PennState

HRP-592 - Protocol for Human Subject Research with Use of Test Article(s)

Protocol Title:

Preoperative application of low-level microcurrent dressing (Jumpstart) for decolonization of *P. acnes* before shoulder surgery

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Table of Contents

1.0 Objectives

1.1 Study Objectives

To evaluate the efficacy of preoperative treatment with a novel, wireless, low-level microcurrent-generating antimicrobial device (brand name: JumpStart) in preventing the spread of *Propionibacterium acnes* in patients receiving open or arthroscopic shoulder surgery. Vomaris distributes Procellera ™ AMT (advanced microcurrent technology) under the name Jumpstart™, exclusively through Arthrex, Inc. The FDA 510 documentation for Vomaris Procellera is attached in a separate document (as well as documentation regarding the distribution through Arthrex).

1.2 Primary Study Endpoints

The primary outcome measures the intraoperative culture results (e.g. positive vs negative, days to positive conversion) for *P. acnes* by evaluating bacterial cultures from punch skin biopsies at the time of the surgery. Any change in the condition of the biopsied area will be recorded and followed, including infections, as part of the routine care visits.

1.3 Secondary Study Endpoints

No secondary endpoints

2.0 Background

2.1 Scientific Background and Gaps

The spread of multi-drug resistant bacteria and financial burden of periprosthetic joint infection exacerbate the need for treatments to address pathogenic contamination and expedite healing. Although rare, these infections can place a great financial burden on the health care system and are often associated with increased hospital length of stay, compromised function, reduced quality of living, and increased likelihood of follow-up surgeries. Bacterial infection can further compound this problem with the widespread, prolonged use of prolonged antimicrobial prophylaxis. It is know that there is a high frequency of infections after open and arthroscopic shoulder surgery caused by *Propionibacterium acnes*. Because P. acnes normally colonizes under the epidermal layer in sebaceous glands, topical skin preparations, skin cleansers, and antibiotics may be unable to completely penetrate the deep layers of the skin to eradicate its colonization in all layers of the skin.

Lee et al. (2014) showed how *P. acnes*, which normally resides in the skin, can continue to persist in the skin despite standard surgical preparation. Ten healthy male subjects had received skin preparation of their upper back with ChloraPrep (2% chlorhexidine gluconate and 70% isopropyl alcohol) and two 3-mm dermal punch biopsy specimens were subsequently obtained. These dermal cultures were positive for P. acnes in 7 out of 10 subjects, where 4 subjects had *P. acnes* grow from 1 of 2 biopsies taken, whereas 3 subjects had it grown on 2 of 2 biopsies taken. This study showed how *P. acnes* persists in dermal tissue even with surface skin preparation that is considered standard in orthopedic surgery, at much higher rate than previously reported.

Namdari et al. (2017) studied the efficacy and safety of preoperative oral administration of doxycycline in decolonizing *P. acnes* from the skin over the shoulder in a randomized controlled trial. Patients, who were prospectively undergoing shoulder arthroscopy, were randomized in either the drug group (n=37) or standard of care (no drug) group (n=37), where the drug group administered oral doxycycline for 7 days before the surgery. Before the surgery, 2 separate 3-mm punch biopsy specimens were obtained from the sites of the anterior and posterior arthroscopic portals and were sent for culture in anaerobic and aerobic medium held for 13 days. Results showed that 22 patients in the no-drug group had at least 1 positive dermal culture, where 10 patients had 1 positive culture and 12 had 2 positive cultures. 16 patients in the drug group had at least 1 positive dermal culture, where 6 patients had 1 positive culture and 10 had 2 positive cultures. This data showed that the administration of oral doxycycline for 7 days before the did not reduce the colonization of P. acnes in a significant manner.

A novel, wireless, low-level microcurrent-generating antimicrobial device has been observed, in vitro, to exhibit electricidal effect in the presence of antibiotic and multidrug resistant clinical wound isolates. These energy-based systems were originally employed to augment wound healing process, reduce infection, and address edema and pain in the recent decades. Low-level microcurrents have been recently expanded into the orthopedic space as a bacterial growth inhibitor both in vitro and in vivo. Procellera (JumpStart) is a sterile single layer dressing consisting of a matrix of alternating silver (Ag) and zinc (Zn) dots that are held in positions on a polyester substrate with biocompatible binder. Dressing is then activated in the presence of a conductive fluid, which may come from wound exudate or exogenous fluids, such as saline.

Many studies have been done already on the wound healing and pain management properties of JumpStart, but only few have explored its bactericidal properties. Below is the summary of current literature related to this topic. The first study didn't look particularly at the antimicrobial effects, but rather the overall benefit of these microcurrent-generating dressings on patients who received knee replacements. The second study summarizes the *in vitro* antimicrobial properties of the dressings against various drug-resistant bacteria.

Chow (2016) performed a single-institution chart review to see the benefit of novel microcurrent-generating antimicrobial dressing (MCD) on patients who received total knee arthroplasty. The study was conducted on 92 patients who were all treated with MCD as a postoperative treatment from 2010 to 2013. MCD was applied using aseptic technique, directly on top of the adhesive skin closure strips, and was electrically activated and maintained moist by saturating with sterile hydrogel upon application. MCD was then covered with semi-occlusive dressing to secure it in place and to maintain a moist healing environment. Dressings were scheduled to be removed after a week post-procedure.

The results show that the use of MCD as an adjunct to standard surgical closure methods is safe and effective. The mean length of stay at the hospital was ~2.3 days, the mean length of treatment with MCD was ~8.3 days, and the mean follow-up time was 341 (+/- 177 days). There was no infection observed, compared to 1.6% reported without MCD (found in literature), and the 30-day post-operative readmission rate was 2%, compared to 4% reported without MCD (found in literature). Knee Society Score function showed statistically significant improvements post-operatively, with a mean 6-month score of 75 (+/- 20.3) and mean improvement of 36.3 (+/- 21.1).

Kim et al. (2014) studied the *in vitro* efficacy of the antibacterial properties of bioelectric dressings containing silver and zinc against clinical wound isolates having unknown antibiotic resistance, including beta-lactamase (ESBL) bacteria, multidrug-resistant (MDR) bacteria, and methicillin-resistant *Staphylococcus aureus* (MRSA). Except for the *E. faecalis* isolates, all types of clinical bacterial isolates were killed completely within 24 hours of exposure to the bioelectric wound dressing, indicating the dressing has broad-spectrum bactericidal activity. For potential bacteriostatic *Enterococcus* isolates were also tested to determine how such isolates would react to longer incubation times of up to 48 hours. With the exception of *E. raffinosus* isolate, all the Enterococcus bacterial isolates had slightly decreased growth at 48 hours compared to with those exposed to the bioelectric wound dressing for 24 hours. The authors hypothesize that the Ag-Zn resistance in *Enterococcus* species may depend on the activation of endogenous silver and/or zinc efflux systems.

To date, no MRSA strains have been found to possess Ag-resistant genes, and there is no known mechanism of bacterial resistance to all heavy metal ions. However, studies have suggested that the widespread and uncontrolled use of Ag+ in wound care may result in more bacteria developing resistance.

2.2 Previous Data

No preliminary data.

2.3 Study Rationale

From current literature search, there is no study that evaluates the antimicrobial prophylaxis of microcurrent-generating antimicrobial dressings (e.g. JumpStart) for shoulder procedures in vivo.

3.0 Inclusion and Exclusion Criteria

3.1 Inclusion Criteria

- 18 years old or older
- Scheduled to receive open or arthroscopic shoulder surgery

3.2 Exclusion Criteria

- 17 years old or younger
- Pregnant women
- Prisoners
- Non-English speaking or unable to understand consent
-
- History of previous shoulder infection or clinical signs of preoperative infection
- History of taking any antibiotic(s) within 4 weeks prior to the scheduled shoulder surgery
- History of allergy to zinc and silver
- No lesions, active acne or skin inflammatory disorders (psoriasis, eczema, etc.) in either shoulder

3.3 Early Withdrawal of Subjects

3.3.1 Criteria for removal from study

Patients will be removed from the study if reasons for safety or if the patient wishes to withdraw from the study.

3.3.2 Follow-up for withdrawn subjects

Patients withdrawn for any reason will be followed up as the standard of care protocol.

4.0 Recruitment Methods

4.1 Identification of subjects

Patients will be identified in the Orthopedics Clinic for indications of open or arthroscopic shoulder surgery. Patients will be asked to join the study if they meet the selection criteria and agree to the plan of care with the microcurrent-generating antimicrobial dressing.

4.2 Recruitment process

Patients will be recruited in the clinic for the study. The shoulder and elbow surgeons will provide the purpose and information of the study to the patient. An investigator will consent patients to the study if they wish to join.

4.3 Recruitment materials

NA

4.4 Eligibility/screening of subjects

Patients will be identified in clinic during their standard of care visit.

5.0 Consent Process and Documentation

5.1 Consent Process

5.1.1 Obtaining Informed Consent

5.1.1.1 Timing and Location of Consent

Written consent will be obtained in the clinic with each patient

5.1.1.2 Coercion or Undue Influence during Consent

An investigator will obtain consent for involvement in the study in the clinic. The investigator will express that this is an academic study and patient involvement is not necessary to their care. The patient has full right to choose to be involved with the study or to decline and it will not affect their care.

5.1.2 Waiver or alteration of the informed consent requirement

Waiver of informed consent is requested to review patients' medical records to identify potential subjects. There is no more than minimal risk to the privacy or welfare of included subjects in this retrospective research study. Data will be entered into study databases only. Only approved investigators may perform the retrospective data collection. No active research intervention is taking place.

5.2 Consent Documentation

5.2.1 Written Documentation of Consent

Written consent form is attached to this IRB submission

5.2.2 Waiver of Documentation of Consent (Implied consent, Verbal consent, etc.)

N/A

5.3 Consent – Other Considerations

5.3.1 Non-English Speaking Subjects

Patients who are non-English speakers will be excluded from this study.

5.3.2 Cognitively Impaired Adults

5.3.2.1 Capability of Providing Consent

Patients not able to provide consent will be excluded. Whether the patient is able to provide informed consent will be decided by the PI.

5.3.2.2 Adults Unable To Consent

N/A

5.3.2.3 Assent of Adults Unable to Consent

N/A

5.3.3 Subjects who are not yet adults (infants, children, teenagers)

5.3.3.1 Parental Permission

N/A

5.3.3.2 Assent of subjects who are not yet adults

N/A

6.0 HIPAA Research Authorization and/or Waiver or Alteration of Authorization

6.1 Authorization and/or Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

Check all that apply:

☐ **Not applicable, no identifiable protected health information (PHI) is accessed, used or disclosed in this study.** *[Mark all parts of sections 6.2 and 6.3 as not applicable]*

☒ **Authorization will be obtained and documented as part of the consent process.** *[If this is the only box checked, mark sections 6.2 and 6.3 as not applicable]*

☒ **Partial waiver is requested for recruitment purposes only (Check this box if patients' medical records will be accessed to determine eligibility before consent/authorization has been obtained).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Full waiver is requested for entire research study (e.g., medical record review studies).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Alteration is requested to waive requirement for written documentation of authorization (verbal authorization will be obtained).** *[Complete all parts of sections 6.2 and 6.3]*

6.2 Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

6.2.1 Access, use or disclosure of PHI representing no more than a minimal risk to the privacy of the individual

6.2.1.1 Plan to protect PHI from improper use or disclosure

Information is included in the "Confidentiality, Privacy and Data Management" section of this protocol.

6.2.1.2 Plan to destroy identifiers or a justification for retaining identifiers

Identifiers will be destroyed when the PI closes the study.

6.2.2 Explanation for why the research could not practicably be conducted without access to and use of PHI

The medical record will be reviewed during the clinic visit to determine eligibility.

6.2.3 Explanation for why the research could not practicably be conducted without the waiver or alteration of authorization

Waiver to view the medical record is necessary to determine eligibility.

6.3 Waiver or alteration of authorization statements of agreement

Protected health information obtained as part of this research will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other permitted uses and disclosures according to federal regulations.

The research team will collect only information essential to the study and in accord with the 'Minimum Necessary' standard (information reasonably necessary to accomplish the objectives of the research) per federal regulations.

Access to the information will be limited, to the greatest extent possible, within the research team. All disclosures or releases of identifiable information granted under this waiver will be accounted for and documented.

7.0 Study Design and Procedures

7.1 Study Design

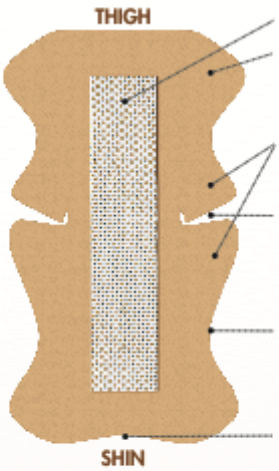
Thirty patients will be identified in the clinic with indications for open or arthroscopic shoulder surgery. Patients will be informed about the current prospective study and written consent will be obtained. Both shoulders of each patient will be included for the study; the surgical side shoulder will serve as a "Treatment shoulder" while the normal non-operative contralateral shoulder will serve as a "Control shoulder". All patients will receive a wireless, low-level microcurrent-generating antimicrobial dressing (JumpStart® Antimicrobial Wound Dressing, Arthrex, Inc., Naples, Florida, USA) (Figure 1) and hydrogel on the posterior aspect of their Treatment shoulder 2 days prior to their surgery. A small amount of hydrogel will be applied to the undersurface of JumpStart dressing. The adhesive dressing will make the JumpStart stick to the skin. The dressing will be kept on the shoulder until the time the patient is transferred to the operating room on the day of surgery. The dressing will be applied by a member of the research team at clinic. Upon transfer to the operating room on the day of surgery, the JumpStart dressing will be removed from the Treatment shoulder. All patients will receive routine preoperative IV antibiotics (either Cefazolin or Clindamycin) at least 5 minutes prior to skin incision and a routine operative skin preparation for both shoulders using standard, alcohol-based preparation (ChloraPrep, 2% chlorhexidine gluconate and 70% isopropyl alcohol; Enturia, El Paso, TX, USA) immediately before skin incision in the operating room.

At the time of the surgery, 2 separate 3-mm punch biopsy specimens will be taken from the posterior shoulder skin of both shoulders using a disposable biopsy punch (Disposable Biopsy Punch; Robbins Instruments, Chatham, NJ, USA) (Figure 2) . The biopsy sites will be closed with an adhesive tape (Steri-Strip, 3M, Maplewood, MN, USA) and covered with a routine gauze dressing. Samples will be transferred directly into separate sterile specimen containers from the biopsy punches using clean, sterile forceps. Specimens will then be transferred directly to a single laboratory for culture. Anaerobic and aerobic culture substrates will be used and held for 14 days for *P. acnes* only, given literature that shows *P. acnes* can grow on either substrate. Anaerobic culture plates will be incubated for 4 days and broth cultures for 14 days before concluding that the final report is negative. To serve as a "negative control," while wearing sterile gloves, in the first 20 patients, a sterile culture swab will be opened in the operating room, wiped through the air, and sealed in a specimen container. Chocolate plate will serve as a settle plate in the OR suite for 10 minutes and incubated for 4 days. Data will include demographic data of patients, positive culture rates, and the number of days before resulting in positive culture. All culture results will be reviewed and the patient will be marked positive if any of the cultures were positive. Patients will be scheduled for postoperative, routine follow-up visits. The rest of patient care will follow our current routine standard care without any modifications or interventions.

JUMPSTART® ANTIMICROBIAL WOUND DRESSING

JumpStart
ADVANCED MICROCURRENT TECHNOLOGY®

New Knee Dressing



Bioelectric Technology

High-Performance Adhesive
- Stretchable for enhanced mobility
- Water-resistant
- Designed for multiday wear time

Fit Flaps
- Adapt to patellar contours
- Seal and protect

Bend Reliefs
- Maximizes range of motion
- Minimizes potential for shear force

Side Contours
- Universal fit to diverse anatomy
- Minimize wrinkling

Shin Contour
- Gap-free fit

Shorter overall dressing length for improved fit and mobility.

New Energel™ Wound Hydrogel

- Compatible with JumpStart antimicrobial wound dressing
- Maintains JumpStart wound dressing's electric field for 5- to 7-day wear time
- Creates a moist wound environment
- Double packaged sterile sachet for use in operating room
- Nonwasteful 7.5 g sachet for true single use
- Available in a box of 10 sachets

Arthrex®
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To order, call 1.800.934.4404

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*Utility and design patents pending
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Figure 2

7.2 Study Procedures

7.2.1 Pre-operation

Patient will be seen in the outpatient clinic during their standard of care 1 week pre-operation visit. Patient will be provided information about the study, consented, and recruited to the study. Following the consent, patients will have a research visit scheduled 2 days before surgery to have the JumpStart dressing material applied to their operative shoulder by a member of the research team. The JumpStart dressing will be kept until the day of surgery. Excessive hair will be removed from the dressing site at the time of dressing application to ensure a secure dressing attachment. All patients will receive standard of care pre-operation routine skin care instructions during the visit as all patients receive having this type of surgery.

7.2.2 Post-operation

Patients will follow our current routine standard care follow-up protocol for each surgical procedure. The biopsy sites will be carefully examined by the PI or his patient care team to ensure proper healing upon each postoperative return visit. The first postoperative visit is at 2 weeks after surgery. Any wound problems such as bleeding, drainage, abnormally increased pain, feeling of local warmth, erythema, and abnormal swelling will be immediately reported to the PI or his patient care team. The duration of the post-operation routine care follow-up can take place between a few weeks to several months depending on the procedure. The culture results will be obtained within 14 days post-operation. Any change in the condition of the biopsied area will be recorded and followed, including infections, as part of the routine care visits.

7.3 Duration of Participation

Patients will be involved in this study only during the time of their shoulder surgery, which include pre-operation consent and post-operation routine follow-up. Pre-operation consent will mark the beginning of the patients' participation and will take place approximately 1 week before the surgery. The patients will use the dressing only during this pre-operation period. The pre-operative visit will take approximately 30 minutes. Application of the dressing in clinic will take approximately 30 minutes. The skin biopsies in the operating room will take about 5 minutes to obtain. The duration of the post-operation routine care follow-up can take place between a few weeks to several months depending on the procedure. The culture results will be obtained within 14 days post-operation. Any change in the condition of the biopsied area will be recorded and followed, including infections, as part of the routine care visits.

7.4 Test Article(s) (Study Drug(s) and/or Study Device(s))

7.4.1 Description

In each patient, the Treatment shoulder will receive preoperative applications of a wireless, low-level microcurrent-generating antimicrobial device (JumpStart® Antimicrobial Wound Dressing, Arthrex, Inc., Naples, Florida, USA) 2 days prior to their surgery. The control will not receive this treatment. On the day of surgery, in the operating room, both shoulders will receive preoperative applications of standard, alcohol-based preparation (ChloraPrep, 2% chlorhexidine gluconate and 70% isopropyl alcohol; Enturia, El Paso, TX, USA) immediately before the surgery. JumpStart is a broad-spectrum antimicrobial wound dressing featuring Advanced Microcurrent Technology™. Embedded in the dressing are microcell batteries made of elemental silver and zinc applied in a dot-matrix pattern to a polyester substrate. In the presence of a conductive medium such as wound exudate, water-based hydrogels or saline, microcurrents are generated at the dressing surface, due to its inherent design.

7.4.2 Treatment Regimen

The dressings will be applied over the posterior aspect of the shoulder above the posterior axilla.

7.4.3 Method for Assigning Subject to Treatment Groups

NA

7.4.4 Subject Compliance Monitoring

7.4.5 Blinding of the Test Article

N/A

7.4.6 Receiving, Storage, Dispensing and Return

7.4.6.1 Receipt of Test Article

All of the standard-of-care alcohol-based prep, iodine-barrier drapes are already available both at the main operating rooms and HOSC operating rooms. The alcohol-based prep and iodine-barrier drapes have been routinely used for shoulder cases in the main operating rooms and HOSC operating rooms. The JumpStart dressing has been used in standard of care, select cases for immediate postoperative dressing and is available in the main operating room.

For this study, we will purchase JumpStart dressings from the vender (Arthrex, Naples, FL) using the PI's personal research fund. Each package will contain 8" x 8" Antimicrobial Wound Dressing that can be cut to fit surgical sites and shape conforms easily to body contours for patient comfort.

7.4.6.2 Storage

The dressing will be stored in dry conditions at controlled room temperature, protected from light. Controlled room temperature is 20°C to 25°C (68°F to 77°F). Excursions are permitted between 15°C and 30°C (59°F and 86°F). Brief exposure to temperatures up to 40°C (104°F) may be tolerated provided the mean kinetic temperature does not exceed 25°C (77°F); however, such exposure will be minimized.

Dressing will be stored in a locked office 30 Hope Drive, Suite 2900 in a locked metal cabinet, separated from other clinical supplies, in the Clinical Research

Office. The room is temperature controlled, and its temperature will be monitored via the thermostat and recorded on a temperature log daily.

7.4.6.3 Preparation and Dispensing

The application of the dressings will be prepared and administered by an investigator on the study team in clinic from the research supply. The dressing will be disposed according to local environmental procedures.

7.4.6.4 Return or Destruction of the Test Article

N/A

7.4.6.5 Prior and Concomitant Therapy

The dressing cannot be applied in conjunction with topical agents such as antimicrobial ointments, enzymatic debriders, antibiotic creams or ointments, silver- or zinc-containing creams, oxidizing agents, or petroleum-based products. The dressing must be removed during energy-based procedures (e.g. radiofrequencies, ultrasound, or radiation) where the dressing may interfere with delivery.

8.0 Subject Numbers and Statistical Plan

8.1 Number of Subjects

Thirty patients will be recruited for this study.

8.2 Sample size determination

A priori sample size calculation was performed using some of the previously published data[1,2]. Assumptions were made as follows: the primary outcome measure was the intraoperative culture results (e.g. positive, negative) for *P. acnes* by evaluating bacterial cultures from two skin biopsies obtained from the posterior aspect of the shoulder at the time of the surgery. Based on a previous study, the positive culture rate in untreated shoulders was set at 60%[5]. We set the minimally clinically significant difference (MCID) of positive culture rate at 30% (a half of 60%) as a previous study described[2]. Using a two-tailed McNemar test for two dependent groups with a power of 0.8 and an alpha of 0.05, the priori sample size calculation suggested a total of 30 patients for the study.

Probability		Treatment shoulder		
		Positive culture	Negative culture	
Control shoulder	Positive culture	0.25	0.35	0.6
	Negative culture	0.05	0.35	0.4
		0.3	0.7	1

Exact - Proportions: Inequality, two dependent groups (McNemar)

Options: α balancing: α/2 on each side, approximation

Analysis: A priori: Compute required sample size

Input:	Tail(s)	=	Two
	Odds ratio	=	7
	α err prob	=	0.05
	Power (1-β err prob)	=	0.8
	Prop discordant pairs	=	0.4
Output:	Lower critical N	=	2.0000000
	Upper critical N	=	10.0000000

Total sample size	=	30
Actual power	=	0.8180007
Actual α	=	0.0385742
Proportion p12	=	0.3500000
Proportion p21	=	0.0500000

8.3 Statistical methods

If at least one of the two cultures from a shoulder turns positive, that shoulder will be counted as a "positive culture" shoulder. The results of the two cultures from each shoulder will be McNemar test will be used to compare the proportions of positive culture rates between paired shoulders. Ordinal or interval Demographic data will be compared between the two groups using parametric vs nonparametric tests depending on their normality. Nominal data will be compared using Fisher's exact test or contingency table. The negative control data will be analyzed in comparison to the results of the treatment and normal control shoulders.

9.0 Confidentiality, Privacy and Data Management

See the Research Data Plan Review Form.

10.0 Data and Safety Monitoring Plan

10.1 Periodic evaluation of data

Data will be reviewed periodically by the PI for the accuracy during the data collection period.

10.2 Data that are reviewed

Previously stated data will be secured with password protection. Staff members will periodically review safety and security protocols for project.

10.3 Method of collection of safety information

The duration of the post-operation routine care follow-up can take place between a few weeks to several months depending on the procedure. The culture results will be obtained within 14 days post-operation. Any change in the condition of the biopsied area will be recorded and followed, including infections, as part of the routine care visits.

10.4 Frequency of data collection

The skin biopsies will be obtained only at the time of surgery. The biopsies will be sent to the microbiology lab for cultures. The culture results will be obtained within 14 days post-operation. No further follow up data collection will be performed directly from patients after their surgery.

10.5 Individuals reviewing the data

Research members will review data.

10.6 Frequency of review of cumulative data

Cumulative data will be reviewed once patient surveys are collected and patient information is de-identified.

10.7 Statistical tests

The proportion of positive cultures will be determined using Fisher's exact test to compare the positive culture rates. Ordinal or interval Demographic data will be compared between the two groups using parametric vs nonparametric tests depending on their normality. Nominal data will be compared using Fisher's exact test or contingency table.

10.8 Suspension of research

Research will be suspended if project is determined unsafe at any time for patients.

11.0 Risks

Loss of patient information during the project. Loss of confidentiality of paper and electronic data. Possible risks of skin biopsies include acute bleeding, localized pain, infection, scarring, and healing problems. Possible risks of dressing use include irritation, increased pain, temporary discoloration of the skin, and allergic reactions to silver or zinc.

12.0 Potential Benefits to Subjects and Others

12.1 Potential Benefits to Subjects

Microcurrent-generating antimicrobial device has been observed, in vitro, to exhibit bactericidal effect in the presence of antibiotic and multidrug resistant clinical wound isolates. Antimicrobial prophylaxis using this device can reduce length of hospital stay, compromised function, and financial burden while increasing quality of living.

12.2 Potential Benefits to Others

Preventing periprosthetic joint infection post-operation can reduce financial burden on the health care system and prevent unnecessary, prolonged use of antibiotics as antimicrobial prophylaxis.

13.0 Sharing Results with Subjects

The patients will be notified if infections are suspected and will be followed up with appropriate revision surgery or any required additional procedures for infections.

14.0 Subject Stipend (Compensation) and/or Travel Reimbursements

No compensation will be provided for this study.

15.0 Economic Burden to Subjects

15.1 Costs

No cost to the patients.

15.2 Compensation for research-related injury

It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Costs for the treatment of research-related injuries will be charged to subjects or their insurance carriers.

16.0 Resources Available

16.1 Facilities and locations

Recruitment will occur at Penn State Bone and Joint Institute or Penn State Camp Hill office. Eligible patients will be identified at clinic during their clinical encounter with Dr. Kim. All surgeries will be done at Hershey Medical Center and HOSC.

16.2 Feasibility of recruiting the required number of subjects

This project aims to recruit 30 patients for this study. Patients will be followed up by the Department of Orthopedics. Patients who decline participation in the study will be removed and a new patient will be recruited.

16.3 PI Time devoted to conducting the research

PI has dedicated research days to ensure time to complete project.

16.4 Availability of medical or psychological resources

Orthopedics clinic will schedule patients if they require an appointment during this study.

16.5 Process for informing Study Team

Team members have monthly meetings in person to review protocols.

17.0 Other Approvals

17.1 Other Approvals from External Entities

No additional approvals required.

17.2 Internal PSU Committee Approvals

Check all that apply:

☒ Anatomic Pathology – Hershey only – Research involves the collection of tissues or use of pathologic specimens. Upload a copy of HRP-902 - Human Tissue For Research Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ Animal Care and Use – All campuses – Human research involves animals and humans or the use of human tissues in animals

☐ Biosafety – All campuses – Research involves biohazardous materials (human biological specimens in a PSU research lab, biological toxins, carcinogens, infectious agents, recombinant viruses or DNA or gene therapy).

☐ Clinical Laboratories – Hershey only – Collection, processing and/or storage of extra tubes of body fluid specimens for research purposes by the Clinical Laboratories; and/or use of body fluids that had been collected for clinical purposes, but are no longer needed for clinical use. Upload a copy of HRP-901 - Human Body Fluids for Research Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ Clinical Research Center (CRC) Advisory Committee– All campuses – Research involves the use of CRC services in any way.

☒ Conflict of Interest Review – All campuses – Research has one or more of study team members indicated as having a financial interest.

☐ Radiation Safety – Hershey only – Research involves research-related radiation procedures. All research involving radiation procedures (standard of care and/or research-related) must upload a copy of HRP-903 - Radiation Review Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ IND/IDE Audit – All campuses – Research in which the PSU researcher holds the IND or IDE or intends to hold the IND or IDE.

☒ Scientific Review – Hershey only – All investigator-written research studies requiring review by the convened IRB must provide documentation of scientific review with the IRB submission. The scientific review requirement may be fulfilled by one of the following: (1) external peer-review process; (2) department/institute scientific review committee; or (3) scientific review by the Clinical Research Center Advisory committee. NOTE: Review by the Penn State Hershey Cancer Institute Scientific Review Committee is required if the study involves cancer prevention studies or cancer patients, records and/or

tissues. For more information about this requirement see the IRB website at:
http://www.pennstatehershey.org/web/irb/home/resources/investigator

18.0 Multi-Site Research

18.1 Communication Plans
Not a multi-site research project.

18.2 Data Submission and Security Plan
Not a multi-site research project.

18.3 Subject Enrollment
Not a multi-site research project.

18.4 Reporting of Adverse Events and New Information
Not a multi-site research project.

18.5 Audit and Monitoring Plans
Not a multi-site research project.

19.0 Adverse Event Reporting

19.1 Adverse Event Definitions

For drug studies, incorporate the following definitions into the below responses, as written:	
Adverse event	Any untoward medical occurrence associated with the use of the drug in humans, whether or not considered drug related
Adverse reaction	Any adverse event caused by a drug
Suspected adverse reaction	Any adverse event for which there is a reasonable possibility that the drug caused the adverse event. Suspected adverse reaction implies a lesser degree of certainty about causality than "adverse reaction". • *Reasonable possibility.* For the purpose of IND safety reporting, "reasonable possibility" means there is evidence to suggest a causal relationship between the drug and the adverse event.
Serious adverse event or Serious suspected adverse reaction	Serious adverse event or Serious suspected adverse reaction: An adverse event or suspected adverse reaction that in the view of either the investigator or sponsor, it results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.
Life-threatening adverse event or life-threatening suspected adverse reaction	An adverse event or suspected adverse reaction is considered "life-threatening" if, in the view of either the Investigator (i.e., the study site principal investigator) or Sponsor, its occurrence places the patient or research subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that had it occurred in a more severe form, might have caused death.
Unexpected adverse event or Unexpected	An adverse event or suspected adverse reaction is considered "unexpected" if it is not listed in the investigator brochure, general investigational plan, clinical protocol, or elsewhere in the current IND application; or is not listed at the

suspected adverse reaction.	specificity or severity that has been previously observed and/or specified.

For device studies, incorporate the following definitions into the below responses, as written:	
Unanticipated adverse device effect	Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or IDE application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

19.2 Recording of Adverse Events

All adverse events (serious or non-serious) and abnormal test findings observed or reported to study team believed to be associated with the study drug(s) or device(s) will be followed until the event (or its sequelae) or the abnormal test finding resolves or stabilizes at a level acceptable to the investigator.

An abnormal test finding will be classified as an adverse event if one or more of the following criteria are met:

- The test finding is accompanied by clinical symptoms
- The test finding necessitates additional diagnostic evaluation(s) or medical/surgical intervention; including significant additional concomitant drug treatment or other therapy

NOTE: Simply repeating a test finding, in the absence of any of the other listed criteria, does not constitute an adverse event.

- The test finding leads to a change in study drug dosing or discontinuation of subject participation in the clinical research study

The test finding is considered an adverse event by the investigator.

19.3 Causality and Severity Assessments

The investigator will promptly review documented adverse events and abnormal test findings to determine 1) if the abnormal test finding should be classified as an adverse event; 2) if there is a reasonable possibility that the adverse event was caused by the study drug(s) or device(s); and 3) if the adverse event meets the criteria for a serious adverse event.

If the investigator's final determination of causality is "unknown and of questionable relationship to the study drug(s) or device(s)", the adverse event will be classified as associated with the use of the study drug(s) or device(s) for reporting purposes. If the investigator's final determination of causality is "unknown but not related to the study drug(s) or device(s)", this determination and the rationale for the determination will be documented in the respective subject's case history.

19.4 Reporting of Adverse Reactions and Unanticipated Problems to the FDA

19.4.1 Written IND/IDE Safety Reports

N/A

19.4.2 Telephoned IND Safety Reports – Fatal or Life-threatening Suspected Adverse Reactions

N/A

19.5 Reporting Adverse Reactions and Unanticipated Problems to the Responsible IRB

In accordance with applicable policies of The Pennsylvania State University Institutional Review Board (IRB), the investigator will report, to the IRB, any observed or reported harm (adverse event) experienced by a subject or other individual, which in the opinion of the investigator is determined to be

(1) unexpected; and (2) probably related to the research procedures. Harms (adverse events) will be submitted to the IRB in accordance with the IRB policies and procedures.

19.6 Unblinding Procedures

The patients will be notified if infections are suspected and will be followed up with appropriate revision surgery or any required additional procedures for infections. In such scenario, the patient will be unblinded to explain the procedural/cautionary steps taken to address the serious adverse event.

19.7 Stopping Rules

Patients should stop using the dressing and consult the PI if allergy, irritation, increased pain, maceration, or any irregular skin discoloration occurs.

20.0 Study Monitoring, Auditing and Inspecting

20.1 Study Monitoring Plan

20.1.1 Quality Assurance and Quality Control

The investigator will permit study-related monitoring, audits, and inspections by the Penn State quality assurance program office(s), IRB, the sponsor, and government regulatory bodies, of all study related documents (e.g., source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g., pharmacy, diagnostic laboratory, etc.).

20.1.2 Safety Monitoring

N/A

21.0 Future Undetermined Research: Data and Specimen Banking

21.1 Data and/or specimens being stored

N/A

21.2 Location of storage

N/A

21.3 Duration of storage

N/A

21.4 Access to data and/or specimens

N/A

21.5 Procedures to release data or specimens

N/A

21.6 Process for returning results

N/A

22.0 References

1. Chow J. Wireless microcurrent-generating antimicrobial wound dressing in primary total knee arthroplasty: a single-center experience. *Orthop Rev*. 2016;8(2):6296.
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3. Lee MJ, Pottinger PS, Butler-Wu S, Bumgarner RE, Russ SM, Matsen FA. Propionibacterium persists in the skin despite standard surgical preparation. *J Bone Joint Surg Am*. 2014;96(17):1447-1450. doi:10.2106/JBJS.M.01474
4. Lorenzetti, A, Wongworawat M, Jobe C, Phipatanakul W. Cyanoacrylate microbial sealant may reduce the prevalence of positive cultures in revision shoulder arthroplasty. *Clin Orthop Relat Res*. 2013; 471(10): 3225-3229
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