Informed Consent Form

You are invited to participate in a clinical efficacy study initiated by Fuwai Hospital, Chinese Academy of Medical Sciences, which aims to evaluate the effect of Bachmann's bundle pacing on improving new-onset atrial fibrillation in patients with cardiac insufficiency. This study has been approved by the Ethics Committee of Fuwai Hospital, Chinese Academy of Medical Sciences (Tel: 010-88396281, 010-88396282). Please read the explanations carefully to understand your rights and obligations in this study, and clarify the nature, content and risks of the study. Participation in this study is completely voluntary, and your treatment in our hospital and other legitimate rights and interests will not be affected regardless of your participation. When the researchers explain and discuss this informed consent form with you, you may ask questions at any time and request the researchers to explain any unclear points. You have ample time to discuss your participation with your family, friends and your doctor, and please make a decision after full consideration.

If you are currently participating in other clinical studies, please inform the researchers.

Sponsor of this study: 2025-ZX183

This is a multicenter study, with Fuwai Hospital, Chinese Academy of Medical Sciences as the leading center. The principal investigator of the project is Chief Physician Fan Xiaohan from this hospital.

Principal investigator of this center:

Fan Xiaohan, Chief Physician

Department of Functional Testing / First Ward of Arrhythmia

1. Rationale for This Study

Chronic heart failure (HF) is one of the most common cardiovascular diseases with a poor prognosis at present and in the future. For specific types of HF patients, cardiac resynchronization therapy (CRT) or implantable cardioverter defibrillator (ICD) can effectively improve cardiac function and prevent sudden death. Atrial fibrillation (AF) is the most common arrhythmia complicated in HF patients; the two often coexist, promote each other and are mutually causal. Traditional atrial pacing involves placing the atrial electrode in the right atrial appendage (RAA). Due to its anatomical

characteristics, RAA has the advantages of reliability and stability for electrode lead implantation, making it a clinically commonly used pacing site. However, RAA pacing prolongs the interatrial conduction, leads to asynchronous atrial contraction and hemodynamic changes, and is prone to induce AF, which is a non-physiological pacing method. Studies have shown that the incidence of new-onset AF in patients with sinus bradycardia receiving RAA pacing is as high as 30% to 40%. How to prevent new-onset AF in chronic HF patients undergoing CRT or ICD therapy has always been a major clinical challenge.

Bachmann's bundle is currently recognized as the most physiological pacing site in the atrium. By placing the pacing electrode in the Bachmann's bundle area, not only the pacing parameters are stable, but also a narrower P wave can be obtained compared with the intrinsic sinus rhythm and traditional RAA pacing, achieving synchronous activation of the left and right atria. The purpose of this study is to verify that Bachmann's bundle pacing helps reduce the risk of new-onset AF and related adverse HF events in HF patients undergoing CRT/left bundle branch pacing (LBBP) or ICD therapy.

2. Study Content

This study is designed as a multicenter, prospective, assessor-blinded, randomized controlled clinical trial. The study population consists of sinus rhythm HF participants with indications for CRT/LBBP or ICD implantation and no previous history of AF. A total of 70 participants are planned to be recruited at this center, and you will be randomly assigned to either the Bachmann's bundle pacing group or the traditional atrial pacing group via central randomization, with a 1:1 allocation ratio.

The study adopts a randomized design, with participants randomly assigned at a 1:1 ratio to the Bachmann's bundle pacing group (experimental group) or the traditional atrial pacing group (control group). For the experimental group: the pacing electrode is implanted in the Bachmann's bundle area during surgery to ensure characteristic electrocardiographic manifestations during pacing; if implantation fails, the procedure will be converted to traditional atrial pacing. For the control group: the pacing electrode is implanted in the right atrial appendage or right atrial septum, both of which are

routine and well-established clinical atrial pacing procedures. Both can effectively achieve atrial pacing function, and standard operation will not bring additional harm to participants beyond routine medical procedures. Participants in both groups will receive guideline-directed medical therapy (GDMT) for at least 3 months continuously.

No special blood samples will be collected for this study; all relevant data will be obtained through routine clinical examinations, without additional specimen collection times or types.

3. Eligibility Criteria for Participation

You will be invited to participate in this study if you meet the following criteria:

Inclusion Criteria

1. Aged ≥18 years and ≤70 years;
2. Diagnosed with chronic cardiac insufficiency in accordance with current guidelines based on symptoms and signs, and has received GDMT for at least 3 months;
3. With indications for CRT/LBBP or ICD implantation, including:

① Symptomatic HF participants with sinus rhythm, QRS duration >120 ms, left bundle branch block (LBBB), and left ventricular ejection fraction (LVEF) ≤35%;

② Symptomatic HF participants with sinus rhythm, QRS duration ≥150 ms, non-LBBB, and LVEF ≤35%;

③ Symptomatic HF participants with sinus rhythm, QRS duration >120 ms, LBBB, and LVEF of 36%~50%;

④ Symptomatic HF participants with LVEF ≤50% and expected ventricular pacing percentage >20%;

⑤ Symptomatic HF participants with LVEF ≤50% who need ICD implantation for primary or secondary prevention of sudden death, and have indications for atrial pacing due to sinus bradycardia or an expected atrial pacing percentage >20%;

⑥ Participants with pacing-induced heart failure requiring upgrade therapy, in sinus rhythm, and undergoing reimplantation of atrial electrodes or extraction of the original atrial electrodes followed by reimplantation.

4. Signed the study informed consent form.

Exclusion Criteria

1. Expected survival time <12 months;
2. Post mechanical tricuspid valve replacement or congenital heart disease (including dextrocardia, transposition of the great arteries, persistent left superior vena cava);
3. Previous history of atrial fibrillation;
4. Previous cardiac surgery or need for surgical treatment due to severe structural heart disease within 1 year;
5. Pregnancy, planned pregnancy or heart transplantation;
6. Refusal of participation by the participant.

We will review your prior treatment methods, medications used, medical history, as well as results of relevant examinations such as blood samples, CT/MRI, and echocardiography, and determine your eligibility for the study based on the inclusion and exclusion criteria specified in the protocol. The final decision on your participation will be made by the principal investigator based on your relevant results.

4. Study Duration and Sample Size

This is a multicenter clinical study, with a total of 110 participants planned to be recruited across 4 research centers, including 70 at this center. The study is scheduled to run from March 2026 to December 2028. Your expected participation duration is 12 months, until 12 months after your surgery. A total of 4 post-operative follow-up visits are required for this study, with each visit taking approximately 1 day of your time.

5. Impact of Participation on Daily Life

Before your enrollment in the study, the doctor may need to inquire about and record your medical history, perform a physical examination, and understand your comorbidities and treatment status to determine your eligibility. Before deciding to participate, please carefully consider the possible impact of the above examinations and follow-up visits on your daily work, family life, etc., as well as the time and transportation for each follow-up visit.

The following precautions should be noted before, during and after your participation in the study:

Precautions Before the Study

Informed Decision-Making

- Fully understand the study purpose, procedures, potential risks and benefits, and be aware that you will be randomly assigned to the Bachmann's bundle pacing group (50% probability) or the traditional atrial pacing group (50% probability), and that Bachmann's bundle pacing may be converted to traditional atrial pacing in case of implantation failure. You may make a decision after full discussion with your family and doctor.
- If you are currently participating in other clinical studies, proactively inform the researchers of this study to avoid potential inter-study interference.
- Before signing the informed consent form, you may ask questions to the researchers (e.g., Principal Investigator Chief Physician Fan Xiaohan) at any time to ensure full understanding of all terms, including your right to withdraw from the study at any time without reason and without affecting subsequent routine treatment.

Screening and Baseline Preparation

- Cooperate with the screening assessment to confirm eligibility; if ineligible, you will receive routine diagnosis and treatment. Plan the screening examination time in advance to ensure the completion of all baseline data collection on schedule; if you need to adjust the examination time due to personal reasons, timely communicate with the study coordinator.

Precautions During the Study

Cooperation in Surgery and Intervention

- Complete pre-operative preparations (e.g., discontinuation of specific drugs, fasting and water restriction) in accordance with the guidance of medical staff before surgery; cooperate with the surgeon to complete electrode implantation during surgery, and promptly inform the medical staff if you experience any discomfort during the operation.
- Pay close attention to changes in your symptoms after surgery; if you experience abnormal conditions such as chest pain, dyspnea, or aggravated palpitations,

immediately contact the researchers (e.g., follow-up doctor) or go to the hospital for treatment to avoid delayed management.

Cooperation in Follow-Up and Data Collection

- Strictly follow the follow-up schedule (3 months, 6 months, 9 months, 12 months) for hospital visits on time, and reserve about 1 day for each follow-up visit. If you are unable to attend the follow-up on time, inform the researchers in advance and reschedule to avoid missed visits affecting data integrity.
- Truthfully inform the researchers of any changes in medications, clinical symptoms (e.g., signs of aggravated heart failure), hospitalizations or other illnesses during follow-up, and cooperate with the completion of routine follow-up examinations without concealing or falsifying information.

Medication and Lifestyle Management

- Continue to receive guideline-directed medical therapy as prescribed by the doctor; do not adjust the drug dosage or stop medication on your own. If medication adjustment is needed due to changes in your condition, it must be carried out under the doctor's guidance and the researchers must be informed.

Adverse Event Management

- If you experience any discomfort (e.g., post-operative wound infection, dyspnea, syncope), contact the researchers (e.g., Doctor Zhu Kailun, Tel: 15699870669) immediately and receive medical treatment as instructed; do not handle the situation on your own to avoid delayed treatment.
- Cooperate with the researchers to record the occurrence time, symptoms, treatment measures and outcomes of adverse events to provide accurate data for the study safety assessment.

Precautions After the Study

Follow-Up and Subsequent Treatment

- After the completion of the study (i.e., the 12-month post-operative follow-up), you need to continue to receive routine cardiac disease treatment as prescribed, and undergo regular pacemaker programming and cardiac function assessment; do not neglect subsequent diagnosis and treatment due to the end of the study.

- If you agree to participate in future studies, cooperate with the researchers for long-term follow-up and provide information on your health status and medications. If your contact information changes, promptly inform the researchers to ensure effective follow-up; if you decline to participate in future studies, the study data will be stored for the specified period in accordance with national regulations.

Information and Privacy Protection

- Understand that your study data will be strictly de-identified and used only for medical research; your personal identifying information will not be disclosed or used in public publications. If you find that your personal information may have been disclosed, you may contact the Ethics Committee of Fuwai Hospital (Tel: 010-88396281, 010-88396282) to report the issue.

Disclosure of Study Results

- After the study results are published, if you wish to know the overall study conclusions, you may consult the researchers, who will explain the results in an accessible manner (e.g., the effect of Bachmann's bundle pacing on new-onset AF). However, detailed individual group assignment data will not be disclosed due to the blinded study design and privacy protection requirements.

6. Risks and Adverse Events for Participants

This study will not bring you any risks beyond routine diagnosis and treatment. All examinations you receive are routine clinical items; no special blood samples are collected for this study, no additional examination items or times are added, and no extra harm is caused.

Risks you may face in routine diagnosis and treatment include:

1. Risks Associated with CRT/LBBP or ICD Implantation Surgery

- Perioperative complications: Pericardial tamponade and pericardial effusion may occur related to the surgery, manifested as chest pain, dyspnea, hypotension, etc.; pneumothorax and hemothorax may also occur, leading to chest pain, chest tightness, dyspnea, and requiring thoracentesis drainage or surgical intervention in severe cases.

- Vascular-related risks: Blood vessels may be injured during the surgical operation, leading to bleeding and hematoma; injury to large blood vessels may cause severe bleeding, requiring compression hemostasis or surgical repair; some participants may develop vascular stenosis or thrombosis, affecting local blood circulation.
- Infection risk: Infection may occur at the surgical incision and implantation site, manifesting as local redness, swelling, pain and exudation in mild cases, and systemic infection symptoms (e.g., fever, chills) in severe cases, requiring antibiotic treatment and even removal of the implanted device in critical situations.

2. Risks Associated with Pacing Electrodes

- Electrode dislodgement: Atrial or ventricular pacing electrode dislodgement may occur after surgery, leading to pacing failure, manifested as palpitations, dizziness, fatigue, etc., requiring reoperation to adjust the electrode position.
- Electrode-related injury: Cardiac structures may be injured during electrode placement, such as ventricular septal perforation, which may cause decreased cardiac function, arrhythmias, etc., requiring further examinations (e.g., echocardiography) for confirmation and intervention; electrodes may break or have insulation layer damage after long-term implantation, affecting pacing function and requiring electrode replacement.

3. Risks Associated with Arrhythmias

- New-onset arrhythmias such as ventricular premature beats and ventricular tachycardia may occur during and after surgery, which may be asymptomatic in mild cases and cause dizziness and syncope in severe cases, requiring drug treatment or device intervention (e.g., ICD shock).
- Even with physiological pacing, some participants may experience aggravation of pre-existing arrhythmias or new-onset arrhythmias due to changes in the cardiac electrophysiological environment.

4. Other Routine Diagnosis and Treatment Risks

- Examination-related risks: Echocardiography, 24-hour ambulatory

electrocardiography, NT-proBNP testing, etc., are required during the study. Echocardiography has no obvious risks, but some participants may experience transient chest tightness due to uncomfortable body positions; NT-proBNP testing requires venous blood collection, which may cause pain, bleeding and hematoma at the puncture site, and phlebitis in a very small number of participants.

- Drug treatment-related risks: Participants need to continue receiving guideline-directed medical therapy. For example, diuretics may cause electrolyte imbalances (hypokalemia, hyponatremia), manifested as fatigue and arrhythmias; ACEI/ARB drugs may cause dry cough and hypotension; β-blockers may cause bradycardia and fatigue. Relevant indicators (e.g., electrolytes, blood pressure, heart rate) need to be monitored regularly and medications adjusted accordingly.

7. Direct Benefits of Participation

You will not receive direct benefits from participating in this study; your condition may or may not improve. Your participation may help us understand the pathogenesis of the disease, promote the improvement of medical standards, facilitate the development of safer and more effective diagnosis and treatment methods, and expand new scientific knowledge.

By participating in this study, you may receive the service of multidisciplinary doctor consultation and may be provided with the best diagnosis and treatment recommendations. Follow-up staff may also provide you with treatment and health care-related suggestions based on your condition.

8. Alternative Treatment Options if Not Participating

You may choose not to participate in this study, which will not have any adverse impact on your access to routine treatment. You may discuss other treatment options with your doctor to decide whether to participate in this study. If you decide not to participate, you also have the right to choose other treatment methods, such as traditional atrial pacing.

Your study doctor will discuss with you the possible risks of participating in this study

and the advantages and disadvantages of other treatment methods, and provide a suitable treatment plan based on your condition.

9. Study-Related Costs and Compensation

You are not required to pay any study-related expenses for your participation. All examinations required during the study screening and follow-up periods are routine clinical diagnosis and treatment items, with no additional examinations added for the project, and the costs shall be borne by you yourself.

No remuneration or compensation will be provided for your participation in this study.

10. Management of Study-Related Injuries

If your health is harmed due to study-related reasons during your participation in this study, please inform the researcher (Doctor Zhu Kailun, Tel: 15699870669). We will take necessary medical measures in a timely manner and determine the liability for compensation in accordance with the relevant laws and regulations of China.

11. Confidentiality of Your Information

If you decide to participate in this study, your participation and personal data in the study are confidential. When your study data is used in this study, your personal information will be kept confidential, and all your information and data will be properly stored and used only for this study. Information in the study database will be strictly de-identified to remove personal identifying characteristics; information that can identify you will not be disclosed to anyone other than the researchers unless your permission is obtained.

To ensure that the study is conducted in accordance with regulations, inspectors from the Ethics Committee and health administrative departments may review your original medical records to verify the study process and data, without violating the confidentiality principle and relevant laws and regulations.

If the study results are published, your personal information will not appear in any public materials and publications, and we will not disclose your personal information to any person or institution.

12. Your Rights During the Study

Your participation in this study is voluntary, and you are free to decide to participate or

refuse. Whether you agree to participate or not will not affect the routine clinical diagnosis and treatment measures you are entitled to during your visit to our hospital.

You may refuse to participate at any time or have the right to withdraw from the study at any stage during the research process without any reason, and you will not be subject to discrimination or retaliation, and your corresponding medical treatment and rights will remain unaffected.

If you wish to withdraw from the study during your participation, please notify the researchers, complete the relevant examinations before withdrawal as required by the researchers, and complete the relevant withdrawal procedures in writing as required; after withdrawal, the researchers will no longer collect and use your study data, but the de-identified data collected before your withdrawal cannot be deleted or withdrawn. After your withdrawal, we may contact you again if new information related to your health and rights is found.

If you wish to participate in this study, you need to carefully read this informed consent form and sign it after confirming full understanding of the relevant issues. Signing this informed consent form will not deprive you of any legal rights endowed by the law.

During the study, you have the right to obtain new information about this study, as well as the right to receive the informed consent form and sign the updated version again, etc.

If you agree to sign this informed consent form, Fuwai Hospital, Chinese Academy of Medical Sciences will obtain your study data free of charge, and the investigators of this project may use your study data for the purpose of this study.

13. Circumstances and Reasons for Termination of Your Participation

The researchers will ask you to withdraw from the study if any of the following situations occur during your participation:

(1) Severe adverse events that make continued participation inappropriate;

(2) Poor compliance on your part;

(3) Other circumstances where the researchers deem it necessary for you to withdraw (the reason for withdrawal must be recorded in detail).

The study sponsor or regulatory authorities may also terminate the study during the

research period. If the study is terminated early, we will notify you in a timely manner, and your researchers will provide suggestions for your subsequent treatment plan based on your health status. For participants who withdraw midway, a final follow-up plan is arranged for safety reasons, and you have the right to refuse. If new information related to your health and rights is found after your withdrawal, we may contact you again.

No new data related to you will be collected after your withdrawal from the study. The researchers will securely store the relevant information collected before your withdrawal until the final destruction, and will not continue to use or disclose it. However, in very rare cases, such information may be required, for example, when government supervision departments conduct supervision, inspection and statistics, they may request to review all study information, including the relevant information of your participation in this study at that time.

14. Willingness to Participate in Future Studies

If you agree, we hope to retain your study data collected during this study. Your de-identified study data, clinical diagnosis and treatment data (including but not limited to medical records, imaging data, clinical laboratory and monitoring data, including examination data from other hospitals, etc.) and follow-up data will continue to be used for subsequent approved medical research to explore the causes, mechanisms and influencing factors of disease occurrence and development, and to research and evaluate disease prevention and treatment measures. If you disagree, after the completion of this study, the study data and clinical diagnosis and treatment data will be stored for the specified period in accordance with national regulations and kept strictly confidential.

We hope to conduct long-term follow-up of you after the study to understand your health status and medication information.

Participation in future studies will not bring you additional risks or economic burdens. All study data used for future research will be properly stored in Fuwai Hospital, Chinese Academy of Medical Sciences and kept strictly confidential. You may voluntarily choose whether to participate in future studies, and may contact the researchers to withdraw in writing at any time.

15. Contact for Questions or Difficulties

You may ask any questions about this study at any time and receive corresponding answers, including any discomfort that may occur during the study. Please contact the researcher Zhu Kailun, Tel: 15699870669.

If you have any questions about your rights, please contact the Ethics Committee of Fuwai Hospital, Tel: 010-88396281, 010-88396282.

Thank you for taking the time to read this informed consent form. If you agree to participate in this study after full consideration, we hope you can complete the study in accordance with the requirements of the researchers. Before participating in the study, please complete and sign the last page (signature page) of this document together with your researcher. The signed informed consent form is in duplicate, with one copy retained by you and the other by our hospital.

Signature Page

Participant's Statement

I have carefully read, understood and agreed to all the terms of this informed consent form.

I have been informed of the study purpose, content, procedures, possible risks, study compensation, and my rights, etc.; I have had sufficient time and opportunity to ask questions and received satisfactory answers.

I agree to participate in this study and authorize your hospital to collect my biological samples and study data for this study.

I promise that the information I provide is true; I am responsible for the consequences if false information is provided.

I have also been informed of whom to contact if I have questions or need further information.

I confirm that the contact information left at the signature is my valid contact information; if the contact information is changed, I shall promptly inform your hospital, otherwise I am willing to bear the corresponding consequences of being unable to be contacted and receive notifications.

I understand that I may withdraw from this study at any time without affecting the

medical treatment and rights I am entitled to, and I also understand that the researchers may terminate my participation in this study at any time.

I will receive an original copy of this informed consent form with the signatures of myself and the researcher.

I agree to participate in this study.

Willingness to participate in future studies: I □ agree / □ disagree (please select) to donate clinical diagnosis and treatment data, study data and long-term follow-up data for future studies, and authorize the researchers and co-research institutions of relevant medical research projects to use and process my anonymous data in approved medical research.

Participant's Name: _____

Signature: _____

Date: _____

(If the participant is a person without capacity for civil conduct or with limited capacity for civil conduct, the guardian shall sign. If the participant has full capacity for civil conduct, there is no need to fill in the guardian's information.)

Guardian's Name: _____

Signature: _____

Relationship with Participant: _____

Date: _____

(If the participant or their guardian is illiterate, a impartial witness is required to read the informed consent form and other written materials to the participant or their guardian and witness the informed consent process. If the participant or their guardian is literate, there is no need to fill in the impartial witness's information.)

I confirm that the information in the informed consent form has been correctly explained and the participant or their guardian has understood the information. The participant participates in this study voluntarily.

Impartial Witness's Name: _____

Signature: _____

Date: _____

Researcher's Statement

I confirm that I have explained the detailed information of this study to the participant, including their rights, benefits and risks, answered the participant's questions, and provided them with a signed copy of the informed consent form. The participant participates in this study voluntarily.

Researcher's Name: _____

Signature: _____

Date: _____