ANCILLARY REVIEWS

Which ancillary reviews do I need and when do I need them? Refer to HRP-309 for more information about these ancillary reviews.			
Select yes or no	**Does your study…**	*If yes…*	***Impact on IRB Review***
☐ **Yes** ☒ **No**	Include Gillette resources, staff or locations	*Gillette Scientific review and Gillette Research Administration approval is required. Contact: research@gillettechildrens.com*	**Required prior to IRB submission**
☒ **Yes** ☐ **No**	Involve Epic, or Fairview patients, staff, locations, or resources?	*The Fairview ancillary review will be assigned to your study by IRB staff Contact:* ancillaryreview@Fairview.org	**Approval must be received prior to IRB committee/ designated review.** **Consider seeking approval prior to IRB submission.**
☒ **Yes** ☐ **No**	Include evaluation of drugs, devices, biologics, tobacco, or dietary supplements or data subject to FDA inspection?	*The regulatory ancillary review will be assigned to your study by IRB staff Contact: medreg@umn.edu* *See: https://policy.umn.edu/research/indide*	
☒ **Yes** ☐ **No**	Require Scientific Review? Not sure? See guidance on next page.	*Documentation of scientific merit must be provided. Contact: hrpp@umn.edu*	
☐ **Yes** ☒ **No**	Relate to cancer patients, cancer treatments, cancer screening/prevention, or tobacco?	*Complete the CPRC application process. Contact: ccprc@umn.edu*	
☐ **Yes** ☒ **No**	Include the use of radiation? (x-ray imaging, radiopharmaceuticals, external beam or brachytherapy)	*Complete the AURPC Human Use Application and follow instructions on the form for submission to the AURPC committee. Contact: barmstro@umn.edu*	**Approval from these committees must be received prior to IRB approval;** **These groups each have their own application process.**
☐ **Yes** ☒ **No**	Use the Center for Magnetic Resonance Research (CMRR) as a study location?	*Complete the CMRR pre-IRB ancillary review Contact: ande2445@umn.edu*	
☐ **Yes** ☒ **No**	Include the use of recombinant or synthetic nucleic acids, toxins, or infectious agents?	*Complete the IBC application via eprotocol.umn.edu Contact:*	
☐ **Yes** ☒ **No**	Include the use of human fetal tissue, human embryos, or embryonic stem cells?	*Contact OBAO for submission instructions and guidance*	

☒ **Yes** ☐ **No**	Include PHI or are you requesting a HIPAA waiver?	*If yes, HIPCO will conduct a review of this protocol.* *Contact: privacy@umn.edu*	
☐ **Yes** ☒ **No**	Use data from the Information Exchange (IE)?	*The Information Exchange ancillary review will be assigned to your study by IRB staff* *Contact: ics@umn.edu*	**Approval must be received prior to IRB approval.** **These groups do not have a separate application process but additional information from the study team may be required.**
☐ **Yes** ☒ **No**	Use the Biorepository and Laboratory Services to collect tissue for research?	*The BLS ancillary review will be assigned to your study by IRB staff.* *Contact: cdrifka@umn.edu*	
☐ **Yes** ☒ **No**	Have a PI or study team member with a conflict of interest?	*The CoI ancillary review will be assigned to your study by IRB staff* *Contact: becca002@umn.edu*	
☐ **Yes** ☒ **No**	Need to be registered on clinicaltrials.gov?	*If you select "No" in ETHOS, the clinicaltrials.gov ancillary review will be assigned to your study by IRB staff* *Contact: kmmccorm@umn.edu*	
☒ **Yes** ☐ **No**	Require registration in OnCore?	*If you select "No" or "I Don't Know" in ETHOS, the OnCore ancillary review will be assigned to your study by IRB staff* *Contact: oncore@umn.edu*	**Does not affect IRB approval.**

PROTOCOL COVER PAGE

Protocol Title	Comparison of normothermia maintenance between resistive blanket and forced air warming systems in renal transplant surgery
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Scientific Assessment	HRPP facilitated scientific assessmentHRPP facilitated scientific assessment
IND/IDE # (if applicable)	N/A
IND/IDE Holder	N/A
Investigational Drug Services # (if applicable)	N/A
Version Number/Date:	Version 43: ~~January~~ June 6, 2022

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
1	9/24/2021 V2	Adding REDCap for data collection	No
2	1/06/2022 V3	Clarified 4.1, 4.2, 5.2 and 5.3; Removed safety monitoring from 15.4 that belongs in 18; added screening patients to 16; and added Oncore to 16.7	No
3	6/6/2022 V4	Remove exclusion criteria of ESRD	No

Table of Contents

ABBREVIATIONS/DEFINITIONS

FA: Forced air [warming system]

RB: Resistive blanket [warming system]

ESRD: end stage renal disease

PA: Pulmonary artery

ICU: Intensive care unit

OR: Operating room

PACU: Post-anesthesia care unit

CRNA: Certified registered nurse anesthetist

NP: Nasopharyngeal

AUC: area under the curve. In this study, the area under the curve is defined as the cumulative summation of the change in temperature from Ti multiplied by the time interval between temperature samplings. This gives a surrogate measurement in effectiveness in maintaining body temperature

DSMB: Date and safety monitoring board

1.0 Objectives

1.1 Purpose:

The purpose of the study is to compare the effectiveness of resistive blanket warming to forced air warming in maintaining body temperature in patients undergoing renal transplantation.

Secondary outcome variables also include:

- AUC of time versus temperature curves
- temperatures at set points during operative period
- Blood loss volumes

2.0 Background

2.1 Significance of Research Question/Purpose:

Patients undergoing general anesthesia are less able to maintain body temperature compared to the awake state due to several factors: 1) Warmer blood normally kept in the torso of the body and organs moves to the limbs and to the skin, where heat is lost more easily to the environment through a cold operating room, moisture evaporation, and heat loss from the patient through heat radiation; 2) The patient is also unable to maintain body temperature since shivering is reduced or abolished. Reduced body temperatures can result in blood being unable to clot appropriately in extreme circumstances, which leads to increased blood loss. The immune system function is also impaired, which results in increased infection rates. Shivering after general anesthesia to increase body temperature also increases oxygen demand of the body, which can also cause increased work of the heart, leading to heart injury. [1,2] For all of these reasons, body temperature is continuously monitored and efforts to maintain body temperature during surgery are a standard of care.

The mainstay of maintaining patient body temperature in the operating room is through active warming techniques, using conductive or convective heat transfer via specially designed blankets. Conductive warming systems work by transferring heat directly through skin contact with an electric blanket or a blanket with circulating warm water. Convective warming continuously circulates warm air at the surface of the skin through air conduits through a blanket that has small holes where the air escapes through. Typically, this forced air warming system (FAWS) is only able to warm the patient in areas where the warm air is constantly refreshed through convective air currents. [3] Areas of the skin that are in contact with the bed or above sterile drapes are not able to be warmed, since warm air cannot circulate to those regions, and becomes a particular challenge with patients who undergo cardiac surgery, since the amount of body surface area available for warming is much lower compared to other surgeries.

2.2 Preliminary Data:

None

2.3 Existing Literature:

Few studies have been done with comparing thermoregulation during prolonged transplant surgeries between different types of warming devices. One quality improvement project showed increased core temperature at ICU handoff for TAVR and open cardiac surgeries with a water-circulation device. [6] FAWS available include upper body, lower body, or under body, however we are interested in investigating whether the resistive blanket warming system (RBWS) may heat more evenly across the surface area and thereby offer advantages over FAWSs.

3.0 Study Endpoints/Events/Outcomes

3.1 Primary Endpoint/Event/Outcome:

Patient temperature at the end of surgery.

3.2 Secondary Endpoint(s)/Event(s)/Outcome(s):

- AUC of temperature vs time curve during hypothermia (core temperature less than 36℃) during the duration of surgery

  Time during surgery spent under 36 degrees through comparison of nasopharyngeal temperature, which is measured by placing a nasopharyngeal temperature probe 10 to 20 cm into the nare (standard of care) [8], between FAWS and RBWS. The study will be conducted as a superiority trial where a 0.5°C difference between the FAWS and RBWS is considered to be significant.
- Minimum body temperature upon arrival in PACU
- Maximum body temperature difference (maximum temperature minus minimum temperature) upon arrival in PACU
- First temperature upon arrive in PACU, last temperature (temperature time weighted average)
- Requiring rescue intervention which will be turning on a second, upper body warming blanket if the temperature is consistently below 35.5 degrees

4.0 Study Intervention(s)/Investigational Agent(s)

4.1 Description:

Forced air warming system (Bair Hugger, Model 635; 3M Medical, St. Paul, MN, USA)

The forced air warming system has a heater unit that blows air through a conduit to an “air blanket” that inflates with forced air that circulates throughout the

blanket, and exits through tiny perforations on the patient-side of that blanket. The heat primarily warms the subject through convective means. As the warmed air escapes through the perforations in the blanket, it creates an environment of continuously circulating warm air that is in contact with the skin. Note, however, that warmed air is only able to move over the skin surface in areas of the body that are immediately adjacent to the blanket and which are not compressing the blanket (and hence blocking airflow). In many surgical cases, the FAWS is placed above the patient so a very large fraction of the patient's skin area is exposed to warm air. Air blankets are placed under the patient by some providers in transplant cases, however, which then results in the blanket conduits then being collapsed/occluded by the weight of the patient - and warm air can circulate only under a small fraction of the patient's upper torso and legs.

The Bair Hugger blanket is the standard of care and will be billed as usual to insurance.

Resistive blanket warming system (Hotdog (U102); Augustine Surgical, Inc., Eden Prairie, MN, USA)

This blanket is equivalent to an operating-room-safe electric blanket. Through a power cord, a separate power source powers a semiconductor layer within the resistive blanket to generate heat. The heat primarily warms the subject by conductive warming through direct skin contact, and, secondarily, by warming the air around the participant in areas where there is no direct skin contact.

The participant will be placed on ether the underbody FAWS or the RBWS on the operating room table depending on which device the patient is randomized to, this will then be the main warming device during the surgery. The main warming device will be turned on once the patient is positioned on the operating table.

An additional upper body FAWS will be placed on top of the patient prior to surgery for rescue purpose and will only be utilized if normothermia cannot be achieved during the surgery with the device the patient is randomized to. During periods when the participant will need to be warmed, the additional upper body device will be switched on to generate heat in addition to the main warming device.

The Hotdog blanket will be donated by the manufacturer. The Anesthesiologist will train CRNA staff on the use of this device and will maintain continual communication with the CRNA Lead to ensure staff is aware of the study and receives proper training. A staff member from the Anesthesiology Research Office will be in charge of the inventory of the donated blankets, stored in the core of the OR department. A research team member will bring the Hotdog device to the OR prior to surgery, if the patient is randomized to Hotdog and will make sure there is a rescue Bairhugger in the OR for all patients. After the surgery, OR staff

will do their normal process of cleaning supplies, including the Hotdog, and will put the device back in the OR core.

The HotDog resistive blanket warming system is FDA approved and available for use in surgery.

4.2 Device Handling:

During the study, the participant will be randomized to lay on top of either the underbody forced air warming system or resistive blanket, this will be the main warming device for the patient. An additional upper body device will be placed on patients in case rescue warming is needed at the discretion of the anesthesiologist. All staff participating in patient care will be instructed that a patient's body temperature of 35.5 degrees Celsius or lower is the threshold for intervention. During periods when the participant will need to be warmed, the additional upper body device will be switched on to generate heat in addition to the main warming device.

Forced air warming blankets are single patient use only. The resistive blankets are reusable. In between use, the resistive blankets will be cleaned and disinfected per manufacturer's instructions.

4.3 Biosafety: N/A

4.4 Stem Cells: N/A

4.5 Fetal Tissue: N/A

5.0 Procedures Involved

5.1 Study Design:

Single institution, prospective, randomized, unblinded superiority study of renal transplant surgery participants, with no history of previous transplant, comparing a resistive blanket warming system (Hotdog (U102); Augustine Surgical, Inc., Eden Prairie, MN, USA) to a forced air warming system (Bair Hugger, Model 635; 3M Medical, St. Paul, MN, USA).

A randomization schedule will be developed using permuted block randomization with blocks of size 2, 4, 6, and 8 assuming 1:1 allocation within each block. Data will be analyzed using an intention-to-treat protocol.

5.2 Study Procedures:

The study will involve two arms: a resistive blanket warming system arm and a forced air warming system arm. Both devices will be set to warm the patient at each device's maximum setting at the beginning and throughout the case. The hotdog's maximum setting is 39C and the Bair Hugger's maximum setting is 41C.

The patient will be randomized to either the FAWS or RBWS before arrival to the operating room. Depending on which arm they have randomized to, the

participant will be placed on either the underbody FAWS or the RBWS. An upper body FAWS will be placed on top of the patient prior to incision but is only to be utilized if normothermia cannot be achieved during the surgery with either device. The warming system that the patient is randomized to will be set up on the table before the participant is brought to the OR and transferred to the operating room table. The main warming device will be turned on once the patient is positioned on the operating table. The CRNA's will be involved in the placement of the blankets. Surgeons, OR Nurse Managers, and CRNA's will be informed by research team regarding patient's involvement in the study.

After the needed standard monitors for surgery have been placed, general anesthesia will be induced and maintained with patient's hemodynamics and other vitals maintained per standard care (no additional measurements beyond standard of care which is recorded in EPIC). Standard anesthetic care of the participant will occur for the duration of the surgery.

Patient core temperature will be measured with a nasopharyngeal temperature probe. The patient's temperature will be monitored and recorded for the duration of surgery with the selected warming system. Vital signs, including continuous blood pressure, heart rate, oxygen saturation, and end-tidal carbon dioxide, will be monitored and recorded in Epic as is routine with all anesthetics performed. Our primary outcome variable is the NP temperature as recorded at the end of the surgery.

After the surgery, the patient will be transported to the PACU in a timely fashion. Temperature measurement in the PACU will be standardized with skin temperature probes (3M Spot-On) that will be placed on the forehead prior to leaving the operating room. If there is an unexpected delay in transporting the patient to the PACU, that will be documented and the temperature upon arrival to PACU will not be valid.

Data to be collected about participants and the source records that will be used to collect those data:

From Epic:

- Age
- Sex
- MRN
- Height
- Weight
- BMI
- Date of procedure
- Procedure performed

- Nasopharyngeal temperature throughout surgery (every minute)
- Time at warming system being switched (resistive blanket or forced air)
- Time when patient reaches 37˚C
- Time at OR departure
- Time sign-out from PACU prior to transfer to regular nursing floor
- Blood product volume administered to patient (red blood cells, fresh frozen plasma, platelets, and cryoprecipitate)
- Recorded incidence of rescue warming used for when patient's temperature is at 35.5˚C (requiring rescue means the need to turn on the additional forced air warming device that may be due to severe hypothermia and uncontrolled bleeding)

Individually Identifiable Health Information: See above

HIPAA Agreement: Attached

5.3 Study Duration:

Individual Subject Participation Duration: Patients will be in the study for their scheduled procedure and for 1 hour following their procedure. Duration of the surgical procedure, is typically 2-5 hours depending on the surgery required. Following the study, participants will not be approached at any time, for any reason as it pertains to their study participation.

Total Study Duration (all Participants): approximately 1 year

Total Study Duration Including Data Analysis: about 14 months

5.4 Use of radiation: N/A

5.5 Use of Center for Magnetic Resonance Research*:* N/A

6.0 Data and Specimen Banking

6.1 Storage and Access: The storage and access to study data will be HIPAA compliant

6.2 Data: Data will be entered in REDCAP and stored in UMN Box Secure storage. Signed Informed Consents in paper form will be stored in the Anesthesia Research Office.

6.3 Release/Sharing: Data will be stored internally within the research group. Data will not be shared with the company providing the RWBS.

7.0 Sharing of Results with Participants

7.1 Individual participant results will not be shared. High-level summary study results may be publicly available in a publication of research results in a scientific journal.

7.2 Sharing of genetic testing: N/A

8.0 Study Population

8.1 Inclusion Criteria:

- Eighteen (18) years to 90 years old
- Undergoing elective renal transplantation

8.2 Exclusion Criteria:

- Previous surgery involving organ transplantation or nephrectomy. These patients are at higher risk of blood loss, making temperature regulation subject to more variables outside our control.
- ~~End stage renal disease with decreased or no urine output from normal.~~
- Previous upper extremity amputations
- Ongoing sepsis or other infection
- Thyroid dysfunction
- Emergency surgery
- Refusal of consent to participate in study
- Pregnancy

8.3 Screening:

First, potential participant's chart in Epic will be accessed to ensure they are not "Research Opt Out" (will not be approached by research team). Participants will be seen in the preoperative holding area before surgery. Participants will be identified before the procedure either by participating anesthesiologists or transplant surgeons when an organ is available and a renal transplant surgery is scheduled. An approved member of the research team will be notified when the case is scheduled and the recipient has been sent for. This individual will then discuss the nature of the study and obtain consent. In all cases, a member of the anesthesia team will be available (either in person or via phone) to directly answer any questions that cannot be addressed by a non-physician member of the team.

9.0 Vulnerable Populations

9.1 Vulnerable Populations:

Population / Group	Identify whether any of the following populations will be targeted, included (not necessarily targeted) or excluded from participation in the study.
Children	Excluded from

	ParticipationExcluded from Participation
Pregnant women/fetuses/neonates	Excluded from ParticipationExcluded from Participation
Prisoners	Excluded from ParticipationExcluded from Participation
Adults lacking capacity to consent and/or adults with diminished capacity to consent, including, but not limited to, those with acute medical conditions, psychiatric disorders, neurologic disorders, developmental disorders, and behavioral disorders	Excluded from ParticipationExcluded from Participation
Non-English speakers	Included/Allowed to ParticipateIncluded/Allowed to Participate
Those unable to read (illiterate)	Excluded from ParticipationExcluded from Participation
Employees of the researcher	Excluded from ParticipationExcluded from Participation
Students of the researcher	Excluded from ParticipationExcluded from Participation
Undervalued or disenfranchised social group	Included/Allowed to ParticipateIncluded/Allowed to Participate
Active members of the military (service members), DoD personnel (including civilian employees)	Included/Allowed to ParticipateIncluded/Allowed to Participate

Individual or group that is approached for participation in research during a stressful situation such as emergency room setting, childbirth (labor), etc.	Included/Allowed to ParticipateIncluded/Allowed to Participate
Individual or group that is disadvantaged in the distribution of social goods and services such as income, housing, or healthcare.	Included/Allowed to ParticipateIncluded/Allowed to Participate
Individual or group with a serious health condition for which there are no satisfactory standard treatments.	Excluded from ParticipationExcluded from Participation
Individual or group with a fear of negative consequences for not participating in the research (e.g. institutionalization, deportation, disclosure of stigmatizing behavior).	Included/Allowed to ParticipateIncluded/Allowed to Participate
Any other circumstance/dynamic that could increase vulnerability to coercion or exploitation that might influence consent to research or decision to continue in research.	Excluded from ParticipationExcluded from Participation

9.2 Additional Safeguards:

Language: Patients with any primary language other than English will be considered for inclusion, so long as there is a professional interpreter available for the consent process and other aspects of the study. The study does not target participants with any specific language. A short form, if available, will be used if the subject is non-English speaking.

Undervalued social group: Research staff will not be asking about this social group, however vulnerability will not be increased by participating.

Military: Research staff will not be asking about this social group, however vulnerability will not be increased by participating.

Stressful Situation: Given that participants are approached in the pre-op area prior to surgery, this may be a stressful situation. Extra caution will be taken as to not coerce the potential participant. They will be encouraged to ask questions of the research team or PI/Sub-PI and will be given adequate time to discuss with

their support. Individuals who are noticeably nervous or stressed at that time will not be consented.

Disadvantaged group: Research staff will not be asking about this social group, however vulnerability will not be increased by participating.

Fear of Participating: Research staff will not be asking about this social group, however vulnerability will not be increased by participating.

10.0 Local Number of Participants

10.1 Local Number of Participants to be Consented: 130

10.2 Basis for Sample Size Calculation:

The sample size of 98 total patients was calculated in consultation with a statistician on the assumption that there would be a significant mean difference of 0.5°C (SD=0.75) (see Section 15.2 for more details). To account for an 80% enrollment rate, we estimate we will need to approach 123 patients for the study.

11.0 Local Recruitment Methods

11.1 Recruitment Process:

Participants who will be undergoing renal transplant surgery at the University of Minnesota – Fairview East Bank. Given the uncertain nature of matching organs to potential recipients, the potential recruits will be identified through the operating room schedule the day of their surgery. The research team will ensure that it does not interrupt that pre-op workflow. The nurses will be informed of the study and ahead of time.

A research assistant or one of the investigators will discuss with the patient the goals of the study and answer any questions the participant and the participant's family may have about the study. Consent will also be obtained by the research staff. Any additional questions the research assistant is unable to answer will be answered by the investigators of this study. A copy of the consent will be given to the patient, one will remain in the patient's medical record and the original will be securely stored by research staff.

11.2 Identification of Potential Participants:

Participants who will be undergoing renal transplant surgery at the University of Minnesota – Fairview East Bank. Potential participants will be approached prior to their surgery by the operating room schedule that day (see above mentioned safeguard in 11.1).

11.3 Recruitment Materials: N/A

11.4 Payment: None

12.0 Withdrawal of Participants

12.1 Withdrawal Circumstances:

The patient's physicians (either surgeon or anesthesiology) may withdraw patients from the study without their consent if there are any concerns for patient safety (whether related to the study or not).

12.2 Withdrawal Procedures:

Participants may withdraw at any time from the study after consenting for participation up to induction of anesthesia and may withdraw from the study after the surgery (the participant will be unconscious after induction of anesthesia and will be unable to withdraw while under anesthesia). Data collected for the study may be retained unless the participant requests otherwise, in which it will then be deleted/destroyed. However, all typical data recorded for the intraoperative anesthetic record will continue to be collected in the patient's chart for patient care and documentation.

12.3 Termination Procedures:

The patient's physicians (either surgeon or anesthesiology) may terminate the study at any time if there are concerns for patient safety (whether related to the study or not).

13.0 Risks to Participants

13.1 Foreseeable Risks:

None beyond those routinely associated with transplant surgery and anesthesia and temperature management. Thermal injury to the skin (with or without actual burns) is listed as a risk for all warming systems that contact the skin (including both forced air and resistive blankets) but such events are exceedingly rare when the equipment is used as intended. We will use the devices according to the manufacturer's recommendations of operating the devices.

Participation in research may involve a loss of privacy due to the nature of the questions that are asked and/or data collected. However, records will be handled as confidentially as possible. No identifying information will be used in any report or publications that may result from this study. All study records will be kept in a UMN box and REDCap which are secure databases. Paper records will be kept in locked cabinets in locked rooms only accessible to study staff.

13.2 Reproduction Risks: None

13.3 Risks to Others: N/A

14.0 Potential Benefits to Participants

14.1 Potential Benefits:

Aside from stated benefits from maintaining normothermia in the perioperative period in this proposal, there are no other additional benefits for subjects in participating in this study.

15.0 Statistical Considerations

15.1 Data Analysis Plan:

1. Our primary outcome variable is the patient's temperature at the end of surgery.

2. Secondary outcome variables also include:

- AUC of time versus temperature curves;
- temperatures at set points during operative period;
- blood loss volumes

All continuous measures will be summarized with mean (standard deviation) or median (interquartile range) based upon evaluation of normality using statistical tests (e.g., Shapiro-Wilk) and graphical representation (e.g., histograms, boxplots). Categorical measures will be summarized by count (percent).

The secondary outcomes are continuous measures and will be compared using two-sided two-sample t-tests for unadjusted comparisons of the groups. Adjusted comparisons will use linear regression models to account for potential confounders that may affect the outcome based upon the clinical literature.

Safety outcomes of interest include the incidence of hyperthermia, rescue warming, and incidence of thermal injury. These are categorical variables and will be compared using the $\chi 2$ test or Fischer's exact test for unadjusted comparisons and with logistic regression models to account for potential confounders.

Final data set will be assessed for missing data, depending on rate of missing data, we will use statistical methods to account for missing data

15.2 Power Analysis:

A mean difference of 0.5°C in patient temperatures between the two devices would be clinically meaningful. However, limited data exists, so a range of standard deviations were explored to examine the different sample sizes needed at 80% and 90% power (assuming a two-sided two-sample t-test with α=0.05).

Power	SD	N per Group	Overall N
0.8	0.25	6	12

	0.5	17	34
	0.75	37	74
	1	64	128
0.9	0.25	7	14
	0.5	23	46
	0.75	49	98
	1	86	172

We will take a conservative approach by enrolling 49 patients per group (98 patients total). As this is a minimal risk study, we expect to an 80% enrollment rate; we will approach (98 + 20% = 123 patients). In 2019, the University of Minnesota Medical Canter performed approximately 240 renal transplants for a total of ~200 eligible patients or ~16 eligible patients/month; 100 total patients approached/16 eligible patients per month = 6.25 months.

15.3 Statistical Analysis:

Data will be collected in REDCap and stored in an excel spreadsheet format in box and analyzed in-house with a statistician.

All analyses will be conducted using R or SAS statistical software. Values of $p<0.05$ will be considered statistically significant. The analyses will use the intention-to-treat approach. The primary outcome will assume a complete case analysis, but when data is missing, methods for imputation will be explored based on the amount and type of missing data, potentially including multiple imputation using the mice package in R or linear interpolation methods for measures repeated over time that are missing for sensitivity analyses.

15.4 Data Integrity:

Data will be recorded automatically into the EPIC electronic health record system and will be extracted using computer algorithms/programs that have been tested for data extraction either by the research team or by the EPIC data team at Fairview. Any data extracted from the Vigilance II monitor with the VitalDB software package will be performed in real-time to a hospital-owned computer dedicated to the research team.

Data will be stored on hospital, password-protected computers via UMN Box. This will include laptops. Data will not be stored on personal computers of any kind,

including smartphones. The computers will be stored in a locked office in the hospital, and only the research team will have access to these computers.

16.0 Health Information and Privacy Compliance

16.1 Select which of the following is applicable to your research:

☐ My research does not require access to individual health information and therefore assert HIPAA does not apply.

☒ I am requesting that all research participants sign a HIPCO approved HIPAA Disclosure Authorization to participate in the research (either the standalone form or the combined consent and HIPAA Authorization).

☐ I am requesting the IRB to approve a Waiver or an alteration of research participant authorization to participate in the research.

Appropriate Use for Research: N/A

☐ An external IRB (e.g. Advarra) is reviewing and we are requesting use of the authorization language embedded in the template consent form in lieu of the U of M stand-alone HIPAA Authorization. Note: External IRB must be serving as the privacy board for this option.

16.2 Identify the source of Private Health Information you will be using for your research (Check all that apply)

☐ I will use the Informatics Consulting Services (ICS) available through CTSI (also referred to as the University's Information Exchange (IE) or data shelter) to pull records for me

☐ I will collect information directly from research participants.

☐ I will use University services to access and retrieve records from the Bone Marrow Transplant (BMPT) database, also known as the HSCT (Hematopoietic Stem Cell Transplant) database.

☒ I will pull records directly from EPIC.

☐ I will retrieve record directly from axiUm / MiPACS

☐ I will receive data from the Center for Medicare/Medicaid Services

☐ I will receive a limited data set from another institution

☐ Other. Describe:

16.3 Explain how you will ensure that only records of patients who have agreed to have their information used for research will be reviewed.

Patients on the surgery schedule for renal transplants will be screened before being approached by research to ensure that they have not opted-out of

research and meet criteria for approaching. For data collection, research staff will only be accessing records of patient's with a signed consent. Participants who have withdrawn from the study will not be included.

16.4 Approximate number of records required for review: 200

16.5 Please describe how you will communicate with research participants during the course of this research. Check all applicable boxes

☐ This research involves record review only. There will be no communication with research participants.

☒ Communication with research participants will take place in the course of treatment, through MyChart, or other similar forms of communication used with patients receiving treatment (consent and assignment to one of two warming methods)

☐ Communication with research participants will take place outside of treatment settings. If this box is selected, please describe the type of communication and how it will be received by participants.

16.6 Explain how the research team has legitimate access to patients/potential participants:

Study staff approaching participants are part of the surgical team (anesthesiology). All study staff involved in this study have successfully completed all regulatory requirements (HIPPA, CITI, GCP, Fairview requirements). Privacy is taken very seriously and only consented patients will be accessed.

16.7 Location(s) of storage, sharing and analysis of research data, including any links to research data (check all that apply).

☐ In the data shelter of the Information Exchange (IE)

☐ Store ☐ Analyze ☐ Share

☐ In the Bone Marrow Transplant (BMT) database, also known as the HSCT (Hematopoietic Stem Cell Transplant) Database

☐ Store ☐ Analyze ☐ Share

☒ In REDCap (recap.ahc.umn.edu)

☒ Store ☒ Analyze ☒ Share

☐ In Qualtrics (qualtrics.umn.edu)

☐ Store ☐ Analyze ☐ Share

☒ In OnCore (oncore.umn.edu)

☒ Store ☐ Analyze ☒ Share

☒ In the University's Box Secure Storage (box.umn.edu)

☒ Store ☒ Analyze ☒ Share

☐ In an AHC-IS supported server. Provide folder path, location of server and IT Support Contact:

☐ Store ☐ Analyze ☐ Share

☐ In an AHC-IS supported desktop or laptop.

Provide UMN device numbers of all devices:

☐ Store ☐ Analyze ☐ Share

☐ Other. Describe:

Indicate if data will be collected, downloaded, accessed, shared or stored using a server, desktop, laptop, external drive or mobile device (including a tablet computer such as an iPad or a smartform (iPhone or Android devices) that you have not already identified in the preceding questions

☐I will use a server not previously listed to collect/download research data

☐I will use a desktop or laptop not previously listed

☐I will use an external hard drive or USB drive ("flash" or "thumb" drives) not previously listed

☐I will use a mobile device such as a tablet or smartphone not previously listed

16.8 Consultants. Vendors. Third Parties: Data will not be shared with the company supplying the product.

16.9 Links to identifiable data: N/A

16.10 Sharing of Data with Research Team Members: Team members will use box to share data. No email or other systems will be used.

16.11 Storage and Disposal of Paper Documents: Signed paper consents will be securely stored in a regulatory binder for 5 years.

17.0 Confidentiality

17.1 Data Security:

Only the core study team (PI, co-PI, and support personnel) will have access to PHI and data during the initial collection process. Intraoperative recording of relevant events for the study will be recorded on paper or in REDCap on an IPAD in the operating room, which will be imported into REDCap and saved in box in a way that de-identifies the data. Intraoperative subject vitals will also be exported

from EPIC into spreadsheet format and be saved on research computers in a de-identified fashion. Data collected by the VitalDB software package will be done in real-time to a hospital-owned computer for use dedicated to the research team, and will have no patient identifiers except for date and time of the data collected, and subject number, and will be merged into the spreadsheet containing the data imported from EPIC. Data will then be processed on these computers that are dedicated solely to the research team. A separate spreadsheet of PHI (patient name, MRN, date of surgery, procedure) will be compiled of study subjects in the case additional information needs to be collected or verified. The spreadsheet with PHI and data spreadsheets will be saved in an encrypted format in BOX. All computers that are dedicated to the research team will not leave the research site (Fairview hospitals, University of Minnesota) and be secured in a locked office when not in use. Transmission of data will be performed within approved University storage and transfer modalities (encrypted e-mail, local network drives, etc.). Original consent documents and data collected on paper, which will include patient information, will be stored in a locked cabinet in a locked research office, accessible only to the core study team.

18.0 Provisions to Monitor the Data to Ensure the Safety of Participants

18.1 Data Integrity Monitoring:

A detailed review of all participants and participant data will be conduct at monthly intervals by the PI or co-PI to ensure data is being recorded and analyzed appropriately. Any missing data or abnormal data findings will trigger a detailed review of raw data from EPIC and measures will be taken to train the staff to minimize the chance for recurrence and to improve the process of data collection and analysis. The PI or co-PI will also review EPIC records of each subject to verify protocols were followed and to note if any adverse events occur, and if any rescue interventions were implemented and implemented correctly.

Any adverse events, whether related to the study or not with regards to temperature management, will be reported to the study team in addition to chart review. An adverse event log will be maintained, with events reported to the IRB. If there is any question as to whether the event was related to the study, the case will be referred to Dr. Michael Todd, the Department of Anesthesiology's Vice Chair for Research and the Departments Quality Assurance Event monitor, for review and adjudication. Dr. Todd will be empowered to temporarily halt enrollment if any safety concerns are noted - although the final decision regarding halting or resuming the study will be referred to the Department of Anesthesiology’s DSMB (see below for details).

18.2 Data Safety Monitoring:

The Department of Anesthesiology has a designated "DSMB" headed by Dr. Joyce Wahr and including Drs. Richard Prielipp and Michael Todd. Given the low risk

nature of this study, our plan is for the DSMB to receive blinded (A vs B) data after the completion of the 55th patient (the halfway point). While statistical stopping rules for non-inferiority studies remain uncertain, we will use a well-established O'Brien-Fleming procedure and will stop the study if the SUPERIORITY of either method is established, based on an intergroup Z-score difference of 2.78.

19.0 Provisions to Protect the Privacy Interests of Participants

19.1 Protecting Privacy:

The participants will be provided written information by the research team about the study and be contacted in person to assess their willingness to participate in the study. After the perioperative period, there is no planned additional follow-up to be performed by the research team. The data and information collected by the research team in relation to the participant will be handled in accordance to HIPAA and will be saved in password-protected file formats and password protected USB drives, if applicable, and data will be transferred within internal network drives and via UMN Box secure internal data storage services. All data, once collected, will be de-identified of participant data for data processing purposes with a spreadsheet linking participant information to datasets saved in a password-protected electronic spreadsheet, and a backup paper spreadsheet secured in a locked cabinet when not in use or being updated.

19.2 Access to Participants*:*

Access to EPIC will be required to collect data relevant to the study. The participant giving consent to participate in this study will also give permission for the research team to use intraoperative anesthesia data for the study.

20.0 Compensation for Research-Related Injury

20.1 Compensation for Research-Related Injury:

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

20.2 Contract Language: N/A

21.0 Consent Process

21.1 Consent Process (when consent will be obtained):

Consent will occur prior to surgery. While it is ideal to consent the patient in the days prior to surgery, it is not feasible for the anesthesiology department to find potential participants in advance as organs have to be matched with appropriate

patients and therefore patients do not know when they will be having surgery. It cannot be scheduled until an organ becomes available.

Patients will be approached in the preoperative holding room the day of surgery. The research team will be in close communication with the clinical care team in the pre-op area so as to not disrupt clinical workflow. The research team will take extra precautions to carefully review of all elements of the ICF with participant, answer questions, verify understanding and give them time to think about or discuss participation and receive signed copy of ICF.

21.2 Waiver or Alteration of Consent Process (when consent will not be obtained): N/A

21.3 Waiver of Written/Signed Documentation of Consent (when written/signed consent will not be obtained): N/A

21.4 Non-English Speaking Participants: Patients with any primary language will be considered for inclusion when a professional interpreter is available for the consent process and other aspects of the study. The study does not target participants with any specific language. A short form, if available, will be used if the subject is non-English speaking. Both the participant and the translator will sign the informed consent. The translator will sign in the witness block.

21.5 Participants Who Are Not Yet Adults (infants, children, teenagers under 18 years of age): N/A

21.6 Cognitively Impaired Adults, or adults with fluctuating or diminished capacity to consent:

The Anesthesia research team recognizes that consenting patients the day of the surgery increases the vulnerability of the patient. If a potential participant is approached to participate in the study in the pre-op holding area, the research team will take extra precautions to carefully review of all elements of the ICF with participant, answer questions, verify understanding and give them time to think about and/or discuss participation. Patients who are noticeably stressed or upset will not be approached for this study.

21.7 Adults Unable to Consent:

- Permission: N/A
- Assent: N/A
- Dissent: N/A

22.0 Setting

22.1 Research Sites:

- The primary research site will be East Bank campus of the University of Minnesota – Twin Cities, and the University of Minnesota Health/Fairview East Bank hospital. The surgeries will be performed at the hospital.

- Data analysis will be conducted within the anesthesiology department in the Mayo building on the campus of the University of Minnesota and at the University of Minnesota Health/Fairview East Bank hospital

22.2 International Research: N/A

23.0 Multi-Site Research: N/A

24.0 Coordinating Center Research

24.1 Role: N/A

24.2 Responsibilities: N/A

24.3 Oversight: N/A

24.4 Collection and Management of Data: N/A

25.0 Resources Available:

Research Assistants to aid in consent and data acquisition. RA's will also be responsible for bringing the hotdog blanket to the OR

CRNAs will be trained by PI/Sub-PI on device setup and device monitoring. CRNA will monitor patient temperature throughout the procedure and 1 hour post op.

Available Patients: On a typical week at the East Bank Medical Center, approximately 3-4 potential participants undergo renal transplant, however, research staff availability to business hours will likely limit the number of enrolled participants

Time to Devote: List approximate time available to faculty and RAs (as percent effort).

10-20% effort

Describe your facilities:

All procedures and surgeries will be performed in the clinical facilities of MHealth/Fairview East Bank. Data storage and analysis can be done using UMN BOX which is available in the Research Office. The research team is located on the 5th floor of the Mayo building. Documents will be kept in a locked cabinet in the research office.

Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions:

RAs and other support faculty will be trained by the principle investigator and Co-PIs. Training will include a review of the protocol, consent form and data collection forms as well as hands-on instructions on the used devices and how to position the patient in the OR. Individuals who are familiar with the study protocol will be available in the OR to assist with participant positioning and optimization of heating system placement for the study

26.0 References

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