COVER PAGE

Official Title of the Study: POSToperative PAcing for Cardiac Efficiency (POSTPACE)

NCT number: NCT ID not yet assigned

Date of the Document: 09/17/2026

POSToperative **PA**cing for **C**ardiac **E**fficiency (POSTPACE)

SHORT PROTOCOL TITLE:

POSTPACE

PRINCIPAL INVESTIGATOR:

Dr. Gregory Webster
Division of Cardiology, Department of Pediatrics
312-227-4397
RGWebster@luriechildrens.org

SPONSOR/FUNDER:

The Graeme McDaniel Foundation

VERSION NUMBER/DATE:

Version 1

Confidentiality Statement:

This protocol is confidential. Please do not circulate outside of Lurie Children's Hospital staff.

Compliance Statement:

This document is a protocol for a human research study. The purpose of this protocol is to ensure this study is being conducted according to applicable guidelines, government regulations, institutional research policies and procedures and other applicable requirements. This includes as applicable ICH GCP guidelines, CFR 21 Part 812, CFR 21 Part 312.

REVISION HISTORY

Include the protocol version number/date for each revision of the protocol along with a summary of changes and an indication of if there was an associated consent change. The oldest version should be listed on the top row and the most recent version should be listed on the bottom row. All version history should remain in the table and never deleted.

Revision #	Version Number/Date	Summary of Changes	Consent Change Y/N

Table of Contents

1.0 Study Summary 4
2.0 Objectives 5
3.0 Background 5
4.0 Study Endpoints 7
5.0 Number of Participants 9
6.0 Inclusion and Exclusion Criteria 9
7.0 Special Populations 10
8.0 Study Intervention/Investigational Agent 10
9.0 Procedures Involved 11
10.0 Study Timelines 19
11.0 Data and Specimen Banking 20
12.0 Sharing of Results with Subjects 20
13.0 Risks to Subjects 21
14.0 Potential Benefits to Subjects 22
15.0 Recruitment Methods 22
16.0 Consent Process 23
17.0 Process to Document Consent in Writing 26
18.0 Withdrawal of Subjects 26
19.0 Data Management and Confidentiality 26
20.0 Provisions to Monitor the Data to Ensure the Safety of Subjects 28
21.0 Provisions to Protect the Privacy Interests of Subjects 31
22.0 Compensation for Research-Related Injury 32
23.0 Costs to Participants 32
24.0 Setting 32
25.0 Resources Available 32
26.0 References 34

1.0 Study Summary

Protocol Information	Description
Study Title	POSTPACE
Study Design	Prospective, randomized interventional study
Primary Objective	The primary objective of this prospective, single-center, randomized within-subject study is to compare 3 clinical approaches to post-operative heart rate management, assessing whether those approaches change postoperative tissue perfusion, measured by renal NIRS, in children. Each participant will serve as their own control across the three clinical approaches.
Secondary Objective(s)	The secondary objectives are to compare the effects of these 3 clinical approaches on cerebral NIRS, blood pressure, oxygen saturation, central venous pressure, lactate, and acid-base status up to 72 hours after surgery. The study will also evaluate clinical and operative predictors of physiologic response and establish postoperative strength-duration curves for temporary epicardial pacing wires.
Research Intervention(s)/ Investigational Agent(s)	No investigational agents are used. Participants are randomized to one of two pathways, each of which contains three clinical approaches. Each approach is within accepted medical practice.
IND/IDE #	Not applicable
IND/IDE # Holder	Not applicable
Study Population	The study population consists of pediatric inpatients younger than 12 years undergoing congenital cardiac surgery with postoperative admission to the CICU at Lurie Children's Hospital. Participants are drawn from the congenital cardiac surgery population and grouped by single-ventricle versus two-ventricle physiology.
Sample Size	46 participants: 23 in cohort 1 and 23 in cohort 2
Study Duration for individual participants	3 days
Study Specific Abbreviations/ Definitions	BPM/bpm — beats per minute CICU — Cardiac Intensive Care Unit Co-I / Co-Is — Co-Investigator / Co-Investigators CRC — Clinical Research Coordinator CTCAE — Common Terminology Criteria for Adverse Events CV — cardiovascular eConsent — electronic consent EMR — electronic medical record HR — heart rate ID — identification LAR / LARs — legally authorized representative / representatives LRL – Lower rate limit (on a cardiac pacing device) MRN — medical record number NIRS — near-infrared spectroscopy OR — operating room PAR — pulmonary artery reconstruction

	REDCap — Research Electronic Data Capture (S)AE — (Serious) Adverse Event VIS — vasoactive-inotropic score
Study Sites	Lurie Children's Hospital (no other sites)

2.0 Objectives

2. 1 Hypothesis

- **Overall Hypothesis:** Temporary atrial pacing above the intrinsic sinus rate during the early postoperative period following congenital heart surgery improves tissue perfusion over the first 10 hours after surgery

2.2 Primary Objectives

- **Primary Objective:** To test whether different clinical strategies affect postoperative tissue perfusion, as measured by renal near-infrared spectroscopy (NIRS) in children following congenital cardiac surgery.

2.3 Secondary Objectives

- **Secondary Objective 1** To compare whether three clinical strategies produce changes in additional physiologic measures, including cerebral NIRS, mean arterial pressure, arterial oxygen saturation, central venous pressure, serum lactate, and acid-base status in the first 72 hours after surgery.
- **Secondary Objective 2** To evaluate the influence of patient characteristics, surgical complexity, vasoactive support, sedation, and heart rate on postoperative tissue perfusion and hemodynamic responses using multivariable predictive modeling.
- **Secondary Objective 3** To establish postoperative strength-duration curves for temporary epicardial pacing wires by measuring pacing capture thresholds across multiple pulse durations during the first 3 days following congenital heart surgery.

3.0 Background

3.1 Preclinical Experience

Not applicable. No new procedures with relevant preclinical data are proposed. All procedures in this study are already in standard clinical use

3.2 Clinical Experience

- Temporary epicardial pacing is routinely used following congenital cardiac surgery to treat postoperative bradycardia, conduction disturbances, and low cardiac output states. Temporary epicardial pacing wires are placed during surgery as part of standard clinical care worldwide, and are routinely used to manage transient bradyarrhythmias, junctional rhythms, low cardiac output, and chronotropic insufficiency. The proposed research evaluates different clinically-acceptable pacing rates using existing standard-of-care equipment. The present study uses only standard temporary epicardial pacing equipment and established pacing techniques currently employed in routine clinical practice.
- Clinical studies evaluating atrial pacing in patients with postoperative sinus rhythm have produced conflicting results. A prospective pediatric crossover study of 30 patients

undergoing congenital heart surgery found that temporary atrial pacing at approximately 15% above the intrinsic sinus rate did not improve cardiac output, blood pressure, lactate, or arteriovenous oxygen saturation difference and was associated with reductions in cerebral and flank near-infrared spectroscopy (NIRS) values[1]. The investigators concluded that routine postoperative atrial pacing did not provide measurable hemodynamic benefit. A subsequent retrospective study evaluating temporary epicardial pacing wires after congenital heart surgery found that only a minority of patients required postoperative pacing and that routine wire placement did not improve clinical outcomes. These findings questioned the routine use of temporary pacing in all patients but did not address whether selected pacing strategies could improve postoperative physiology[2]. More recently, a retrospective study demonstrated that atrial pacing at 10–20 beats per minute above the intrinsic sinus rate was associated with improved renal NIRS values in children following the Norwood operation, suggesting that controlled augmentation of heart rate may improve tissue perfusion in selected postoperative patients[3]. In addition, contemporary postoperative management has evolved substantially since the earlier prospective study, including widespread use of dexmedetomidine, which produces negative chronotropic effects that may increase the physiologic relevance of atrial pacing during the early postoperative period[4-6]. These observations provide the clinical rationale for the present prospective study.

- **This study compares three accepted standards of care; it does not test an experimental therapy, nor test the efficacy of the pacemaker itself.** All three study conditions evaluated in this protocol represent current standards of clinical practice in our Cardiac Intensive Care Unit. Patients are routinely managed either without temporary pacing or with atrial pacing at modest chronotropic augmentation (approximately 10-20 beats per minute above the intrinsic sinus rate), depending on the clinical judgment of the treating cardiac intensivist. The purpose of this study is not to introduce a novel pacing intervention, but to prospectively compare three pacing strategies that are already in routine clinical use. Randomization simply assigns participants to the timing of these standard management approaches to permit rigorous within-subject comparison while minimizing bias. Because all pacing strategies fall within accepted clinical practice and use standard temporary epicardial pacing equipment already placed for routine postoperative care, participation in the study does not expose patients to a novel pacing modality or investigational device.
- Each participant serves as his or her own control, allowing comparison of unpaced sinus rhythm with two pacing strategies while minimizing inter-patient variability.

3.3 Problem Statement

Congenital heart surgery is frequently followed by a period of hemodynamic instability during which optimization of cardiac output and tissue perfusion is a major focus of intensive care management. Temporary epicardial pacing wires are routinely placed at the time of surgery and atrial pacing is commonly used in the postoperative period to increase heart rate in patients with sinus rhythm. Despite the widespread use of this intervention, there is limited prospective evidence demonstrating whether routine chronotropic augmentation improves postoperative hemodynamics or tissue oxygen delivery.

As noted above, the available literature is limited and conflicting. Unsurprisingly, post-pacing strategies differ from provider-to-provider. In addition, there have been major innovations in the last decade that may change the risk-benefit analysis for post-operative pacing. These include advances in perioperative care, high-fidelity physiologic monitoring, and the widespread use of dexmedetomidine and other medications that reduce intrinsic heart rate. Consequently, there remains genuine clinical uncertainty regarding the optimal use of temporary atrial pacing in the modern cardiac intensive care unit.

In addition to the uncertainty surrounding postoperative atrial pacing, there are limited data describing the electrophysiologic properties of the postoperative neonatal myocardium. Specifically, postoperative strength-duration relationships for temporary epicardial pacing have not been systematically characterized in infants following congenital heart surgery. Existing data are derived primarily from adult patients or chronic pacing systems and may not accurately reflect the transient physiologic changes associated with cardiopulmonary bypass, myocardial edema, ischemia-reperfusion injury, and postoperative inflammation. These data are increasingly important as novel implantable pacing technologies for neonates are being developed and require evidence-based programming parameters.

This study addresses both knowledge gaps by prospectively evaluating the physiologic effects of commonly used postoperative atrial pacing strategies and by establishing postoperative strength-duration curves in neonates and infants. The results have the potential to inform evidence-based postoperative pacing practices and improve the physiologic understanding of temporary epicardial pacing in this vulnerable population.

4.0 Study Endpoints

4.1 Primary and Secondary Study Endpoints

Primary Endpoint

The primary study endpoint is the within-subject change in renal near-infrared spectroscopy (NIRS) during the three protocol-defined pacing conditions: intrinsic sinus rhythm, atrial pacing at 10 beats per minute above the intrinsic sinus rate, and atrial pacing at 20 beats per minute above the intrinsic sinus rate.

The primary analysis will compare the mean renal NIRS values obtained during the final 30 minutes of each pacing phase. Our goal is to detect a clinically meaningful absolute target of 5 percentage-point change in renal NIRS (Cohort 1 baseline is estimated at 90%; Cohort 2 baseline is estimated at 80%).

Renal NIRS was selected as the primary outcome because it provides continuous, noninvasive, high temporal resolution assessment of somatic tissue oxygenation and is therefore well suited to detecting short-term, within-subject physiologic changes during the protocol-defined pacing conditions. Renal NIRS has been extensively studied following pediatric cardiac surgery and has been associated with measures of systemic oxygen delivery, renal injury, vasoactive support, and postoperative outcomes. Importantly, it is used here as a physiologic marker of regional oxygen

delivery rather than as a direct measure of cardiac output or a diagnostic test for acute kidney injury[7-9]. Alternative measures, including echocardiographic cardiac output, lactate, venous oxygen saturation, urine output, and clinical outcomes, are less suitable as the primary endpoint because they are intermittent or insufficiently sensitive to changes occurring over the duration of individual pacing phases; these measures are retained as secondary outcomes where appropriate. Renal NIRS also adds essentially no incremental participant risk and permits direct comparison with prior postoperative pacing data using the same physiologic measure[3]. For these reasons, we believe that renal NIRS is a sufficient outcome measure and will not expose participants to additional risk without meeting the planned study objectives.

Secondary Endpoints

- Cerebral NIRS
- Mean arterial pressure
- Arterial oxygen saturation
- Central venous pressure
- Mean airway pressure
- Serum lactate concentration
- Arterial pH
- Arterial bicarbonate concentration
- Intrinsic heart rate during each pacing phase

Secondary electrophysiologic endpoints include:

- Pacing capture thresholds measured across multiple pulse durations
    - Rheobase
    - Chronaxie
    - Changes in strength-duration curves over the first 72 postoperative hours

Additional exploratory endpoints include identification of clinical and operative factors associated with postoperative physiologic response to atrial pacing using multivariable predictive modeling.

4.2 Primary and Secondary Safety Endpoints

Because all pacing strategies evaluated in this study are currently used as part of routine postoperative clinical care, no unique safety endpoint is designated as the primary study outcome. Safety will be assessed by monitoring for clinically significant adverse events occurring during protocol-directed pacing.

Safety endpoints include:

- Development of clinically significant tachyarrhythmias
- Cardiac arrest
- Initiation of extracorporeal mechanical circulatory support
- Death during the study period
- Discontinuation of protocol-directed pacing because continuation is deemed not to be in the participant's best clinical interest by the treating clinical team
- Development of any protocol-defined exclusion criterion after enrollment requiring cessation of study pacing (e.g., requirement for ventricular pacing, or other predefined stopping criteria)

5.0 Number of Participants

Each cohort requires 19 patients who complete the protocol. We have inflated by ~20% to account for non-completion due to clinical instability or early discontinuation. This design provides adequate power to detect clinically meaningful NIRS changes at each pacing transition while preserving the within-subject efficiency of the study framework.

A total of 46 participants will be enrolled

- 23 patients in Cohort 1 (single-ventricle pathway)
- 23 patients in Cohort 2 (two-ventricle pathway).

6.0 Inclusion and Exclusion Criteria

6.1 Screening for eligibility

Potential participants will be identified prospectively from the congenital cardiac surgery schedule at Lurie Children's Hospital and other routine communications from the CV surgery team.

6.2 Inclusion/Exclusion

Inclusion Criteria

- Age less than 12 years (all potential recruitment)
  - Age less than 12 months at enrollment (target recruitment)
  - Children aged 13-36 months will be eligible for recruitment if we do not meet the target recruitment goals for infants according to the study timeline, and then all patients < 12 years if recruitment is still below targets.
- Scheduled for congenital cardiac surgery at Lurie Children's Hospital
- Planned postoperative admission to the CICU
- Informed consent from parent or legally authorized representative

Exclusion Criteria

- Pregnant patient at time of surgery
- Category 2 and category 3 patients on the pulmonary artery reconstruction (PAR) program
- Junctional or ventricular rhythm at baseline
- Uncontrolled tachyarrhythmia (for example, but not limited to, atrial or ventricular tachycardia, atrioventricular re-entrant arrhythmias)
- Hemodynamically significant bleeding, defined as active bleeding that, in the judgment of the treating clinical team, requires ongoing blood product transfusion, surgical or catheter-based intervention, or results in hemodynamic instability requiring escalation of clinical support
- Postoperative cardiac arrest prior to protocol initiation or during the protocol period
- Requirement for mechanical circulatory support
- Requirement for ventricular pacing
- Arterial pH less than 7.10
- Determination by the treating clinical team that participation is not in the patient's best clinical interest

Study Procedures Following Enrollment

Participants who develop an exclusion criterion after enrollment will discontinue protocol-directed pacing and will continue to receive standard clinical care. Data collected prior to discontinuation of the pacing protocol will be retained for analysis. Participants who have a phase skipped or are discontinued from the pacing intervention may continue to contribute routinely collected clinical and physiologic data obtained during standard postoperative care, unless consent for study participation is withdrawn.

6.3 Specific Populations

- **Adults unable to consent:** Excluded.
  The study is limited to patients younger than 12 years age undergoing congenital cardiac surgery. Adults, including adults unable to provide informed consent, will not be enrolled.
- **Individuals who are not yet adults (infants, children, teenagers):** Included.
  The study specifically enrolls patients younger than 12 years age who undergo congenital cardiac surgery and are admitted postoperatively to the CICU. Parental or legally authorized representative permission will be obtained prior to enrollment in accordance with institutional and federal regulations.
- **Pregnant women:** Excluded.
  Pregnant women are not eligible for enrollment. Most patients will be below the age of viable pregnancy, and any child ≤ 12 years of age who is pregnant will be excluded.
- **Non-English speaking participants:** Included.
  Non-English-speaking families will be eligible to participate. Informed consent will be obtained using IRB-approved translated consent documents and/or qualified medical interpreters in accordance with institutional policies to ensure that parents or legally authorized representatives fully understand the study prior to providing permission.
- **Participants of diverse racial and ethnic backgrounds:** Included.
  Participants will be recruited without regard to race, ethnicity, sex, or socioeconomic status. All eligible patients meeting the study criteria will be considered for enrollment, and no racial or ethnic group will be excluded.

7.0 Special Populations

The study recruits children/minors. Our study team has extensive experience with assent, permission, and informed consent for children/minors. The process will comply with the HRP-416 checklist.

The study does not include neonates of uncertain viability.

8.0 Study Intervention/Investigational Agent

8.1 Description of the Study Intervention

The study intervention consists of sequentially assigning participants to 3 protocol-directed clinical strategies. Temporary epicardial pacing wires are placed by the cardiac surgeon during congenital heart surgery as part of routine clinical care. Participants will undergo three clinically accepted pacing conditions: intrinsic sinus rhythm (no atrial pacing), atrial pacing at 10 beats per minute above the intrinsic sinus rate, and atrial pacing at 20 beats per minute above the intrinsic sinus rate. The order of these clinical strategies will be determined by study randomization (Figure 1). In addition, pacing capture thresholds will be measured at predetermined pulse durations to establish postoperative strength-duration curves during

the first 72 hours after surgery. The study does not involve the use of any investigational drug, biologic, or investigational medical device.

8.2 Drug/Device Handling

Not applicable. No investigational drugs or investigational medical devices are used in this study.

Temporary epicardial pacing wires and external temporary pacemakers are standard clinical equipment routinely used in the Cardiac Intensive Care Unit for postoperative management of patients undergoing congenital heart surgery. All equipment will remain under the control of the treating clinical team and will be stored, maintained, and used according to Ann & Robert H. Lurie Children's Hospital policies, manufacturer recommendations, and applicable institutional procedures. Only physicians, advanced practice providers, nurses, and other clinical personnel who are authorized and appropriately trained in the use of temporary cardiac pacing equipment will perform pacing or threshold testing. No study-specific storage, dispensing, accountability, or investigational device control procedures are required.

This protocol compares three clinical care approaches and does not evaluate the safety or effectiveness of external pacemakers or temporary pacing wires. Based on the Device Worksheet HRP-307, Device Applicability checklist, FDA device regulations do not apply to this study:

CRITERIA	**STUDY-SPECIFIC RESPONSE**
In the United States: The use of a device in one or more persons that evaluates the safety or effectiveness of that device,	No
Data regarding subjects or control subjects submitted to or held for inspection by FDA	No
Data regarding the use of a device on human specimens (identified or unidentified) submitted to or held for inspection by FDA	No
Does this involve a humanitarian use device	No

9.0 Procedures Involved

9.1 Study Design

This is a prospective, single-center, randomized, within-subject physiologic study conducted in the CICU at Ann & Robert H. Lurie Children's Hospital of Chicago. The study is designed to evaluate the physiologic effects of temporary atrial pacing in neonates and infants during the first 10 hours following congenital cardiac surgery and to characterize postoperative strength-duration relationships of temporary epicardial pacing wires during the first 72 postoperative hours.

Eligible participants will be assigned to one of two predefined clinical cohorts based on surgical physiology: a single-ventricle pathway cohort and a two-ventricle pathway cohort. Within each cohort, participants will be randomized in a 1:1 ratio. Randomization determines the timing of the pacing strategies while ensuring that all participants are exposed to the same three clinical conditions: intrinsic sinus rhythm (no pacing), atrial pacing at 10 beats per minute above the intrinsic sinus rate, and atrial pacing at 20 beats per minute above the intrinsic sinus rate. The two randomized pacing sequences are designed to minimize the potential for predictable postoperative physiologic changes over time to confound comparisons between pacing strategies.

Each participant will serve as his or her own control, allowing within-subject comparison of physiologic responses to the three pacing conditions while reducing inter-patient variability. Continuous physiologic data will be collected using the institutional Sickbay platform throughout the first 72 postoperative hours.

Participants who complete at least two of the three protocol-defined pacing conditions will be included in the primary analyses. Following completion of the pacing protocol, clinical management will proceed according to the treating clinical team's judgment while physiologic data collection continues through the remainder of the 72-hour study period.

To accomplish the secondary aim, pacing capture thresholds will be measured at multiple pulse durations at baseline and daily for 3 days after CICU admission to construct postoperative strength-duration curves. These measurements will be performed only when the treating clinical team determines that threshold testing can be conducted safely.

This is a single-center study; therefore, no site-specific differences in study procedures are applicable.

9.2 Research Procedures

Following parental permission, study procedures will begin after admission to the CICU following congenital cardiac surgery. Prior to initiation of the study intervention, eligibility will be confirmed, including review of the participant's cardiac rhythm, intrinsic heart rate, hemodynamic status, and protocol-defined eligibility criteria. Participants may be paced as they leave the operating room before the research protocol begins, at the discretion of the surgical team. If the participant is receiving atrial pacing upon CICU admission, pacing will be discontinued for the last 15 minutes of the first postoperative hour to determine the intrinsic sinus heart rate, which will serve as the participant's baseline heart rate for the study (Figure 1). If the clinical team determines that it is clinically inappropriate to pause pacing to establish a baseline heart rate, then the phase will be skipped, and the intrinsic sinus heart rate will be assessed at start of the next phase, according to protocol.

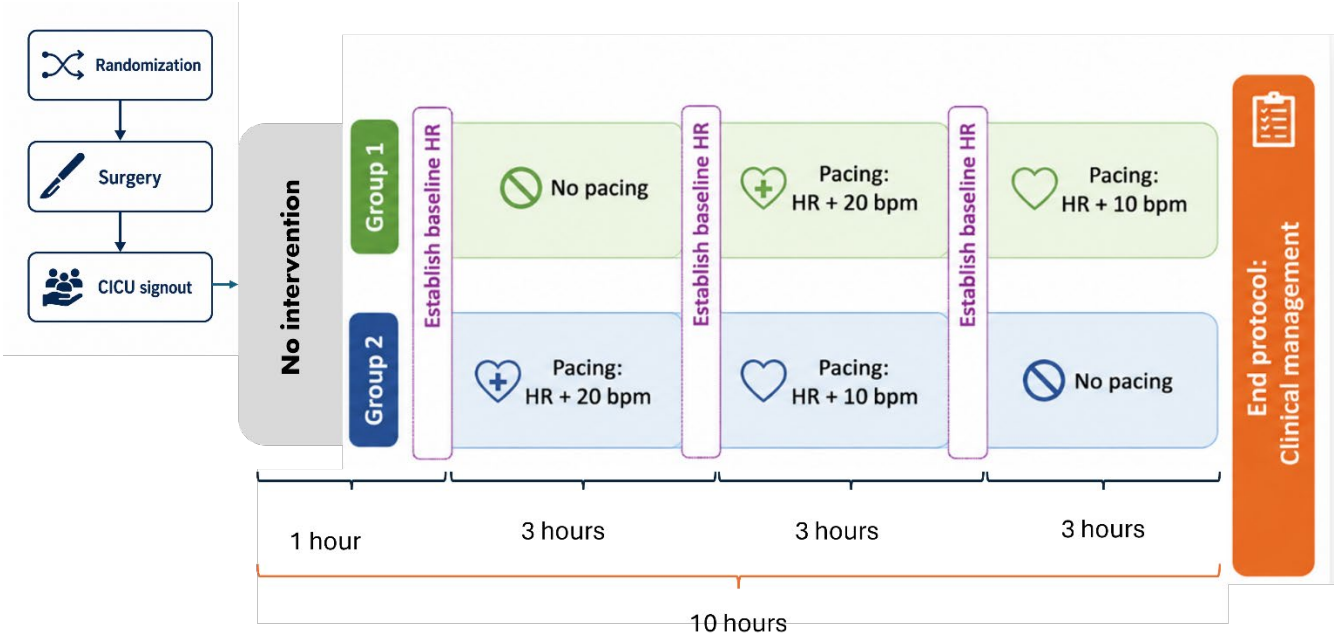
Participants will be assigned to one of two physiologic cohorts (single-ventricle or two-ventricle circulation) based on the planned surgical pathway and operative interventions. Within each cohort, participants will be randomized in a 1:1 ratio to one of two protocol-defined pacing sequences. The two randomized sequences differ only in the timing of the pacing phases to minimize bias from predictable physiologic changes in the post-operative period.

The pacing intervention consists of three clinically accepted management conditions: intrinsic sinus rhythm without atrial pacing, atrial pacing at 10 beats per minute above the intrinsic sinus rate, and atrial pacing at 20 beats per minute above the intrinsic sinus rate. Each pacing phase will be maintained for approximately three hours according to the assigned randomization sequence. Participants who complete at least two of the three protocol-defined pacing phases will be included in the primary analyses. After completion of the protocol-directed pacing intervention, all subsequent pacing and medical management will be determined solely by the treating clinical team.

Protocol-Directed Pacing Algorithm

The protocol-directed pacing algorithm standardizes temporary atrial pacing during the first 10 postoperative hours while allowing the treating clinical team to skip phases or discontinue study procedures whenever clinically indicated (Figure 1). In addition to skipping or discontinuing, physicians can temporarily pause pacing (e.g. 1 minute) to check underlying heart rate for clinical management purposes without otherwise disrupting or changing the protocol.

Figure 1. Protocol-Directed Pacing Algorithm.



The time intervals in Figure 1 and elsewhere in this protocol are approximate. We recognize that there will be small variations in intervals to account for the time required for signout, intervals to assess baseline heart rates, and other transitional periods. The overall 10-hour study period is also approximate, taking into account that there will be time periods when the study team will wait for a clinician to arrive to make changes to the pacemaker and otherwise account for transitional adjustments.

Pacing Readiness Review. At surgical bedside signout in the CICU, before initiation of protocol-directed pacing, the treating clinical team will complete a final Pacing Readiness Review. The clinical team will be asked explicitly: *"Are there features of this patient's anatomy, operative findings, surgical repair, or current physiology that would make atrial pacing up to 20 beats/min above the intrinsic heart rate substantially higher risk than in a typical postoperative patient?"* If the clinical team determines that the answer is yes, the participant will not undergo protocol-directed pacing. The participant may remain enrolled for observational data collection and strength-duration testing, provided these activities remain clinically appropriate.

Baseline Heart Rate Determination

Following CICU admission and confirmation of study eligibility, the participant will undergo a one-hour baseline observation period during intrinsic sinus rhythm without protocol-directed atrial pacing. That 1-hour period starts after CICU signout finishes. For the purposes of the study, we consider CICU signout to be over when the team has finished the bedside discussion, which includes the fellow or attending's conversation with the bedside nurse and the family, not just the multi-specialty huddle that occurs immediately after bringing the patient back to the bedside. In addition, the post-signout "no intervention" period means no protocol-directed pacing. Temporary pacing can be used for routine clinical care during this period at the discretion of the CICU team. If temporary pacing is used for routine clinical care during

this period, pacing will be discontinued for last 15 minutes of this one-hour baseline observation period, to determine the participant's intrinsic sinus heart rate.

The baseline heart rate will be defined as the maximum intrinsic sinus heart rate during the final 15 minutes of the baseline observation period. The maximum heart rate is the approximate maximum heart rate, based on the overall trend, not the minimum RR interval based on ectopy, sinus arrhythmia, or temporary beat-to-beat acceleration. A new reference heart rate will be calculated for each phase as shown in Figure 1.

Calculation of Pacing Rates

Two protocol pacing rates will be determined from the baseline heart rate:

- Baseline heart rate +10 beats per minute, rounded upward to the nearest 5 beats per minute.
- Baseline heart rate +20 beats per minute, rounded upward to the nearest 5 beats per minute.

In some pacing rate ranges, the clinical pacing device used at Lurie Children's only allow adjustments in increments of 2 bpm (not adjustments of 1 bpm). Therefore, if the calculated rate falls at a heart rate that cannot be exactly programmed on the temporary pacemaker, the heart rate will be rounded up to the next paced rate available on the device.

The maximum paced rate (pacing cap) will be 170 bpm. Table 1 provides the specific implementation of this cap.

Table 1: Procedure to handle heart rates near the pacing cap

Heart rate at the time of rate determination for the phase	Study process	When to re-evaluate
≤ 150 bpm	Standard study intervention	End of phase
> 150 and ≤ 160 bpm	Pacing cap = 170 bpm	End of phase
> 160 bpm	Skip phase (no intervention; allow intrinsic rhythm through the phase)	End of phase

Put into technical terms specific to pacemakers, maximum lower rate limit (LRL) of the temporary pacemaker during protocol-directed pacing will be 170 bpm. If the calculations indicate a study-directed pacing rate above 170 bpm, the LRL will be set to 170 bpm. We recognize that the terminology "maximum lower rate limit" is potentially confusing to lay readers, but this is an appropriate technical term specific to pacemakers.

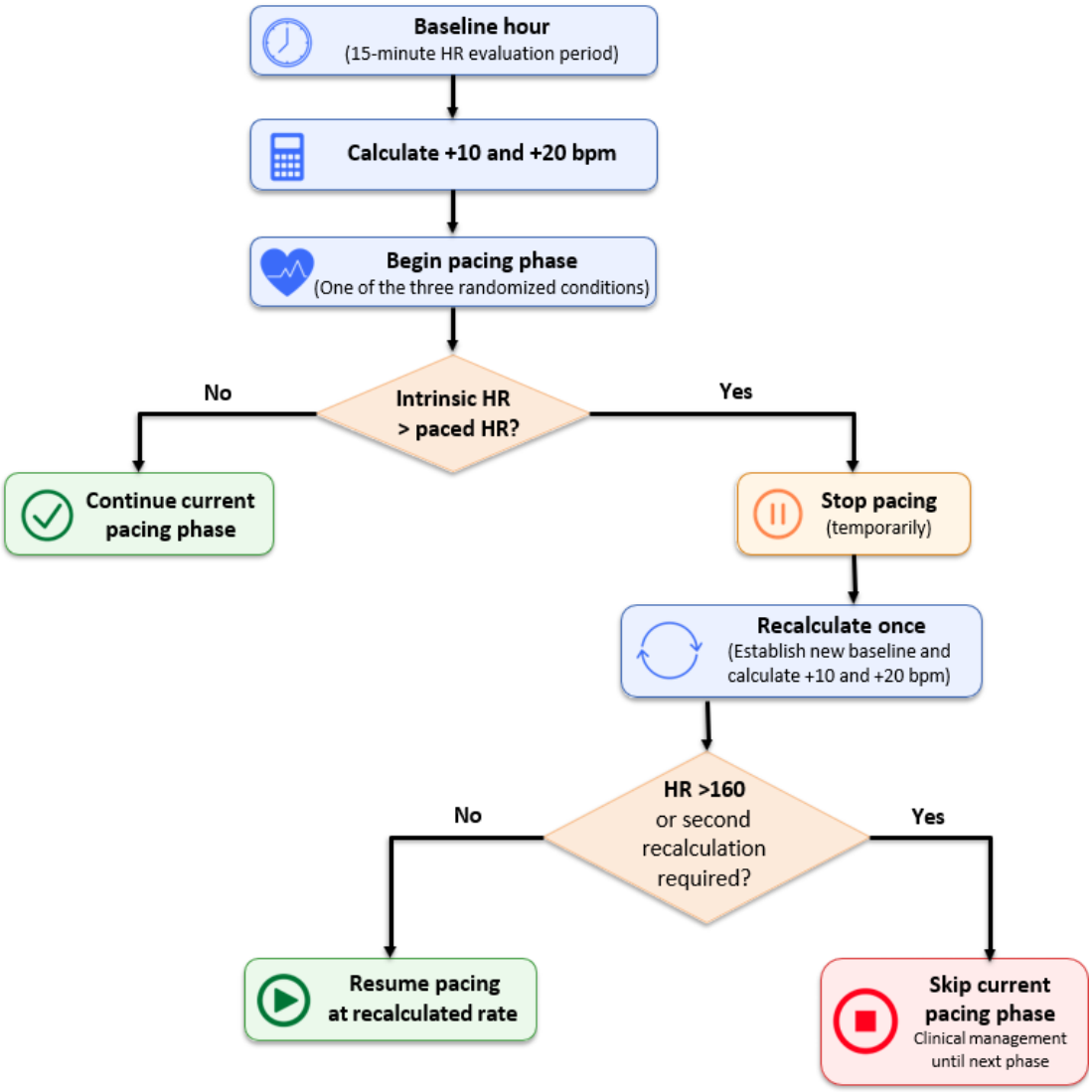
Management of Intrinsic Heart Rate Exceeding the Programmed Pacing Rate

If the participant's intrinsic sinus rhythm exceeds the programmed pacing rate during any pacing phase, protocol-directed pacing will be temporarily suspended.

A new intrinsic baseline heart rate will then be established using the participant's prevailing sinus rhythm. New protocol pacing rates (+10 beats per minute and +20 beats per minute, rounded upward to the nearest 5 beats per minute) will be calculated from this revised baseline, and protocol-directed pacing will resume at the appropriate recalculated rate.

Recalculation of pacing rates may occur once during each protocol pacing phase (Figure 2).

Figure 2. Process for adjusting rate during a pacing phase



Removing a patient from the atrial pacing protocol ("skipping" or "discontinuation")

We define two different mechanisms to take a patient out of the protocol: (1) Skipping a phase, which means changing to clinically-directed care for the remainder of the phase and rejoining protocol at the end of the phase; and (2) discontinuing the protocol, which means that no further protocol-directed pacing will occur and the remainder of the post-operative care will be determined by the clinical team.

1. Criteria for Skipping Atrial Pacing Phases

Protocol-directed pacing for the current pacing phase will be skipped if any of the following occur:

- A second recalculation would be required during the same pacing phase because the intrinsic sinus rate exceeds the programmed pacing rate for a second time.
- The recalculated intrinsic baseline heart rate exceeds 160 beats per minute, following the protocol in Table 1
- The treating clinical team determines that continuation of current protocol-directed pacing phase is not in the participant's best clinical interest, but is willing to continue with other phases

Skipping a pacing phase does not automatically exclude the participant from subsequent study phases if eligibility criteria are again satisfied.

2. Criteria for Discontinuing the Atrial Pacing Protocol

The protocol will be fully discontinued if any of three events occur:

- A protocol-defined exclusion criterion develops after enrollment.
- The clinical team requests that the patient be removed from the pacing study
- The family withdraws consent to participate

Participants who discontinue protocol-directed pacing will continue to receive care as directed by the CICU clinical team. All subsequent treatment decisions, including pacing strategy, will be determined solely by the treating clinical team.

Clinical and physiologic data obtained before, during and after protocol skipping or discontinuation will be retained for study analysis. Unless parental permission is withdrawn, participants who discontinue protocol-directed pacing may continue to contribute observational clinical and physiologic data collected as part of routine postoperative care.

Clinical management can supersede the research protocol at any time. The treating clinical team may skip phases or discontinue protocol-directed pacing without restriction whenever necessary to provide optimal patient care.

3. Continuation of strength duration testing

Skipping phases or discontinuing atrial pacing does not affect the strength duration portion of the protocol.

Strength duration testing occurs over approximately 1 minute of time, is performed as part of routine clinical care, and does not affect the patient once the test is complete. Strength duration testing will continue to occur daily until post-operative day 3 (subject to the limitations stipulated elsewhere in the protocol), unless the family withdraws consent to participate.

Data Collection

Continuous physiologic data will be collected for the first 72 postoperative hours using the institutional Sickbay platform. Physiologic variables include heart rate, arterial blood pressure, arterial oxygen saturation, cerebral and renal near-infrared spectroscopy (NIRS), central venous pressure, and mean airway pressure. No additional physiologic monitoring devices will be placed for research purposes.

Laboratory values obtained as part of routine clinical care, including arterial pH, bicarbonate concentration, and serum lactate, will be recorded with their corresponding collection times. Baseline demographic information, operative variables, vasoactive-inotropic score, and sedation medication doses will also be collected from the medical record[10].

For the secondary study objective, pacing capture thresholds will be measured across multiple pulse durations to construct postoperative strength-duration curves. Threshold testing will be performed at baseline and again daily for 3 days after CICU admission using standard clinical threshold testing techniques and routine temporary pacing equipment[11,12]. These measurements will only be performed when the treating clinical team determines that threshold testing can be safely completed without compromising patient care.

Safety Monitoring and Risk Minimization

All pacing strategies evaluated in this study are routinely used during standard postoperative care in the CICU. Participants will remain under continuous clinical monitoring throughout the study, including continuous electrocardiographic, hemodynamic, and pulse oximetry monitoring, as is standard for all postoperative cardiac surgical patients. Research procedures will not delay or interfere with routine clinical management.

The pacing protocol will be discontinued immediately if a protocol-defined exclusion criterion develops after enrollment, including clinically significant bleeding, uncontrolled tachyarrhythmia, need for ventricular pacing, severe metabolic acidosis, cardiac arrest, initiation of mechanical circulatory support, or any other condition that, in the judgment of the treating clinical team, makes continued participation inadvisable. If a participant's intrinsic sinus rate exceeds the protocol pacing rate, one attempt will be made to establish a new baseline heart rate and resume protocol pacing. If pacing adjustments are required more than once during a study phase or the participant no longer meets eligibility criteria, protocol-directed pacing for that phase will be discontinued. At all times, the treating clinical team retains full authority to skip phases or discontinue pacing whenever clinically indicated, and participant safety will take precedence over all research procedures.

Timeline

A schedule of study events (screening, enrollment, randomization, pacing phases, physiologic data collection, laboratory data collection, strength-duration testing, and study completion) are provided as Appendix A.

9.3 Procedures Performed to Lessen the Probability or Magnitude of Risks

All pacing strategies evaluated in this study are currently used as part of routine postoperative clinical care in the CICU. No participant will receive an investigational pacing modality or pacing rate outside the range of accepted clinical practice. Participants will remain under continuous electrocardiographic and hemodynamic monitoring throughout the study, consistent with standard postoperative care.

The pacing protocol will be discontinued immediately if a participant develops any protocol-defined exclusion criterion after enrollment or if the treating clinical team determines that continued participation is not in the patient's best clinical interest. Clinical management will always take precedence over research procedures, and treating physicians may skip phases or discontinue pacing at any time without regard to study participation. Strength-duration testing will only be performed when the treating clinical team determines that threshold testing can be conducted safely.

Drugs and Devices Used in the Research

No investigational drugs, biologics, or investigational medical devices are used in this study.

The study utilizes standard temporary epicardial pacing wires and external temporary cardiac pacemakers that are routinely used for postoperative management following congenital cardiac surgery. These devices are used in accordance with their intended clinical purpose. Temporary pacing wires are placed during surgery as part of routine clinical care and are not implanted specifically for research purposes. Continuous physiologic monitoring is performed using the institutional Sickbay platform, which is an FDA-cleared physiologic data acquisition system routinely used in the CICU and is not implanted specifically for research purposes.

Source Records

Research data will be obtained from the following source records:

- Electronic medical record (Epic)
- Sickbay continuous physiologic monitoring database
- Operative and anesthesia records
- Cardiac surgery and intensive care documentation
- Medication administration records
- Clinical laboratory reports
- Standardized study case report forms used for pacing threshold measurements
- REDCap study database used for research data entry and management

Study Data Collection

Please see Appendix B for a detailed list of study data to be collected

Long-Term Follow-up

There is no long-term follow-up associated with this study. Research procedures conclude after completion of the 72-hour strength-duration assessment. Data collection is limited to information obtained during the participant's routine postoperative hospitalization, and no additional research-specific clinic visits, telephone contacts, or long-term chart reviews are planned.

Blinding

This is an open-label physiologic study. Neither the treating clinicians nor study personnel will be blinded to pacing status or pacing rate. No blinding or unblinding procedures are required.

Clinical Management Supersedes Research Procedures

A participant may be withdrawn from the study at any time if the treating clinical team determines that continued participation is not in the patient's best clinical interest. Clinical judgment will always take precedence over research procedures. Under no circumstances will the study protocol delay, alter, or supersede routine clinical care, and the treating team may skip phases or discontinue any study-related procedure as necessary to ensure participant safety.

9.4 Humanitarian Use Device (HUD) uses

Not applicable.

9.5 Software and Technology

The following software and technology platforms will be used during the conduct of this study:

- **REDCap eConsent:** The REDCap eConsent platform will be used to facilitate the electronic informed consent process. Parents or legally authorized representatives will review the IRB-approved consent document electronically, have the opportunity to ask questions of study personnel, and provide electronic signatures in accordance with institutional policies and applicable regulatory requirements. Electronic consent records will be securely maintained within the REDCap platform.
- **Epic (Electronic Medical Record):** Epic will be used to identify potentially eligible participants, verify eligibility, and obtain demographic, clinical, operative, medication, laboratory, and outcome data documented during routine clinical care.
- **Sickbay (Medical Informatics Corp.):** Sickbay, an FDA-cleared physiologic data acquisition platform that is routinely used in the CICU, will be used to collect, store, and export high-fidelity physiologic data, including heart rate, arterial blood pressure, cerebral and renal near-infrared spectroscopy (NIRS), arterial oxygen saturation, central venous pressure, and mean airway pressure. Continuous physiologic data are captured at one-second resolution as part of routine clinical monitoring.
- **REDCap (Research Electronic Data Capture):** REDCap will be used as the secure electronic data capture system for study data entry, management, and storage. Study personnel will enter pacing threshold measurements and other research variables into REDCap using standardized electronic case report forms.
- **Statistical Software:** Statistical analyses will be performed using Stata (StataCorp LLC) and R (R Foundation for Statistical Computing), including mixed-effects modeling and random forest regression analyses as described in the statistical analysis plan.

All software and technology used in this study will be institutionally approved and deployed in accordance with the policies and procedures of Ann & Robert H. Lurie Children's Hospital of Chicago. Only authorized study personnel will have access to research data, and all electronic data will be maintained on institutionally approved secure systems in accordance with institutional information security and data privacy policies.

10.0 Study Timelines

10.1 Enrollment Duration and Recruitment Monitoring

Enrollment is anticipated to require 12 months, with a target enrollment of 46 participants. Recruitment progress will be formally reviewed at three predefined enrollment checkpoints (3, 6, and 9 months after study initiation). At each checkpoint, cumulative enrollment will be compared with the projected enrollment required to achieve full accrual within 12 months. An enrollment rate of 90% or greater of the projected target will be considered on track.

The study will initially enroll **neonates and infants younger than 12 months of age**.

Checkpoint 1 (3 months after study initiation)

- If cumulative enrollment is ≥90% of the projected target at checkpoint 1, eligibility will remain limited to children <12 months of age.
- If cumulative enrollment is <90% of the projected target at checkpoint 1, eligibility will be expanded to include children <36 months of age for all subsequent enrollment.

Checkpoint 2 (6 months after study initiation)

- If cumulative enrollment is ≥90% of the projected target at checkpoint 2, no changes will be made to the current eligibility criteria.
- If cumulative enrollment is <90% of the projected target at checkpoint 2:
  - If eligibility has not been altered (still limited to <12 months of age), eligibility will be expanded to include children <36 months of age.
  - If eligibility has already been expanded to <36 months of age, eligibility will be further expanded to include children <12 years of age.

Checkpoint 3 (9 months after study initiation)

- If cumulative enrollment is ≥90% of the projected target at checkpoint 3, no changes will be made to the current eligibility criteria.
- If cumulative enrollment is <90% of the projected target at checkpoint 3:
  - If eligibility has not been altered (still limited to <12 months of age), eligibility will be expanded to include children <36 months of age.
  - If eligibility has already been expanded to <36 months of age, eligibility will be further expanded to include children <12 years of age.

This staged recruitment strategy is intended solely to facilitate timely completion of enrollment while preserving the primary scientific objective of studying the youngest postoperative patients whenever feasible. Expansion of the eligible age range will not alter the study intervention, pacing protocol, outcome measures, safety monitoring, or statistical analysis plan. Participant age will be recorded for all enrolled subjects and incorporated as a prespecified covariate in the planned analyses. This is a recruitment contingency plan that broadens eligibility only if enrollment is inadequate, not an adaptive study design.

11.0 Data and Specimen Banking

11.1 Data or specimen banking

No biological specimens will be collected or stored as part of this study. Research data will be retained in accordance with institutional record retention requirements. Data without identifying information may be stored for future research.

11.2 Procedures for release of data or specimens

Not applicable. This study does not include banking of biological specimens or creation of a repository for future research. Accordingly, no procedures for release of banked data or specimens are applicable. Data collected for this study will be used only for the research purposes described in this protocol and will be accessible only to authorized members of the study team. Any future sharing or use of study data outside the scope of this protocol would require appropriate Institutional Review Board review and approval, as applicable, and would be conducted in accordance with institutional policies governing the protection of participant confidentiality.

12.0 Sharing of Results with Subjects

Individual research results and overall study results will not be routinely shared with participants or their families. No investigational diagnostic testing, genetic testing, or research-specific clinical testing is performed as part of this study. The study uses physiologic and clinical data collected during routine

postoperative care, and research analyses will not be used to guide individual patient management or be communicated to participants or their primary care providers

13.0 Risks to Subjects

13.1 Foreseeable Risks

The incremental risks associated with participation in this study are expected to be minimal, as all pacing strategies evaluated are currently used as part of routine postoperative clinical care in the CICU. Temporary epicardial pacing wires are placed during cardiac surgery as part of standard clinical management and are not implanted specifically for research purposes. Participants will remain under continuous electrocardiographic and hemodynamic monitoring throughout the study, allowing prompt recognition and management of any clinically significant changes.

Potential risks related to protocol-directed atrial pacing include increased myocardial oxygen demand, induction of atrial or ventricular arrhythmias, transient hypotension or hypertension, or reduced cardiac output if the selected pacing rate is not optimal for an individual patient. These events are uncommon, are generally reversible with adjustment or discontinuation of pacing, and are routinely monitored for during standard postoperative care. In addition, the pacing rates chosen for this study are currently used routinely in clinical care and all of these risks are possible during routine clinical care.

Measurement of pacing capture thresholds may require brief changes in pacing output. Threshold testing is routinely performed during postoperative management of patients with temporary epicardial pacing wires and is expected to pose no risk beyond standard clinical care. If the treating clinical team determines that threshold testing is not clinically appropriate, the procedure will not be performed.

Participation also carries a small risk of loss of confidentiality associated with collection and storage of research data. This risk will be minimized through the use of secure, institutionally approved data systems, restriction of data access to authorized study personnel, and adherence to institutional policies governing the protection of participant information.

The study does not involve additional blood draws, radiation exposure, anesthesia, surgical procedures, or administration of investigational drugs or devices.

13.2 Unforeseeable Risks

No unforeseeable risks are anticipated beyond those associated with routine postoperative temporary atrial pacing and standard clinical threshold testing. As with any clinical research, there is a possibility that previously unrecognized risks may emerge. Participants will remain under continuous clinical monitoring, and the protocol may be modified or discontinued if unexpected safety concerns arise.

13.3 Risks to an Embryo or Fetus

Not applicable. The study population consists exclusively of children undergoing congenital cardiac surgery.

13.4 Risks to Others

Not applicable.

13.5 Investigational Product Risk Information

Not applicable. This study does not involve an investigational drug, biologic, or medical device. Temporary epicardial pacing wires, external temporary pacemakers, and physiologic monitoring equipment are FDA-

cleared devices used in accordance with their approved clinical indications and routine institutional practice.

14.0 Potential Benefits to Subjects

14.1 Potential Benefits to Individual Subjects

All three pacing strategies evaluated in this study are currently used as part of routine postoperative clinical care. Because participants will receive each of these standard-of-care pacing strategies for a limited period (approximately three hours each), we do not anticipate that participation will provide a lasting direct clinical benefit beyond that expected from routine postoperative management.

A potential theoretical benefit is that the participant's physiologic response to each pacing strategy may become apparent to the treating clinical team. After completion of the protocol, the treating clinicians may elect to continue the pacing strategy that appears to provide the most favorable hemodynamic profile for that individual patient. However, this potential benefit is speculative, is not an objective of the study, and may not occur for any given participant. All subsequent pacing decisions will be made solely at the discretion of the treating clinical team based on the participant's clinical condition.

14.2 Direct Benefit

There is **no anticipated direct benefit** from study participation beyond standard postoperative care. Participants should not expect to receive any additional therapeutic benefit as a result of participating in the research.

15.0 Recruitment Methods

15.1 Recruitment Procedures

Potential participants will be identified prospectively from the congenital cardiac surgery schedule at Lurie Children's Hospital. Members of the study team will screen the daily CICU census and surgical schedule to identify potentially eligible patients. Once eligibility has been confirmed, a member of the study team will approach the participant's parent or legally authorized representative (LAR) to discuss the study, answer questions, and obtain informed consent. Recruitment and informed consent will occur only after the clinical team determines that the parent/LAR is available and that discussion of research participation is appropriate. Parents/LARs will receive an informational handout describing the study prior to the consent discussion. Eligible participants and their parents/LARs will be approached for the study on or around the pre-surgery clinical visit which typically takes place days to weeks before the surgery.

15.2 Source of Subjects

Participants will be recruited from patients receiving routine clinical care at Ann & Robert H. Lurie Children's Hospital of Chicago. Potential subjects will be identified from the congenital cardiac surgery schedule at Lurie Children's Hospital and other routine communications from the CV surgery team. Clinical information used to determine eligibility will be obtained from the electronic medical record and routine clinical documentation.

15.3 Identification of Potential Subjects

Potential participants will be identified through review of the daily congenital cardiac surgery schedule and other routine communications from the CV surgery team. Members of the study team who are authorized to access protected health information for research purposes will review clinical records to determine whether patients meet the study eligibility criteria. Information reviewed for screening purposes may include age, cardiac diagnosis, operative procedure, postoperative location, cardiac rhythm, presence of

temporary epicardial pacing wires, arterial catheter status, and other eligibility criteria specified in the protocol. No biospecimens will be accessed for screening or recruitment purposes.

15.4 Recruitment Materials

A parent/LAR informational handout will be used during recruitment to introduce the study and facilitate discussion with the parent or legally authorized representative. The informational handout will be provided directly by study personnel during the recruitment process and is included with this IRB submission. No public advertisements, flyers, social media, websites, or other recruitment materials will be used.

15.5 Compensation

Participants and their parents or legally authorized representatives will receive a payment of $100 for participation in the study.

15.6 MyChart Messaging

MyChart messaging will not be used for recruitment.

16.0 Consent Process

Process	Mark all that apply
Written Parental Permission	☒
Written Adult Consent/LAR	☐
Written Adolescent Assent (ages 12-17)	☐
Verbal Adolescent Assent (ages 7-11)	☐
Waiver or Alteration of Informed Consent	☐
Waiver of Parental Permission	☐
Waiver of Adolescent Assent	☐

16.1 Informed Consent Process

Written parental permission will be obtained for all participants, as the study population consists exclusively of children who are unable to provide consent. The informed consent process will be conducted in accordance with HRP-090 – SOP – Informed Consent Process for Research.

Consent may be obtained either in person or through the institutionally approved REDCap eConsent platform.

In-person Consent

- The consent discussion will be conducted by authorized study personnel who have completed all required human subjects protection and study-specific training.
- The discussion will take place in a private location within the pre-operative clinic or another appropriate clinical setting that allows for a confidential conversation.
- Parents or legally authorized representatives (LARs) will be given sufficient time to review the consent document, ask questions, and consider participation before making a decision.
- The investigator or delegated study personnel will explain the purpose of the study, study procedures, potential risks and benefits, alternatives to participation, and the voluntary nature of participation in language understandable to the parents/LARs.

- Consent will only be obtained after study personnel are satisfied that the parent/LAR understands the study and has had all questions answered.

Electronic Consent

- Electronic informed consent may be obtained using the institutionally approved REDCap eConsent platform in accordance with institutional policies and applicable regulatory requirements.
- Parents/LARs will have the opportunity to review the consent document electronically, discuss the study with study personnel, ask questions, and electronically sign the IRB-approved consent form.

Participation in this study is entirely voluntary. Parents/LARs may decline participation or withdraw their child from the study at any time without affecting the child's medical care or relationship with the hospital or treating clinicians.

Because participation lasts only through the postoperative hospitalization, ongoing consent will be maintained through continued communication between the study team and the parent/LAR. If new information becomes available that may affect a parent's willingness to continue participation, it will be communicated promptly, and additional consent will be obtained if required by the IRB.

16.2 HIPAA Authorization and Specific Case

Non-English Speaking Subjects

- Participants with non-English speaking parents/LAR will be recruited. If Spanish or Arabic speaking parents/LAR are consented, the approved Parental Permission form in their language will be used and the consent will be done with an interpreter, according to the practices described in HRP-090 - SOP - Informed Consent Process for Research. For additional languages, a short form will be utilized with a translator according to the practices described in HRP-090 - SOP - Informed Consent Process for Research.

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

- **Not applicable.** This study does not request a waiver or alteration of informed consent or parental permission. Written parental permission will be obtained from the parents or legally authorized representatives of each participant in accordance with HRP-090 – SOP – Informed Consent Process for Research prior to enrollment. The study is not emergency research and does not request a waiver of consent under emergency research regulations. No deception is involved.

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

- All research will be conducted in the State of Illinois. For the purposes of this study, children are individuals who have not attained the legal age for consent to medical treatment or research participation under applicable Illinois law. Because the study population consists exclusively of children younger than 12 years of age, all participants are considered children.

- Written parental permission will be obtained from both parents or legally authorized representatives (LARs) prior to study enrollment, consistent with institutional policy. The process for obtaining signatures from both parents will follow the guidance in the HRP-090 - SOP - Informed Consent Process for Research 3.5.25.docx.
- If parents are unavailable, permission may be obtained from individuals who are legally authorized under applicable law and institutional policy to make medical decisions on behalf of the child. The authority of the legally authorized representatives will be verified through review of the medical record and institutional registration documentation, consistent with HRP-013 – SOP – LARs, Children, and Guardians.
- Written assent will not be obtained because all participants are younger than 12 years of age. Verbal assent will be obtained from children 7 - 11 years of age. Documentation of verbal assent will be recorded by the study team member providing consent and assent. Since 7-11 year-old participants are not part of the initial recruitment goal, the IRB will be notified if recruitment will be expanded to include them. A modification will be submitted to the IRB with details of the assent process and an adolescent assent form so that verbal assent can be documented.

Cognitively Impaired Adults

- Not applicable

Adults Unable to Consent

- Not applicable

Assessment of Capacity to Consent

- Study participants will be children who are younger than 12 years of age (accounting for expansion of eligibility criteria as described above). Because all study participants will be minors, informed consent will be obtained from the participant's parent or legally authorized representative (LAR).
- After using typical procedures to verify that the consenting adults are the participant's parents or legally authorized representatives (LARs), study personnel will assess the individual's ability to understand the purpose of the study, study procedures, potential risks and benefits, alternatives to participation, and the voluntary nature of participation. Parents/LARs will be encouraged to ask questions, and consent will only be obtained after study personnel are satisfied that the individual understands the information presented and is capable of making an informed decision.

Humanitarian Use Device (HUD)

- **Not applicable.** This study does not involve the use of a Humanitarian Use Device (HUD) or a device approved under a Humanitarian Device Exemption (HDE). Temporary epicardial pacing wires and external temporary pacemakers used in this study are standard-of-care devices used in accordance with their approved clinical indications.

Waiver of Adolescent Assent – Choose one criterion option	Study Specific Justification
☐ The capability of these children (considering the ages, maturity, and psychological state of the children involved) is so limited that they cannot reasonably be consulted.	N/A
☐ The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research	N/A

17.0 Process to Document Consent in Writing

17.1 Written Documentation of Consent. Written informed consent will be documented in accordance with HRP-091 – SOP – Written Documentation of Consent. Written parental permission will be obtained from the participant's parents or legally authorized representatives (LARs) before any study-specific procedures are performed. Consent may be documented either by a handwritten signature on the IRB-approved consent form or by an electronic signature using the institutionally approved REDCap eConsent platform, in accordance with institutional policies and applicable regulatory requirements. Signed consent documents will be maintained as required by institutional policy and regulatory requirements.

18.0 Withdrawal of Subjects

18.1 Participant withdrawal

A participant may be withdrawn from the study at any time if the treating clinical team determines that continued participation is not in the patient's best clinical interest. Clinical judgment will always take precedence over research procedures. Under no circumstances will the study protocol delay, alter, or supersede routine clinical care, and the treating clinical team may skip phases or discontinue any study-related procedure as necessary to ensure participant safety. Participants may also be withdrawn if they develop a protocol-defined exclusion criterion that precludes continued study participation.

18.2 Orderly Termination

If a protocol-defined exclusion criterion develops after protocol-directed pacing has begun, the pacing intervention will be discontinued immediately, and the participant will return to routine clinical management under the direction of the treating clinical team. Data collected prior to discontinuation will be retained for analysis unless the parent or legally authorized representative requests otherwise, as permitted by applicable regulations.

19.0 Data Management and Confidentiality

19.1 Data Analysis Plan

Analyses will be performed separately within the two prespecified physiologic cohorts (single-ventricle and two-ventricle circulation). The primary analyses will first be completed independently within each cohort. If the direction and magnitude of treatment effects are similar between cohorts, pooled analyses may be performed to increase statistical power.

Enrollment will initially be limited to children younger than 12 months of age. If enrollment criteria are expanded during the study according to the prespecified recruitment plan (<36 months and, if necessary,

<12 years), participant age will be incorporated as a prespecified covariate in all multivariable analyses. Age-stratified subgroup analyses will also be performed, when appropriate, to evaluate whether physiologic responses differ across age groups.

Aim 1

The primary endpoint is renal near-infrared spectroscopy (NIRS) measured during the three protocol-defined pacing conditions (intrinsic sinus rhythm, pacing at +10 beats/minute, and pacing at +20 beats/minute). Continuous physiologic data will be obtained from the Sickbay platform at one-second resolution and summarized into one-minute intervals for analysis.

The primary analysis will compare within-subject physiologic responses across the three pacing conditions using mixed-effects regression models to account for repeated measurements within each participant. Participant identity will be modeled as a random effect. Prespecified covariates may include age, weight, surgical cohort, cardiopulmonary bypass duration, STAT category, vasoactive-inotropic score (VIS), sedation medications, mean airway pressure, and other clinically relevant variables.

Secondary analyses will evaluate cerebral NIRS, mean arterial pressure, arterial oxygen saturation, central venous pressure, serum lactate, arterial pH, bicarbonate concentration, and other physiologic variables collected during routine clinical care.

Exploratory machine learning analyses using random forest regression will be performed to identify predictors of renal NIRS, cerebral NIRS, mean arterial pressure, and serum lactate. Predictor importance, calibration, and partial dependence analyses will be used to characterize the relationship between heart rate and postoperative physiologic outcomes.

Aim 2

Pacing capture thresholds measured at approximately 1, 24, 48, and 72 hours after surgery will be used to construct individual strength-duration curves using the Weiss-Lapicque equation to estimate rheobase and chronaxie[13-15].

Descriptive statistics will summarize pacing parameters at each time point. Longitudinal changes in rheobase and chronaxie will be evaluated using repeated-measures ANOVA or, when assumptions of normality are not met, the Friedman test. Correlations between pacing parameters and relevant clinical variables, including age, serum potassium, body temperature, medications, and vasoactive-inotropic score, will be evaluated using Pearson or Spearman correlation coefficients, as appropriate.

Sample Size

The planned enrollment is 46 participants, with 23 participants in the single-ventricle pathway cohort and 23 participants in the two-ventricle pathway cohort. The sample size is based on the primary physiologic endpoint: within-subject change in renal near-infrared spectroscopy (NIRS) across the three protocol-defined pacing conditions: intrinsic sinus rhythm, atrial pacing at 10 beats/min above the intrinsic sinus rate, and atrial pacing at 20 beats/min above the intrinsic sinus rate.

For sample-size planning, we anticipate a clinically meaningful absolute within-subject change in renal NIRS of approximately 5 percentage points between pacing conditions, with a within-subject standard deviation of paired differences of approximately 8 percentage points. The study does not directly measure renal blood flow; renal NIRS is the prespecified physiologic measure of regional renal tissue oxygenation used as the primary endpoint. With 19 protocol-complete participants per cohort, a two-sided paired comparison at $\alpha=0.05$ provides approximately 80% power to detect a 5-percentage-point difference, corresponding to

a standardized paired effect size of approximately 0.68. To account for approximately 20% non-completion due to postoperative clinical instability, early discontinuation of protocol-directed pacing, inadequate NIRS data, or inability to complete all pacing phases, enrollment will be increased from 19 to 23 participants per cohort, for a total planned enrollment of 46 participants. Secondary endpoints and multivariable predictive analyses will be considered exploratory and are not separately powered.

19.2 Data Security

Study data will be stored in secure, institutionally approved REDCap databases maintained by Lurie Children's Hospital or similar protected data directories provided by Lurie Children's Hospital. Continuous physiologic data will be obtained from the institutional Sickbay platform, and clinical data will be abstracted from the electronic medical record (Epic). Access to study data will be restricted to authorized study personnel who have completed required institutional training in human subjects research and data security. Electronic data will reside on institutionally managed, password-protected servers with appropriate access controls, encryption, and routine system backups. Identifiable data will be maintained separately from analytic datasets whenever feasible, and only the minimum necessary identifiable information will be retained. Data transmission will occur only through institutionally approved secure systems.

19.3 Quality Control

Standardized case report forms and REDCap data entry forms will be used for all study data collection. Study personnel will receive protocol-specific training before participating in the study. Data entered into REDCap will undergo routine quality assurance procedures, including range checks, logic checks, and periodic review for completeness, consistency, and accuracy. Continuous physiologic data obtained from Sickbay will be reviewed for physiologically implausible values and artifact before analysis using predefined quality control criteria. Any discrepancies identified during data review will be resolved through comparison with the original source records.

19.4 Study-Wide Data Handling

Study data will include demographic information, clinical history, operative variables, physiologic monitoring data, laboratory values obtained during routine clinical care, medication administration records, pacing threshold measurements, and study-derived variables including rheobase and chronaxie. Biological specimens will not be collected.

Source data will be obtained from the electronic medical record, the Sickbay physiologic monitoring platform, standardized study forms, and REDCap. The Principal Investigator and authorized study personnel will be responsible for receipt, entry, transmission, and maintenance of study data.

Electronic data will be transmitted only through institutionally approved secure systems. No paper records or biological specimens will be transported outside the institution. Study data will be retained in accordance with Ann & Robert H. Lurie Children's Hospital policies, applicable sponsor requirements, and federal regulations governing research record retention. Identifiable information will be removed from analytic datasets whenever possible before statistical analysis.

20.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

20.1 Data Evaluation to Ensure Safety of Subjects

Oversight and general approach. Participants will remain under continuous bedside monitoring by the CICU clinical team throughout protocol-directed pacing. The attending physician responsible for the

participant's clinical care retains final authority for all clinical and treatment decisions and may skip or discontinue protocol-directed pacing at any time if doing so is considered to be in the participant's best clinical interest. While a physician study investigator will not necessarily be present at the bedside throughout the protocol, a physician study investigator will be available to the attending physician at all times during protocol-directed pacing by pager or cellular telephone for protocol-related questions or consultation. Clinical management will take precedence over the research protocol at all times.

An independent data monitoring committee is not planned because this is a single-center study of 46 participants comparing pacing strategies that are already used in routine care, with continuous bedside monitoring and immediate authority of the treating team to stop study procedures. Safety oversight will be performed by the Principal Investigator and study co-investigators.

Collection of safety information. Safety information will be obtained from continuous bedside monitoring, the electronic medical record, Sickbay physiologic data, laboratory results, medication administration records, operative and CICU documentation, direct observation by the treating and research teams, and standardized study case report forms and REDCap forms. Safety collection will begin with initiation of the first study-specific procedure (the protocol baseline observation) and continue through completion of the 72-hour strength-duration assessment. Any serious adverse event occurring after consent but before protocol initiation will also be documented if it affects eligibility or study participation. Serious adverse events assessed as possibly related or related to a study procedure will be followed through resolution, stabilization, or hospital discharge, whichever occurs first.

Individual and cumulative review. Research staff will review the medical record, monitoring data, laboratory results, and participant status at least daily during the study period and will document new safety events promptly. The Principal Investigator or a physician co-investigator will review each new adverse event within 24 hours of its identification; serious or potentially study-related events will be communicated to the Principal Investigator immediately. Cumulative safety data will be reviewed by the Principal Investigator and study co-investigators after the first 5 participants and after each subsequent 10 participants, or at least quarterly, whichever occurs first. Reviews will be documented and will assess event type, severity, relatedness, expectedness, pacing condition, cohort, timing, reversibility, clinical management, and whether protocol or consent changes are needed. Findings indicating a new or increased risk will be reported to the IRB and sponsor in accordance with institutional and sponsor requirements. Aggregate safety findings will also be included in required continuing-review or progress reports.

Statistical evaluation of safety. Because the study is small and is not powered to detect differences in uncommon safety events, safety monitoring will be primarily descriptive and clinical rather than dependent on statistical significance. Adverse events will be summarized as counts and proportions, with exact 95% confidence intervals, overall and by physiologic cohort and pacing condition. Continuous physiologic safety measures will be summarized as within-subject changes from baseline using means and standard deviations or medians and interquartile ranges, as appropriate. Mixed-effects models specified for the primary analysis may be used to evaluate repeated within-subject physiologic changes, and Fisher's exact test may be used exploratorily to compare event proportions when cell sizes permit. Bedside stopping criteria and clinical judgment, rather than a P-value threshold, will determine whether an individual study procedure is stopped.

Immediate suspension of research. Study-directed pacing and threshold testing will be suspended immediately pending safety review if any of the following occurs:

- A death, cardiac arrest, initiation of extracorporeal mechanical circulatory support, sustained clinically significant tachyarrhythmia requiring urgent treatment judged possibly related or related to a study procedure.
- Cumulative review identifies a recurring pattern of clinically important hemodynamic or perfusion deterioration temporally associated with a study procedure.
- A device, equipment, or procedural problem is identified that could place additional participants at risk.
- The Principal Investigator, treating clinical leadership, IRB, sponsor, or an institutional safety official requests suspension.

Following suspension, no new participants will begin study procedures until the event or pattern has been reviewed. Patients in the cardiac intensive care unit are in a high-risk situation. We expect death, cardiac arrest, and initiation of ECMO to occur in the post-operative period, even in the absence of a clinical research study. The Heart Center keeps meticulous records on these major adverse events, and we will track run sheets and other QI-based frequency data to ensure that we are not encountering adverse events at a higher frequency than anticipated within this population.

20.2 Adverse Events

Definitions and Assessment

Adverse Event (AE): An untoward medical occurrence arising after initiation of the first study-specific procedure, requiring intervention from the clinical team, regardless of whether it is considered related to the research. We will not record clinical changes that are expected during the usual course of clinical care, and the PI and co-investigators will have responsibility for determining whether events are within or outside of standard of care. Events occurring after consent but before protocol initiation will be recorded when they affect eligibility or study participation.

The following are our predetermined serious adverse events:

- Clinically significant tachyarrhythmias
- Cardiac arrest
- Initiation of extracorporeal mechanical circulatory support
- Death
- Development of a protocol-defined exclusion criterion after enrollment, other than maximum heart rate criteria

The following are our predetermined adverse events:

- Skipped pacing phases
- Discontinuation of protocol-directed pacing because of clinical concern
- Any untoward event associated with pacing capture-threshold testing.

Causality: The Principal Investigator or physician co-investigator will classify each AE/SAE as related, possibly related, or not related to the study intervention. Assessment will consider temporal relationship, known effects of temporary pacing or threshold testing, alternative clinical explanations, and improvement after adjustment or discontinuation of the study procedure.

Expectedness: An event will be considered expected when its nature and severity are consistent with the risks described in the protocol and consent. Expected study-related events include transient hypotension or hypertension, reduced cardiac output or tissue-perfusion measures, increased myocardial oxygen

demand, and atrial or ventricular arrhythmia. These events are anticipated to be uncommon and generally reversible with adjustment or discontinuation of pacing. Cardiac arrest, mechanical circulatory support, and death are monitored as serious safety endpoints but are not expected consequences of the study intervention.

Severity grading. AEs will be graded using the applicable Common Terminology Criteria for Adverse Events when an appropriate term exists. When no directly applicable criterion exists, the following five-level clinical scale will be used:

- Grade 1 (mild): Transient or asymptomatic event requiring no intervention beyond observation.
- Grade 2 (moderate): Event requiring a nonurgent clinical intervention or adjustment in management, without major escalation of support.
- Grade 3 (severe): Medically significant event requiring urgent intervention, substantial escalation of support, or prolongation of hospitalization.
- Grade 4 (life-threatening): Event requiring immediate life-sustaining intervention.
- Grade 5: Death.

Time Frame and Process for Collection: AEs and SAEs will be collected from initiation of the protocol baseline observation through completion of the 72-hour strength-duration assessment. Serious or potentially study-related events will be reported immediately to the Principal Investigator; all other new AEs will be reviewed by the Principal Investigator or a physician co-investigator within 2 days, excluding holidays and weekends. Serious events assessed as possibly related or related will be followed through resolution, stabilization, or hospital discharge, whichever occurs first.

Management of Adverse Events. For any event that may be related to protocol-directed pacing or threshold testing, the research procedure will be paused or stopped immediately and the treating clinical team will assume unrestricted management. Expected events will be managed according to institutional standards of care, including pacing-rate or output adjustment, discontinuation of pacing, treatment of arrhythmia, and escalation of hemodynamic support as clinically indicated.

Reporting. The Principal Investigator is responsible for ensuring that AEs and SAEs are documented and reported. The Lurie Children's Hospital IRB Incident Assessment Tool will be used to determine whether an event constitutes a reportable incident or unanticipated problem. Reportable events will be submitted to the IRB, sponsor, and other institutional offices within applicable required timelines. Any event or cumulative finding that suggests a new or increased risk will be reported promptly and will be evaluated for protocol, consent, or recruitment changes. Non-reportable events will be summarized in cumulative safety reviews and in required continuing-review or progress reports.

21.0 Provisions to Protect the Privacy Interests of Subjects

21.1 Subject Privacy

Subjects' privacy will be protected by conducting all study activities within the CICU, where access is limited to authorized clinical personnel and approved visitors. The informed consent discussion will be conducted in a private setting whenever feasible, such as the patient's clinic room prior during the pre-operative evaluation or another private location. Participation is voluntary, and families may decline or withdraw from the study at any time without affecting the patient's medical care. Research procedures will be performed in conjunction with routine clinical care and will not require unnecessary interactions or disclosure of personal information beyond what is needed for the conduct of the study. The research team will access medical records and other sources of information only with proper authorization and in compliance with privacy regulations. Access will be limited to the information necessary for the study.

21.2 Steps to put subjects at ease

The study is designed to minimize any sense of intrusiveness by integrating research activities into routine postoperative clinical care. Parents or legally authorized representatives will receive a thorough explanation of the study during the informed consent process and will have the opportunity to ask questions before deciding whether to participate. No sensitive personal questions will be asked beyond those necessary for the study. Study procedures will be performed by clinicians familiar with the patient's care, and participation may be discontinued at any time at the request of the parent or the clinical treatment team without affecting the patient's medical care.

21.3 Access to information

The research team will access study information through the electronic medical record under HIPAA authorization obtained as part of the informed consent process. Study personnel will also access physiologic data collected through the institutional Sickbay platform and study data entered into REDCap. Access to all study information will be limited to authorized study personnel who have completed the required institutional training and have permission to access these systems for research purposes.

22.0 Compensation for Research-Related Injury

Not applicable.

23.0 Costs to Participants

There are no costs for participants in this study

24.0 Setting

24.1 Sites and locations

All study activities will be conducted at Lurie Children's Hospital. Research procedures will be performed in the CICU during routine postoperative clinical care. Study data will be obtained from the electronic medical record, the institutional Sickbay physiologic monitoring platform, and REDCap.

Informed consent may be obtained in person or through the institution's approved electronic consent (eConsent) process, depending on family preference and logistical considerations.

This study does not involve a community advisory board. The research will be conducted only at Lurie Children's Hospital and does not involve any external research sites or international locations.

25.0 Resources Available

Due to the number of congenital heart surgeries performed each year and the eligibility criteria for the study, we do not anticipate any issues meeting our recruitment goals.

Lurie Children's Hospital performs approximately 450 congenital heart surgeries each year with 51% being <12 months, 9% being from 12 months to 36 months and 25% being between 36 months and 12 years, providing a sufficient population of potentially eligible subjects to meet the planned enrollment of 46 participants within the anticipated recruitment period. Based on the annual surgical volume and study eligibility criteria, we do not anticipate difficulty achieving our recruitment goals.

The investigators have protected time to conduct the study. The research will take place in the CICU, where the necessary clinical infrastructure, temporary pacing equipment, bedside physiologic monitoring, Sickbay data acquisition platform, and REDCap data capture system are routinely available. A dedicated research professional with clinical expertise will provide protocol support, including visual reminders and phone

check-ins with attending physicians and bedside nurses to facilitate protocol implementation and timely pacing transitions without disrupting routine clinical care.

No additional medical or psychological resources are anticipated to be required as a result of participation in this minimal-risk study. Participants will continue to receive all routine postoperative care. Families will have access to the hospital's social work, psychology, child life, and other support services that are routinely available to all patients undergoing congenital heart surgery.

All research personnel will complete required institutional human subjects protection training and will be trained on the study protocol, informed consent process, and study procedures before participating in the research. All study personnel will be listed on the IRB-approved study team roster and will receive ongoing protocol updates through regular investigator meetings. The Principal Investigator is responsible for ensuring that all study personnel are adequately trained and informed regarding the protocol, study procedures, participant safety, and their individual responsibilities throughout the study.

26.0 References

1. Barker GM, Affolter J, Saenz J, et al. Temporary atrial pacing for cardiac output after pediatric cardiac surgery. Pediatr Cardiol 2013;34:1605–11. PMID: 23503930

2. Chauhan M, Prentice E, Zidan M, Walters HL, 3rd, Delius RE, Mastropietro CW. Necessity of temporary epicardial pacing wires after surgery for congenital heart disease. Ann Thorac Surg 2014;97:2148–53. PMID: 24681035

3. Loomba RS, Villarreal EG, Farias JS, Flores S, Wong J. Factors associated with renal oxygen extraction in mechanically ventilated children after the Norwood operation: insights from high fidelity haemodynamic data. Cardiol Young 2024:1–6. PMID: 38783789

4. Mendel B, Christianto C, Setiawan M, Prakoso R, Siagian SN. A Comparative Effectiveness Systematic Review and Meta-analysis of Drugs for the Prophylaxis of Junctional Ectopic Tachycardia. Curr Cardiol Rev 2022;18:e030621193817. PMID: 34082685

5. Wang Q, Chen C, Wang L. Efficacy and safety of dexmedetomidine in maintaining hemodynamic stability in pediatric cardiac surgery: a systematic review and meta-analysis. J Pediatr (Rio J) 2022;98:15–25. PMID: 34252370

6. Ergul Y, Unsal S, Ozyilmaz I, Ozturk E, Carus H, Guzeltas A. Electrocardiographic and electrophysiologic effects of dexmedetomidine on children. Pacing Clin Electrophysiol 2015;38:682–7. PMID: 25753681

7. Niezen CK, Modestini M, Massari D, et al. Prognostic Value of Perioperative Near-Infrared Spectroscopy Monitoring for Postoperative Acute Kidney Injury in Pediatric Cardiac Surgery: A Systematic Review. Semin Cardiothorac Vasc Anesth 2025;29:209–18. PMID: 39928846

8. Owens GE, King K, Gurney JG, Charpie JR. Low renal oximetry correlates with acute kidney injury after infant cardiac surgery. Pediatr Cardiol 2011;32:183–8. PMID: 21085945

9. Zaleski KL, Kussman BD. Near-Infrared Spectroscopy in Pediatric Congenital Heart Disease. J Cardiothorac Vasc Anesth 2020;34:489–500. PMID: 31582201

10. Gaies MG, Gurney JG, Yen AH, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. Pediatr Crit Care Med 2010;11:234–8. PMID: 19794327

11. Barold SS, Ong LS, Heinle RA. Stimulation and sensing thresholds for cardiac pacing: electrophysiologic and technical aspects. Prog Cardiovasc Dis 1981;24:1–24. PMID: 7019961

12. Barold SS, Winner JA. Techniques and significance of threshold measurement for cardiac pacing. Relationship to output circuit of cardiac pacemakers. Chest 1976;70:760–6. PMID: 1001053

13. Coates S, Thwaites B. The strength-duration curve and its importance in pacing efficiency: a study of 325 pacing leads in 229 patients. Pacing Clin Electrophysiol 2000;23:1273–7. PMID: 10962751

14. Jastrzębski M, Moskal P, Bednarek A, Kiełbasa G, Vijayaraman P, Czarnecka D. His bundle has a shorter chronaxie than does the adjacent ventricular myocardium: Implications for pacemaker programming. Heart Rhythm 2019;16:1808–16. PMID: 31181375

15. Kiełbasa G, Jastrzębski M, Bednarek A, et al. Strength-duration curves for left bundle branch area pacing. Heart Rhythm 2024;21:2262–9. PMID: 38759916

Appendix A. Study Timeline for each patient

Study Activity	Screening / Pre-op	Enrollment	CICU Admission	Post-op Hour 1	Hours 1-4	Hours 4-7	Hours 7-10	Post-op Day 1	Post-op Day 2	Post-op Day 3	Study Completion
Eligibility assessment	X										
Informed consent / eConsent	X	X									
Assignment to Cohort (single- vs. two-ventricle pathway)		X									
Randomization		X									
Baseline clinical data collection			X	X							
Determine intrinsic baseline heart rate				X							
Protocol pacing phase					X	X	X				
Continuous physiologic data collection (Sickbay)			X	X	X	X	X	X	X	X	
Routine clinical laboratory data collection[1]			X	X	X	X	X	X	X	X	
Strength-duration testing[2]			Baseline					Day 1	Day 2	Day 3	
Adverse event assessment			X	X	X	X	X	X	X	X	X
Data integrity evaluation, case finalization											X

1. Laboratory values (*e.g.* arterial pH, bicarbonate, and serum lactate) are obtained only as part of routine clinical care. No laboratory tests are performed solely for research purposes.

2. Strength-duration testing is performed using standard pacing threshold assessment techniques and only when the treating clinical team determines that it is clinically appropriate and safe.

Appendix B. Study Data Collection

A. Protocol-directed data collection:

- Strength duration pacing curves, as established by existing clinical protocols at 4 times: baseline, post-operative day 1, post-operative day 2, post-operative day 3. These strength duration curves are typically established as part of routine clinical care.

B. Tabulation of clinical data collection:

All clinical data are obtained as part of routine postoperative care. The clinical treatment team retains full responsibility for patient management and determines which laboratory studies, physiologic measurements, medications, imaging studies, and clinical assessments are obtained. Accordingly, the variables listed below are representative of typical postoperative care but are not mandated by the study protocol. Individual patients may have more or fewer data elements available depending on their clinical condition and the judgment of the treating team.

B1. Baseline Demographic, Clinical, and Operative Variables

- Age
- Sex
- Weight
- Height or length, if available
- Cardiac diagnosis
- Surgical procedure
- Single-ventricle versus two-ventricle pathway
- STAT surgical category
- Cardiopulmonary bypass time
- Aortic cross-clamp time
- Circulatory arrest time, if applicable
- Prior cardiac surgery
- Relevant medical history
- Cardiac rhythm prior to surgery
- Other demographic or baseline clinical characteristics relevant to postoperative physiology

B2. Continuous Physiologic Data Obtained Through Sickbay

- Heart rate
- Cardiac rhythm
- Arterial blood pressure
- Mean arterial pressure
- Central venous pressure
- Arterial oxygen saturation
- Cerebral near-infrared spectroscopy (NIRS)
- Renal near-infrared spectroscopy (NIRS)
- Respiratory rate
- Mean airway pressure
- Ventilator parameters
- Temperature

- Other continuously monitored physiologic variables routinely captured by the institutional Sickbay platform

B3. Intermittent Clinical Data Obtained from the Electronic Medical Record

The following variables may be collected when obtained as part of routine clinical care:

Laboratory studies

- Arterial blood gas measurements
- Serum lactate
- Hemoglobin / Hematocrit
- Electrolytes
- Glucose
- Creatinine
- Blood urea nitrogen
- Other laboratory values obtained during routine postoperative care

Clinical and physiologic variables

- Vasoactive Inotropic Score (VIS)
- Vasoactive medication doses
- Sedation medication doses, including dexmedetomidine and opioid infusions
- Antiarrhythmic medications
- Mechanical ventilation settings
- Fluid balance
- Urine output
- Chest tube output
- Temporary pacing settings
- Echocardiographic findings, if clinically obtained
- Clinically significant arrhythmias
- Cardiac arrest
- Initiation of extracorporeal mechanical circulatory support
- Other clinically relevant postoperative observations documented in the medical record

B4. Study Specific Measurements

- Pacing capture thresholds measured across multiple pulse durations. Pacing threshold measurements will be recorded on standardized study forms and entered into the REDCap study database.
- Derived electrophysiologic parameters, including rheobase and chronaxie

Appendix C. Clinical Research Coordinator Eligibility and Study Checklist

** This checklist is submitted as an example,
but it may be changed in format or specific fields if needed to accurately capture data.
The formal data collection request is provided in Appendix B.**

Participant ID		MRN	
First Name		Last Name	
Study eligibility range (check with PI if uncertain): ☐ <12 months ☐ 12-36 months ☐ 36 months -12 years			

Section 1. Screening, Enrollment, and Randomization

- ☐ Age within age range on projected date of surgery
- ☐ Congenital cardiac surgery planned
- ☐ Cohort: ☐ Cohort 1 [Single Ventricle] ☐ Cohort 2 [Biventricular]
- ☐ Written consent/eConsent obtained
- ☐ Randomization completed
- Randomization Assignment: ☐ Group 1 ☐ Group 2
- Date & Time Randomized: _____
- CRC who randomized (First and last name): _____

Section 2. Protocol Execution

Initiation

- ☐ Temporary epicardial pacing wires present
- ☐ Intrinsic sinus rhythm present
- ☐ No uncontrolled tachyarrhythmia
- ☐ No ventricular pacing required
- ☐ Arterial pH ≥7.10
- ☐ No postoperative cardiac arrest
- ☐ No mechanical circulatory support
- ☐ No hemodynamically significant bleeding
- ☐ Baseline intrinsic heart rate documented: _____ bpm

Protocol Phase 1

- Projected Start Time: _____
- Actual Start Time: _____
- Protocol Phase: ☐ Sinus rhythm ☐ Pacing +10 bpm ☐ Pacing +20 bpm

CALCULATION
Baseline heart rate + 10 bpm, rounded up to the nearest 5 bpm: _____ bpm
Baseline heart rate + 20 bpm, rounded up to the nearest 5 bpm: _____ bpm

- ☐ Rate readjusted during this phase
- Cause of rate readjustment
  - ☐ Sinus rhythm > paced rate
  - ☐ Other _____

  New Baseline intrinsic heart rate: _____ bpm
- ☐ Phase skipped
- Reason for skipping phase
  - ☐ Second rate readjustment required
  - ☐ Other _____
- ☐ Phase Completed
- ☐ Protocol discontinued during this phase

Protocol Phase 2

- Projected Start Time: _____
- Actual Start Time: _____
- Protocol Phase: ☐ Sinus rhythm ☐ Pacing +10 bpm ☐ Pacing +20 bpm

CALCULATION
Baseline heart rate + 10 bpm, rounded up to the nearest 5 bpm: _____ bpm
Baseline heart rate + 20 bpm, rounded up to the nearest 5 bpm: _____ bpm

- ☐ Rate readjusted during this phase
- Cause of rate readjustment
  - ☐ Sinus rhythm > paced rate
  - ☐ Other _____

  New Baseline intrinsic heart rate: _____ bpm
- ☐ Phase skipped
- Reason for skipping phase
  - ☐ Second rate readjustment required
  - ☐ Other _____
- ☐ Phase Completed
- ☐ Protocol discontinued during this phase

Protocol Phase 3

- Projected Start Time: _____
- Actual Start Time: _____
- Protocol Phase: ☐ Sinus rhythm ☐ Pacing +10 bpm ☐ Pacing +20 bpm

CALCULATION
Baseline heart rate + 10 bpm, rounded up to the nearest 5 bpm: _____ bpm
Baseline heart rate + 20 bpm, rounded up to the nearest 5 bpm: _____ bpm

- ☐ Rate readjusted during this phase
- Cause of rate readjustment
  - ☐ Sinus rhythm > paced rate
  - ☐ Other _____

  New Baseline intrinsic heart rate: _____ bpm
- ☐ Phase skipped
- Reason for skipping phase
  - ☐ Second rate readjustment required
  - ☐ Other _____
- ☐ Phase Completed
- ☐ Protocol discontinued during this phase

Continuous Data Collection

- ☐ Sickbay recording verified
- ☐ Routine clinical laboratory data available
- ☐ Study forms completed

Monitoring During Study (Discontinue protocol-directed pacing if any occur)

- ☐ Postoperative cardiac arrest
- ☐ Mechanical circulatory support initiated
- ☐ Ventricular pacing required
- ☐ Uncontrolled tachyarrhythmia
- ☐ Hemodynamically significant bleeding
- ☐ Arterial pH <7.10
- ☐ Treating clinical team requests protocol discontinuation

Protocol Discontinued?

- ☐ No ☐ Yes
- Date/Time: _____
- Clinician Discontinuing Protocol, if clinician-directed (Name): _____

- Reason for discontinuation:

Strength-Duration Testing

- Baseline ☐ Completed ☐ Deferred
- Post-op Day 1 ☐ Completed ☐ Deferred
- Post-op Day 2 ☐ Completed ☐ Deferred
- Post-op Day 3 ☐ Completed ☐ Deferred

Study Completion

- ☐ All study forms complete
- ☐ Data entered into REDCap
- ☐ Queries resolved
- CRC (First and last name): _____ Date: _____

APPENDIX D. Text of parent handout

Help Us Improve Care for Children After Heart Surgery

Your child may be eligible to participate in the POSTPACE Research Study: POSToperative PAcing for Cardiac Efficiency

What is the study about?

- After heart surgery, many children have temporary pacing wires placed as part of routine care to adjust their heart rate if needed.
- Doctors use different pacing approaches after surgery, but we do not yet know which approach is best.
- This study compares standard pacing strategies to learn the best way to improve blood flow and oxygen delivery for the first 10 hours after heart surgery.

Why is the study important?

Your child's participation could help us improve care for future children recovering from heart surgery.

What would happen if my child participates?

If you choose to participate:

- Your child's care will continue to be directed by the CICU team.
- Your child will be randomly assigned to one of two timing schedules for routine pacing strategies already used in clinical care.
- We will record information obtained by the medical team as part of your child's normal care.
- We do not expect this study to cause pain or discomfort for your child. No additional blood draws or samples are required for the study.
- You would receive a $100 gift card for your child's participation.

Are there any risks?

The pacing methods used in this study are all standard approaches currently used in the CICU. No investigational pacemakers or devices are used.

Do I have to participate?

No. Participation is completely voluntary. Choosing not to participate will not affect your child's medical care in any way. If you decide to participate, you may withdraw your child from the study at any time.

Questions?

If you would like more information, please speak with your child's physician or a member of the study team. The study team can be reached at 312-227-2525.

This study is Lurie Children's IRB #STUDY00001292, POSToperative PAcing for Cardiac Efficiency (POSTPACE), PI: Dr. Greg Webster. The content of this flier has been approved by the Lurie Children's IRB