A Virtual Reality based intervention for surgical patients: study protocol of a randomized controlled trial

Raluca Georgescu  
Babes-Bolyai University

Anca Dobrean (anca.dobrean@ubbcluj.ro)  
Babeș-Bolyai University  
https://orcid.org/0000-0001-8329-0063

Cristina Alina Silaghi  
Iuliu Hatiganu University of Medicine and Pharmacy Cluj-Napoca

Horațiu Silaghi  
Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca

Study protocol

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Abstract

Background: Pain after surgery is normal, and treatments, including both pharmacological and psychological components, are fundamental for a proper postoperative care. While several trials have investigated the analgesia analgesic effect of traditional non-pharmacological treatments, such as Cognitive Behaviors Therapies, the newer ways of delivering psychological interventions for pain after surgery are scarcely investigated. The aim of this randomized controlled trial (RCT) is to determine if delivering the psychological content through Virtual Reality (VR) along with the standard pharmacological treatment return better pain relief outcomes than standard care in adults patients following surgery. Methods: This is a protocol of a parallel RCT conducted in one community hospital. In order to test the efficacy of VR environments for reducing pain intensity, in the following day after surgery, adults (18 to 65 years) will be randomly assigned to either (1) standard treatment after surgery (control group) or (2) VR based intervention along with standard treatment. It is intended that a minimum of 27 patients be recruited in each group. For estimating the intensity of pain, both self-report and physiological measures will be used. Repeated measures of pain outcomes will be taken before and after the intervention. Moreover, for allowing an in-depth investigation on of the effect of VR environments, the primary outcome will be complemented with measures of the adverse effects, level of immersion, and level of presence in the VR environment. Keywords: pain; postsurgical pain; virtual reality; psychological interventions; VR-based interventions; Trial registration status: ClinicalTrials, NCT03776344. Retrospectively registered in December 14, 2018, https://clinicaltrials.gov/ct2/show/NCT03776344.

Background

As defined by the International Association for the Study of Pain (IASP), pain is an unpleasant sensory and an emotional experience associated with actual or potential tissue damage or described in terms of such damage (1). Often, acute pain results from trauma or surgery and represents a warning to the brain that noxious stimuli are present or that tissue is continually affected (2). Whereas acute symptoms of pain decrease after cessation of painful stimuli, chronic pain remains beyond the helpful duration of pain signals and often continues despite treatment of initial tissue damage (1). According to one report (3) using data from National Health Interview Survey (NHIS) Sample Adult Core and the NHIS Adult Functioning and Disability Supplement pinpointed that in the year of 2012, 86.6 million US adults reported having pain in some days in the last three months while 25.5 million reported having chronic (daily) pain. Similarly, a subsequent analysis conducted on 300 post-surgical patients (4) relived that up to 85% of people experienced acute postoperative pain and pain severity was rated as moderate, severe or extreme in 75% of those cases. Besides, postoperative pain was associated with prolonged hospitalization (5), alveolar ventilation, tachycardia, insomnia, flawed wound healing (6), as well as with an increased risk of chronic post-surgery pain (CPSP) (7). Described as the pain which persists beyond the expected recovery time after a surgical procedure (8), CPSP is reported in 10% to 70% of cases depending on the type of surgery (7,9,10), and several biological and psychological factors (11,12).
Although in the last years, pain management gained a lot of attention in both research and practice areas with enormous gains, the management of postoperative pain remains a tremendous challenge with high costs for patients and health care providers (4).

Currently, evidence-based treatments including pharmacological and psychological, are promoted by the clinical practice guidelines of postoperative management (5). The majority of non-pharmacological strategies for postoperative care are interventions based on Cognitive Behavioral Therapy (CBT) which prove their efficacy in decreasing pain and distress in different surgical settings, such as lumbar spinal fusion (6,7), abdominal surgery (8), cardiac surgery (9) or orthopedic surgeries (10). Results of a recent meta-analysis (11) which estimate the efficacy of psychological interventions on postoperative pain management after orthopedic surgery, showed a small to medium effect size ($g = 0.26$) of these interventions in decreasing pain intensity, a medium effect in improving recovery ($g = 0.38$), and no significant improvements on the frequency of the analgesic used. These results were also evidenced in primary studies estimating the efficacy of psychological interventions (12–15).

However, face to face CBT interventions were associated with several threats regarding their applicability on a large scale. Specifically, one of the biggest challenges of non-pharmacological treatments for being implemented on large scales is to synchronize the hospitalization time and patients’ availability as some of these interventions are designed to be conducted in pre-surgical settings. In addition, other interventions were designed to be conducted in several sessions in order to be effective, and often patients did not have this amount of time during their hospitalization. In consequence, most of the CBT interventions are applied in the management of chronic pain while the treatment of acute pain remains mainly pharmacological (16). The consequences of treating pain mainly through pharmacological options are the array of side effects derived from opioids consumptions such as vomiting, nausea, respiratory depression and physical dependence (7,8) which increase the costs of pain care and places pain medicine in a peerless crisis (9).

One potential approach for increasing the applicability of CBT in cases of acute pain during short hospitalization could be to develop shorter protocols, respectively to deliver the psychological content through technology, such as virtual reality (VR). The VR technology already proved his effectiveness in case of adults in other hospital settings, such as burn units (17–19) or cancer units (20–23) and is currently under evaluation for pain relief during venipuncture in pediatric patients (24).

By using a combination of technologies (i.e., head-mounted display-HMD, vibro-tactile gloves, individualized sounds, and gesture-sensing joysticks) VR environments create immersive (25) and multi-sensorial experiences (26). Immersion in the virtual world is believed to facilitates the shifting of attention away from the painful stimuli or from the experience of pain, to more engaging or enjoyable stimuli, developing effective distraction strategies and reshaping the pain perception (27,28). A recent meta-analysis (29) estimating the efficacy of VR interventions for acute pain management in clinical settings found a medium effect size of these interventions (SMD $= -0.49$, 95% CI $-0.83$ to $-0.14$). A subsequent meta-analysis (30) relying on 27 randomized controlled trials (RCT) conducted in hospital settings,
showed significant effects of VR-based interventions in reducing pain intensity during medical procedures \((g = 0.95, 95\% \text{ CI} 0.32 \text{ to } 1.57)\) and after the medical procedures \((g = 0.87, 95\% \text{ CI} 0.54 \text{ to } 1.21)\). Moreover, based on a smaller number of studies, comparable results were founded when interventions aimed to reduce the cognitive \((g = 0.82, 95\% \text{ CI} 0.39 \text{ to } 1.26)\) or affective components of pain \((g = 0.55, 95\% \text{ CI} 0.34 \text{ to } 0.77)\). However, although these are reassuring results in using VR in acute procedural pain management none of the analyses includes studies on post-surgical patients and even though VR technology could be effectively exported in medical care settings \((29)\) as a potentially cost-effective tool \((31)\) to date in postoperative care only few studies examined his efficacy. In this sense, one study conducted by Mosso-Vazquez and colleagues \((32)\) found that 30 minutes of VR exposure can reduce pain intensity after cardiac surgery regardless if the pain relief was self-reported or assessed through physiological measurements \((\text{i.e.}, \text{breathing rate, arterial pressure, and heart rate})\). One subsequent study of Mosso-Vazquez and colleagues \((33)\) comparing two different VR devices \((\text{i.e.}, \text{HMD and mobile VR})\) for pain relief during ambulatory surgery revealed that both technologies decreased pain intensity, with better outcomes for VR environments delivered through HMD. This result is consistent with other results proving that high-quality VR environments create a better distractor from pain \((34)\) although the estimates was not in postoperative settings. Although these studies conducted by the Mosso-Vazquez and colleagues \((32,33)\) had positive and clinically significant results, highlighting the potential usefulness of VR in the postoperative pain management, these studies were uncontrolled leading to possible overestimation of the VR efficacy. Consequently, as far as we know, there are no studies testing the effectiveness of VR for postoperative pain following surgery under general anesthesia in a randomized clinical manner. In addition, the VR contents used in previous studies were intended only to distract patients from pain. Using environments that promote relaxation stimuli rather than distraction stimuli can be particularly useful because a relaxed state of mind was associated with a reduced demand of tissues oxygen and a reduced level of lactic acid, both being harbingers of a decreased level of pain \((35)\). In addition, relaxation was associated with an increased level of endorphins, lower levels of anxiety and skeletal muscle tension.

Consequently, we propose a confirmative, randomized controlled trial, in order to assess the effectiveness of relaxing VR environments for pain relief at patients in the first days after surgery.

**Objectives**

The aim of this study is to assess whether exposure to VR environments is associated with decreased levels of pain after surgery after varicose veins, hernia repair or gallbladder surgeries. Surgeries of varicose veins, hernia repair, and gallbladder, were aggregated due to similarities across (1) the incidence rate \((36–38)\); (2) levels of pain intensity after surgery \((39–41)\); and (3) odds of acute pain to be translated into CPSP \((39–41)\). We hypothesize that VR based intervention will have a better result in decreasing pain when it is used as a complementary treatment of standard care compared with the standard care alone. Additionally, we will assess the safety of VR based intervention in patients after surgery.

**Methods And Analysis**
Study design

This study is a prospective, randomized controlled trial with two parallel groups. After randomization, participants will receive either (1) standard care after surgery (control group) or (2) VR based intervention along with standard care for testing the superiority of the intervention delivered through VR environments for reducing postoperative pain.

The study protocol follows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) (42) instructions and received the ethical approval from the Babes-Bolyai University committee as from the committee of Municipal Hospital of Cluj-Napoca and is retrospectively registered on ClinicalTrials.gov (NCT03776344).

Study sample size

Using G*Power 3.1.9.2 (43), we estimated a minimum of 54 participants (27 in each group) needed to detect an effect size of 0.80, with \( \alpha = 0.05 \) and power =0.80. The expected effect size of 0.80 was chosen in the light of the results found by the most recent meta-analyses (29,30), being a conservative effect size given that in their analysis Chan and colleagues (29) found a medium effect size (SMD= -0.49, 95% CI -0.83 to -0.14) and the analysis of Georgescu and colleagues (30) a large effect size was found (g=1.08, 95% CI 0.46 to 1.70) for studies with parallel design aiming to decrease pain at hospitalized patients. However, we expect to have some incomplete or unusable data, especially on the physiological measure, therefore, we aim to recruit 30 participants in each group.

Participants

All the participants are recruited from one community hospital from Romania. Starting October 2018, each patient admitted to the hospital for surgery is screened for eligibility criteria to this trial.

Inclusion/exclusion criteria

The below criteria should be cumulative met in order that a participant be included in the trial.

Inclusion criteria:

- Adults aged 18-65 years, after surgery of varicose veins, hernia repair or gallbladder surgery.
- Patient in the acute care units, 1-3 days following surgery.
- Willing and able to provide informed consent and participate in the study visit and study follow-up questionnaire.

Presence of any criteria listed below will conduct at the exclusion of the participant from the trial.

Exclusion criteria:

- Patients with neoplastic pathologies.
Patients with a history of motion sickness.

Patients with severe visual impairment (i.e. not able to clearly see without glasses; patients with contact lenses will not be excluded).

Patients with severe/profound cognitive impairments measured with Six-item Cognitive Impairment Test (6CIT).

Use of strong opioids (i.e. morphine)

Other reasons for exclusion (Non-Romanian speaking patients, patients with severe psychological problems, etc.)

Randomization and blinding

Randomization is conducted within the type of surgery using a random number generator, with an equal number of participants in the control and experimental group. An independent researcher conducted the randomization sequence and the allocation sequence is stored on a secured computer until the participants are assigned to one of the interventions. For ensuring blindness of medical personnel and participants through the entire procedure every participant is invited in a separate room - the treatment room - where only the research assistant conducting this phase of the study is allowed. In the treatment room those from the experimental group will be exposed to the VR content and psychological along physiological measures will be taken, while those from the control group psychological and physiological measures will be taken without exposure to the VR content. After this, each participant will be conducted to their hospital room. In this manner the participants from the control and experimental group will not be mixed and the entire procedure is secured. In the case that a participant explicitly requests to end the study procedure for any reasons, the procedure will be stopped and will be counted as a dropout. Those patients, who ask to end the procedure earlier, will be asked to respond at a short interview to quantify the reasons.

Recruitment procedure and interventions

The process of recruitment and data collection is presented in Figure 1. The day following the surgical procedure, all patients from the acute care unit who meet the primary criteria for inclusion (i.e., age, type of surgery, type of opioids used, free of visual impairments, able to fluently speak in Romanian and without recorded psychological problems) are invited to participate. Information regarding duration, procedure, implications, and conditions for withdrawing are presented and explained. Those who are interested and sign the informed consent are invited in the treatment room where they complete the Six-item Cognitive Impairment Test for assessing the eligibility regarding executive functions. Subsequently, patients are randomly allocated to one of the two groups:

a) Treatment group: VR based intervention

Patients allocated to the VR based intervention will follow the standard protocol after surgery as prescribed by the current medical personnel and are exposed for 15 minutes to an interactive virtual
environment (i.e., Nature Treks® VR). This application is a commercially available app from the Oculus store (available at https://www.oculus.com/experiences/go/1723271804396968/), promoting relaxation through fifteen highly immersive environments. Every environment recreates a different natural scene (e.g., a tropical beach, savannas at sunset, snowy forests) which can be explored by the patients through a controller. Concomitant with the activities (e.g., walking on the beach, climbing the mountains) environmental effects are changing smoothly to create a vivid experience. Additionally, in some environments (i.e., deep blue and black beginning), patients can freely explore the scenes in 360 degrees for enhancing the feeling of presence and immersion.

As previous studies testing the efficacy of the analgesic effect of VR (34) showed that better immersion is associated with lower scores for pain intensity, the device used is an Oculus Rift® (available at https://www.oculus.com/). This device is the premium device from Oculus, equipped with a highly immersive headset, one controller, and integrated headphones.

Five minutes before and during the VR exposures, the fluctuations of skin conductance are measured for all patients. Before and after the intervention, pain intensity, relaxation, and VR adverse effects are recorded. Additionally, the catastrophizing level, anxiety, and depression related to health and presence in the VR environment are measured.

b) Control group: standard of care intervention

Patients allocated to the standard of care group follows the treatment after surgery as prescribed by current medical personnel. They are also following the same protocol as the patients in the intervention group regarding psychological and physiological measures. Specifically, they will be conducted in the treatment room, will be asked to indicate the non-dominant hand and the equipment for measuring SC will be setted up. After that, the SC will be measured continuously for 20 minutes without to be exposed to the VR environments. At the end, they will complete de psychological measures and will be conducted in their hospital room.

Data collection procedure

Figure 2 offers an overview of the process of the data collection and measures. All psychological and physiological measures will be collected by a previously trained researcher. The level of pain intensity and relaxation will be collected before and after the exposure to VR environments in the experimental group and before and after the measurement of skin conductance (SC) in the control group. The SC will be measured during the exposure to VR content in the experimental group and for a period of 15 minutes in the control group. For ensuring an accurate baseline for the physiological measure and for controlling the individual differences in SC, the signal of SC for each participant will be taken before the study procedure start for five minutes. During this time, participants will have no other instructions, and the communication will be maintained at the minimum level. The amount of analgesic consumption for each
participant will be extracted from the medical records. Excepting for the fluctuations of skin conductance, all measures will be collected through an online platform.

Outcomes

The present study assesses the efficacy of a Nature Track® VR to decrease pain intensity in surgical patients. The primary outcome will be pain intensity measured right before the exposure to the VR content and after. The secondary outcomes will measure the effects of the application on relaxation and the amount of time spent thinking about pain. Also, to allow for an in-depth investigation on the effect of VR environments, the primary outcome will be complemented with measures of the adverse effects, level of immersion and level of presence in the VR.

Measures

Primary measures

Pain

The pain intensity will be measured using the Numerical Rating Scale (NRS) (44) by asking participants to report their intensity before and after the intervention on a scale from 0 (“no pain”) to 10 (“extremely painful”). To help patients to discriminate between different pain levels, we will ask them to report the mean level of pain intensity in the last 24 hours, the peak of intensity in the same period and the intensity right before the intervention. We chose NRS for this study rather than other measures more extensively used, such as Visual Analog Scales (VAS), due to the consensus of the better psychometrics properties (45–48). The value of pain right before the intervention will be used in the analysis of VR effectiveness.

Concomitantly, as a physiological indicator of postoperative pain we will measure the fluctuations of the SC (49–51). The SC will be measured using the BIOPAC MP150 system (52). The two finger electrodes were attached to the first phalange of the index and medius fingers from the non-dominant hand with Velcro straps. The electrodes were connected to the computer using the USB connection input. In order to ensure good contact with the skin, isotonic gel was added to the electrodes prior to attaching to the fingers. At the beginning, participants were allowed to relax, get ready and comfortable with the experimental structure in a variable time (i.e., five minutes). In this time participants were invited to find a comfortable position for both hands, which they were instructed not to move for the duration of the recording.

Secondary measures

Relaxation

As the level of relaxation could affect the perception of the pain intensity, the state of relaxation will be measured using the NRS from 0 (“extremely stressed” to 10 (“relaxed”) before and after the
intervention. We chose to measure through an NRS rather than other scale designed to measure relaxation due to his factual effect and similarities with the pain intensity measures.

*Time spent thinking about pain*

Another factor which can contribute to an increased perception of pain intensity is the time spent thinking about pain (53). Consequently, we will ask patients to report after the interventions, on NRS from 0 (“not at all”) to 10 (“all the time”), the amount of time they spent thinking about their pain during the exposure to the VR content in the experimental group and during the measuring of SC conductance in the control group.

*Adverse effects*

Potential adverse effects will be evaluated using the Simulator Sickness Questionnaire (SSQ) (54). As some of the unintended effects of VR could also be effects of the opioid's consumptions (e.g., headaches, nausea), we will ask participants to complete the scale twice, before and after the exposure of VR. The SSQ was previously validated and proved robust psychometrics properties (54,55) being the most widely measure of cyber-sickness. The patients will be instructed to answer on a 4-point Likert scale, corresponding to not at all, slight, moderate and strong sensations regarding the occurrence of possible side effects such as general discomfort, fatigue, headache, and dizziness.

*Treatment satisfaction and presence*

The presence in VR was assessed using Igroup presence questionnaire (IPQ, available at [http://www.igroup.org/projects/ipq/](http://www.igroup.org/projects/ipq/)). This is a 14 items questionnaire assessing different aspects of presence and immersion into VR world through items such as: “In the computer generated world I had a sense of "being there" or “How aware were you of the real world surrounding while navigating in the virtual world? (i.e. sounds, room temperature, other people, etc.)?”. In the end, once the IPQ completed, the patients will be instructed to answer an additional question (i.e., Are you willing to use VR systems in the future?) with dichotomous response developed by the authors for assessing the willingness for further sessions with VR system.

*Covariates and measures for baseline imbalances*

*Opioids used*

The amount of analgesic used will be extracted from the medical records and will be used as a covariate in the estimation of the intervention effect. The usage of opioids will be coded as present and absent. The mean drug metabolism time will be calculated in order to determine if an opioid agent is active, coding 1 if the opioid agent is active and 0 if is out of his action range.

*Pain catastrophizing*
Level of catastrophizing will be measured through the Pain Catastrophizing Scale (PCS) (56). This scale is a self-report measure with 13 items structured in three subscales, namely rumination, magnification, and helplessness, and proved good psychometrics properties. Patients will be instructed to answer on a scale from 0 (“not at all”) to 4 (“all the time”).

Assessment of mood

Anxiety and depression levels will be assessed through the Hospital Anxiety and Depression Scale (HADS)(57). This scale is a self-report measure with 14 items, with half of the items measuring anxiety symptoms (e.g., items targeting tension, panic attacks) and the other half measuring depression symptoms (e.g., items targeting anhedonia or inability to enjoy things or experiences). Responses are recorded on a scale from 0 to 3, and each item has a different response in accordance with the item content.

Cognitive abilities

Cognitive abilities were measured though the Six-item Cognitive Impairment Test (6CIT) (58), a screening tool for measuring the global cognitive status. The items of the 6CIT cover six questions; one assessing the memory (remembering a 5-item name and address), two items including calculation (reciting numbers backward from 20 to 1 and months of the year backward) and three items assessing orientation (year, month, and time of day). The cutoff of seven from the total score was used for excluding patients with low cognitive abilities (59).

Statistical analysis

Preliminary analyses and preprocessing data of skin conductance

Demographic characteristics and psychological measures will be explored for missing data, and distribution abnormalities. Means and standard deviations will be used to characterize the sample. Baseline imbalances between groups regarding continuous variables (i.e., age, level of pain catastrophizing, anxiety and depression related to health problems) will explored using t-test statistics, and gender respectively the opioids usage using \( \chi^2 \) test. Preprocessing of skin conductance measure will performed using AcqKnowledge 4.1 first though the visual inspection of the raw signal, and then applying the Smoothing function with a smoothing factor of three samples. This function has the same effect as the low pass filter by replacing the high-frequency signal with the mean values across three milliseconds in order to subtract the artifacts, without changing the waves form.

Main analyses

Behavioral data will analyzed using SPSS 20 (IBM Corporation, Armonk, NY) in accordance with the intent to treat principal (Gupta, 2011). Physiological data will be processed using the AcqKnowledge 4.1 software, and for each patient, a difference score in the area under the curve between the last five minutes of measurement and baseline level of SC was extracted. In order to account the changes in pain
intensity and relaxation scores, separate repeated measure analysis of variance (RM-ANOVA) will be employed. The effect size of intervention will be estimated by computing a d value using the means and standard deviations (SD) of the control and treatment group. A value of d less than .20 will be considered small, medium when d ≤ .50 and large when d ≥ .80. For clinical significance purposes, we will code for each patient the percentages of dropping in pain score, coding with 1 all pre-post differences above 30% on NPRS and 0 differences below this threshold. Subsequently, χ² test will be employed to determine if are significant differences across the two groups. To estimate differences in time spent thinking about pain, treatment satisfaction, and adverse effects of VR intervention, t-test statistics will be used. Pearson correlation will be employed to examine the relationship between the level of skin conductance and pain intensity (as a difference score between pre-post intervention). A P-value will be used to estimate statistical significance for all analyses.

**Discussion**

Treating pain after surgical interventions is a very complex and challenging process (61,62), and the integration of non-pharmacological approaches has been one of the priorities of healthcare reform in the last years (5). Additional interventions along the standard pharmacological treatments are strongly recommended by the guidelines for postoperative pain management (5). Limited medical personnel resources and short periods of hospitalization are widely known problems of the postoperative management, highlighting the need for additional interventions that are requiring very little set-up time to co-occur with the standard pharmacological treatment. Addressing these problems, VR interventions can be used as a non-pharmacological tool for reducing pain after surgery. The present protocol offers a detailed description of a randomized and controlled clinical trial to determine the effectiveness of VR environments in reducing pain intensity in surgical patients.

Should the hypotheses suggested in this study be proven, this would add empirical evidence about the benefits and feasibility of VR for the pain treatment in surgical patients. Our expectation is to obtain greater pain relief compared with studies employing non-technological interventions. Moreover, we expect that the results of the present study to be in line with the ones conducted by Mosso-Vazquez and colleagues (32) as well with studies that use VR for non-surgical patients (29,30). In addition, we expect to find minimal side effects in those patients exposed to VR and the level of willingness to use VR sessions in the future treatment of pain to be high.

However, the present protocol is exposed to several threats. First, by recruiting participants from a single hospital is possible to affect the external validity of the study. Will be unknown if the characteristics of our participants will be representative for a broader population of surgical pain sufferers. Moreover, our results cannot be extrapolated to other VR environments, being strictly linked to Nature TreksVR®. Second, although we take the measures for ensuring blinding of participants is possible that in some cases the participants guess the treatment arm. Therefore, the planned study is single-blinded only. In some therapeutical areas, sham or placebo intervention is not always feasible. In this study, patients cannot be completely blinded to the actions of the study intervention. Nonetheless, the assessors and
researchers conducting data analysis will be blinded in order to improve the internal validity of the study and maintain a low detection bias (63). Not lastly, our results will be subtracted in the absence of other non-pharmacological treatment, thus, in the case of hypothesis confirmation we can conclude that the Nature TreksVR® produce significant reductions in pain intensity but we cannot know the effects when other non-pharmacological interventions are applied or when VR-based interventions are integrated in more comprehensive treatments of pain intensity.

Concluding, although several threats exist, this study is to our knowledge, the first to test the efficacy of a modern, market-ready VR application for the treatment of pain after surgery, and his results will assist in the development of a new method for the delivery of evidence-based treatments.

Data storage

During data collection, all the data will be safely stored at the Municipal Hospital. After the implementation phase is completed, all the data will be transferred in a secured PC at the International Institute of Psychotherapy, accessible only by the principal investigator (RG) and the corresponding author (AD).

Dissemination

Following the recommendations of the Consolidated Standards of Reporting Trials (CONSORT) (60) statement for reporting RCTs, results will be submitted to peer-reviewed journals and presented as oral or poster presentation at international scientific conferences. Additionally, we will make available all the results to patients if required. After the results are published in a peer-review journal, all the materials used will be made public at request.

Trial status

This trial is currently continuing to recruit participants and collect data. The cessation of participant recruitment is planned for July 31, 2019, but is likely to continue to the end of September 2019. This manuscript is written based on protocol version 1.2 (March 23, 2020).

Abbreviations

RCT: randomized controlled trial

VR: Virtual reality

IASP: International Association for the Study of Pain

CPSP: chronic post-surgery pain

CBT: Cognitive Behavioral Therapy
HMD: head-mounted display

SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials

SC: Skin Conductance

NRS: Numerical Rating Scale

VAS: Visual Analog Scales

SSQ: Simulator Sickness Questionnaire

SEQ: Suitability Evaluation Questionnaire

PCS: Pain Catastrophizing Scale

HADS: Hospital Anxiety and Depression Scale

6CIT: Six-item Cognitive Impairment Test

Declarations

Ethics approval and consent to participate

The trial has been reviewed and given a favorable opinion by the Babeș-Bolyai Committee (ref. number 7150/03/05/2018). In order to be included in the study, every participant should complete and sign the study consent form. The supplementary information contains the consent form.

Consent for publication Not Applicable

Availability of data and material Not Applicable

Competing interests. The authors declare that they have no competing interests. All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf (available upon request from the corresponding author) and have nothing to disclose.

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Authors' contributions (with author initials): Conceptualization (RG,AD); Writing - original draft (RG); Writing - reviews & editing (AD, HS, AS). All the authors have reviewed the present version of the manuscript and approved it for submission. No conflicts of interest have been disclosed for any of the authors.
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Figures
Assessed for eligibility patients aged 18-65 years of age referred to the surgical department of the hospital (n=x)

Enrollment

Excluded (n=x)
- Not meeting inclusion criteria (n=x)
- Declined to participate (n=x)
- Other reasons (n=x)

Randomized (n=x)

Allocation

Allocated to VR based intervention
- Received allocated intervention (n=x)
- Did not receive allocated intervention (give reasons) (n=x)

Allocated to standard as care intervention
- Received allocated intervention (n=x)
- Did not receive allocated intervention (give reasons) (n=x)

Follow-Up

Post intervention evaluation (n=x)
Discontinued intervention (give reasons) (n=x)

Post intervention evaluation (n=x)
Discontinued intervention (give reasons) (n=x)

Analysis

Analysed (n=x)
- Excluded from analysis (give reasons) (n=x)

Analysed (n=x)
- Excluded from analysis (give reasons) (n=x)

Figure 1

Flowchart of the study based on the Consolidated Standards for Reporting of Trials
### Figure 2

Overview of the enrollment, intervention and assessment measures.

#### Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- completedSPIRITchecklist.docx