Music Therapy versus Control during Total Knee Replacement under Spinal Anesthesia

Study Protocol and Statistical Analysis Plan

NCT03569397

November 9, 2020

Promil Kukreja, M.D., Ph.D. Principal Investigator
University of Alabama at Birmingham
Birmingham, AL 35294

Human Subjects Protocol (HSP)

Form Version: February 1, 2017

- You are applying for IRB review of the research described in this form.
- To avoid delay, respond to all items in order and include all required approvals and documents. For more tips, see the UAB IRB website.
- To complete the form, click the underlined areas and type or paste in your text; double-click checkboxes to check/uncheck.
- All responses should be Times New Roman, Bold, and Underlined.
- Submit all materials to AB 470, 701 20th Street South, Birmingham, AL 35294-0104.

Indicate the type of review you are applying for:

☐ Convened (Full) IRB ***-OR-***

☒ Expedited - See the Expedited Category Review Sheet, and indicate the category(ies) here:

☐1 ☐2 ☐3 ☒4 ☐5 ☐6 ☐7

1. IRB Protocol Title: Music Therapy versus Ambient Noise during Total Knee Replacement under Spinal Anesthesia

2. Investigator and Contact Person

a. Name of Principal Investigator: **Promil Kukreja, M.D., Ph.D.**

Degree(s)/Title: **M.D., Ph.D.** BlazerID: **pkukreja**

Dept/Div: **Anesthesiology** Mailing Address: **JT 862** UAB ZIP: **6810**

Phone: **996-7025** Fax: **996-4489** E-mail: **pkukreja@uab.edu**

b. Name of Contact Person: **Adam Sturdivant** Title: **Researcher III** Phone: **205-934-4042**

E-mail: **adamsturdivant@uabmc.edu** Fax: **205.975.0761**

c Name of Contact Person: **Avesha Bryant, MSPH, MD** Title: **Assoc Professor** Phone: **205-996-7383**

E-mail: **asbryant@uabmc.edu** Fax: **205.975.0761**

INVESTIGATOR ASSURANCE STATEMENT & SIGNATURE

By my signature as Principal Investigator, I acknowledge my responsibilities for this Human Subjects Protocol, including:

- Certifying that I and all key personnel comply with reporting requirements of the UAB Conflict of Interest Review Board;
- Certifying that the information, data, and/or specimens collected for the research will be used, disclosed and maintained in accordance with this protocol and UAB policies;
- Following this protocol without modification unless (a) the IRB has approved changes prior to implementation or (b) it is necessary to eliminate an apparent, immediate hazard to a participant(s);
- Verifying that all key personnel listed on the protocol have completed initial IRB training and will complete continuing IRB training as required;
- Verifying that all personnel are licensed/credentialed for the procedures they will be performing, if applicable;
- Certifying that I and all key personnel have read the *UAB Policy/Procedure to Ensure Prompt Reporting of Unanticipated Problems Involving Risks to Subjects or Others to the IRB, Institutional Officials, and Regulatory Agencies* and understand the procedures for reporting;
- Applying for continuing review of the protocol at least annually unless directed by the IRB to apply more frequently;
- Conducting the protocol as represented here and in compliance with IRB determinations and all applicable local, state, and federal law and regulations; providing the IRB with all information necessary to review the protocol; refraining from protocol activities until receipt of initial and continuing formal IRB approval.

Signature of Investigator: _____ **Date:** 11/1/16

3. Protocol Personnel

Including the PI, list all key personnel (each individual involved in the design and conduct of this protocol). See the Key Personnel Flowchart.

Complete the UAB (3.a.) and non-UAB (3.b) tables, as applicable. Use the checkboxes to show each individual's role, whether the individual has financial interests as defined by the UAB CIRB, and briefly describe the individual's protocol responsibilities and qualifications to perform those responsibilities. **Insert additional rows as needed.**

FDA: For studies involving investigational drugs, list all investigators who will be listed on FDA Form 1572 and include a copy of the 1572. Send the IRB a copy of Form 1572 any time you update the form with the FDA.

a. UAB Personnel (includes UAB affiliates and Children's of Alabama personnel)

Name, Degree, and Dept.	Blazer ID	Role	Financial Interest?*	Protocol Responsibilities and Qualifications (indicate if this person obtains consent)
Name: **Promil Kukreja** Degree: **M.D., Ph.D.** Department: **Anesthesiology**	**pkukreja**	Principal Investigator	☒No ☐Yes	**Oversees all aspects of project and study team, obtains consent, screening, recruitment, data analysis interpretation, manuscript writing**
Name: Elie Ghanem **Degree: MD** **Department: Orthopedic Surgery**	**eghanem**	☒Sub-Investigator ☐Other	☒No ☐Yes	Helps with recruiting, monitoring for adverse outcomes, data analysis
Name: **Lisa MacBeth** Degree: **MD** Department: **Anesthesiology**	**ldspeake**	☒Sub-Investigator ☐Other	☒No ☐Yes	Recruiting, monitoring for adverse outcomes, data analysis interpretation, manuscript writing
Name: **Katherine Talbott** Degree: MD Department: **Anesthesiology**	**ktalbott**	☒Sub-Investigator ☐Other	☒No ☐Yes	Screening, consenting, recruitment, data collection, analysis, data interpretation, manuscript writing
Name: Adam Sturdivant Degree: MPH Department: Anesthesiology	**absturdi**	☐Sub-Investigator ☒Other	☒No ☐Yes	Screening, consenting, data collection and entry, regulatory compliance, protocol adherence, quality assurance
Name: Shanna Graves Degree: Department: Anesthesiology	**shannagraves**	☐Sub-Investigator ☒Other	☒No ☐Yes	Screening, consenting, data collection and entry, regulatory compliance, protocol adherence, quality assurance
Name: Ayesha Bryant Degree: MSPH, MD Department: Anesthesiology	**shiekh**	☐Sub-Investigator ☒Other	☒No ☐Yes	Protocol development, data analysis, interpretation, manuscript writing
Name: Kyle Cichose Degree: BS Department: Orthopedics	**kcichos**	☐Sub-Investigator ☒Other	☒No ☐Yes	Screening, consenting, data collection and entry, regulatory compliance, protocol adherence, quality assurance
Name: Ben Wilson Degree: BS Department: Anesthesiology	**bewilson**	☐Sub-Investigator ☒Other	☒No ☐Yes	Screening, consenting, data collection and entry, regulatory compliance, protocol adherence, quality assurance
Name: Cynthia Bass Degree: CRNA Department: Anesthesiology	**csbass**	☐Sub-Investigator ☒Other	☒No ☐Yes	Screening, consenting, data collection and entry, regulatory compliance, protocol adherence, quality assurance

b. Non-UAB Personnel Relying on UAB IRB - If you are requesting that the UAB IRB serve as the IRB of record for anyone not affiliated with UAB, list these individuals below.

Name and Degree	From Institution with or without own IRB?	Financial Interest?*	Protocol Responsibilities and Qualifications (indicate if this person obtains consent)

Name: _____ Degree: _____ Institution: _____ Email: _____	☐Has own IRB but requests that UAB IRB serve as IRB of record?-***OR***- ☐Does not have own IRB and needs to rely on UAB IRB.	☐No ☐Yes	_____

***Financial Interest** – for each individual listed above, answer **Yes** or **No** as to whether the individual or an immediate family member has any of the following:

- An ownership interest, stock options, or other equity interest related to the investigator's institutional responsibilities of any value.
- Compensation greater than $5,000 in the previous two years when aggregated for the immediate family
- Proprietary interest including, but not limited to, a patent, trademark, copyright, or licensing agreement.
- Board of executive relationship, regardless of compensation.
- Any other Financial Interest as defined by the UAB CIRB.

UAB Personnel: If the individual or his/her spouse or dependent child has a Financial Interest, a disclosure has to be made to the UAB CIRB. A completed CIRB evaluation has to be available before the IRB can complete its review.

Non-UAB Personnel: If the individual has a Financial Interest, ***include a copy of the report from his/her own institution's conflict of interest review with this submission to the UAB IRB.***

c. Do the investigators listed above include any students using this research for their thesis or dissertation?

☒ No, continue with Item 3.d.

☐ Yes, complete the following

Student Name	Thesis/Dissertation Title
_____	_____

d. Is the principal investigator a student, fellow, or resident? ☐Yes ☒No

If Yes, complete items below and obtain signature of faculty advisor or supervisor:

Supervisor's Name: _____

Degree(s) / Job Title: _____

Additional Qualifications pertinent to the protocol: _____

Telephone: _____

E-Mail: _____

Signature: _____

e. Describe the principal investigator's activities related to this protocol and provisions made by the PI to devote sufficient time to conduct the protocol: **As an attending anesthesiologist, the PI is able to devote sufficient time to conduct and provide oversight for this protocol.** _____

f. Is medical supervision required for this research? ☒Yes ☐No

If Yes, who will provide the medical supervision?

☒ PI will provide -***OR***-

☐ Other:

Name: _____ Telephone: _____

If other than PI, obtain signature of person providing medical supervision:

Signature _____

g. Describe your process for ensuring all key personnel are adequately informed about the protocol and their research-related duties and functions: **All personnel who are involved in the design or conduct of this research study will have successfully completed and maintained UAB IRB required human subjects research training, which includes the importance of measures to protect patient confidentiality.**

4. Funding

Is this protocol funded? ☐Yes ☒No

If No, specify that costs of the protocol will be covered by funds from the UAB department or other source named: **Department of Anesthesiology and Perioperative Medicine and Department of Orthopedic**

Surgery. The STAI questionnaire costs $2.50 each time it is administered, totaling $5.00 per patient enrolled.

If Yes, attach one copy of completed application or request for funding sent to sponsor, and complete a-d.

a. Title of Grant, Contract, or Agreement: _____

b. UAB PI of Grant, Contract, or Agreement: _____

c. Office of Sponsored Programs (OSP) Assigned Number: _____
(If not yet available, enter "Pending" and provide upon receipt from OSP.)

d. Sponsor, Funding Route:
(Check and describe all that apply)
(If subaward, list both the funding source and the institution receiving the direct award)

☐ Gov't Agency or Agencies—Agency name(s): _____
- ☐ Department of Defense (DoD): Identify DoD component: _____
- ☐ Department of Energy (DOE)
- ☐ Department of Justice (DOJ)
- ☐ Department of Education

☐ NIH Cooperative Group Trial - Group name: _____

☐ Private Nonprofit (e.g., Foundation) - Name: _____

☐ Industry, investigator-initiated - Name: _____
Describe the funding arrangement: _____
NOTE: The UAB IRB typically only reviews industry-sponsored protocols that are investigator initiated or when the protocol qualifies for expedited review or involves gene therapy.

☐ UAB Departmental/Division Funds—Specify: _____

5. Locations Involved

a. Indicate all performance sites that will provide space, services, or facilities for the conduct of this protocol.

☒ UAB Hospital
☒ UAB Hospital - Highlands
☐ The Kirklin Clinic of UAB Hospital
☐ The Kirklin Clinic at Acton Road
☐ UAB Callahan Eye Hospital
☐ UAB Clinical Research Unit
☐ Children's of Alabama
☐ Birmingham Veterans Affairs Medical Center
☐ Jefferson County Department of Health
☐ Other (i.e., any performance site not listed above, including those covered by subawards related to this protocol) - Describe: _____
NOTE: Documentation of IRB approvals from sites receiving subawards must be received by the UAB OIRB before funding will be released for that subaward.

b. Describe the space, service, or facilities available for the conduct of the research in the performance sites listed in Item 5.a (For research on UAB campus, include building names): **This research will take place in the same area in which standard of care surgery occurs daily, including the preoperative area and the operating rooms at UAB Hospital – Highlands.**

c. Is this protocol a clinical trial requiring clinical services at one of the performance sites listed in Item 5.a above? ☒Yes ☐No

If Yes, will any of the services be billed to either participants/their insurance or to the study account through the Hospital Billing Office (PFS) or the HSF Billing Office (MSO)? ☐Yes ☒No

If Yes, submit a Full Fiscal Approval Process (FAP)-designated unit submission to s complete a FAP submission and send to fap@uab.edu. For more on the UAB FAP requirements, go to FAP - SiteMinder Processes.

d. Is this a field study? ☐Yes ☒No

If Yes, describe the community and include information about how the community will be involved in the design, implementation and analysis of the research. This would include focus groups, training local facilitators/community health advisors: _____

e. Has this protocol been rejected or disapproved by another review board (another IRB, similar review board, or departmental review committee(s)) that authorizes the use of its patient populations? ☐Yes ☒No

If Yes, provide name(s) of the review board(s) and reason(s) not approved: _____
Attach copies of the disapprovals.
NOTE: If this protocol is subsequently rejected or disapproved by another review board, promptly notify UAB IRB.

f. Will the protocol be conducted at or recruit participants from the Birmingham Veterans Affairs Medical Center (BVAMC)? ☐Yes ☒No

If Yes, describe the involvement of the BVAMC: _____
Attach the VA IRB approval and VA IRB-stamped consent form(s), if applicable.
NOTE: See the BVAMC section of the IRB Guidebook for more information.

g. Will the protocol be conducted at or recruit participants from the Jefferson County Department of Health (JCDH)? ☐Yes ☒No

If Yes, describe the involvement of the JCDH and list the JCDH clinics being used: _____
Attach the JCDH Research Review Panel approval, if applicable.
NOTE: Human subjects research conducted at certain JCDH clinics requires review by the JCDH Research Review Panel. See the JCDH section of the IRB Guidebook for more information.

6. Clinical Trial

Does this protocol meet the following definition of a clinical trial? ☒Yes ☐No
**A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. For more information, see the full definition of clinical trial here.*

If Yes, you will need to fulfill the following requirements (regardless of funding):

a. All key personnel must complete the Good Clinical Practices (GCP) training. For information on this requirement, visit the IRB website here.

b. This protocol must be registered on ClinicalTrials.gov. Provide the National Clinical Trial (NCT) identifier number: **NCT03569397**
If you have any questions regarding registering a study on ClinicalTrials.gov, email the UAB Center for Clinical and Translational Science at ccts@uab.edu.

7. Multi-Site Studies

a. Is this a multi-site study with the UAB investigator as the lead investigator? ☐Yes ☒No

b. Is this a multi-site study with UAB as a coordinating site? ☐Yes ☒No

c. If Yes to a or b, describe the management of information obtained in multi-site research that might be relevant to the protection of participants. Include, at a minimum, how the following items are managed:

- IRB approvals from other sites

- Unanticipated problems involving risks to participants or others. (For example, if there is an unanticipated problem involving risks to participants or others, which site is responsible for reporting it?)
- Interim results
- Protocol modifications

_____

8. Drugs

Will any drugs or supplements be *used or studied* in this protocol? ☐Yes ☒No
If Yes, attach the completed Drug Review Sheet.

9. Devices

a. Will any devices be *studied* in this protocol? ☐Yes ☒No

b. Will any *not FDA-approved* devices be *used or studied* in this protocol? ☐Yes ☒No
If Yes to a or b, attach the completed Device Review Sheet.

10. Special Approvals

a. Does this protocol involve the use of radioisotopes? ☐Yes ☒No
If Yes, attach documentation of approval from the Radiation Safety Division.

b. Does this protocol include patients with contagious infections (e.g., mumps, measles, chickenpox, TB, meningitis)? ☐Yes ☒No
If Yes, attach documentation of approval from the Infection Control Committee of the appropriate facilities.

c. Does this protocol involve obtaining remnant biopsy or surgical material from the Department of Pathology or any other source? ☐Yes ☒No
If Yes, attach documentation of approval from the entity or individual providing the materials (e.g., the UAB Division of Anatomic Pathology Release of Pathologic Materials).

d. Does this protocol require obtaining any remnant clinical laboratory specimens, body fluids, or microbiological isolates from the Department of Pathology or any other source? ☐Yes ☒No
If Yes, attach documentation of approval from the entity or individual providing the materials (e.g., the UAB Division of Laboratory Medicine Release of Pathologic Materials).

e. Does this protocol use stored (existing) specimens from a repository? ☐Yes ☒No
If Yes, attach documentation of approval for use of specimens, and describe how existing specimens are labeled: _____

11. Use of Specimens

Does this protocol involve the collection of specimens? ☐Yes ☒No
If Yes, complete 11.a-11.h.
If No, skip to Item 12.

a. How will specimens be obtained, processed, distributed, and stored? _____

b. How will specimens be labeled (e.g., unique identifier, medical record number, Social Security number, name, date of birth)? _____

c. How will clinical data associated with the specimens be collected and stored? _____

d. What participant-identifying information will be collected and linked to the specimens? _____

e. What steps will be taken to maximize the confidentiality of linked identifiers? For example, procedures could include using a password-protected computer database to link identifiers, with limited personnel knowledgeable of the password, or coded identifiers released without the ability to link to clinical data (also called "stripped" or "anonymized" specimens). _____

f. Is genetic testing planned as part of this protocol? ☐Yes ☐No
If Yes, describe the planned genetic testing here. _____

g. Will specimens be stored for future use? ☐Yes ☐No
If Yes, indicate whether they will be used for the disease under study in this protocol or research on other diseases. _____

h. Will specimens be shared with other investigators in the future? ☐Yes ☐No
If Yes, answer i. and ii.
i. What identifiers, clinical information and demographic information will be shared; or will the specimens be stripped of identifiers (i.e., anonymized)? _____
ii. Outline your procedure for assuring IRB approval for release and use prior to release of specimens.

_____

NOTE: Investigators who receive and/or use these specimens must document approval from the appropriate IRB(s) before the specimens may be released.

12. Gene Therapy
Does this protocol involve gene therapy or administering recombinant materials to humans? ☐Yes ☒No
If Yes, submit the Gene Therapy Project Review Panel Report ***-OR-*** the Protocol Oversight Review Form For Clinical Vaccine Trials, as applicable.

13. HIPAA Privacy and Security
Will the PI or others obtain, review, or make other use of participants' "protected health information" (i.e., information, whether oral or recorded in any form or medium that (a) is created or received by a health care provider and (b) relates to past, present, or future physical or mental health or condition of an individual; or provision of health care; or payment for provision of heath care)? ☒Yes ☐No
If Yes, complete Items 13.a-13.f.
If No, skip to 14.

a. Will the data/information be stored or managed electronically (on a computer)?
☒Yes ☐No

b. Is the principal investigator requesting that the UAB IRB waive patient HIPAA authorization from another institution or entity (e.g., insurance company, collaborating institution)? ☐Yes ☒No
If Yes, attach copies of the privacy notices from each institution/entity, and provide the name of each institution/entity: _____

c. Indicate which of the entities would provide health information for this protocol, maintain health information as it was collected for this protocol, and/or store health information after it has been collected for this protocol.
☒ UAB Hospital or UAB Hospital - Highlands
☐ The Kirklin Clinic of UAB Hospital or Acton Road (and/or associated clinics)
☐ UAB Callahan Eye Hospital
☐ Children's of Alabama
☐ Jefferson County Department of Health
☐ School of Dentistry
☐ School of Health Professions
☐ School of Medicine
☐ School of Nursing
☐ School of Optometry
☐ University of Alabama Health Services Foundation
☐ UAB Health Centers
☐ Viva Health

☐ Ophthalmology Services Foundation
☐ Valley Foundation
☐ Medical West - UAB Health System Affiliate
☐ None - **If None, skip to Item 14.**

d. Indicate any information systems that will be the sources of information used for the protocol.

☒ A system maintained centrally by UAB Health System (these include the following: HealthQuest for registration, billing, and patient administration; PowerInsight (clinical data warehouse); Cerner IMPACT for PowerNotes for meds, Lab, Radiology, UED, Surgery

NOTE: If a researcher needs information in a specified format or a specified time, the researcher must confirm with the unit who can supply the information/service that the request can be met before writing the information/service into the research protocol. In addition, the researcher must be aware that these services may have a cost attached that should be considered in the research budget.

To request access to clinical systems for research purposes, visit https://www.oneuabmedicine.org/web/hsis/technical-support, click "Accounts Request" and complete the form indicating access for research purposed.

☐ Another system on a UAB server - Describe: _____

e. Indicate which of the listed identifiers will be accessed, associated and/or linked with the protected health information (PHI) used for this protocol.

☒ Names
☐ Geographic subdivisions smaller than a state
☒ Elements of dates (except year) related to an individual
☐ Telephone numbers
☐ Fax numbers
☐ Email addresses
☐ Social security numbers
☒ Medical record numbers
☐ Health plan beneficiary numbers
☐ Account numbers
☐ Certificate/license numbers
☐ Vehicle identifiers and serial numbers
☐ Device identifiers and serial numbers
☐ Biometric identifiers
☐ Web universal resource locators (URLs)
☐ Internet protocol address numbers
☐ Full-face photographic images
☐ Any other unique identifying number - Describe: _____
NOTE: Codes are not identifying as long as the researcher cannot link the data to an individual
☐ None - **If None, skip to Item 14.**

f. Choose one plan to describe your use of the personal health information:

☐ The data collected meet the specifications for a "limited data set" (LDS)
-If the LDS will leave the covered entity or will be received from another covered entity you will need a Data Use Agreement

☒ Research staff will obtain authorization from each participant to use the information
-Include the HIPAA Authorization form, complete except for participant name and IRB protocol number, as the final page of the consent form

☐ PI requests waiver of authorization to use the information
-Attach Waiver of Authorization and Informed Consent form

PROPOSED RESEARCH

- The IRB will not accept grant applications and/or sponsor's protocols in lieu of the items as outlined below.
- Do not separate responses from items. Instead, insert your response to each item below the item, keeping the information in the order of this form.

14. Purpose - in nontechnical, lay language

a. Summarize the purpose and objectives of this protocol in one short paragraph.

The purpose of this study is to examine the effects of music therapy during spinal anesthesia for patients having total knee arthroplasty. Specifically, we would like to assess if intraoperative music therapy impacts patient anxiety, sedation requirements during surgery, stress response to surgery and postoperative satisfaction.

b. Describe how outcomes will be measured for this protocol.

The primary end points are as follows:

1. Patient anxiety levels
2. Sedation requirements during surgery
3. Postoperative patient satisfaction

15. Background - in nontechnical, lay language

Summarize in 2-3 paragraphs past experimental and/or clinical findings leading to the design of this protocol. Include any relevant past or current research by the PI. For drug and device studies, summarize the previous results (i.e., Phase I/II or III studies).

For millennia, people have listened to and enjoyed music for entertainment, as a distraction from daily troubles, and as a means to relax and relieve stress. It is no real surprise that the relaxing and stress-relieving effects of music have been shown in patients having surgery. For patients having surgery with spinal anesthesia, music therapy during the operation decreases sedation requirements, anxiety and may improve patient satisfaction.[1, 2, 3, 4, 5, 6, 7] Music therapy during surgery may also lead to a decreased stress response, as evidenced by more stable cortisol levels.[8] Studies done previously have included patients undergoing various surgical procedures, however no studies have been done specifically for patients undergoing total knee arthroplasty. Because total knee arthroplasty is a common procedure usually done under spinal anesthesia at our institution, we would like to study the effects music therapy could have on our patient population.

16. Participants (Screening and Selection)

a. How many participants are to be enrolled at UAB (if other sites relying on UAB IRB, list the number for each site)? **100**

If multi-site study, total number at all sites/institutions: _____

b. Describe the characteristics of anticipated or planned participants (if multiple groups, repeat list for each group).

Sex: **M,F**

Race/Ethnicity: **any**

Age: **≥18 years**

Health status: **ASA Physical Status I, II, III**

c. From what population(s) will the participants be derived? **The study population will be derived from those patients scheduled for total knee arthroplasty**

Describe your ability to obtain access to the proposed population that will allow recruitment of the necessary number of participants: **Between several weeks to days before surgery, patients will report to the Highlands Preoperative assessment Clinic (HPAC) for standard of care preoperative health examination and testing by the anesthesiologist attending in HPAC. This visit occurs routinely for patients having surgery in our health system and does not occur because of this study. The anesthesiology attending physician in HPAC, who has routine access to the patient's medical history, will contact the PI or co-investigator should a patient appear to be a candidate for this study based on their routine review of records.**

During the patient's visit they will be given a "Patient Information Sheet," describing the study. On the day of surgery, patients scheduled for surgery will be seen in the preoperative holding area and enrolled in the study if they choose and are appropriate candidates.

d. Describe the inclusion/exclusion criteria:

Inclusion Criteria:

Patients undergoing total knee arthroplasty under spinal anesthesia.
Patients 18 years of age or older.
Patients classified by the American Society of Anesthesiology (ASA) class I, II, or III.

Exclusion Criteria;

Any patient not classified as an ASA I, II, or III.
Patients with hearing impairment, defined by personal endorsement of hearing impairment or use of hearing aids.
Patients with contraindication to spinal anesthesia.

e. If participants will comprise more than one group or stratification, describe each group (e.g., treatment/intervention, placebo, controls, sham treatment) **and** provide the number of participants anticipated in each group.

Upon enrollment in the study, participants will be randomized 1:1 to either the investigational group ("Music Therapy" group) or the control group ("No Music" group). Participants will be randomized using a random number generator.

f. Indicate which, if any, of the special populations listed below will be involved in the protocol. Include the Special Populations Review Form (SPRF) if indicated.

☐ Pregnant Women: Attach SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
☐ Fetuses: Attach SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
☐ Neonates/Nonviable Neonates: SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
☐ Prisoners: Attach SPRF—Prisoners
☐ Minors (<18 years old): Attach SPRF—Minors
☒ Employees or students at institution where research conducted
☐ Persons who are temporarily decisionally impaired
☐ Persons who are permanently decisionally impaired
☐ Non-English Speakers

For each box checked, describe why the group is included **and** the additional protections provided to protect the rights and welfare of these participants who are vulnerable to coercion: **Employees and students may be eligible to participate and should be allowed to do so. It is an undue burden to exclude them. The suggested language has been included in the informed consent document to**

fully disclose that this project is separate from the expectations and their relationship with UAB as an employee or a student.

g. List any persons other than those directly involved in the protocol who will be at risk. If none, enter "None": **None**

h. Describe the recruitment process (e.g., medical record review, referrals, letter of invitation, existing patients) that will be used to seek potential participants (e.g., individuals, records, specimens). Research recruitment by non-treating physicians/staff may require completion of Partial Waiver of Authorization for Recruitment/Screening. **Days to weeks prior to surgery, patients scheduled for total knee arthroplasty will receive an information sheet about the study at their appointment at Highlands Preoperative Assessment Clinic (HPAC). On the day of surgery, patients scheduled for surgery will be seen in the preoperative holding area and enrolled in the study if they choose and are appropriate candidates.**

i. If you will use recruitment materials (e.g., advertisements, flyers, letters) to reach potential participants, attach a copy of each item. If not, identify the source (e.g., IRB Protocol Number for approved databases) from which you will recruit participants. **N/A**

j. Describe the screening process/procedures for potential participants.
Study personnel will confirm eligibility requirements using a standardized eligibility checklist. This will be completed by the PI or another member of the research team prior to consenting and enrolling subjects in the study. This eligibility screening will occur in the preoperative holding area where each patient is in a private room.

17. Protocol Procedures, Methods, and Duration - in nontechnical, lay language

Describe the procedures for all aspects of your protocol. Tell us what you are doing.

A. **Patients who consent to the study will be randomized 1:1 to either the investigational group ("Music Therapy" group) or the control group ("No Music" group). Participants will be randomized using a random number generator.**
B. **Consent and study enrollment will occur in the preoperative area prior to surgery. After enrollment, all patients will complete a State-Trait Anxiety Assessment (STAI) questionnaire. Patients in the "Music Therapy" group will be asked to choose a genre of music that they would like to listen to during the operation (instrumental, jazz, classical, rock, R&B/hip-hop, pop, country, Christian/gospel, musical theatre). All patients enrolled in the study will continue to receive routine preoperative care.**
    a. **After proceeding to the operating room, all patients will receive routine preoperative care during placement of spinal anesthesia. In addition to monitors routinely placed prior to spinal block, a BIS (Bi-Spectral Index) monitor will be placed on the patient's forehead to monitor sedation levels during the procedure. A BIS monitor is a noninvasive series of patches placed on the patient's forehead that, through a propriety equation creates a number (1-100) from processed EEG waves that correlates with depth of sedation or anesthesia. After the spinal anesthetic block is placed, the patients in the "Music Therapy" group will wear headphones that will play their pre-selected music. The "No Music" group will receive intraoperative standard of care with no headphones. Headphones will be worn by the "Music Therapy" patients until the procedure is finished (skin incision is closed).**

C. **During the procedure, routine intraoperative sedation consisting of propofol, fentanyl and midazolam will be administered. All patients <70 years old will be given 1 mg midazolam, 50 mcg fentanyl and propofol dosing titrated to a BIS level of 60-70 (or as respiratory rate allows), which correlates to moderate sedation.[9] Those patients of age >/= 70 years will receive 50mcg of fentanyl after the spinal with an additional 50mcg only if needed. Again, propofol dosing should be titrated to reach a BIS of 60-70 (or as respiratory rate allows).**

D. **All patients will receive standard postoperative care in the post-anesthesia care unit (PACU).**

E. **On postoperative day 1, all patients will again complete a STAI questionnaire. Additionally, they will complete a Satisfaction survey.**

F. **The amount of pain medication you received in the operating room will be recorded.**

G. **Failed or unsuccessful spinals will be excluded from the study.**

b. What is the probable length of time required for the entire protocol (i.e., recruitment through data analysis to study closure)? **1 year**

c. What is the total amount of time each participant will be involved? **Each participant will be involved in the study for approximately 24 hours. Each procedure time period is listed below.**

d. If different phases are involved, what is the duration of each phase in which the participants will be involved? If no phases are involved, enter "None." **None**

e. List the procedures, the length of time the procedure takes, the total # of times the procedure is performed, and indicate whether each is performed solely for research or would already be performed for treatment or diagnostic purposes (routine care) for the population.
-Insert additional table rows as needed.
-If procedure is sometimes research and sometimes routine care, include on separate lines with number of times as each.

Procedure	Length of Time Required of Participants	Frequency of Repetition	Research (Res) – OR- Routine Care
Presurgical Evaluation on the day of surgery	**30 minutes**	**once**	☐Res ☒Routine
Obtaining informed consent from patient	**20 minutes**	**Once**	☒Res ☐Routine
Randomization on day of surgery	**5 minutes**	**Once**	☒Res ☐Routine
Choosing music genre, completing STAI Questionnaire	**Approximately 30 min.**	**Once**	☒Res ☐Routine
Postoperative day 1: Completing STAI Questionnaire, Satisfaction Survey	**20 minutes**	**Once**	☒Res ☐Routine

f. Will an interview script or questionnaire be used? ☒Yes ☐No

If Yes, attach a copy.

g. Will participants incur any costs as a result of their participation? ☐Yes ☒No

If Yes, describe the reason for and amount of each foreseeable cost. _____

h. Will participants be compensated? ☐Yes ☒No

If Yes, complete i-v.

i. Type: (e.g., cash, check, gift card, merchandise): _____

ii. Amount or Value: _____

iii. Method (e.g., mail, at visit): _____

iv. Timing of Payments: (e.g., every visit, each month): _____

v. Maximum Amount of Compensation per Participant: _____

18. Benefits

Describe the potential benefits of the research. **Music could be a cost-effective way to lower sedation requirements, decrease the stress response to surgery and improve patient experience and satisfaction during total knee arthroplasty surgery. With lower sedation requirements, patients may recover sooner, which could impact their recovery in a favorable manner.**

19. Risks - in nontechnical, lay language

a. List the known risks for participants as a result of participation in the research. This should not include the minimal risk of loss of confidentiality. However, it should include any physical, psychological, social, economic, and/or legal risks. If there is a greater than minimal risk of loss of confidentiality describe why this is so. Do not list risks associated with the standard-of-care procedures.

NOTE: Risks included here should be included in the consent form or information sheet, as applicable.

Assessment of Level of Risk: Minimal risk. Participants in this study have the risk associated with wearing headphones, including discomfort from the headphones, dysphoria from music selection.

b. Estimate the frequency, severity, and reversibility of each risk listed.

Patients will be encouraged to communicate with their anesthesia provider if they are experiencing discomfort from the headphones or music choice.

c. Is this a therapeutic study or intervention? ☒Yes ☐No

If Yes, complete i.-iii.

i. Describe the standard of care in the setting where the research will be conducted: **The standard of care during total knee replacement under spinal anesthesia is currently sedation intraoperatively. This study will test the therapeutic effects of adding music via headphones to the intraoperative experience of the patient.**

ii. Describe any other alternative treatments or interventions: **None**

iii. Describe any withholding of, delay in, or washout period for standard of care or alternative treatment that participants may be currently using: **None**

d. Do you foresee that participants might need additional medical or psychological resources as a result of the research procedures/interventions? ☐Yes ☒No

If Yes, describe the provisions that have been made to make these resources available. _____

e. Do the benefits or knowledge to be gained outweigh the risks to participants? ☒Yes ☐No

If No, provide justification for performing the research: _____

20. Precautions/Minimization of Risks

a. Describe precautions that will be taken to avoid risks and the means for monitoring to detect risks.
Patients will be encouraged to communicate with their anesthesia provider if they are experiencing discomfort from the headphones or music choice. Headphones will be sanitized between uses, using the standard of care cleaning of other monitors in the operating room.

A data and safety monitoring plan will be implemented by Drs. Kukreja and MacBeth to ensure that there are no changes in the risk/benefit ratio during the course of the study and that confidentiality of research data is maintained. This will be achieved by close following of study participants to screen for adverse events and interim results analysis during data collection phase. Investigators and study personnel will meet either electronically or in person, monthly (more often if needed) during active participant enrollment to discuss the study (e.g., study goals and modifications of those goals; subject recruitment and completion; progress in data coding and analysis; documentation, identification of adverse events or research subject complaints; violations of confidentiality) and address any issues or concerns at that time.

If the protocol involves drugs or devices skip Items 20.b. and 20.c. and go to Item 21. Instead include this information in the Drug Review Sheet or Device Review Sheet, as applicable.

b. If hazards occur to an individual participant, describe (i) the criteria that will be used to decide whether that participant should be removed from the protocol; (ii) the procedure for removing such participants when necessary to protect their rights and welfare; and (iii) any special procedures, precautions, or follow-up that will be used to ensure the safety of other currently enrolled participants.
If patients who have been enrolled in the study cannot tolerate wearing the intraoperative headphones, they will be removed from the study. Patient request to be removed from the study at any time during the procedure will be adequate for immediate withdrawal from the study.

c. If hazards occur that might make the risks of participation outweigh the benefits for all participants, describe (i) the criteria that will be used to stop or end the entire protocol and (ii) any special procedures, precautions, or follow-up that will be used to ensure the safety of currently enrolled participants.
We anticipate very few risks involved with this study. However, we will closely monitor all study patients. If at any time, this study presents risks to the patients other than the mild anticipated risks listed above, measures will be taken to modify the procedure to ameliorate these risks. If unacceptable risks cannot be eliminated, the study will be stopped.

A data and safety monitoring plan will be implemented by Drs. Kukreja and MacBeth to ensure that there are no changes in the risk/benefit ratio during the course of the study and that confidentiality of research data is maintained. This will be achieved by close following of study participants to screen for adverse events and interim results analysis during data collection phase. Investigators and study personnel will meet either electronically or in person, monthly (more often if needed) during active participant enrollment to discuss the study (e.g., study goals and modifications of those goals; subject recruitment and completion; progress in data coding and analysis; documentation, identification of adverse events or research subject complaints; violations of confidentiality) and address any issues or concerns at that time.

21. Informed Consent

a. Do you plan to obtain informed consent for this protocol? ☒Yes ☐No

If Yes, complete the items below.

If No, complete and include the Waiver of Informed Consent or Waiver of Authorization and Informed Consent, as applicable.

b. Do you plan to document informed consent (obtain signatures) for this protocol? ☒Yes ☐No
If Yes, complete the items below.
If No, complete the items below **and** include the Waiver of Informed Consent Documentation.

c. How will consent be obtained? **The interviewing investigator will confirm eligibility and absence of any exclusionary criteria. Details of the study (including risks) will be explained to prospective participant to their satisfaction and consent forms will then be signed.**

d. Who will conduct the consent interview? **Principal Investigator or Co-investigators.**

e. Who are the persons who will provide consent, permission, and/or assent? **Patient or a legally authorized representative (LAR).**

f. What steps will be taken to minimize the possibility of coercion or undue influence? **Participation is voluntary, and the potential participant will have the opportunity to ask any questions or raise any concerns. The PI or Co-investigators conducting the consent interview will do nothing to coerce or unduly influence a potential study participant.**

g. What language will the prospective participant and the legally authorized representative understand? **English**

h. What language will be used to obtain consent? **English**

i. If any potential participants will be, or will have been, in a stressful, painful, or drugged condition before or during the consent process, describe the precautions proposed to overcome the effect of the condition on the consent process. If not, enter "None." **None**

j. If any protocol-specific instruments will be used in the consenting process, such as supplemental handouts, videos, or websites, describe these here and provide a copy of each. If not, enter "None." **None**

k. How long will participants have between the time they are told about the protocol and the time they must decide whether to enroll? If not 24 hours or more, describe the proposed time interval and why the 24-hour minimum is neither feasible nor practical.

Patients scheduled for total knee arthroplasty will receive a "Patient Information Sheet" on this study during their routine presurgical examination at the Highlands Preoperative Assessment Clinic (HPAC), one day to weeks prior to their surgery date. Patients arriving for same day surgery will be evaluated by the anesthesiologist in the preoperative holding area and will be given the option to enroll in the study. There is at least 24 hours between the time of the patient's visit to the HPAC and the day of surgery.

22. Procedures to Protect Privacy

Describe how you will protect the privacy interest of the participants. Include how you will make sure others cannot overhear your conversation with potential participants and that individuals will not be publicly identified or embarrassed. **All patient information is gathered during the routine pre-surgical evaluation on the day of surgery in the preoperative holding area, which consists of private patient evaluation rooms with closed doors. Patient information is gathered in a private setting in the preoperative holding area and in a HIPAA-compliant manner, in which no one else can overhear the conversation.**

23. Procedures to Maintain Confidentiality

a. Describe how you will store research data to maintain confidentiality (both paper records and electronic data), including how access is limited. If data will be stored electronically anywhere other than a server maintained centrally by UAB, identify the department and all computer systems used to store protocol-related data. **The list of patients participating in the study with their medical record numbers and dates of surgery will be kept separately and securely in a locked filing cabinet in a locked office and will be destroyed, after final data analysis, using the UAB contracted confidential shredding service. The original paper data collection forms will be disposed of using the UAB contracted confidential shredding service after the de-identified data have been transferred to the password-protected, electronic computer database. The data will only be stored in an electronic database on a clinical research drive that is located on the UAB's Department of Anesthesiology's central server. It is password protected and behind a firewall. Only the PI and limited IRB-trained personnel on the protocol will have access to the data.**

b. Will any data from this protocol be given to any person, including the subject, or any group, including coordinating centers and sponsors? ☒Yes ☐No

If Yes, complete i-iii.

i. Who will receive the data? **Information will be shared with the UAB Anesthesiology faculty and residents, and other entities within the UAB Health System for quality improvement. Information may be presented at scientific meetings, conferences or may be published.**

ii. What data will be shared? **Findings from study. Information regarding participant demographics will only be presented in aggregate form – age, sex, ASA (American Society of Anesthesiologists) status. . Additionally, results obtained from the study may be shared, including anxiety level scores, cortisol levels, and satisfaction scoring.**

iii. How will the data be identified, coded, etc.? **Information will be de-identified and will be presented in aggregate form. None of the 18 HIPAA Identifiers will be disclosed**

24. Genomic Data Sharing (GDS)

Researchers who collect genomic data as part of a NIH grant funded after January 25, 2008 may be required to submit those data to a NIH database for broad scientific sharing. See Genomic Data Sharing in the IRB Guidebook for more information.

a. Does this protocol involve the proposed submission of genetic data into genomic repositories created to share genetic information for research purposes? ☐Yes ☒No

b. Will UAB be uploading the final genomic data to the central repository (e.g., dbGaP)? ☐Yes ☐No

If Yes to both a and b, submit a Detailed Data Sharing Plan to the IRB for review. This plan should include any known data use limitations and indicate whether aggregate-level data are appropriate for general research use. For guidance see the NIH Genomic Data Sharing Policy.

c. Submit a copy of the NIH Institutional Certification Form.

To determine which certification form to include, answer i-ii.

i. Was this protocol funded prior to January 25, 2015? ☐Yes ☐No

- **If yes,** and consent will be obtained, submit the Extramural Institutional Certification - Before January 25 - With Consent.
- **If yes,** and consent will not be obtained, submit the Extramural Institutional Certification - Before January 25 - Without Consent.

ii. Was this protocol funded after January 25, 2015? ☐Yes ☒No

- **If yes,** submit the Extramural Institutional Certification - After January 25.

25. Additional Information

In the space below, provide any additional information that you believe may help the IRB review the proposed research, or enter "None." **None**

References:

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3. Ilkkaya NK, Ustun FE, Sener EB, Kaya C, Ustun YB, Koksal E, Kocamanoglu IS, Ozkan F. The effects of music, white noise, and ambient noise on sedation and anxiety in patients under spinal anesthesia during surgery. Journal of PeriAnesthesia Nursing. 2014; 29(5): 418-426.
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6. Palmer JB, Lane D, Mayo D, Schluchter M, Leeming R. Effects of music therapy on anesthesia requirements and anxiety in women undergoing ambulatory breast surgery for cancer diagnosis and treatment: a randomized controlled trial. Journal of Clinical Oncology 2015; 33(28): 3162-3170.
7. Zhang XW, Fan Y, Manyande A, Tian YK, Yin P. Effects of music on target-controlled infusion of propofol requirements during combined spinal-epidural anaesthesia. Anaesthesia 2005; 60: 990-994.
8. Tabrizi EM, Sahraei H, Rad SM, Hajizadeh E, Lak M. The effect of music on the level of cortisol, blood glucose and physiological variables in patients undergoing spinal anesthesia. EXCLI Journal 2012; 11: 556-565.
9. Covidien. BIS™ Brain Monitoring During TIVA Procedures. Accessed 16 March 2018. http://www.medtronic.com/covidien/en-us/products/brain-monitoring/bis-complete-4-channel-monitor.html

10/25/2017

Music therapy versus Control during Total Knee Replacement under Spinal Anesthesia

STATISTICAL CONSIDERATIONS

General Data Analysis Plan: All demographic and clinical variables with continuous measures will be expressed as means and standard deviations; categorical factors will be expressed as proportions. For non-normal data, the medians and inter quartile ranges will be displayed. The distribution of the continuous factors will be examined using the Kolmogorov-Smirnov test. For data that are normally distributed, the one-way ANOVA and Student's t-test will be used to compare groups of data. For data that are not normally distributed, the Kruskal-Wallis and Mann-Whitney tests will be used for comparisons. Chi-square and Fisher's exact tests will be used to analyze categorical data. For all comparisons, a value of $p < 0.05$ will be considered statistically significant.

Primary Outcome Analysis: Statistical analyses will be performed using SAS for Windows, version 9.2. Student's t-test will be used to compare score from preoperative and postoperative STAI assessment, intraoperative propofol use, and to compare patient satisfaction.

Statistical Power and Sample Size Estimates (if applicable) : Sample size (100) was determined using a Cohen's d table assuming a mean STAI anxiety score of 35 (SD = 10) on a scale of 20-80 for control subjects. A difference of STAI score of 5 between two study groups will be clinically relevant. A sample of 50 participants (25 patients per group) will have approximately 85% power to detect a reduction in anxiety score difference of 5 with significance level alpha of 0.05.