SUCCESS STUDY

SUccess in **C**omaneci-assist **C**oils **E**mbolization **S**urveillance **S**tudy

SURVEILLANCE PLAN

PS190001

ClinicalTrials.gov ID: CT04518670

Protocol #: CLN-Co-001

VERSION: 2.0

DATE: March 6, 2023

Study Sponsor:
Rapid Medical
P.O. Box 337
Carmel Building
Yokneam 2069205
Israel

SURVEILLANCE PLAN (SP) APPROVAL

Study Title: SUCCESS Study

CIP Version: 2.0

CIP Date: March 6, 2023

Signatures:

Dr. Walid Haddad
VP Clinical Operations
Rapid Medical

Sponsor Representative

Date

Ricardo Hanel, Baptist Neurological Institute, Baptist Health System Jacksonville, FL

Coordinating Principal Investigator

Date

Jason Davies, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, New York

Co-Coordinating Principal Investigator

SP SIGNATURE PAGE

Study Title: SUCCESS Study

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I have read the Surveillance Plan and agree to adhere to the surveillance plan contained herein. Deviations from the surveillance plan will not be made prior to sponsor notification, except when necessary to protect the safety, rights, or welfare of study Subjects.

I agree to conduct or supervise the conduct of the described Surveillance and ensure all participating investigators and research staff are appropriately trained regarding the study conduct prior to participating in any study related activities.

I will ensure that the requirements relating to obtaining informed consent and Institutional Review Board (IRB) review and approval, as they pertain to 21 CFR Part 50, ICH E6 are met.

I agree to maintain adequate and accurate records in accordance with 21 CFR 812.140 and to make those records available for inspection in accordance with 21 CFR 812.145 and ICH E6.

I will ensure that the IRB complies with the requirements of 21 CFR Part 56 and ICH E6 and will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB any changes in research activity and all unanticipated problems involving risks to human Subjects or others. Additionally, I will not make any changes in research without IRB approval, except where necessary to eliminate apparent immediate hazards to human Subjects.

I agree to comply with all other clinical investigator obligations and pertinent requirements in 21 CFR Part 812 and ICH E6.

_____

Site Principal Investigator (please print or use stamp)

_____ _____

Site Principal Investigator Signature Date

LIST OF ABBREVIATIONS

ADE	**Adverse Device Effect**
AE	**Adverse Event**
A-P	**Anterior-Posterior**
CFR	**Code of Federal Regulations**
CIP	**Clinical Investigation Plan**
CRO	**Clinical Research Organization**
CTA	**Clinical Trial Agreement**
CT	**Computed Tomography**
CV	**Curriculum Vitae**
DSA	**Digital Subtraction Angiography**
DSMB	**Data Safety Monitoring Board**
eCRF	**Electronic Case Report Form**
eIC	**electronic Informed Consent**
EDC	**Electronic Data Capture**
EVT	**Endovascular Treatment**
FDA	**Food and Drug Administration**
GCP	**Good Clinical Practice**
IA	**Intracranial Aneurysm**
ICF	**Informed Consent Form**
ICH	**Intracranial Hemorrhage**
ID	**Identification**
IFU	**Instructions for Use**
INR	**International Normalized Ratio**
IRB	**Institutional Review Board**
ISO	**International Organization for Standardization**
LAR	**Legally Authorized Representative**
MDR	**Medical Device Reporting**
MRI	**Magnetic Resonance Imaging**
mRS	**Modified Rankin Score**
NIH	**National Institutes of Health**
NIHSS	**National Institutes of Health Stroke Score**
PI	**Principal Investigator**
PT	**Prothrombin Time**
PTT	**Partial Thromboplastin Time**
RFA	**Rankin Focused Assessment**
SAE	**Serious Adverse Event**
SADE	**Serious Adverse Device Effect**
sICH	**Symptomatic Intracranial Hemorrhage**
SOC	**Standard of Care**

PROTOCOL SUMMARY
Postmarket Surveillance Plan (PS190001)
-SUCCESS Study-

Title	**SU**ccess in **C**omaneci-assist **C**oils **E**mbolization **S**urveillance **S**tudy
Short title	SUCCESS Study
Sponsor	Rapid Medical
Coordinating Principal Investigators	Ricardo Hanel, Baptist Neurological Institute, Baptist Health System Jacksonville, FL Co-Investigator: Jason Davies, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, New York
Product	Comaneci Embolization Assist Device
Objective	The objective of the Postmarket Surveillance Plan is to assess safety and performance as used in postmarket clinical practice in the U.S.
Study Design	This study is a multicenter, single arm, open, prospective, postmarket safety surveillance in up to 30 US centers
Device Description and Intended Use	The Comaneci Embolization Assist Device is indicated for use in the neurovasculature as a temporary endovascular device used to assist in the coil embolization of wide-necked intracranial aneurysms with a neck width ≤ 10 mm. A wide-necked intracranial aneurysm (IA) defines the neck width as ≥ 4 mm or a dome-to-neck ratio < 2. The Comaneci is comprised of a collapsible, fully retrievable, fine wire construction mounted on a wire shaft that expands to comply with the vessel diameter. It is delivered through a neurovascular microcatheter. The Comaneci is provided with a 3.5 French (F) peelable loading sheath.
Endpoints	**Safety** • Periprocedural events*: Rates of all adverse events occurring within 24 hours post-procedure and hospital discharge status. • All adverse events at discharge and up to 30 days post procedure. • Functional status at discharge and 30 days assessed using the modified Rankin Scale (mRS). **Secondary safety endpoint:** evaluation of the extent of any relationship between adverse event rate to operator experience. (*) Including vessel perforation or dissection, intracranial aneurysm rupture, stroke, hemorrhage, death, inability to deploy or remove the device, and coil entanglement **Efficacy**

	• Successful intracranial aneurysm occlusion (measured by Raymond Roy classification I or II) at the end of procedure, using digital subtraction angiography (DSA). • Successful intracranial aneurysm (IA) occlusion, that is a stable IA occlusion, measured by Raymond Roy classification I or II taken at 6 months (± 21d) post procedure without the need for re-treatment of the target IA, using DSA. • Good clinical outcome- mRS shift @ 6 months (change @ 6 months from pre procedure) and tetrachotomized (0,1, 2, 3-6) mRS analysis.
Number of Subjects: Surveillance is to continue until complete data on the deployment of 90 devices with complete 30-day patient status are obtained	Number of Study Centers: Up to 30 centers total in the US
Population	The Postmarket Surveillance Study will include male or female patients with wide-necked ruptured and/or unruptured intracranial aneurysms that may require adjunctive assistance with coil embolization during the surgical procedure.
Inclusion Criteria	In order to assure that the probable benefits outweigh the probable risks for the Comaneci Embolization Assist Device, as indicated in the IFU, the subjects must meet all of the following inclusion criteria: 1. Patient has a documented intracranial ruptured or unruptured aneurysm, suitable for embolization by coils. 2. Patient is considered for treatment with coil embolization assisted by the Comaneci Device for wide-necked intracranial aneurysms with neck width ≤ 10 mm. A wide-necked intracranial aneurysm is defined by the neck width as ≥ 4 mm or a dome-to-neck ratio < 2. 3. A signed informed consent by the patient or legally authorized representative
Exclusion Criteria	Patient should be treated by the Comaneci device in accordance with the approved device label. (i.e. doesn't meet the contraindication criteria, as described in the IFU): 1. Patient with known hypersensitivity to nickel-titanium
Study Duration	Enrolment: 30 months Follow-up period: 180 days
Committees and Core lab	• DSMB – Data Safety Monitoring Board • Imaging Core Lab- UCLA

Statistical Analysis	The rates of all adverse events occurring within 24 hours post procedure, hospital discharge status and after discharge for all opened devices at each participating clinical site during the surveillance period will be summarized. The numbers of individual adverse events of each type and the per subject incidence rate for each type of adverse event will be determined and reported along with 90% two-sided exact binomial confidence intervals. Separate event counts and incidence rates with corresponding confidence intervals will be summarized for adverse events determined to be serious, device-related, serious and device-related, procedure-related, serious and procedure-related, and severe. Listings for all adverse events will be compiled that provide full descriptions of each adverse event including determination of the severity, seriousness, and relationship to the device or procedure. Discharge status will be described with counts and percentages. Effectiveness at six months will be descriptively summarized in terms of the number and percentage of subjects achieving successful aneurysm occlusion measured by Raymond scale grade I and II and by clinical outcome as measured by mRS shift analysis comparing preprocedure mRS (up to 24 h prior to treatment) with 6 month mRS. In addition, tetrachotomized (0,1, 2, 3-6) mRS analysis will also be performed. mRS will also be evaluated at discharge and 30 days. Successful aneurysm occlusion will also be evaluated at the end of procedure. Stability of occlusion will be evaluated by comparing the two angiographic studies that are 6 months apart. The distribution of scores will be summarized by counts and percentages. If only three month Raymond scale value is available but not the six month, the three month value will be used in these analyses. Similarly, the last available earlier mRS values will be used if the six month value is not available.

Schedule of Events

Elapsed time/Study procedures	Baseline/ Procedure	24 hours (-6/+12)	Discharge if different than 24 hours (-6/+12)	30 (±7) days	180 (±21) days**
Informed Consent	X				
Demographics	X				
Medical History and Concomitant Medications	X				
Brain CT Scan	X	X*			
Vital Signs	X				
mRS score+	X		X	X	X
NIHSS	X			X	
Clinical Laboratory	X				
Raymond scale	X***				X***
Intraoperative data	X				
Prior/concomitant medications	X	X	X	X	X
Adverse Events	X	X	X	X	X

(*) If performed as a standard of care any time up to 24 hours post procedure

(**) Will be collected if performed also at 90 (±14) days as a standard of care.

(***) Post-procedure and 6 months imaging should use Digital Subtraction Angiography (DSA) for Raymond scale assessments.

(+) If in-person visits are not possible, mRS assessments may be performed remotely by structured telephone interviews.

Summary of Surveillance Plan Changes

Version History	Effective Date
1.0	June 29, 2020

Version 2.0, March 6, 2023

Section	Change From	Change To	Rationale for Change
Synopsis, section 6, section 8.1	Sample size 120	Sample size 90	The primary effectiveness endpoint is successful intracranial aneurysm occlusion (measured by Raymond Roy classification I or II) at the end of procedure, using digital subtraction angiography (DSA). The performance goal (PG) for evaluating effectiveness is based on outcomes as reported in the Comaneci de novo, which was successful aneurysm occlusion of 79.7%. With a hypothesized true incidence rate of 82.6% for successful intracranial aneurysm occlusion at the end of procedure and desired power of ≥ 80%, using a normal approximation test with a nominal 0.025 one-sided significance level (equivalent to a two-sided alpha=0.05), the required evaluable sample size for primary efficacy is 90 evaluable patients with a power of 80%.
Section 5.1	No maximum of enrolled subjects in each clinical center.	No more than 13 subjects should be enrolled at each clinical center.	In order to ensure reasonable patient diversity and user diversity.
Synopsis	Study duration: enrollment 24 months	Study duration: enrollment 30 months	To reflect the actual rate of patients' enrollment

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1. INTRODUCTION AND BACKGROUND

1.1 Background

An aneurysm is an abnormal local dilatation in the wall of a blood vessel, usually an artery, due to a defect, disease, or injury. A rupture is the main risk associated with an aneurysm. Other less common risk is thromboembolic events. A ruptured aneurysm can lead to bleeding, serious injury and death. This risk increases as the aneurysm increases in size[1].

Aneurysms are particularly risky when they occur in intracranial blood vessels. A ruptured aneurysm in the brain is one of the most common cause of hemorrhagic stroke; which is a serious medical condition often leading to severe neurological deficit or death (Two-thirds of patients with aneurysm rupture either die or have a disabling neurological deficit[2]).

The incidence of intracranial aneurysms (IAs) is estimated to be between 1.8% and 2%[3], a number that is supported by recent MRI investigations[4]. The yearly rupture rate for IAs was calculated to be as low as 0.05%[5]. Recent publications have raised the risk figure to 1.3-1.4%[6,7].

Intracranial aneurysms can be classified using several schemes. The most obvious division is considering the ruptured and unruptured lesions separately. With respect to morphology, aneurysms are classified as saccular or non-saccular. Saccular aneurysm refers to any aneurysm with a saccular outpouching. Non-saccular intracranial aneurysms involve widening of an entire blood vessel, such as a fusiform aneurysm.

The primary treatment goal of cerebral aneurysms is prevention of rupture. Treatment methods include two major intervention options: clipping of the aneurysm neck and endovascular methods such as coiling and flow diversion as reconstructive therapy and permanent vessel occlusion (PVO) as deconstructive therapy (if the aneurysm is uncoilable). Traditionally, surgical clipping has been the only treatment modality for both ruptured and unruptured cerebral aneurysms until 20 years ago; however, since the introduction of controlled detachable coils (GDC) for packing of aneurysms in 1991[8], endovascular aneurysm therapy has become an acceptable as well as preferable alternative to conventional neurosurgical treatment. There is well-established clinical evidence demonstrating that endovascular coiling is more likely to result in independent survival at 1 year when compared to neurosurgical clipping and that the survival

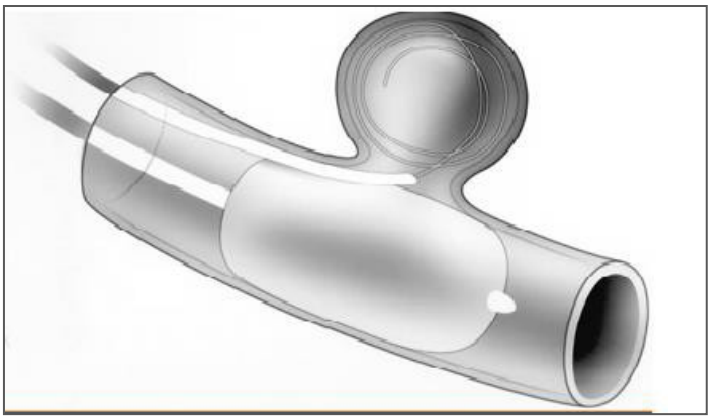
benefit continues for at least 7 years. After both treatment strategies the risk of late rebleeding is low, but is more common after endovascular coiling than after neurosurgical clipping[9].

The most common endovascular technique used to treat aneurysm is utilizing intrasaccular coils for embolization of the aneurysm. However, this technique is somewhat limited by the shape of some of these aneurysms. Wide-necked aneurysms (aneurysm absolute neck diameter of 4.0 mm[10] and/or dome-to-neck ratios of <2.0[11]) are difficult to treat because of their unfavorable geometry, which reduces the possibility of achieving dense packing and elimination of the aneurysm from circulation. One of the major risks is the possibility of coil herniation through the broad neck into the parent vessel. This can cause thromboembolic events, which are serious complications associated with endovascular treatment (EVT) of intracranial aneurysms (IA). Thromboembolic events with partially or completely persisting neurological deficits are reported in 2.4% to 5.2% of endovascular-treated patients[12,13,14].

To overcome this complication, the use of an adjunctive device to support coil embolization treatment was introduced by Moret, et al. in 1997[15 16]. In this groundbreaking study, Moret utilized an intracranial balloon to treat 52 wide neck or badly shaped aneurysms that were untreatable without this technique. The results of occlusion with the assistance of a balloon (“balloon remodeling technique” or "balloon-assisted coiling" - BAC) were better than those in the series of normal GDC treatment, and complications related to the technique were fewer. This technique thereby extended the spectrum of treatable aneurysms without increasing the risk recurrence or aneurysm regrowth and recanalization by treatment.

The balloon remodeling technique (BAC) involves placing a balloon mounted to a microcatheter in the parent artery along the aneurysm neck. An additional microcatheter is positioned in the sac of the aneurysm, while the balloon deflated. The balloon is inflated during the deployment of the coil (Figure 1 - Balloon remodeling technique: the balloon is inflated during coil delivery) and deflated before its detachment to assess its stability inside the aneurysm. The balloon serves two purposes during embolization; to stabilize the microcatheter in the aneurysm during coil delivery, and to force the coil to assume the shape of the aneurysm without impinging on the parent vessel.

Figure 1 - Balloon remodeling technique: the balloon is inflated during coil delivery



1.2 The Comaneci device

Similar to a remodeling balloon the Comaneci is a temporary device intended to support neurovascular coil embolization procedure. Specifically, it is designed to provide visible temporary support during coil embolization of intracranial aneurysms. It integrates the advantages of existing adjuvant devices without the risk of parent vessel occlusion during coiling procedure or the need for long-term antiplatelet medication in case of permanent stenting.

The Comaneci is comprised of a collapsible, fully retrievable, fine wire construction mounted on a wire shaft that expands to the vessel diameter. It is delivered through an intracranial microcatheter and is intended to prevent coil protrusion towards the vessel lumen during aneurysm closure. The long and soft atraumatic tip of the Comaneci protects the vessels wall from perforation and enables better deliverability and navigability. The Comaneci is manufactured from superelastic Nitinol wire with tantalum core and is fully radioopaque. It also includes a soft, floppy loading device, which enables easy insertion of the shaft and Comaneci to the micro catheter. The outer diameter of the mesh is controlled via a handle.

Figure 2 - Comaneci Temporary Support Aneurysm Coiling Device

2. DEVICE DESCRIPTION

2.1 Comaneci Device

The Comaneci is intended for use in the neurovasculature to assist in the coil embolization of wide-necked intracranial aneurysms under fluoroscopic guidance. The Comaneci is comprised of a collapsible, fully retrievable, fine wire construction mounted on a wire shaft that expands to comply with the vessel diameter. It is delivered through a neurovascular microcatheter. The Comaneci is provided with a 3.5 French (F) peelable loading sheath.

2.1.1 Device Versions:

Three versions of the Comaneci are available. The standard Comaneci has a length of 32 mm, which shortens to 25 mm when deployed in a straight vessel of 4 mm diameter. The Comaneci Petit measures 24 mm before deployment and contracts to 21 mm when fully deployed in a straight vessel of 3 mm diameter. The Comaneci 17 measures 22 mm before deployment and contracts to 16 mm when fully deployed in a straight vessel of 3 mm diameter.

2.1.2 Microcatheter Compatibility:

The Comaneci and Comaneci Petit should be introduced through a microcatheter with a minimum inner diameter of 0.021 inches. The Comaneci 17 should be introduced through a microcatheter with a minimum diameter of 0.017 inches. The Comaneci was introduced in a bench top model test using the following microcatheters shown in Table 1:

Table 1: Sizes and Microcatheters Compatibility

	Diameter	Compatibility	Net Length
COMANECI	1.5 mm - 4.5 mm	0.021" ID microcatheter	32 mm
COMANECI Petit	1.5 mm - 3.5 mm	0.021" ID microcatheter	24 mm
COMANECI 17	0.5 mm - 3 mm	0.017" ID microcatheter	22 mm

2.1.3 Device Indication Use

The Comaneci Embolization Assist Device is indicated for use in the neurovasculature as a temporary endovascular device used to assist in the coil embolization of wide-necked intracranial aneurysms with a neck width ≤ 10 mm. A wide-necked intracranial aneurysm defines the neck width as ≥ 4 mm or a dome-to-neck ratio < 2.

2.1.4 Labeling

The Comaneci device is required to be used per the protocol and as specified in the Instructions for Use (IFU) document (attached as Appendix A).

3. STUDY OBJECTIVES

The objective of the Postmarket Surveillance Plan is to assess safety and performance as used in postmarket clinical practice in the U.S.

3.1 Endpoints

Safety

- Periprocedural events*: Rates of all adverse events occurring within 24 hours post-procedure and hospital discharge status.
- All adverse events at discharge and up to 30 days post procedure.
- Functional status at discharge and 30-days assessed using the modified Rankin Scale (mRS).

Secondary safety endpoint: evaluation of the extent of any relationship between adverse event rate to operator experience

(*) Including vessel perforation or dissection, intracranial aneurysm rupture, stroke, hemorrhage, death, inability to deploy or remove the device, and coil entanglement

Efficacy

- Successful intracranial aneurysm occlusion (measured by Raymond Roy classification I or II) at the end of procedure, using digital subtraction angiography (DSA).
- Successful intracranial aneurysm (IA) occlusion, that is a stable IA occlusion, measured by Raymond Roy classification I or II taken at 6 months (± 21d) post procedure without the need for re-treatment of the target IA, using DSA.
- Good clinical outcome- mRS shift @ 6 months (change @ 6 months from pre procedure) and tetrachotomized (0,1, 2, 3-6) mRS analysis.

4. ENDPOINT JUSTIFICATION AND RATIONALE

Due to the fundamental design of the Comaneci Embolization Assist Device and the novel use of a core wire to expand and contract the mesh region to set the size of the device in the target vessel, the purpose of this postmarket surveillance plan is to capture real world safety data as the device is used in practice by physicians in the United States (U.S.).

5. SITES AND SUBJECTS

5.1 Subjects

5.1.1 Enrolment and Informed Consent

Ninety (90) subjects with device deployment will be enrolled in up to 30 US clinical centers, while no more than 13 subjects should be enrolled at each clinical center.

Subject's informed consent must be obtained and documented according to the principles of informed consent.
Any subject who is consented for endovascular treatment of an IA that may potentially require use of the Comaneci device at the participating centers in the study will be approached for consenting prior to device use, using separate consent for the subject's participation in and data collected to be included in the SUCCESS study.
Subjects with ruptured aneurysms: due to the emergent nature of acutely ruptured aneurysms, informed consent may be obtained from the point of arrival at the medical treatment facility up to 72 hours after the study procedure.
For all subjects, consent must be obtained before any data is captured in the eCRF.
Accounting for all unsealed Comaneci devices in each IA case that may potentially require use of the Comaneci device at a clinical site for the period of enrollment to the study will be provided. The accounts will not provide patient information but will provide some indication of the device disposition.

A patient informed consent form (ICF) will be given to each Subject or their Legally

Authorized Representative [(LAR); as defined by the local Institutional Review Board (IRB)]. The ICF will include an explanation of surveillance plan, duration, explanation of

medical record access and patient anonymity, and how their coded data may be transferred, used for publications or in submissions for reimbursement support. The ICF will contain language that is non-technical and understandable to the patient or his/her LAR.

Consent can be obtained electronically (Electronic Informed Consent, eIC), and the eIC materials be provided for both on-site and remote access. The eIC process may take place at the study site when both the investigator and subject are at the same location, or it may take place remotely where the subject reviews the consent document in the absence of the investigator or other study personnel. If the entire process takes place at the study site, the study personnel can personally verify the subject's identification, review the eIC content, answer questions about the material, have follow-up discussions, and witness the signing of the eIC. If any or all of the consent process takes place remotely and is not personally witnessed by study personnel, the electronic system must include a method to ensure that the person electronically signing the informed consent is the subject who will be participating in the research study or is the subject's LAR (see 21 CFR 11.100(b)).

Each potential Subject will be provided with written and verbal information regarding the nature of the study in an understandable manner. Adequate time will be allowed for the Subject to consider participation in the surveillance study. Signed, written consent will be obtained for each Subject prior to data collection and entry into the study. Coercion or undue influence of potential Subjects to participate will be avoided, and the Subject's legal rights should not be waived. The Investigator or an appropriately designated member of the study staff shall co-sign the consent form, indicating they believe the Subject or LAR understands the nature and risks of the study and scope of the consent.

If the Subject is not able to sign the ICF but has given his/her oral consent to participate, a third party can sign the informed consent for the Subject if allowable per IRB policy. The consenting process will be documented in the medical record and reason for Subject not signing the consent (in case of verbal confirmation). If the Subject is not able to give his/her informed consent to participate in the study, a LAR can sign the informed consent for the Subject if this is approved by the local IRB. If a LAR signs on behalf of a minor (12-17 years), a separate assent form must be given to the minor, and the minor must sign to acknowledge their understanding and willingness to participate.

Short form informed consent may be utilized if approved by the IRB. Each institution must follow their institutional IRB policy for obtaining informed consent. If the short form informed consent is used, the summary must include all the basic elements of informed consent (21 CFR §50.25; ICH E6 4.8.10).

The signed consent forms will be retained by the Investigator and made available (for review only) to the study monitor and auditor upon request.

Subjects are considered enrolled once appropriate informed consent has been obtained.

5.1.2 Study Subject Numbering

Sites participating in the SUCCESS Study will each be assigned a site number prior to enrolling Subjects. Each enrolled Subject will be assigned a Subject number. Site study staff will use the electronic case report form (eCRF) assigned Subject number to complete documentation of the screening/enrolment log following appropriate consenting. Subject study identification numbers will consist of the aggregate of site number followed by a sequential number, where “01” is the first enrolled Subject as the corresponding site.

5.1.3 Subject Terminations

Subjects will be considered discontinued from the study if any of the following occur:

1. Subject voluntarily withdraws from the study. Participation in the SUCCESS Study is voluntary. Subjects may withdraw consent at any time by completing an informed withdrawal form. Reasonable attempts will be made to determine the reason for withdrawal of consent. Data obtained prior to withdrawal enrolled will be included in endpoint data analysis, but no data will be obtained subsequent to withdrawal.

2. Investigator withdraws Subject from the study due to safety concerns. If, during the conduct of research, an Investigator determines that participation in the study may increase the hazard to a subject that is not acceptable, an Investigator may withdraw the Subject from the study due to safety concerns.

3. Lost to Follow Up: In the event that a Subject fails to return for the 30 days and/ or 6 months follow-up visits and is unable to be reached at the Subject’s last known telephone number, a certified letter will be sent to the Subject’s last known mailing address to remind the Subject of study obligations. Once all reasonable attempts to contact the Subject have been made, including contacting through the Subject’s general practitioner, the Subject is considered lost to follow-up. Each attempt to contact a Subject will be documented.

If, during the conduct of the study, a Subject dies, all available information related to the event should be obtained. Within 24 hours from study staff becoming aware of the event, an appointed Rapid Medical representative/study monitor should be notified by completing the appropriate study termination forms in the Subject’s eCRF.

Maximal completeness of the CRF for subject that died should be attempted and ensured by the following:

- If death occurs while the Subject is in the hospital, a copy of the death summary report should be submitted. In case of an autopsy, a copy of the autopsy report should also be submitted.

- If death occurs outside the hospital setting, effort should be made to obtain all information related to the death along with an Investigator's summary of the events associated with the death.

5.2 Site Selection, Training and Initiation

5.2.1 Selection

Sites will be selected by their ability to provide complete data sets with robust analyses for all safety and effectiveness outcomes with minimal risk to the subjects (i.e. CT up to 24h post procedure and 6 months angio to determine Raymond Scale score).

5.2.2 Training

Investigators and Site Personnel will be trained on the surveillance plan prior to site initiation of enrollment. Training will be documented on the Training Log and cover the following topics:

1. Study objectives
2. Surveillance plan review
3. Delegation of authority
4. Process for Informed Consent as well as IRB requirements
5. Electronic case report form use and completion guidelines
6. Enrolment procedures
7. Protocol Deviation documentation
8. AE and SAE event reporting
9. Device malfunction reporting
10. Comaneci Instructions for Use
11. Device traceability
13. Image collection and core lab submission
14. Investigator responsibilities and obligations
15. General Good Clinical Practice (GCP) guidelines
16. Regulatory requirements including essential documents

Changes to existing SUCCESS Study staff responsibilities, as documented on the Delegation Log, or addition of new study personnel will require investigational plan training, as appropriate.

5.2.3 Initiation

Rapid Medical, or a representative of Rapid Medical, will conduct study training as described in section 5.2.2.

Prior to actively recruiting/enrolling Subjects, Clinical sites must provide the following documentation to Rapid Medical:

1. IRB approval for the Surveillance Plan
2. IRB and sponsor approved Informed Consent Form for the study
3. Investigator(s') *curriculum vitae* (CV)
4. Financial Disclosure(s) for the PI and Sub-I(s)
5. Signed Clinical Trial Agreement (CTA) including Confidentiality Agreement
6. Training Log documentation to verify the appropriate study staff has been trained on the protocol, device, eCRFs and study conduct.

Sites will be officially notified of site activation through receipt of an activation letter or email.

6. STUDY DESIGN

The SUCCESS Study is a multi-center, prospective, postmarket safety surveillance study in up to 30 US centers. The Surveillance is to continue until complete data on the deployment of 90 devices with complete 30-day patient status are obtained in order to assess safety and performance as used in postmarket clinical practice in the U.S.

6.1 Study Duration

All patients who are treated with the Comaneci device and consented to allow data collection will be followed for 180 (±21) days post-procedure.

6.2 Subject Inclusion/Exclusion Criteria

Subjects are considered enrolled in the SUCCESS Study only after an attempt is made to introduce the Comaneci device through the arterial sheath and subject was properly consented.

6.2.1 Inclusion Criteria

In order to assure that the probable benefits outweigh the probable risks for the Comaneci Embolization Assist Device, as indicated in the IFU, the subjects must meet all of the following inclusion criteria:

1. Patient has a documented intracranial ruptured or unruptured aneurysm, suitable for embolization by coils.
2. Patient is considered for treatment with coil embolization assisted by the Comaneci Device for wide-necked intracranial aneurysms with neck width ≤ 10 mm. A wide-necked intracranial aneurysm is defined by the neck width as ≥ 4 mm or a dome-to-neck ratio < 2.
3. A signed informed consent by the patient or legally authorized representative.

6.2.2 Exclusion Criteria

Patient should be treated by the Comaneci device in accordance with the approved device label. (i.e. doesn't meet the contraindication criteria, as described in the IFU):

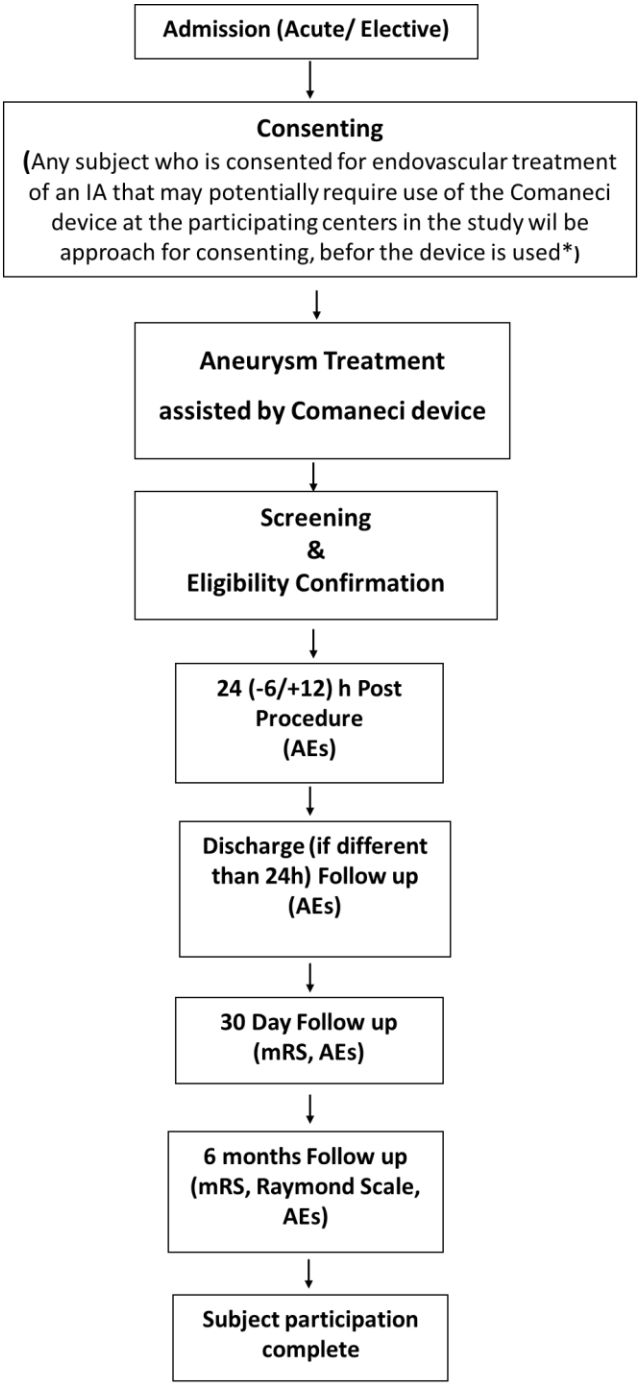
1. Patient with known hypersensitivity to nickel-titanium.

7. Data Collection

All procedures will be according to the standard practice at each site and determined by the treating physician including 6 months follow up. Procedures such as routine hospital examinations, brain CT scan or MRI will be performed according to each site's standard management protocol and relevant data will be properly documented in the patient's medical records.

7.1 Study

Study flow of Subjects through the SUCCESS Study is illustrated in Figure 3.



*Subjects with ruptured aneurysms: Due to the emergent nature of acutely ruptured aneurysms, informed consent may be obtained from the point of arrival at the medical treatment facility up to 72 hours after the study procedure. Consent must be obtained before any data is captured in the eCRF

Figure 3: Study Flow

7.2 Screening and Baseline Visit

Any subject who is consented for endovascular treatment of an IA that may potentially require use of the Comaneci device at the participating centers in the study will be approached for consenting prior to device use, using separate consent for the subject's participation in and data collected to be included in the SUCCESS study.
Subjects with ruptured aneurysms: due to the emergent nature of acutely ruptured aneurysms, informed consent may be obtained from the point of arrival at the medical treatment facility up to 72 hours after the study procedure.
For all subjects, consent must be obtained before any data is captured in the eCRF.
To reduce selection bias, accounting for all unsealed Comaneci devices in each IA case that may potentially require use of the Comaneci device at a clinical site for the period of enrollment to the study will be provided. The accounts will not provide patient information but will provide some indication of the device disposition.

An electronic Screening & Enrollment Log will include all IA patients treated at each site whether or not they are included in the study. Screening against study inclusion/exclusion criteria will be completed to determine potential eligibility. For each patient considered but not treated with Comaneci, the reason for not attempting to use Comaneci will be indicated. In addition, for patients where Comaneci was introduced into the body but who were not enrolled for follow up and data collection, or who denied post procedure consenting, the reason will be indicated in the electronic Screening & Enrollment Log by the attending physician. Sites will maintain this electronic log for the duration of the recruitment period of the study.

7.2.1 Patient Details:

- Year of Birth
- Gender
- Date of Treatment

7.2.2 Medical History:

- Presence or absence of multiple intracranial aneurysms
- Smoking history
- Presence or history of hypertension
- History of prior rupture of an intracranial aneurysm
- Family history of intracranial aneurysm
- Vital Signs (Hight, Weight, Blood Pressure, Heart Rate)
- Concomitant diseases
- Laboratory- Standard Biochemistry and CBC, PT, PTT, INR
- Prior/Concomitant Medications (Coagulation and Antiplatelet)

7.2.3 Pre- Treatment Data:

- Aneurysm size and location
- Pre-procedure mRS score (modified Rankin Scale)-up to 24h prior to treatment.
- Pre symptoms mRS
- NIHSS
- Pre op antiplatelet and/or coagulation medications

NIHSS will be performed by certified Study personnel.
mRS will be assessed by an independent clinician who is not a member of the investigational team.

7.2.4 Screen Failures

Subjects who were consented and not treated with the Comaneci device (device was not introduced to the body) due to not meeting the indication of the device, such as aneurysm size and anatomy, will be considered screen failures and will not be followed up, but the reason for not introducing the Comaneci will be documented. Screen failures will not be included in the primary safety endpoint analysis.

7.3 Procedure

7.3.1 Angiography

Intraprocedural diagnostic catheter angiography will be conducted prior to device deployment to determine location and aneurysm morphological features. Diagnostic angiograms will be obtained as per standard of care. A final post-procedure angiogram (full A-P lateral image) will be obtained once all treatments have concluded, including rescue therapy, if necessary. CT of up to 24h postprocedure if performed as a standard of care will be analyzed for safety parameters, such as hemorrhage.
Angiography at end of procedure and 6 months, will be analyzed to determine Raymonds scale at both time points and stability of Raymond Roy score.
All images are to be de-identified and submitted to the core lab for review:

The University of California at Los Angeles with the following address:
Angiography and Noninvasive Imaging Core Lab
David S Liebeskind, MD, FAAN, FAHA, FANA
UCLA Department of Neurology
Neuroscience Research Building
635 Charles E Young Drive South, Suite 225
Los Angeles, CA 90095-7334

Procedure will be handled as standard of care, according to Comaneci device IFU, appendix A.

7.3.2 Intraoperative Data

Intraoperative data will be collected as described below:

- Devices, Coils
- Medications
- Comaneci Performance (such as deployment/removal success, neck coverage)
- Total procedure time
- Total time Comaneci was inflated
- Raymond Scale at the end of procedure, using post procedure DSA
- Intra- Procedural Complications and AEs (including a determination of the severity, seriousness, and relationship to the device or procedure). These will specifically include vessel perforation or dissection, intracranial aneurysm rupture, stroke, hemorrhage, death, inability to deploy or remove the device, and coil entanglement.

7.4 24 Hour (-6/+12) Follow-up

24 hours (-6/+12 hours) from time of procedure

- Complications and any AE's (including a determination of the severity, seriousness, and relationship to the device or procedure). These will specifically include stroke, hemorrhage and death.
- Concomitant antiplatelet and/or anticoagulant medications
- mRS Score (if performed) mRS should be assessed by an independent clinician who is not a member of the investigational team.
- CT (if performed up to 24 hours post procedure as a standard of care)
- If subject discharged within 24 h- Discharge status (for example, by CMS Patient Discharge Status Code)

Note: CT images will be sent to the Imaging Core Lab for evaluation.

7.5 Discharge, if different than 24 hours (-6/+12 hours)

If Subject is discharged in a time that is different than the 24 hours (-6/+12 hours), the following data will be collected:

- Discharge status (for example, by CMS Patient Discharge Status Code)
- mRS Score- should be assessed by an independent clinician who is not a member of the investigational team.
- Complications and any AE's (including a determination of the severity, seriousness, and relationship to the device or procedure). These will specifically include stroke, hemorrhage and death.

- Antiplatelet and/or anti-coagulant Medications, if was changed from previous visit

7.6 30 days (± 7 days), can be performed over the phone

If an in-person visit cannot be performed, it is possible to perform via structured telephone interviews, with the exception of NIHSS.
30 days (± 7 days) from time of procedure

- mRS Score- should be assessed by an independent clinician who is not a member of the investigational team.
- NIHSS
- Complications and any AE's (including a determination of the severity, seriousness, and relationship to the device or procedure). These will specifically include stroke, hemorrhage and death.
- Antiplatelet and/or anti-coagulant Medications, if was changed from previous visit

NIHSS will be performed by certified Study personnel.

7.7 180 days (± 21 days)

- mRS Score (If an in-person visit cannot be performed, it is possible to perform via structured telephone interviews)-should be assessed by an independent clinician who is not a member of the investigational team.
- Raymonds scale, using DSA
- Complications and any AE's (including a determination of the severity, seriousness, and relationship to the device or procedure). These will specifically include stroke, hemorrhage and death.
- Antiplatelet and/or anti-coagulant Medications, if was changed from previous visit

In some cases, this visit is also performed at 3 months (90 ± 14 days) as a standard of care, then the same information will be collected at 3 months as well.
Also note, if in-person visits are not possible, mRS assessments may be performed remotely by structured telephone interviews.

7.8 Unscheduled Visits

When clinically indicated, unscheduled assessments should be completed with corresponding data documented in the eCRF.

7.9 Adverse Events

Adverse events that occur during participation in the SUCCESS Study will be recorded. See section 11 for more information on AEs.

Table 2: Schedule of Events

Elapsed time/Study procedures	Baseline/ Procedure	24 hours (-6/+12)	Discharge if different than 24 hours (-6/+12)	30 (±7) days	180 (±21) days**
Informed Consent	X				
Demographics	X				
Medical History and Concomitant Medications	X				
Brain CT Scan	X	X *			
Vital Signs	X				
mRS score+	X		X	X	X
NIHSS	X			X	
Clinical Laboratory	X				
Raymond scale	X***				X***
Intraoperative data	X				
Prior/concomitant medications	X	X	X	X	X
Adverse Events	X	X	X	X	X

(*) If performed as a standard of care any time up to 24 hours post procedure

(**) Will be collected if performed also at 90 (±14) days as a standard of care.

(***) Post-procedure and 6 months imaging should use Digital Subtraction Angiography (DSA) for Raymond scale assessments.

(+) If in-person visits are not possible, mRS assessments may be performed remotely by structured telephone interviews.

7.10 Clinical Outcomes Assessment

Assessments to be performed as indicated in Table 2 are as follows:

Modified Rankin Scale (mRS): Measures the global degree of disability or dependence of an individual on an ordinal scale. Must be assessed by an independent clinician who is not a member of the investigational team, who is trained to conduct the mRS assessment.
To the extent possible, the same examiner should examine all subjects at a single site.

8. STATISTICAL ANALYSIS-

8.1 General Principles

The detailed hypothesis generation and statistical method is provided below:

The primary effectiveness endpoint is successful intracranial aneurysm occlusion (measured by Raymond Roy classification I or II) at the end of procedure, using digital subtraction angiography (DSA).

The performance goal (PG) for evaluating effectiveness is based on outcomes as reported in the Comaneci de novo, which was successful aneurysm occlusion of 79.7% (51/64). The PG for the primary effectiveness is defined as success rate cited above minus a margin of 10%, therefore giving a PG of 69.7%.

The resulting null and alternative statistical hypotheses are as follows:

H0: $p \leq PG$

HA: $p > PG$

The hypothesis test will be performed at an overall two-sided alpha level of 0.05 using Chi-square test, in which the lower confidence bound on the observed incidence of success is compared to the PG.

With a hypothesized true incidence rate of 82.6% for successful intracranial aneurysm occlusion at the end of procedure and desired power of ≥ 80%, using a normal approximation test with a nominal 0.025 one-sided significance level (equivalent to a two-sided alpha=0.05), the required evaluable sample size for primary efficacy is 90 evaluable patients with a power of 80%.

The objective of this postmarket surveillance study is to reduce uncertainty regarding the safety profile of the device and its real-world performance. This objective will be met by capturing safety data as the device is used in practice by physicians in the United States. As specified by FDA's order to conduct a postmarket surveillance study under section 522 of the Federal Food, Drug and Cosmetic Act (the act), 21 U.S.C. 360l, a total N=120 deployed devices with complete 30 day post procedure patient status. This number of deployments was later adjusted and approved by the FDA to 90 in the current version of the protocol (version 2.0) as explained above. The focus of the study is to characterize the incidence and nature of periprocedural events occurring within 24 hours post-procedure as well as hospital discharge status and to characterize 30-day post-procedure status including 30-day functional status and all adverse events after discharge to day 30 for each use of the Comaneci Embolization Assist Device. Longer terms effectiveness at six months will be also descriptively summarized in terms of the Raymond scale and mRS.

Attempt to use the Comaneci device is defined as: in each IA case that may potentially require use of the Comaneci device where the sterile seal on the packaging was broken, whether or not the device is ever delivered to the target site of its intended use. The procedural case report form (CRF) will record all attempts to use the Comaneci device. All reasons the device may not have been used after the sterile seal

has been broken, including whether consent was obtained or not, will be provided.

Accounting for all unsealed Comaneci devices in each IA case that may potentially require use of the Comaneci device at a clinical site for the period of enrollment to the study will be provided: for devices unsealed and not used in the SUCCESS intent to treat (ITT) group described below, the accounts will not provide patient information but will provide some indication of the device disposition. There will be a separate CRF to track the disposition of all devices for which the sterile seal has been broken, including whether the device was used in a subject in the ITT group.

Any patient who is consented for endovascular treatment of an intracranial aneurysm (IA) that may potentially require use of the Comaneci device at the participating centers in the study, and a Comaneci device's package sterile seal was broken will form the basis of ITT. ITT patients that Comaneci device was not introduced to the body will be considered screen failure, and will not be followed up, but the reason for not introducing the Comaneci will be documented.
The primary safety endpoint analysis will be performed using the ITT population without screen failures.

All patients who meet all of the inclusion criteria and no exclusion criteria will form the basis for FAS primary analysis- for whom primary safety and efficacy analysis will be performed.

Descriptive summaries of the peri-operative and post-operative adverse events in both the ITT cohort and the FAS cohort will be reported.

8.2 Evaluation of Periprocedural Events

The rates of all adverse events occurring within 24 hours post procedure and hospital discharge status for all opened devices at each participating clinical site during the surveillance period will be summarized. Adverse events of special interest include vessel perforation or dissection, intracranial aneurysm rupture, stroke, hemorrhage, death, inability to deploy or remove the device, and coil entanglement. The numbers of individual adverse events of each type and the per subject incidence rate for each type of adverse event will be determined and reported along with 90% two-sided exact binomial confidence intervals. The upper bounds of 90% two-sided exact binomial confidence intervals are equivalent to the upper bounds of 95% one-sided exact binomial confidence intervals. While the estimated incidence rates for each type of adverse event will be taken as the most likely value of the true incidence rate, the corresponding upper bound of the one-sided 95% exact binomial confidence interval will be taken as the largest possible incidence rate consistent with the observed sample results.

Separate event counts and incidence rates with corresponding confidence intervals will be summarized for adverse events determined to be serious, device-related, serious and device-related, procedure-related, serious and procedure-related, and severe. Listings for all adverse events will be compiled that provide full descriptions of each adverse event including determination of the severity, seriousness, and relationship to the device or procedure. The following listings will be compiled:

- AE Listing 1 All AEs Sorted by Event Type
- AE Listing 2 All AEs Sorted by Subject and Relative Time of Onset
- AE Listing 3 Serious AEs
- AE Listing 4 Severe AEs
- AE Listing 5 Device-Related AEs
- AE Listing 6 Procedure-Related AEs
- AE Listing 7 Serious Device or Procedure Related AEs
- AE Listing 8 Severe Device or Procedure Related AEs

Discharge status will be described with counts and percentages.

Evaluation of the extent of any relationship between adverse event rate to operator experience will be evaluated. Operator experience will be evaluated by credentialing the investigators by years of training, number of aneurysms treated endovascularly in the last two years.

In addition, Successful intracranial aneurysm occlusion (measured by Raymond Roy classification I or II) at the end of procedure will be descriptively summarized in terms of the number and percentage of subjects.

8.3 30-day post-procedure status

30-day functional status will be assessed using the modified Rankin Scale (mRS). This scale runs from 0-6, from no symptoms to death as follows:

- 0 - No symptoms
- 1 - No significant disability. Able to carry out all usual activities, despitesome 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 - Dead.

The frequency distribution and cumulative frequency distribution of the 30-day mRS will be summarized using counts and percentages.

All adverse events after discharge (device-related and non device-related) for each use of the Comaneci Embolization Assist Device will be summarized similarly to how periprocedural events will be summarized as described above. This includes counts, per subject incidence rate, exact binomial confidence intervals, and a separate set of adverse event listings that contain full descriptions of each adverse event including determination of the severity, seriousness, and relationship to the device or procedure.

8.4 Six Month Effectiveness and Clinical Status

Effectiveness at six months will be descriptively summarized in terms of the number and percentage of subjects achieving stable IA occlusion, measured by Raymond Roy classification I or II without the need for re-treatment of the target IA and good clinical outcome defined by mRS and shift tetrachotomized (0,1, 2, 3-6) analysis. 95% two-sided confidence intervals will be provided to evaluate the statistical precision of the estimates. If these endpoints are available at three months but not at six months, the three month values will be used for these analyses.

8.5 Subgroup Analysis

Selected adverse event rates will be provided for subgroups including wide-necked ruptured versus unruptured intracranial aneurysms.

8.6 Missing Data

Since the primary safety endpoint is defined immediately post-procedure and up to 30 days, the amount of missing data for this study is anticipated to be low and so no imputation of missing data will be performed. For the analysis of six month effectiveness, if the six month Raymond score or mRS values are missing and any earlier data are available, the most recent earlier value will be used.

8.7 Heterogeneity Among Investigational Sites

An objective of this study is to evaluate variability in outcome among 'real world' users. To this end, an evaluation of heterogeneity among investigational sites may be important for this evaluation. Key summary adverse event endpoints such the per subject occurrence of any serious event, any device-related event, and any serious device-related event will be stratified by investigational site. If there is sufficient data, the site stratified event rates will be subjected to a random effects analysis on arcsine transformed proportions. Sites contributing fewer than 5 subjects will be pooled. True site-effects are assumed to be normally distributed with mean M and variance t^2. By imposing a specified distribution on the site-to-site variability, i.e., a normal distribution with mean M and variance t^2, sensitivity to small sample sizes in individual sites is reduced, and the parameters reflecting the magnitude of site-to-site variability are naturally derived. The quantitative measure of the magnitude of heterogeneity is I^2. I^2 is the fraction of total site-to-site variance that is due to event rate heterogeneity across sites, as opposed to sampling variance. If σ^2 is the total variance, then $I^2 = t^2 / \sigma^2$. Fractions of 25% and less are considered small and not clinically significant (Higgins and Thompson 2002)[1]. Site variability will be visually evaluated using a Forrest plot. If these analyses reveal specific sites that are outliers, further quantitative and qualitative analyses will be performed to investigate potential reasons.

8.8 Deviations from the Statistical Plan

Any departure or deviation from these planned statistical methodologies will be documented and discussed in the Clinical Study Report summarizing the results from this study.

8.9 Software

Statistical analyses will be performed using SAS version 9.4 or later and/or R version 3.4 or later.

9. RISK/BENEFIT ANALYSIS

This is an observational study only; therefore, data collection does not introduce additional risks to the patients, apart from the procedure's possible risks.

The IFU attached as Appendix A, describes the procedure's potential complications and technical success analysis.

[1] Higgins JPT and Thompson SG. Quantifying Heterogeneity in a Meta-Analysis. Statistics in Medicine 21(11): 1539-1555.

10. DEVIATIONS FROM THE CLINICAL SURVEILLANCE PLAN

10.1 Surveillance Plan Deviations

A surveillance plan deviation is defined as any change or alteration from the procedures stated in the surveillance plan, consent document, recruitment process, or study materials that were originally approved by the IRB where the change or alteration itself is not IRB approved. Surveillance plan deviations can be either major or minor.

All surveillance plan deviations must be reported to Rapid Medical or their authorized representatives (study monitors) through the eCRF surveillance plan deviation form. All deviations, regardless of whether medically justifiable (Subject's safety) or pre-approved by Rapid Medical and/or the IRB of record, shall be reported. In addition, the Investigator is required to adhere to IRB of records' procedures for reporting surveillance plan deviations.

Prior approval for deviation from the surveillance plan shall be obtained by the Investigator from Rapid Medical, except in situations where necessary to protect the safety of a Subject (emergency) or for situations beyond the Investigator's control such as Subjects missing scheduled follow-up visits. Approval for deviations shall be documented in writing and maintained in the Investigator and clinical study management files.

Investigators are required to maintain accurate, complete and current records, including documentation showing the dates of, and reasons for, each deviation from the Surveillance Plan Deviations

Any surveillance plan deviations will be reported to the study sponsor and IRB, as required. Deviations will be documented in the final study report.

11. SAFETY AND ADVERSE EVENTS

Safety of study Subjects is of critical importance for the SUCCESS study. Site Investigators are responsible for the safety of Subjects under his/her care. In order to more clearly understand data and potential confounders, assessment of all Adverse Events observed by the site investigators will be recorded in the case report form and reported to the Data and Safety Monitoring Board for period review.

11.1 Adverse Event Data Collection

Recording of adverse events commence from time that a Subject is appropriately consented and culminate through the 180-day (± 21) follow up. All available information related to the AE must be obtained by the Investigator so that proper determination of

causality and outcome can be made and classification as a SAE can be made if warranted. Adverse Events will be documented on the appropriate eCRF. Data captured include the event description, onset, resolution status, seriousness, severity, causality (if known), relationship to the device or procedure and treatment, if done. The Investigator will follow all AEs until resolution or completion of the 6 months follow-up.

11.2 Definitions

11.2.1 Adverse Events

Per ISO 14155:2011 section 3.2, an Adverse Event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in Subjects, users or other persons, whether or not related to the Comaneci medical device.

In the event that a Subject participates in the SUCCESS Study with signs of prior disease and/or symptoms, these conditions would not be considered AEs unless the condition recurs after the Subject has recovered from the previously occurring condition or the condition worsens in intensity or frequency during participation in the SUCCESS Study.

11.2.2 Adverse Device Effect

Per ISO 14155:2011 Section 3.1, an Adverse Device Effect (ADE) is any AE related to the use of an investigational medical device.

11.2.3 Serious Adverse Events

Per ISO 14155:2011 Section 3.37, an SAE is an AE that:

1. Led to death,
2. Led to serious deterioration in the health of the Subject, that resulted in:
    a. a life-threatening illness or injury, or
    b. a permanent impairment of a body structure or a body function, or
    c. in-patient or prolonged hospitalization, or
    d. medical or surgical intervention to prevent permanent life-threatening illness or injury or permanent impairment to a body structure or a body function.
3. Led to fetal distress, fetal death or a congenital anomaly or birth defect

11.2.4 Serious Adverse Device Effect

Per ISO14155:2011 3.36, a Serious Adverse Device Effect (SADE) is an adverse device effect that has resulted in any of the consequences characteristic of a SAE.

Examples of SADE for the SUCCESS Study include vessel dissections or perforations caused by the Comaneci Device.

11.2.5 11.2.7 Procedure-Related

Definite Related: Must have all 3 of the following:

1. Has a reasonable temporal relationship to the intervention procedure
2. Could not possibly have been produced by the Subject's clinical state or have been due to environmental or other interventions.
3. Follows a known pattern of response to the intervention procedure.

Possible Related: Must have at least 2 of the following 3 conditions:

1. Has a reasonable temporal relationship to the intervention procedure
2. Could not possibly have been produced by the Subject's clinical state or have been due to environmental or other interventions.
3. Follows a known pattern of response to intervention procedure.

Unlikely Related: Has a reasonable or tenuous temporal relationship to intervention procedure, but also has BOTH of:

1. Could readily have been produced by the subject's clinical state, or environmental or other interventions.
2. Does not follow known pattern of response to intervention procedure.

Unrelated: The temporal relationship between intervention procedure and the adverse event is unreasonable or incompatible and/or adverse event is clearly due to extraneous causes (e.g., underlying disease, environment).

11.2.6 11.2.8 Device-Related

Definite Related: Must have all 3 of the following:

1. Has a reasonable temporal relationship to the intervention device
2. Could not possibly have been produced by the Subject's clinical state or have been due to environmental or other interventions.
3. Follows a known pattern of response to the intervention device.

Possible Related: Must have at least 2 of the following 3 conditions:

1. Has a reasonable temporal relationship to the intervention device

2. Could not possibly have been produced by the Subject's clinical state or have been due to environmental or other interventions.
3. Follows a known pattern of response to intervention device.

Unlikely Related: Has a reasonable or tenuous temporal relationship to intervention device, but also has BOTH of:

1. Could readily have been produced by the subject's clinical state, or environmental or other interventions.
2. Does not follow known pattern of response to intervention device.

Unrelated: The temporal relationship between intervention device and the adverse event is unreasonable or incompatible and/or adverse event is clearly due to extraneous causes (e.g., underlying disease, environment).

11.3 Determination of Event Severity and Relatedness

Using all available information, Site Investigators will independently categorize event severity as Serious or Non-serious, using the above definitions.

Using all available information, Site Investigators will categorize the relationship of non-serious adverse events (NSAEs) and SAEs to study procedure and study device. In addition, a central Data and Safety Monitoring Board will independently adjudicate the relationship of all SAEs to study procedure and study device.

11.4 Event Notification

SUCCESS Study Investigators are required to report all deaths, serious injuries or malfunction at any time during the study to Rapid Medical, or Sponsor representative, within 24 hours after first learning of the event or as soon as they are known to investigators. In addition, the Investigator must follow the IRB of record's policies for SAE.

All Medical Device Reporting (MDR) reportable events will conducted in accordance with Rapid- Medical SOP 017-046- Vigilance System Procedure.

11.5 Data and Safety Monitoring Board

The DSMB will consist of at least one independent trained vascular neurologist, a neuroendovascular surgeon, and a Biostatistician. All DSMB members will not be affiliated with any of the participating sites.

All AEs observed by the site investigators will be reported to the DSMB for quarterly review.

Major responsibilities of the DSMB are:

1. Monitor the rates of all adverse events
2. 3. Recommend revisions to the SUCCESS Study plan regarding safety of the study Subjects
4. quarterly review and monitor aggregated and individual Subject data related to safety, data integrity, scientific validity and overall conduct of the study, to ensure the rights, safety, and welfare of the study participants
5. Monitor Subject accrual and retention
6. Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or on the ethical conduct of the study
7. Ensure the confidentiality of trial data and the results of monitoring

12. STUDY MONITORING

The study will be monitored regularly by trained clinical trial monitors to ensure the protection of Subject rights and safety, as well as, data quality and integrity.

The monitor will verify information entered into the eCRFs against source documents and the Subject's medical records to ensure validity of data. Source documents may be photocopied if required but will be anonymized prior to a monitor leaving the performance site. The following on-site visits will occur: site initiation visit; first monitoring visit shortly after the first 1-3 subjects are enrolled; additional monitoring visits determined by site enrollment rates.

On the occasion that a monitor requests additional data or clarification of data for the eCRF, the request must be addressed appropriately prior to the next monitoring visit. Once completed eCRF data are verified against source data, the study monitor will electronically sign off to indicate that data has been monitored for correctness. The Investigator must sign all eCRFs prior to site close.

In the event that a monitor discovers potential SAEs or SADEs which were not previously reported, Rapid Medical or the appointed representative/study monitor will inform the Investigator for their review and submission to the IRB, if applicable.

There will be a site close out visit to ensure all documentation is in place and all outstanding items have been addressed. Record retention policies will be reviewed, and post-study Investigator responsibilities discussed.

Device traceability will also be conducted by the study monitor at each monitoring visit. damaged, malfunctioning, or expired devices will be returned to Rapid Medical.

12.1 Source Documentation

Investigators are required to record and maintain adequate and accurate case histories for all Subject observations, assessments, and data pertinent to SUCCESS Study conduct.

12.2 Access to Source Documents

The Investigator and Institution, as participants in the SUCCESS Study, will be responsible for providing direct access to source data to Rapid Medical, their designated representatives, and to appropriate authorities for the purposes of monitoring, audit, IRB review or regulatory inspection. Subjects will be notified of such access to study records as part of the consenting process.

13. DATA COLLECTION AND OWNERSHIP

13.1 Protected Health Information and Confidentiality

The Investigator and members of the IRB of record shall consider all data or findings generated during the conduct of the study, other than that information to be disclosed by law, as confidential. Disclosure of such data or findings to any third party shall not occur without the prior written consent of Rapid Medical.

All reports and communications relating to Subjects in the study will identify Subjects by their Subject ID number only.

13.2 Data Management

Every effort will be taken to ensure the accuracy and reliability of data including the selection of qualified Investigators and appropriate study centers, review of protocol procedures with the Investigator and associated personnel before the study commences, and periodic onsite monitoring visits by the Sponsor, or their representatives, as deemed appropriate by the Sponsor. Guidance for eCRF completion will be provided and reviewed with the study personnel prior to the start of the study. The Sponsor will review eCRFs for accuracy and completeness and any discrepancies will be resolved with the Investigator or designee, as appropriate.

13.3 Electronic Case Report Forms

Study staff, as indicated in the Delegation log, who will use the EDC system will have adequate training in order to perform assigned tasks (21 CFR §11.10(i)). Training will be conducted by Rapid Medical and/or their qualified designated appointee as part of the Site Initiation Visit or as needed.

Data collected during the conduct of the SUCCESS Study will be entered into a 21CRF §11 compliant eCRF database. Accuracy and data quality will be ensured through implementation of data edit checks. Responses to requests for clarification of eCRF recorded data will be answered, dated, and electronically signed by the Investigator or designee. Any required changes to the Sponsor's eCRF/database will be followed by data review and validation procedures.

Once the study is closed and all data has been monitored and signed by study Investigators, the database will be locked and analyzed for statistical evaluation and reporting.

13.4 Record Retention and Storage

13.4.1 Sponsor Record Retention

Rapid Medical will retain all study documentation for a period of at least five (5) years or in accordance with GCP regulations in force in the Sponsor's jurisdiction, whichever is greater, following formal discontinuation of the SUCCESS Study.

13.4.2 Investigator Record Retention

The Investigator shall retain all study documentation for a period of at least (3) years or in accordance with retention policies of the IRB of record, whichever is longer.

13.5 Publication Policy

As part of the SUCCESS Study, information related to the Comaneci Device (such as pre-clinical data and other device materials) may be supplied to SUCCESS Study Investigators. Any information not previously published is considered confidential and shall remain the sole property of Rapid Medical. The Investigator agrees to use any such information as it pertains to study conduct and not use data generated from the study for other purposes without first obtaining the written consent of Rapid Medical.

Every effort will be made to publish the results of this study regardless of whether the findings are in favor of the Comaneci device. To achieve this goal, and to avoid publication bias, the SUCCESS study will be registered, prior to enrollment commencing, on the clinicaltrials.gov database.

Rapid Medical will form a Publications Committee for the purpose of reviewing and publishing data from the study. This committee will include, at a minimum, the SUCCESS Study Principal Investigators (PIs) and a representative of Rapid Medical. The Publications Committee will be tasked with creating a publication policy describing the authorship criteria. Abstracts and manuscripts will be written and/or reviewed by the Publication Committee prior to submission for journal or meeting acceptance.

14. AUDITS OR INSPECTIONS

Representatives of Rapid Medical or any regulatory body reviewing study results may visit study sites to conduct a SUCCESS Study audit in compliance with company policy and regulatory guidelines. Audits will require access to all study related documentation for inspection. Investigators will immediately notify Rapid Medical upon learning of announced audits or inspections by regulatory agencies.

15. REFERENCES

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Appendix A- Instructions For Use