STUDY PROTOCOL

Evaluation of Virtual Reality Intervention after Pediatric Idiopathic Scoliosis Surgery to Reduce Postoperative Pain and Opioid Consumption

NCT number NCT04584970
Document Date 05/17/2020

PROTOCOL TEMPLATE: INTERVENTIONAL STUDY

Complete Title: Evaluation of Virtual Reality Intervention after Pediatric Idiopathic Scoliosis Surgery to Reduce Postoperative Pain and Opioid Consumption

Short Title: Virtual Reality after Pediatric Scoliosis Surgery (VRAS-PS)

Drug or Device Name(s): Applied VR

Sponsor: University of North Carolina Hospitals

Protocol Date: April 20, 2020

Amendment 1 Date: May 17, 2020
Amendment 2 Date:
Amendment 3 Date:
Amendment 4 Date:

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PROTOCOL TITLE: Evaluation of Virtual Reality Intervention after Pediatric Idiopathic Scoliosis Surgery to Reduce Postoperative Pain and Opioid Consumption

SHORT TITLE: Virtual Reality after Pediatric Scoliosis Surgery

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Protocol Version: 1.1
Version Date: May 17, 2020

I confirm that I have read this protocol and understand it.

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Date: May 17, 2020

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ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
E-consent	**Electronic consent**
ERAS	**Enhanced Recovery After Surgery**
FLACC	**Face, Legs, Arms, Cry and Consolability**
PACU	**Post anesthesia care unit**
PCA	**Patient controlled analgesia**
PHBQ-AS	**Post Hospitalization Behavior Questionnaire for Ambulatory Surgery**
POD	**Postoperative day**
STAI	**State-Trait Anxiety Inventory**
VR	**Virtual reality**

PROTOCOL SYNOPSIS

Study Title	Evaluation of Virtual Reality Intervention after Pediatric Idiopathic Scoliosis Surgery to Reduce Postoperative Pain and Opioid Consumption
Funder	UNC Department of Anesthesiology Research Department
Clinical Phase	N/A
Study Rationale	• Pain is common after surgery, and can be influenced by many factors, including anxiety • Distraction methods are commonly used with pediatric patients at UNC including the use of iPads postoperatively • Studies have shown that pain, anxiety and patient satisfaction are improved with the use of distraction • Studies have compared these standard distraction methods to the use of virtual reality and have shown that VR is an effective way to reduce anxiety, decrease pain, and improve patient satisfaction • The majority of these studies have been done either during minor procedures or preoperatively as an introduction to the patient experience • Little has been done to study VR in the postoperative period, particularly on the first postoperative day • Scoliosis surgery is a common pediatric procedure that can be associated with significant postoperative pain
Study Objective(s)	Primary • To evaluate postoperative pain scores and postoperative opioid use in pediatric idiopathic scoliosis surgical patients using virtual reality as a method of immersive distraction compared with standard electronic use postoperatively. Secondary • To evaluate patient satisfaction with use of virtual reality as a method of distraction.
Device Description	The Applied VR is a lightweight mobile virtual reality headset with embedded software, creating an immersive experience. The Applied VR is specifically designed for medical use.
Study Design	Randomized controlled pilot study comparing virtual reality to standard electronic use (iPad) after idiopathic scoliosis surgery. Patients age 11-17 years old will be included and randomized to either the virtual reality or control (iPad) group. The randomization-and-concealment feature of REDCap data capture system will be utilized.

Subject eligibility will be verified by the research coordinator through chart review and patient questionnaire prior to enrollment in the study.

In the VR arm, VR devices will be used with pre-selected virtual reality program options. In the control arm, patients will be offered an iPad preloaded with a variety of games. Both groups of participants will also receive the postoperative standard of care including a PCA for pain control.

Preoperatively:

- Baseline anxiety score (STAI score) will be assessed
- Baseline pain scores will be obtained: FACES scale (patient reported) and FLACC score (measured by the trained research assistant)
- Baseline vitals will be measured
- Patients will be oriented to their respective devices

Intraoperatively:

- Must be on ERAS idiopathic scoliosis pathway at our institution

Postoperatively:

- Must be admitted to the general pediatric floor post-operatively (versus intensive care unit)
- On POD #1 in the morning, patients in both groups will be visited by the research assistant. Patients in the VR arm will be offered the VR device for up to 30 minutes, and patients in the control arm will be offered an iPad for up to 30 minutes
- Number of hours since anesthesia end will be recorded
- Pain scores (FACES scale by the patient, FLACC scores by the research assistant) will be recorded immediately prior to intervention (T=0) and at end of intervention (T=30); FLACC score by research assistant will also be recorded at 10 minute mark (T=10)
- PCA use (in mcg or mg as appropriate) for previous hour prior to intervention (T=-60-0), during intervention (T=0-30), and one hour after intervention is complete (T=30-90) will be recorded; PCA use will be converted to morphine equivalents at time of data entry
- Total number of minutes of electronic device use will be recorded. The electronic device will be applied for a total of 30 minutes maximum, after which time the session will end
- On POD #1 in the afternoon, research assistant will return for patients in both groups, for another session up to 30 minutes. Data for both groups will be recorded as above

	• If a patient declines to participate, the reason for declining will be asked for and recorded Post-intervention: • Patients and caregivers in the VR group will be given a survey regarding acceptance and effectiveness of the VR device in the postoperative period at approximately 48-72 hours • Patients and caregivers in both groups will be given a follow-up survey at approximately 48-72 hours and 7-10 days • Surveys will be conducted by phone, email or in person
Subject Population key criteria for Inclusion and Exclusion:	Inclusion Criteria 1. Subjects age 11 – 17 2. Patients undergoing idiopathic scoliosis surgery on ERAS spine protocol (which includes postoperative PCA) 3. No contraindication to using an iPad or VR device Exclusion Criteria 1. Patient/caregiver refusal 2. Patients with developmental delay 3. Patients with seizure disorder 4. Non-English-speaking patients 5. Patients with daily opioid use ≥ two weeks 6. Patients with uncorrected visual or hearing impairment 7. Patients admitted to pediatric intensive care unit on POD#1
Number of Subjects	At most 24 enrollees (goal 10 completed participants in each arm)
Study Duration	Each subject's participation will last ~120 minutes • Day of surgery: 30 minutes, which includes recruitment and consent, baseline anxiety and pain scores, and orientation • Postoperative (POD #1): 35 minute visits x 2, which include pain scores, 30 minutes of electronic device use, and PCA use data • Postoperative (approximately 48-72 hours and 7-10 days postoperatively): 10 minutes for each survey The anticipated duration of the study is 3-4 months
Study Phases	(1) Screening: screening for eligibility and obtaining consent (2) Intervention: study intervention and data collection (3) Follow up: post intervention surveys and data analysis
Efficacy Evaluations	To evaluate efficacy of VR for pain control, the following will be recorded: • Postoperative pain scores • Postoperative PCA usage surrounding intervention

	• Patient & caregiver satisfaction scores • Presence of dizziness/nausea • Time of discontinuation of VR if less than 30 minutes
Safety Evaluations	Safety and feasibility of VR in postsurgical populations has been proven in previous studies, some of which include specific spine surgery populations.
Statistical And Analytic Plan	Quantitative data analysis will be conducted under the supervision of the biostatistician, using SAS or R. *All* statistical estimates (e.g., means, medians, proportions, incidence rates, mean differences, correlations, etc.) will be tabulated along with corresponding confidence intervals (CIs). To avoid over-reliance on p-values, the magnitudes of estimates and the corresponding confidence intervals will be the primary focus of the analyses.
Data and Safety Monitoring Plan	The data collected during this study will be on hospital or School of Medicine computers with security features installed to protect the data. Data will be collected by a research assistant and will be monitored by members of the research study and other members of the Department of Anesthesiology research division. The Information Technology group within the Department of Anesthesiology provides secure data storage for the proposed study. Servers for the group are located in a locked office on the UNC campus. Study data on these servers is stored on SQL Server 2005s and backed up with nightly full backups. The web server is behind a firewall and only known and approved site users have access via ASP.NET forms authentication. This data management system meets or exceeds NIH security guidelines, safeguards participant data, and adheres to the Certificate of Confidentiality. Any adverse events will be collected in the data and reported to the PI and IRB as applicable. Based on the results, modifications in the postoperative management protocols at UNC will be considered as appropriate.

1 BACKGROUND AND RATIONALE

1.1 Introduction

Pain is a common complaint after surgery, and can be influenced by many factors, including anxiety. Distraction methods are commonly used with pediatric patients in the perioperative period to decrease patient and caregiver anxiety both before and during procedures. UNC and the Child Life team routinely use a variety of games and videos to assist in easing the pre- and postoperative experience for children and their families. Studies have shown that pain, anxiety and patient satisfaction are improved with the use of distraction methods as compared to treatment with medications alone. Studies have also compared these standard distraction methods to the use of virtual reality during minor procedures (dressing changes, IV lines, vaccines) and have shown that VR is an effective way to reduce anxiety, decrease pain, and improve patient satisfaction during these procedures. The majority of these studies have been done either during minor procedures or preoperatively as an introduction to the patient experience. In addition, studies show improvement in rehabilitation in certain populations. Little has been done to study VR in the postoperative period, particularly on the first postoperative day. Our group previously investigated VR use in the PACU following a broad range of pediatric surgeries last year, with favorable results. This study will focus on patients specifically undergoing pediatric scoliosis surgery, and will examine the use of VR on the first postoperative day. Scoliosis surgery is a common pediatric procedure that can be associated with significant postoperative pain. This study and data collection will be done at UNC Hospitals, including the Children's preoperative holding area and the Children's inpatient floors postoperatively.

1.2 Name and Description of Investigational Product or Intervention

The Applied VR is a lightweight mobile virtual reality headset with embedded software, creating an immersive experience. The Applied VR is specifically designed for medical use. Our group has received funding approval for a UNC Department of Anesthesiology grant to acquire 2 Applied VR units. (date of request 4/9/2020, date of approval 4/13/2020). These funds grant us the ability to purchase 2 AppliedVR devices which includes the 12 month research subscription plan – software license, tech support, training, Pico G2 4K hardware ($5000 total). We have successfully purchased these devices.

In comparison with the Oculus Go headsets used in our prior research study, the Applied VR carries several advantages including: lighter weight headsets; specific design for medical intervention with a HIPAA compliant platform; enhanced immersion including improved audio-visual synchronization, higher pixel count, 4K device (vs 3K device); improved infection control capability due to rubber straps instead of Velcro. Applied VR is manufactured by a leading virtual reality company that is defined as a wellness company; they have not achieved FDA approval given that they are considered as wellness devices. They have numerous studies demonstrating their software's impact on pain and anxiety. In addition, their headsets' more lightweight and comfortable design will be important in our pediatric patents.

In keeping with our group's accepted IRB application last year regarding postoperative virtual reality research, we plan to request a device determination from the IRB. We have determined that the device as used in this investigation meets the criteria for a non-significant risk (NSR) device.

1.3 Non-Clinical and Clinical Study Findings

By exploring non-pharmacologic methods of postoperative pain management in the form of virtual reality distraction, we hope to contribute to effective means of management for the common condition of postoperative pain. Postoperative risks associated with children are related to opioid administration and include over-sedation, respiratory depression, nausea and vomiting, and increased PACU stay. By providing a non-pharmacologic distraction method, we plan to minimize postoperative pain, opioid requirements, and lessen their possible adverse effects. As a result, children may receive fewer opioids, while benefiting from a positive hospital experience that is patient centered and age appropriate. There is a known small risk of motion sickness and nausea with the use of VR, but we believe that this risk will not be different in our study population, as evidenced by our previous VR study.

1.4 Relevant Literature and Data

Arane K, Behboudi A, Goldman RD. Virtual reality for pain and anxiety management in children. *Can Fam Physician*. 2017;63(12):932-934.

Eijlers R et al. Development of a virtual reality exposure tool as psychological preparation for elective pediatric day care surgery: Methodological approach for a randomized controlled trial. *JMIR Res Protoc*. 2017;6(9):e174.

Gold JI, Mahrer NE. Is virtual reality ready for prime time in the medical space? A randomized control trial of pediatric virtual reality for acute procedural pain management. *J Pediatr Psychol*. 2018;43(3):266-275.

Jenkins BN et al. Revisiting a common measure of child postoperative recovery: Development of the post hospitalization behavior questionnaire for ambulatory surgery (PHBQ-AS). *Paediatr Anaesth*. 2015;25(7):738-745.

Nilsson S et al. Assessing children's anxiety using the modified short state-trait anxiety inventory and talking mats: A pilot study. *Nursing Research and Practice*. 2012;932570.

Nilsson S et al. School-aged children's experiences of postoperative music medicine on pain, distress, and anxiety. *Paediatr Anaesth*. 2009;19(12):1184-90.

Parsons TD et al. Virtual reality in paediatric rehabilitation: A review. *Dev Neurorehabil*. 2009;12(4):224-38.

Piskorz J, Czub M. Effectiveness of a virtual reality intervention to minimize pediatric stress and pain intensity during venipuncture. *J Spec Pediatr Nurs*. 2018;23(1).

Ryu JH et al. Randomized clinical trial of immersive virtual reality tour of the operating theatre in children before anaesthesia. *Br J Surg.* 2017;104:1628–1633.

Won AS et al. Two virtual reality pilot studies for the treatment of pediatric CRPS. *Pain Med*. 2015;16(8):1644-7.

2 STUDY OBJECTIVES

The purpose of this study is to determine whether the use of virtual reality after pediatric idiopathic scoliosis surgery influences pain perception. We hypothesize that the use of virtual reality programs will provide superior distraction to standard electronic use and will result in improved pain scores and reduced opioid consumption after surgery.

2.1 Primary Objective

To evaluate postoperative pain scores and postoperative opioid use in pediatric idiopathic scoliosis surgical patients using virtual reality as a method of immersive distraction compared with standard electronic use (iPad) postoperatively.

2.2 Secondary Objective

To evaluate patient satisfaction with use of virtual reality as a method of distraction.

3 INVESTIGATIONAL PLAN

3.1 Study Design

This will be a randomized controlled pilot study comparing virtual reality to standard electronic use after pediatric idiopathic scoliosis surgery. Patients age 11-17 years old undergoing idiopathic scoliosis surgery will be included. Patients will be randomized to either the virtual reality or control (iPad) group. The randomization-and-concealment feature of REDCap data capture system will be utilized.

Subject eligibility will be verified by the research coordinator through chart review and patient questionnaire prior to enrollment in the study. The patients will be blinded to their study arm until they agree to be part of the study. Participants will be properly oriented to their respective device (VR or iPad) before surgery. While the use of VR may be new to the patients, VR is a very popular, trending and mainstream concept that is not likely to be unfamiliar to patients in the study age group. The patients will have the ability to stop using the VR device at any time if they choose.

Study phases are as follows:

Screening/Consent/Baseline: Randomization and consent will be obtained preoperatively. A baseline anxiety score will be assessed on a self-report form (STAI short form). Patients in the VR arm will be oriented to the VR device before surgery. All patients will be oriented to the Wong-Baker FACES pain scale. Baseline pain scores will be obtained through the following method: FACES scale (patient reported) and FLACC score (measured by the trained research assistant). Baseline vital signs will be measured and recorded. The STAI, FACES, and FLACC scoring tools have all been used and previously validated in the pediatric population.

Intervention/Treatment: On postoperative day (POD) #1 in the morning, patients in both groups will be visited by the research assistant. Standardized scripts will be utilized by the research assistant for the entirety of the data collection. Patients in the VR arm will be offered the VR device for up to 30 minutes. Patients in the control arm will be offered an iPad for up to 30 minutes. After a total of 30 minutes maximum, the session will end. Routine data will be collected on pain scores and PCA use as below for both groups. On POD #1 in the afternoon, a research assistant will return for patients in both

groups, for another session of the respective electronic device for up to 30 minutes. If a patient declines to participate, the reason for declining will be asked for and recorded.

In the control arm of the study, the iPad will have a variety of vetted and screened games available. The content on the iPads will include puzzles, games, and movies that have been previously vetted and approved by the Child Life team, separate from this study, and are currently used as standard of care at UNC. The Child Life team is an integral part of pediatric postoperative recovery at UNC.

In the VR arm of the study, there will be selected programs to choose from. All of the content will be pleasant games or exploring programs, avoiding unpleasant and fast-moving settings such as fighting or racing. All of the content will be age appropriate, vetted and screened by the research team for violence or otherwise stressing scenarios, content requiring rapid eye motion or head movement, and content requiring more body movement than what can comfortably be done in a sitting or reclined position.

Both iPads and VR devices are interactive (regardless of fingers versus head movement) and this type of movement difference should not confound results. Our study aims to assess whether the VR immersive experience provides superior distraction to the standard of care (iPad use), thus by nature of the study design we are studying the difference in the two distinct types of experiences. Finger versus head movement use is inherent to the types of distraction and central to the distinct experiences. Similarly, there will be different apps between VR and iPad platforms by nature of the differences in platforms. Our goal is to examine whether an immersive experience is more beneficial than an iPad-based experience, rather than examine specific styles of games.

There will be no restriction to personal electronic use. Both groups will have access to their personal devices (cell phones, iPads) as is the standard of care. The study iPad will only be offered at specific times as designated twice a day on POD#1 for participants in the control group. Outside of the study windows, participants will not be provided with hospital iPads. Personal electronic devices including iPads are acceptable, as is the standard of care for patients to bring whatever they see fit into the hospital.

There will be a variety of popular games and apps, deemed to be content- and age-appropriate by the Child Life specialists. Program offerings will not vary by specific age or gender; our study will only include ages 11-17 and per discussion with Child Life the programs do not need to be subdivided to remain appropriate within this age range.

Standard of care for both groups will include PCA use as ordered by the surgical team as well as routine Child Life visits. The Child Life team is an integral part of pediatric postoperative recovery at UNC.

The following will be recorded: Number of hours since anesthesia end. Pain scores including FACES scale by the patient and FLACC scores by the research assistant will be recorded immediately prior to intervention (T=0) and at end of intervention (T=30); FLACC score will also be recorded at the 10 minute mark (T=10). PCA use, in mcg or mg as appropriate, for the hour prior to intervention (T=-60-0), during intervention (T=0-30), and one hour after intervention is complete (T=30-90) will be recorded. Total number of minutes of electronic device use will be recorded. PCA use will be converted to morphine equivalents at time of data entry.

The anesthetic management of the patients will be left to the discretion of the anesthesia provider on the day of surgery but will follow the guiding principles of the pediatric spine ERAS protocol, which standardizes many aspects of anesthetic care including multimodal analgesia, fluid management, etc.

We are limiting our scope to POD#1 opioid usage. We do not hypothesize that VR use on POD#1 will affect opioid usage following hospital discharge.

Follow up: A follow up survey will be given using the Post Hospitalization Behavior Questionnaire for Ambulatory Surgery (PHBQ-AS) form at approximately 48-72 hours postop and 7-10 days postop via a phone call, email or in person from a member of the research team. The PHBQ-AS form is used to assess new onset behavior change associated with hospitalization, which has been documented in numerous studies. We believe that by assessing preoperative anxiety and preventing perioperative pain, which can lead to behavioral changes, the use of VR may decrease the chance of post hospitalization behavior change.

3.2 Allocation to Treatment Groups and Blinding (if applicable)

Patients will be randomized to one of two study arms. Each patient will have a private area preoperatively and postoperatively and no information about the other arm of the study will be disclosed, as to keep the study subjects blinded to the study. All study families and subjects will be consented/assented preoperatively, whether by phone in advance or in person on the morning of surgery. Patients will be blinded to the device upon consent for the study with the description of the use of an "electronic device" in the postoperative setting. This is deliberate, as to minimize any chance of bias. We feel that this is necessary due to the popularity and growing public interest in VR.

3.3 Study Duration, Enrollment and Number of Subjects

The anticipated duration of the study is 3-4 months, with total enrollment time of up to 13 days for each patient. This enrollment period includes: preoperative screening and consent, as well as the postoperative intervention and data collection (roughly 100 minutes); follow up survey 48-72 hours post op (roughly 10 minutes); and follow up survey 7-10 days postop (roughly 10 minutes). We plan to enroll at most 24 patients for this pilot study, with a final goal of 10 completed participants in each arm.

3.4 Study Population

Inclusion Criteria:

- Subjects age 11 – 17 years of age
- Patients undergoing idiopathic scoliosis surgery on ERAS spine protocol (which includes postoperative PCA)
- No contraindication to using an iPad or VR device

Exclusion Criteria:

- Patient/caregiver refusal
- Patients with developmental delay
- Patients with seizure disorder
- Non-English-speaking patients

- Patients with daily opioid use ≥ two weeks
- Patients with uncorrected visual or hearing impairment
- Patients admitted to pediatric intensive care unit on POD#1

4 STUDY PROCEDURES

4.1 Screening/Baseline Visit procedures

Baseline anxiety score will be assessed on a self-report form (STAI short form). The patients will be oriented to their study arm and to the VR device if assigned to that arm. The patient will be oriented to the Wong-Baker FACES pain scale. Baseline pain scores will be obtained through the following method: FACES scale (patient reported) and FLACC score (measured by the trained research assistant). Baseline vital signs will be measured and recorded in the preoperative area. All assessment modalities have been used and validated in the pediatric population.

4.2 Intervention/Treatment procedures (by visits)

There will be two intervention/treatment visits, both occurring on POD#1. On POD#1 in the morning, patients in both groups will be visited by the research assistant. Patients in the VR arm will be offered the VR device for up to 30 minutes. Patients in the control arm will be offered an iPad for up to 30 minutes. After a total of 30 minutes maximum, the session will end. Routine data will be collected on pain scores and PCA use as above for both groups. On POD #1 in the afternoon, a research assistant will return for patients in both groups. For participants in the intervention group, this VR session will be again offered for up to 30 minutes. Patients in the control arm will be offered an iPad for up to 30 minutes. If a patient declines to participate, the reason for declining will be asked for and recorded.

To evaluate efficacy, the following will be recorded:

- Primary outcomes:
    - Postoperative pain scores
    - Postoperative PCA opioid use surrounding intervention (morphine equivalents)

- Secondary outcomes:
    - Patient and caregiver satisfaction scores
    - Presence of dizziness/nausea
    - Time of discontinuation of VR if less than 30 minutes

4.3 Follow-up procedures (by visits)

There will be a follow-up survey using the PHBQ-AS form to assess new onset behavior change at approximately 48-72 hours postop and 7-10 days postop via a phone call from a member of the research team. These scores will be recorded and analyzed between both study groups.

4.4 Unscheduled visits

Not applicable

4.5 Concomitant Medication documentation

PCA opioid use surrounding intervention (morphine equivalents), at time intervals as detailed above, will be recorded. Any anti-nausea medication requested during the intervention will be recorded. Given that our study will take place on POD#1, perioperative medications given intra-operatively will not be included for analysis.

4.6 Rescue medication administration

Addressed in section 4.5

4.7 Subject Completion/ Withdrawal procedures

Patients and/or caregivers can withdraw from the study at any time for any reason, and this will be documented. Standard of care practices will not be influenced by inclusion, exclusion or withdrawal from the study. If patients are excluded from the study at any point, the reason(s) will be noted, and every effort will be made to replace that patient with another subject within the same subgroup. The goal is to have 10 patients in each arm complete the study. Study duration will be up to 13 days for each patient and will conclude following the second postoperative telephone survey or after postoperative day 13, whichever comes first.

4.8 Screen failure procedures

Patients that fail to be screened and considered for the study will not be included.

5 STUDY EVALUATIONS AND MEASUREMENTS

- Variables that will be abstracted from the medical charts:
  - Name, medical record number, phone number
  - Age (years), gender (male or female), race or ethnicity, weight (kg), BMI (kg/m2), heart rate (0-200 beats/min), and blood pressure (0-250/0-150 mmHg) pre-operatively
  - Surgery type, current medications
  - Pain scores, vital signs
  - Intraoperative record
- Baseline evaluation will include chart review, by phone or in person assessment for inclusion and exclusion criteria, vital sign assessment, study consent and orientation.
- Preoperatively, baseline vital signs will be obtained and recorded by nursing staff per UNC standard of care practices. Additionally, two pain scores will be assessed: FACES by the patient and FLACC by the research assistant.
- Postoperatively, pain scores including FACES scale by the patient and FLACC scores by the research assistant will be recorded immediately prior to intervention (T=0) and at end of intervention (T=30); FLACC score will also be recorded at the 10 minute mark (T=10). PCA use, in mcg or mg as appropriate, for the hour prior to intervention (T=-60-0), during intervention (T=0-30), and one hour after intervention is complete (T=30-90) will be recorded. Total number of minutes of electronic device use will be recorded. This data will be recorded by the research assistant.
- PCA use will be converted to morphine equivalents at time of data entry.

Descriptions of each questionnaire and scale, including total score computations:

Short State-Trait Anxiety Inventory (STAI) – 6 statements (i.e., 'I feel calm', with 1=Not at all, 2=Somewhat, 3=Moderately, 4=Very much). Scores 6-24, with 6 signifying no anxiety and 24 points signifying the highest level of anxiety. This short form of the STAI was used and validated in children aged 5-16 years (Schisler et al, 1998; Apell et al, 2011)

FACES (Wong-Baker) Pain Rating Scale – Self-assessment scale; patients select a face that illustrates the pain they are experiencing. Scores 0-10, with 0=No hurt and 10=Hurts worst (wongbakerfaces.org)

FLACC (Face, Legs, Activity, Cry, Consolability) – Observer assessment scale, with 5 categories (i.e., 'Face', with 0=No particular expression or smile, 1=Occasional grimace or frown, 2=Frequent to constant quivering chin, clenched jaw). Scores 0-2 in each category, for total scores 0-10, with 0=No observed pain and 10=Most observed pain

PHBQ-AS (Post Hospitalization Behavior Questionnaire for Ambulatory Surgery) – 11 items on a five-point scale (i.e., 1=Much less than before, 5=Much more than before). Total scores 11-55 (Jenkins et al, 2015)

These are all validated scoring systems in pediatric populations.

We will utilize the short STAI, as above.

Units of measurement for all variables of interest: Questionnaires and scales as above. In addition, hours since anesthesia end to start of visit (hours), PCA use (mcg or mg, at T=-60-0, 0-30, 30-90 min; converted to morphine equivalents at time of data entry), patient declines (0=Yes, 1=No), total duration of electronic device use (min), presence of dizziness (0=No, 1=Yes), presence of nausea (0=No, 1=Yes), anti-nausea medication requested during intervention (0=No, 1=Yes).

Patient and caregiver satisfaction: Qualitative satisfaction will be documented, divided into positive and negative comments.

5.1 Efficacy Evaluation

During data analysis, number of hours since anesthesia end to start of visit will be extracted from chart review. PCA use conversion to morphine equivalents will be performed. Pain and anxiety scores and PCA opioid usage will be compared between the two study arms. These data will allow us to compare the two study arms and evaluate for efficacy.

5.2 Pharmacokinetic Evaluation

Not applicable

5.3 Safety Evaluations

Safety and feasibility of VR in postsurgical populations has been proven in previous studies, some of which include specific spine surgery populations. As we are limiting the use of the virtual reality headset to 30 minutes, there is a possibility that patients may experience anxiety and/or notice an increase in pain following cessation of VR. As such, the patients will be permitted to freely use personal electronic devices without restriction, which is the standard of care at present. We feel that by doing this, the chance of anxiety related to complete withdrawal of electronic distraction will be low, as will

the possibility of any adverse effects such as nausea or dizziness. The incidence of dizziness and nausea with the use of virtual reality is not precisely known and is not agreed upon in the literature. As it is mentioned in various studies as a potential side effect, we will limit the use of the virtual reality headsets to 30 minutes to minimize the risk.

6 STATISTICAL CONSIDERATIONS

6.1 Primary Outcomes

Postoperative pain scores and postoperative PCA opioid usage surrounding intervention (in morphine equivalents).

6.2 Secondary Outcomes

Our secondary outcomes and efficacy measures include: patient and caregiver satisfaction scores, presence of dizziness/nausea, time of discontinuation of VR/iPad if less than 30 minutes, and PHBQ-AS scores postoperatively at 48-72 hours and 7-10 days.

6.3 Statistical Methods

All statistical estimates (e.g., means, medians, proportions, incidence rates, mean differences, correlations, etc.) will be tabulated along with corresponding confidence intervals (CIs). To avoid over-reliance on p-values, the magnitudes of estimates and the corresponding confidence intervals will be the primary focus of the analyses. Quantitative data analysis will occur using SAS or R and will be conducted under the supervision of a UNC Department of Anesthesiology biostatistician along with other members of the UNC Department of Anesthesiology research division.

We will work closely with our departmental statistician in all statistical analyses. After discussion with our biostatistician, we do plan to utilize a completely randomized study design. For our post-study analysis, we will perform analyses with and without gender stratification to assess whether gender is a contributing factor in opioid usage and pain scores.

For Aim 1 (comparing postoperative pain and anxiety scores), the following questionnaires and scales with validated scoring as above will be analyzed: short STAI, FACES, FLACC, PHBQ-AS.

For Aim 2 (comparing postoperative opioid usage), opioid usage will be converted into morphine equivalents at the time of data entry and analyzed.

For Aim 3 (assessing patient and caregiver satisfaction), qualitative satisfaction will be documented, divided into positive and negative comments. Patient satisfaction and overall experience are commonly linked to pain experienced during a hospitalization, and as a result, satisfaction with the use of VR as a method of pain control will be one of our outcomes.

We hypothesize that the use of virtual reality programs will provide superior distraction to standard of care and will result in improved pain scores and reduced opioid consumption after surgery. We will utilize two-sample t-test to compare the pain scores and opioid consumption in VR and control groups.

We will have the p-values reported and Bonferroni correction will be used to adjust for multiple comparison. P-values not reaching the significance level will be deemed as inconclusive.

If a value is missing, the measure will be negated for that participant, and we will have an incomplete data point. These incomplete data points will not be included in the analyses. This study is based on prior work by our group with a quite rare occurrence of not being able to collect all data points, given the nature of the collected data. We do not anticipate that missing values will systematically introduce any selection bias.

6.4 Sample Size Rationale

We would like to present this study as a pilot study of 20 completed patients. There are approximately 2 idiopathic scoliosis repairs per week in the pediatric population at UNC, thus we would hope to be able to complete the pilot portion of this study in a reasonable timeframe. Since the effect size is unknown at this stage, we consulted with our UNC Department of Anesthesiology statistician and discussed among our team. We feel that the study design is substantially different from any published studies or our group's study last year - all-comers to the PACU, versus this homogenous population undergoing a specific ERAS protocol with the intervention taking place on postoperative day 1. We would like to proceed with a pilot study that can then be used to estimate the effect size of our intervention on the primary outcome based on the data we collect from the pilot study (N=20). The pilot study will also be used to assess the feasibility of the logistics and study procedure.

6.5 Study Stopping Rules

Any adverse events throughout the study will be reported to the PI and further safety evaluations will be made as necessary for the remainder of the study. If it is determined that the study exposes patients to more than the normal risk associated with standard of care practices, then the study will be stopped. We will conduct a data analysis at the conclusion of the pilot study (N=20). Given the small sample size, no interim analysis of the data will be performed.

7 STUDY INTERVENTION (drug, device or other intervention details)

The Applied VR is a lightweight mobile virtual reality headset with embedded software, creating an immersive experience. The Applied VR is specifically designed for medical use. The devices will be stored in a locked room within the Department of Anesthesiology. There will be no modifications to the packaging or labeling of the devices, as this may interfere with the application and functionality of the devices. During the intervention phase of the study, a research assistant will be monitoring the patients to assist with technical issues with the device, as well as to monitor for compliance and adherence.

8 STUDY INTERVENTION ADMINISTRATION (if applicable)

Randomization and blinding procedures addressed in section 3.2.

9 SAFETY MANAGEMENT

Any and all adverse events and any safety concerns will be reported to the PI and IRB as applicable. Standard of care practices will continue to be followed throughout this study, which includes serious or adverse event monitoring and reporting and medical emergency procedures.

10 DATA COLLECTION AND MANAGMENT

- The research coordinator will manage all of the data through the use of a RedCap database which will be created prior to the start of the study. A codebook of variables will be created in consultation with a UNC Department of Anesthesiology biostatistician. All data entries which are missing will have (whenever possible) a comment associated with that data point to explain its reason for being missing.
- The data collected during this study will be on hospital or School of Medicine computers with security features installed to protect the data. Data will be collected by a research assistant and will be monitored by members of this research study noted on the IRB and other members of the Department of Anesthesiology research division.
- The Information Technology group within the Department of Anesthesiology provides secure data storage for the proposed study. Servers for the group are located in a locked office on the UNC campus and backed up with nightly full backups. The web server is behind a firewall and only known and approved site users have. This data management system meets or exceeds NIH security guidelines, safeguards participant data, and adheres to the Certificate of Confidentiality.
- All data collected on paper forms will be kept in a locked file cabinet in a locked office area. All electronic files will be stored on the Department of Anesthesiology secured intranet without identifiable information.
- Data will be stored separate from identifiable information and shared with the research team electronically on hospital or School of Medicine computers within the secured networks.

11 RECRUITMENT STRATEGY

Subjects will be identified by looking at surgery schedules and type of surgery. All subjects 11-17 years old undergoing idiopathic scoliosis surgery will be identified and considered for this study. The subjects will be identified and then recruited either by phone 1-3 days in advance or in person on the day of their proposed surgery in the preoperative holding area.

12 CONSENT PROCESS

The recruitment and consent process will be done either by phone with electronic consent (e-consent) or in person. A research assistant or member of the research team will be the recruiters for this study.

E-consent will be conducted via RedCap, which has e-consent capability and knowledge tracks, with the ability for participants to give a physical signature and download a copy of the consent for their own reference. A member of the research team will call patients and their guardians 1-3 days prior to surgery and go through the informed consent process by phone, and will share a RedCap link so families can pull up the consent and go through it while on the phone with the researcher. The recruiter will be immediately available to answer questions by staying on the phone while participants complete the consent. The benefit of offering e-consent is to allow a higher enrollment of interested patients, given the significant time restraints on the morning of surgery that can preclude a successful completion of consent. The in person, day-of surgery consent option will still be offered for families who do not have access to a computer or prefer in person consent.

For in person consents on the day of surgery, each subject will have a private room on the day of surgery in the preoperative area. Consent in person will be obtained in the preoperative area, in person and in a private room with closed doors, preventing those not involved with the study from hearing any private information about the study or the subjects.

13 PLANS FOR PUBLICATION

The goal is to complete a manuscript for publication by June 1, 2021.

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15 APPENDIX

No items for appendix at this time.