Informed Consent Form (ICF)

Name of investigational medical device:	mechanical thrombectomy system
Specification/Model of investigational device:	FG-004-001-CH, FG-004-002-CH, FG-004-003-CH, FG-004-014-CH, FG-004-016-CH, FG-004-018-CH, FG-004-035-CH, FG-004-037-CH, FG-004-039-CH
Sponsor:	NeuroVasc Technologies Inc.
Agent:	Neurovasc (Weihai) Medical Device, Ltd.
Name of clinical trial protocol:	A prospective, multicenter, randomized controlled clinical study to evaluate the safety and efficacy of mechanical thrombectomy system for endovascular treatment of acute ischemic stroke
Clinical trial protocol No.:	NWSKLC-202001
ICF version No.:	V1.1
ICF version date:	2020-11-13
Clinical trial institution:	Henan Provincial People's Hospital
Principal investigator:	Li Tianxiao

Distinguished sir/madam,

We would like to invite you to participate in a clinical trial, "A prospective, multicenter, randomized controlled clinical study to evaluate the safety and efficacy of mechanical thrombectomy system for endovascular treatment of acute ischemic stroke", sponsored by NeuroVasc Technologies Inc. The study protocol number is NWSKLC-202001. The clinical study should be approved by the Ethics Committee of Henan Provincial People's Hospital. The study will be carried out by Li Tianxiao, Professor in the Department of Cerebrovascular Disease. The study should be performed upon the approval of Human Genetic Resource Administration of China. You are invited to participate in this study as you are eligible to be enrolled in the acute ischemic stroke study. Your study doctor or investigator will fully explain the contents of the informed consent form to you.

The following items describe the study background, purpose and method of the investigational medical device, benefits and risks or inconveniences that may arise from the study process, and your rights and interests. Please read them carefully before you participate in the clinical trial. The informed consent form provides you with information that can help you decide whether to participate in this clinical trial. The study doctor will answer your questions about the test product and the study. When your doctor or investigator discusses the informed consent form with you, you can always ask the investigator questions in case of any doubt or any content that cannot be fully understood, so as to ensure full understanding of related contents. Please inform us if you are participating in other drug or medical device trials/studies.

Your participation in this trial is based on voluntary principle. Please sign the statement in the informed consent form after reading the following data, if you participate in the clinical study of your own accord.

The background, purpose, process and other important information of this study are as follows:

I. Background

Cerebral stroke is one of the diseases that cause the greatest damage to human beings. Acute ischemic stroke accounts for 60%-80%.

The Report on the Third National Retrospective Sampling Survey of Death Causes in China showed that acute ischemic stroke has become the first cause of death in China with the aging of the population and 75% of survivors still had different degrees of disability. Cases aged over 40 years with cerebral stroke in China have exceeded ten million, showing a tendency of younger patients, of which cases with ischemic stroke account for 80%. The disease has constituted heavy social and economic burdens. At present, the intravenous recombinant tissue plasminogen activator (rt-PA) is an effective approach to treating acute ischemic stroke. However, the treatment time window is narrow, only 4.5 hours, so patients beyond the time window cannot be treated in time. In addition, for stroke caused by large vessel occlusion and cardiogenic embolism, the recanalization rate using intravenous thrombolysis is low and the therapeutic effect is poor. With the development of interventional materials and technologies in recent years, endovascular treatment has significantly improved the recanalization rate of occluded vessels and expanded the treatment time window, showing a good application prospect. Mechanical thrombectomy and emergency angioplasty were developed relatively late. As to advantages, these techniques can avoid or reduce the use of thrombolytic drugs and have a higher recanalization rate for large vessel occlusion and cardiogenic embolic stroke, which become important treatments for acute ischemic stroke. "Mechanical thrombectomy" attracts widespread attention due to many theoretical advantages including rapid recanalization, low bleeding conversion rate, and extended time window of interventional therapy for stroke. For thrombectomy devices, a temporary stent is used to capture the thrombus and restore blood flow by moving the thrombus through squeezing against peripheral vessel wall. In stent withdrawal, the thrombus is captured into the stent space and removed with the stent. The treatment has advantages of navigation and rapid recanalization, and lower risk of long-term complications. Therefore, the invention of thrombectomy devices is a great advance in the endovascular treatment of stroke.

The current treatment results have demonstrated that the endovascular treatment of mechanical thrombectomy can bring additional benefits, including significantly decreased disability rate, faster and more complete reperfusion, and increased survival rate and functional independence in patients with ischemic stroke. However, successful recanalization is very difficult when the pathway vessel is seriously tortuous. At the turn of vessels, the stent will twist, collapse, and lose its ability to catch the thrombus due to structural changes. Since 2004, the US Food and Drug Administration (FDA) has approved Merci™ Retrieval and Penumbra Aspiration Systems™ as the first generation of mechanical thrombectomy devices successively. In 2012, FDA approved Solitaire™ and Trevo™ as thrombectomy devices.

The mechanical thrombectomy system manufactured by NeuroVasc Technologies Inc. is of multi-section design. The system still remains stretched even when being pulled and twisted and can hold onto the thrombus when passing through the turns of vessels. In addition, when the multi-section stent loaded with the thrombus is withdrawn, its distal end remains open, which is helpful to prevent broken thrombus from escaping to the distal end.

The mechanical thrombectomy system has been subject to the type test in the National Institutes for Food and Drug Control and granted the test qualification report. Furthermore, the animal experimental studies have been completed for the product. Based on the above conditions, this clinical study is planned to be performed.

II. Name and Purpose

(I) Study name:

A prospective, multicenter, randomized controlled clinical study to evaluate the safety and efficacy of mechanical thrombectomy system for endovascular treatment of acute ischemic stroke

(II) Purpose

To verify the safety and efficacy of the mechanical thrombectomy system manufactured by NeuroVasc Technologies Inc. for endovascular treatment of patients with acute ischemic stroke.

III Scope, Method and Related Information:

(I) Number of subjects:

The study will be conducted in multiple clinical trial institutions in China. The competitive enrollment model will be adopted across China. A total of 268 subjects are planned to be enrolled,

including 238 subjects for the randomized controlled study and 30 subjects for the small sample study. It is expected that 30 subjects are enrolled in the randomized controlled study

and the small sample study respectively in our center.

(II) Scope and method:

This trial is mainly to verify the safety and efficacy of the mechanical thrombectomy system manufactured by NeuroVasc Technologies Inc. for the surgery for intracranial vascular acute stroke and evaluate its usability.

The study consists of two parts: (1) Patients with acute ischemic stroke within 8h of symptom onset are enrolled in the randomized control study. Based on randomized results, thrombectomy is carried out with the experimental device or the control device. (2) Patients with acute ischemic stroke within 8-24 h of symptom onset are included in the small sample study and receive thrombectomy with the experimental mechanical thrombectomy system.

1. Randomized controlled study:

In this part, a prospective, multicenter, randomized controlled, non-inferior study is designed. Subjects who meet the inclusion criteria within 8 hours after symptom onset are enrolled and randomized into the experimental group and the control group at a ratio of 1:1 through central randomization system.

① Experimental group: mechanical thrombectomy system manufactured by NeuroVasc Technologies Inc. (the product is not commercially available yet).

② Control group: intracranial stent retriever (trade name: Solitaire FR) approved by the National Medical Products Administration (NMPA).

2. Small sample study:

Subjects who meet the inclusion criteria within 8-24 hours after symptom onset are enrolled. There is currently no appropriate thrombectomy device for the indications of such subjects, so no control group is established.

IV. Process and Period:

Subjects who are successfully enrolled after screening will receive intravascular thrombectomy, and related examinations and follow-ups 24±6 hours after surgery and 7±2 days after surgery (or before discharge). Further outpatient/telephone follow-up will be carried out 90±14 days after surgery. The doctors will ask about drug use and the subjects' general health condition. Specific contents are as follows:

(I) Subject screening and preoperative routine examination

If you are willing to participate in this study, your doctor will review your past and current treatment, including medicines you are taking, past medical history and history of present illness. In your participation in this study, the doctor will ask you to cooperate in related examinations. These examinations are part of routine medical examinations and they are also required even if you do not participate in the study. The examples include CT/CTA or MR, MRI-DWI or CTP-rCBF, physical examination, blood test, pregnancy test (if necessary) (if you are female patients, this test should be performed when pregnancy signs are suspected during screening).

1. Signature of the informed consent form by the subject or guardian.
2. Collection of medical history/demographics.
3. Vital sign examinations.
4. Laboratory examinations: blood routine, chemistry panel (only creatinine and random blood glucose), and pregnancy test if necessary.
5. ECG, brain CT (CTA) or MR (MRA), MRI-DWI or CTP-rCBF (small sample study).
6. NIHSS score and mRS score.
7. Review of inclusion/exclusion criteria.
8. Concomitant medication record: thrombolytic therapy (if any).

(II) Inclusion/exclusion criteria

1. Inclusion criteria (you should meet all of the following conditions)

(1) Randomized controlled study:

① Clinical symptoms and signs consistent with acute ischemic stroke;

② mRS score before this acute ischemic stroke ≤ 1;

③ 18 years ≤ age ≤85 years;

④ 6≤ NIHSS score ≤30;

⑤ Expected to complete arterial puncture within 8 hours of onset;

⑥ Patients whose imaging examination should meet MR/CT: infarction core volume < 70 ml; or whose ASPECTS score is 6 to 10;

⑦ DSA radiography findings: ICA (intracranial segment), MCA (M1 or M2) or ACA (A1 or A2) occlusion;

⑧ Subjects who can receive IV-tPA treatment should receive IV-tPA and it is required that the investigators confirm that the subjects have received/are receiving the correct dose of IV-tPA within 4.5 hours of stroke onset;

⑨ Subjects or their Agents that are able to understand the purpose of the trial, voluntarily participate and sign written informed consent forms and receive follow-up.

(2) Small sample study:

① Clinical symptoms and signs consistent with acute ischemic stroke;

② mRS score before this acute ischemic stroke ≤ 1;

③ 18 years ≤ age ≤85 years;

④ 6≤ NIHSS score ≤30;

⑤ Expected to complete arterial puncture within 8-24 hours of onset;

⑥ Patients whose imaging should meet "clinical-image mismatch" (mismatch between baseline NIHSS score and core infarct volume on MRI-DWI/CTP-rCBF), defined as:

a: 80-85 years old (inclusive), NIHSS score ≥ 10, core infarction volume < 21 ml;

b: < 80 years old, NIHSS score ≥ 10, core infarction volume < 31 ml;

c: < 80 years old, NIHSS score ≥ 20, 31 ml≤ core infarction volume <51 ml.

⑦ DSA radiography findings: ICA (intracranial segment), MCA (M1 or M2) or ACA (A1 or A2) occlusion;

⑧ Subjects who can receive IV-tPA treatment should receive IV-tPA and it is required that the investigators confirm that the subjects have received/are receiving the correct dose of IV-tPA within 4.5 hours of stroke onset;

⑨ Subjects or their Agents that are able to understand the purpose of the trial, voluntarily participate and sign written informed consent forms and receive follow-up.

2. Exclusion criteria (randomized controlled study and small sample study)

(1) Life expectancy possibly less than 90 days;

(2) Pregnant or lactating women, or those who are planned to be pregnant in the next 90 days;

(3) Allergy to contrast agent, nickel-titanium metal or alloy; and other materials;

(4) Renal failure suspected. Renal failure is defined as serum creatinine > 3.0 mg/dL (264 μmol/L) or glomerular filtration rate (GFR) < 30 ml/min;

(5) Severe sustained hypertension (systolic blood pressure > 185 mmHg or diastolic blood pressure > 110 mmHg) that cannot be controlled by medication;

(6) Patients with active bleeding or known bleeding tendency;

(7) Platelet count<50×10^9/L;

(8) RBG <50mg/dL (2.78mmol/L) or >400mg/dL (22.20mmol/L);

(9) Subjects with occlusion in multiple vascular areas (e.g. bilateral anterior circulation or anterior/posterior circulation);

(10) Intracranial hemorrhage or massive cerebral infarction suggested by CT or MR (infarct volume ≥ 70ml or infarct volume > 1/3MCA blood supply area);

(11) Failure to obtain accurate results of NIHSS assessment at the onset of stroke;

(12) Radiography suggesting occlusion of intracranial artery due to arterial dissection or arteritis;

(13) DSA angiography suggesting tortuous vessel path, making investigational/control device difficult to reach the target location or be recovered;

(14) Presuming as embolism due to septic emboli or bacterial endocarditis;

(15) CT or MR suggesting intracranial tumor (except for tentorial meningiomas);

(16) Treatment with any thrombectomy device or other intra-arterial (neurovascular) therapy within the last three months;

(17) Unable to complete 90±14 days of follow-up;

(18) Stroke within the past 3 months;

(19) Previous clinical manifestations of AVM rupture or aneurysm rupture;

(20) Serious organic diseases in heart, lung, kidney, etc.;

(21) Patients participating in other drug or medical device clinical trials but failing to complete the primary study endpoint;

(22) Other conditions not suitable for inclusion judged by investigators.

You cannot participate in the study if meeting any of the following exclusion criteria.

(III) Post-operation examination and clinical follow-up

1. Post-operation to 24±6 hours

(1) Vital signs;

(2) Brain CT (CTA) or MR (MRA);

(3) NIHSS score

(4) Adverse event record;

(5) Concomitant medication record (antiplatelet, anticoagulant and statin drugs).

2. 7±2 days after operation or before discharge (whichever is earlier)

(1) Laboratory examination: blood routine, chemistry panel and coagulation profile;

(2) NIHSS score;

(3) Adverse event record;

(4) Concomitant medication record (antiplatelet, anticoagulant and statin drugs).

3. 90 days after operation (± 14 days)

(1) mRS score;

(2) Adverse event record;

(3) Concomitant medication record (antiplatelet, anticoagulant and statin drugs).

V. Source of Funds and Potential Conflict of Interest

Neurovasc (Weihai) Medical Device, Ltd. is the organizer and agent of the clinical study. The Company shall pay the relevant costs of the clinical study, without any conflict of interest with other institutions or organization.

VI. Possible Benefits, Risks and Discomforts of Subjects

(I) Possible benefits to subjects

You may be benefited from the study, but we cannot guarantee improvement in your health condition, and we hope future subjects with the same medical conditions as you may be benefited from the information obtained from your participation in the study. Whether participating in the study or not, you will receive reasonable examination and treatment.

(II) Possible risks and discomfort

When feeling any discomfort during the study, please immediately report to your physician. This is very important. The study physician may arrange for you relevant examination, adjust the drug dosage, or add other drugs for treatment or controlling the medical condition. If you think or your study physician thinks you are not suitable to participate in the study, you may withdraw from the study.

1. Potential risks from investigational product and/or surgery:

The Sponsor shall ensure any risk related to the product is within the acceptable range, according to Medical device - Application of risk management to medical devices. The potential risks for this clinical trial are basically the same as those for receiving normal intracranial artery thrombectomy, including but not limited to the following symptoms:

- Adverse reactions to antiplatelet/anticoagulant drugs or contrast agent
- Air embolus
- Arterio-venous fistula
- Change of mental state
- Death
- Device deformation, folding, rupture or malfunctions
- Distal embolism not covered before
- Hematoma and hemorrhage of puncture position
- Infection
- Intracranial hemorrhage
- Focal ischemia

- Neurological dysfunction
- Neurological deterioration including stroke and death
- Vessel perforation and dissection
- Postoperative hemorrhage
- Pseudoaneurysm formation
- Thrombus
- Vascular occlusion
- Vasospasm

2. Risks and discomfort related to blood sampling

The risks from blood sampling from arms include transient discomfort and/or cyanosis. With low possibility, though, infection, excessive bleeding, blood coagulation or syncope may occur.

3. Reproductive risk:

For female subjects: If necessary, pregnancy test may be conducted for females of childbearing age during screening, so if you are in lactation, pregnancy or you think you may be pregnant or are preparing for pregnancy, you cannot participate in the study. If you are in pregnancy or lactation, potential risks that are uncertain now may be caused to you and your child.

For male subjects: Currently no data is available to demonstrate the impact on reproduction from the study, while it cannot be excluded potential damage may be caused to your child conceived during the study. With low possibility, though, such damage is beyond estimation now.

Therefore, we strongly recommend you not to prepare conception during the study. If you are/your wife is pregnant or might be pregnant during your participation in the study, please immediately inform the study physician. This is very important. The study physician may therefore adjust your drug administration, and if necessary, terminate your participation, discuss with you on what you should do, and ask you about pregnancy and the child after the end of the study.

4. Other risks

Administration of aspirin, cilostazol, clopidogrel, ticagrelor and other antiplatelet drugs may cause the risks of gastro-intestinal discomfort, blood coagulation disorder, allergy, and thrombopenia. In addition, there may be some unpredicable risks, discomforts, drug interaction or adverse reactions.

VII. Alternative Diagnostic and Treatment Approaches:

You may choose not to participate in the study, and it will not cause any adverse impact on your conventional treatment. Considering your health condition, the following conventional diagnostic and treatment approaches are now available, apart from the study:

(1) Arterial thrombolysis;

(2) Emergency angioplasty;

(3) Other marketed mechanical thrombectomy devices and other medical products.

VIII. Diagnostic and Treatment Items and Other Subsidies Available During Trial:

When participating in the trial, you need not pay any additional cost for examination. According to the requirements of the study, the costs for the thrombectomy devices (mechanical thrombectomy system or Solitaire FR intracranial stent retriever) and related laboratory examination (once) in the study shall be paid by the Agent Neurovasc (Weihai) Medical Device, Ltd.

Laboratory examination after operation to 7±2 days after operation/before discharge, including:

(1) Vital signs (after operation to 24±6 hours after operation): Blood pressure, pulse (heart rate), respiration and temperature.

(2) Blood routine: White blood cell count, red blood cell count, platelet count and hemoglobin.

(3) Chemistry panel: Alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, direct bilirubin, creatinine, random blood glucose (including blood glucose testing in any case).

(4) Cruor examination: Activated partial thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT), and international normalized ratio of prothrombin (INR).

To better protect your rights and interest, we will provide you with RMB200 as the blood sampling subsidy for this examination. Furthermore, we will arrange a phone call or outpatient clinical follow-up 90 days (±14 days) after operation, and you shall come to the hospital for the follow-up, for which we shall provide additionally RMB200 as the traffic subsidy.

IX. Treatment and Economic Compensation for Damage Related to Trial:

The Agent of the study Neurovasc (Weihai) Medical Device, Ltd. has covered the insurance for subjects participating in the study, and you will receive the timely treatment and compensation in case of any damage related to the clinical trial, even if you withdraw from the study during the follow-up. Upon any damage related to the investigational product, the insurance company is required to provide relevant compensation according to legal requirements, and when the compensation is lower than the deductibles or exceeds the indemnity limit, the shortage shall be on account of Neurovasc (Weihai) Medical Device, Ltd.

X. Confidentiality of Medical Records:

Your medical records shall be kept at the clinical trial institution. The Investigator, competent authorities and the ethics committee are allowed to access your medical records.

Any open report related to the study results shall not disclose your personal identity. We shall use all reasonable efforts to protect the privacy of your personal medical information to the extent permitted by law.

XI. Voluntary and Privacy Principles

1. Voluntary principles

Whether you are fully voluntary to participate in the study? If so, we hope you can hold on and complete the study; but, you may choose to withdraw from the study at any time without any loss of your benefits. You may choose not to participate in or withdraw from the study midway at any time without giving any reason, and you will not meet with any discrimination or retaliation, or any impact on your medical benefits, rights and interests.

If you decide to withdraw from this study during the study, we encourage you to consult with your study physician first. Considering you safety, our study staff shall provide you with a health evaluation upon your withdrawal from the study, and possibly another relevant examination after withdrawal.

2. Privacy principles

With the understanding and assistance of you and other subjects, the results of this study may be published in medical journals, but we will keep your study records confidential pursuant to relevant laws. The personal information of you as a study subject will be kept strictly confidential, and will not be disclosed as required by laws. If necessary, the medical administration authorities, the ethics committee of the hospital and other relevant staff may get access to your data as required.

XII. Responsibilities of Subject

If you choose to participate in this study, you need to:

1. Provide true information of accurate past medical history and current physical condition;
2. Tell the study physician any discomfort and health problem of you during the study;
3. During the study, follow the medical advice and requirements to receive examination and administer relevant drugs;
4. Disclose whether you are participating in other trials or studies (on drugs and medical devices) and relevant information;
5. Follow the instruction of the study staff and study physician, and ask them about the same when you have any question;
6. Assist the study physician to receive the phone call or outpatient follow-up visit 90±14 days after operation according to the required window time.
7. Upon follow-up, inform the study personnel what drugs you actually administered during the study (including discontinuing and adding drugs).

XIII. Criteria for Termination of Study

For your safety, you may need to withdraw from the study under any of the following circumstances:

1. If it finds that your rights and interests cannot be guaranteed, the ethics committee may suspend or terminate the clinical trial at any time in writing;

2. The clinical trial institution and investigators may propose to suspend or terminate the clinical trial when they find that the risks exceed the possible benefits, or the results sufficient to determine the safety and efficacy of the investigational medical device have been obtained;

3. When finding any matter that may affect the safety of the subjects, or if implementation of the trial may change the Ethics Committee's approval for continuing such trial, the sponsor shall immediately notify the investigator to terminated the study.

XIV.Relevant Consultation

You can learn about the progress related to the study at any time, and if you have any questions related to the study (e.g. rights and interests of the participant), or you have any discomfort or injury during the study, please contact (Investigator) _____at _____(Tel or mobile No.); and if you have any questions related to your rights and interests,

contact the ethics committee of the Site at: _____.

Subject Informed Consent Statement

I have carefully read through the Informed Consent Form, and been given the opportunity to ask questions, and all the questions have been answered. I understand participating in the trial is subject to one's own choice, and I may choose not to participate in this study, or withdraw from this study at any time after notifying the investigator without discrimination or retaliation, and my medical benefits, rights and interests will not be affected.

If I need other diagnosis/treatment, or if I failed to comply with the study plan, or if I have any other sound reason, the Investigator can terminate my participation in the clinical trial.

I am willing to participate in the clinical trial "A prospective, multicenter, randomized controlled clinical study to evaluate the safety and efficacy of mechanical thrombectomy system for endovascular treatment of acute ischemic stroke", sponsored by NeuroVasc Technologies Inc. I will receive a signed copy of the “Informed Consent Form”.

Signature of the subject: _____ **Date:** _____

Tel: _____

Note: If the subject cannot sign the informed consent due to incapacity and other reasons, it will be signed by the guardian.

Signature of guardian: _____ **Date:** _____

Relationship with subject: _____ **Tel:** _____

Reason why the subject cannot sign: _____

Statement of Investigator

I confirm that I have accurately informed the subject of the contents of the Informed Consent Form and answered the questions raised by the subject, and the subject is willing to participate in this clinical trial.

Signature of the Investigator: _____ **Date:** _____

Tel: _____