Study Title	**Assessment of *Cu*tting-Balloon Angioplasty with Novel Bioabsorbable *P*olymer-Coated, Everolimus-Eluting Stent in the Treatment of Calcified Coronary Lesions Guided by *I*ntravascular Ultrasoun*d*: Study Design and Protocol**
Study Title (Short Description)	**CUPID trial**
Principle Investigator	**Jon Suh, MD., PhD.**
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Participant Description Document

Research Title: Assessment of Cutting-Balloon Angioplasty with Novel Bioabsorbable Polymer-Coated, Everolimus-Eluting Stent in the Treatment of Calcified Coronary Lesions Guided by Intravascular Ultrasound (CUPID trial)

Research Institution and Principal Investigator: Soonchunhyang University Bucheon Hospital / Jon Suh

Before deciding whether to participate in this study, please read the following information carefully, listen to the explanation, and make sure you fully understand and accept the content of this study before making your decision based on your own will. This document provides important information related to the study (research purpose, methods, risks and discomfort factors, precautions, possible alternative procedures, and the right to withdraw from the study at any time), and the research staff will explain the study to you. You may ask any questions while reading this document or while listening to the explanation. Participation in the study is entirely voluntary and based on your decision. If you decide to participate, you must sign this form for voluntary participation, and you will receive a copy of the signed consent form. Those who agree to participate and do so will be referred to as study subjects, and this term will be used throughout this document and consent form. If you refuse to participate or decide to withdraw later, you will not suffer any disadvantages in your relationship with our medical staff or hospital and will still receive the best treatment. If you wish to withdraw from the study, please contact the principal investigator or research staff.

This study is supported by Boston Scientific.

1. Purpose and Background of the Study

Severe calcified lesions do not respond well to traditional balloon angioplasty, and if a stent is inserted into a lesion where calcification is not fully alleviated, the stent may expand incompletely and asymmetrically. Inadequate relief of calcification and atherosclerotic plaques can not only lead to poor clinical outcomes but also increase the number of balloons used, the amount of contrast agent, and the duration of the procedure, which negatively affects the success of stent implantation. Moreover, procedural factors such as the amount of contrast agent and procedure time are known to be associated with negative clinical outcomes and in-hospital complication rates.

Currently, various devices such as cutting balloons, scoring balloons, and rotational atherectomy devices are used to alleviate calcified lesions. The principle of the cutting balloon involves four micro blades around the balloon which create incisions in the plaque as the

balloon inflates, and the shear force applied by subsequent balloon inflation propagates these cracks, thereby expanding the vessel. However, clinical evidence for the expansion of calcified lesions of varying degrees with the use of cutting balloons remains limited. Despite the advantages of cutting balloons in the treatment of calcified lesions, there are not many studies focused on procedural and operator-centric outcomes, such as the number of balloons used, procedure time, and total amount of contrast agent used.

On the other hand, bioresorbable polymer-coated coronary artery stents have been proven to be safe and effective in the treatment of coronary artery diseases, including calcified lesions. Therefore, this study aims to analyze and compare the safety and efficacy of vessel expansion using the new cutting balloon (Wolverine™, Boston Scientific, Natick, MA, USA) against conventional non-compliant balloons during the insertion of a bioresorbable polymer-coated everolimus-eluting coronary artery stent (Synergy™, Boston Scientific Corporation, Marlborough, MA, USA) in patients with calcified lesions of varying degrees from mild to severe, using intravascular ultrasound.

2. Research Procedures

This research is available to individuals like you who have been diagnosed with coronary artery stenosis, suspected due to severe calcification, following a coronary angiography performed because of typical chest pain or myocardial ischemia. If you listen to the explanation about this research and agree to participate, you will sign a consent form, and the following procedures will occur:

To assess your coronary artery condition, the following coronary examination will be conducted. This examination is frequently performed in clinical settings to assess the coronary arteries regardless of this study. Before the examination, local anesthesia will be applied to your wrist or groin while you are conscious. A small catheter will be inserted through a puncture or incision at the anesthetized area of the arm or leg, which allows access to the diseased coronary artery to administer a contrast agent to confirm the presence of calcific coronary artery stenosis and determine if a coronary intervention (drug-eluting stent insertion) is needed.

If a coronary intervention is deemed necessary, intravascular ultrasound (IVUS) will be performed to assess the degree of calcification and the cross-sectional area of the vessel lumen. Prior to stent insertion, one of the following two methods will be applied for vessel expansion. The choice between the two methods will be randomly assigned (like flipping a coin, with a 1:1 ratio). Random assignment will only proceed if you agree to participate in the study.

- Vessel expansion of calcified lesions using the Wolverine cutting balloon

After the coronary angiography, intravascular ultrasound will be used to assess the degree

of calcification, lesion length, and reference diameter in real-time, determining the size of the stent to be inserted. Before stent insertion, a balloon expansion using the Wolverine cutting balloon is performed to minimize residual stenosis after stent insertion. After the final procedure, IVUS is repeated to verify the stent's cross-sectional area. If there are areas smaller than the reference vessel's cross-section distally or insufficiently expanded, additional high-pressure balloon expansion is performed to minimize residual stenosis.

- Vessel expansion of calcified lesions using a non-compliant balloon

  Similar steps are followed as with the cutting balloon but using a high-pressure balloon expansion with a non-compliant balloon to minimize residual stenosis after stent insertion.

After the procedure, medical staff will closely observe you, and you may need to remain lying down for 4-6 hours to prevent bleeding from the puncture site in your arm or leg. Blood tests and electrocardiogram (ECG) will be conducted, and you will receive various drug treatments to prevent blood clotting in the treated vessel. Depending on your condition, you may need to be admitted for one to two days. The use of intravascular ultrasound will be funded by the research budget, and since all procedures are performed according to general coronary stent procedures, no additional costs are expected.

The following research procedures will be carried out after stent implantation:

You will be followed up regularly over a year according to a set schedule through outpatient visits or phone calls. The first visit will occur one month after discharge, the second visit at six months, and the third visit at one year. This schedule is a typical outpatient treatment plan for patients diagnosed with coronary artery disease, but if it's difficult for you to visit according to the schedule, the research team will contact you by phone to check on you.

The purpose of follow-up through outpatient visits or phone calls is to check on your health status, including whether there has been a need for re-intervention or re-admission after coronary angiography or intervention, control status of underlying diseases, and to check if new issues have arisen.

Below are the tests and procedures you will undergo at each time point:

- Registration ~ Discharge: Medical history, medication review, symptom check, electrocardiogram, blood tests (complete blood count, kidney function, lipid profile, myocardial enzyme levels), vascular imaging
- 1 Month: Review of medical history, symptom check, review of medication, blood tests as needed (complete blood count, kidney function, lipid profile, etc.)

- 6 Months: Review of medical history, symptom check, review of medication, blood tests as needed (complete blood count, kidney function, lipid profile, etc.)
- 1 Year: Review of medical history, review of medication, blood tests as needed (complete blood count, kidney function, lipid profile, etc.)

The above-described tests will be performed only if necessary for standard care and are not additional tests conducted for research purposes.

3. Compliance Requirements for Research Participants

As a research participant, you must adhere to the following:

1) Follow the instructions of the principal investigator and research staff.
2) Keep the appointments related to the research outpatient visits. If you need to change an outpatient visit schedule, please call the research staff to reschedule.
3) Take medications as directed.
4) If you wish to withdraw from the research, please inform the principal investigator or research staff.
5) During participation in this clinical study, you must not participate in other clinical studies without the permission of the research team. This is to protect you from excessive blood draws, X-ray examinations, and drug interactions.
6) If you visit other medical institutions for treatment or consultation, please inform the research team.

4. Expected Risks and Discomforts Due to Participation in the Research

The Wolverine cutting balloon has been proven to have improved lesion passability, resulting in a higher stent delivery success rate compared to conventional cutting balloons. Therefore, the expected risks and inconveniences due to participation in the study are not anticipated to be different from the usual treatment of other patients with calcified coronary lesions who do not participate in the study. However, the procedure may take about 15 minutes longer than usual due to performing intravascular ultrasound before and after stent insertion.

The known risks associated with coronary interventions (stent treatments) include, but are not limited to:

- Myocardial infarction
- Infection/pain at the puncture site
- Allergic reactions to contrast agents or medications
- Bleeding
- Hypotension
- Delayed or unstable angina

- Myocardial ischemia
- Aneurysm or pseudoaneurysm
- Nausea/vomiting
- Cardiac arrhythmia
- Embolism
- Cardiac tamponade
- Pain
- Death
- Failure to deliver the stent to the insertion site
- Fever
- Thrombosis (acute, subacute, late)
- Vasospasm
- Vascular infection
- Adverse reactions to antithrombotic/anticoagulant medications
- Renal failure (due to contrast agent)
- Peripheral or stent thrombosis
- Restenosis of the vessel
- Emergency coronary artery bypass surgery
- Stent dislodgment or compression
- Vascular damage: dissection, perforation, acute rupture, fistula
- Stroke

5. Expected Duration of Participation and Total Number of Study Participants

This study involves 5 institutions within Korea, including Soonchunhyang University Bucheon Hospital, and aims to enroll a total of 250 participants nationwide. If you decide to participate, your expected research participation period will be a total of one year, including the time after discharge and the outpatient visit period.

6. Compensation/Treatment for Injuries Related to the Study

The risk of injury from participating in this study is no different from that of patients who do not participate. However, if an unexpected adverse reaction or emergency situation occurs during the research, the best possible treatment will be provided based on the individual situation. If a serious adverse reaction occurs, prompt and appropriate action will be taken to minimize any consequences, which will be immediately reported to the principal investigator and dealt with accordingly. If an adverse reaction is determined to be a direct result of the research procedure, compensation will be provided according to victim compensation regulations. However, compensation will not be provided for adverse reactions resulting from non-adherence to this protocol by the research physician or yourself.

7. Additional Costs and Financial Compensation Anticipated from Participation in the

Study

All procedures and tests conducted in this study are performed according to the standard treatment guidelines, regardless of participation in this trial, and the costs will be covered by you according to insurance standards. However, the Wolverine cutting balloon needed for stent insertion will be supported by the study for participants assigned to Wolverine.

8. Expected Benefits

The information used in this study (test results, treatment details, subsequent prognosis, etc.) will enhance the understanding of interventional treatment for cardiovascular diseases and contribute to medical advancements both domestically and internationally.

9. Types of Alternative Treatment Options and Their Potential Risks and Benefits

If you choose not to participate in this study, other standard treatments for calcified coronary artery stenosis that causes chest pain or myocardial ischemia include rotational atherectomy, high-pressure balloon angioplasty using non-compliant balloons, and coronary artery bypass graft surgery. The cost and insurance standards for Wolverine cutting balloons are similar to those for general non-compliant balloons, and the likelihood of complications is also similar. If you wish to receive a specific treatment and not follow the random assignment result for any reason, you cannot participate in this study, and your attending physician will review other treatment options with you.

10. Voluntary Participation and Right to Refuse

The decision to participate in this study is entirely up to you. You can decide freely to participate or withdraw from all aspects of the study. You may cancel your participation at any time after joining. If you refuse to participate or decide to withdraw, you will not suffer any disadvantage in your relationship with our medical staff or hospital and will still receive the best treatment. If you wish to participate after reading this explanatory document, the study will proceed with those who voluntarily sign the consent. If important reasons arise to stop participating in the study or to withdraw, please contact the principal investigator or research staff. If you decide to discontinue participation during the study, the research team will discuss options for follow-up investigation with you. This will be conducted through a separate form, and you will be able to choose one of several options for how your information will be handled and whether to maintain further contact from the point of discontinuation.

Moreover, the researchers can withdraw your participation without your consent in the following cases:

- If you do not follow the instructions from the research staff
- If the researcher determines that continuing participation could harm you
- In the case of pregnancy (for women)
- If you require treatment not permitted in the study
- If the study is canceled
- In other unforeseen circumstances

11. Confidentiality of Data and Personal Information Collected in Relation to the Study

By agreeing to participate in this study and signing this consent form, you permit the following:

Your medical information such as age, gender, weight, medical history, surgical history, medication history, and various other types of information related to the study, including test results, will be recorded and stored in a specific format (paper or computer).

The personal information collected for this study includes:

- Your date of birth, age, gender, contact information.

Your sensitive information collected for this study includes:

- Height, weight
- Health-related information, including medical records and data generated during routine medical care by your doctor
- Health-related information including past medical records, medical history, and disease information
- Information related to tests such as blood tests, electrocardiograms, angiography.

The collected information will be handled and used for the following purposes:

- To conduct the research
- To verify the accuracy of the research
- To ensure that the research is conducted in the best manner according to the relevant laws and regulations
- To obtain approval from regulatory authorities when a product resulting from this research is introduced to the market.

In some countries, as per relevant laws and regulations, the research data might be disclosed to researchers not involved with this study upon request by regulatory authorities. However, all personally identifiable information will be removed before disclosure. The following departments may handle your information:

- Research team (including direct researchers and those assisting them)
- The Institutional Review Board (IRB) that approved the research
- Relevant regulatory authorities responsible for managing and monitoring studies
- Individuals or entities involved in research-related work by contract with the principal investigator
    - Companies that create and manage computer systems for handling data collected from the research
    - Quality control personnel or companies that ensure the research is conducted properly.

The period during which your information will be retained and used is up to 3 years after the publication of the research results, which includes all periods necessary for participant recruitment, follow-up observation, and document retention required by law. This information will be shared among the research team and will be managed to prevent others from viewing it by using locks or passwords, and records that can identify individuals will be protected in confidence. The research team will take all reasonable measures to protect your personal information. Records that can identify you will be kept strictly confidential, and health information will be processed anonymously so that it cannot be known from the data who or where you are. Also, your personal information will remain confidential even when the results are published.

The outline of this study is registered on www.clinicaltrials.gov and can be accessed at any time. No personal information of study participants will be disclosed in any papers or presentations published on www.clinicaltrials.gov or elsewhere.

12. New Information That May Affect Your Willingness to Continue Participation

If new scientific data or information related to safety that may affect your willingness to continue participation in the study is collected, the research team will inform you or your representative.

13. Inquiries

This consent form uses some technical terms. If there is anything you do not understand or have questions about, please ask the research team. After thoroughly reviewing this study and the consent form, please decide whether to participate. A copy of this consent form will be kept by both the research team and you. If you have any inquiries related to the study, please contact the principal investigator or the person in charge.

- Principal Investigator's affiliation, position/name/contact: Cardiology/Professor Jon Suh/ 032-621-6825
- 24-hour contact: Research staff/Eun Bin Park/ 010-9180-7781

  170 Jomaru-ro, Bucheon-si, Gyeonggi-do

If you have questions about the welfare and rights as a study participant during the study, or if you wish to consult with someone not directly related to the study, please contact the following number:

- Institutional Review Board (IRB) of Soonchunhyang University Bucheon Hospital 032-624-6363