Protocol No.: SN-CBC-202201

A Prospective, Multicenter, Randomized Controlled Study to Evaluate the Safety and Effectiveness of Coronary Scoring Balloon Catheter for the Treatment of Coronary Artery Disease

Clinical Trial Protocol

(NCT05509296)

Name of Investigational Medical Device:	**Coronary Scoring Balloon Catheter**
Models/Specifications:	**2.0-3.5 mm in diameter, 10-15 mm in length**
Class III Medical Device Requiring Clinical Trial Approval:	**Yes☐ No☑**
Protocol Version No. and Date:	**V1.1/June 01, 2022**
Study Site:	**Peking University First Hospital**
Principal Investigator:	**Professor Li Jianping**
Leading Site/Coordinating Investigator of Clinical Trial:	**Peking University First Hospital/Professor Li Jianping**
Sponsor:	**Sino Medical Sciences Technology Inc.**

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Protocol Abstract

Study Title	A Prospective, Multicenter, Randomized Controlled Study to Evaluate the Safety and Effectiveness of Coronary Scoring Balloon Catheter for the Treatment of Coronary Artery Disease
Study Objective	To evaluate the safety and effectiveness of Coronary Scoring Balloon Catheter manufactured by Sino Medical Sciences Technology Inc. in the treatment of coronary artery stenosis
Test Devices	● Investigational Medical Device: Product Name: Coronary Scoring Balloon Catheter Manufacturer: Sino Medical Sciences Technology Inc. ● Control Device: Product Name: NSE Coronary Dilatation Catheter Manufacturer: Goodman Co., Ltd. Medical Device Registration Certificate No.: NMPA (I) 20163035067
Estimation of Sample Size	After literature review, according to the results of relevant literature and clinical experience of the scoring balloon catheter in the treatment of coronary artery disease, assuming that the SINOMED Coronary Scoring Balloon Catheter in the test group and Goodman NSE Coronary Dilatation Catheter in the control group can reach the equivalent level, and the device success rate (lesion level) is expected to reach 96%, with one-sided test α as 0.025, test power (1-β) as 0.8 and non-inferiority margin δ as -10%, the number of cases to be included in each group is 61 as calculated by PASS software. In consideration of a 10% dropout rate, this study requires 136 subjects, 68 each in test group and control group.
Study Method	This study is a prospective, multicenter, randomized, parallel controlled, non-inferiority design to evaluate the safety and effectiveness of Coronary Scoring Balloon Catheter. It is planned to recruit a total of 136 patients with coronary artery stenosis. After all subjects sign the ICF, the investigators will judge whether the subjects meet the patient-related inclusion criteria and do not meet the patient-related exclusion criteria. Then the subjects undergo coronary angiography, and if their imaging results meet the inclusion criteria and do not meet the exclusion criteria, they will be randomized to the test group or control group (the probability of being assigned to the test group or control group is 50%) for balloon dilation of lesions. The subjects in the test group use the Coronary Scoring Balloon Catheter developed by Sino Medical Sciences Technology Inc., and those in the control group use the NSE Coronary Dilatation Catheter (NMPA (I) 20163035067) developed by Goldman Co., Ltd. The visit time points during this trial include pre-PCI, during procedure, and follow-up from post-procedure to pre-discharge. In this study, the device success rate (lesion level) is the primary endpoint, and the secondary endpoints is the procedural success rate (subject level). At the same time, the incidences of target lesion failure (TLF) composite endpoint and its composite events, patient-oriented composite endpoint (PoCE) and its composite events, as well as other procedure-oriented adverse events (AEs), serious adverse events (SAEs) (such as balloon rupture, vascular dissection, in-stent thrombosis) and device defects from the beginning of procedure to pre-discharge are taken as the safety endpoints.
Effectiveness Endpoints	**Primary efficacy endpoint: Device success rate (lesion level)** To achieve device success (lesion level), the following conditions should be met simultaneously: a. The whole balloon dilatation procedure, including delivery, passing through the lesion, inflation and dilatation, deflation and retraction and withdrawal of the balloon, is successfully completed. b. ≤30% residual stenosis of target lesion immediately after PCI (For ISR and drug balloon-related restenosis, residual stenosis <50% post-procedure) **Secondary efficacy endpoints: Procedural success rate (subject level)** To achieve procedural success (subject level), the following conditions should be met simultaneously: a. ≤30% residual stenosis of at least one target lesion immediately after PCI (For ISR

	and drug balloon-related restenosis, residual stenosis <50% post-procedure) b. No major adverse cardiac events (MACE) during post-procedure hospitalization: all-cause death, myocardial infarction (MI) and target lesion revascularisation (TLR).
Safety Endpoints	**(1) Incidence of target lesion failure (TLF) composite endpoint** Any of the following events is considered as a TLF: a. Cardiac death (the death with uncertain cause is also considered cardiac death); b. Target vessel myocardial infarction (TV-MI); c. Clinically indicated target lesion revascularisation (CI-TLR). **(2) Incidence of patient-oriented composite endpoint (PoCE)** Any of the following events is considered as a PoCE: a. All-cause death; b. All myocardial infarction; c. All revascularisation events, including target lesion revascularisation (TLR), target vessel non-target-lesion revascularisation (TVR), and non-target vessel revascularisation. **(3) Occurrence of single AE and SAE** Other possible AEs such as balloon rupture, vessel perforation, dissection, acute occlusion, vasospasm, thrombosis (including in-stent thrombosis), arrhythmia requiring intervention. **(4) Incidence of device defects**
Case Selection	**Inclusion criteria:** 1) Patients are at least 18 to 75 years of age, male or not pregnant female; 2) Patients with asymptomatic ischemic evidence, stable or unstable angina pectoris or old myocardial infarction; 3) In situ or restenotic lesion(s) in coronary arteries, including in-stent restenosis (ISR); 4) Target lesion(s) must have a diameter of 2.0 mm ~ 3.5 mm and a length of ≤ 30 mm; 5) Target lesion(s) must have a percent diameter stenosis of ≥70%% or ≥50% with evidence of ischemia; 6) Patients have a planned intervention at no more than two lesions, in different target vessels; 7) Investigators believe that target lesion atherosclerotic plaques require the scoring balloon treatment, in which the balloon can be passed through by pre-dilation. 8) Able to understand the purpose of the trial, voluntarily participate and sign the ICF. **Exclusion criteria:** 1) Evidence of ongoing acute myocardial infarction within a week. 2) Chronic total occlusion (TIMI 0 pre-procedure), left main lesion, intervention-required three-vessel lesions, and bypass lesion. 3) Severe calcification and target lesion in a severe angulation (≥ 45 degrees). 4) Patients with severe heart failure (NYHA Class III or above) or left ventricular ejection fraction <40% (ultrasound or left ventricular angiography). 5) Patients with severe liver and renal dysfunction, as Cr >176.82 umol/L or Cr >2.0 mg/dl. 6) Patients with history of active digestive tract ulcer, history of cerebral hemorrhage or subarachnoid hemorrhage, history of ischemic stroke 6 months before procedure, as well as patients with bleeding tendency, antiplatelet preparation and anticoagulant therapy contraindications that cannot be treated with anticoagulant therapy. 7) Patients with allergies to heparin and contrast agent. 8) Target lesion demonstrating severe dissection prior to planned deployment of the study balloon. 9) Visible thrombus at the target lesion. 10) Patients to receive heart transplantation. 11) Patients who participated in other clinical trials of drugs or medical devices, but did not reach the primary endpoint. 12) Patients who are judged by the investigators to have poor compliance, are unable to complete the study as required, or are judged by the investigators to be unsuitable for participation in the study. 13) Patients who are not suitable for coronary artery bypass grafting (CABG).

Schedule of Tests and Procedures Table

Item / Time points	Screening period	Treatment period	Follow-up period
	Pre-procedure (-14d-0d)	Procedure details (0d)	From post-procedure to pre-discharge
Signing of ICF	▲		
Demographic data	▲		
Medical history	▲		
Vital signs[1]	▲	▲	▲
Pregnancy test[2]	▲		
Blood routine and blood biochemistry[3]	▲		▲
Myocardial enzyme spectrum[4]	▲		▲(Within 48 hours post procedure)
ECG[5]	▲		▲(Within 48 hours post procedure)
Inclusion/exclusion criteria	▲		
Center random	▲		
Clinical evaluation		▲	
Coronary angiography[6]		▲	
Coagulation functions[7]	▲		
Adverse cardiovascular event[8]		▲	▲
AE and SAE		▲	▲
Device defect		▲	
Cardiovascular concomitant medications	▲	▲	▲

Notes:

(1) Vital signs: Systolic blood pressure, diastolic blood pressure and heart rate.

(2) Pregnancy test: Only applicable to women of childbearing potential.

(3) In order to protect the rights and interests of subjects, the examination results of blood routine and blood biochemistry within one month before procedure (the recent results shall prevail for those who have undergone examinations for many times) will be accepted: ① Blood routine: white blood cell count (WBC), red blood cell count (RBC), platelet count (PLT) and hemoglobin (HB); ② Renal function: serum creatinine (SCr); ③ Liver function: alanine aminotransferase (ALT) and aspartate aminotransferase (AST); ④ Blood lipids: triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C).

(4) Myocardial enzyme spectrum: creatine kinase (CK), creatine kinase isoenzyme (CK-MB), cardiac troponin T (cTnT)/cardiac troponin I (cTnI) (choose one, not all are mandatory). Note: Post-procedure myocardial enzyme spectrum should be completed within 48 hours after procedure, and should be reexamined before discharge if the results are abnormal and clinically significant.

(5) Post-procedure ECG should be done within 48 hours after procedure.

(6) Coronary angiography is completed immediately after procedure and made into CD in each site.

(7) Coagulation functions: Prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), fibrinogen (FIB). In order to protect the rights and interests of subjects, the examination results within one month before procedure will be accepted.

(8) Adverse cardiovascular event includes major adverse cardiac events (MACE: including all-cause death, myocardial infarction [MI], and target lesion revascularisation [TLR]), target lesion failure (TLF, including cardiac death, target vessel myocardial infarction [TV-MI], and clinically indicated target lesion revascularisation [CI-TLR]), patient-oriented composite endpoint (PoCE, including all-cause death, all MIs, and all revascularisation events (target lesion revascularisation [TLR], target vessel non-target-lesion revascularisation [TVR] and non-target vessel revascularisation), etc.

List of Abbreviations

Abbreviation	Complete spelling
%DS	percent diameter stenosis
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
APTT	Activated Partial Thromboplastin Time
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CI-TLR	clinical indicated target lesion revascularisation
CK	creatine kinase
CK-MB	creatine kinase-myocardial band
cTnI	Cardiac troponin I
cTnT	Cardiac troponin T
FIB	Fibrinogen
HDL-C	High density lipoprotein cholesterol
ISR	in-stent restenosis
LDL-C	Low density lipoprotein cholesterol
MACE	major adverse cardiovascular events
MI	myocardial infarction
PCI	percutaneous coronary intervention
PoCE	patient-oriented composite endpoint
PT	prothrombin time
PTCA	percutaneous transluminal coronary angioplasty
RVD	reference vessel diameter
SCr	Serum creatinine
TC	Total cholesterol
TG	Triglyceride
TIMI	Thrombolysis In Myocardial Infarction
TLF	target lesion failure
TLR	target lesion revascularisation
TV-MI	target vessel myocardial infarction
TVR	target vessel revascularisation
TT	Thrombin Time

Text of Study Protocol

1. Sponsor Information

1.1 Name of Sponsor

Sino Medical Sciences Technology Inc.

1.2 Address of Sponsor

F2, Building B, TEDA Bio-pharmaceutical, No. 5 The Fourth Avenue, Tianjin Economic-Technological Development Area

1.3 Contact Information of Sponsor

Contact Person: Yu Xiaoyan

Tel.: 18614030565

E-mail: yuxiaoyan@sinomed.com

2. Information on Study Sites and Principal Investigators

The list of study sites and principal investigators (PIs) is present in Appendix 1.

During the clinical study, if the existing participating sites fail to obtain the approval of the clinical trial management department or the EC, resulting in the progress of the study significantly slower than the expected schedule, the sponsor should fully communicate and discuss with the coordinating investigator, and then make adjustments to the participating sites (abandonment or addition), and may file the list of clinical study sites in the Appendix without amending the text of the protocol. The final list of participating sites should be submitted to the clinical trial management departments and ECs of all participating sites for filling.

3. Background Information of Clinical Trial

3.1 R&D Background

Since the success of the first percutaneous transluminal coronary angioplasty (PTCA) on September 16, 1977, with the continuous iteration and improvement of angioplasty techniques, PTCA has now become the most basic method of percutaneous coronary intervention (PCI), which is of great value for application to coronary artery disease (CAD).

The principle of PTCA is that the mechanical extrusion of vessel wall by balloon causes the atherosclerotic plaque to rupture irregularly, thus dilating the narrow lumen [1]. However, some lesions, especially coronary artery calcification or dense fibrosis, are extremely difficult to be properly dilated with traditional balloons, which is often related to the failure of stent delivery or insufficient stent dilation. When the stent is placed at the poorly dilated lesions, it is very likely to lead to stent malapposition, incomplete expansion and poor symmetry, resulting

in a significant increase in periprocedural complications and an increase in risks of in-stent thrombosis and restenosis [2]. Because of the stent incomplete expansion, even post-dilation, the effect is also poor, thus leading to an increase in the incidence of adverse events such as in-stent thrombosis [3]. In recent years, some functional balloons, such as scoring balloons, have obviously improved the effect of complex coronary pre-dilation, greatly improving the acute procedural success rate and long-term prognosis.

Functional balloons are designed to combine their surface with a rigid metal or plastic element to enhance the interaction between the balloon surface and the plaque underneath. This improved interaction has two main advantages: the creation of a controlled plaque detachment that is not easily spread, and in addition, a reduction in longitudinal displacement or balloon slippage during dilation. Functional balloons currently on the market include cutting balloons with rigid microblades parallel to the longitudinal axis on the balloon surface, AngioSculpt balloons with Ni-Ti alloy wound along the balloon surface in a spiral shape on the longitudinal axis, and scoring balloons with nylon elements wound along the balloon surface parallel to the longitudinal axis. Compared with common balloons, functional balloons have shown certain advantages in the clinical application for the treatment of ISR, coronary ostial lesions, bifurcation lesions, small vessel lesions, and calcified lesions [4].

However, cutting balloons (such as Scoreflex) have a potential "relaxation" phenomenon in design and cannot produce multiple cutting effects [5]. At the same time, for cutting balloons, their inflexibility in clinical settings, difficulty in delivery, and poor passage at lesions (due to their high cross profile: 0.041–0.046 ″) lead to a higher incidence of intra-procedural perforation [6]. It is particularly important to optimize the flexibility and other processes of existing functional balloons and reduce the risk of complications such as intra-procedural vessel perforation and damage to normal vessel walls, so as to benefit the large population of coronary artery disease, especially those PCI patients with calcified lesions.

A new generation of the scoring balloon catheter (Coronary Scoring Balloon Catheter) independently developed by Sino Medical Sciences Technology Inc. (hereinafter referred to as SINOMED) has undergone the type test at Tianjin Medical Devices Quality Supervision and Testing Center of the NMPA, and has been granted the test qualification report; meanwhile, Coronary Scoring Balloon Catheter has undergone the animal experimental study, verifying its safety. This study is intended to evaluate the safety and effectiveness of the new generation scoring balloon catheter (Coronary Scoring Balloon Catheter) developed and manufactured by SINOMED for human use, so as to provide the basis for its eventual formal marketing and application in China.

3.2 Basic Information of Product

(1) Product Characteristics

The Coronary Scoring Balloon Catheter has the following characteristics: (1) the scoring element made of Ni-Ti alloy with shape memory can restore its original shape, which is conducive to the safe withdrawal of the product from the blood vessel; (2) the spiral winding scoring element can act on the lesion at 360°, with a wide range of action; (3) the trapezoidal scoring similar to a triangle is conducive to the scoring element embedded in the plaque.

(2) Structural Composition and Operating Principle

1) Device Composition

The balloon catheter consists of TIP, balloon protective sheath, balloon, scoring element, balloon inner tube, Marker, balloon outer tube, metal catheter, sleeve, connector, opening, and two markers of metal catheter. The product structure diagram is shown in Figure 1:

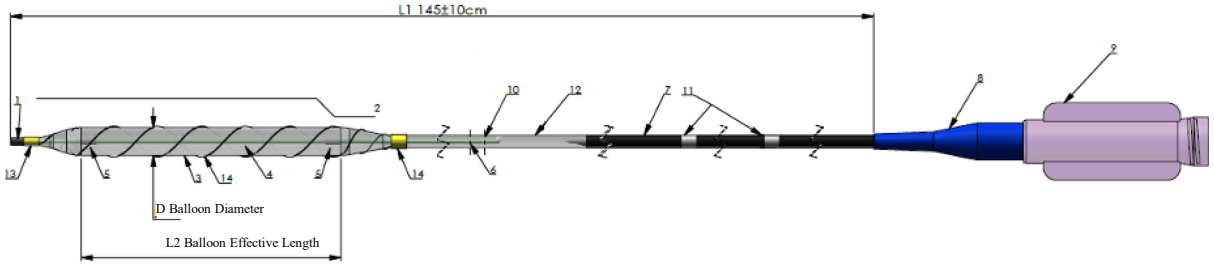


Figure 1 Structure diagram of Coronary Scoring Balloon Catheter

1) TIP
2) Balloon protective sheath
3) Balloon
4) Balloon inner tube
5) Marker [Two Markers are placed on the balloon inner tube (7), with their outer edges flush with the balloon neck]
6) Distal outer tube
7) Metal catheter (hypotube)
8) Sleeve
9) Connector
10) Opening (guidewire exit port)
11) Two markers of metal catheter
12) Proximal outer tube
13) Distal retainer
14) Scoring element

15) Proximal retainer

Note 1: D indicates the diameter of balloon post-dilation.

Note 2: L2 indicates the balloon effective length on the balloon catheter.

Note 3: L1 indicates the effective length of the balloon catheter.

Note 4: The complete Coronary Scoring Balloon Catheter is put into a protective sheath

The two developing points located on the balloon inner tube can accurately mark the position of the balloon under X-ray, which is helpful for checking the length of balloon dilated. The Ni-Ti alloy scoring element is spirally wound on the balloon, which is only attached to the balloon catheter at the distal and proximal ends, reducing the likelihood of slippage during balloon dilation. There are two markers (93 cm and 103 cm away from the distal end of the catheter, respectively) at the proximal end of the catheter, which are used to determine the position of the dilatation catheter relative to the front end of the guiding catheter in femoral artery puncture or brachial puncture. The guidewire exit port located at the front end of the catheter is about 24 cm away from the distal end. The Coronary Scoring Balloon Catheter can be used in combination with a guiding catheter with a minimum inner diameter of 1.68 mm (6Fr/0.066 inch); all the products can be used in combination with a guidewire with a maximum outer diameter of 0.36 mm (0.014 inch).

2) **Operating Principle**

The Coronary Scoring Balloon Catheter is a rapid exchange scoring balloon catheter. In interventional procedure, the Coronary Scoring Balloon Catheter is punctured percutaneously and travels along the blood vessel to the lesion site. The scoring element wound on the balloon in a spiral way can reduce the slippage of the balloon during dilation.

3.3 Intended Use and Related Information

(1) Intended Use (Indications, Intended Population, Application Site)

The Coronary Scoring Balloon Catheter is intended for the treatment of coronary artery stenosis, including in-stent restenosis (ISR) and complex type C lesions, to improve myocardial perfusion.

(2) Use Conditions and Method

This study product is intended for lesion localization and dilation under coronary angiography conditions and cannot be reused. The use method and steps of the product include pre-use inspection, unpacking, pre-procedure preparation, balloon catheter preparation, balloon catheter placement, balloon dilation process and balloon catheter withdrawal process. See the instructions for use (IFU) for details.

(3) Contraindications

- All contraindications to angioplasty are contraindications to this product;
- Coronary artery spasm without organic stenosis;
- Left main lesion without bypass grafting or collateral circulation protection;
- Bifurcated lesions covered by stents;
- Stent fracture lesions;
- Patients with allergic reaction to the contrast agent;
- Patients with obvious abnormal coagulation function or hemorrhagic tendency;
- Patients who are contraindicated for antiplatelet or anticoagulant therapy;
- Other lesions that are not conducive to balloon dilation;
- Patients with severe infection or organ dysfunction;
- Patients who are not suitable for coronary artery bypass grafting (CABG);
- Except for the above matters, patients diagnosed by physicians as unsuitable for the use of relevant medical devices.

(4) Warnings

- Please read the IFU carefully prior to use. Please pay special attention to all warnings and precautions so as to avoid accidents.
- Please carefully select the patients with indications. Using this product has the same risks as the general angioplasty, including acute vascular occlusion, acute and sub-acute thrombosis, vascular dissection, vascular hemorrhage, etc.
- The Coronary Scoring Balloon Catheter has been sterilized before release from the factory, and it is sterile, non-pyrogenic, and intended for single-use only. Re-use, re-processing or re-sterilization may result in product structure deformation, failure and contamination, and may cause patient infection or cross infection, and evenly patient injury, illness or death.
- The procedure shall be performed by qualified professionals who have received professional training in coronary angioplasty, and the product should be used in the clean interventional operating room of a hospital.
- Check the product packaging carefully before use. If the carton package is opened, damaged, or the primary packaging is broken, Do Not use the product.
- Before use, please pay attention to the shelf life of the product and do not use an expired product.

- Intravascular procedures should be performed under high-resolution X-ray fluoroscopy, and if resistances encounter or abnormalities occur, please terminate the procedure immediately and confirm the cause.
- When using multiple devices in the body, Do Not let the Coronary Scoring Balloon Catheter wind with other devices. If resistances encounter or abnormalities occur, please terminate the procedure immediately and confirm the cause.
- To prevent vascular injury, the inflated diameter of the balloon should be similar to the diameter of the coronary artery at the proximal or distal stenosis. When using this product, pre-dilate the lesion appropriately according to its characteristics.
- Caution should be exercised when dealing with distal lesions with newly implanted drug-eluting stents (drug-eluting stents may delay intimal repair).
- The maximum inflation pressure of the balloon cannot exceed the labeled rated burst pressure (RBP).
- This product is not intended for power injection.
- In the process of a procedure, patients should be given appropriate anticoagulants and vasodilators.

4. Study Objective

To evaluate the safety and effectiveness of Coronary Scoring Balloon Catheter manufactured by Sino Medical Sciences Technology Inc. in the treatment of coronary artery stenosis.

5. Study Design

5.1 Overall Design and Its Determination Basis

This clinical trial is a prospective, multicenter, randomized, parallel controlled, non-inferiority design.

Multicenter clinical trial: refers to the clinical study conducted in two (inclusive) or more medical device clinical trial institutions under the same clinical trial protocol.

Parallel controlled design: Based on the Guidance for the Design of Medical Device Clinical Trials, the controlled clinical trial is conducted using the marketed devices with recognized efficacy/safety. The Coronary Scoring Balloon Catheter is a class III medical device, and there are few similar products on the market. In order to evaluate the effectiveness and safety of Coronary Scoring Balloon Catheter, the NSE Coronary Dilatation Catheter (NMPA (I) 20163035067), which is similar in structure and operating principle, relatively widely used in clinical practice and has positive efficacy in China and abroad, is

selected as the control device after investigation.

Randomization: Randomization is the basic principle to be followed by parallel controlled clinical trials. Each subject in a clinical trial has the same opportunity (the ratio of cases in test group to control group is 1:1) to be assigned to test group or control group, without affection of subjective wishes of the investigator and/or subject, to ensure the subjects in test group and control group comparable in various known and unknown baseline variables that may affect the trial result.

Blinding: Due to the different inherent characteristics (appearance, marking, etc.) of the investigational medical device and the control device, the subjects and investigators cannot be blinded in the trial, so an open-label design is adopted.

Non-inferiority test: The non-inferiority test is selected to confirm the efficacy/safety of the investigational medical device, which if lower than that of the control device but the difference between them is less than the pre-set non-inferiority margin, the difference is clinically acceptable.

5.2 Subject Enrollment

5.2.1 Inclusion Criteria

(1) Patients are at least 18 to 75 years of age, male or not pregnant female;

(2) Patients with asymptomatic ischemic evidence, stable or unstable angina pectoris or old myocardial infarction;

(3) In situ or restenotic lesion(s) in coronary arteries, including in-stent restenosis (ISR);

(4) Target lesion(s) must have a diameter of 2.0 mm ~ 3.5 mm and a length of ≤ 30 mm;

(5) Target lesion(s) must have a percent diameter stenosis of ≥70%% or ≥50% with evidence of ischemia;

(6) Patients have a planned intervention at no more than two lesions, in different target vessels;

(7) Investigators believe that target lesion atherosclerotic plaques require the scoring balloon treatment, in which the balloon can be passed through by pre-dilation.

(8) Able to understand the purpose of the trial, voluntarily participate and sign the ICF.

5.2.2 Exclusion Criteria

(1) Evidence of ongoing acute myocardial infarction within a week.

(2) Chronic total occlusion (TIMI 0 pre-procedure), left main lesion, intervention-required three-vessel lesions, and bypass lesion.

(3) Severe calcification and target lesion in a severe angulation (≥ 45 degrees).

(4) Patients with severe heart failure (NYHA Class III or above) or left ventricular ejection fraction <40% (ultrasound or left ventricular angiography).

(5) Patients with severe liver and renal dysfunction, as Cr >176.82 umol/L or Cr >2.0 mg/dl.

(6) Patients with history of active digestive tract ulcer, history of cerebral hemorrhage or subarachnoid hemorrhage, history of ischemic stroke 6 months before procedure, as well as patients with bleeding tendency, antiplatelet preparation and anticoagulant therapy contraindications that cannot be treated with anticoagulant therapy.

(7) Patients with allergies to heparin and contrast agent.

(8) Target lesion demonstrating severe dissection prior to planned deployment of the study balloon.

(9) Visible thrombus at the target lesion.

(10) Patients to receive heart transplantation.

(11) Patients who participated in other clinical trials of drugs or medical devices, but did not reach the primary endpoint.

(12) Patients who are judged by the investigators to have poor compliance, are unable to complete the study as required, or are judged by the investigators to be unsuitable for participation in the study.

(13) Patients who are not suitable for coronary artery bypass grafting (CABG).

5.2.3 Criteria and Procedures for Subject Withdrawal

Subjects who have signed the ICF and have been screened and enrolled into the trial but withdraw before the end of the observation period as required by the protocol, regardless when and why they withdraw, should be deemed as dropout cases.

(1) Withdrawal at the investigator's discretion

1) Those who experience SAEs that, in the judgment of the investigators, warrant discontinuation of the trial.

2) During the trial, the subjects suffer from complications and special physiological changes, and thus are not suitable to continue the trial.

3) Poor compliance of subjects.

(2) Self-withdrawal of subjects

1) Subjects who, for whatever reason, are unwilling or unable to continue the clinical trial, propose withdrawal from the trial to the investigators and

terminate the trial.

2) Subjects who are lost to follow-up since they refuse the further treatment and follow-up despite not specifically proposing withdrawal from the trial.

(3) Management of drop-out

1) All drop-out subjects should be recorded in the original medical records with study conclusions and reasons for drop-out.

2) After the subjects are dropped out, the investigators should communicate with the subjects as much as possible, ask them the reasons for drop-out, and make the evaluation items as complete as possible.

3) In the event of withdrawal, the investigators should take appropriate treatment measures for alternative therapy according to the subjects' actual conditions.

5.2.4 Criteria and Procedures for Discontinuation or Termination of the Trial

(1) Criteria for Discontinuation or Termination of the Trial

Discontinuation of the trial means that the clinical trial has not been completed as per its protocol, but discontinued prematurely. Discontinuation of the trial is to protect the rights and interests of subjects, ensure the quality of the trial and avoid unnecessary economic losses. Criteria for Discontinuation of the Trial:

1) If serious safety issues occur during the trial, the trial should be discontinued immediately.

2) Major defects are found in the clinical trial protocol during the trial, making it difficult to evaluate the effect of the investigational medical device; Or although there are no obvious defects in the trial protocol, significant deviations occur during implementation, making it difficult to evaluate the effectiveness and safety of the investigational medical device if continued.

3) The sponsor requests the discontinuation of the trial for funding reasons, management reasons, etc.;

4) The EC finds that the rights and interests of subjects cannot be guaranteed and asks for the discontinuation of the trial.

5) The medical products regulatory authority orders the discontinuation of the trial for some reasons.

(2) Procedures for Discontinuation or Termination of the Trial

The sponsor, if decides to discontinue or terminate the clinical trial, should report to all management departments of the medical device clinical trial institutions, ECs and PIs, and report to the medical products regulatory authority of the province, autonomous region or municipality directly under the central government where the sponsor is located, report to the medical products

regulatory authorities and health administrations of the provinces, autonomous regions or municipalities directly under the central government where the medical device clinical trial institutions are located within the time specified in the Good Clinical Practice for Medical Devices ([2022] Announcement No. 28). If the medical products regulatory authority or the EC requests suspension or termination of the trial, the trial shall be suspended or terminated within the prescribed time limit. When suspended or terminated, the trial is ended only after the enrolled subjects have completed the treatment and the post-treatment visits have been made according to the protocol, ensuring that the subjects receive appropriate treatment and follow-up.

5.3 Evaluation Methods

5.3.1 Effectiveness Evaluation

(1) Description on Effectiveness Endpoint

1) Primary efficacy endpoint: Device success rate (lesion level)

To achieve device success (lesion level), the following conditions should be met simultaneously:

a. The whole balloon dilatation procedure, including delivery, passing through the lesion, inflation and dilatation, deflation and retraction and withdrawal of the balloon, is successfully completed.

b. ≤30% residual stenosis of target lesion immediately after PCI (For ISR and drug balloon-related restenosis, residual stenosis <50% post-procedure)

2) Secondary efficacy endpoints: Procedural success rate (subject level)

To achieve procedural success (subject level), the following conditions should be met simultaneously:

a. ≤30% residual stenosis of at least one target lesion immediately after PCI (For ISR and drug balloon-related restenosis, residual stenosis <50% post-procedure)

b. No major adverse cardiac events (MACE) during post-procedure hospitalization: all-cause death, myocardial infarction (MI) and target lesion revascularisation (TLR).

(2) Basis for Determination

PTCA technique is relatively mature in clinical application. In its clinical studies published, especially pre-marketing registry studies, the use effect of PTCA in coronary artery in situ lesions or restenosis lesions (including ISR) is evaluated at the same time, with device success rate and procedural success rate as the endpoints. Regarding the definition of device success rate, on the one hand, it focuses on the successful use of the product itself, for example, the FDA-registered clinical trials such as Scoreflex NC PTCA Scoring Catheter (P200041)

[7] and Lacrosse PTCA Scoring Catheter (NCT04985773) [8], and the study of Auer et al. [9] defined the device success rate as the smooth delivery, inflation and dilation, deflation and retraction and withdrawal of the product throughout the balloon dilation procedure; on the other hand, it focuses on the immediate post-procedure residual stenosis following completion of the procedure, for example, the FDA-registered clinical trials such as Scoreflex NC PTCA Scoring Catheter (P200041) [7], Lacrosse PTCA Scoring Catheter (NCT04985773) [8] and AngioSculpt PTCA Scoring Catheter (P050018) [10] reported the device success rate as that at least one target lesion has achieved < 50% residual stenosis immediately after procedure and no MACE-related events occur during post-procedure hospitalization, which is also a criterion to be met as defined in the procedural success rate. At the same time, the provisions for residual stenosis after PCI in relevant clinical studies and clinical practice are taken into account, for example, the studies such as by Auer et al. [9] defined the balloon procedure success as residual stenosis of lesion < 30%, and the studies such as by Lee SH et al. [11] defined the procedural success as at least residual stenosis of < 30% post-procedure, and freedom of major AEs (death, MI, or emergency coronary artery bypass grafting) during post-procedure hospitalization.

In summary, referring to clinical study design literature of similar PTCA balloons in China and at abroad, the PIs decide that the device success rate (lesion level) is set as the primary efficacy endpoint, and the procedural success rate is set as the secondary efficacy endpoints in combination with the indications for use of the test devices and the previous clinical procedure experience of the investigators.

5.3.2 Safety Evaluation

(1) Description on Safety Evaluation Endpoints

1) **Incidence of target lesion failure (TLF) composite endpoint**

Any of the following events is considered as a TLF:

a. Cardiac death (the death with uncertain cause is also considered cardiac death);

b. Target vessel myocardial infarction (TV-MI);

c. Clinically indicated target lesion revascularisation (CI-TLR).

Evaluation method: The observation time range is from the start of procedure to pre-discharge. The incidences of single and composite events are counted, respectively, by lesions.

2) **Incidence of patient-oriented composite endpoint (PoCE)**

Any of the following events is considered as a PoCE:

a. All-cause death;

b. All myocardial infarction;

c. All revascularisation events, including target lesion revascularisation (TLR), target vessel non-target-lesion revascularisation (TVR), and non-target vessel revascularisation.

Evaluation method: The observation time range is from the start of procedure to pre-discharge. The incidences of single and composite events are counted, respectively, by subjects.

3) **Occurrence of single AE and SAE**

Evaluation method: The observation time range is from the start of procedure to pre-discharge. Other possible AEs such as balloon rupture, vessel perforation, dissection, acute occlusion, vasospasm, thrombosis (including in-stent thrombosis), arrhythmia requiring intervention. The incidences of single events are counted, respectively.

4) **Incidence of Device Defects**

(2) Basis for Determination

By referring to study design literature on PTCA balloons with equivalent functions and similar structures in China and at abroad, the target lesion failure (TLF) composite endpoint and patient-oriented composite endpoint (PoCE) are set as the primary safety endpoints based on the decision of the PIs, taking into account the safety endpoints of relevant interventional procedures and clinical experience of the investigators, and the definitions of guidelines such as AHA/ACC [12] and ARC-2 [13] are used to more comprehensively and fully evaluate the safety of the study product.

5.4 Investigational Medical Device and Control Device

(1) Investigational Medical Device

Product Name Coronary Scoring Balloon Catheter

Manufacturer Sino Medical Sciences Technology Inc.

Model/specification 2.0-3.5 mm in diameter, 10-15 mm in length (see Table 1)

Table 1 Model/specification of investigational Medical device

Diameter (mm)	Length (mm)	
	10	**15**
2.00	●	●
2.50	●	●
2.75	●	●
3.00	●	●
3.50	●	●

Table 2 Relationship between balloon diameter and inflation pressure

Balloon diameter/mm	Pressure/atm										
	4	5	6	7	8	9	10	11	12	13	14
2.00	1.90	1.95	2.00	2.05	2.08	2.12	2.15	2.17	2.19	2.21	2.22
2.50	2.42	2.49	2.50	2.60	2.64	2.68	2.72	2.75	2.78	2.80	2.84
2.75	2.62	2.70	2.75	2.82	2.87	2.90	2.93	2.96	2.99	3.03	3.05
3.00	2.85	2.93	3.00	3.06	3.11	3.17	3.21	3.26	3.31	3.36	3.41
3.50	3.29	3.39	3.50	3.56	3.61	3.66	3.71	3.75	3.79	3.83	3.87

Nominal balloon pressure
Rated burst pressure of balloon

*The rated burst pressure of balloon is obtained according to the test results of in vitro tests. At least 99.9% of balloons will not burst at the rated burst pressure or below (95%CI). During the balloon inflation, it is recommended that a pressure detection device should be used to prevent the excessive inflation of the balloon. The size of actual dilation in vivo should be determined by angiography.

(2) Control Device

Product Name NSE Coronary Dilatation Catheter
Manufacturer Goodman Co., Ltd.
Medical Device Registration Certificate No. NMPA (I) 20163035067
Model/specification 2.0-4.0 mm in diameter and 13 mm in length (see Table 3)

Table 3 Model/specification of control device

Specification	Balloon diameter (mm)	Length (mm)
NS20013	2.00	13
NS22513	2.25	13
NS25013	2.50	13
NS27513	2.75	13
NS30013	3.00	13
NS32513	3.25	13
NS35013	3.50	13
NS37513	3.75	13
NS40013	4.00	13

Table 4 Relationship between balloon diameter and inflation pressure

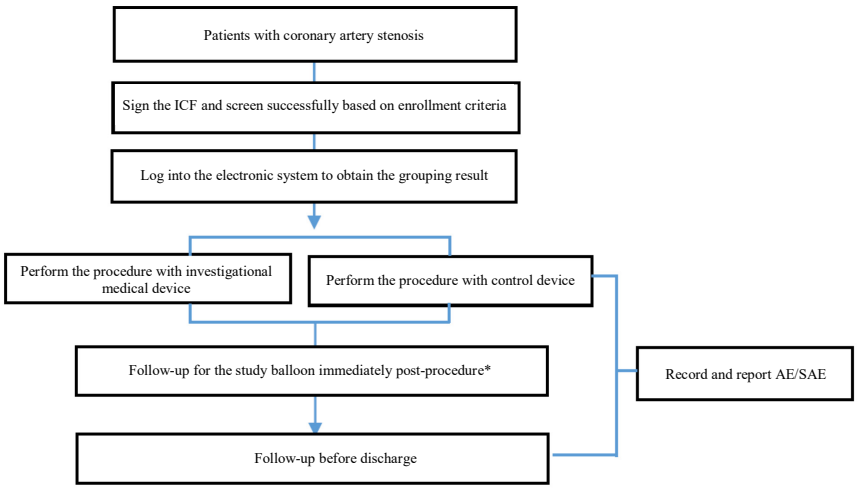
Balloon diameter/mm	Pressure/atm					
	4	6	8	10	12	14
2.00	1.93	2.00	2.06	2.10	2.14	2.18
2.25	2.16	2.25	2.31	2.36	2.40	2.45
2.50	2.38	2.50	2.59	2.66	2.70	2.74
2.75	2.65	2.75	2.81	2.86	2.90	2.94
3.00	2.89	3.00	3.07	3.12	3.16	3.20
3.25	3.13	3.25	3.32	3.38	3.43	3.48
3.50	3.37	3.50	3.57	3.64	3.69	3.73

3.75	3.61	3.75	3.85	3.91	3.96	4.00
4.00	3.86	4.00	4.10	4.17	4.22	4.26

Nominal pressure (NP) Rated burst pressure (RBP)*

5.5 Study Process

5.5.1 Study Flowchart



Note: * According to pre- and post-procedure conditions of the target lesion for the study balloon, pre-dilation of common balloon and stent implantation or post-dilation balloon can be selected for further treatment.

5.5.2 Conduct of Clinical Trial

(1) Screening Assessment (-14 d to 0 d)

Before the trial, all patients planning to be enrolled in this study must pass the screening assessment after voluntarily signing the ICF by themselves or their legally acceptable representatives. The following items shall be tested and evaluated before procedure:

1) Collection of demographic data (age, gender, BMI), clinical diagnosis, and comorbidities of patients.
2) Pregnancy test and blood/urine HCG test for women of childbearing potential when necessary;
3) Pre-procedure examination of vital signs (systolic blood pressure, diastolic blood pressure and heart rate);
4) Pre-procedure examination or review of blood routine, blood biochemistry and coagulation function test results within one month before procedure (the recent results shall prevail for those who have undergone examinations for many times): ① Blood routine: white blood cell count (WBC), red blood cell count (RBC), platelet count (PLT) and hemoglobin (HB); ② Renal function: serum creatinine (SCr); ③ Liver function: alanine aminotransferase (ALT) and aspartate aminotransferase (AST); ④ Blood lipids: triglyceride (TG),

total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C); ⑤ Prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT) and fibrinogen (FIB).

5) Pre-procedure examination of myocardial enzyme spectrum: creatine kinase (CK), creatine kinase isoenzyme (CK-MB), cardiac troponin T (cTnT)/cardiac troponin I (cTnI) (choose one, not all are mandatory)
6) Pre-procedure examination of 12-lead ECG;
7) Verification of inclusion and exclusion criteria.

(2) Procedure details (0d)

According to the routine procedure of the hospital, no special operation requirements are added. During this period, the following visit contents need to be completed:

1) Vital signs (systolic blood pressure, diastolic blood pressure and heart rate);
2) Coronary angiography (patient's lesions, residual stenosis after PCI, etc.);
3) Clinical evaluation (study balloon operation, including balloon pushability, passing ability, withdrawal ability, dilation frequency, dilation pressure, etc.; device defects; balloon and stent usage);
4) AEs (such as procedure-related complications, including puncture hematoma, vascular dissection, vessel perforation, acute occlusion, etc.);
5) Cardiovascular adverse events (including major adverse cardiac events - MACE, target lesion failure - TLF, patient-oriented composite endpoint - PoCE);
6) Cardiovascular concomitant medications (anticoagulants, antiplatelets, and statins).

(3) Follow-up period (from post-procedure to pre-discharge)

1) Vital signs (systolic blood pressure, diastolic blood pressure and heart rate);
2) Post-procedure reexamination of blood routine and blood biochemistry: ① Blood routine: white blood cell count (WBC), red blood cell count (RBC), platelet count (PLT) and hemoglobin (HB); ② Renal function: serum creatinine (SCr); ③ Liver function: alanine aminotransferase (ALT) and aspartate aminotransferase (AST); ④ Blood lipids: triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C);
3) Myocardial enzyme test 48 hours post-procedure. If the results are abnormal and clinically significant, re-examination should be performed before

discharge (the highest test value is recorded for those with multiple examinations);

4) 12-lead ECG examination 48 hours post-procedure.
5) AEs (such as procedure-related complications, including puncture hematoma, vascular dissection, vessel perforation, acute occlusion, etc.);
6) Cardiovascular adverse events (including major adverse cardiac events - MACE, target lesion failure - TLF, patient-oriented composite endpoint - PoCE);
7) Cardiovascular concomitant medications (anticoagulants, antiplatelets, and statins).

5.5.3 Norms for Using Device

Before using the test devices, the investigators should carefully read the relevant product IFU or materials and perform the procedures in strict accordance with IFU. (The following are recommended operations, and the operator may make slight modification according to the actual situations)

- The diameter, length, and number of balloons are selected, and the dilation pressure is determined by the operator according to the lesion condition.
- In use, the balloon should be dilated according to the nominal pressure specified in the IFU. A pressure monitoring device is recommended during the procedure to prevent excessive pressure.
- According to pre- and post-procedure conditions of the target lesion for the study balloon, pre-dilation of common balloon and stent implantation or post-dilation balloon can be selected for further treatment.
- Patients have a planned intervention at no more than two lesions, in different target vessels.
- When treated at the same time, the target and non-target lesions must be located in different vascular branches.
- If the target lesion and non-target lesion are treated at the same time, the target lesion can only be treated after the non-target lesion has been treated successfully.
- If a study balloon fails to dilate the target lesion, the operator will decide the follow-up treatment measures according to the lesion condition.
- In the event of a flow-limiting dissection or rupture during dilation, the operator will decide what treatment measures will be taken.

5.5.4 Specifications for Concomitant Therapy (e.g., Medication)

Based on interventional guidelines in China and at abroad, dual antiplatelet

therapy is recommended to minimize the risk of thrombosis. The initial oral loading dose for all patients without contraindications to aspirin is 100~300 mg, which will be maintained for a long time at 100 mg/d. A P2Y12 receptor antagonist is added in addition to aspirin and maintained for at least 12 months, unless there are contraindications (e.g. higher risk of hemorrhage). Options include:

- Ticagrelor: Loading dose of 180 mg, maintenance dose of 90 mg, bid;
- Clopidogrel: loading dose of 300~600 mg, maintenance dose of 75mg, qd.

Investigators can make decisions on the use of dual-antiplatelet drugs in patients according to clinical conditions, including whether pre-procedure loading dose is required.

Low-density lipoprotein control with an optimal lipid-lowering regimen is recommended, with an LDL target of ≤ 1.8 mmol/L (≤ 70 mg/dL), moderate-intensity statins recommended, and a combination with non-statins recommended if the OPC is not reached.

5.6 Measures to Control Bias

(1) In terms of trial design, the randomized, parallel-controlled clinical trial design is used, which can make the distribution of clinical trial influencing factors between the test group and control group tend to be balanced, reducing the selection bias and implementation bias. The objective judgment endpoints are adopted to avoid measurement bias.

(2) In terms of trial implementation, the investigators in various sites use the same methods, follow the same standard operating procedures (SOPs), and receive uniform trainings before the trial to reduce observer bias. Subjects will be screened in strict accordance with the inclusion and exclusion criteria in the clinical trial protocol to reduce selection bias. The clinical research associate (CRA) appointed by the Sponsor shall regularly conduct monitoring on the study sites, making sure that all contents in the trial protocol are strictly followed. The raw materials are inspected to ensure consistent contents with the Case Report Form (CRF).

(3) In terms of independent imaging evaluation, the addition of independent imaging analysis is not excluded in this trial.

(4) To minimize bias, blinded data review may be considered. For possible confounding bias, appropriate control may be considered in the data analysis phase.

6. Statistical Considerations

6.1 Estimation of Sample Size

6.1.1 Overall Sample Size

After literature review, according to the results of relevant study literature and clinical experience of the scoring balloon catheter in the treatment of coronary artery disease, assuming that the SINOMED Coronary Scoring Balloon Catheter in the test group and Goodman NSE Coronary Dilatation Catheter in the control group can reach the equivalent level, then the device success rate is expected to reach 96% [10, 14-17]. Considering the influence of factors such as the procedure level of different investigators, the complexity of lesions, and the comorbidities and severity of illness of subjects, the sponsor, clinical experts, investigators and statistical experts jointly decide that the non-inferiority margin δ is taken as -10%, the one-sided test α is set to be 0.025, and the test power (1-β) is 0.8. The total sample number is calculated as 122 using the PASS software, with 61 each in test group and control group. In consideration of a 10% dropout rate, this study requires 136 subjects, 68 each in test group and control group. The formula for calculation of sample size is shown as follows:

$$n_T = n_C = \frac{\left(Z_{1-\alpha/2} + Z_{1-\beta}\right)^2 [P_C(1-P_C) + P_T(1-P_T)]}{(|D| - \Delta)^2}$$

Note: n_T and n_C are the sample sizes of test group and control group, respectively, and $Z_{1-\alpha/2}$ and $Z_{1-\beta}$ are the quartiles of the standard normal distribution; when α=0.025, $Z_{1-\alpha/2}$ = 1.96, and when β=0.2, $Z_{1-\beta}$=0.842; $(Z_{1-\alpha/2}+Z_{1-\beta})^2$=7.85; P_T and P_C are the predictive incidences of events in test group and control group, respectively, and $|D|$ is the absolute value of the expected rate difference between the two groups $|D| = |P_T - P_C|$, and Δ is the non-inferiority margin, being negative.

6.1.2 Allocation of Sample Size

The inclusion/exclusion criteria for the selected subjects are strictly restricted in this trial protocol, and all selected 136 subjects are diagnosed with coronary artery stenosis (including in situ or restenotic lesions). The subjects screened are randomized at 1:1 to receive the investigational medical device or the control device for treatment, and the device success rate is set as the primary endpoint.

6.1.3 Minimum and Maximum Number of Subjects in Each Site and Justification

This trial will be carried out at the same time in multiple study sites. In principle, the number of subjects enrolled in each site will be distributed as evenly as possible to ensure adequate site representation. However, considering the feasibility and progress of the selection, the number of subjects enrolled in each participating site will be adjusted according to the actual situation, so as to ensure that the enrollment scale at each site is relatively balanced, and that the final enrollment scale for a specific site should not exceed 50% of the total number of

cases.

6.2 Analysis Data Sets

Statistical analysis will be carried out on the basis of the following analysis populations. The analysis populations will be clearly defined before the start of statistical analysis. And the analysis populations in this study include:

(1) Full Analysis Set (FAS): the set of subjects determined following the intent-to-treat (ITT) principle refers to the data set constituted by all subjects who participate in the randomized study and receive the investigational product. The worst observation carried forward (WOCF) is used for imputation of the patients in whom the Primary efficacy endpoint is unable to be observed.

(2) Per-Protocol Set (PPS): refers to the subgroups of treatment population where the study has been completed with the major protocol violations excluded (which means that the subjects violate the inclusion criteria or exclusion criteria, etc.).

(3) Safety set (SS): refers to the subject dataset using investigational medical devices and having recorded safety endpoints.

The efficacy analysis will be performed based on the FAS and PPS. All baseline demographic data analysis will be performed on the FAS while the safety evaluation will be on the SS.

6.3 Subject Elimination Criteria

(1) The subjects seriously violate the inclusion/exclusion criteria, affecting the evaluation of the primary endpoint.

(2) The subjects do not use the test devices for treatment after inclusion, or have no any visit record although they meet the inclusion criteria.

6.4 Statistical Methods

6.4.1 Statistical Design

This study is a prospective, multicenter and randomized controlled design, with comparison type of non-inferiority test. It is to demonstrate that the investigational medical device also meets the needs of clinical application through comparison with the similar products that have been marketed, with the primary endpoint set as device success rate (lesion level); the corresponding statistical hypothesis test is:

$$H_0 : p_T - p_C \leq -\Delta$$

$$H_1 : p_T - p_C > -\Delta$$

Where, P_T is the expected device success rate in the test group, P_C is the expected device success rate in the control group, and Δ is the non-inferiority margin.

6.4.2 Statistical Analysis Methods

(1) General Principles for Statistical Analysis

In this study, SAS software is used for data description and analysis. All statistical tests are conducted by two-sided test (unless otherwise specified). The 95% confidence is adopted for the confidence interval (CI). In addition to the statistical methods listed below, detailed and additional exploratory analyses may be required and confirmed in the Study Reports and Statistical Analysis Plan (SAP).

1) Statistical description: For the description of quantitative indicators, the mean, standard deviation (SD), median, minimum, maximum, lower quartile (Q1) and upper quartile (Q3) will be calculated; for the categorical indicators, the number of cases and percentage for each category will be described.
2) Statistical inference: The inter-group comparison in general condition will be conducted by using appropriate method according to the types of indicators. The inter-group comparison in quantitative data will be conducted by the group t-test (homogeneity of variance and normal distribution) or Wilcoxon rank sum test according to the data distribution. The categorical data will be analyzed by the Chi-squared Test or Exact Test (if the Chi-squared Test is not applicable), while the ranked data will be analyzed by the Wilcoxon rank sum test or CMH test.

(2) Completion and Baseline Analysis

The number of subjects enrolled and the completion status of enrollment of each site should be summarized, and the drop-out cases should be listed. Different data set sizes in each group, case distribution of each site, total drop-out rate comparison and reasons for discontinuation, should be tabulated in detail. The demographic characteristics (age and gender), the relevant medical history and the treatment history of the patients are described, and the comparison of age and gender, etc. between the two groups will be conducted to measure the comparability between the two groups. Demographic analysis is based on FAS.

(3) Primary efficacy endpoint

The Primary efficacy endpoint of this study is the device success rate (lesion level), and the hypothesis test is as follows:

Null hypothesis: $P_T - P_C \leq -10\%$

Alternative hypothesis: $P_T - P_C > -10\%$

Under $\alpha=0.025$ (one-sided test) and $ß=0.2$, the device success rate (lesion level) is compared between the test group and control group, and the difference between the two groups and the 95%CI of such difference are calculated to determine whether the non-inferiority margin is met based on the lower limit of CI. Non-inferiority is established if the lower limit of 95%CI is not lower than -10%. If

central effect is to be considered, CMH's chi-square test is used.

(4) Secondary efficacy endpoints

The secondary efficacy evaluation is based on FAS and PPS. For the statistical description and inference of the data, the applicable descriptive indicators and hypothesis test methods are selected based on the characteristics of the data.

(5) Safety endpoints

Descriptive analysis is performed on safety endpoints data, and the number, incidence and case-times of all AEs, related AEs and SAEs in the two groups are calculated. The cases who discontinue the study due to AEs and who experience SAEs are presented in a list.

6.4.3 Significance Level and Power of Clinical Study

In this trial, for the primary endpoint, the significance level of statistical test is 0.025% one-sided, and the power of test is taken as 80%. For other indicators, the significance level of statistical test is taken as 0.05 two-sided.

6.4.4 Expected Drop-out Rate

In determining the sample size, the highest possible drop-out rate during the study is expected to be 10%, including all conditions that make the subjects ultimately excluded from the primary analysis, often referring to major deviation of trial protocol (affecting the primary efficacy evaluation and/or safety evaluation) adjudicated by the PIs.

6.4.5 Pass/Fail Criteria for Clinical Trial Results

Determining whether the study result is acceptable from a statistical perspective is equivalent to verifying the initial hypothesis testing. For this study, the primary evaluation indicator is the device success rate (lesion level). In comparison type, this is non-inferiority test. It is planned to prove through the study results that the test group had the same therapeutic effect as compared with the control group.

In conclusion, the judgment of the study results will be based on the difference in device success rate between the test group and control group. If the results show that the lower limit of 95%CI for the difference in device success rate between test group and control group is greater than -10% (the pre-specified non-inferiority margin), the non-inferiority is established. Otherwise, the non-inferiority conclusion is not established.

6.4.6 Criteria for Termination of Trial Based on Statistics and Justification

The interim analysis and its corresponding early termination criteria are not pre-established in this trial, so this section is not applicable. All statistical analyses are conducted after the completion of data collection, cleansing and final locking.

6.4.7 Procedures for Reporting Deviation from Original Statistical Plan

The statistical analysis plan needs to be confirmed by the sponsor and the PIs, and finalized before database locking. Prior to finalization, the initial analysis plan should be modified according to the actual conditions in the trial process. In principle, the main analysis principles, methods and analysis sets should not be modified, and all the modifications will be recorded.

6.5 Missing Data and Outliers

Method for the treatment of missing data: The missing data will be processed according to the division of the data set; primary efficacy data will be imputed with the use of the WOCF (Worst Observation Carry Forward).

Wrong data handling method: In the process of data management, the quality management will be performed for the data in the database, wrong data found will be questioned in the form of Query to investigators, and the wrong data will be adjusted according to the written reply of investigators until all wrong data is corrected before locking the database.

Unreasonable data handling method: In the process of data management, the data in the database will be checked logically, unreasonable data found will be questioned in the form of Query to investigators, and the unreasonable data will be adjusted according to the written reply of investigators until all unreasonable data is solved before locking the database.

7. Monitoring Plan

The sponsor should assume the responsibility for the monitoring of the medical device clinical trial, establish the SOPs for monitoring and choose qualified CRA to perform the monitoring duties. The monitoring plan is as follows:

(1) Monitoring visits include: before start-up visit, start-up visit, routine process visit, unconventional visit, and closing visit;

(2) Monitoring frequency: The number of CRAs and the monitoring frequency should depend on the complexity of the medical device clinical trial and the number of study sites involved in the trial.

(3) CRA qualification: The CRA should be trained accordingly, be familiar with the GCP and relevant laws and regulations, have relevant professional knowledge, be familiar with relevant study data of the investigational medical device, clinical information of the similar products, clinical trial protocol and related documents, and be able to effectively fulfill the monitoring duties; the CRA should abide by the SOPs for monitoring developed by the sponsor, and urge the medical device clinical trial to be carried out according to the clinical trial protocol.

(4) Monitoring contents: compliance of medical device study sites and investigators with the clinical trial protocol, the GCP and relevant laws and

regulations in the implementation of clinical study; signing of ICF by subjects, screening of subjects, follow-up, rights and interests, and safety guarantee; the management and use of investigational medical devices and control devices (if applicable); the management and use of biological samples (if applicable); handling of adverse events and device defects; reporting of safety information; recording of clinical trial data and filling of CRFs.

8. Data Management

The Electronic Data Capture (EDC) system is used to collect the trial data. The EDC system has been strictly tested and fully complies with the requirements of Good Clinical Practice for Medical Devices and Technical Guidance for Data Management in Clinical Trials. Before the system is formally launched, the relevant users need to be trained and assessed to ensure that the system meets the trial requirements. After the official launch, relevant personnel will be provided with the account and password. The account is bound with the role and authority of the user who is required to properly keep and not to disclose the account information to others or exercise corresponding rights on behalf of others.

8.1 Data Collection

The EDC directly transmits data from the client to the server through the Internet. Investigators can directly enter the source data into the EDC system to complete data collection. Investigators should be responsible for the quality of the entered data and ensure the authenticity and integrity of the data. The EDC system provides an interface printing function that allows the investigators to print the electronic case report form (eCRF) as required.

8.2 Data Verification and Modification

The EDC system provides on-line and off-line verification methods. When investigators have entered abnormal data, the EDC system will issue real-time warnings to remind them to check; and the data administrator performs logical check on the data stored in the server and issues the wrong data through EDC in the form of manual query. Investigators need to answer all published queries. The CRA needs to periodically remind and assist the investigators in answering queries to ensure that each query is handled correctly. The system will record all queries and answers thereto.

8.3 Database Locking

When all data entry is completed and submitted, and all queries are answered, the system enters a soft locking status. The data administrator will generate a blinded review report based on the database. If it is confirmed that the data would not be modified, the sponsor, the person in charge of data administration and the person in charge of statistics will sign the database locking form, and the data administrator would complete the database locking operation according to the

form. The locked database cannot be modified again. If there is any wrong data that affects the primary efficacy endpoint or safety endpoints, the sponsor, the person in charge of data administration and the person in charge of statistics will confirm the unlocking for modification and sign the database unlocking form, and the data administrator will modify the wrong data according to the unlocking reason and carry out quality control. The sponsor, the person in charge of data administration and the person in charge of statistics will sign the database locking form again once the error has been corrected.

9. Risk-Benefit Analysis

9.1 Benefit Analysis

PTCA, as the most basic method in the PCI of coronary artery stenosis lesions, has been widely used in patients with coronary artery in situ lesions or ISR. Based on data of its previous clinical applications, PTCA shows potential benefits in improving patients' symptoms and quality of life that outweigh possible risks associated with the use of such products. This also benefits from the design of the scoring balloon itself, with three wound Ni-Ti alloy elements to the outside of the common balloon. Therefore, compared with the risks such as late stent delivery failure and stent incomplete expansion caused by the blunt, disorderly dilated lesion with the common balloon, the scoring balloon dilates lesions in such a way that plaque cracks can be formed in an effective and relatively regular manner, thus obtaining ideal stent implantation, effectively reducing the restenosis and the risk of in-stent thrombosis, and ultimately affecting the whole procedure time and procedural success rate [18-20].

In addition, there is also a possibility that subjects do not directly benefit from enrollment in this trial, but the results of the trial will also help to improve existing treatment methods and benefit the patients with coronary artery stenosis requiring balloon dilation in the future.

9.2 Potential Risk Analysis

There may be some risks involved in participating in this trial, but the risks are not expected to be substantially different from those experienced by individuals receiving balloon dilation or PCI outside of the trial. Patient risks are managed and reduced by fully evaluating the potential risks and benefits of subjects, providing comprehensive trainings to the investigators, and conducting regular monitoring visits during the clinical trial process, and adhering to the recommended peri-procedural medication regimen.

10. Quality Control of Clinical Trial

(1) Quality Control Measures of the Laboratory

The laboratories of the participating clinical trial institutions should have quality

control procedures for all observed indicators of this trial.

(2) Training for Clinical Trial

Before the initiation of the clinical trial, the relevant personnel of the clinical trial will be trained, and the investigators of each site will be trained by organizing the kick-off meeting, including the clinical protocol, informed process, device use, and document filling, etc. In the course of the trial, targeted training will be provided to the investigators and the relevant personnel of the trial according to the actual clinical situation.

(3) Monitoring of Clinical Trial

During the clinical trial, the CRA will conduct regular monitoring visits at the study site according to the monitoring plan, to ensure that all the contents in the study protocol are strictly observed, and will check the raw data to ensure that the filled contents of EDC are true, complete and correct.

(4) Retention of Raw Data

The raw data of this trial include the signed ICF, release records of test products, relevant laboratory test reports, case records and other related records, which should be retained at the clinical trial institute of the hospital where the study site is located. All raw data and printed CRF should be retained for 10 years after completion or termination of the clinical trial.

11. Ethical Issues and Informed Consent in Clinical Trial

11.1 Ethical Considerations

This clinical trial is conducted in compliance with the Declaration of Helsinki of the World Medical Association and applicable laws and regulations of China. Before the clinical trial, the investigators need to submit the clinical trial protocol, ICF and other related documents to the Medical Ethics Committee of hospitals where the study sites are located. The clinical trial will be started only after obtaining the approval of the EC. Any amendment to the study protocol must be approved by the EC before it can be implemented. SAEs during the clinical trial shall be submitted to the EC in writing timely.

11.2 Informed Consent Process

The investigators should comply with the codes of ethics and relevant ethical requirements of the Declaration of Helsinki of the World Medical Association. Before subjects participate in the clinical trial, the investigators should inform the subjects of the details of the investigational medical device and clinical trial, as well as the possible benefits and known and foreseeable risks. After full and detailed explanation by the investigators, both the subjects and investigators should sign and date the ICF; where a subject is a person without or with limited capacity for civil conduct, the written informed consent should be obtained from

his/her guardian; if any subject lacks reading ability, an impartial witness should be present to witness the whole informed consent process, and sign and date the ICF. The investigators should not compel or otherwise improperly induce the subjects to participate in the clinical trial;

The investigators should use the latest version of the ICF approved by the EC and other information provided to subjects. Where the ICF is revised in the course of the trial, the revised ICF should not be implemented until the written consent of the EC has been obtained again. When the ICF is updated and reviewed and approved by the EC, the investigators should ensure that all the subjects who have been affected and have not finished the trial procedures sign the newly revised ICF.

12. Provisions for AE and Device Defect Reporting

12.1 Definition of AE and Provisions for AE Reporting

Adverse event (AE) refers to an adverse medical event that occurs during the medical device clinical trial, related or unrelated to the investigational medical device.

AEs after treatment with the investigational product must be recorded truthfully in the Adverse Event Form. Record the duration of AEs (that is, from start to end), severity, and correlation with the clinical study as well as the corresponding treatment and other management measures. Follow-up shall be made to the end of the trial or the outcome of adverse events.

In this clinical trial, the following conditions may not be recorded as an AE: 1) hematoma less than 6 cm or a small amount of bleeding at the puncture site; 2) common stress reactions post-procedure, such as fever and weak dorsalis pedis artery pulse; 3) abnormal laboratory indicators post-procedure are clinically significant, but the investigators do not take corresponding treatment measures, and the subjects resolve spontaneously.

12.2 Device Defect

The device defect refers to the unreasonable risk that may endanger the human health and life safety in the normal use of the medical device during the clinical trial, such as label errors, quality problems and failures.

The investigators should record the device defects occurred or found during the clinical trial and analyze the cause of the event together with the sponsor, form a written analysis report, propose the opinions on continuing, suspending or terminating the trial and report to the EC through the management department of medical device clinical trials of the clinical study sites for review.

The investigators and subjects can make complaints against the test devices at any phase of this clinical study.

12.3 Definition of SAE

The SAE refers to the event that causes death or serious deterioration of health in the process of clinical trial, including:

(1) Fatal disease or injury;

(2) Permanent impairment of a body structure or a body function;

(3) Requiring in-patient hospitalization or prolongation of existing hospitalization;

(4) Requiring medical measures to prevent permanent impairment of the body structure or body function;

(5) Leading to fetal distress, fetal death or congenital abnormality, or congenital defect, etc.

Hospitalization or prolongation of hospitalization cannot be considered an SAE if at least one of the following exceptions is met:

- Pre-planned hospitalizations (e.g., scheduled elective or scheduled operations or examinations prior to study start)
- Hospitalization not related to an AE (e.g., community hospitalization for short-term or long-term care purposes)

However, any interventional therapy performed during hospitalization may meet the criteria for an "Important Medical Event" and may be reported as a SAE based on clinical judgment. In addition, if local regulatory authorities specifically require stricter definitions, local regulations shall prevail.

12.4 Reporting Procedures and Contact Information

In case of SAEs in the medical device clinical trial, the investigators should immediately take appropriate treatment measures for subjects; at the same time, the investigators should report to the sponsor, the management department of medical device clinical study site and the EC within 24 hours after awareness of SAEs; follow up these SAEs according to the provisions of the clinical trial protocol, and submit the follow-up report of SAEs;

The sponsor should, within 7 days after being aware of death or life-threatening SAEs related to the investigational medical device, or within 15 days after being aware of non-death or non-life-threatening SAEs related to the investigational medical device and other serious safety risk information, report to other medical device clinical trial institutions, ECs and PIs participating in the clinical trial, report to local medical products regulatory authority of the province, autonomous region or municipality directly under the central government where the sponsor is located, report to the medical products regulatory authorities and health administrations of the provinces, autonomous regions or municipalities directly under the central government where the medical device clinical trial institutions

are located, and take risk control measures.

See Appendix 2 for the contact information.

13. Deviation from Clinical Trial Protocol and Regulations for Protocol Amendment

Before the start of the clinical verification, the trial protocol is discussed, revised, finalized and signed by each investigator and the sponsor, and then reported to the EC for approval, which the trial can be initiated then.

If this protocol has problems in clinical verification and actual implementation that need to be revised, the investigators should be informed of. After the multicenter discussion, the protocol shall be revised by the leading site.

During the clinical study, if the existing participating sites fail to obtain the approval of the clinical trial administrative department or the EC, resulting in the progress of the study significantly slower than the expected schedule, the sponsor should fully communicate and discuss with the coordinating investigator, and then make adjustments to the participating sites (abandonment or addition), and may update the list of clinical study sites in the Appendix without amending the text of the protocol. The final list of participating sites should be submitted to the clinical trial management departments and ECs of all participating sites for filling.

If the important new information regarding the investigational medical device becomes available, the ICF must be revised in writing and re-approved by the EC before obtaining consent from subjects once again.

In the event of deviation from the protocol during the course of the trial, the investigators should promptly notify the sponsor and the EC.

14. Direct Access to the Source Data and Documents

In this clinical study, the PIs and their authorized investigators can access and generate inpatient medical records, ICF of subjects, EDC and original medical records in HIS system.

The laboratory inspection personnel and investigators can access and generate the inspection result report issued by them. The data administrator can access and generate the data of data management; the statistical analyst can access and generate the statistical analysis data. The access and editing permissions of the remaining source data shall, in accordance with the requirement of the relevant laws and regulations and technical specifications in China, be specified in detail by SOP of the corresponding department.

15. Contents to be Covered in Clinical Trial Report

The clinical trial report generally includes basic information on the medical device clinical trial, implementation, statistical analysis methods, trial results,

AEs and device defect reporting and handling, analysis and discussion of trial results, clinical trial conclusions, ethical situation, existing problems and suggestions for improvement, etc.

16. Confidentiality Principle

This Protocol and the contents of this clinical trial and all the attached data are confidential and proprietary information of the sponsor, and the investigators shall be held responsible for confidentiality, including the patent application, manufacturing process and unpublished data available to the investigators provided by the sponsor, which shall not be disclosed to any third party unless the consent of the sponsor is obtained and the obligation of confidentiality shall survive the termination or end of this trial.

17. Responsibilities Assumed by All Parties

All parties shall strictly implement the relevant provisions in accordance with the Good Clinical Practice for Medical Devices ([2022] Announcement No. 28, hereinafter referred to as "GCP").

17.1 Responsibilities of Investigators

(1) The investigators should participate in the training related to the medical device clinical trial organized by the sponsor, and participate in the medical device clinical trial within the scope authorized by the PIs.

(2) The investigators should be familiar with the principle, indications for use or intended use, product performance, operation methods, installation requirements and technical indicators etc. of the investigational medical device, and understand the pre-clinical study related data of the investigational medical device.

(3) The investigators should fully understand and comply with the clinical trial protocol, the GCP and applicable laws and regulations, as well as responsibilities related to the medical device clinical trial.

(4) The investigators should bear management responsibilities for the investigational medical device and control device (if applicable) provided by the sponsor, ensure that they are only used for subjects participating in the medical device clinical trial, store and keep them as required during the clinical trial, and handle them according to relevant laws and regulations as well as the contract with the sponsor after the completion or termination of the clinical trial.

(5) The investigators should ensure that the collection, processing, storage, transportation, and destruction of biological samples comply with the clinical trial protocol and applicable laws and regulations during the medical device clinical trial.

(6) When receiving the SAE and other safety information related to the investigational medical device provided by the sponsor, the PIs should sign in and read it in a timely manner, consider whether to make corresponding adjustment to the treatment for subjects, and communicate with the subjects as soon as possible if necessary.

(7) When receiving a notice from the sponsor or the EC that needs to suspend or terminate the medical device clinical trial, the PIs should inform the subjects timely and ensure that the subjects are properly treated and followed up.

(8) The PIs should ensure that the medical device clinical trial follows the latest version of clinical trial protocol approved by the EC; and ensure that the medical device clinical trial is conducted in accordance with the GCP and applicable laws and regulations within the agreed time limit.

(9) The PIs may authorize the investigators that have received clinical trial related trainings to organize the enrollment and informed consent of subjects, screening and follow-up, management and use of the investigational medical device and the control device (if applicable); management and use of biological samples (if applicable); handling of AEs and device defects, and recording of clinical trial data and filling of CRF according to the needs of the medical device clinical trial.

(10) The PIs should inform the EC of the progress of the medical device clinical trial, events affecting the rights and interests as well as the safety of subjects, as well as the deviation from the clinical trial protocol on time.

17.2 Responsibilities of Medical Device Clinical Trial Institutions

(1) Medical device clinical trial institutions should meet the filing requirements, and establish the management organizational structure and management system for clinical trials. Medical device clinical trial institutions should have corresponding clinical trial management department to undertake the management of medical device clinical trials.

(2) The management departments of medical device clinical trial institutions should be responsible for filling in, managing and changing the filing information of medical device clinical trial institutions in the filing management information system of medical device clinical trial institutions, including the information of clinical trial specialties and PIs; online submitting the summary report of medical device clinical trials of the previous year in the filing system; organizing the evaluation on the qualifications of the PIs of the clinical trial and completing the filing before the review of the medical device clinical trial by the EC.

(3) Medical device clinical trial institutions should establish a quality

management system, covering the whole implementation process of medical device clinical trials, including such systems as training and assessment, implementation of clinical trials, management of medical devices, management of biological samples, handling of adverse events and device defects and reporting of safety information, recording, and quality control, so as to ensure that the PIs fulfill their responsibilities related to the clinical trials, guarantee that subjects can receive proper medical treatment and ensure the authenticity of data generated in the trial.

(4) Before accepting a medical device clinical trial, medical device clinical trial institutions should evaluate relevant resources according to the characteristics of the investigational medical device to ensure that appropriate qualifications, personnel, facilities, and conditions are available.

(5) Medical device clinical trial institutions and investigators should cooperate with the monitoring and audit organized by the sponsor and the inspection conducted by medical products regulatory authorities or health administrations.

(6) Medical device clinical trial institutions should properly keep the clinical trial records and essential documents according to applicable laws and regulations and the contract with the sponsor.

(7) Where the sponsor seriously or continuously violates the GCP and applicable laws and regulations, or requires changes in trial data and conclusion, medical device clinical trial institutions and investigators should report in writing to the medical products regulatory authority of the province, autonomous region or municipality directly under the central government where the sponsor is located.

17.3 Responsibilities of Sponsor

(1) The sponsor should be responsible for the authenticity and compliance of the medical device clinical trial.

(2) The sponsor should have its quality management system cover the whole process of medical device clinical trials, including the selection of medical device clinical trial institutions and PIs, design of clinical trial protocol, and the implementation, recording, result reporting and document archiving of medical device clinical trials. Its quality management measures should accommodate to the risks of the clinical trial.

(3) Before initiating a medical device clinical trial, the sponsor should ensure that the product design has been finalized, the pre-clinical study of the test medical devices has been completed and its results should be able to support the medical device clinical trial.

(4) Before initiating a medical device clinical trial, the sponsor should, according

to the characteristics of the investigational medical device, select medical device clinical trial institutions, specialties and PIs that have completed the filing.

(5) In a multicenter clinical trial, the sponsor should be responsible for selecting and determining the coordinating investigator for the medical device clinical trial, and the medical institution where the coordinating investigator works is the leading site. The coordinating investigator undertakes the coordination of various sites in the multicenter clinical trial, and ensure communication among PIs in various sites.

(6) Before initiating a medical device clinical trial, the sponsor should be responsible for organizing the formulation of the investigator's brochure (IB), clinical trial protocol, ICF, CRF, SOPs and other relevant documents, and provide them to medical device clinical trial institutions and PIs.

(7) The sponsor should sign a contract with medical device clinical trial institutions and the PIs to specify their respective rights and obligations in the medical device clinical trial.

(8) The sponsor should file the clinical trial at the medical products regulatory authority of the province, autonomous region and municipality directly under the central government where it is located after the medical device clinical trial has been approved in EC review and the contract with medical device clinical trial institutions has been signed. After a medical device clinical trial has been filed, the medical device clinical trial institution can start the informed consent and screening of the first subject.

(9) Before the start of the medical device clinical trial, the sponsor should be responsible for organizing trainings related to the medical device clinical trial, such as trainings on the rationale, indications for use, product performance, operation methods, installation requirements and technical indicators of the investigational medical device, and the clinical trial protocol and SOPs as well as other relevant documents.

(10) The sponsor should provide the investigational medical device free of charge, and should meet the requirements of Article 42 of the GCP.

(11) The sponsor should pay the expenses related to the medical device clinical trial for subjects.

(12) The sponsor should be responsible for the evaluation and reporting of the safety information during the medical device clinical trial.

(13) The sponsor should assume the responsibility for the monitoring of the medical device clinical trial, establish SOPs for monitoring and choose qualified CRAs to perform the monitoring duties.

(14) The sponsor should ensure that the medical device clinical trial is

implemented in strict accordance with the clinical trial protocol. The sponsor should promptly point out and rectify the noncompliance of medical device clinical trial institutions and investigators with the clinical trial protocol, the GCP and relevant laws and regulations; where the situation is serious or continued, the sponsor should terminate the participation of such clinical trial institutions and investigators in the clinical trial and report it to the medical products regulatory authorities of the provinces, autonomous regions or municipalities directly under the central government where such clinical trial institutions are located.

(15) The sponsor should report to all the PIs, management departments of medical device clinical trial institutions and the ECs within 10 working days upon the suspension, termination or completion of the medical device clinical trial. The sponsor should report to the medical products regulatory authority of the province, autonomous region or municipality directly under the central government where it is located within 10 working days upon the termination or completion of the medical device clinical trial.

18. Other Contents to Be Addressed

None.

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Investigator's Statement

I hereby agree that:

1. I will carry out this clinical trial in strict compliance with the Declaration of Helsinki, current regulations of China and the requirements of this trial protocol.
2. I will accurately record all data required in the CRF to complete the clinical trial report.
3. I will make sure that the investigational medical device will be used only for the purpose of this clinical trial; and will completely and accurately record the receipt and use of the investigational medical device, with such records retained throughout the clinical trial.
4. I will allow the CRA and auditors authorized or designated by the sponsor as well as regulatory authorities to conduct monitoring, audit and inspection on the clinical trial.
5. I will strictly implement the terms in the clinical trial contract/agreement signed among parties.

I have already read the clinical trial protocol entirely, including the above statement and I fully agree with all the above contents. Principal Investigator

Principal Investigator Signature: <signed> July 08, 2022

Medical Device Clinical Trial Institution Seal <stamped> July 11, 2022

Sponsor Seal <stamped> July 5, 2022

Appendix 1 List of Study Sites and Principal Investigators

Site name	Principal Investigator	Professional title
Peking University First Hospital	Li Jianping	Chief Physician
Peking University Third Hospital	Tang Yida/Wang Guisong	Chief Physician
Chest Hospital of Tianjin City	Cong Hongliang/Li Ximing	Chief Physician
Tianjin Fourth Center Hospital	Wen Shangyu	Chief Physician
Xuzhou Cancer Hospital	Zhang Yaojun	Chief Physician
The First People's Hospital of Lianyungang	Yin Delu	Chief Physician
Wuxi People's Hospital	Wang Qiang	Chief Physician
Kaifeng Central Hospital	Qin Lei	Chief Physician

Appendix 2 List of Contact Information for AE and Device Defect Reporting

Site name	Contact	Tel.	E-mail address
Peking University First Hospital	Yu Ronghui	010-66119025	bdyyec@163.com
Peking University Third Hospital	Hong Xue	010-82265571	bysygcp@163.com
Chest Hospital of Tianjin City	Pang Ruonan	022-88185557	xkyydb@126.com
Tianjin Fourth Center Hospital	Liu Haiyang	022-26181877	tjsszxjg@163.com
Xuzhou Cancer Hospital	Cao Shengya	0516-85537719	XZZLLL@126.com
The First People's Hospital of Lianyungang	Yang Jian	0518-85767557	irb_lygyyy@163.com
Wuxi People's Hospital	Duan Ru	0510-85351101	wuxillwyh@163.com
Kaifeng Central Hospital	Qiu Yang	0371-25672861	kflcsyllwyh@126.com

Note: Any increase or decrease of the site during the course of the trial will be documented separately as a separate document without amendment to the protocol.

Appendix 3 Definition of Composite Endpoint

Patient-oriented composite endpoint (PoCE)	• All-cause death; • All myocardial infarction; • All revascularisation events, including target lesion revascularisation (TLR), target vessel revascularisation (TVR), and target vessel non-target lesion revascularisation.
Target lesion failure (TLF)	• Cardiac death (the death with uncertain cause is also considered cardiac death); • Target vessel myocardial infarction (TV-MI); • Clinically indicated target lesion revascularisation (CI-TLR).

Appendix 4 Definition of Death

Type of death	Definition
Cardiac death	Refers to death due to cardiovascular causes, as detailed in the table below:
	1. Death due to acute myocardial infarction
	2. Death due to cardiac arrest, including deaths of unknown cause
	3. Death due to heart failure
	4. Death due to stroke
	5. Death due to cardiovascular procedure
	6. Death due to hemorrhage of cardiovascular system
	7. Death due to other cardiovascular diseases

Type of death	Definition
Non-cardiac death	Refers to death due to non-cardiovascular causes, as detailed in the table below:
	1. Death due to malignancies
	2. Death due to pulmonary causes
	3. Death due to infection (including septicemia)
	4. Death due to digestive system
	5. Death due to accident/trauma
	6. Death due to organ failure other than the cardiovascular system
	7. Death due to other non-cardiovascular causes
Death unexplained	Death with undetermined cause or classification due to lack of relevant data will be considered cardiac death.

Appendix 5 Myocardial Infarction (MI) (UD 2018) [21]

Type 1 MI: thrombosis due to plaque disruption (rupture or erosion)

Detection of a rise and/or fall of cTn values with at least one value above the 99th percentile upper reference limit (URL), and clinical evidence of acute myocardial ischemia, requiring at least one of the following:

- Symptoms of acute myocardial ischaemia;
- New ischemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology;
- Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy [a]

Note [a]: Post-mortem demonstration of an atherothrombus in the artery supplying the infarcted myocardium, or a macroscopically large circumscribed area of necrosis with or without intramyocardial haemorrhage, meets the type 1 MI criteria regardless of cTn values.

Type 2 MI: MI secondary to ischemia or mismatch between oxygen supply and demand

Detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL, and evidence of an imbalance between myocardial oxygen supply and demand unrelated to coronary thrombosis, requiring at least one of the following:

- Symptoms of acute myocardial ischaemia;
- New ischemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology;

Type 3 MI: MI that causes death and unable to provide the cardiac biomarker value

Patients who suffer cardiac death, with symptoms suggestive of myocardial ischaemia accompanied by presumed new ischaemic ECG changes or ventricular fibrillation, but die before blood samples for biomarkers can be obtained, or before increases in cardiac biomarkers can be identified, or MI is detected by autopsy examination.

Type 4a MI: PCI-related MI ≤ 48 h after the index procedure

An elevation of cTn values > 5 times the 99th percentile URL in patients with normal baseline values; in patients with elevated pre-procedure cTn in whom the cTn level are stable (≤ 20% variation) or falling, the post-PCI cTn must rise by > 20%. However, the absolute post-procedural value must still be at least 5 times the 99th percentile URL. In addition, one of the following elements is required:

- New ischemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology;
- Angiographic findings consistent with a procedural flow-limiting complication such as coronary

dissection, occlusion of a major artery or a side branch occlusion/thrombus, or distal embolization.
Type 4b MI: In-stent thrombosis-related MI A subcategory of PCl-related Ml is in-stent thrombosis, using the same criteria utilized for type 1 MI, and what is special about this type of MI is that it occurs after stent implantation. It is important to indicate the time of the occurrence of the stent thrombosis in relation to the timing of the PCI procedure. The following temporal categories are suggested: acute, 0-24 h; subacute, > 24 h to 30 days; late, > 30 days to 1 year; and very late > 1 year after stent implantation.
Type 4c MI: restenosis-related MI During angiography in some patients with suspected MI, it is found that ISR or balloon dilation-related restenosis is the only possible explanation for the occurrence of MI. This PCI-related MI type is designated as type 4c MI, associated with a rise and/or fall of cTn values with at least one value above the 99th percentile URL.
Type 5 MI: CABG-related MI ≤ 48 hours after the index procedure An elevation of cTn values > 10 times the 99th percentile URL in patients with normal baseline values; in patients with elevated pre-procedure cTn in whom the cTn level are stable (≤ 20% variation) or falling, the post-CABG cTn must rise by > 20%. However, the absolute post-procedural value must still be > 10 times the 99th percentile URL. In addition, one of the following elements is required: ● Development of pathological Q waves; ● Angiographic documented new graft occlusion or new native coronary artery occlusion; ● Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology;

Appendix 6 Definition of Revascularisation

Type	Definition
Target lesion	Refers to the vascular segments within the lesion to be intervened, and within 5 mm in front and behind the lesion
Target lesion revascularisation (TLR)	PCI or CABG performed again at the lesion in order to treat target lesion restenosis or other complications
Target vessel	The main coronary artery in which the target lesion is located, containing its branches
Target vessel revascularisation (TVR)	Any, repeated PCI or CABG for any segment of target vessels (including target lesions)
Target vessel non-target lesion revascularisation	PCI or CABG intervention required again for target vessel non-target lesion (due to previous non-treatment, progression of stenosis, or other reasons, and this lesion is unrelated to the target lesion).
Non-target lesion revascularisation (Non-TLR)	Revascularisation performed on lesions other than target lesions on target vessels
Non-target vessel revascularisation (Non-TVR)	Revascularisation performed on non-target vessel lesions
Clinically and physiologically indicated revascularisation (CPI-Resvasc)	Revascularisation is considered a clinical indication if related to any of the following: • Unplanned emergency revascularisation with positive troponin • Positive assessment of invasive functional ischemia (e.g., FFR, iFR, Doppler flow velocity reserve) • Positive assessment of ischemia based on angiography (QFR) • Angiographic percent diameter stenosis ≥ 50%, and

	positive assessment of non-invasive ischemia (e.g., dobutamine stress test, radionuclide myocardial imaging, exercise test, FFR-CT) • Angiographic percent diameter stenosis ≥ 90%