WakeMed Health & Hospitals
3000 New Bern Ave., Raleigh, NC 27610

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Title:	**A Prospective Pilot Study of the Combination of CardiaMend and Amiodarone for the Prevention of Postoperative Atrial Fibrillation (POAF) in Patients Undergoing Isolated Cardiac Arterial Bypass Grafting or Isolated Valve Surgery (CAMP POAF)**
Protocol and Date:	**CAMP POAF SEPTEMBER 26, 2022**
Principal Investigator:	Judson Williams, MD, MHS 3000 New Bern Ave. Raleigh, NC 27610 919-231-6333

A Prospective Pilot Study of the Combination of CardiaMend and Amiodarone for the Prevention of Postoperative Atrial Fibrillation (POAF) in Patients Undergoing Isolated Cardiac Arterial Bypass Grafting or Isolated Valve Surgery

CONCISE SUMMARY

The purpose of this study is to evaluate the combination of CardiaMend, an FDA cleared surgical patch designed to provide soft tissue reinforcement, repair, and reconstruction of the pericardium (sac which holds the heart) following cardiac surgery, with the addition of amiodarone (a medication to prevent irregular heart rhythms) in the prevention of atrial fibrillation in patients undergoing coronary artery bypass grafting (CABG) or valve surgery. Atrial fibrillation is an irregular heart rhythm that occurs when the two top chambers of the heart quiver instead of beating normally. Atrial fibrillation is extremely common after open heart surgery, affecting 20-50% of patients. Atrial fibrillation, if not treated, could lead to the development of blood clots that can travel to the brain, lungs, arms, and legs.

This is a single-center, prospective, pilot study, enrolling adult subjects undergoing isolated CABG or isolated valve surgery, via complete median sternotomy (cutting the bone in the center of the chest open). A total of up to 30 patients will be enrolled in the study.

Patients will be followed for the duration of hospitalization until discharge. No further follow up will be required for the study.

Risks of the trial include those associated with CABG or valve surgery. These may include bruising, swelling, infection, bleeding, redness at surgical site, fluid around surgical site, cyst formation, scarring, reactions from anesthesia medications, excessive fluid loss, damage to skin or nerves, abnormal heart rhythm, and death.

If you are interested in learning more about this study, please continue to read below.

Your participation in any research study is voluntary. To decide whether you want to participate in a research study, you should understand the study risks and benefits to make an informed decision. This process is known as informed consent. The purpose of this document is to give you information about the purpose, procedures, and possible benefits and risks of this study. This form also explains how your personal identifying and medical information will be used and who may see it.

An institutional review board has approved the information in this consent document and has given approval for the study doctor to do the study. An institutional review board is an independent committee established to help protect the rights of research subjects. This does not mean the institutional review board has approved your participation in the study. You must think about the information in this consent document for yourself. You must then decide if you want to be in the study.

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Please read this document carefully and do not hesitate to ask any questions you might have about this form or the study. The form may contain words you do not understand. Please ask the study doctor or staff to explain the words or information that you do not understand. You may have a copy of this form to review at your leisure and/or ask the advice of others. Once you understand the study, you will be asked to sign this form if you wish to participate.

Why is this research study being conducted? What is the purpose?

The purpose of this study is to evaluate the combination of CardiaMend, with the addition of amiodarone, in the prevention of an abnormal heart rhythm called atrial fibrillation after open heart surgery (also known as post-operative atrial fibrillation, or POAF) in patients undergoing isolated coronary artery bypass grafting (CABG) or valve surgery. WakeMed will enroll up to 30 patients in this investigator-initiated trial.

Atrial fibrillation is an irregular heart rhythm that occurs when the two top chambers of the heart quiver instead of beating normally. POAF is extremely common after open heart procedures, such as CABG or valve surgeries, affecting 20-50% of patients. If not treated, atrial fibrillation could lead to the development of blood clots that can travel to the brain, lungs, arms, and legs. This study will evaluate CardiaMend, an FDA cleared (K210331) pericardial reconstruction matrix used in combination with amiodarone as a prevention of POAF.

Amiodarone is an antiarrhythmic drug which is currently approved by the FDA for oral and intravenous (IV) administration to treat and prevent arrhythmias. Most patients receive an IV bolus (a single, large dose given at one time) of amiodarone prior to surgery to prevent atrial fibrillation. If patients develop POAF, they are then treated with additional doses of IV and/or oral amiodarone. In this study, we will soak the CardiaMend patch in amiodarone for local, topical administration of amiodarone to the heart instead of administering the pre-procedure IV bolus. You will receive a one-time local dose of 450mg of amiodarone via the CardiaMend patch at the time of pericardium closure.

The primary mode of action of CardiaMend is to serve as a physical patch to repair and reconstruct the sac which holds the heart (pericardium) following cardiac surgery. This repair mimics the role of the body's pericardium by providing a physical barrier to separate the heart from the rest of the chest structures, including the sternum (bone in the middle of the chest) which is a site of significant injury. The CardiaMend provides an additional layer of protection and support for the heart, which aids in healing and reducing infection risk.

While being used primarily to repair the pericardium, the CardiaMend device can also act as a short-term reservoir for local delivery of amiodarone to the heart to help reduce the occurrence

of POAF. This is possible because of CardiaMend's ability to absorb liquid, and being in close proximity to the heart.

Previous studies have shown that local administration of amiodarone is safe and still offers antiarrhythmic benefit. These studies have also shown that local delivery of amiodarone reduces the risks that are associated with oral or IV administration, such as lung and liver problems.

What will I have to do if I am in this research study?

Patients who are undergoing isolated CABG or isolated valve surgery, via open chest approach who meet all criteria for eligibility and have no exclusionary criteria met are candidates for the trial.

All study patients will undergo a screening interview wherein their medical history will be reviewed to verify they qualify for the study. The patients meeting the criteria for enrollment in the study will sign the informed consent form and be assigned a patient identification number. Unique patient identification numbers will be created and assigned only to patients who qualified for the study signed the informed consent form. Patients will be assigned a unique identification number for the purpose of the trial, which will be stored in a secure location. All information obtained will be reported using the unique identification number. The 30 patients enrolled will receive treatment with the CardiaMend with Amiodarone.

Patients will be monitored while in the hospital for the development of atrial fibrillation with telemetry (a heart monitor) and through review of the medical record. There will be no required follow up post discharge from the hospital.

How long will I have to participate in this research study – how many other participants will be in the study?

You will participate in the trial as long as you are hospitalized for your initial CABG or isolated valve surgery. There is no required follow up after discharge from the hospital.

How are individuals selected for this research study?

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You will be eligible to participate in the study **if you meet all of the following criteria**:

Inclusion Criteria:

- Subject aged 20-85 years old.
- Patients able to provide written informed consent, understand, and be willing to comply with study-related procedures.
- Participants who are scheduled to undergo open-chest cardiac surgery via complete median sternotomy (cutting open the chest). Includes:
    - Coronary artery bypass graft (CABG) or valve repair/replacement, or
    - Inclusionary valve repair/replacement procedures for the primary reason for surgery include: aortic valve repair/replacement, mitral valve repair/replacement.
    - Note: Left atrial appendage (LAA) procedures are allowed if CABG and/or valve repair or replacement is the qualifying surgical procedure but is not a qualifying surgical procedure on its own.
- In sinus rhythm (the heart's normal rhythm) at the time of office visit and prior EKG (note: continuous EKG monitoring for 48 hours is not required).

And **do not have any of the following criteria**:

Exclusion Criteria:

- Subject unable to give voluntary written informed consent, is unlikely to cooperate or is legally incompetent, including subjects who are institutionalized by court or official order, or in a dependency relationship with, testing center or investigator.
- Any condition which could interfere with the subject's ability to comply with the study.
- Ongoing participation in an interventional clinical study or during the preceding 30 days.
- Female subjects who are pregnant, breastfeeding, were pregnant within the last three months, or are planning to become pregnant during the study.
- Active skin or deep infection at the site of implantation.
- History of non-healing wounds or wound-healing disorders.
- Known connective tissue diseases (e.g., Ehlers-Danlos syndrome, Epidermolysis bullosa, Marfan syndrome, Osteogenesis imperfecta).

- Immune-suppressed subjects, immune-deficiency subjects (properly managed diabetes mellitus is not an exclusion criterion).
- Use of IV or oral systemic steroid therapy and/or other constant anti-inflammatory therapies.
- The subject has an implantable cardiac device (i.e., cardiac resynchronization therapy devices with and without defibrillator capabilities (CRTs and CRT-Ds), implantable cardioverter-defibrillators (ICD) and pacemakers).
- Known history of atrial fibrillation or paroxysmal (temporary) atrial fibrillation.
- History of ablation for atrial fibrillation.
- Patients already receiving amiodarone as a treatment for atrial fibrillation or ventricular arrhythmias

What are the risks of this research study – what could go wrong?

As with any surgical procedure or research study, there are risks involved, some of which may be unforeseen. The most common risks associated with this procedure are:

Complications of the open heart procedure, which is part of your routine care, may include:

- Bruising, swelling
- Infection
- Bleeding
- Erythema—redness at surgical site
- Seroma—fluid surrounding surgical site
- Cyst
- Microcalcifications—small benign calcium deposits that develop after surgery
- Scarring
- Anesthesia toxicity—reaction to medication administered during surgery to keep you asleep

- Excessive fluid loss
- Damage to skin or nerves
- Abnormal heart rhythms requiring treatment, such as atrial fibrillation or heart block
- Death

Your surgeon will discuss these complications of the routine surgical procedure with you in depth.

Amiodarone (given at high doses and for a prolonged period) intravenously (IV) or orally (by mouth) can cause:

- Hypotension (low blood pressure)
- Corneal deposits (calcification in eye)
- Photosensitivity (sensitive to light)
- Possible lung toxicity
- Thyroid dysfunction
- Hepatic (liver) toxicity

Previous studies have shown that local administration of amiodarone reduces the risk of these systemic effects (entire body).

What are the benefits of this research study?

There are no guaranteed benefits of participating in this research study. Previous studies have shown that local administration of amiodarone reduces the systemic effects (entire body) of the medication, which reduces the risk of eye, thyroid, lung, and liver injury. The local delivery of amiodarone may also reduce the possibility of developing post-operative atrial fibrillation.

If I do not want to take part in this research study, what are my options?

Participation in the trial is voluntary. Your decision whether or not to participate will not alter the type of surgery or care received prior to, during, or after the surgery.

What if there is new information I should be informed about?

Should there be new information available regarding the study, this information will be provided to you.

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Are there any costs associated with this research study?

There are no costs to you for participating in the research study. The CardiaMend patch with Amiodarone will be supplied at no cost to you or your insurer. Your surgery and associated care costs will be billed to you and/or your insurer as routine care. There are no additional procedures, tests, or medications required of you while participating in the trial.

Will my study doctor or members of the study team receive any type of compensation for this research study? Is there any reason why the study doctor or study team should not participate in this research study?

Helios Cardio, Inc., the maker of CardiaMend, will be providing support to WakeMed and the study doctor for the conduct of this study. There are no conflicts of interest or other reasons why the study doctor or study team should not participate in this research study.

Will I get paid for participating in this research study?

You will not receive any compensation for participating in the trial**.**

What if I need to see another doctor while participating in this research study?

Participation in this trial will not keep you from receiving care from any other provider while hospitalized. Your participation in the research study will be over at the time of discharge from the hospital.

Do I have to participate in this research study?

You do not have to participate in this research study.

If you sign this consent form, you are hereby freely and voluntarily are consenting to participate in the study described above. This consent is given based on verbal and written information provided to you and on the understanding that you are medically and physically qualified to participate in this study. You understand that you do not have to participate in this study and that choosing not to participate will not affect your current or future medical care by your physician or this institution.

What are my rights as a research participant?

If you do not want to participate in this study, you do not have to. If you do want to participate, however, you must sign this form. You acknowledge that your participation is voluntary, and you have been told that you are able to withdraw your consent and stop your participation in this study at any time. If you do withdraw, it will not affect your current or future medical care by your provider or this institution, and will involve no penalty or loss of benefits to which you are otherwise entitled. If you intend to withdraw from the study, please inform the Investigator immediately.

Your data may be stored and shared for future research without additional informed consent if identifiable private information, such as your name and medical record number, are removed. If your identifying information is removed from your data, we will no longer be able to identify and destroy them.

Why would I be taken off the study early?
You may be taken off the study early by the Investigator without your consent for any reason, including, but not limited to:

- Investigator's judgment that any condition or circumstance may jeopardize your welfare or the integrity of the study.
- If you fail to follow the instructions of the Investigator and study requirements.
- If the study is stopped by the Investigator prior to its completion.

Who may see, use, or share my health information?

You have the right to privacy. All information obtained from this research that can be identified with you will remain confidential within the limits of the law. You authorize your protected health information to be used and disclosed in accordance with the study protocol. Your identifying information (e.g., name, address, social security number, date of birth) will not be revealed in reports or publications resulting from this study without your expressed consent. WakeMed and/or the Principal Investigator for this study will allow the following organizations/individuals to review your study information/medical records:

- Monitors from the Food and Drug Administration (FDA)
- The study investigator and clinical research staff
- Members of the Institutional Review Board (IRB) at WakeMed
- Office for Human Research Protections in the U.S. Department of Health and Human Services
- Helios Cardio, Inc.

(which include identifying information) created and maintained for the research study when appropriate and necessary. These groups will treat such information as confidential; however,

absolute confidentiality cannot be guaranteed. Medical records created after the end of the research study or after you revoke this authorization will not be used or disclosed without your expressed consent except when required by state or federal law.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the study results. You can search this Web site at anytime.

What if I get hurt while participating in this research study?

If you feel you need medical care because of participation in this research study, you should contact the principal investigator, Judson Williams, at (919) 231-6333, 24 hour a day, 7 day a week access, at 3000 New Bern Ave., Raleigh, NC 27610. Financial compensation for the cost of this care cannot be provided by WakeMed. However, every effort will be made to make available to you the facilities and professional skills of WakeMed.

Institutional Review Board (IRB) Approval:

The Institutional Review Board (IRB) at WakeMed has reviewed the protocol for this study using certain federal and local laws that relate to research and experiments involving human subjects. However, approval of this protocol by the WakeMed IRB is not the same as endorsing this study or its consequences.

Contact Information:

I understand that I may use the following contact information to reach the appropriate person/office (anonymously, if you like) to address any questions or concerns I may have about this study. I know:

I can call…	At	If I have questions or concerns about
Investigator: **Judson Williams** **3000 New Bern Ave.** **Raleigh, NC 27610**	Phone: **(919) 231-6333**	▪ General questions about the study ▪ Research-related injuries or emergencies ▪ Any research-related concerns or complaints
IRB Chair **Adeyemi Lawal**	Phone: **(919) 350-7335**	▪ Rights of a research subject ▪ Use of protected health information.

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3000 New Bern Ave.
Raleigh, NC 27610

- Compensation in event of research-related injury
- Any research-related concerns or complaints.
- If investigator/study contact cannot be reached.
- If I want to speak with someone other than the Investigator, Study Contact or research staff.

Documentation of Informed Consent and Authorization

- I have read the information provided in this consent form and have been given enough time to consider the decision to participate in this study.
- This research study has been satisfactorily explained to me, including possible risks and benefits
- All my questions were satisfactorily answered
- I understand that participation is voluntary and that I can withdraw at any time.
- I am signing this consent form prior to participating in **any** research activities
- By signing this consent form, I acknowledge that I have not waived any of my legal rights or released any party from liability for negligence and I hereby authorize the Principal Investigator, Judson Williams, or those that he/she may designate to perform the research described in this document.

I understand that I will receive a signed copy of this consent form.

My authorization will expire at the completion of the research study.

_____ _____
Signature of Research Participant Date

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Printed Name of Research Participant

"Either I have, or my designee has explained to the study subject named above the nature of the research described above. To the best of my knowledge, the study subject signing this consent form understands the nature, demands, benefits and risks involved in participating in this research study."

_____ _____
Signature of Person Obtaining Consent Date

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Printed Name of Person Obtaining Consent

Note: If you are enrolled in this study, a copy of your informed consent will be given to you. The original copy of your informed consent will go into your study file with the Principal Investigator.