**Informed Consent Form**

# Minimally Invasive Transapical Septal Myectomy in the Beating Hearts for the Treatment of Hypertrophic Obstructive Cardiomyopathy: Safety and Efficacy Results of a Phase I First-in-man Clinical Trial

**Informed Consent Form • Informed Notification Page**

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Sponsor: Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology

**Dear _____Sir/Madam:**

We invite you to participate in a clinical trial to evaluate the safety and efficacy of the Minimally Invasive Transapical Septal Myectomy in the treatment of hypertrophic obstructive cardiomyopathy.

Before deciding whether to participate in this study, please read the following content as carefully as possible. It can help you understand the study and why it was conducted, the program and duration of the study, and the potential benefits, risks, and discomfort that participating in the study may bring to you. If you are willing, you can also discuss with your relatives and friends, or ask your doctor for an explanation to help you make a decision.

## 1. Research background and purpose

Operative method: Minimally Invasive Transapical Septal Myectomy

Efficacy: relieve obstruction of left Ventricular outflow tract

Indications: Hypertrophic obstructive cardiomyopathy

Background: Hypertrophic cardiomyopathy (HCM) is the most common Autosome inherited heart disease that is characterized by obvious left ventricular hypertrophy, usually without enlargement (normal or narrowing) of the left ventricular cavity, and excludes other



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factors that can cause ventricular wall thickening. According to hemodynamics, HCM can be divided into hypertrophic obstructive cardiomyopathy and hypertrophic non-obstructive cardiomyopathy. Hypertrophic obstructive cardiomyopathy can be divided into left ventricular outflow tract obstruction (LVOTO), middle obstruction and apical obstruction according to the site of obstruction. According to epidemiological surveys, the crude prevalence of HCM in the overall population in China is 0.16%, the prevalence in men is 0.22% higher than that in women 0.10%, and the prevalence adjusted for age and sex is 0.08%, according to which it is estimated that there are more than 1 million HCM patients in China. The clinical manifestations of hypertrophic obstructive cardiomyopathy mainly include exertional dyspnea, chest pain, palpitations, and syncope. For patients with symptoms and the presence of LVOTO, the first-line treatment is medication. Patients who cannot effectively control symptoms despite sufficient medication can undergo invasive treatment, with surgical septectomy being the preferred treatment option for ventricular septal reduction. Foreign studies have shown that there is no statistically significant difference in 1-year, 5-year, and 10-year survival rates between patients with hypertrophic obstructive cardiomyopathy after surgery and the general population, and they are significantly better than patients who have not undergone surgery. Due to the limitations of conventional scalpel operation of traditional open-heart surgery to remove hypertrophic myocardial tissue, the difficulty of operation, angle and thickness of hypertrophic myocardial tissue resection are high, according to the "Guidelines for the Management of Hypertrophic Cardiomyopathy 2017", common complications in the early stage after surgical ventricular septectomy include ventricular septal perforation, aortic regurgitation and residual obstruction, so it is still necessary to explore safer and more effective treatment methods clinically.

In recent years, a number of minimally invasive treatments for HOCM have emerged, aiming to shorten the operation time, reduce trauma, reduce the incidence of surgery-related complications and their incidence, and improve the quality of life of patients. These include percutaneous ventricular septal alcohol ablation, percutaneous femoral ventricular septal


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radiofrequency ablation, percutaneous intramyocardial intraventricular septal radiofrequency ablation, etc. The main complications of percutaneous ventricular septal alcohol ablation were perioperative death (perioperative mortality is 1.0%-1.4%), myocardial infarction at coronary artery injury and non-target ablation sites, intraoperative and postoperative ventricular arrhythmias. The main complication of percutaneous femoral ventricular septal radiofrequency ablation was complete atrioventricular block, and the proportion of complete atrioventricular block with percutaneous femoral septal radiofrequency ablation requiring dual-chamber pacemaker implantation was about 21.1%. Experience and long-term safety follow-up data on percutaneous intraventricular septal radiofrequency ablation are limited. Combining the limitations of traditional open-heart surgery and minimally invasive surgery, upgrading existing open-heart surgical instruments or upgrading existing surgical approaches is an effective way to explore safer and more effective treatment methods in the clinic.

Research purpose: The main purpose of this clinical trial is to evaluate the safety and effectiveness of the minimally invasive transapical septal myectomy in the beating hearts for the treatment of hypertrophic obstructive cardiomyopathy under the premise of ensuring the safety of the subjects and ensuring the scientific nature of the clinical trial.

Duration of the study: 2022-01-12——2023-12-31。

**2. Who can participate in the study**

You can participate in the study if you

[1] had a resting or provoked left ventricular outflow tract gradient (LVOTG) > 50 mmHg and a maximal ventricular septal wall thickness ≥ 15 mm;

[2] had heart function ≥ New York Heart Association (NYHA) class II;

[3] presented with drug refractory symptoms or were intolerant of pharmaceutical therapies;

[4] were aged greater than 12 years; and

[5] were informed of the first-in-man nature of the clinical trial, consented to participate in all of the activities, and signed an informed consent form.

**3. Who should not participate in the study**


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You should not participate in the study if you

[1] were pregnant;

[2] had concomitant diseases, such as native valvular disease or coronary artery disease, that needed open-heart surgery;

[3] presented with severe heart failure with an LV ejection fraction < 40%;

[4] had an estimated life expectancy < 1 year;

[5] were non-compliant; or

[6] had circumstances that were considered to be unsuitable or prohibitive for participating in the clinical trial at the discretion of the attending medical team and the researchers.

**4. What to do if you participate in the research**

1) Before you are included in the study, you will receive the following information consultation and inspection to determine whether you can participate in the study.

[1] Sign the informed consent form;

[2] Check the inclusion/exclusion criteria;

[3] Record past or current medical history, accompanying disease and treatment history, family history, surgery history, trauma history, allergy history

[4] Demographic information: including gender, age (date of birth), ethnicity, weight, etc.

[5] Vital signs include body temperature, respiration, heart rate, blood pressure;

[6] Physical examination: including general condition, skin and mucous membranes, lymph nodes, head, neck, chest, abdomen, spine and limbs, nervous system and other routine examinations;

[7] Blood routine: red blood cell, white blood cell, platelet count, hemoglobin, neutrophil percentage, lymphocyte percentage;

[8] Urine routine: urine sugar, hydrogen ion concentration index, bilirubin, urine protein, ketone body, urine specific gravity, red blood cell count, white blood cell count;

[9] Blood biochemistry: aspartate aminotransferase, alanine aminotransferase, total protein, albumin, globulin, total bilirubin, indirect bilirubin, direct bilirubin, alkaline phosphatase,


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γ-glutamyl transpeptidase, Total cholesterol, lactate dehydrogenase, urea, creatinine, uric acid, hydrocarbons, eGFR, potassium, sodium, chloride, calcium, corrected calcium;

[10] Coagulation function: prothrombin time, prothrombin activity, international normalized ratio, fibrinogen, activated partial thrombin time, thrombin time;

[11] Echocardiography: left ventricular outflow tract pressure gradient (LVOTG), left ventricular outflow tract diameter, end-diastolic interventricular septal thickness, end-diastolic left ventricular inner diameter, end-systolic left ventricular inner diameter, end-diastolic left ventricular volume, end-systolic left ventricular Volume, left ventricular ejection fraction, peak E and peak A velocity of mitral valve during diastole;

[12] Cardiac MRI or chest enhanced CT

[13] Cardiac enzymes: high-sensitivity cardiac troponin I, myoglobin, creatine kinase MB type isozyme;

[14] B-type natriuretic peptide;

[15] Electrocardiogram;

[16] NYHA assessment;

[17] 6-minute walk test;

[18] Fill out the quality of life scoring questionnaire;

[19] Evaluation of combined medication;

[20] Adverse event evaluation: record adverse events/serious adverse events that occurred/existed during the screening period of subjects;

[21] Make an appointment for the next visit.

2) If you pass the above inspection, you will conduct research according to the following steps.

[1] Check the inclusion/exclusion criteria;

[2] Perfect preoperative examination and preparation

[3] Use beating-heart myectomy device for surgery;

[4] Product device performance evaluation;



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[5] Record the combined drug use;

[6] Record the occurrence of adverse events;

[7] Evaluation of device defects;

[8] Make an appointment for the next visit.

3) Other matters that require your cooperation

The expected duration of participation is 3.3 months, which includes a screening period of 1 week, the day of surgery, and a follow-up period of 3 months.

[1] Objectively fill out the quality of life scoring questionnaire;

[2] NYHA assessment;

[3] 6-minute walk test;

[4] Complete relevant examinations (blood test, echocardiogram, electrocardiogram, etc.) within the agreed time period;

[5] Record the combined drug use;

[6] Record the occurrence of adverse events;

[7] Evaluation of device defects;

[8] Make an appointment for the next visit until the end of the follow-up visit.

If you participate in this study, please cooperate with medication and related inspections.

**5. Possible benefits of participating in the research**

The benefits of participating in this research include: it may improve your condition (direct benefit), improve the medical diagnosis and treatment level of the whole society and indirectly increase the possibility of treating the disease (social benefit/indirect benefit), etc.

If you agree to participate in this study, you will have the potential to receive direct medical benefits. However, we cannot guarantee this.

We hope that the information obtained from your participation in this study will help to provide more information for the diagnosis and treatment of this disease in the future, and to develop new treatments for patients with this disease in the future.

**6. Possible adverse reactions, risks, discomfort and inconvenience of participating in**



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**the research**

Adverse reactions and countermeasures: arrhythmia, mitral valve injury, aortic valve injury, pericardial effusion, stroke and ventricular septal defect.

- Arrhythmia

When ventricular septal hypertrophy tissue is resected, the cardiac atrioventricular conduction system running in the ventricular septum may be destroyed by tissue resection. There are many types of arrhythmias, including atrioventricular block, left bundle branch block, and atrial fibrillation.

Strengthening training for investigators, improving the investigator's proficiency in operation, clarifing the range of myocardiectomy that is not easy to damage, strengthening the monitoring of the patient's heart rhythm during the operation, and observing the changes of the ECG at all times when the myocardial tissue is removed. If there is an abnormality, it needs to be dealt with in a timely manner. Asymptomatic patients with first-degree or mild second-degree atrioventricular block do not need special treatment, and pacemaker implantation is required for complete atrioventricular block; asymptomatic patients with left bundle branch block do not need treatment, and complete atrioventricular block occurs. Cardiac resynchronization therapy can be performed in patients with chronic left bundle branch block; those with atrial fibrillation who are assessed as high risk of embolism can start anticoagulation therapy in time, and prepare for drug or electrical cardioversion and catheter ablation therapy.

- Mitral valve injury

Mitral valve injury may occur when ultrasound-guided transapical myocardial acacitomy system enters the left ventricle and excisional tissue is localized.

Strengthening the training of researchers, improving their proficiency in operation, and fully understanding the anatomical landmarks of the heart under ultrasound imaging can effectively reduce the occurrence of mitral valve injury. If mitral regurgitation or mitral regurgitation is found during surgery, mitral valve injury is judged according to


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regurgitation, and no treatment, mitral valve repair or mitral valve replacement is required.

- Aortic valve injury

Ultrasound-guided access to the left ventricle via the apical myocardial acatrotomy system for excisional tissue localization may cause aortic valve injury.

Strengthening the training of researchers, improving operational proficiency, fully understanding cardiac anatomy, and adjusting according to the actual situation of individual patients can effectively reduce the occurrence of aortic valve injury. Aortic valve injury is found during surgery, and the degree of injury is mild (transapical ultrasound shows reverse stroke flow) and does not require special treatment; The degree of injury is more severe, and aortic valve repair can be performed during surgery; If the injury cannot be repaired, aortic valve replacement is required.

- Pericardial effusion

The cause of pericardial effusion may be due to postoperative incision exudate, apical tear, etc. The most common symptom of pericardial effusion is dyspnea; Large pericardial effusions can cause tamponade and the triad of hypotension, weak heart sounds, and jugular venous distention.

Strengthening the training of researchers, operate cautiously during surgery, and ensuring tight suture and suture treatment when the apical is closed after apical surgery. Accurately determine the cause of pericardial effusion. The occurrence of pericardial effusion requires urgent pericardial puncture to relieve the symptoms of pericardial tamponade, and to identify the primary cause of pericardial effusion and treat the primary disease.

- Stroke

Thrombosis occurs after surgery due to atrial fibrillation, and cerebral artery embolism can occur when the thrombus flows through the aorta and carotid artery through the internal cerebral artery, resulting in ischemic stroke.

Postoperative monitoring of patients' electrocardiograms, patients with atrial fibrillation, high risk of thrombosis, early use of anticoagulants, drug or electrical cardioversion, and


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those who are allowed can receive radiofrequency catheter ablation.

- Ventricular septal defect

The negative pressure of the beating-heart myectomy device attracts myocardial tissue into the negative pressure tube, and the ultrasound imaging is not clear. When too much tissue is attracted, it may cause ventricular septal defect. When the size of the ventricular septal defect is small, the left-to-right shunt flow of the heart is small, which has almost no effect on the daily activities of the patient.

Fully evaluate the condition of ventricular septal hypertrophy before operation, operate carefully during operation, and perform rotary resection on the target hypertrophic tissue. Ventricular septal defect found during operation can be repaired at the same time.

- Hemorrhagic shock

There is a risk of blood loss at the purse string suture during and after the apical approach, and hemorrhagic shock will occur when the rapid blood loss reaches 30%-35% of the total blood volume.

Strengthening training for investigators, operating cautiously during the operation, find ingabnormal bleeding, finding the bleeding point and performing emergency hemostasis.

Risks: Mild to moderate adverse events are often transient and usually occur within 1 week after surgery; severe adverse events are mainly the risks of the operation itself.

Discomfort and inconvenience: Follow the doctor's advice to cooperate with examination and treatment, nursing and rest after the operation.

If any adverse reaction related to this device occurs during this trial, you will receive timely and necessary treatment, and the cost of treatment will be borne by the sponsor. If you have any discomfort during the study, or any unexpected situation, whether related to surgery or not, you should promptly notify your doctor, and he/she will make judgments and treat it medically.

Physicians and sponsors will make every effort to prevent possible harm due to this research. If an adverse event occurs in a clinical trial, a medical expert committee will


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identify whether it is related to the test device. The sponsor will provide treatment costs and corresponding economic compensation for the damage related to the trial, which has been stipulated in my country's "Quality Management Standards for Clinical Trials of Medical Devices".

**7. Research fees, compensation and damages**

1) Medical devices used in research and related inspection fees

By taking part in this research study, you may benefit by being given a free trial product and a free examination related to the trial. The treatment and examinations you need for other diseases will no longer be covered for free.

[1] Screening period: blood routine (red blood cell, white blood cell, platelet count, hemoglobin, neutrophil percentage, lymphocyte percentage); urine routine (urine sugar, hydrogen ion concentration index, bilirubin, urine protein, ketone body, urine specific gravity, red blood cell count, white blood cell count); blood biochemistry (aspartate aminotransferase, alanine aminotransferase, total protein, albumin, globulin, total bilirubin, indirect bilirubin, direct bilirubin, alkaline phosphatase, γ- Glutamyl transpeptidase, total cholesterol, lactate dehydrogenase, urea, creatinine, uric acid, hydrocarbons, eGFR, potassium, sodium, chloride, calcium, corrected calcium); coagulation function (prothrombin time, prothrombin activity, international normalized ratio, fibrinogen, activated partial thrombin time, thrombin time); cardiac enzymes (high-sensitivity cardiac troponin I, myoglobin, creatine kinase MB type isoenzyme); type B sodium Urinary peptides; echocardiography; cardiac MRI or chest CT with contrast; electrocardiography;

[2] On the day after surgery: echocardiogram; electrocardiogram;

[3] 1 day after operation: electrocardiogram;

[4] 1 week after operation: blood routine (red blood cell, white blood cell, platelet count, hemoglobin, neutrophil percentage, lymphocyte percentage); urine routine (urine sugar, hydrogen ion concentration index, bilirubin, urine protein, ketone body , urine specific gravity, red blood cell count, white blood cell count); blood biochemistry (aspartate


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aminotransferase, alanine aminotransferase, total protein, albumin, globulin, total bilirubin, indirect bilirubin, direct bilirubin, alkaline phosphatase, γ-glutamyl transpeptidase, total cholesterol, lactate dehydrogenase, urea, creatinine, uric acid, hydrocarbons, eGFR, potassium, sodium, chloride, calcium, corrected calcium); B-type natriuretic peptide; echocardiography ; Cardiac MRI or chest enhanced CT; ECG;

[5] One month after operation: blood routine (red blood cell, white blood cell, platelet count, hemoglobin, percentage of neutrophils, percentage of lymphocytes); blood biochemistry (aspartate aminotransferase, alanine aminotransferase, total protein, albumin, globulin, Total bilirubin, indirect bilirubin, direct bilirubin, alkaline phosphatase, gamma-glutamyl transpeptidase, total cholesterol, lactate dehydrogenase, urea, creatinine, uric acid, hydrocarbons, eGFR, potassium , sodium, chloride, calcium, corrected calcium); cardiac enzymes (high-sensitivity cardiac troponin I, myoglobin, creatine kinase MB-type isozyme); B-type natriuretic peptide; echocardiography; cardiac MRI or chest Enhanced CT; ECG;

[6] 3 months after operation: blood routine (red blood cell, white blood cell, platelet count, hemoglobin, percentage of neutrophils, percentage of lymphocytes); blood biochemistry (aspartate aminotransferase, alanine aminotransferase, total protein, albumin, globulin, Total bilirubin, indirect bilirubin, direct bilirubin, alkaline phosphatase, gamma-glutamyl transpeptidase, total cholesterol, lactate dehydrogenase, urea, creatinine, uric acid, hydrocarbons, eGFR, potassium , sodium, chloride, calcium, corrected calcium); cardiac enzymes (high-sensitivity cardiac troponin I, myoglobin, creatine kinase MB-type isozyme); B-type natriuretic peptide; echocardiography; cardiac MRI or chest Enhanced CT; ECG.

2) Compensation for Study Participation

If you go back to the hospital for relevant follow-up examinations, you will be provided with a corresponding transportation subsidy (RMB 200 for each follow-up visit).

3) Compensation for damages

If you suffer damage due to participating in the research, you can get free treatment provided by the researcher, and you will be compensated according to law.


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**8. Is personal information confidential?**

Your medical records will be kept intact at the hospital. Investigators, sponsor representatives, ethics committees and drug regulatory authorities will be allowed to review your medical records. Any public reporting of the results of this research will not reveal your personal identity. We will make every effort to protect the privacy of your personal medical data within the scope permitted by law.

It is possible that your medical records may be reused in future studies other than this study. You can also now declare your refusal to use your medical records for research other than this one.

**9. How to get more information?**

You can ask any questions about this study at any time.

Your doctor will leave you his/her phone number so that he or she can answer your questions.

Your doctor will promptly notify you if there is any important new information during the study that may affect your willingness to continue participating in the study.

**10. You can voluntarily choose to participate in the research and quit the research halfway**

Participation in research is entirely up to you. You may refuse to participate in this study, or withdraw from this study at any time during the study. You will not be discriminated against or retaliated against for refusing to participate in this study, or withdrawing at any time during the study, and your medical treatment and rights will not be affected.

Your doctor or investigator may discontinue your participation in this study at any time in your best interest.

If you withdraw from the study for any reason, you may be asked about your use of the trial drug. You may also be ordered to have laboratory tests and a physical examination if deemed necessary by the doctor.

If you choose to take part in this study, we hope that you will stick to it for the full


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duration of the study.

**11. What should I do now?**

Participation in this research study is at your own discretion. You can discuss it with your family or friends before making a decision.

Before you decide to take part in a study, ask your doctor as many questions as you can until you fully understand the study.

Thank you for reading the above material. If you decide to take part in this study, please tell your doctor and he or she will make all the arrangements for you.

Please keep this document.


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**Informed Consent Form • Signature Page**

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**Research physician commitment**

As a research physician, I confirm that I have clearly explained the details of this trial to the subjects, including their rights and possible benefits and risks, and gave them a copy of the signed informed consent form.

Physician's signature:_____ Date:_____/_____/_____

Tel:_____

**Subject promises**

I have read and understood the introduction of this study in the informed notice page, and have the opportunity to ask relevant questions. I understand the research doctor's explanation very well.

I know the possible risks and benefits of participating in this study. I know that participating in the study is voluntary, and I confirm that I have had enough time to consider and voluntarily participate in this experiment. I can ask the doctor for more information at any time, or I can withdraw from this study at any time without being discriminated against or retaliated against, and my medical treatment and rights will not be affected.

I also know that if I withdraw from the study halfway, especially due to drugs, if I tell the doctor about the change of my condition and complete the corresponding physical and chemical examinations, it will be very beneficial to me and the whole study. If I need to take any other medication due to my illness, I will ask the doctor for advice in advance or tell the doctor truthfully afterwards.


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I agree□ or refuse□ other research than this study uses my medical records.

I decided to agree to participate in this study and promised to follow the doctor's advice as much as possible. I will receive a signed and dated copy of the informed consent form.

Subject’s signature:_____ Date:_____/_____/_____

Guardian's signature:_____ Date:_____/_____/_____

Tel:_____



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