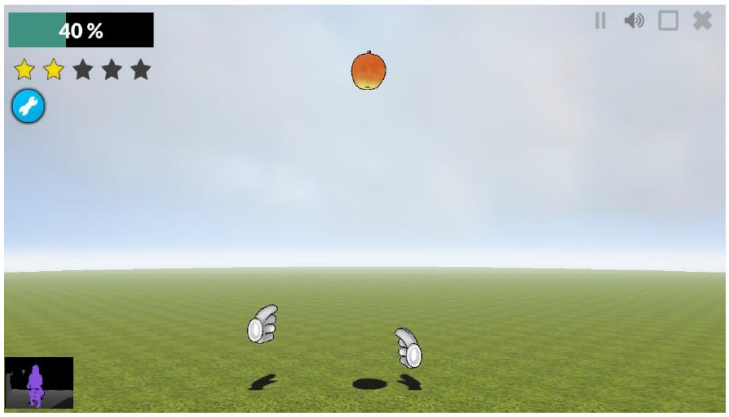

Figure 4. Jintronix “Activities” for Bilateral Upper Limb Coordination involving Catch and Carry Motions

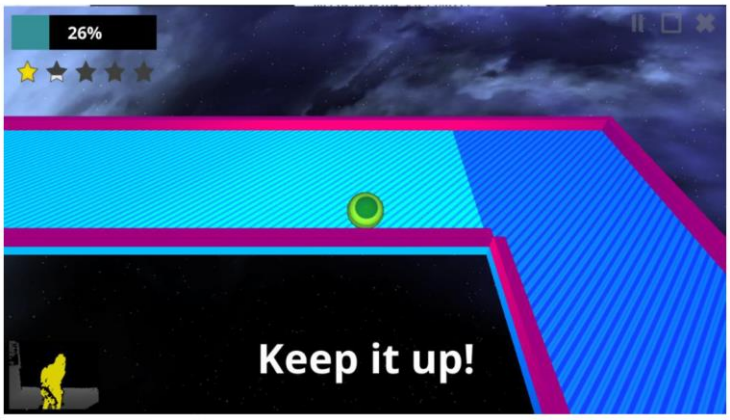

Figure 5. Jintronix “Activities” for Trunk Control involving Weight Shifting Motions in Sitting Positions

Figure 6. Jintronix “Activities” for Balance in Standing Position Involving Kicking Motions

Before performing an activity on Jintronix, the system guides the user through trunk and range of motion calibrations, where applicable.

ii. Phase 1 Clinic-based Training

Subject will be instructed and assisted by the therapist for this phase with the carer present.

In addition, the carer will be trained on understanding and ability on ensuring a safe physical environment at home, ability to use Jintronix Virtual Reality System, ability to safely guide and handle subject and fall management.

For the last 3 sessions (i.e. 7,8 and 9) of this Phase 1, therapist will let carer handle the subject with the therapist supervising and evaluating carer's ability in ensuring participant's safety.

The carer will then be evaluated with the Carer Education and Competency Form at the end of this Phase 1. Phase 2 will commence only if carer is competent, i.e., all statements in the Carer Education and Competency Form is rated as "C" (for Competent).

iii. Phase 2 Home-based Training

Equipment will be set up and tested to be operational at the subject's home and will be loaned to subject at no cost for the duration of the subject's participation. This will include:

- computer with installed Jintronix Virtual Reality Platform
- Kinect sensor
- WIFI connection

Carer:

Therapist will evaluate with carer his/her competency by re-evaluating with the Carer Education and Competency Form after the home set-up. This is to ensure carer's understanding and ability on ensuring a safe physical environment at home, ability to use Jintronix Virtual Reality System, ability to safely guide and handle subject and fall management.

Subject:

Each subject is expected to login and perform prescribed exercises everyday (Mondays to Fridays only) for 4 weeks with carer's guidance and assistance. Each exercise session duration is 45 minutes. The subject can decide regarding preferred exercise time (i.e. before 3 pm).

Therapist:

Therapist will review each subject's performance and re-adjust program games parameters to upgrade or downgrade level of challenge via remote processing in-clinic within the same day of each training day if needed (i.e. after 3pm). Any change of program games parameters will be documented.

6. METHODS AND ASSESSMENTS

These include subjects' performances and feedback, carer competency and therapists' operations and feedback and technical usability:

(i) Subjects' Physical Performance: To be carried out at week 0 (pre-Phase 1), week 3 (post-Phase 1), week 7 (post-Phase 2), and 1-month Post Phase 2. Standard stroke outcome measures will be used:
- Upper Limb measurement: Fugl Meyer Upper Limb Motor Assessment
- Balance measurement: Berg Balance Test
- Endurance: 6 minute Walk Test
- Gait Speed: 10 metre Walk Test
- Pain: Visual Analogue Scale
- Stroke Self-Efficacy Questionnaire

(ii) Subjects' Performance: include compliance, ease of system utilisation (measured by rating scale), ability to carry out exercises with changes done remotely by therapist, and user satisfaction.

(iii) Carer Competency: include carer's understanding and ability on ensuring a safe physical environment at home, ability to use Jintronix Virtual Reality System, ability to safely guide and handle subject and fall management.

(iv) Therapists' Operations: include ease of system utilisation (measured by rating scale), total number of remote monitoring sessions per day, actual man-hours required to review and re-adjust after each subject exercise session, and documentation of each remote monitoring.

(v) Therapists' Feedback: include user satisfaction and system usefulness.

(vi) Technical Issues: include system reliability and need for support service trips to subjects' homes – measured by i) number of visits required for technical support due to system breakdown/problems; ii) number of man-hours to solve the technical problems.

6.1. Randomisation and Blinding

No randomization and blinding needed for this feasibility trial.

6.2. Contraception and Pregnancy Testing

Not applicable in this study.

6.3. Study Visits and Procedures

a. Screening Visits and Procedures

Screening will be done by either the Principal Investigator or Co-investigators based on the inclusion and exclusion criteria stated above.

b. Study Visits and Procedures

Subjects will be undergoing outpatient and/or home based rehabilitation during the trial period.

c. Final Study Visit:

Will be at 1-month Post Phase 2 for outcomes evaluation in outpatient clinic as stated in Point 6 above.

d. Post Study Follow up and Procedures

Not applicable in this study.

e. Discontinuation Visit and Procedures

If the subject decides to withdraw from the study for any reasons without any adverse effects, he/she will receive standard care for his/her condition. This will include outpatient and/or home based conventional rehabilitation therapy if indicated and occasional use of commercial off the shelf gaming consoles if clinically indicated at intervals determined by clinicians.

If the subject is withdrawn from the study due to adverse effects, he/she will be given appropriate care under medical supervision until the symptoms of any adverse event resolve or the condition becomes stable.

7. TRIAL MATERIALS

7.1. Trial Product (s)

Not applicable in this study.

7.2. Storage and Drug Accountability

Not applicable in this study.

8. TREATMENT

8.1. Rationale for Selection of Dose

The number of training sessions within the training period is determined by principles of exercise prescription (3-5 times per week, 45 minutes each session).

8.2. Study Drug Formulations

Not applicable in this study.

8.3. Study Drug Administration

Nil drug administered.

The Jintronix telerehabilitation system will be supervised by experienced physiotherapists and occupational therapists.

8.4. Specific Restrictions / Requirements

No restrictions or limitations on existing rehabilitation therapies, no alterations or restrictions in patients' own medications, herbs, vitamins and mineral supplements while participating in the study.

8.5. Blinding

No blinding needed for this feasibility trial.

8.6. Concomitant therapy

No interruptions or alterations to existing medical or rehabilitation therapies will be enforced during the research trial.

9. SAFETY MEASUREMENTS

9.1. Definitions

Define terms e.g. what would be regarded as UPIRTSO events, Serious adverse events etc.. Include details of the protocol specific reporting, procedures, including the individual responsible for each step (e.g. the Investigator, the medical monitor, etc.), how decisions will be made regarding determining relatedness and grading severity, how reports will be distributed and what follow up are required. Include specific details of reporting procedures for:

- Deaths and life threatening events
- other SAEs
- Other adverse events

9.2. Collecting, Recording and Reporting of "Unanticipated Problems Involving Risk to Subjects or Others" – UPIRTSO events to the NHG Domain Specific Review Boards (DSRB)

9.3. Collecting, Recording and Reporting of Serious Adverse Events (SAEs) to the Health Science Authority (HSA)

1. **For Industry sponsored Trials**

   Not applicable in this study.

2. **For Principal Investigator initiated Trials**

   Not applicable in this study.

9.4. Safety Monitoring Plan

Data and subject feedback will be reviewed after every 5 subjects recruited. In addition, any negative feedback in terms of subject feedback or therapist opinion will be discussed at 4 weekly meetings.

9.5. Complaint Handling –

Complaints will be reported to the PI and data will be stored in safe and secure rooms under locked cabinets.

10. DATA ANALYSIS

10.1. Data Quality Assurance

Data will be reviewed after every 5 subjects recruited. Random checks will be undertaken by co-investigators and PI.

10.2. Data Entry and Storage

Hard copies of research data (case record forms - CRF) will be stored in locked cupboards within locked rooms. Soft copies of the data will be stored in password protected computers accessed only by members of the study team (PI, Co-I).

The electronic data can be accessed by Jintronix company as the system runs on an online platform. All subjects' Jintronix accounts will be fully de-identified and coded.

All subjects' data and Jintronix coded accounts will be stored up to 6 years after the completion of the study, then deleted.

11. SAMPLE SIZE AND STATISTICAL METHODS

11.1. Determination of Sample Size

Not applicable in this pilot feasibility trial.

11.2. Statistical and Analytical Plans

Descriptive statistics will be used to present the demographic and baseline characteristics for all patients. If the outcome data is normally distributed, one-way analysis of variance (ANOVA) will be used to analyse the differences in outcome between time points. If the data is not normally distributed, the Kruskal-Wallis *H* Test will be used to analyse the differences in outcome between time points.

All data analysis will be conducted using SPSS version 21.

12. ETHICAL CONSIDERATIONS

12.1. Informed Consent

Patients will be approached prior to initiation of any study procedure, by the treating physician, PI, co-investigators or research associates involved in study. They will be given copy of Informed Consent Form (ICF) and adequate time to read through and understand the procedures and ask for clarifications prior to informed consent. Consent will be taken in the outpatient gymnasium or clinic and to protect patient confidentiality and no coercion or force will be used during the consent process and patient will be given the option to volunteer. Only the PIs, Co-Is or study administrators will be involved in taking informed consent.

12.2. IRB review

This protocol is submitted together with the associated informed consent documents to NHG DSRB.

12.3. Confidentiality of Data and Patient Records

Hard copy data will be coded with code numbers/subjects initials only and the list of subjects' full names and NRIC numbers matching these codes will be kept in the investigator file located in a locked cupboard. Hard copy records will be kept in locked cupboard within locked rooms and soft copy records will be kept in password protected computers in the clinic within locked room premises.

The electronic data can be accessed by Jintronix company as the system runs on an online platform. All subjects' Jintronix accounts will be fully de-identified and coded.

All subjects' data and Jintronix coded accounts will be stored up to 6 years after the completion of the study, then deleted.

13. PUBLICATIONS

As per data sharing agreements and research collaborative agreements, joint and independent publications will be permitted with non-identification of research patients.

14. RETENTION OF TRIAL DOCUMENTS

Records for all participants, including CRFs, as well as IRB records and other regulatory documentation will be retained by PI in locked cupboard within locked rooms. Soft copy records will be stored in password protected computers located in locked rooms.

Hard copy and soft copy data will be destroyed 6 years after completion of the study.

List of Attachments

Appendix 1 **Study Schedule: Located on main English ICF**

Appendix 2 **Blood Sampling Summary : Not applicable**

Appendix 3 **Questionnaires used in the Trial: Not applicable**

Appendix 4 **Laboratory Tests: Not applicable**

Appendix 5 **Sample Patient Information Sheet and Informed Consent Form: Located on NHG ROAM ethics submission attachments**