Protocol title:

EVALUATION OF THE PERFORMANCE OF VRP-CLINIC IN HEALTHY SUBJECTS IN THE SUPPORT OF REHABILITATION: A PROSPECTIVE, OPEN LABEL, SINGLE ARM STUDY

Protocol number: VRP02

Version number: 1

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PRINCIPAL INVESTIGATOR: Yair Barzilay, M.D.

CO INVESTIGATOR: Lilach Gavish, Ph.D

PROTOCOL APPROVAL

I confirm that I have read this protocol named "EVALUATION OF THE PERFORMANCE OF VRP-CLINIC IN HEALTHY SUBJECTS IN THE SUPPORT OF REHABILITATION "; I understand it and I will work according to its contents and the applicable laws and regulations of Israel.

PRINCIPAL INVESTIGATOR:

Yair Barzilay, MD _____ _____ _____

Signature **Date**

CO-INVESTIGATOR:

Lilach Gavish, PhD _____ _____ _____

Signature **Date**

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SYNOPSIS

Study Sponsor	**VRHealth, Shocken 32, Tel-Aviv 6105101, Israel**	
Protocol Number	VRP02	
Study Title	Evaluation of the Performance of VRP-Clinic in the Support of Rehabilitation in Healthy Subjects: A prospective, open label, single arm study design	
Projected Study Period	Initiation Date: **July 2017**	Completion Date: **August 2017**
Study Device	VRP-Clinic	
Device Description and Indication for Use	VRP-Clinic is a software system that is coupled with virtual reality hardware and head movement sensors, aimed at gamification of physiotherapy training	
Study Objectives	**Primary objective** To verify that the movements included in a VRP-Clinic VR training session are self-explanatory and recognized by clinicians **Secondary objectives** To verify that these movements are considered useful for rehabilitation.	
Study Design	Single center, prospective, open label, single arm. Following screening visit, eligible subjects will be enrolled into the study. Each subject will perform a series of neck movements guided by the VRP-Clinic software. The duration of the actual training session is expected to be 5 minutes. Every session will be recorded by video during which the face of the subject will be covered by the VR headset. The video will be evaluated by clinicians. They will identify each movement seen on the video from a predefined list and define if such a movement is recommended as part of a rehabilitation training program	
Study Duration	Study duration from the first enrollment to completion is expected to be four months.	

Study Population	Twenty (n=20) healthy subjects will be recruited
Main Inclusion Criteria:	1. Healthy male or female 2. Age 18-65
Main Exclusion Criteria:	1. History of neck related disorders (Whiplash, disc degeneration disease or other acute cervical spine conditions) 2. Current neck pain 3. Under medical treatment or observation for any health-related issue during the study 4. Recent trauma 5. Oncology background 6. Acute disease/illness 7. Pregnancy. 8. Using drugs that could potentially affect physical function and balance (such as corticosteroids, antipsychotics or antidepressants) 9. Vision problems that require glasses (not all frame types can fit into the headset)
Study Endpoints	**Primary Endpoint:** Number of VRP-Clinic neck movements that the evaluator recognizes as useful for rehabilitation. Success acceptance criteria defined as: 80% **Secondary Endpoint:** Safety – Record of any adverse event occurring during the study. All AEs will be recorded and evaluated as part of the risk management for the device

INTRODUCTION

One of the most common musculoskeletal dysfunctions in the population is dysfunction of the cervical spine reaching an annual prevalence of 30-50% in western societies and associated with considerable pain, disability, and costs [1, 2].

Physical therapies are first line treatments aimed at improving muscle strength and range of motion, often requiring considerable commitment by subjects over a long period of time [3] and frequently requiring a home exercise program for a successful outcome [4]. However, compliance to home exercises is not as high as desired therefore, it is imperative to include new motivational interventions to increase compliance.

Virtual reality (VR) technology has been used for several decades for a variety of psychosocial interventions. The use of VR was studied for a variety of rehabilitation conditions [5, 6]. Specifically, the effect of neck exercises using VR was previously tested on both asymptomatic individuals and patients with chronic neck pain and was shown to be useful in increasing cervical motion [7-9].

STUDY RATIONAL

In recent years, commercial and research groups have been studying the effect of VR systems on the rehabilitative progress and developing new platforms. As the variety of available products widens, each system focuses on specific hardware and different rehabilitation aspects. The software presented in the current study focuses on the rehabilitation of the upper body.

STUDY OBJECTIVES

The current study was designed to evaluate neck movements performed according to the VRP-Clinic software, and to verify that they promote physical activities that correspond with physical rehabilitation.

STUDY DEVICE

Indications for Use

VRHealth's VRP-Clinic software, coupled with compatible VR (virtual reality) hardware (headset and supporting PC) is intended to promote physical rehabilitative processes of individuals requiring training of their head and neck muscles/joints as part of a physical therapy session.
Prior to the first session using VRP-clinic, a medical practitioner will assess the patient and will determine the selection of movements included in such training.

Device Description

VRP-clinic Software

VRP-Clinic software is used with several supported hardware platforms, delivering the same experience in each. Currently, the VRP-Clinic software supports Oculus rift and HTC VIVE

platforms – both systems use a PC based virtual reality platform and infra-red sensors to detect head movement of the user.

A description of the software algorithm, a major routine/function level flow chart, a signed validation document, and a risk analysis table can be found in the Investigator Brochure.

Hardware platform

VRP-Clinic software is used with several supported hardware platforms, delivering the same experience in each. Currently, the VRP-Clinic software supports Oculus rift and HTC VIVE platforms – both systems uses a PC based virtual reality platforms and used infra-red sensors to detect head movement of the user. In the current study, the Oculus rift platform will be used. A description of the Oculus rift device and the manufacturer details can be found in Investigator Brochure.

STUDY DESIGN

Overview

Single center, prospective, open label, single arm.

The study will take place at Shaare Zedek Medical Center (SZMC). The study will include a single visit. Twenty (n=20) healthy subjects will be recruited to this study. Subjects must meet the eligibility criteria detailed in the protocol and sign the informed consent form prior to any study procedure.

Each subject will receive an explanation from the study team on the device and study procedures. Medical and demographic information will be collected.
The subject will put on the VR headset and perform a series of neck movements guided by graphic instructions appearing in the VR environment. The study team will record any adverse event (AE) if such happens during/post training.

The session will be recorded with a video camera. Camera recording will start after the VR headset is placed on the subjects' head and terminate before removing it, to ensure the participants' privacy.

The video will be viewed and evaluated separately by 4 clinicians. The clinicians will identify each movement seen on the video from a predefined list and determine if such a movement is recommended as part of a rehabilitation training program for neck related pathologies.

Endpoints:

Primary Endpoint

Number of VRP-Clinic neck movements that the assessing clinician recognizes as rehabilitation movements.

Success acceptance criteria defined as: 80%

Secondary Endpoint:

Safety – Record of any adverse event occurring during the study.

All AE's will be recorded and evaluated as part of the risk management for the device

Study Duration

Duration of subject's participation: 30 minutes of which the actual exercise is expected to take not more than 5 minutes

Study duration: The total study duration from recruitment to final data collection is estimated to be four months

STUDY POPULATION AND SUBJECT SELECTION

Source and sample size

Twenty (n=20) healthy adult subjects will be included in this study. The subject will be recruited by the investigator by use of an IRB approved advertisement.

Eligibility

Each subject will be evaluated by the Investigator to assess his/ her suitability for entry into this study according to the following criteria:

Inclusion Criteria

Eligible subjects must meet all of the following inclusion criteria:

1. Healthy male or female
2. Age 18-65

Exclusion Criteria

Eligible subjects must not meet any of the following exclusion criteria:

1. History of neck related disorders (Whiplash, disc degeneration disease or other acute cervical spine conditions)
2. Current neck pain
3. Under medical treatment or observation for any health-related issue during the study
4. Recent trauma
5. Oncology background
6. Acute disease/illness
7. Pregnancy.
8. Using drugs that could potentially affect physical function and balance (such as corticosteroids, antipsychotics or antidepressants)
9. Vision problems that require glasses (not all frame types can fit into the headset)

The investigator may withdraw a subject if, in his clinical judgment, it is in the best interest of the subject or if the subject cannot comply with the protocol. At the discretion of the investigator, these subjects may be replaced. Attempt should be made to complete any examinations.

Subject Termination

In case of dropout or subject removal the investigator will describe the reason for discontinuing the subject's participation in the Termination CRF.

Compensation

At the end of the session, subjects will receive a coupon for use at the local cafeteria for purchase of a hot drink and cake ("café u maafe") approximately worth 15 NIS as compensation for their time.

STUDY PROCEDURES

Screening

Eligibility: the volunteer will be screened to determine if he/she meets the study inclusion/exclusion criteria.

Informed consent Prior to the study visit, informed consent will be obtained. When the participant fully understands the procedure, possible benefits and risks of the study, the subject will be asked to sign and date the informed consent document.

Subject number If the subject meets the study inclusion/exclusion criteria , the subject will be assigned the next consecutive number.

Medical history and demographic information: Basic medical and demographic information will be collected including age, gender, height, weight, head circumference, general medical background and specific information related to head/neck.

Interventions and procedures:

Subject Preparation and Instructions

The subject will sit on a steady chair, with back support, in front of a desk were the device sensors are located. Once starting the training program, the subject will receive instructions appearing in the graphic VR environment:

Neck movements

The software will guide the subjects to perform neck movements.

EVALUATIONS

Physiotherapist Evaluation and Assessment of Videos

1. Identification of each movement seen in the video from the list detailed in "Neck Movement" section
2. Determining if the use of such movement is recommended for rehabilitation

Safety

All adverse events (AEs) will be documented and evaluated as part of the risk management for the device

STATISTICAL CONSIDERATIONS AND ANALYSIS

Sample Size Justification

The rationale for the sample size is based on obtaining exact 95% confidence intervals for the activity movements which achieved 80% success. When the sample size is 20, a one-sided 95.0% confidence interval for a single proportion using the large sample normal approximation will extend at most 0.18 from the observed proportion.

Subject Accountability

A CONSORT flow diagram will be presented that will include the number of subjects screened and reasons for screening failures; the number of subjects, who were enrolled, as well as the reasons for all enrollment discontinuations grouped by major reason; A list of discontinued subjects, protocol deviations, and subjects excluded from the analyses.

Data Analysis

Descriptive statistics and summary tables will be provided giving sample size, absolute and relative frequency of categorical variables and sample size, arithmetic mean, standard deviation, median, minimum and maximum, percentiles and 95% CI (Confidence Interval) for means of continuous variables. All measured variables and derived parameters will be listed individually and, if appropriate, tabulated by descriptive statistics.

Study Hypothesis – Primary Endpoint:

The number and percentage of neck movements which achieve a success rate of at least 80% will be tabulated. Exact 95% binomial confidence intervals will be calculated for the rate of neck movements which achieve 80% success.

Safety - Secondary Endpoint

Adverse events will be coded according to coding dictionaries (MedDRA version 13.1 or higher) and presented in tables by system organ class, preferred term. The number and percentage of subjects who experienced any adverse events will be tabulated.

ADVERSE EVENTS

In this study, Serious Adverse Experience (SAE) is to be reported by the investigator within 24h to the IRB. The “Adverse Experience” CRF should be filled in all events of SAE and in other cases of Adverse Experience (AE) which, in the judgment of the investigator, affect this protocol.

Anticipated Side Effects

In this study, we are not anticipating any side effects.

Anticipated Adverse Effects/Risks

The movements not expected to cause any pain or discomfort.

MISCELLANEOUS

Ethical Considerations

Prior to study initiation the site shall obtain an Institutional Review Board (IRB)/Helsinki approval of the study. Any changes in the study protocol, informed consent forms, or investigator must be re-approved by the IRB and the approval documented. All subjects enrolled in the study will provide their consent prior to entering the study. An informed consent form shall be signed by the subject. The investigator will retain the forms as part of the study records.

This study will be performed in accordance with the Declaration of Helsinki, in agreement with the guidelines for conducting a clinical investigation in accordance with the principles of ICH GCP outlined in the E6 document and IRB guidelines. By signing the present protocol, participants in the study commit themselves to carry it out in accordance with local legal requirements

Protocol Amendments

Possible with IRB approval.

Study Monitoring

Study monitoring visits include a pre-study site evaluation and site initiation visit, periodic monitoring visits during the course of the investigation, and a final termination visit at the conclusion of the study. The frequency of the monitoring visits will vary depending on the subject enrollment rate, the quantity and quality of data collection.

Study Documentation

Study documents include protocol and MOH documents, approvals, insurance, signed ICFs, copy of CRFs, training materials, SAE reports, investigator site file

Case Report Forms (CRFs)

Case Report Forms will be established to collect the required demographic and clinical information, as described by this protocol and the variables to be analyzed. Case Report Forms will be completed by the investigator or a designee who will be properly trained on study procedures and data recording requirements. The investigator will maintain a separate enrollment log with the corresponding subject name, initials and subject code. All CRFs will have 1 original clearly filled with a ball point pen. Any changes, amendments or additions to the forms will have to be marked though with a single line, dated, and initialed. The investigators will maintain a copy of the CRFs.

Study Termination

If the Principal Investigator determines that the conditions do not allow the continuation of the study, then it will be terminated. Among the conditions that may justify the study termination without limitation are the followings:

- Subject safety
- Inability to enroll subjects at acceptable rate
- Insufficient adherence to the protocol that could have a potential impact on the study outcomes

Maintenance and Retention of Records

The records will be kept at least two years after the study.

Use of Information and Publication

Specified in contract with the Investigators, research records will be available to study personnel, and the Institutional Review Board, where applicable. Research records may be used after removal of subject names or other identifying information as specified in the Informed Consent. Information collected in this study that was not previously published is considered confidential information and is the property of VRHealth.

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