Protocol No.: SNSC202101

Study on Effectiveness and Safety of Ghunter Revascularization Device for Endovascular Treatment of Acute Ischemic Stroke

(A Prospective, Multicenter, Randomized Controlled, Non-inferiority Study)

Clinical Trial Protocol of Medical Devices

(NCT04973332)

Name of investigational medical device:	**Ghunter Revascularization Device**
Models/Specifications:	**See the text**
Management category of investigational medical device:	**Class III medical device**
Class III medical device requiring clinical trial approval:	**Yes ☐ No ☑**
Similar product in China:	**Yes ☑ No ☐**
Home-made similar product in China:	**Yes ☑ No ☐**
Protocol version No. and date:	**V3.0/February 9, 2022**
Study site:	**General Hospital of Eastern Theater Command, PLA**
Principal investigator (coordinating investigator):	**Professor Liu Xinfeng <signed>**
Sponsor:	**Sinomed Neurovita Technology Inc.**
Statistical analysis:	**Medical Statistics Office of Peking University First Hospital** **Professor Yao Chen**
Contract research organization:	**JetMed (Beijing) Co., Ltd.**

Statement of Confidentiality

All information contained in this protocol is the proprietary information of Sinomed Neurovita Technology Inc. and is only available for review by the investigator, the coordinating investigator, Ethics Committee, supervisory and regulatory authorities and other relevant medical institutions. Without the written approval of the sponsor, any information cannot be disclosed to the third parities not associated with the study unless this disclosure is made to make the subjects who may participate in the study sign the informed consent form (ICF).

<For the seal, refer to the source document>

Table of Contents

Protocol Abstract **5**
1. Sponsor Information **9**
1.1. Name of Sponsor 9
1.2. Address of Sponsor 9
1.3. Contact Information of Sponsor 9
1.4. Relevant Qualification Documents of Sponsor 9
1.5. Name, Address, Contact Information and Relevant Qualification Documents of Agent 9
2. List of Study Sites and Investigators **9**
3. Purpose and Content of Clinical Trial **9**
3.1. Purpose 9
3.2. Contents 10
4. Background of Clinical Trial **10**
5. Characteristics, Device Composition, Working Principle, Mechanism of Action and Study Scope of the Product **13**
5.1. Product Characteristics 13
5.2. Device Composition, Operation Principle and Mechanism of Action 13
5.2.1. Device Composition *14*
5.2.2. Working Principle and Mechanism of Action *14*
5.3. Study Scope 14
6. Overall Design **15**
6.1. Study Design 15
6.1.1. Study Objective *15*
6.1.2. Selection of Study Method and Justification *15*
6.1.3. Measures to Reduce and Avoid Bias *15*
6.1.4. Investigational Medical Device and Control Device/Control Diagnostic and Therapeutic Method *16*
6.1.5. Subject Enrollment *17*
6.1.6. Effectiveness Evaluation Methods *20*
6.1.7. Safety Evaluation Methods *22*
6.2. Study Process 23
6.2.1. Study Process *23*
6.2.2. Device Specifications (recommend the operation method, and the operator may make slight modification according to the actual situations) *29*
6.3. Monitoring Plan 34
7. Statistical Analysis Method and Evaluation Method **34**
7.1. Statistical Design, Method and Analysis Procedure 34
7.1.1. Statistical Design (Hypothesis Testing) *34*
7.1.2. Statistical Analysis Methods *35*

7.2. Calculation of Sample Size....36
7.2.1. Total Sample Size....36
7.2.2. Number of Subjects for Each Disease and Rationale for Determination....37
7.2.3. Minimum and Maximum Number of Subjects in Each Site and Justification....37
8. Significance Level and Power of Clinical Study....37
8.1. Expected Drop-out Rate....37
8.2. Pass/Fail Criteria for Clinical Trial Results....38
8.3. Criteria for Termination of Trial Based on Statistics and Justification....38
8.4. Data Statistical Method, with the Handling Method of Missing, Unused and Wrong Data (Including Discontinuation and Withdrawal) and Unreasonable Data....38
8.5. Procedures for Reporting Deviation from Original Statistical Plan...38
8.6. Selection Criteria for Subjects Included in the Analysis and Justification....38
8.7. Exclusion of Special Data During Hypothesis Test and Justification (if applicable)....39
9. Data Management....39
9.1. Data Collection....39
9.2. Data Verification and Modification....39
9.3. External Data Management....40
9.4. Database Locking....40
10. Feasibility Analysis....40
10.1. Possibility Analysis on Success....40
10.2. Possibility Analysis on Failure....41
11. Quality Control of Clinical Trial....41
11.1. Monitoring of Clinical Trial....41
11.2. Filling of Case Report Form....42
11.3. Retention of Raw Data....42
12. Ethical Issues and Informed Consent in Clinical Trial....42
12.1. Ethical Considerations....42
12.2. Approval of Trial Protocol....42
12.3. Informed Consent Process and Contents of Informed Consent Form42
13. Provisions for AE and Device Defect Reporting....43
13.1. AE....43
13.1.1. Definition of AE....43
13.1.2. Determination of AE Severity....43
13.1.3. Recording of AE....43
13.2. Device Defect....43
13.3. SAE....44

13.4. Reporting Procedures and Contact Information 44
14. Deviation from Clinical Trial Protocol and Regulations for Protocol Amendment 45
15. Direct Access to the Source Data and Documents 46
16. Finance and Insurance 46
17. Contents to be Covered in Clinical Trial Report 46
18. Confidentiality Principle 47
19. Agreement on Publication of Trial Results 47
20. Responsibilities Assumed by All Parties 48
20.1. Responsibilities of the Sponsor: 48
20.2. Responsibilities of Study Site and Investigator: 48
References 50
Investigator's Statement 51
Appendix 1 List of Study Sites and Investigators 52
Appendix 2 ASPECTS Scale 53
Appendix 3 mTICI Image Grading Criteria: 54
Appendix 4 mRS: 55
Appendix 5 NIHSS: 56

Protocol Abstract

Protocol title	Study on Effectiveness and Safety of Ghunter Revascularization Device for Endovascular Treatment of Acute Ischemic Stroke (A Prospective, Multicenter, Randomized Controlled, Non-inferiority Study)
Protocol version No. and date	V3.0/February 9, 2022
Sponsor	Sinomed Neurovita Technology Inc.
Device name	Ghunter Revascularization Device
Device classification	Class III medical device
Study objective	To verify the effectiveness and safety of Ghunter Revascularization Device for endovascular treatment of acute ischemic stroke
Sample size	220 subjects
Number of study sites	No less than 10 sites, competitive enrollment
Indications for use	Ghunter Revascularization Device is indicated for use in ischemic stroke patients whose symptom onset are within 24 h.
Control setting	Test group: Sinomed Neurovita Ghunter Revascularization Device Control group: Solitaire FR
General inclusion criteria	1) ≥ 18 years old; 2) NIHSS ≥ 6 at randomization; 3) Pre-onset mRS < 2; 4) Acute ischemic stroke was diagnosed; 5) Within 24h from the stroke onset to the completion of femoral artery puncture (regardless of whether intravenous thrombolysis has been performed); the time point of stroke onset is defined as the time point at which the patient is last known to be normal; 6) The subject (or his/her guardian) agrees to participate in this study and signs the informed consent form (ICF).
Angiographic inclusion criteria	1) Cerebral CT or MR should be performed when the time from the stroke onset to the completion of femoral artery puncture of a patient is ≤ 6h; 2) Cerebral CT or MR should be performed when the time from the stroke onset to the completion of femoral artery puncture of a patient is 6 (exclusive)-24h (inclusive), and his/her ASPECTS score should be ≥ 6. (If immediate CT perfusion imaging or MR perfusion imaging is feasible, it is recommended to perform CTP or MRP simultaneously to assist in the assessment of the infarct core, and his/her ASPECTS score should also be ≥ 6); 3) DSA angiography shows acute occlusion of large intracranial arteries, including intracranial internal carotid artery (C4-C7), middle cerebral artery (M1/M2), basilar artery and intracranial vertebral artery (V4).
General exclusion criteria	1) Those who could undergo neither MRI nor CT; 2) Those with hemorrhagic stroke or major ischemic stroke within 6 months before enrollment; 3) Those with severe persistent hypertension that could not be controlled by intravenous injection for blood pressure reduction, i.e. patients with sustained SBP > 185 mmHg or sustained DBP > 110 mmHg; 4) Those with presumed septic emboli or suspected bacterial endocarditis; 5) Renal failure, defined as creatinine > 3.0 mg/dL (264 μmol/L); 6) Those with blood glucose < 2.78 mmol/L (50 mg/dL) or > 22.20 mmol/L (400 mg/dL);

	7) Decreased platelet count (< 40 × 10^9/L); 8) Those with known hemorrhage tendency, coagulation factor deficiency, are taking anticoagulants and with INR > 3.0; 9) Pregnant or lactating women; 10) Those with known severe allergy to contrast media or known allergy to nickel materials; 11) Those with disorders possessing possibility of affecting neurological assessment (e.g., neurological and psychiatric disorders); 12) Those who are unable to undergo interventional operations due to heart, lung, liver failure or other serious diseases; 13) Participating in clinical trials of other drugs or devices; 14) Life expectancy less than 6 months; 15) Other conditions judged by the investigator to be not suitable for inclusion.
Angiographic exclusion criteria	1) There is evidence of intracranial hemorrhage on CT or MR or known hemorrhage tendency; 2) CT/MR/DSA angiography suggests > 1 vascular occlusion (e.g., simultaneous occlusion of bilateral internal carotid artery vessels, or simultaneous occlusion of intracranial vessels in anterior and posterior circulation, or simultaneous occlusion of intracranial and extracranial internal carotid artery); 3) Those with carotid artery dissection, occlusion of the initial segment of the carotid artery or arteritis; 4) Those whose access vessels are severely tortuous, making the revascularization device difficult to reach the target location.
Primary endpoint	Success rate of instant recanalization
Secondary endpoints	Proportion of subjects with mRS scores of 0-2 on 90d postoperatively, time from femoral artery puncture to recanalization/the end time of operation for subjects whose recanalization failed, proportion of subjects with NIHSS score decrease > 4, and success rate of device operation
Safety endpoints	Incidence of symptomatic intracranial hemorrhage within 24h postoperatively, all-cause mortality within 90d, incidence of SAE, incidence of AE, and incidence of device defects
Clinical examination items	◆ Vital signs: heart rate, blood pressure ◆ Cerebral CT or MR ◆ Blood routine: Red blood cell, hemoglobin, white blood cell count, and platelet count ◆ Blood chemistry: Urea nitrogen (urea), serum creatinine, blood glucose ◆ Coagulation: Prothrombin time, activated partial thromboplastin time and INR ◆ Pregnancy testing (Only for women of childbearing potential who are planning to become pregnant) ◆ Cerebral vascular DSA
Expected duration of participation	Screening/baseline period (-1 d ~ 0 d preoperatively), treatment period (day of operation/0d), observation period (24 ± 12 h postoperatively), follow-up period (7 ± 2 d postoperatively (before discharge in case of premature discharge)), and follow-up period (90 ± 14 d postoperatively). The expected duration of participation of each subject is about 90 days.
Statistical analysis	Medical Statistics Office of Peking University First Hospital Professor Yao Chen
Contract research organization	JetMed (Beijing) Co., Ltd.
Expected	About 30 months

duration of trial	

List of Abbreviations

Abbreviation	Terms and Definitions
AE	Adverse event
SAE	Serious adverse event
FAS	Full Analysis Set
PPS	Per Protocol Set
SS	Safety Analysis Set
eCRF	Electronic Case Report Form
AIS	Acute ischemic stroke
rt-PA	Recombinant tissue plasminogen activator
sICH	Symptomatic intracranial hemorrhage
SAH	Subarachnoid hemorrhage
NIHSS	National Institutes of Health Stroke Scale
TIMI	Thrombolysis in Myocardial Infarction
mTICI	Modified Thrombolysis in Cerebral Infarction
mRS	Modified Rankin Scale
ASPECTS	Alberta Stroke Program Early CT Score
INR	International Normalized Ratio
RHV	Rotating Hemostatic Valve

1. Sponsor Information

1.1. Name of Sponsor

Sponsor: Sinomed Neurovita Technology Inc.

1.2. Address of Sponsor

Factory Building 3, Shicheng Sci.&Tech. Park, No.1566 Yinzhong South Road, Wuzhong Economic Development Zone, Suzhou

1.3. Contact Information of Sponsor

Contact person: Xia Ligang

Tel.: 18612448465

E-mail: xialigang@sinomed.com

1.4. Relevant Qualification Documents of Sponsor

Unified social credit code: 91320506MA2288DA27

1.5. Name, Address, Contact Information and Relevant Qualification Documents of Agent

N/A

2. List of Study Sites and Investigators

See Appendix 1 List of Study Sites and Investigators for details.

During the clinical study, if the existing participating sites fail to obtain the approval of the clinical trial administrative department or the Ethics Committee, 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 administrative department and Ethics Committee of all participating sites for filling.

3. Purpose and Content of Clinical Trial

3.1. Purpose

To verify that Ghunter Revascularization Device manufactured by Sinomed Neurovita Technology Inc. (hereinafter referred to as “Sinomed Neurovita”) is not inferior to Solitaire FR in success rate of instant recanalization for endovascular treatment of acute ischemic stroke, and to verify the effectiveness and safety of this product by clinical trial in accordance with the Good Clinical Practice for Medical Devices.

3.2. Contents

The study is a prospective, multicenter, randomized controlled, non-inferiority clinical trial, of which the investigational device is Sinomed Neurovita Ghunter Revascularization Device and the control device is Solitaire FR (hereinafter referred to as the control product under the trade name Solitaire FR) distributed by Covidien Healthcare International Trading (Shanghai) Co., Ltd.; the study is planned to be conducted in more than 10 sites and include 220 subjects. The subjects who meet the inclusion criteria will be randomized into the test group or control group in 1:1. The study is to collect and evaluate whether the success rate of instant recanalization is not inferior to Solitaire FR when Sinomed Neurovita Ghunter Revascularization Device is used for endovascular treatment of acute ischemic stroke, and to evaluate whether there is a statistically significant difference in the proportion of subjects with mRS score of 0 - 2 on 90d postoperatively, the time from femoral artery puncture to recanalization/the end time of operation for subjects whose recanalization failed, the proportion of subjects with NIHSS score decrease > 4, and the success rate of device operation as compared with Solitaire FR when Ghunter Revascularization Device is used for endovascular treatment of acute ischemic stroke. Also, whether there is statistical difference in incidence of symptomatic intracranial hemorrhage within 24h postoperatively, all-cause mortality within 90d, incidence of SAE, incidence of AE, and incidence of device defects between Ghunter Revascularization Device and Solitaire FR for endovascular treatment of acute ischemic stroke will be evaluated.

4. Background of Clinical Trial

Stroke is one of the leading causes of disability and death in humans, and acute ischemic stroke (AIS) accounts for about 80% of all strokes. Recent studies have shown that the 1-month mortality rate of hospitalized acute ischemic stroke patients in China is 2.3%-3.2%; the 3-month mortality rate is 9%-9.6%, and the death/disability rate is 34.5%-37.1%; the 1-year mortality rate is 14.4%-15.4%, and the death/disability rate is 33.4%-33.8% [1]. The key to AIS treatment lies in early recanalization of obstructed vessels and saving the ischemic penumbra. Current treatment modalities mainly focus on intravenous thrombolysis and endovascular treatment, of which endovascular treatment mainly includes arterial thrombolysis, non-stented mechanical thrombectomy, and stented mechanical thrombectomy [2, 3].

At present, the proven effective treatment for early recanalization of AIS is intravenous recombinant tissue plasminogen activator (rt-PA) thrombolysis [4-6]. A pooled analysis of 9 randomized controlled studies of thrombolysis published in 2014 further confirmed the benefit of intravenous rt-PA thrombolysis within 4/5h of ischemic stroke onset, and the earlier the time, the more the benefit [7]. However, because intravenous thrombolysis has strict time window restrictions,

less than 3% of patients can benefit from it, and there is still a huge room for optimization of its therapeutic effect: compared with the control group, the mortality rate at 3-6 months after intravenous thrombolysis is not significantly reduced, still as high as 17.9%, and two-thirds of patients are still left with different degrees of disability, especially for patients with great vascular occlusion or severe disease, and its recanalization rate is low (13%~18%) [8].

Therefore, domestic and foreign scholars have been exploring the AIS endovascular treatment regime for patients with great vascular occlusion. Since September 2014, a series of studies have published more consistent findings: endovascular treatment based on mechanical thrombectomy can bring definite benefits [9-17].

Mechanical thrombectomy devices have gained much attention because of their many theoretical advantages: rapid recanalization, lower hemorrhage conversion rate, and prolonged stroke intervention time windows [15]. Merci Retrieval™ (2004) and Penumbra Stroke Systems™ (2008) were approved by the US Food and Drug Administration (FDA) as the first-generation mechanical thrombectomy devices.

The invention of stent thrombectomy devices represents a great advance for endovascular treatment of stroke, and revascularization devices have the advantage of navigability and rapid recanalization without the risk of long-term complications. The stent thrombectomy device uses a temporary stent to capture the thrombus and to restore flow by moving the thrombus against the intracranial vessel wall; upon stent withdrawal, the thrombus is captured in the stent space and removed with the stent. Solitaire (Medtronic/ev3) and Trevo (Stryker) stent thrombectomy devices were approved by the US FDA in 2012 for treatment of great-vessel occlusive stroke. The Solitaire device versus Merci device for AIS treatment trial (SWIFT) [18] compared the Solitaire and Merci devices (non-stented mechanical revascularization device) and terminated prematurely mid-term due to a significant difference in effectiveness; in the primary endpoint, recanalization was defined as a TIMI grade of 2 or 3. More recanalization with the Solitaire device, more patients with mRS scores $\leq$ 2 after 3 months. The multicenter randomized clinical trial of AIS endovascular treatment (MRCLEAN) [10] was a prospective, multicenter, randomized controlled study and was the first to exhibit a significant benefit of endovascular treatment compared with the standard internal medicine treatment; the results demonstrated a higher rate of 24h recanalization for endovascular treatment group, a smaller median infarct volume at 1 week, and a better 3-month mRS grade. The study, with endovascular mechanical thrombectomy as the primary endovascular treatment for AIS (SWIFT PRIME) [13] was conducted in 39 hospitals in the United States and Europe to compare the effectiveness of intravenous rt-PA thrombolysis with combined endovascular treatment (both using Solitaire), while it was terminated

prematurely as the interim analysis suggested a significant benefit of endovascular treatment; the results demonstrated that patients in the thrombectomy group had a higher proportion in mRS scores of 0-2 on 90d and a tendency to reduce mortality. In the EXTEND-IA [11], a prospective, randomized controlled study to prolong the time from acute neurological deficit to intra-arterial thrombolysis, subjects were randomized into the intravenous r-tPA thrombolysis group and intravenous r-tPA thrombolysis + Solitaire thrombectomy group; the results demonstrated that the early reperfusion rate of ischemic tissue at 24h after Solitaire thrombectomy, the early neurological improvement rate on 3d, and the proportion of patients with mRS scores of 0-2 on 90d in patients with thrombectomy were significantly higher than those in the control group, showing a tendency to reduce mortality. In summary, there is clear evidence to support the use of stent thrombectomy devices for early or ultra-early thrombectomy [2].

DEFUSE-3 [19] was a multicenter, randomized, open-label, blinded evaluation outcome (PROBE) clinical study to determine whether patients with great vascular (ICA or M1) occlusion within 6 - 16 h from the last time being normal could benefit from thrombectomy. The results demonstrated that the 90-d mRS score of mechanical thrombectomy + drug treatment group was significantly better than that of the drug treatment group, and the 90-d mortality was significantly reduced. The incidences of symptomatic intracranial hemorrhage and 24h vascular patency rate were similar to those of the drug treatment group. DEFUSE-3 focused more on mismatch between perfused ischemic area and core infarct. DAWN [20] was a study of thrombectomy taking a treatment time window of 6 - 24 h in patients with sleep stroke and out-of-time window stroke with clinical image mismatch, and its evaluation endpoints were similar to DEFUSE-3. In addition, 90-d mRS, 90-d mortality, 24-h infarct size increased, and symptomatic intracranial hemorrhage were also evaluated. The results demonstrated that the 90-d mRS was significantly improved in the thrombectomy group, and DAWN focused more on the mismatch between the patient's clinical symptoms and infarct size.

In the Chinese Guidelines for the Endovascular Treatment of Acute Ischemic Stroke (2018), mechanical thrombectomy for acute anterior circulation great-vessel occlusive stroke within 6h of onset is classified into Class I recommendation (Level A evidence). According to the results of DEFUSE-3 and DAWN studies, patients with onset at 6 - 16 h and 16 - 24 h met the corresponding inclusion and exclusion criteria and were classified into Class I recommendation (Level A evidence) and Class IIa recommendation (Level B evidence), respectively. According to the 2018 AHA/ASA [4], mechanical thrombectomy is recommended as Class I recommendation (Level A evidence) for acute ischemic stroke patients within 6-16h from the last time being normal and target lesions in

the anterior circulation great vessels if the enrollment meets the DOWM or DEFUSE-3 criteria. Mechanical thrombectomy is recommended as Class IIa recommendation (Level B evidence) in acute ischemic stroke patients within 6-24h from the last time being normal and target lesions in the anterior circulation great vessels if the enrollment meets the DOWM or DEFUSE-3 criteria.

At present, the self-expanding revascularization devices marketed in China include the ReVive SE (Self-Expanding) Thrombectomy Device (Trade Name: ReVive SE, NMPA (I) No. 2014 3773354), Solitaire FR Revascularization Device (Trade Name: Solitaire FR, NMPA (I) 2013 3774122) and Trevo ProVue (Trade Name: TrevoProVue, NMPA (I) 20153773927). Those products are all imported and are expensive. In view of this, on the premise of ensuring the safety and effectiveness, the localization and cost reduction of revascularization devices break the monopoly of foreign products, so that more stroke patients can receive advanced interventional therapy with mechanical thrombectomy, meeting the clinical and patient needs.

As independently developed by Sinomed Neurovita, Ghunter Revascularization Device has passed the test of Tianjin Medical Device Quality Supervision and Testing Center, NMPA (Test Report No.: 2021-GJ-0081). The safety and effectiveness of the product were further verified through animal experiment and therefore the conditions for conducting a clinical trial are met.

5. Characteristics, Device Composition, Working Principle, Mechanism of Action and Study Scope of the Product

5.1. Product Characteristics

The revascularization device is designed with open loop structure. When the diameter of the stent changes with the diameter of the vessel, the stent pattern remains unchanged, only the size of the overlapping region in the circumferential direction changes. This design allows the thrombectomy stent to overlap in the vessel, increases the contact area with the thrombus, and can better capture the thrombus; meanwhile, the stent has the greatest support force at the beginning of deployment, and rapidly reduces the support force at the later stage of deployment, thus reducing the damage to the vascular intima; in addition, when withdrawn, the stent can maintain the screening area and reduce the risk of thrombus shedding during cutting. This design has excellent stent wall apposition, and will not separate from the thrombus when the stent is withdrawn, reducing the risk of thrombus shedding. Meanwhile, several precious metal developing wires are embedded in the stent, so that the outline of the stent can be clearly displayed under DSA device, ensuring the effectiveness and safety of the product in clinical use.

5.2. Device Composition, Operation Principle and Mechanism of

Action

5.2.1. Device Composition

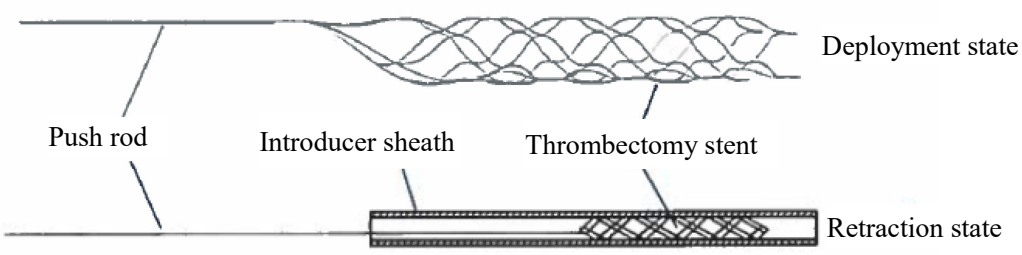
The Ghunter Revascularization Device is composed of a thrombectomy stent, a push rod and an introducer sheath.

The thrombectomy stent is formed by laser engraving of nitinol material, with strong radial support force and excellent flexibility; the stent is connected distal to multiple radiopaque developing devices, so that the placement and deployment of the distal stent can be observed under DSA; multiple radiopaque wires are embedded on the main body of the stent, so that the deployment of the main body of the stent can be observed under DSA; the stent is also connected proximal to a radiopaque device, so that the relative position of the proximal stent and the distal microcatheter can be observed under DSA.

The push rod is fabricated with a specially processed wire to ensure sufficient push force is provided. It is subjected to multi-step mechanical processing and heat treatment while being composited with multiple materials, so that its distal end has good over-bending capacity while providing pushing force, for adapting to the complex intracranial vascular path.

The thrombectomy stent is retracted inside the introducer sheath during storage and transport, and during the operation, the introducer sheath is inserted into the proximal microcatheter, allowing the thrombectomy stent to be easily pushed into the inner lumen of the microcatheter and then into the target vessel.

The structure of revascularization device is as shown in the figure below:



5.2.2. Working Principle and Mechanism of Action

The revascularization device, by means of interventional therapy, delivers a metal thrombectomy stent into the intracranial target vessel. After fully deployed, the stent has a strong capacity to capture the thrombus, and then the thrombus is withdrawn to the outside body with the revascularization device to achieve the purpose of recanalization.

5.3. Study Scope

The revascularization device is intended to remove the thrombus from large intracranial blood vessels of ischemic stroke patients within 24 hours after symptom onset, so as to restore blood flow.

6. Overall Design

6.1. Study Design

6.1.1. Study Objective

To verify that the success rate of instant recanalization of Ghunter Revascularization Device is not inferior to Solitaire FR for endovascular treatment of acute ischemic stroke.

6.1.2. Selection of Study Method and Justification

The therapeutic effect and prognosis of AIS patients are related to whether the infarcted vessels can be opened in time. Therefore, whether the vessels are successfully opened will be the primary endpoint of the thrombectomy effect. This trial assumes that the recanalization success rate of the investigational product is not inferior to that of the control product, and this hypothesis will be verified by a sufficient sample size.

Study method: Prospective, multicenter, randomized controlled, non-inferiority test.

1) Prospective: research method that start from the present and track into the future is used.
2) Multicenter: More than 10 clinical sites are planned to be selected to conduct the clinical trial.
3) Randomized control: Randomization is performed using the Interactive Web Response System (IWRS), with competitive block randomization and competitive enrollment by each site. After signing the ICF and passing the screening, the subjects are randomized into the test group and control group in 1:1, with 110 each in the test group and control group. Randomization numbers and groups are distributed by randomization personnel in the randomization system of each site to avoid selection bias.
4) Non-inferiority test: to evaluate that the success rate of instant recanalization is not inferior to the control product when the investigational product is used for endovascular treatment of acute ischemic stroke.
5) Blind reading: The thrombectomy procedure will be burned on a CD in DICOM format, and the target vessel will be blindly evaluated for recanalization by a central interpretation room independent of the trial.

6.1.3. Measures to Reduce and Avoid Bias

6.1.3.1. Multicenter:

The samples from multi sites are more representative than those from a single site, and the latter may lead to bias of study results due to its systematic errors. Therefore, the conclusion obtained can be more reliable. In order to reduce

differences in procedures between sites, trainings of study personnel in each site on the use of the same standards in the study should be performed. Clear evaluation criteria are adopted for effectiveness and safety indicators.

6.1.3.2. Investigator Training:

Before the start of the clinical trial, the CRA shall coordinate with the director of the study sites to train the investigators on the trial protocol so that the investigators can understand and be familiar with the test products, and shall also grasp all new information related to this product found during the trial.

6.1.3.3. Monitoring of Clinical Trial:

The monitoring plan is developed and the CRA appointed by the sponsor shall conduct regularly on-site monitoring visit to the hospitals conducting the clinical trial to ensure that all the contents in the trial protocol are strictly observed and the EDC is checked to ensure consistency with the raw data.

6.1.3.4. Management of Clinical Trial:

A clinical research coordinator (CRC) will assist the investigator in performing the specific non-medical judgment affairs of the clinical trial to ensure that all aspects of the trial protocol are strictly adhered to and that the EDC data is consistent with the raw data.

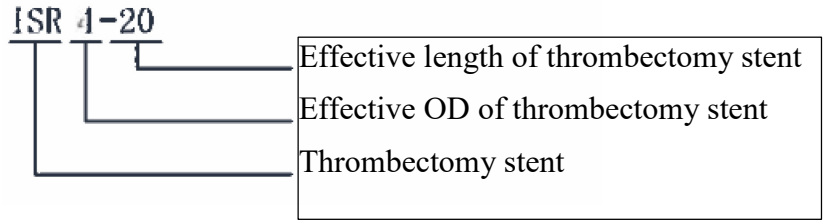
6.1.4. Investigational Medical Device and Control Device/Control Diagnostic and Therapeutic Method

6.1.4.1. Investigational Product:

Product name: Ghunter Revascularization Device

Models: ISR3-20, ISR3-25, ISR3-30, ISR4-20, ISR4-30, ISR4-40, ISR6-20, ISR6-30, ISR6-40

The naming rule of Ghunter revascularization device is ISR XYY, and each letter represents the meaning as follows:



According to the target vessel diameter and thrombus length, the revascularization device is divided into the following specifications:

Model	Recommended vessel diameter[1]		Compatible microcatheter minimum ID		Diameter × effective length[2]	Total length of thrombectomy stent	Total length of revascularization device	Distance from proximal marker to distal radiopaque marker	Quantity of radiopaque markers	
	Minimum (mm)	Maximum (mm)	(mm)	(inch)	(mm×mm)	(mm)	(cm)	(cm)	Distal	Proximal
ISR3-20	1.5	3.0	0.43	0.017	3×20	31	200	<130	3	1
ISR3-25	1.5	3.0	0.43	0.017	3×30	36	200	<130	3	1
ISR3-30	1.5	3.0	0.43	0.017	3×40	41	200	<130	3	1
ISR4-20	2.0	4.0	0.53	0.021	4×20	31	200	<130	3	1
ISR4-30	2.0	4.0	0.53	0.021	4×30	41	200	<130	3	1
ISR4-40	2.0	4.0	0.53	0.021	4×40	51	200	<130	3	1
ISR6-20	3.0	5.5	0.69	0.027	6×20	31	200	<130	4	1
ISR6-30	3.0	5.5	0.69	0.027	6×30	41	200	<130	4	1
ISR6-40	3.0	5.5	0.69	0.027	6×40	51	200	<130	4	1

1. XX revascularization device is selected based on the minimal diameter, listed in Table 1, of the thrombus-located vessel.
2. The effective length of XX revascularization device should be no less than the thrombus length.

Manufacturer: Sinomed Neurovita Technology Inc.

6.1.4.2. Control Product:

Product name: Solitaire FR

Specification/model (mm × mm): 4 × 15, 4 × 20, 6 × 20, 6 × 30

Manufacturer: Covidien Healthcare International Trading (Shanghai) Co., Ltd.

6.1.5. Subject Enrollment

6.1.5.1. Inclusion Criteria

General inclusion criteria:

1) ≥ 18 years old;
2) NIHSS ≥ 6 at randomization;
3) Pre-onset mRS < 2;
4) Acute ischemic stroke was diagnosed;
5) Within 24h from the stroke onset to the completion of femoral artery puncture (regardless of whether intravenous thrombolysis has been performed); the time point of stroke onset is defined as the time point at which the patient is last known to be normal;
6) The subject (or his/her guardian) agrees to participate in this study and signs

the informed consent form (ICF).

Angiographic inclusion criteria:

1) Cerebral CT or MR should be performed when the time from the stroke onset to the completion of femoral artery puncture of a patient is ≤ 6h;
2) Cerebral CT or MR should be performed when the time from the stroke onset to the completion of femoral artery puncture of a patient is 6 (exclusive)-24h (inclusive), and his/her ASPECTS score should be ≥ 6. (If immediate CT perfusion imaging or MR perfusion imaging is feasible, it is recommended to perform CTP or MRP simultaneously to assist in the assessment of the infarct core, and his/her ASPECTS score should also be ≥ 6);
3) DSA angiography shows acute occlusion of large intracranial arteries, including intracranial internal carotid artery (C4-C7), middle cerebral artery (M1/M2), basilar artery and intracranial vertebral artery (V4).

6.1.5.2. Exclusion criteria

General exclusion criteria:

1) Those who could undergo neither MRI nor CT;
2) Those with hemorrhagic stroke or major ischemic stroke within 6 months before enrollment;
3) Those with severe persistent hypertension that could not be controlled by intravenous injection for blood pressure reduction, i.e. patients with sustained SBP > 185 mmHg or sustained DBP > 110 mmHg;
4) Those with presumed septic emboli or suspected bacterial endocarditis;
5) Renal failure, defined as creatinine > 3.0 mg/dL (264 μmol/L);
6) Those with blood glucose < 2.78 mmol/L (50 mg/dL) or > 22.20 mmol/L (400 mg/dL);
7) Decreased platelet count (< 40×10^9/L);
8) Those with known hemorrhage tendency, coagulation factor deficiency, are taking anticoagulants and with INR > 3.0;
9) Pregnant or lactating women;
10) Those with known severe allergy to contrast media or known allergy to nickel materials;
11) Those with disorders possessing possibility of affecting neurological assessment (e.g., neurological and psychiatric disorders);
12) Those with heart, lung, liver failure or other serious disorders leading to disablement of interventional operation;

13) Participating in clinical trials of other drugs or devices;

14) Life expectancy less than 6 months;

15) Other conditions judged by the investigator to be not suitable for inclusion.

Angiographic exclusion criteria:

1) There is evidence of intracranial hemorrhage on CT or MR or known hemorrhage tendency;
2) CT/MR/DSA angiography suggests > 1 vascular occlusion (e.g., simultaneous occlusion of bilateral internal carotid artery vessels, or simultaneous occlusion of intracranial vessels in anterior and posterior circulation, or simultaneous occlusion of intracranial and extracranial internal carotid artery);
3) Those with carotid artery dissection, occlusion of the initial segment of the carotid artery or arteritis;
4) Those whose access vessels are quite tortuous, making the revascularization device difficult to reach the target location.

6.1.5.3. Criteria and Procedures for Withdrawal from/Discontinuation of Trial Treatment

The subjects may withdraw from the study at any time during the course of the study without giving a reason: moreover, subjects may choose not to undergo any study procedures after signing the ICF, and if subjects choose not to undergo any study procedures after signing the ICF, the investigator must be informed. However, subjects have the right to continue receiving the standard of care regardless of the cases.

Any subject may also be withdrawn from the study by the investigator based on medical judgement.

Subject's premature discontinuation or withdrawal from the study can be any of the following cases, but not limited to:

1) The subject is unwilling to continue participating in this study for any reason;
2) For medical or safety reasons, the investigator believes that the subject should be withdrawn from the study;
3) Serious protocol violation (confirmed by the principal investigator);
4) The investigator or the sponsor requests to terminate the study for any reason; or
5) Death.

For all subjects who terminate the study early, the investigator should make every effort to find out the reasons for withdrawal from the trial, for example: adverse

events, failure of corrective treatment, the investigator's decision or other reasons. The reasons for withdrawal should be recorded in the EDC. Subjects who withdraw early should be requested to complete an early withdrawal visit according to the visit schedule.

Subjects who withdraw from the study will not be replaced, i.e. the randomization number will be uniquely related to each subject and cannot be reused.

6.1.5.4. Expected Overall Duration of Clinical Trial and Its Rationale

Overall duration: About 30 months.

The overall duration of the clinical study includes the time of obtaining EC approval letters from all the study hospitals, time of signing the clinical study agreement, filling time, time of study initiation, enrollment and follow-up of subjects, time of collection and statistics of study data, and summary report writing, etc. The expectation is from March 2021 to September 2023.

Rationale: The overall duration of this trial is predicted based on the number of the investigational devices used for the cases in each hospital to ensure adequate source of cases for the study, as well as the patient follow-up schedule and the process systems of each hospital.

6.1.5.5. Expected Duration of Participation for Each Subject

The duration of each subject participation is defined as a period from the time that the patient signs the ICF to the end time of the final follow-up. According to the study design, the visit time of each subject: screening/baseline period (-1 d~ 0 d preoperatively), treatment period (day of operation/0d), observation period (24 ± 12 h postoperatively), follow-up period (7 ± 2 d postoperatively (before discharge in case of premature discharge)), and follow-up period (90 ± 14 d postoperatively). Therefore, the expected duration of participation of each subject is around 90 days.

6.1.5.6. Number of Subjects for Confirmatory Clinic Trial

220 subjects are enrolled into this clinical study in total.

6.1.6. Effectiveness Evaluation Methods

1) Description of effectiveness endpoints
    a) Primary effectiveness endpoint: success rate of instant recanalization
    b) Secondary effectiveness indicators: Proportion of subjects with mRS scores of 0-2 on 90d postoperatively, time from femoral artery puncture to recanalization/the end time of operation for subjects whose recanalization failed, proportion of subjects with NIHSS score decrease > 4, and success rate of device operation
2) Selection of Method and Time to Evaluate, Record and Analyze Effectiveness

Indicators

Primary endpoint:

- **Success rate of instant recanalization**

Recording time and method: During thrombectomy, cerebral vascular DSA examination will be performed to analyze whether the recanalization success is achieved. If the recanalization is affected due to in situ atherosclerotic stenosis, vascular dissection and vasospasm after thrombectomy, the investigator can handle it in an appropriate way and determine whether the target vessel is successfully revascularized according to the recanalization after treatment.

* Recanalization success was evaluated separately by clinicians and a central interpretation room independent of the study, and when the evaluation results were inconsistent, the results of the blind evaluation by the central interpretation room prevailed.

Formula: Success rate of instant recanalization = Number of subjects with instant recanalization success in this group/Number of subjects treated with revascularization devices in this group × 100%.

Criteria for instant recanalization success: target vessel recanalization, with mTICl grade of 2b or 3. The mTICI grading is shown in Appendix 3.

Secondary endpoint:

- **Proportion of mRS scores of 0-2**

Recording time and method: preoperatively and 90 ± 14 d postoperatively. Postoperative subjects' degree of disability will be analyzed by 90-d mRS scores postoperatively. The mRS score is based on mRS scale (as shown in Appendix 4).

Proportion of subjects with mRS scores of 0-2 = Subjects with mRS scores of 0-2 on 90d postoperatively/Number of subjects treated with intracranial thrombectomy device × 100%.

- **Time from femoral artery puncture to recanalization/the end time of operation for patients whose recanalization failed**

Evaluation time: Intraoperatively

Evaluation site: target vessel

Evaluation method: The recanalization time will be judged by intraoperative procedure and the vascular condition shown by imaging.

Formula: Recanalization time = Recanalization success time - Femoral artery puncture time

Precautions: The recanalization time is the time from the completion of femoral

artery puncture to recanalization success. If the vessel is not revascularized, the end time point is recorded as the time point at the end of operation. Criterion for instant recanalization success: target vessel recanalization with mTICI grade of 2b or 3 after thrombectomy with the investigational device. The investigator's judgment intraoperatively shall prevail.

- **Proportion of subjects with NIHSS score decrease > 4**

Recording time and method: The preoperative and postoperative NIHSS scores are compared by three time points: pre-operation, 24 ± 12h postoperatively and 7± 2d postoperatively (before discharge in case of premature discharge) to analyze the degree of impairment and improvement of neurological functions preoperatively and postoperatively. The NIHSS score is the total score based on NIHSS scale (as shown in Appendix 5).

Proportion of subjects with NIHSS score decrease > 4 = Number of subjects with NIHSS score decrease > 4 postoperatively in this group/Number of subjects treated with thrombectomy through stents in this group × 100%.

- **Success rate of device operation**

Definition: The success rate of device operation is the proportion of device operation success. Device operation success is defined as successful delivery of the investigational device to the diseased vessel site to complete accurate deployment and withdrawal.

Evaluation time: Intraoperatively (evaluation endpoint)

Evaluation site: target vessel

Evaluation method: The success rate of device operation is calculated by intraoperative evaluation of whether the delivery, deployment and withdrawal of the thrombectomy device are completed.

Formula: Device operation success = Number of devices delivered, deployed and withdrawn/Number of all investigational devices used in this group × 100%.

6.1.7. Safety Evaluation Methods

6.1.7.1. Description of Safety Endpoints

1) Safety Endpoints

- Safety endpoints: Incidence of symptomatic intracranial hemorrhage within 24 h postoperatively, mortality within 90d, incidence of SAE, incidence of AE, and incidence of device defects.

2) Selection of Method and Time to Evaluate, Record and Analyze the Safety Endpoints

- **Incidence of symptomatic intracranial hemorrhage within 24h**

Recording time and method: Symptomatic intracranial hemorrhage within 24h, specifically refers to intracranial hemorrhage (parenchymal hematoma, subarachnoid hemorrhage, ventricular hemorrhage) accompanied by neurological deterioration (NIHSS score increases by ≥ 4 compared with that preoperatively).

Incidence of symptomatic intracranial hemorrhage within 24 h = Number of subjects who develop symptomatic intracranial hemorrhage on CT or MR within 24 h in this group/Number of subjects who receive revascularization device for thrombectomy in this group × 100%.

* Subjects with symptomatic intracranial hemorrhage postoperatively who show additional hemorrhage on CT or MR within 24 h postoperatively will not be re-evaluated.

- **All-cause mortality within 90 days**

Recording time and method: Throughout the clinical trial. All-cause mortality = Number of deaths in this group/Number of subjects who receive revascularization device for proximal thrombectomy in this group × 100%.

- **Incidence of device defects**

Recording time and method: During the thrombectomy. Incidence of device defects = Number of defective devices / Total number of devices × 100%.

Note: The investigational device defects that occur during the clinical trial, such as device fracture and mislabeling.

- **Incidence of SAE**

Recording time and method: Throughout the clinical trial. Incidence of SAE = Number of subjects with SAE/Number of subjects treated with intracranial thrombectomy device for thrombectomy in total × 100%.

- **Incidence of AE**

Recording time and method: Throughout the clinical trial, incidence of AE = Number of subjects with AE/Number of subjects who receive intracranial thrombectomy device for thrombectomy × 100%.

6.2. Study Process

6.2.1. Study Process

6.2.1.1. Enrollment

The investigator will screen the subjects according to the inclusion and exclusion criteria after obtaining the ICF signed by the subjects (or their guardians). After the subjects pass the screening, at the end of cerebral DSA angiography and before using the revascularization device, the investigator will randomize the subjects into the test group and the control group in the randomization order, and the enrollment will be considered successful.

6.2.1.2. Randomization

Randomization will be performed via an electronic randomization system after screening for inclusion and exclusion criteria. The investigator will log into the randomization system, fill in the subject information and then submit, and the system will automatically give the randomization results. The investigator should select the corresponding test product to treat the subject according to the results given by the electronic randomization system. In Group A, Sinomed Neurovita Ghunter Revascularization Device will be used, and in Group B, Covidien Solitaire FR will be used. Once the subject information is entered into the electronic randomization system, no deletion will be allowed, and all operations will be automatically left on the system for verification.

6.2.1.3. Visit Schedule

1) Visit 1: Screening/baseline period (-1 d ~ 0 d)

After all the subjects (or their guardians) sign the ICF, the investigator will screen the subjects according to the inclusion/exclusion criteria of the study. During this period, the following visit contents need to be completed:

i. Signing of ICF;

ii. Recording of basic information of the subject;

iii. Present medical history: onset time and admission time;

iv. Medical history: history of allergy, history of stroke, history of other significant diseases (e.g., presumed septic emboli or suspected bacterial endocarditis), history of neurological diseases;

v. Vital signs (blood pressure, heart rate);

vi. NIHSS score;

vii. MRS score, ASPECTS score (required within 6 - 24 h of onset);

Laboratory examination:

viii. Pregnancy testing (Only for women of childbearing potential who are planning to become pregnant)

ix. Administration of anticoagulant and antiplatelet drugs;

x. Cerebral CT or MR will be performed, and the following information will be recorded:

   a) When the onset time is ≤ 6h, cerebral CT or MR is performed;

   b) Cerebral CT or MR is performed when the onset time is 6 (exclusive)-24h (inclusive) to determine whether ASPECTS score ≥ 6 is met; (if immediate CT perfusion imaging or MR perfusion imaging is feasible, CTP or MRP is recommended to assist in the assessment of the infarct

core to determine whether ASPECTS score ≥ 6 is met).

* For laboratory tests and imaging tests, the results after this admission and the results of external hospital examinations within 24h preoperatively are acceptable.

c) Other significant abnormal conditions.

2) Visit 2 (0 d):

i. Recording of cerebral vascular DSA:

a) Name of target vessel and lesion segment, proximal diameter of occluded vessel

b) mTICI image grading postoperatively

c) Does the patient suffer from carotid origin occlusion or carotid dissection or arteritis?

d) Is the vessel access so tortuous that makes it difficult for the investigational/control device to reach the target location?

ii. Recording of the operations:

a) Date of operation, femoral artery puncture time, operation start and recanalization time (or end time)

b) Intraoperative treatment method (Are implant stent, balloon dilatation and antithrombotic drugs used)

c) Model of each revascularization device, the frequency of thrombectomy procedure, evaluation of success rate of device operation, whether the vessel is successfully revascularized, recanalization success time, and reason for failure

iii. Administration of anticoagulant and antiplatelet drugs;

iv. Recording of adverse events;

v. Recording of device defects:

Note: The frequency of thrombectomy procedure with the thrombectomy device will be determined by the investigator on a case-by-case basis. If recanalization fails, the investigator may use other diagnostic and therapeutic measures (including but not limited to dual-stent technique, stent implantation, and aspiration device) according to specific case characteristics.

3) Visit 3: Observation period (V3: 24 ± 12 h postoperatively)

The subjects undergo clinical follow-up 24 h ± 12 h postoperatively. All the visit information will be analyzed and recorded by investigators. In this visit, the following visit contents need to be completed:

i. Vital signs;

ii. NIHSS score;

iii. Laboratory tests;

iv. Cerebral CT or MR will be performed, and the following information will be recorded:

a) Is there intracranial hemorrhage (parenchymal hematoma, subarachnoid hemorrhage, ventricular hemorrhage)

b) Is there is a new cerebral infarction

c) Other significant abnormal conditions

v. Administration of anticoagulant and antiplatelet drugs;

vi. Recording of adverse events;

4) Visit 4: Follow-up period (V4: 7 ± 2 d postoperatively (before discharge in case of premature discharge))

The subjects undergo clinical follow-up 7 ± 2 d postoperatively. All the visit information will be analyzed and recorded by investigators. In this follow-up visit, the following visit contents need to be completed:

i. Vital signs;

ii. NIHSS score;

iii. Laboratory tests (if laboratory test results had already been collected at Visit 3, they might not be collected here);

iv. Administration of anticoagulant and antiplatelet drugs;

v. Recording of adverse events;

5) Visit 5: Follow-up period (V5: 90 ± 14 d postoperatively)

The subjects undergo outpatient/telephone follow-up 90 ± 14 d postoperatively. All the visit information will be analyzed and recorded by investigators. In this follow-up visit, the following visit contents need to be completed:

i. mRS score;

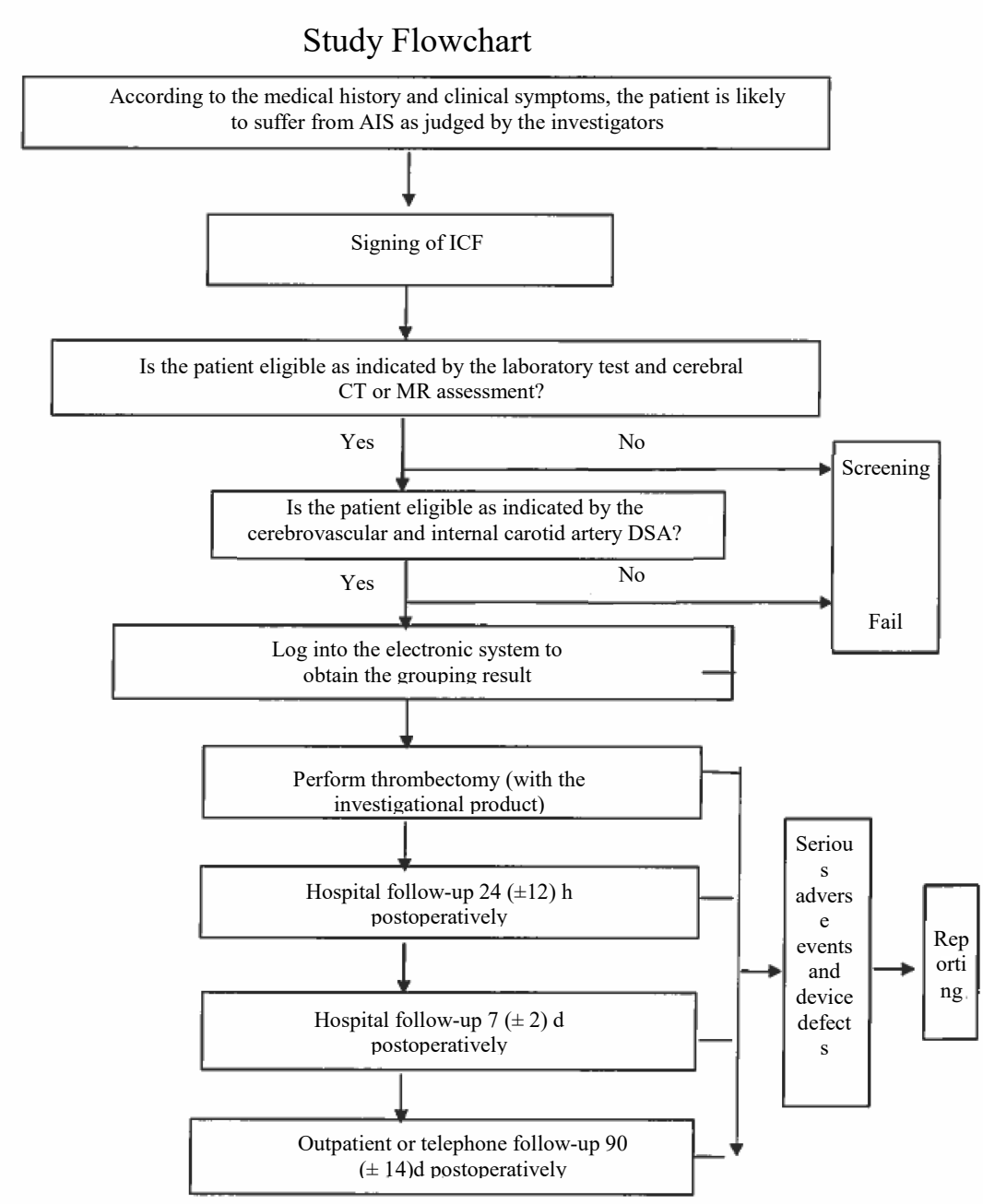
ii. Administration of anticoagulant and antiplatelet drugs;

iii. Recording of adverse events;

6) Premature termination of visit

Subjects can withdraw from the study at any time, and once a subject withdraws prematurely from the study before the end of the follow-up period, an premature termination visit must be completed as soon as possible and the reason for termination will be recorded. Evaluations to be performed during this follow-up

period is the same as Visit 5. All information will be analyzed and documented by the investigator.



Data Collection:

Visit time / Visit contents	Screening/Baseline period	Treatment period	Observation period	Follow-up period	
	Preoperatively -1 d ~ 0 d	Day of operation/ 0 d	Postoperatively 24 h ± 12 h	Postoperatively 7 d ± 2 d	Postoperatively 90 d ± 14 d
Signing of ICF	×				
Medical history	×				
Preoperative diagnosis	×				
Vital signs[1]	×		×	×	
NIHSS score[2]	×		×	×	
mRS score[3]	×				×
Laboratory test[1]	×		×		
Pregnancy test[5]	×				
Cerebral CT or MR[6,7]	×		×		
Cerebrovascular DSA[7]	×				
Verification of eligibility criteria		×			
Randomization		×			
Operations		×			
Antiplatelet and anticoagulant medication	×	×	×	×	×
Adverse event		×	×	×	×
Device defect		×			

Note:

1) Vital signs include heart rate and blood pressure.
2) NIHSS score: assessing the degree of neurological impairment of the subject.
3) MRS score: assessing the degree of disability of the subject.
4) Laboratory tests (The laboratory test results at 24 h preoperatively are accepted during the screening period, and one laboratory test within 9d postoperatively is sufficient):

   Blood routine: Red blood cell, hemoglobin, white blood cell count, and platelet count

   Blood chemistry: Urea nitrogen (urea), serum creatinine, blood glucose

   Coagulation: Prothrombin time, activated partial thromboplastin time and

INR

5) Only for women of childbearing potential who are planning to become pregnant, blood or urine pregnancy test result is acceptable.
6) Cerebral CT or MR is performed when the onset time is ≤ 6h; cerebral CT or MR is performed when the onset time is 6 (exclusive)-24h (inclusive) to determine whether ASPECTS score ≥ 6 is met; (if immediate CT perfusion imaging or MR perfusion imaging is feasible, CTP or MRP is recommended to assist in the assessment of the infarct core to determine whether ASPECTS score ≥ 6 is met).
7) CT or MRI images and DSA images during thrombectomy are burned on a CD in DICOM format and evaluated by a central interpretation room.
8) Randomization: An electronic randomization system is logged into for randomization.

   * If any of the micro-guidewire and microcatheter does not pass through the thrombus segment of the target vessel during the operation, or if the thrombectomy device is not used for thrombectomy, this subject is statistically processed as having a blank randomization number;

6.2.2. Device Specifications (recommend the operation method, and the operator may make slight modification according to the actual situations)

6.2.2.1. Preparations

1. Administer anticoagulant and antiplatelet drugs according to standard guidelines.
2. With the aid of angiography, determine the location and size of the area for recanalization.
3. Select a revascularization device based on the product specification/model.
4. To achieve optimal use of the revascularization device and reduce the risk of thromboembolic complications, maintain continuous flushing of the following lumens:

   a) Between femoral sheath and guiding catheter;

   b) Between guiding catheter and microcatheter;

   c) Between microcatheter and push rod/revascularization device.

   Check all connections to ensure that no air enters the guiding catheter or microcatheter during continuous flushing.
5. Deliver the appropriate guiding catheter as close as possible to the thrombus site by standard methods. If required in subsequent steps, the size of the

guiding catheter should be appropriate for thrombus recovery. Connect the RHV to the guiding catheter and then connect an infusion line for continuous flushing.

6. Based on the product specification/model, select the microcatheter suitable for delivering the revascularization device.
7. Attach a second RHV to the microcatheter and then connect an infusion line for continuous flushing.
8. Set the flushing speed according to standard guidelines.
9. Deliver the microcatheter over the appropriate guidewire until the end of the microcatheter is distal to the thrombus so that the effective length portion of the revascularization device covers each side of the thrombus in the vessel when fully deployed. Tighten the RHV around the microcatheter.

6.2.2.2. Delivering Revascularization Device

10. Insert the distal portion of the introducer sheath into the RHV connected to the microcatheter. Tighten the RHV and verify that fluid exits the proximal end of the introducer sheath.
11. Loosen the RHV and push the introducer sheath until its distal end is securely seated in the microcatheter hub. Tighten the RHV around the introducer sheath to prevent blood backflow, but the damage may occur to the device if tightened too tightly as the stent is pushed into the microcatheter. Verify that there are no air bubbles in the system.
12. Push the push rod in a smooth continuous manner so that the thrombectomy stent is delivered into the microcatheter. Once the flexible portion of the push rod enters the microcatheter, loosen the RHV and remove the introducer sheath from the proximal end of the push rod. Upon completion, tighten the RHV around the push rod. Continued tight attachment of the introducer sheath to the inner lumen of the microcatheter will block normal flushing of the RHV and lead to backflow of blood into the microcatheter.
13. After visually confirming that the flushing fluid input is normal, loosen the RHV and push the push rod.
14. Once the proximal marker of the revascularization device enters the microcatheter, start the X-ray imaging system. With the aid of the x-ray imaging system, carefully deliver the stent until its distal marker is aligned with the distal microcatheter, and the stent remains in such a position that, when the device is completely deployed, its effective length portion covers each side of the thrombus in the vessel.

    ✧ Warning: If excessive resistance encounters in the advancement of the stent, stop and identify the cause. Advancing the thrombectomy stent

against heavy resistance may damage the device and/or injure the patient.

6.2.2.3. Deploying Revascularization Device

15. Loosen the RHV around the microcatheter. Fix the push rod so as to maintain the position of the thrombectomy device while carefully withdrawing the microcatheter to the proximal end.
16. Withdraw the microcatheter until it approaches the proximal marker of the revascularization device. Tighten the RHV to prevent movement of the push rod. The effective length of the revascularization device should be greater than each side of the thrombus.
17. Tighten the RHV around the microcatheter. Angiographically assess the target vessel for flow patency.
18. Ancillary medical techniques (i.e. thrombolytics, etc.) may be used according to standard guidelines.

6.2.2.4. Withdrawing the Device

19. If using a balloon guiding catheter, inflate the balloon as directed on the balloon catheter label to occlude the vessel.
20. Ensure that the proximal marker of the stent is inside the microcatheter and loosen the RHV around the microcatheter so that it moves but remains sealed.
21. Slowly withdraw the microcatheter and the revascularization device as a whole to the end of the guiding catheter while aspirating the guiding catheter with a 60 cc syringe. Do not advance the stent deployed to the distal end.

    Caution: Ensure that the proximal marker of the revascularization device remains within the microcatheter.
22. Perform vigorous aspiration of the guiding catheter with a syringe, while withdrawing the revascularization device and microcatheter into the guiding catheter. Continue aspiration of the guiding catheter until the thrombectomy stent and microcatheter are almost withdrawn from the guiding catheter.

    Note: If it is difficult to withdraw the guiding catheter, first deflate the balloon (if the balloon guiding catheter is used), and then withdraw the guiding catheter, microcatheter and revascularization device to the arterial sheath while maintaining aspiration, and withdraw together with the arterial sheath if necessary.

    ✧ Warning: If excessive resistance encounters in the withdrawal of the revascularization device, discontinue thrombectomy and identify the cause.
23. Open the RHV of the guiding catheter, and allow the microcatheter and revascularization device to be smoothly withdrawn. Take care of device

interference and prevent air from entering the system.

24. Continue aspiration of the guiding catheter and ensure there is no thrombus material in the guiding catheter.
25. Deflate the balloon if the balloon guide catheter is used.
26. If an additional attempt to restore flow is required, take the following steps:
    a) Use a new revascularization device, and then:
        i. Repeat the above steps from the "Preparations" section.
    b) Use the same revascularization device, and then:
        i. Clean the device with normal saline.

            Caution: Do not use other solvents or autoclaves.

        ii. Inspect the device for damage carefully.
        iii. In case of any damage, use a new device and follow the steps described above (starting with the "Preparations" section) for subsequent flow restoration attempt.
        iv. Use of a damaged device may result in further damage to the device and/or patient injury.

6.2.2.5. Re-deploying Revascularization Device

If the revascularization device should be re-deployed (e.g., repositioning), take the following steps:

✧ Warning: When the device has been combined with thrombus, pushing the microcatheter may result in embolization fragments. No resistance encounters when advancing the microcatheter.

1. Loosen the RHV around the microcatheter and around the push rod. With the help of radiographic monitoring, securely fix the push rod to prevent the revascularization device from moving.
2. Carefully advance the microcatheter forward to the distal end of the revascularization device until the distal marker of the thrombectomy stent is aligned with the distal end of the microcatheter to complete re-sheathing. If great resistance encounters during one more sheathing, stop immediately. Proceed to the above "Withdrawing Revascularization Device" section.

6.2.2.6. Precautions

- Only physicians trained in neurointerventional techniques and ischemic stroke can use this device.
- Inspect packaging and devices for damage in transit prior to use. Please do not use a bent or damaged device.

- Use before the "Shelf-life" indicated on the label.

6.2.2.7. Contraindications

- Patients who are known to be allergic to nickel titanium alloy.
- Patients with stenosis near the thrombus site and/or pre-existing stents, since safe withdrawal of a revascularization device may be hindered.
- Patients with angiographic evidence of carotid artery dissection.

6.2.2.8. Potential complications

Potential complications include, but are not limited to, the following:

- Hematoma and bleeding at the puncture site
- Vascular injury (e.g., perforation)
- Angiospasm
- Confusion
- Nervous system failure (including stroke and death)
- Ischemia
- Infection
- Aeroembolism
- Intracranial hemorrhage
- Vascular embolization
- Pseudoaneurysm formation
- Postoperative bleeding
- Distal embolization, including previously unaffected areas
- Adverse reaction to antiplatelet/anticoagulation agents or contrast media
- Device deformation, collapse, fracture or malfunction
- Thrombosis (acute and subacute)
- Arteriovenous fistula

6.2.2.9. Warnings

- Appropriate anti-platelet and anti-coagulation therapy should be used in accordance with standard guidelines.
- No twisting of the revascularization device
- For each new revascularization device, use a new microcatheter
- Electrical detachment cannot be performed during thrombectomy

- To prevent device detachment:
  a. Do not use oversized device.
  b. Do not withdraw the device if excessive resistance encounters. The device should be re-sheathed with a microcatheter and the entire system should be removed under aspiration. If resistance encounters during one more sheathing, stop entry and remove the entire system under aspiration.
  c. Do not treat patients with pre-existing stenosis proximal to the thrombus site.
- The device is provided sterile and for single use. Do not re-use or re-sterilize. Reuse and re-sterilization increase the risks of patient infection and compromise device performance.

6.3. Monitoring Plan

The sponsor will entrust a contract research organization (CRO) for the monitoring of this trial, assign qualified CRA based on the complexity degree of this trial and the quantity of sites, and develop a corresponding monitoring plan, so as to ensure that the rights and interests of subjects are protected, data presented in trial records and reports is accurate and complete, and the trial is conducted in accordance with the approved protocol and relevant regulations.

Monitoring before the trial mainly includes: investigational device, study documents, trial personnel and trial training; monitoring during the trial mainly includes: regular visits, documents to be submitted to the Ethics Committee during the trial, monitoring of adverse events; monitoring after end of (or before prematurely terminating) the trial mainly includes: recovery and destruction of investigational products, EDC data entry and data query, validation of trial document integrity, notification of Ethics Committee, site closure and clinical trial report.

7. Statistical Analysis Method and Evaluation Method

7.1. Statistical Design, Method and Analysis Procedure

7.1.1. Statistical Design (Hypothesis Testing)

This study is a prospective, multicenter and randomized controlled design, with comparison type of non-inferiority test. It is to demonstrate that the investigational device also meets the needs of clinical application through comparison with the similar products that have been marketed, with the primary evaluation endpoint set as success rate of recanalization; 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 success rate of recanalization in the test group; P_C is the expected success rate of recanalization in the control group; and $\triangle$ is the non-inferiority margin (taken as a positive value here).

7.1.2. Statistical Analysis Methods

7.1.2.1. General Principles

Statistical description: The categorical data are described as frequency and proportion; while the continuous data are described as mean, standard deviation, maximum, minimum, median, 25th quantile, and 75th quantile.

Statistical inference: For the comparison of general situation of the two groups, the quantitative indicators between groups are compared using group t test or Wilcoxon rank sum test according to the data distribution, classification indicators using chi-square test or accurate probability method (if the chi-square test is not applicable), and ordinal data using Wilcoxon rank sum test or CMH test.

All statistical tests, if not specified, are two-sided and the difference is considered statistically significant when P value is <0.05 (two-sided). 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).

7.1.2.2. Study Completion and Demographic Analysis

The number of subjects enrolled and the completion status of enrollment of each site should be summarized, and the dropout cases should be listed. Different data set sizes in each group, case distribution of each site, total dropout 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.

7.1.2.3. Primary Efficacy Indicator

For the primary endpoint of recanalization success rate, at the level of $\alpha = 0.025$ (one-sided test) and $\beta = 0.2$, the success rate of target vessel recanalization in the study and control groups are compared, respectively. The 95% CI for their difference is calculated. If the lower limit of 95% CI for their difference is greater than -12.5%, it is considered that the test group is non-inferior to the control group. The inter-group comparison will be performed using the center effect-modified CMH chi-squared analysis, and the Logistics regression model can be considered for the inter-group comparison as appropriate to correct for the effects

of factors such as the center.

7.1.2.4. Secondary Efficacy Indicators

The secondary efficacy evaluation is based on Full Analysis Set (FAS) and Per-Protocol Set (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.

7.1.2.5. Safety Indicator

The number and proportion of cases with normal conditions before treatment and abnormal conditions after treatment will be described respectively by the test group and the control group. AEs are described by the number and the incidence of AEs, where the likelihood ratio X^2 test or Fisher's exact probability test is used. Also, the manifestations and degree of AEs occurred in each group and their relationship to the investigational product will be described in detail.

7.2. Calculation of Sample Size

7.2.1. Total Sample Size

The primary endpoint of the study is the success rate of recanalization, using non-inferiority test. A total of 220 patients are planned to be enrolled and randomly assigned to the test or control group in a 1:1 ratio, with 110 subjects in each group. mTICI can reach 76% at 6-16h according to DEFUSE-3 and 84% at 6-24h according to DAWN. Within 6 h, mTICI is 86% in EXTEND-IA, 88% in SWIFT PRIME, and 87% in PISTE.

According to the estimation combined with the existing clinical evidence and the experience of clinical experts, assuming that the recanalization success rate after treatment is 89% in both the test group and control group within 24h [10-19], the non-inferiority margin is set at 12.5% after discussion between the clinical investigator and the sponsor. When the significance level α of statistical test is set as one-sided 0.025 and the power 1-β is set as 80%, the sample size is calculated as 99 in each group. In consideration of the maximum possible dropout rate of 10% in the study, the sample size in each group is 110. Therefore, 220 subjects are required in total It is calculated according to statistical principles that,

the corresponding sample size formula is:

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

where, n_T and n_C are the respective sample size of the test group and control group; $Z_{1-a/2}$ and $Z_{1-\beta}$ are the percentiles in standard normal distribution; P_T is the expected success rate of recanalization in the test group, Pc is the expected success rate of recanalization in the control group; $|D|$ is the absolute value of the

difference between groups in the expected recanalization, $|D| = |P_T - P_C|$; Δ is the non-inferiority margin (taking the negative value).

7.2.2. Number of Subjects for Each Disease and Rationale for Determination

In this trial protocol, the inclusion/exclusion criteria for selected patients are strictly limited. It can be considered that the current study is only conducted for patients with a single indication. The above 220 patients have the same disease and are no longer further divided.

7.2.3. 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.

8. Significance Level and Power of Clinical Study

8.1. 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 principal investigator.

It may include the following conditions:

a) Subjects who, for whatever reason, are unwilling or unable to continue the clinical trial, propose withdrawal from the clinical trial to the investigator and terminate the clinical trial;

b) Subjects who are lost to follow-up despite not specifically proposing withdrawal from the clinical study but no longer receiving treatment and examination;

c) Subjects, who experience SAE, should be withdrawn from the clinical study as judged by the investigator;

d) Subjects, due to poor compliance, fail to complete follow-up for primary outcome;

e) Lost to follow-up (The investigator cannot reach the subject to return to the

clinic for visit assessment and examination via telephone or mail for two consecutive times).

8.2. Pass/Fail Criteria for Clinical Trial Results

If the lower limit of the 95% CI of the difference in recanalization success rate between the test group and control group is greater than -12.5% (the pre-specified non-inferiority margin), and there are no clinically unacceptable safety issues related to the investigational device, the study is qualified, otherwise it is unqualified.

8.3. 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, cleaning and final locking.

8.4. Data Statistical Method, with the Handling Method of Missing, Unused and Wrong Data (Including Discontinuation and Withdrawal) and Unreasonable Data

Missing data handling method: 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.

8.5. Procedures for Reporting Deviation from Original Statistical Plan

The statistical analysis plan needs to be confirmed by the sponsor and the principal investigator and finalized before the database is locked. 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.

8.6. Selection Criteria for Subjects Included in the Analysis and

Justification

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:

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. For patients in whom the primary effectiveness endpoint is not observed, missing data are proposed to be carried forward using the WOCF (Worst Observation Carry Forward).

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.).

Safety Set (SS): refers to the set of all subjects who receive the investigational device and complete safety evaluation at least once.

8.7. Exclusion of Special Data During Hypothesis Test and Justification (if applicable)

N/A

9. 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.

9.1. 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 investigator to print the electronic case report form as required.

9.2. 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 questions. 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.

9.3. External Data Management

External data in the study, such as device parameters and review results of central interpretation room, require pre-defined transmission mode, format requirements, transmission frequency and encryption and must meet the requirements for later data management and statistical analysis. For data management, the completeness, consistency and accuracy of external data should be verified, and in case of any problematic data, the external data output party should explain or modify it to ensure that it can be combined with the ECRF database.

9.4. Database Locking

When all data entry is completed and submitted, and all queries are answered, the system enters a soft locking status. The statistician will generate a masked 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 effectiveness endpoint or safety indicators, the sponsor, the person in charge of data management and the person responsible for 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 had been corrected.

10. Feasibility Analysis

10.1. Possibility Analysis on Success

According to the clinical trial and clinical application of similar products, the application of mechanical revascularization device for treatment of acute ischemic stroke is safe and effective, because of its navigation and rapid recanalization advantages, and freedom from risk of long-term complications. In the Chinese Guidelines for the Endovascular Treatment of Acute Ischemic Stroke (2018), mechanical thrombectomy for acute anterior circulation great-vessel occlusive stroke within 6h of onset is classified into Class I recommendation

(Level A evidence). According to the results of DEFUSE-3 and DAWN studies, patients with onset at 6-16h and 16-24h meet the corresponding inclusion and exclusion criteria and are classified into Class I recommendation (Level A evidence) and Class IIa recommendation (Level B evidence), respectively. According to the 2018 AHA/ASA, mechanical thrombectomy is recommended as Class I recommendation (Level A evidence) for acute ischemic stroke patients within 6-16h from the last time being normal and target lesions in the anterior circulation great vessels if the enrollment meets the DOWM or DEFUSE-3 criteria. Mechanical thrombectomy is recommended as Class IIa recommendation (Level B evidence) in acute ischemic stroke patients within 6-24h from the last time being normal and target lesions in the anterior circulation great vessels if the enrollment meets the DOWM or DEFUSE-3 criteria.

The design of Ghunter Revascularization Device of Sinomed Neurovita Technology Inc. is optimized on the basis of similar products that have been marketed, and there is no difference in their main technical indicators. Before conducting the clinical trial, animal experiments have been performed to verify that Sinomed Neurovita Ghunter Revascularization Device is not inferior to the marketed product in terms of effectiveness and safety.

The clinical sites participating in this study are equipped with complete instruments and equipment and are the hospitals with rich clinical experience; the physicians participating in this study have rich experience in using mechanical intracorporeal thrombectomy stents.

10.2. Possibility Analysis on Failure

The main reasons for failure or poor results may be related to the following factors: 1) The product is seen very special device defects. 2) Too many subjects dropped out due to the development of SAEs. 3) The training for the personnel of the study site is not in place, and the use of the device is not skilled, with the result that the effectiveness of the product fails to meet the requirements.

In addition to the above reasons, there are other unpredictable risks that may exist in this study, leading to its failure. But the risk may be minimized by adherence to this protocol, treatment in the prescribed study sites, compliance with the inclusion/exclusion criteria of the subjects, and close monitoring of the physical condition of the subjects during the treatment or follow-up period.

11. Quality Control of Clinical Trial

11.1. 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.

11.2. Filling of Case Report Form

Permissible users perform data entry to ensure that the raw data are consistent with EDC data.

11.3. Retention of Raw Data

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

12. Ethical Issues and Informed Consent in Clinical Trial

12.1. Ethical Considerations

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 Ethics Committee. Any amendment to the study protocol must be approved by the Ethics Committee before it can be implemented. SAEs during the clinical trial shall be submitted to the Ethics Committee in writing timely.

12.2. Approval of Trial Protocol

The approval of the clinical trial protocol is performed by the Ethics Committee, and the clinical trial can be performed only after obtaining the final ethical approval.

12.3. Informed Consent Process and Contents of Informed Consent Form

The investigators must specify to the subjects or their guardians, prior to their enrollment, the details of this clinical trial, including the contents and purpose of the trial, intended efficacy, possible adverse events and countermeasures. The subjects can only be enrolled when they have fully understood this trial and signed the ICF.

For incompetent subjects, if the Ethics Committee agrees in principle and the investigators believe that it is in their own interests for the subjects to participate in the clinical trial, they may also enter the clinical trial, but their guardians should sign and date before the trial. Although acute ischemic stroke patients may not be clinically comatose, their cognitive ability and hand function are affected, and such subjects should be signed and dated by their guardians before the trial.

When the subjects or their guardians have no reading ability, a witness shall be present in the informed process. After the detailed explanation of the ICF, the

witness's reading of the ICF shall be consistent with the oral informed content. After the subjects or their guardians show verbal consent, the witness shall sign and date the ICF and the signatures of the witness and the investigator shall be on the same day.

13. Provisions for AE and Device Defect Reporting

13.1. AE

13.1.1. Definition of AE

An AE is defined as any untoward medical occurrence after treatment with the investigational product, regardless of its relationship to the investigational medical device. This includes the events related to the followings:

- All events related to the investigational or control device.
- All events related to the study process (all processes in the clinical study plan).
- Other adverse events.

13.1.2. Determination of AE Severity

The process, degree, handling and outcome of the adverse events should be observed in detail and be filled in the Adverse Event Report Form. According to the following criteria, the severity of adverse events can be divided into mild (inquired), moderate (active narration, but able to endure) and severe (objective manifestation, unendurable).

13.1.3. Recording of AE

AEs after treatment with the investigational product must be recorded truthfully in the Adverse Event Form. Record the duration of adverse events (that is, from start to end), severity, and correlation with the clinical study of adverse events 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.

13.2. 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 Ethics Committee through the administrative department for medical device clinical trials of the clinical trial institution for review.

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

13.3. SAE

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

- Fatal disease or injury;
- Permanent impairment of a body structure or a body function;
- Requiring in-patient hospitalization or prolongation of existing hospitalization;
- Requiring medical treatment or surgical intervention so as to avoid permanent impairment of the body structure or body function;
- Leading to a fetal distress, fetal death or a congenital abnormality;
- Congenital defect, etc.

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

1) Pre-planned hospitalizations (e.g., scheduled elective or scheduled operations or examinations prior to study start)
2) Hospitalization not related to an AE (e.g., community hospitalization for short-term or long-term care purposes)
3) Measures such as tracheal intubation or tracheotomy to help stroke patients breathe better with sputum
4) Not symptomatic intracranial hemorrhage as judged by the investigators

Note: Symptomatic intracranial hemorrhage refers to intracranial hemorrhage (parenchymal hematoma, subarachnoid hemorrhage, ventricular hemorrhage) accompanied by neurological deterioration (NIHSS score increases by ≥ 4 compared with that preoperatively)

However, any interventional therapy performed during hospitalization may meet the criteria for a "significant 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.

13.4. Reporting Procedures and Contact Information

In case of any SAE during the clinical trial, whether related to the investigational device or not, the investigators should immediately take appropriate therapeutic measures for subjects and report the event in writing to the administrative department for medical device clinical trials of the clinical trial institution, and

then the clinical trial institution reports the same to the Sponsor in writing. The administrative department for medical device clinical trials should send written reports to corresponding Ethics Committee, the food and drug administrative authorities, the competent authority of health and family planning in local province, autonomous region and municipality within 24 h. Regarding any death event, the clinical trial institutions and investigators should provide all required data to corresponding Ethics Committees and sponsor;

The sponsor should promptly investigate the SAE with the investigator and take necessary measures to ensure the safety and rights and interests of the subjects. Any SAE or device defect that may cause serious adverse events should be reported to the food and drug administrative authorities and the competent department of health and family planning at the same level where the device is filed within 5 working days after being informed. Meanwhile, other clinical trial institutions and investigators that participate in the trial should also be informed, and the Ethics Committee of such clinical trial institution should also be timely informed through its administrative department for medical device clinical trials. If it is determined to be a test device-related SAE, the sponsor shall bear the cost of rescuing the subject and the corresponding economic compensation.

14. 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 the investigators and the sponsor, and then reported to the Ethics Committee for approval before the trial can be initiated.

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 and submitted to the investigators and the study sites in writing for signature and approval, and then reported to the Ethics Committee for approval before implementation.

During the clinical study, if the existing participating sites fail to obtain the approval of the clinical trial administrative department or the Ethics Committee, 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 administrative department and Ethics Committee of all participating sites for filling.

If the important new information regarding the investigational device becomes available, the informed consent form must be revised in writing and re-approved

by the Ethics Committee 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 ethics committee.

15. Direct Access to the Source Data and Documents

In this clinical study, the principal investigator and authorized investigators thereof can access and generate out-patient medical records, ICF (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, in accordance with the requirement of the relevant laws and regulations and technical specifications in China, shall be specified in detail by SOP of the corresponding department.

16. Finance and Insurance

In this clinical study, the sponsor shall sign a written agreement with clinical trial institutions, with the financial situation and payment methods for this clinical trial specified in detail in the agreement. The specific content is detailed in the signed agreement.

In case of any injury or death related to the clinical trial, the sponsor should assume corresponding compensation, which should be fully in accordance with relevant laws and regulations and GCP requirements.

17. Contents to be Covered in Clinical Trial Report

Each participating institution should complete the clinical trial summary of each sub-site, and the medical statistics office should complete the statistical analysis report. The leading site of this clinical trial should complete the clinical trial summary report according to the contents of statistical analysis report, which should include the clinical trial summary of each sub-site.

The clinical trial summary of each sub-site should include at least the clinical trial overview, general clinical data, description on investigational medical devices, safety and effectiveness data set, incidence and treatment of adverse events, description of protocol deviation, etc., with CRFs attached.

According to the requirements of the Good Clinical Practice for Medical Device (CFDA Order No. 25) issued by the China Food and Drug Administration (CFDA) and National Health and Family Planning Commission of China (NHFPC), the clinical trial report should be consistent with the clinical trial

protocol and should cove:

(I) General information:

(II) Abstract;

(III) Brief introduction;

(IV) Objective of clinical trial;

(V) Method of clinical trial;

(VI) Contents of clinical trial;

(VII) General clinical data;

(VIII) Investigational medical device and control device or control diagnostic and therapeutic method;

(IX) Statistical analysis methods and evaluation methods adopted;

(X) Clinical evaluation criteria;

(XI) Organizational structure of clinical trial;

(XII) Description of ethics;

(XIII) Clinical trial results;

(XIV) AEs observed in the clinical trial and their treatment;

(XV) Analysis and discussion of clinical trial results, especially the indications, intended use, contraindications and precautions;

(XVI) Conclusion of clinical trial;

(XVII) Existing problems and suggestions for improvement;

(XVIII) List of personnel involved in the trial;

(XIX) Other conditions that need to be described.

18. Confidentiality Principle

This agreement 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.

19. Agreement on Publication of Trial Results

The investigators have the right to prepare sub-site papers, reports, etc., but the

investigators should notify the sponsor in writing before publishing to the public, and shall not violate the confidentiality obligations agreed in this protocol.

20. Responsibilities Assumed by All Parties

All parties shall strictly implement the relevant provisions in accordance with the Good Clinical Practice for Medical Devices (Order No. 25).

20.1. Responsibilities of the Sponsor:

(1) Provide the medical institutions with test devices, trial protocol, EDC and ICF free of charge;

(2) Provide relevant training for clinical investigators before trial;

(3) Bear the costs related to the trial;

(4) Before terminating a medical device clinical trial, the sponsor should issue a notice to the medical institution, Ethics Committee and municipal medical products regulatory authority and National Medical Products Administration that have accepted the application for the registration of this medical device, and describe the reasons;

(5) Any SAE once occurred should be investigated with the investigators promptly, necessary measures should be taken to ensure the safety and interests of subjects, and the SAE should be reported to the medical products regulatory authorities and health administrative authorities in a timely manner;

(6) The sponsor should bear the treatment cost and relevant economic compensation for the clinical trial-related injury or death of subjects, with the exception of damage due to the fault of medical institution and medical staff in the diagnosis and treatment.

20.2. Responsibilities of Study Site and Investigator:

(1) The study site should properly keep the records and basic documents of clinical trial according to the agreement with the sponsor;

(2) Fulfill the clinical trial protocol, report any deviation from the clinical trial protocol to the sponsor, and reach an agreement with the sponsor;

(3) Use devices according to the clinical trial protocol. Whether it is for devices or for the clinical trial protocol, any change must be reported to the sponsor;

(4) Ensure that personnel and facilities can carry out the clinical trial safely and effectively;

(5) Clinical trial personnel always have an appropriate number of subjects;

(6) Obtain the ICF;

(7) According to the national laws and regulations, the CRF should be recorded

in a timely manner, and its data should be consistent with the recorded data of the subjects;

(8) Record and report AEs and device defects to the sponsor according to procedures;

(9) Keep records of withdrawal of subjects, non-compliance with the physician's orders and any termination of clinical trial;

(10) Provide the clinical trial report to the sponsor in a timely manner together with the clinical study site, and bear legal responsibility for the correctness, clarity and reliability of the report after the completion of device use.

References

[1] Chinese Society of Neurology, Chinese Stroke Society. Chinese guidelines for diagnosis and treatment of acute ischemic stroke 2018 [J]. Chin J Neuro,2018,51 (9):666-682.

[2] Gao F，Xu AD. Chinese guidelines for endovascular treatment of acute ischemic stroke 2015 [J]. Chin J Stroke,2015.10(7):590-606.

[3] Cheng YM. Current status of thrombolytic therapy for acute ischemic stroke (review) [J]. Chinese journal of urban and rural enterprise hygiene,2012(6):25-28.

[4] Powers W J, Rabinstein A A, Ackerson T, et al. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association [J]. Stroke,2018,49(3):158.

[5] An-Ding X, Yong-Jun W, Wang D Z. Consensus statement on the use of intravenous recombinant tissue plasminogen activator to treat acute ischemic stroke by the Chinese Stroke Therapy Expert Panel [J]. Cns Neuroscience & Therapeutics,2013,19(8):543-548.

[6] Levy E I, Siddiqui A H, Annemarie C, et al. First Food and Drug Administration-approved prospective trial of primary intracranial stenting for acute stroke: SARIS (stent-assisted recanalization in acute ischemic stroke) [J], Stroke; a journal of cerebral circulation,2009,40(11):3552.

[7] Jonathan E, Lees K R, Patrick L, el al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials[J]. Lancet,2014,384(9958): 1929-1935.

[8] Asadi H, Dowling R, Yan B, el al. Advances in endovascular treatment of acute ischaemic stroke[J]. Internal Medicine Journal,2015,45(8):798-805.

[9] Zaidat O O. North American Solitaire Stent Retriever Acute Stroke registry: post-marketing revascularization and clinical outcome results. [J]. Journal of Neurointerventional Surgery,2014,6(8):584-588.

[10] Berkhemer O A, Fransen P S, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke [J], N Engl J Med,2015,372(1):11 -20.

[11] Campbell B C V, Mitchell P J, Kleinig T J, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection[J], N Engl J Med,2015,372(11): 1009-1018.

[12] Alakeson N, Flettt T, Hunti V, et al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke[J]. N Engl J Med,2015,49(2): 1019-1030.

[13] Saver J L, Goyal M, Bonafe A, et al. Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke[J]. N Engl J Med,2015,372(24):2285-2295.

[14] Jovin T G, Angel C, Erik C, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke[J]. New England Journal of Medicine,2015,372(24):2296-2306.

[15] Ferrell A S, Britz G W. Developments on the horizon in the treatment of neurovascular problems[J]. Surgical Neurology International,2013,4:S31-S37.

[16] Saver J L, Jahan R, Levy E I, el al. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomized, parallel-group, non-inferiority trial [J]. Lancet,2012,380(9849): 1241- 1249.

[17] Goyal M, Menon B K, Zwam W H V, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: A meta-analysis of individual patient data from five randomised trials[J]. Lancet,2016,387(10029): 1723-1731.

[18] Albers G W, Mp M, S K, et al. Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging [J]. N Engl J Med,2018,378(8):708.

[19] Nogueira R G, Jadhav A P, Haussen D C, et al. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct[J]. N Engl J Med,2017,378(I):a 1706442.

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 undertake that the EDC data will be true, valid and complete, and the electronic data signature will be completed on time.
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 accept monitoring, verification and inspection of the CRA and auditor authorized by the sponsor as well as regulatory authorities 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.

Comments of the investigator	
Approved	<signed> Signature: February 17, 2022

Comments of the sponsor	
Approved	<stamped> Signature (stamp): February 10, 2022

Comments of the medical device study sites	
Approved	<stamped> Signature (stamp): February 25, 2022

Appendix 1 List of Study Sites and Investigators

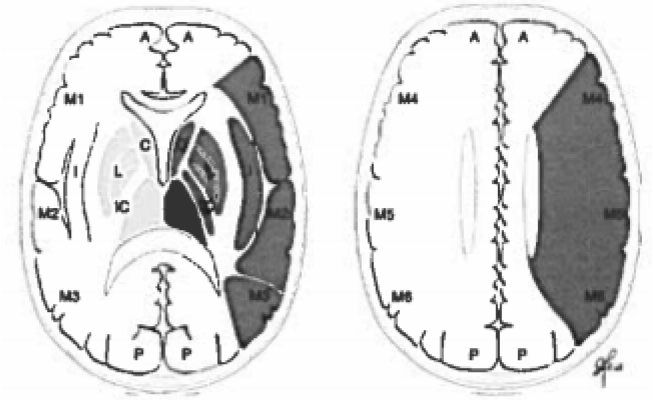
Clinical Study on Safety and Effectiveness of Ghunter Revascularization Device for Endovascular Treatment of Acute Ischemic Stroke

List of Study Sites and Investigators

Site #	Name of site	Investigator
01	General Hospital of Eastern Theater Command, PLA	Liu Xinfeng
02	The First Affiliated Hospital of USTC (Anhui Provincial Hospital)	Hu Wei
03	The Second Affiliated Hospital of Soochow University	Xiao Guodong
05	The First Affiliated Hospital of Nanchang University	Fang Pu
07	The First Affiliated Hospital of Wannan Medical College (Yijishan Hospital)	Zhou Zhiming
13	Ganzhou People's Hospital	Zeng Guoyong
15	Taiyuan Central Hospital	Wen Chao
17	Zhuhai People's Hospital	Cheng Guangsen
18	Jiangmen Wuyi Hospital of Traditional Chinese Medicine	Shi Qing
19	Central Hospital of Xiang Tan city	Yuan Guangxiong
20	Meizhou People's Hospital	Wei Tongguo
21	General Hospital of Northern Theater Command, PLA	Chen Huisheng
22	Jinan Central Hospital	Zhao Yanxin
23	Qingdao Center Hospital	Yuan Haicheng
24	Ganzhou Municipal Hospital	Liu Hanwen
25	Xinxiang Central Hospital	He Wenlong
26	Handan Central Hospital	Ma Wenqun

Appendix 2 ASPECTS Scale

Alberta Stroke Program Early CT Score (ASPECTS)



Subcortical structural area:	(1) Caudate nucleus (C)	(2) Lenticular nucleus (L)	(3) Internal capsule (IC)
Middle cerebral artery cortex:	(4) Anterior cortical area of middle cerebral artery (M1)	(5) Insular cortex (I)	
	(6) Lateral cortical area of middle cerebral artery insular (M2)	(7) Posterior cortical area of middle cerebral artery (M3)	
	(8) Middle cerebral cortex above M1 (M4)	(9) Middle cerebral cortex above M2 (M5)	
	(10) Middle cerebral cortex above M3 (M6)		

Appendix 3 mTICI Image Grading Criteria:

mTICI image grading criteria

Classification	Criteria
Grade 0	No perfusion
Grade 1	Trace flow through occluded segment with minimal or no perfusion
Grade 2a	Partial antegrade perfusion of less than 50% downstream ischemic area
Grade 2b	Partial antegrade perfusion of more than 50% downstream ischemic area
Grade 3	Complete antegrade perfusion of downstream ischemic area

Note: Perfusion is defined as capillary visualization or parenchymal staining

Appendix 4 mRS:

mRS

Score	Description
0	No symptoms at all
1	No significant disability; able to carry out all usual duties and activities, despite some symptoms
2	Slight disability; able to look after own affairs without assistance, but unable to carry out all previous activities
3	Moderate disability; requires some help, but able to walk unassisted
4	Moderately severe disability; unable to attend to own bodily needs without assistance, and unable to walk unassisted
5	Severe disability; requires constant nursing care and attention, bedridden, incontinent
6	Death

Appendix 5 NIHSS:

The National Institutes of Health Stroke Scale (NIH Stroke Scale, NIHSS)

Item	Scoring criteria
1a. Level of consciousness: The investigator must choose a response if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.	0 Alert; keenly responsive 1 Somnolence, but arousable by minor stimulation to obey, answer, or respond 2 Lethargic or slow in response, requires repeated stimulation to attend, or requires strong or painful stimulation to make movements (not stereotyped) 3 Stuporous; responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, and areflexia
1b. Level of consciousness questions: The patient is asked the month and his/her age. It is important that only the initial answer be graded. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier, or any other problem not secondary to aphasia are given a 1. Written responses will be available.	0 Answers both questions correctly. 1 Answers one question correctly. 2 Answers neither question correctly.
1c. Level of consciousness commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Only the first attempt is scored. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to him or her (pantomime), and the result scored. Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands.	0 Performs both tasks correctly. 1 Performs one task correctly. 2 Performs neither task correctly.
2. Gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis, score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or fields should be tested with reflexive movements, and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.	0 Normal 1 Partial gaze palsy gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present). 2 Forced deviation, or total gaze paresis is not overcome by the oculocephalic maneuver.

3. Visual: If the patient can see the finger on the side, record it as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia, is found. If patient is blind from any cause, score 3. If there is extinction, patient receives a 1, and the results are used to respond to item 11.	0 No visual loss 1 Partial hemianopia 2 Complete hemianopia 3 Bilateral hemianopia (blind including cortical blindness)
4. Facial palsy	0 Normal 1 Minor paralysis (flattened nasolabial fold, asymmetry on smiling). 2 Partial paralysis (total or near-total paralysis of lower face) 3 Complete paralysis of one or both sides (absence of facial movement in the upper and lower face).
5 and 6. Motor arm and motor leg: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine); hold the leg at 30 degrees (always tested supine). Score 1~4 if the arm falls before 10 seconds and the leg falls before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm.	Arm: 0 No drift; limb holds 90 (or 45) degrees for full 10 seconds. 1 Limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. 2 Some effort against gravity; limb cannot get to or maintain 90 (or 45) degrees. 3 No effort against gravity; limb falls rapidly. 4 No movement. 9 Amputation or joint fusion, explain: 5a Left arm; 5b Right arm
	Leg: 0 No drift; leg holds for full 5 seconds. 1 Leg falls by the end of the 5 second period but does not hit the bed. 2 Leg falls to bed by 5 seconds but has some effort against gravity. 3 No effort against gravity; leg falls to bed immediately. 4 No movement. 9 Amputation or joint fusion, explain: 6a Left leg; 6b Right leg
7. Limb Ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. In case of blindness, test by having the patient touch nose from extended arm position. Only in the case of amputation or joint fusion, score 9 and explain.	0 Absent 1 Present in one limb. 2 Present in two limbs, ataxia in: Right arm 1 = yes, 2 = no 9 Amputation or joint fusion, explain: Left arm 1 = yes, 2 = no 9 Amputation or joint fusion, explain: Right arm 1 = yes, 2 = no 9 Amputation or joint fusion, explain: Left leg 1 = yes, 2 = no 9 Amputation or joint fusion, explain: Right leg 1 = yes, 2 = no

8. Sensory: Sensation or grimace to pinprick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas [arms (not hands), legs, trunk, face] as needed to accurately check for hemisensory loss. A score of 2 is given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will, therefore, probably score 1 or 0. The patient with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in a coma (1a = 3) are scored 2.	0 Normal 1 Mild-to-moderate sensory loss; patient feels pinprick is less sharp or is dull; or there is a loss of pinprick, but patient is aware of being touched. 2 Severe to total sensory loss; patient is not aware of being touched in the face, arm, and leg.
9. Language: Naming and reading tests. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in a coma will automatically score 3 on this item. The examiner must choose a score for the patient with stupor or limited cooperation, but a score of 3 should be used only if the patient is mute and follows no one-step commands.	0 Normal 1 Mild-to-moderate aphasia; some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. 2 Severe aphasia; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited. 3 Mute, global aphasia; no usable speech or auditory comprehension.
10. Dysarthria: Read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barriers to producing speech, the examiner should record the score as 9 and clearly write the explanation for this choice. Do not tell the patient why he or she is being tested.	0 Normal 1 Mild-to-moderate dysarthria; patient slurs at least some words and, at worst, can be understood with some difficulty. 2 Patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric. 9 Intubated or other physical barrier, explain:
11. Neglect: If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may also be taken as evidence of abnormality.	0 Normal 1 Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 Profound hemi-inattention or extinction to more than one modality; does not recognize own hand; or orients to only one side of space.