MINNETRONIX® NEURO

ExtracorPoreal FILtration of Subarachnoid Hemorrhage via SpinaL CAtheteR EXTension

PILLAR-XT

PILLARXT Study

Clinical Protocol
IDE #G150184
NCT03607825

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1. SYNOPSIS

Objective	The objective of this study is to further demonstrate safety and characterize effectiveness of the Neurapheresis™ System (extracorporeal system and catheter) to remove red blood cells (RBCs) and lysed blood by-products from hemorrhagic cerebrospinal fluid (CSF) following aneurysmal subarachnoid hemorrhage (aSAH).
Investigational System	The Neurapheresis System consists of custom and off-the-shelf components designed for use in an intensive care setting.
Intended Use	The Neurapheresis System is intended for use in the filtration of cerebral spinal fluid in order to remove targeted, disease causing agents from the central nervous system.
Study Design	Prospective, multi-center, non-randomized single arm study.
Sample Size	N=30 subjects treated with Neurapheresis (study therapy) are expected to be enrolled.
Centers	Up to 8 investigative centers within the United States
Primary Endpoint(s)	**Primary endpoints:** 1. Mean reduction of cisternal blood via CT post study therapy 2. Proportion of subjects with Neurapheresis Catheter, System or Therapy related serious adverse events
Secondary Endpoints	**Secondary safety endpoints:** • Proportion of subjects with successful catheter placement of those attempted • Proportion of subjects with study device or therapy related adverse events • Proportion of subjects with systemic CNS infection within 5 days of catheter removal **Secondary efficacy endpoints:** • Mean reduction of RBCs and total protein by CSF sample post study therapy • Mean length of Neuro ICU stay
Exploratory Endpoints	• Proportion of subjects requiring additional CSF management during Neurapheresis or on-going CSF management post study therapy • Reduction in biomarkers of inflammation as seen in CSF, blood and physiologic manifestations post study therapy • Proportion of subjects with symptomatic complications from aSAH • Analysis of endpoints by the following sub-groups for any groups that have at least 5 subjects that meet the criteria for the group; o Age: <45, ≥45-<60, 60 – 70 years o Gender: male, female o Enrollment Modified Fischer grade: 2, 3, 4 o Baseline cisternal Hijdra score: ≤15, 16-20, 21-25, 26-30 o Study therapy time: <16hrs, ≥16-32hrs, >32-48hrs, >48hrs o Other sub-groups not yet defined
Enrollment Categorization	All patients who provide written consent to participate in the study will be considered enrolled study subjects, however not all subjects will contribute to

	the enrollment cap of N=30 treated subjects. Only "Treated" subjects, as defined below, will contribute to the enrollment cap. As such, it is expected that up to 40 subjects may be enrolled to meet the enrollment cap of N=30 Treated Subjects. Informed consent may be obtained prior to or after aneurysm securement as able based on patient status upon admission and legally authorized representative (LAR) availability if needed. Intent to Treat Subjects: • Subjects who provide written informed consent but do not have placement of the study catheter attempted. This would include placement tools such as the epidural needle and guidewire. Intent to Treat subjects will be exited immediately as they have not received any portion of the study catheter or study therapy. They will not count towards the enrollment cap of N=30 treated subjects. Attempt to Treat Subjects: • Subjects who provide written informed consent and have any portion of the catheter placement procedure attempted (including the epidural needle and guidewire) but placement was unsuccessful. Attempt to Treat subjects will be followed through 2 days post-attempt for safety then exited. They will not count towards the enrollment cap of N=30 treated subjects. They will be included in the analysis of safety endpoints but will not be included in the analysis of efficacy endpoints. Treated Subjects: • Subjects who provide written informed consent, have successful placement of the study catheter and have study therapy initiated. These subjects will be followed out to 30 days according to the study protocol then exited. They will count towards the enrollment cap of N=30 treated subjects and used in all analyses.
Inclusion Criteria	• Male or female patient age: 18 – 70 years • Informed consent by the patient or his/her legally authorized representative • Modified Fisher Grade 2, 3 or 4 • Hunt & Hess I-IV • First aneurysmal SAH that has been confirmed by CT scan and secured or planned securement via clipping or coiling per institutional SOC • Patient is ≤ 48 hours post bleeding event • World Federation of Neurosurgeons (WFNS) Grades I-IV • Patient is indicated for a ventriculostomy

Exclusion Criteria	• Pregnancy • Patients with a SAH due to mycotic aneurysm or AV malformation • Patients who present with an acute MI or unstable angina • Patients with uncontrolled diabetes at the time of catheter placement • Patients who present with a creatinine > 2.0mg/dl • Imaging demonstrates supratentorial mass lesions ≥15 cc • Imaging demonstrates ≥2 mm of mid-line-shift associated with infarction and or edema • Imaging demonstrates infratentorial mass lesion ≥10cc • Imaging demonstrates presence of any subdural hematoma • Effacement of the basilar cisterns (suprasellar, ambient, chiasmatic and quadrageminal) • Vasospasm on admission as defined by angiographic evidence • Patients with a coagulopathy that cannot be reversed per the professional discretion of the investigator • Patients with a connective tissue disorder that may impact the integrity of the dura • Thrombocytopenia def. platelet count < 100,000 • Patients on low molecular weight heparin such as Lovenox • Patients on Clopidogrel bisulfate (Plavix) or other chronic platelet inhibitors • Patients with a documented history of cirrhosis • Non-communicating Obstructive hydrocephalus • Patients with a lumbar or thoracic spinal anatomy (e.g. severe spinal stenosis) or history of posterior fusion hardware that would interfere with placement or appropriate in-dwelling of the catheter • Existing hardware that prevents accurate CT imaging • Pre-existing Lumbar Drain • Local skin infections or eruptions over the puncture site • Signs of CNS systemic infection, sepsis or pneumonia • Lumbar puncture within 6 hours • Concurrent participation in another study which is not observational or retrospective in nature without prior approval from the Sponsor
Catheter Placement	During catheter placement, an MNeuro clinical field specialist will be available to support the accurate assembly, placement, priming and testing of the system prior to beginning study therapy. Fluoroscopy is required for catheter placement and as such it is expected to be performed in an IR/OR with preservative free saline available from the site to adequately prime the system. Consent may be obtained prior to aneurysm securement to allow for catheter placement immediately following clipping or coiling in the same IR/OR session. Alternatively, consent may be obtained following aneurysm securement to ensure the patient continues to meet I/E criteria prior to enrollment or if applicable due to LAR availability. In this scenario, the subject must be brought back to the IR/OR in a separate session. The catheter must be placed ≤48 hours from ictus.
Neurapheresis Therapy	The study catheter can remain in-dwelling for up to 72 hours (± 4hr) in treated subjects during which study therapy can be completed. Neurapheresis therapy

	will be incrementally extended during the study such that, the first five (n=5) treated subjects enrolled under this protocol, will have a maximum of 36 hours (± 4hr) of Neurapheresis therapy (pump time) allowed during the 72 hours (± 4hr) of catheter in-dwelling. Following positive DSMB review of the safety data from the first five subjects, the remaining up to n=9 treated subjects (for a study total of N=30 Treated Subjects) will have no limit on maximum therapy time and instead be limited only by the maximum catheter in-dwelling time of 72 hours (± 4hr). If the DSMB does not agree that it is safe to remove the Neurapheresis therapy limit after review of data from the first ten subjects, the maximum of 36 hours (± 4hr) of Neurapheresis therapy (pump time) will remain in place for the remaining subjects.
Neurapheresis Surveillance	Following aneurysm securement and prior to initiating study therapy, a head CT is required to establish safety for beginning study therapy as well as provide a baseline to which the follow-up CTs may be compared. This may be done following catheter placement but needs to be done in a department scanner. Subjects will be monitored regularly during study therapy according to institutional SOC for Neuro ICU monitoring with additional protocol requirements as defined below. Protocol required neuro monitoring should begin following catheter securement. The catheter can remain in-dwelling for up to 72 hours (± 4hr) in Treated Subjects during which study therapy can be performed. • Intracranial pressure (ICP), Glasgow coma score (GCS), Lumbar pressure and Peripheral checks performed hourly (± 1hr) while the catheter is in-dwelling • CSF Sampling every 8 hours while the catheter is in-dwelling • Venous blood sample will be taken at 36 hours and 72 hours or end of catheter in-dwelling (± 4hr) To ensure the pressures are accurately obtained, the system will be paused temporarily for completion of each study-required neuro check. If the lumbar pressure reads below 4.4 mmHg (6.0 cmH2O), the Investigator will be notified for review of clinical symptoms and system data prior to re-starting therapy unless a pre-defined treatment plan has already been directed by the Investigator. If the ICP recorded at a study-required neuro check is higher than the lumbar pressure at the same neuro check. The system should remain paused until the ICP is equal to or lower than lumbar pressure for at least two consecutive neuro checks and the Investigator has approved restarting the system. Additionally, at 36 hours and 72 hours or end of catheter in-dwelling (± 4hr), a head CT will be required. The CTs must be taken using a department scanner and will be used to compare to the baseline CT and document the amount of blood removal from the basal cisterns for the primary endpoint. Additional data related to the clinical status of the subjects will be collected throughout study therapy such as the development of complications or study adverse events.

	The study therapy may be paused or terminated at any time by the Investigator or Subject but will be required to terminate under the following conditions: • Brainstem herniation • Lower extremity paralysis • Subdural spinal hematoma • Subdural hematoma or hygroma • Abnormal gram stain • Re-bleeding event requiring intervention e.g., re-coiling, re-clip • Subject previously extubated requires new or re-intubation • ICP is greater than Lumbar pressure at five consecutive study-required neuro checks • Subject requires inversion (such as Trendelenburg position) If study therapy must be terminated early (prior to 72 hrs of catheter in-dwelling), a head CT within (± 4hr) of catheter removal must be obtained to document the final amount and location of blood within the basal cisterns to allow for comparison to baseline. The subjects' EVD should be clamped upon beginning study therapy and remain closed unless ICP goes above 20 mmHg or is trending in a way that cannot be managed with the study therapy and the investigator feels it is in the best interest of the subject to open it. If it is opened, the set pressure should be 20 mmHg. Subjects with an EVD will have ICP values recorded at the same time as the neuro checks are completed. As CSF filtration is considered an adjunct to standard of care, subjects will continue on the prescribed medical and physical therapy regimen as directed by the treating Investigator during the time of enrollment through study exit.

Follow-up Surveillance Schedule	Following removal of the catheter, subjects will have follow-up assessments at 2 days, at Neuro ICU discharge and 30 days. Collection of required study data, assessment of adverse events and evaluation of clinical status will be completed at these follow-up time points. After completion of the 30 day follow-up, the subject will be exited from the study. 2 Day Post-Neurapheresis Follow-up Requirements: • General Clinical and Hospital Data • Glasgow Coma Scale • Head CT • Venous blood sample Neuro ICU Discharge: • General Clinical and Hospital Data • Glasgow Coma Scale • Modified Rankin Scale • Copies of all SOC head CTs performed through ICU discharge 30 Day Post-Neurapheresis Follow-up Requirements: • General Clinical Data • Hospital Data (if applicable) • Glasgow Outcome Scale Extended • Modified Rankin Scale • Barthel • MoCA
Study Duration	It is estimated that it will take 12-16 months to complete enrollment and protocol required data collection, analysis and reporting requirements.
Sponsor	Minnetronix Neuro, Inc. (MNeuro) Toll-Free: 888-301-1025 1635 Energy Park Drive Phone: 651-917-4060 St. Paul, MN 55108 Fax: 651-917-4066
Sponsor Contact	Julie M Messer Director Clinical & Regulatory Affairs 651-348-3138 jmesser@minnetronix.com

2. Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a catastrophic neurological condition occurring as the result of a ruptured cerebral aneurysm. There are roughly 30,000 cases per year in the US, with worldwide estimated incidence of 9 people per 100,000[1]. After securement of a ruptured aneurysm, patients are closely observed in the hospital for an average of 12-14 days to monitor for complications. aSAH patients can develop severe complications post-aneurysm securement,

[1] de Rooij, N. K., Linn, F. H. H., van der Plas, J. A., Algra, A. & Rinkel, G. J. E. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. Journal of Neurology, Neurosurgery & Psychiatry 78, 1365–1372 (2007)

ranging from vasospasm[2,3,4] and stroke to hydrocephalus[5] resulting in the need for permanent shunting of cerebrospinal fluid (CSF). The lasting effects of these complications can be devastating, possibly resulting in permanent disability and even death. Thus, there remains a significant unmet need to reduce complications and improve outcomes for these patients.

Other common complications of SAH include the following;[6,7,8]

- Re-bleeding of the rupture
- Delayed cerebral ischemia (DCI)
- Delayed ischemic neurological deficit (DIND)
- Seizures and epilepsy
- Cardiac dysfunction
- Systemic inflammatory response syndrome (SIRS)
- Cerebral edema

The treatment for aSAH has evolved from an established standard of care (SOC) craniotomy to clip the aneurysm, to less invasive image guided techniques of endovascular coil placement to pack and exclude the aneurysm from circulation. Despite advancements in technical approaches, the cited clinically significant comorbid state remains unchanged regardless of the therapeutic technique. It is posited that this state of transient compromised cerebral circulation, is related to spasmogenic substances e.g., cytokines, generated during the lysis of hemorrhagic cells[9] that then taint the CSF. Early removal of blood and blood products (e.g. hemoglobin, oxyhemoglobin, and downstream inflammatory proteins) from the CSF has been shown to reduce the incidence of vasospasm, stroke, hydrocephalus and shunting, and result in a shorter hospital course[10].

The PILLAR-XT study uses an extracorporeal investigational pump and filtration system with an investigational double lumen catheter for the rapid removal of red blood cells (RBC's) post SAH. The system removes the hemorrhagic CSF, filters out RBCs and lysed by-products and returns the filtered CSF to the subarachnoid space (SAS) via the same catheter. Minnetronix Neuro (MNeuro) calls this tailored process of the filtration and return of CSF "Neurapheresis™" Therapy which is based on blood plasma filtration or "Apheresis." The active removal of degrading RBC's and their released cytotoxic by-products can be accomplished more efficiently with Neurapheresis Therapy than with a standard, passive ventricular or lumbar drain (LD) which are often indwelling for up to 10 days.

[2] Neal F Kassell et al., "Cerebral Vasospasm Following Aneurysmal Subarachnoid Hemorrhage," *Stroke* 16 (1985): 562–72.
[3] JT Hughes and PM Schianchi, "Cerebral Artery Spasm. A Histological Study at Necrospy of the Blood Vessels in Cases of Subarachnoid Hemorrhage," *Journal of Neurosurgery* 48 (1978): 515–25.
[4] Paul Klimo Jr et al., "Marked Reduction of Cerebral Vasospasm with Lumbar Drainage of Cerebrospinal Fluid after Subarachnoid Hemorrhage," *Journal of Neurosurgery* 100, no. 2 (February 2004): 215–24, doi:10.3171/jns.2004.100.2.0215.
[5] Hasan, D., Vermeulen M., Wijdicks EFM., Hijdra A., & van Gijn J. Management problems in acute hydrocephalus after subarachnoid hemorrhage, Stroke V 20: no. 6, 747-753 (1989)
[6] de Oliveira Manoel A.L. and Macdonald R.L. Neuroinflammation as a Target for Intervention in Subarachnoid Hemorrhage. Front. Neurol. 9:292. (2018)
[7] Solenski, N.J., Haley, E. Clark JR., Kassell, N.F., Kongable, G.R.N., Germanson, T., Truskowski, L., & Torner, J.C. Medical complications of aneurysmal subarachnoid hemorrhage: A report of the multicenter, cooperative aneurysm study. Crit Care Med, 23(6), 1007-1017. (1995)
[8] Suarez, J.I., Tarr, R.W., and Selman, W.R. Aneurysmal Subarachnoid Hemorrhage. N Engl J Med, 354, 387-396. (2006)
[9] GS Allen, HS Ahn, and Tj Preziosi, "Cerebral Arterial Spasm - a Controlled Trial of Nimodipine in Patients with Subarachnoid Hemorrhage," *New England Journal of Medicine* 308 (1983): 619–24.
[10] Paul Klimo Jr et al., "Marked Reduction of Cerebral Vasospasm with Lumbar Drainage of Cerebrospinal Fluid after Subarachnoid Hemorrhage," *Journal of Neurosurgery* 100, no. 2 (February 2004): 215–24, doi:10.3171/jns.2004.100.2.0215

2.1 Previous Clinical Data

In April 2018 the first-in-human cohort of PILLAR subjects (N=15) treated with Neurapheresis therapy was completed. The study was performed at four clinical sites in the U.S. and concluded by MNeuro and Data Safety Monitoring Board (DSMB) review the Neurapheresis System and associated therapy were safe for continued investigational use. A summary of the data is provided below.

PILLAR Study Baseline Subject Status

Status Prior to Neurapheresis N=15	**Summary**
Gender % Female (n/N)	73% (11/15)
Height (mean [range])	5'5" [5'2" – 6']
History of Smoking % Yes (n/N)	40% (6/15)
History of Hypertension % Yes (n/N)	73.3% (11/15)
Family History of SAH % Yes (n/N)	26.7% (4/15)
WFNS (Median [range])	2 [1 – 4]
Hunt & Hess (Median [range])	3 [1 – 3]
Glasgow Coma Scale (GCS) (Median [range])	14 [9 – 15]
Fisher/Modified Fisher Grade (Median [range])	3 [3 – 4]

Considering the typical aSAH population and study inclusion/exclusion criteria, the subject baseline profile proved to be as expected. One subject did not have catheter placement attempted and is not included in further tables.

PILLAR Aneurysm Securement

Aneurysm Securement Data N=14	**Summary % Yes (n/N)**
EVD in place	84.6% (11/13*)
Aneurysm Type, Saccular	85.7% (12/14)
Aneurysm Type, Wide Neck	42.9% (6/14)
Coiled	64.3% (9/14)
Clipped	35.7% (5/14)

*EVD placement not recorded for one subject

Thirteen of Fourteen subjects 92.9% (13/14) in whom catheter placement was attempted had the catheter successfully placed. The one failed attempt was due to the subject being morbidly obese with an unusual distribution of fatty tissue over the lumbar spine thus causing the catheter to bend in the tissue rather than continue over the guidewire. This subject is not included in further tables as the study therapy was not performed.

PILLAR Neurapheresis Summary

Neurapheresis N=13	Summary mean [range]
Total Pump Time (hrs)	15:07 hrs [5:32 – 24:00]
Total processed volume (mL)	632.0 ml [180.6 – 1447.6]
Catheter in-dwelling	30:23 hrs [15:15 – 36:22]

The PILLAR study protocol, under which subjects were enrolled, limited catheter in-dwelling time to 36 hours and total pump time (therapy time) to 24 hours. As can be seen in the table above, the average pump time was shorter than anticipated with only one subject receiving the complete 24 hour allotted time for study therapy. Despite this, clearance of red blood cells (RBCs) from the lumbar cistern was seen as noted in the table below. Longer pump times will be necessary for more complete blood clearance. Pre and Post-Neurapheresis total protein measures were also taken to account for removal of by-products from lysed blood.

PILLAR Post-Neurapheresis Outcomes

Outcome Measured N=13	Pre-Neurapheresis mean ± STD	Post-Neurapheresis mean ± STD	Percent Decrease of Means
Concentration of Total Protein	537.36 ± 500.70 mg/dL	144.09 ± 188.44 mg/dL	73.2%
Concentration of CSF Red Blood Cells (RBCs)	2.78e5 ± 2.43e5 cells/µL	1.17e5 ± 1.30e5 cells/µL	57.9%

Subjects were followed at 2-weeks and 30-days post-Neurapheresis. Other notable outcomes include; a mean of 12 days to discharge from the Neuro ICU with a range of [6 – 18 days]. By the 2-week visit, 38.5% (5/13) were discharged home which increased to 69.2% (9/13) by 30 days.

PILLAR Follow-up Outcomes

Follow-up Status N=13	Two Week Median [range]	30 Day Median [range]
GCS	15 [11-15]	NR*
WFNS	1 [1-5]	NR*
mRS	2 [1-5]	1 [0-4]
GOS	NR*	5 [3-5]
Barthel	NR*	100 [20-100]

*These neuro assessments were not required per protocol

Finally, the primary safety endpoint for the study was the assessment of adverse events associated with the placement of the catheter and operation of the system. As there were no (0) adverse events associated with the placement of the catheter and minimal, expected, non-serious adverse

events (as seen below) during Neurapheresis, the end points of this study were considered to have been met.

The adverse events (AEs) reported below is site reported and was also reviewed by the independent DSMB. While the AEs were reported as potentially related to Neurapheresis therapy, they are also known AEs for subarachnoid hemorrhage patients.

PILLAR Device or Procedure Related Adverse Events During Neurapheresis

Event	Timeframe	Serious Adverse Event (SAE)	Related to System	Related to Neurapheresis	n/N (%)
Headache with Vomiting	Neurapheresis	No	No	Yes	1/13 (7.7%)
Vomiting	Neurapheresis	No	No	Yes	1/13 (7.7%)

PILLAR Device or Procedure Related Adverse Events After Neurapheresis

Event	Timeframe	Serious Adverse Event (SAE)	Related to System	Related to Neurapheresis	n/N (%)
Pain (back/leg)	2 Week F/U	No	Unknown	Unknown	1/13 (7.7%)

Further, no (0) subjects experienced the following:

- No serious adverse events (study device or study procedure related)
- No unanticipated adverse device effects (UADEs)
- No localized infection or systemic CNS infection
- No organisms seen on any gram stain (no abnormal gram stain)
- No growth on CSF culture (including those out to the standard testing of 96 hours)
- No subdural spinal hematomas
- No subdural hematomas
- No brainstem herniation
- No re-bleeding events
- No deaths

Pillar study endpoints were assessed and all were considered to have been met by internal (MNeuro) and independent DSMB review.

2.2 Current Clinical Data

Please see the 2019 Pillar-XT Annual Report for the most current summary of study progress and study data. There have been 16 subjects enrolled and treated with Neurapheresis under a previous version of this protocol.

As documented in the 2019 annual report, one subject previously enrolled in this study had a herniation event. The event was identified early by the Investigator and resolved with no further complication. Terminating therapy and use of the Trendelenburg position resolved the event. Upon investigation, the event was determined to be a result of evolving mass effect in combination with the use of the device that created a sustained negative pressure gradient between the intracranial and lumbar pressures.

PILLAR-XT Adjudicated Adverse Events During Neurapheresis

Event	Timeframe	Serious Adverse Event (SAE)	Resolved	Unanticipated AE	n/N (%)
Pain (back/leg)	Neurapheresis	No	Yes	No	1/16 (6.3%)
Other: Diencephalic Herniation	Neurapheresis	Yes	Yes	No	1/16 (6.3%)

3. DEVICE / SYSTEM DESCRIPTION

A description of the device herein referred to as the "Neurapheresis System" is comprised of dual lumen catheter used in conjunction with a medical cart based extracorporeal pump and filtration system (Figure 1 below). The pump and filtration system include custom and off-the-shelf (OTS) disposable and non-disposable components, with custom software to run and monitor the systems operation. The system was designed in accordance with all applicable design controls and standards.

Figure 1: Neurapheresis System Medical Cart

3.1 Intended Use

The Neurapheresis System is intended for use in the filtration of cerebral spinal fluid in order to remove targeted, disease causing agents from the central nervous system.

3.1.1 Indications for Use

The Neurapheresis System is indicated for the treatment of cerebral spinal fluid in order to remove red blood cells and lysis byproducts in patient with aneurysmal subarachnoid hemorrhage.

3.2 Component Summary

The Neurapheresis System access tools and accessories are a combination of OTS and custom developed tools designed to gain access to the lumbar SAS and to facilitate catheter placement. A summary of the system components can be found below or in the associated Instructions For Use (IFU).

Table 1: Neurapheresis System Component Summary

Component Name	Component Description	Disposable Status
Neurapheresis Catheter	Dual lumen spinal catheter	Disposable
Flow Assembly	Blue and red coiled tubing with flow sensor	Disposable
Filter Assembly	Tangential flow filters with pressure sensors	Disposable
Waste Assembly	Pump tubing and Waste Bag connection	Disposable
Epidural Needle	15g straight epidural needle	Disposable
Uncoated Guidewire	0.018 diameter guidewire	Disposable
Waste Bag	Merit Disposal Depot Bag and tubing	Disposable
Neurapheresis System Enclosure	Houses pumps, pressure sensors and flow sensors	Non-Disposable
Main System Pumps	Two Peristaltic pumps, one for main system other for waste assembly	Non-Disposable
Data Acquisition System	Fanless medical station PC with LabVIEW software	Non-Disposable

3.3 Disposable Component-Catheter

The Neurapheresis catheter has not been tested for MRI compatibility.

The Neurapheresis system catheter follows 510(k) approved predicates in size and length for which the intended use is within the lumbar and thoracic spinal spaces. The catheter materials, Nylon 12, Pebax® and Polytetrafluoroethylene (PTFE) are well established composites for construct of vascular catheters. The dual-lumen catheter employs a tapered co-axial design that is coil reinforced to assist with handling and, to resist kinking or crushing when navigating the spinal anatomy.

There are radiopaque marker bands at both the proximal inlet and distal outlet sections to assist the Investigator with positioning the proximal holes in the lumbar cisterns and the distal outlet in the thoracic anatomy as seen in the figures below.

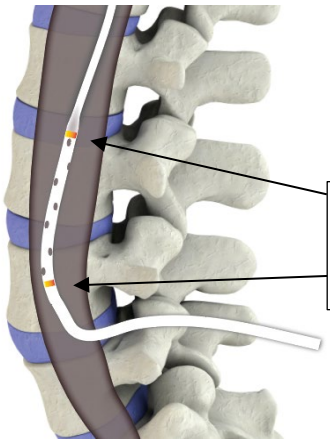


Figure 2: Lumbar Proximal Inlet Holes

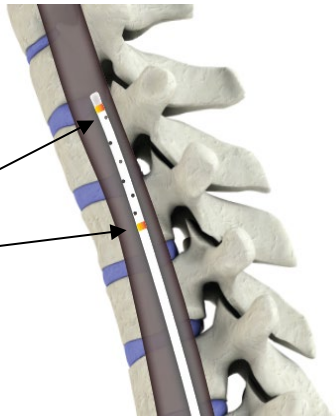


Figure 3: Thoracic Distal Outlet Holes

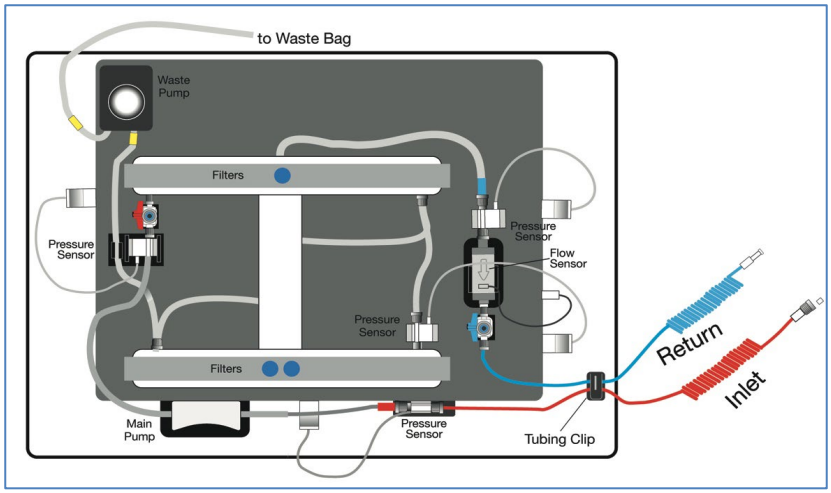
3.4 OTB Disposable Component-Filter and Flow Assemblies

The Neurapheresis System out-of-the-body (OTB) disposable "Filter Assembly" is pre-configured and packaged in a clamshell tray for ease of transfer on to the sterile field. The Filter Assembly is comprised of various lengths of tubing, two (2) OTS 100 kDa Millipore Pellicon™ tangential flow filters (TFF), and (4) OTS PendoTECH pressure sensors. The sensors are not intended to replace SOC patient monitoring devices, nor should they be used for making clinical assumptions or decisions.

The Neurapheresis System OTB disposable "Flow Assembly", is pre-configured and packaged in a clamshell tray for ease of transfer on to the sterile field. The disposable Flow Assembly connects to the catheter and to the Filter Assembly. The Flow Assembly contains an OTS flow sensor and two (2) 3-way stopcock sample ports on the inlet and outlet hubs of the system catheter.

The integrated sensor readings are used to facilitate the automated algorithm, to allow for manual adjustments to the pump settings or to trouble shoot system issues. The 3-way stopcocks of the Flow Assembly are used to facilitate CSF sampling and priming of the system. The figure below is a diagram of the filter, flow and waste assemblies as appropriately set up for use.

Figure 4: Filter, Flow and Waste Assemblies



3.5 Non-Disposable Component-Data Acquisition System

The Neurapheresis System utilizes PC and data acquisition system. The system operates with customized software for the user interface, data logging (archive, analysis and data transfer), motor control, pressures and flow rate monitoring. This system software is considered investigational and is not commercially available. The figure below provides a visual of the touch screen user interface.

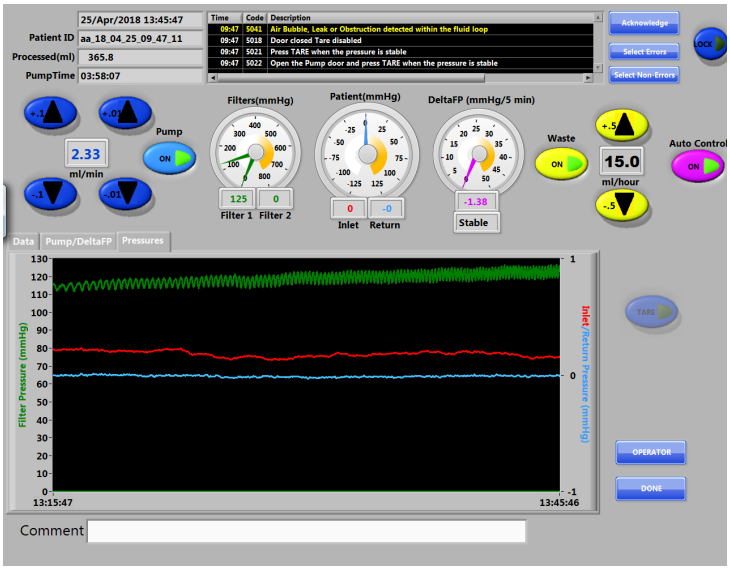


Figure 5: Neurapheresis System Touch Screen User Interface

The system has an integrated battery back-up for use during transport or a systemic power loss at a center. When not in use, the cart shall be connected to a power supply in the identified center storage area.

3.6 Shipping and Device Accountability of the Investigational System

The investigational catheter and non-disposable components of the Neurapheresis System will be shipped and tracked in accordance with 21CFR§812.140 (b)(2) requirements. and will only be shipped to sites and Investigators who have been selected by MNeuro to participate in this study.

A Device Accountability Log will be maintained to catalogue receipt and disposition of the catheter and non-disposable components. The Sponsor will provide a shipping mechanism or instructions for return of the system and individual components as needed through completion of the clinical study.

3.6.1 Required Disposable Component Return

The Neurapheresis system catheter is the only disposable that is required to be returned to the Sponsor. While the guidewire is considered to be investigational due to their off-label use, they may be destroyed at the study site. The MNeuro Clinical Field Specialist (CSF) (i.e. technical representative) has the discretion to request return of other disposable components if there is a performance question that could be answered by further analysis. Catheters or other used disposables are to be returned to the Sponsor in the biohazard shipping containers provided. Returns of any components will be documented on the Device Accountability Log.

4. STUDY DESIGN

The PILLAR-XT study is a prospective, multi-center, non-randomized single arm study that is an extension of the first-in human PILLAR study.

4.1 Objective

The objective of this study is to further demonstrate safety and characterize effectiveness of the Neurapheresis™ System (extracorporeal system and catheter) to remove red blood cells (RBCs) and lysed blood by-products from hemorrhagic cerebrospinal fluid (CSF) following aneurysmal subarachnoid hemorrhage (aSAH).

4.2 Scale and Duration

The Study will enroll N=30 "Treated" subjects, as defined by the protocol. The study will be performed at up to 8 centers within the United States. Subjects will have assessments and data collection at enrollment, during catheter placement and Neurapheresis procedure, 2 days (±1 days), at Neuro ICU discharge and 30 days (±3 days) post removal of the catheter.

Based on the incidence of occurrence of SAH in the US population, it is estimated that it will take approximately 12-16 months to complete enrollment and protocol required data collection, analysis and reporting requirements.

4.3 Study Endpoints

The PILLAR-XT Study does not have a hypothesis based statistical endpoint due to the feasibility nature of the investigation.

Primary Endpoints:

1. Mean reduction of cisternal blood via CT post study therapy
2. Proportion of subjects with Neurapheresis Catheter, System or Therapy related serious adverse events

Secondary Safety Endpoints:

- Proportion of subjects with successful catheter placement of those attempted
- Proportion of subjects with study device or therapy related adverse events
- Proportion of subjects with systemic CNS infection within 5 day of catheter removal

Secondary Efficacy endpoints:

- Mean reduction of RBCs and total protein by CSF sample post study therapy
- Mean length of Neuro ICU stay

Exploratory endpoints:

- Proportion of subjects requiring additional CSF management during study therapy or on-going CSF management post study therapy
- Reduction in biomarkers of inflammation as seen in CSF, blood and physiologic manifestations post study therapy
- Proportion of subjects with symptomatic complications from aSAH
- Analysis of endpoints by the following sub-groups for any groups that have at least 5 subjects that meet the criteria for the group;
    - Age: <45, ≥45-<60, 60 – 70 years

- Gender: male, female
- Enrollment Modified Fischer grade: 2, 3, 4
- Baseline cisternal Hijdra score: ≤15, 16-20, 21-25, 26-30
- Neurapheresis time: <16hrs, ≥16-28hrs, >28-40hrs, >40hrs
- Other sub-groups not yet defined

4.4 Justification for Study and Design

The previous first-in-human study, PILLAR study, was completed to substantiate the feasibility and safety of Neurapheresis in aneurysmal SAH patients. As described in section 2.1, the study endpoints were met. The PILLAR-XT study is designed to further confirm safety and characterize efficacy of Neurapheresis therapy. Additionally, this study is expected to generate foundational data for development of the Neurapheresis treatment curve (e.g. time or volume processed needed to clear blood from the subarachnoid cisterns and lumbar spine). The study works in tandem with the current SOC treatments for SAH and does not detract from the established care pathways, or deny enrolled subjects proven therapies. The PILLAR-XT study utilizes the established skill sets of chosen Investigators who are already trained in the treatment and care of SAH patients and insertion/management of lumbar drains.

5. SUBJECT SELECTION

5.1 Study Population and Eligibility

Subjects considered for the PILLAR-XT study will be identified from a pool of patients, who are admitted to the investigational center and have experienced a SAH. Subjects will be eligible for enrollment based on adherence to the inclusion/exclusion criteria outlined below. The Investigator and/or designated site staff is responsible for screening patients to determine the appropriateness of the PILLAR-XT study for each patient based on compliance to study criteria and the overall patient status.

5.2 Screening and Subject Enrollment

Screening for potential study subjects can be done either prior to or after aneurysm securement depending on the institutional work flow, IR/OR availability, LAR availability or patient status. Inclusion or exclusion criteria that can be assessed by institutional SOC may be done so prior to written informed consent, however no study specific procedures may be performed until informed consent is obtained. Informed consent is considered the point of enrollment.

5.3 Institutional Standard of Care Treatment

The PILLAR-XT study does not require a uniform method for the treatment to secure the aneurysm i.e., Clip vs. Coil. Additionally, the Investigator may use accepted institutional SOC and professional discretion for interventions and treatments which include, but are not limited to:

- SOC neurological assessments
- SOC imaging
- ICP monitoring
- EVD placement
- “Triple H” therapy (hypertension, hypervolemia, hemodilution)

- Hyperventilation
- Nimodipine
- Seizure prophylaxis
- Antimicrobial prophylaxis

5.4 Inclusion Criteria

Subjects who meet all of the following criteria may be given consideration for inclusion in this clinical investigation:

- Age: 18 – 70 years
- Informed consent by the patient or his/her legally authorized representative
- Modified Fisher Grade 2, 3 or 4 SAH
- Hunt & Hess I-IV
- First aneurysmal SAH that has been confirmed by CT scan and secured or planned securement via clipping or coiling per institutional SOC
- Patient is ≤ 48 hours post bleeding event
- World Federation of Neurosurgeons (WFNS) Grades I-IV
- Patient is indicated for a ventriculostomy

5.5 Exclusion Criteria

Subjects who meet any of the following criteria will be excluded from this clinical investigation:

- Pregnancy
- Patients with a SAH due to mycotic aneurysm or AV malformation
- Patients who present with an acute MI or unstable angina
- Patients with uncontrolled diabetes at the time of catheter placement
- Patients who present with a creatinine > 2.0mg/dl
- Imaging demonstrates supratentorial mass lesions ≥15 cc
- Imaging demonstrates ≥2 mm of mid-line-shift associated with infarction and or edema
- Imaging demonstrates infratentorial mass lesion ≥10cc
- Imaging demonstrates presence of any subdural hematoma
- Effacement of the basilar cisterns (suprasellar, ambient, chiasmatic and quadrageminal)
- Vasospasm on admission as defined by angiographic evidence
- Patients with a coagulopathy that cannot be reversed per the professional discretion of the investigator
- Patients with a connective tissue disorder that may impact the integrity of the dura
- Thrombocytopenia def. platelet count < 100,000
- Patients on low molecular weight heparin, such as Lovenox
- Patients on Clopidogrel bisulfate (Plavix) or other chronic platelet inhibitors
- Patients with a documented history of cirrhosis
- Non-communicating obstructive hydrocephalus
- Patients with a lumbar or thoracic spinal anatomy (e.g. severe spinal stenosis) or history of posterior fusion hardware that would interfere with placement or appropriate in-dwelling of the catheter
- Existing hardware that prevents accurate CT imaging
- Pre-existing Lumbar Drain
- Local skin infections or eruptions over the puncture site
- Signs of CNS infection, sepsis or pneumonia
- Lumbar puncture within 6 hours

- Concurrent participation in another study which is not observational or retrospective in nature without prior approval from the Sponsor

5.6 Informed Consent

The Sponsor will provide to each center, an FDA approved Informed Consent Form (ICF) template which may be edited to include center specific language or compliance requirements. The Sponsor and Institutional Review Board (IRB) must approve any changes to the form prior to use for consent of a patient. A central IRB, Western IRB (WIRB), will be utilized for this study. Each enrolled subject must also consent to data transfers affected by HIPAA; the center may use their own HIPAA consent form to document this data transfer.

Informed Consent is a process by which a patient voluntarily confirms their willingness to participate in the study after being informed of all risks and requirements. Informed Consent is documented by means of a signed and dated ICF. Once the patient or their legally authorized representative (LAR) signs and dates the ICF, the patient is considered enrolled in the study and becomes a study subject.

Study enrollment without consent must be reported by Minnetronix, to the IRB and the FDA. Any violations of the informed consent process must be reported as deviations to the sponsor and local regulatory authorities as appropriate.

The process of obtaining Informed Consent shall:

- Process of obtaining Informed Consent must be documented in the Subject's medical record or study binder,
- Be conducted by the Principal Investigator or designee authorized to obtain informed consent,
- Include a description of all aspects of the clinical study that are relevant to the patient's decision to participate throughout the clinical study,
- Avoid any coercion of or undue influence of patient to participate,
- Not waive or appear to waive patient's legal rights,
- Use native language that is non-technical and understandable to the patient or his/her legal representative,
- Provide ample time for the patient or LAR to consider participation and ask questions if necessary,
- Ensure important new information is provided to new and existing Subjects throughout the clinical study.

The ICF shall always be signed and personally dated by the subject or LAR and by the Investigator or an authorized designee responsible for conducting the Informed Consent process. If a LAR provides signatory authority, the subject shall be notified of the informed consent and study participation as soon as his/her medical condition allows. The original signed ICF will be retained by the center and a copy of the signed and dated document and any other written information must be given to the subject or LAR signing the form.

If new information becomes available that can significantly affect a subject's future health and medical care, that information shall be provided to the affected subject(s) in written form via an amended informed consent form or other format as requested by the IRB or FDA. Further, if requested by the IRB or FDA, all affected subjects shall be asked to confirm their continuing informed consent in writing.

Other situations may necessitate revision of the ICF, e.g., amendments to the protocol, a change in Principal Investigator, administrative changes or requests following annual review by the IRB. The new version of the ICF must be approved by the IRB and Minnetronix before implementation at investigative centers. The IRB will determine the subject population to be re-consented, if applicable.

Once the patient or their LAR provides consent, data collection may begin. The Investigator shall continue the institutional SOC for the treatment of SAH while providing the Sponsor with the data required for the study.

5.7 Subject ID Assignment and Enrollment Notification

Once Centers have identified a study candidate and Informed Consent has been obtained, the Sponsor must be notified as soon as possible to ensure rapid deployment of the Sponsor's Technical Personnel. Specific instructions on the study communication/notification process will be covered at site specific training. Subject ID's will be assigned via the study database and documented on a screening log.

5.7.1 Subject Enrollment Classifications

All patients who provide written consent to participate in the study will be considered enrolled study subjects, however not all subjects will contribute to the enrollment cap of N=30 Treated Subjects. Only treated subjects, as defined below, will contribute to the enrollment cap. As such, it is expected that up to 40 subjects may be enrolled to meet the enrollment cap. FDA, IRBs and Investigational sites will be notified when enrollment is complete.

Intent to Treat Subjects:

- Subjects who provide written informed consent but do not have placement of the study catheter attempted. This would include placement tools such as the epidural needle and guidewire. Intent to Treat subjects will be exited immediately. They will not count towards the enrollment cap of N=30 treated subjects. Only enrollment and study exit data will be collected in the study database.

Attempt to Treat Subjects:

- Subjects who provide written informed consent and have any portion of the catheter placement procedure attempted (including the epidural needle and guidewire) but placement was unsuccessful. Attempt to Treat subjects will be followed through 2 days post-attempt for safety then will be exited. They will not count towards the enrollment cap of N=30 treated subjects. They will be included in the analysis of safety endpoints but will not be included in the analysis of efficacy endpoints. Enrollment, catheter placement attempt, 2 day follow-up and study exit data will be collected along with any adverse events or protocol deviations if applicable.

Treated Subjects:

Subjects who provide written informed consent, have successful placement of the study catheter and had Neurapheresis initiated. These subjects will be followed out to 30 days according to the study protocol then exited. They will count towards the enrollment cap of

N=30 treated subjects and used in all analyses. All study data through the 30 day follow-up will be collected.

6. RISKS AND POTENTIAL BENEFITS

Subjects participating in this study are exposed to the same inherent risks shared by all patients undergoing treatment for SAH and who receive a lumbar drain as SOC for a number of clinical applications. These risks include but are not limited to headache, nausea/vomiting, transient pain, re-bleed, infection, CSF leak, changes in intracranial pressures, cognitive defects or poor neurological outcomes, other SAH complications and complications from associated interventions (e.g., IA therapy, angiography) and death.

The Study protocol does not prevent SOC for the management of SAH patients and utilizes well established techniques for lumbar puncture for diagnostic purposes, therapeutic applications or interventions. Only Investigators trained in the management of SAH patients, the associated care pathways and/or placement and management of lumbar drains are included in this study. Further, Investigators are trained on the Clinical Protocol to further minimize subject risks.

6.1 Risks Associated with the Device, Components or Procedure

The table below outlines the risks that are associated with the Neurapheresis System (catheter, components and study procedure). In the event of a catheter or disposable replacement, the risk profile remains unchanged.

Table 2:Neurapheresis System Risks

Risks
Additional radiation exposure
Brainstem herniation
Headache
Nausea / Vomiting
Fluctuation in CSF volume or pressure
CSF leak
Retained catheter
Localized transient pain (back/leg)
Peripheral neuropathy / Paralysis
Re-Bleed / Hemorrhage
Infection / Sepsis
Subdural spinal hematoma
Death

6.2 Potential Benefits

It is hypothesized that utilizing the Neurapheresis System post SAH could improve neurological outcomes by the rapid removal of the CSF contaminants (blood and those generated during the lysis of the subarachnoid hemorrhage[11]). Other potential benefits may include a reduced likelihood

[11] Klimo et al., "Marked Reduction of Cerebral Vasospasm with Lumbar Drainage of Cerebrospinal Fluid after Subarachnoid Hemorrhage."

of common SAH complications. These benefits are only theoretical at this time; therefore, subjects may receive no direct benefit from participation in this study.

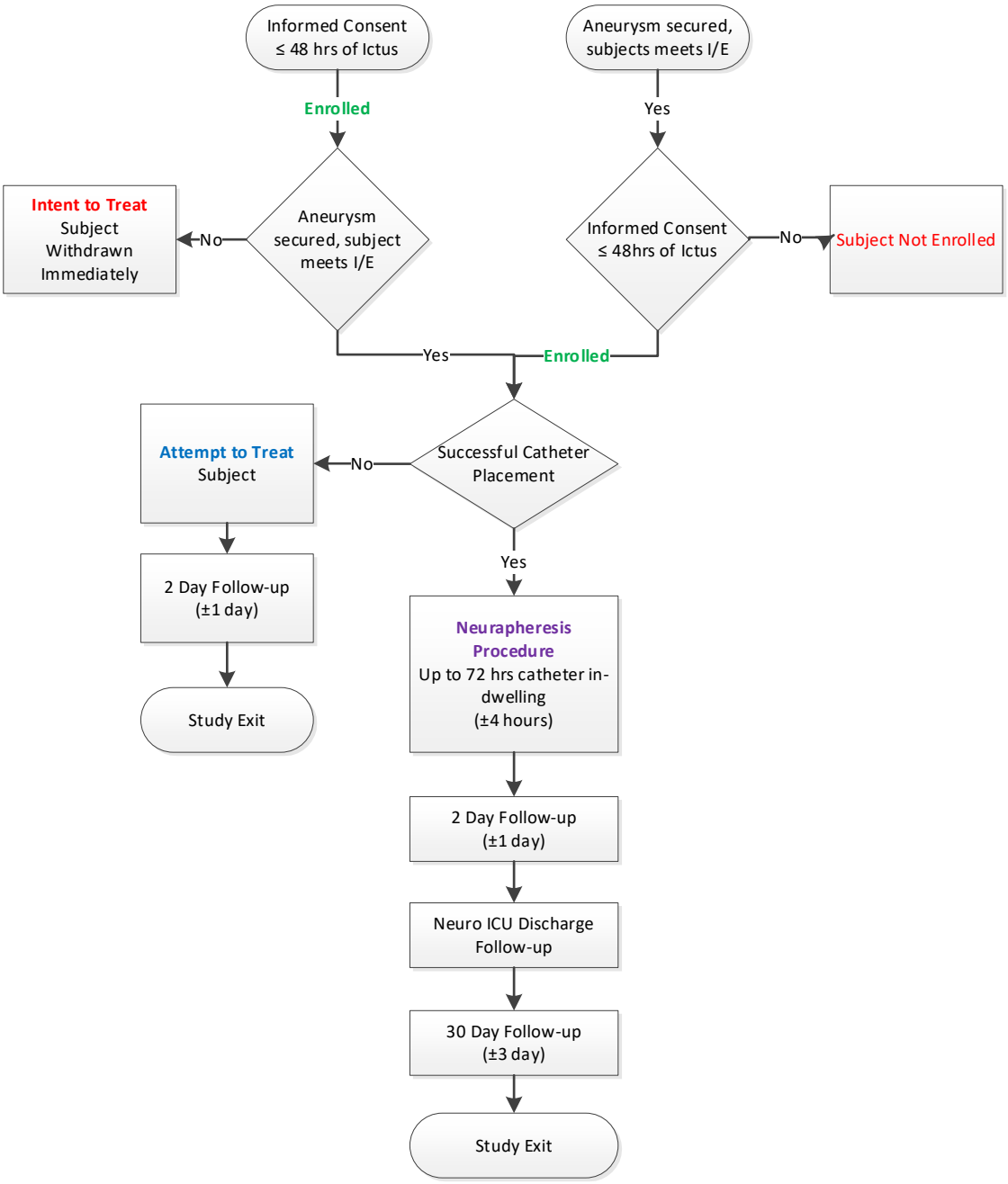


Figure 6: Expected PILLAR-XT Subject Flow

7. STUDY REQUIREMENTS

Once the subject or LAR provide consent, study data collection should begin as the subject is considered enrolled. The Investigator shall follow the institutional SOC for the treatment of SAH while providing the Sponsor with the data required for the study.

Outlined in Figure 6 is the PILLAR-XT Subject flow which describes how subjects would move through the study and the associated surveillance requirements. It is expected that subjects will participate in the study for a maximum of 36 days from the time of enrollment to the time of exit.

7.1 Screening Requirements

Standard of care assessments may be used to screen potential subjects against inclusion/exclusion (I/E) criteria for the study. Testing that is outside of SOC, cannot be performed until after a subject has been enrolled (i.e. written informed consent obtained). Once the subject has been enrolled and it has been determined that screening criteria are met, the subject can be prepared for catheter placement. If instead it is determined that a subject no longer meets study criteria after completing all screening assessments, they are to be withdrawn immediately and classified as an "Intent to Treat" subject. Enrollment data collected to that point and the reason for study exit should be entered into the case report forms for submission to the sponsor.

A screening CT is required to assess I/E criteria and is expected to be a SOC test for the diagnosis and treatment planning of aSAH. If a subject has been transferred from another institution at which a CT was obtained, a new screening CT is not required provided that an electronic copy of the CT can be obtained from the referring institution. It is expected that the volume of any identified mass lesions as noted in the study exclusion criteria will be calculated using the standard of care formula used by most radiologists in practice today. The formula should be based on the estimated volume of an ellipsoid ($L \times W \times H \times 0.52$ (where 0.52 is an approximation for $\pi/6$).

Volume = A x B x C / 2

- A = greatest hemorrhage diameter in the axial plane
- B = hemorrhage diameter at 90º to A in the axial plane
- C = originally described as the number of CT slices with hemorrhage multiplied by the slice thickness, but can simply be substituted with the craniocaudal diameter of the hemorrhage where there is access to multiplanar reformats

A venous blood sample is also required for screening and to establish baseline values for certain inflammatory markers (platelets and white blood cells including neutrophils and lymphocytes). Sample amounts should be based on site specific laboratory requirements for completion of tests including a Complete Blood Count (CBC) with Differentials and a Comprehensive Metabolic Panel (CMP). Current laboratory certificates are required by the sponsor with laboratory processes to be made available upon request.

7.2 Pre-Neurapheresis Imaging (CT) Requirements

As aneurysm securement (especially clipping) may change the amount of blood in the subarachnoid space, a CT is required following aneurysm securement but prior to beginning Neurapheresis. This CT will serve as the Baseline CT (pre-Neurapheresis CT) which, along with the screening CTs, will be compared to the post-Neurapheresis CTs. The Baseline CT is expected to be taken in a department scanner using optimal metal artifact reduction settings at the conclusion of aneurysm securement or following catheter insertion but prior to initiation of Neurapheresis therapy. The baseline CT must be reviewed to determine safety, via intracranial

stability, prior to beginning Neurapheresis therapy. In particular, the Investigator must assess the CT for the following criteria:

- no evidence of re-bleeding;
- no increasing mass effect;
- no effacement of the basilar cisterns;
- continued communication between the ventricles and subarachnoid space

In addition to the CT requirements above, study therapy cannot begin for at least 8 hours following aneurysm securement for subjects who underwent a clipping procedure.

If the subject meets these criteria, study therapy can be initiated. If the subject does not meet these criteria, either the subject can be exited, or another CT can be taken to determine baseline stability. If the subject still does not meet the safety criteria to begin study therapy after the second baseline CT, the subject is to be exited. If the study catheter was not placed prior to the baseline CT, the subject should be exited as an Intent to Treat Subject and no further follow-up is required. If however the study catheter was placed prior to the baseline CT, a 2-day follow-up is to be completed and the subject exited as an Attempt to Treat Subject.

7.3 Heparinization/Anti-Platelet Guidance/Aneurysm Stability

If Heparin is to be administered as a center SOC for a coiling procedure, study subjects must have a baseline Activated Clotting Time (ACT) drawn *prior to administration of the initial heparin* bolus. An additional ACT must be checked prior to the Neurapheresis catheter insertion. When the ACT reads baseline ±10 sec it is deemed safe to proceed. ACT's must be recorded on the case report form and are considered to be source documentation if not captured elsewhere in the medical record.

If a subject requires an additional platelet aggregation inhibitor e.g., Integrilin as part of the coiling procedure, the Investigator may wait to insert the Neurapheresis catheter but must initiate catheter insertion *within the window of 48hours post ictus* and, coagulation is deemed safe to proceed. Subjects who are enrolled and do not meet these criteria of time or coagulation should be withdrawn and are classified as "Intent to Treat subjects". Documentation of adequate coagulation metrics is a protocol requirement regardless of method used to secure the aneurysm.

Prior to proceeding with catheter insertion, the Investigator uses professional judgement to determine if the Subject and aneurysm is stable. If stability is in question, the Investigator may wait to insert the catheter but insertion must still fall within the 48 hour from ictus time frame.

7.4 Catheter Insertion

The Investigator should be mindful of a history of lumbar or thoracic stenosis or any existing spinal instrumentation when placing the catheter. Initial insertion of the investigational catheter is to be timed to be as close as possible to completion of the initial treatment/securement of the SAH but no later than 48 hours post-bleeding event. Ideally, the catheter should be inserted immediately after the coiling or clipping procedure; see the previous Section for guidance concerning Heparin and anti-platelet administration. Insertion of the Neurapheresis catheter is expected to have a similar pain profile as that of lumbar drain insertion and should be treated

accordingly. It is recommended that adequate local anesthetic and sedation/analgesia is in place at the time of catheter insertion. An MNeuro CFS will be onsite to support the catheter placement and system prep.

The Investigator may choose the position which affords the most technical comfort level for insertion e.g., lateral decubitus or prone; there is no protocol requirement for positioning, but the position of the subject must be documented on the Neurapheresis CRF. If the catheter placement occurs immediately following a clipping procedure, a C-arm and an OR table that can accommodate portable fluoroscopy will be needed. Continuous lateral fluoroscopy is recommended during guidewire insertion to ensure that there is no looping of guidewire and that catheter follows the guidewire appropriately and tracks dorsally. Elapsed time to place the catheter is a required data item.

Catheter insertion and system set up are to be performed according to the Instructions For Use (IFU). While highlights of the insertion are included in this protocol, the current IFU should be referenced prior to and/or during each procedure. Investigators delegated to perform catheter placement are required to acknowledge their review and understanding of the IFU prior to being approved to place the catheter. The investigational catheter is expected to be inserted under fluoroscopic guidance using the tools provided by the Sponsor, however if the subject anatomy is unusual, use of different delivery tools e.g., guidewires, and access needles may be allowed. Documentation on the case report forms will be required.

To minimize the risk of infection and nerve damage, insertion and placement of the catheter is limited to two (2) discrete events**.** If the catheter ceases to function effectively e.g., positional migration, kink or clot, the Investigator may remove the catheter once and replace it with another catheter. Subjects must be transported to an interventional procedure room for catheter replacement; re-insertion ***may not*** be facilitated at the bedside with a C-arm. The catheter change-out is be performed according to the IFU. If a catheter change out is needed, it is ***required*** that the system disposables are also replaced to mitigate the risk of infection e.g., meningitis. Reconnecting to an existing system would result in a protocol deviation.

7.4.1 Catheter Insertion Highlights

- Soak and flush catheter in preservative free saline prior to insertion
- SOC patient prep, positioning and anesthesia for lumbar puncture
- Insert epidural needle through intervertebral spinous processes to the dural level (skin nick or pilot hole may be used to help with passage of the needle
- Remove the needle stylet and observe for CSF drainage, advance slowly until CSF is returned
- A 5ml CSF sample to be taken from the needle
    - 3ml submitted for Cell counts with Differential and Chemistries
    - 2ml for biomarkers (cytokines) which must be stored in a -80^{o} freezer until shipped to the core lab
- An additional level or re-positioned attempt can be made if no CSF is returned
- Do not perform excessive attempts to avoid potential complications such as CSF leakage, spinal headache or nerve root damage
- Insert guidewire and advance to low-mid thoracic spine, tracking dorsally

- Remove epidural needle and leave guidewire in place
- Using an OTW technique, advance catheter over the guidewire (with tension on the end of the guidewire to prevent further advancement
- Upon reaching the guidewire tip, advance both the wire and catheter together until the catheter proximal inlet holes rest within the lumbar cistern (approximately L2-L3)
- When the catheter is in position remove the guidewire

If there is significant difficulty in gaining access, placing or positioning the catheter, abort the procedure and dress the wound per SOC. Those Subjects who have the procedure aborted due to an inability to gain access or obtain an acceptable position are classified as an "Attempt to Treat" subject and are followed according to the protocol through 2 day follow-up to assess the wound and potential adverse events related to the attempted access or catheter insertion. Subjects in the Attempt category are exited from the study after the protocol required 2 day follow-up visit.

It is highly recommended to have the Neurapheresis System assembled and prepped either prior to or while the catheter is being placed to minimize IR/OR time for the subject. However, if the system is not prepped completely by the time of catheter securement is complete, Investigators or center staff should carefully join the male and female ends of the catheter together to form a sterile loop to avoid CSF leakage while waiting to connect the catheter to the system. Do not overtighten the catheter hubs. The figure below demonstrates how to properly connect the catheter to maintain sterility of the catheter hubs.

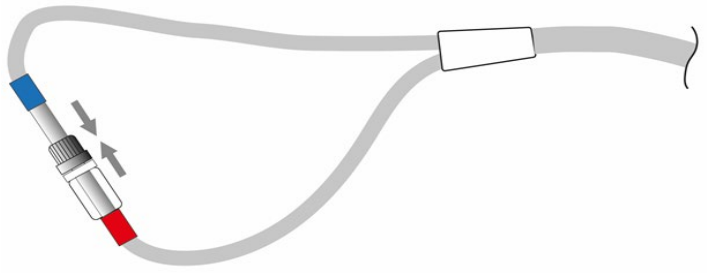


Figure 7: Temporary Connection of the Catheter Male and Female Ends

Upon connection of the catheter to the system a flow test is required to ensure the connections are secure, the system has been appropriately set up and a flow loop has been established (refer to the IFU for proper system assembly and details on the required flow test). Following completion of a successful flow test, the catheter can be externally secured to the subject.

7.4.2 Guidance-Securing the Catheter/Dressing the Wound

Investigators are required to use a fixation device to secure the catheter to the subject to eliminate catheter movement and pullout. Commercially available devices (StayFix by Merit Medical) will be provided by the Sponsor to ensure availability. The fixation device contains a dressing but the choice of a topical antibiotic ointment is discretionary per the Investigator. Center personnel may also shave any excess hair from around the insertion site to assist with skin preparation for the application of the fixation device. Other institutional SOC surgical tape may be placed over the StayFix if preferred, however not underneath the StayFix.

The catheter is designed with extra length such that the pressure points can be avoided and that access to the system ports can easily be facilitated. Avoid positioning the extra catheter length over a bony prominence by taping the catheter to the Subject's abdomen or torso for easy access.

An ongoing dialogue with the MNeuro CFS will assure that the exteriorized catheter is properly positioned to optimize system functionality, however, guidance is provided below.

- Use the protocol required Stay-Fix device to dress the puncture wound site. Ensure that the orientation of the catheter and application of the dressing afford the least amount of bend/stress on the catheter (see Figure 8). The catheter should be positioning snugly over the blue support pad before securement.

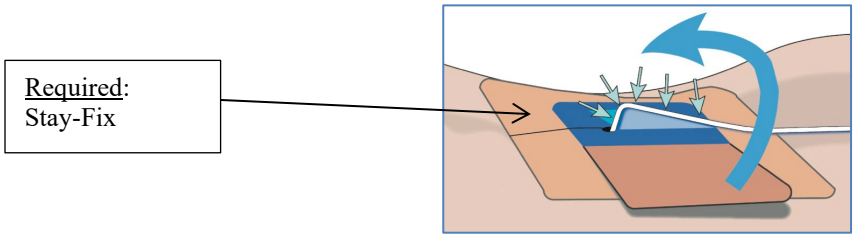


Figure 8: Catheter Positioning within StayFix

- On smaller patients, a single coil with the catheter is to be created and may be secured with surgical tape.
    - While not required, previous Investigators preferred to cover the StayFix and single catheter coil with Tegaderm™ or OpSite™.
- For proper oversight of system functionality, it is imperative that the bifurcation (Y joint) and catheter luer hubs are visible at all times.
    - As such, they should not be hidden under the bed sheets or taped to bed rails
- It is necessary and appropriate to have a lengthy "tail" on the catheter.
    - When positioning the tail, it is recommended to tape the catheter to the torso, with a loop of coiled tubing to act as strain relief (see Figure 9).
    - Ensure placement of the catheter does not create a pressure point if the subject should roll over or move. Chux or gauze may be placed beneath the catheter hubs to further protect the connections.
- A second StayFix device may be used to further secure the coiled tubing to the patient's abdomen (Figure 9).

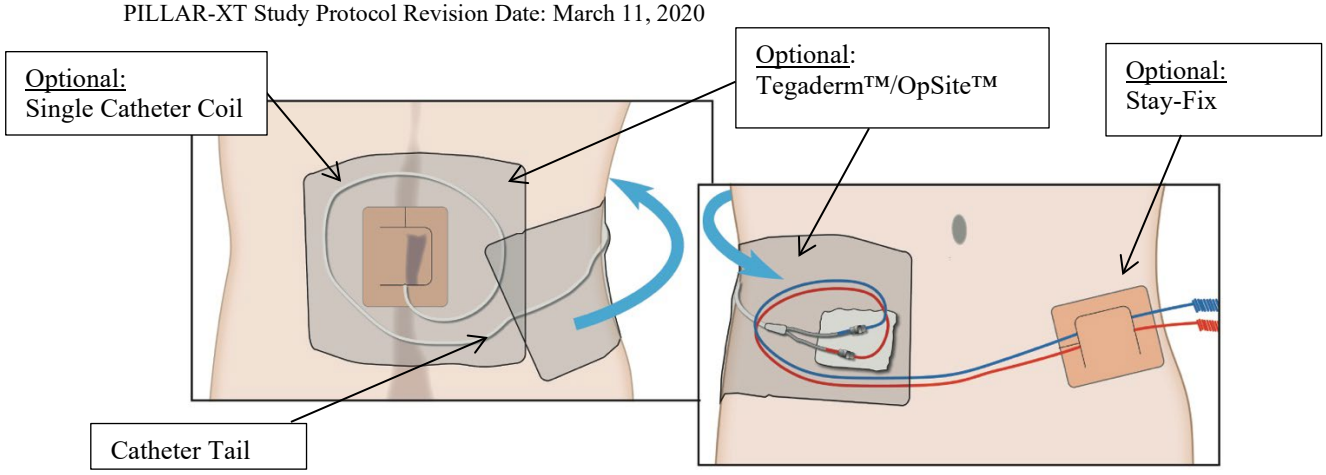


Figure 9: Catheter Fixation Device and Protective Dressing

7.4.3 OTB System Disposables Replacement

It is possible that a change of the OTB system disposables i.e., Filter and Flow Assemblies, Luer fill set and the waste bag, may be required during the Neurapheresis procedure. Change-out of the OTB system disposables can be driven by physical causes e.g., accidental cutting/crush of tubing or, driven by system data e.g., suspicious component behavior etc.

The Sponsor will track change outs of the disposables and the rationale for each action. Change-outs dictated by a component behavior may require return of the affected component to the Sponsor for analysis for product development purposes.

Change out of the OTB system disposables may be facilitated at the bedside; it is not necessary to return to the IR/OR, subject transfer is left to the discretion of the Investigator.

When changing the system disposables, Investigator will disconnect the catheter from the system and join the two ends (male→female) forming a sterile loop that maintains the sterility of the catheter ends (Figure 7). A sterile field should be established to connect the filter and flow assemblies and to facilitate priming of the system. The MNeuro CFS will guide center personnel in the catheter disconnection, component assembly, handing, and reconnection as needed based on the components being replaced. The IFU should also be referenced during this time for detailed instructions on disposable component replacement.

7.5 Neurapheresis Therapy

As this is an investigational system, Investigators and study staff expected to place, use or monitor the system will be trained in the applicable information, techniques and troubleshooting. Despite training, Investigators and applicable site staff should refrain from making medical decisions based on any data point or trend displayed on the Neurapheresis system interface and instead continue to reply on SOC devices or data.

The study catheter may remain in-dwelling for up to 72 hours (± 4hr) in treated subjects during which study therapy can be completed. Neurapheresis therapy will be incrementally extended during the study such that, the first five (n=5) treated subjects enrolled under this protocol will have a maximum of 36 hours (± 4hr) of Neurapheresis therapy (pump time) allowed during the 72 hours (± 4hr) of catheter in-dwelling.

Following positive DSMB review of the data from the first five subjects, the remaining up to n=9 treated subjects (for a study total of N=30 Treated Subjects) will have no limit on maximum therapy time and instead be limited only by the maximum catheter in-dwelling time of 72 hours (± 4hr).

If the DSMB does not agree that it is safe to remove the Neurapheresis therapy limit after review of data from the first five subjects enrolled under this protocol, the maximum of 36 hours (± 4hr) of Neurapheresis therapy (pump time) will remain in place for the remaining subjects. s.

The sponsor will notify FDA, the IRB and clinical sites of the results from the DSMB review.

The start of catheter indwelling time is the time of catheter securement completion. The end of catheter indwelling time is marked by catheter removal and is not to exceed a total of 72-hours (±4hrs). Center personnel must document required catheter times in the case report forms and medical record source as applicable.

Neurapheresis therapy start time is documented when study therapy is initiated. Therapy end is captured as the time the pump is stopped to allow for catheter removal. Study therapy will not be continuous for the 72-hours of catheter in-dwelling. Pausing of therapy may be required for SOC activities and potential fluctuations in the clinical status of the subject. The protocol also requires pausing of study therapy at the study required neuro checks and for study required CTs.

7.5.1 Neurapheresis Therapy Rates

Neurapheresis therapy will commence slowly at a nominal flow rate of 0.5mL/min. to accommodate the volume of hemorrhagic CSF pooled in the lumbar cistern. An increase of flow shall not occur until 1 hour of aggregate pump time has elapsed to optimize the system operation during the initial access of the pooled hemorrhage. At this time, a baseline CSF sample will be taken, see Section 7.5.7.

After the CSF sample has been taken, the MNeuro CFS will transition the system to auto mode. In this mode, an automated algorithm will adjust the flow rates to continuously optimize the Neurapheresis therapy based on system pressures. The MNeuro CFS will be present while the system is in auto mode for system oversight. During study therapy, the waste rate will be generally maintained within a range of 12-15 mL/hr as determined by the Investigator. However, at any time the Investigator may choose to manually adjust the system waste rate based on subject status.

7.5.2 Neurapheresis Termination Criteria

Investigators should engage in an ongoing dialogue with the MNeuro CFS to address starting and stopping the pump for CSF sampling, change in clinical status, emergent situations and SOC concerns e.g., transport, extubation, physical therapy, study-required neuro checks or other. If a subject meets any of the criteria below, Neurapheresis should be stopped immediately (if not previously stopped) and the subject should be scheduled for catheter removal.

Change(s) in Subject conditions that ***require*** Neurapheresis termination are:

- Brainstem herniation
- Lower extremity paralysis
- Subdural spinal hematoma

- Subdural hematoma or hygroma
- Abnormal gram stain
- Re-bleeding event requiring intervention e.g., re-coiling, re-clip
- Subject previously non-intubated/extubated requires new or re-intubation
- ICP is greater than Lumbar pressure at five consecutive study-required neuro checks
- Subject requires inversion (such as Trendelenburg position)

As the MNeuro CFS will be on site during Neurapheresis therapy, the sponsor will be notified immediately if any subject has the Neurapheresis procedure terminated due to reasons above. Source documents may be requested for the Sponsor to adequately review the termination.

The Investigator may pause the system or terminate the procedure at any time. The Subject also has the right to terminate the procedure at any time. If study therapy must be terminated early, a head CT within (± 4hr) of catheter removal must be obtained to document the final amount and location of blood within the basal cisterns to allow for comparison to baseline.

7.5.3 Role of the MNeuro Clinical Field Specialist (CFS)

MNeuro clinical field specialists or their trained representatives are responsible for training and directing the applicable site staff in the placement, assembly, priming, replacement and removal of all components of the Neurapheresis System. The MNeuro CFS is also responsible for the general operation and trouble-shooting of the investigational system under guidance from Investigators and site staff to confirm the system does not present any care concerns and is functioning properly. The attending MNeuro CFS or representative will not practice medicine, alter data or make any clinical suggestions based on collected data or observed data trends.

During the Neurapheresis procedure, the MNeuro CFS is also responsible for addressing any system alert states. System data includes but is not limited to, inlet and return pressure(s), flow and waste rates, processed volume etc. System data collected during a Neurapheresis procedure will be recorded on the LabView Software and is saved to the PC hard drive and retrieved to USB pen drives. The MNeuro CFS will also help the site staff document the lumbar pressure from the system during the study-required neuro checks.

If the system experiences an issue e.g., pump failure, filter clot, catheter kink or obstruction, breach of sterility etc.., MNeuro CFS or representative will facilitate replacement or removal of the affected component after discussing “next steps” with the Investigator.

7.5.4 CSF Pressure Guidance During Neurapheresis

Subjects must have an EVD as part of the SOC for post SAH intracranial pressure management. Study Investigators should consult with the MNeuro CFS to coordinate the EVD maintenance with the Neurapheresis System waste control rate. Investigators are asked to clamp the EVD and open if ICP goes to ≥20mmHg while the Neurapheresis system is operating. The Investigator has the medical discretion to open the EVD at a lower pressure limit as clinical status for a specific subject may require. Alternatively, the Investigator may increase the therapy waste rate to manage an increasing trend in ICP with the Neurapheresis system rather than open the EVD. If the EVD is opened, it should be set to a pressure of 20 mmHg. Also, the Investigator may reduce the system waste rate or pause the system if unusually low ICP or clinical symptoms indicate continued drainage at the current rate may be unsafe.

Brain herniation is a known risk for intracranial hemorrhage patients, including aneurysmal subarachnoid hemorrhage, as the blood can create excess pressure in the brain. Likewise, herniation is a known risk of lumbar drainage as it may lead to cranial pressure changes.

SAH patients with increased risk for herniation may include those with:

- CNS infection or abscess;
- Excessive cranial edema/swelling that increases mass effect;
- Hydrocephalus or other complication that could compromise CSF communication;
- Other mass effect (tumor, hematoma, etc.) that may lead to high intracranial pressure (ICP);
- A sustained negative pressure change between intracranial and lumbar pressure due to high ICP or low lumbar pressure.

During Neurapheresis therapy, the protocol requires measurement of both lumbar pressure and ICP for assessment of subject status administered hourly (±1hr). This should be performed at the same time as the study required neurological assessments. Centers will not be deviated for obtaining ICP measurements at a greater frequency if that is the center SOC. ICP is to be captured on the applicable CRF. It is acceptable to have the attending critical nursing staff obtain the measurements if that is the SOC of the center's critical care unit.

To ensure accurate pressure measurements, the system will be paused, and the inlet pressure sensor will be leveled to the lumbar region of the subject. The lumbar pressure will then be recorded. The site staff will use their normal process for leveling and recording the ICP measurement. The system will remain paused if the lumbar pressure falls below 4.4 mmHg (6.0 cmH2O), and the Investigator will be notified to review clinical symptoms and system data prior to restarting. Alternatively, if the Investigator has pre-defined and documented a treatment plan, the system may be re-started according to the plan and on-going communication with the Investigator maintained to ensure adequate oversight of subject safety.

If during any pressure check the ICP recorded is higher than the lumbar pressure taken at the same neuro check, the system will remain paused until the ICP is equal to or lower than the lumbar CSF pressure for at least two consecutive neuro checks AND the Investigator has approved restarting the system. If the ICP remains higher than the lumbar pressure for five consecutive study-required neuro checks, then therapy will be terminated, and the site should prepare to gather the end of treatment data.

In cases where the Neurapheresis procedure is terminated early, the protocol required *ICP measurements are to be continued* until the catheter has been removed.

7.5.5 Neurologic Assessments During Neurapheresis

During Neurapheresis therapy, the protocol requires neurological assessments including GCS and Peripheral neurological checks for assessment of subject status to be administered hourly (±1 hr). Peripheral neurological checks will include assessment of leg strength and sensory changes to identify potential adverse events such as subdural spinal hematoma. Centers will not be deviated for performing assessments at a greater frequency if that is the center SOC or if additional assessments are administered. Assessments are to be captured on the applicable CRF. It is

acceptable to have the attending critical nursing staff conduct the assessments if that is the SOC of the center's critical care unit. The Investigator may reduce the system waste rate or pause the system if clinical symptoms indicate continued drainage at the current rate may be unsafe.

In cases where the Neurapheresis procedure is terminated early, the protocol required *neurological assessments are to be continued* until the catheter has been removed.

Neurological monitoring is required hourly during study therapy and similar to standard practice, this monitoring is intended to identify changes to neurological status that may be suggestive of neurological decline. Note that the protocol requires that study therapy be stopped if herniation is identified, regardless of whether the Investigator believes the herniation to be related to study therapy.

7.5.6 Neurologic Assessments for Intubated Subjects

To ensure the identification of deterioration in intubated subjects, the following data collection and criteria related to the GCS are established to pause the Neurapheresis procedure and allow for adequate assessment of the subject's status. Specifically, GCS will be captured each hour while the subject is intubated.

GCS should be captured noting that the subject is intubated (t) and it would be expected that the highest score for an intubated subject will be 10(t) due to inability to provide a verbal response. Further, Neurapheresis is required to be paused in an intubated subject if the motor component of the GCS drops below 6. Neurapheresis can begin upon improvement in the motor component score back to 6 or at a motor component of 5 that is stable for at least 4 consecutive hours during which a cause for the deficiency is identified such that the investigator concludes is not related to Neurapheresis. If the motor component or total GCS score continues to decline Neurapheresis should be terminated and the subject scheduled for catheter removal.

Finally, if a subject who was previously extubated/non-intubated requires new or re-intubation, Neurapheresis is to be terminated.

7.5.7 CSF Sampling During Neurapheresis

During catheter in-dwelling and Neurapheresis therapy, CSF samples will be obtained at regular intervals until the catheter is removed. A maximum of 11 CSF samples total per subject will be taken. Ten of those during catheter indwelling, though fewer may be taken if the catheter must be removed early.

Samples will be taken according to the schedule in Table 10 below. The initial CSF sample will be taken during catheter placement however, the first sample taken during catheter in-dwelling will be considered the Baseline CSF sample (pre-Neurapheresis sample) to which the later samples will be compared. The last CSF sample taken will be considered the Final sample or (post-Neurapheresis sample) which will be compared to the Baseline sample for applicable endpoint analyses. To account for different assay requirements, CSF sample volumes are different for the initial and seventh (40 hr) sample than those in between.

It is allowable to collect less CSF sample volume for completion of the Cell counts with Differentials based on site specific laboratory requirements. Current laboratory certificates are

required by the sponsor with laboratory processes to be made available upon request. Care should be taken to ensure laboratory samples are handled and processed consistently for accurate data reporting.

During catheter in-dwelling, the first sample (#2 on Table 10 below) should be taken after 1 hour (±30min) of Neurapheresis therapy. The MNeuro CFS will assist in monitoring the therapy time in order to prepare for the sample. The next CSF sample should be taken at 8 hours (±2hr) from catheter securement (8 hours of catheter in-dwelling) then each subsequent sample taken every 8 hours (±1hr) from the previous scheduled sample (i.e. every 8 hours during catheter in-dwelling).

Table 3: Required CSF Samples

Sample #	Sample Metric	Required Assay	CSF Sample Volume
1	During Catheter Placement (needle stick)	Cell counts with Differential: RBC, WBC, neutrophils, lymphocytes, etc. Chemistries: Total protein, Glucose, Culture	3ml
		CSF Biomarkers (requires -80° storage until shipped)[β]	2ml [β]
2	1hr (±30min) of Neurapheresis	Cell counts with Differential and Chemistries	3ml
3	8hr (±2hr)*	Cell counts with Differential and Chemistries	3ml
4	16hr (±2hr)*	Cell counts with Differential and Chemistries	3ml
5	24hr (±2hr)*	Cell counts with Differential and Chemistries	3ml
6	32hr (±2hr)*	Cell counts with Differential and Chemistries	3ml
7	40hr (±2hr)*	Cell counts with Differential and Chemistries	3ml
		CSF Biomarkers (requires -80° storage until shipped)	2ml
8	48hr (±2hr)*	Cell counts with Differential and Chemistries	3ml
9	56hr (±2hr)*	Cell counts with Differential and Chemistries	3ml
10	64hr (±2hr)*	Cell counts with Differential and Chemistries	3ml
11	72hr (±2hr)*[¥]	Cell counts with Differential and Chemistries	3ml

*time measured from catheter securement (beginning of indwelling time)
[β]if a CSF sample for biomarkers was not obtained during catheter placement (sample #1), it can be done with sample #2
[¥]if the catheter is removed prior to reaching the 72hr indwelling limit, a final CSF sample should be taken just prior to catheter removal

Center personnel shall work with the MNeuro CFS to time the CSF sampling as to not interfere with SOC patient care. To ensure sample consistency and minimize subject impact, samples are to be taken using the automated sampling process within the system. The system is switched to "sample mode" then using sterile technique, a syringe is inserted into the three-way sample stopcock. Sample mode should be set at the nominal flow rate of 0.5ml/minute. The system will automatically fill the syringe. Once the appropriate amount of CSF has been retrieved, sample

mode can be stopped and the syringe removed. The MNeuro CFS will pause the system prior to the sample acquisition, and will leave the system paused for a short period post sampling e.g., approx. 15 min, to allow for the CSF fluid balance to recover.

Also reference the IFU for additional details in regard to CSF sampling. A de-identified laboratory print-out of the required CSF assay analyses must be provided to the Sponsor. The original laboratory results must be available for monitoring.

7.5.8 Additional Testing Requirements During Neurapheresis

At 36 hours (±4hr) and 72 hours (±4hr) or end of catheter in-dwelling (whichever comes first), a venous blood sample and CT are required. Timing should be aligned with a study require neuro check for efficiency. The 36 hour CT and the 72 hour (end of catheter in-dwelling) CT must be obtained using a department scanner at optimal metal artifact reduction settings as it will be used for primary endpoint analysis. The 72 hours (±4hr) or end of catheter in-dwelling CT can be obtained after catheter removal to minimize the risk of compromising sterility of the fluid loop. However, if it obtained prior to catheter removal, steps to maintain sterility during patient transport should be followed as described in 7.5.9 below.

The venous blood sample should be submitted for a Complete Blood Count (CBC) with Differentials and a Comprehensive Metabolic Panel (CMP) to allow for comparison to pre-therapy values.

7.5.9 Patient Transport during Neurapheresis

If it is necessary to transport the study subject during the Neurapheresis procedure, ensure that the Sponsor's representative is present and the system is stopped for transport. Care should be taken to protect the integrity of tubing connections during transport. If possible, transport the system connected to the Subject, keeping the fluid loop intact or, remove the tubing and filters from the mounting bracket and place the components on the bed. If a system disconnect is required, connect the two catheter ends to one another (male→female) keeping the catheter sterile, see Figure 7. If sterility is compromised when connecting, the ends of catheter should be cleansed with Betadine for three minutes per AANA guidelines or SOC at center for sterile line technique when reconnecting to the Neurapheresis System.

The patient may sit up, stand, or move from their hospital bed as permitted or recommended by SOC. Center personnel should work with the MNeuro CFS to position the system cart in such a way to minimize strain on the catheter and tubing and allow proper movement of the patient. The system should remain connected to the patient, and depending on the type of movement, the system may continue running.

7.5.10 Catheter Removal

As described in Section 7.5.8, above, it is a protocol requirement to obtain a CT scan of the head within 4 hours of catheter removal (± 4hr from catheter removal) to document the post-therapy status. This post-Neurapheresis CT will be compared to the pre-Neurapheresis CT (Baseline CT) to analyze applicable study endpoints. This CT cannot be obtained bedside.

An image of the catheter position prior to removal is required showing proximal (lumbar cistern) and distal catheter (thoracic anatomy) locations. It is preferable that this is captured by fluoro to be consistent with the intra-procedural images captured during catheter placement, but X-ray capture of the image is acceptable it better accommodates work flow at the center.

It is recommended that the Investigator employ the following steps for catheter removal and be mindful of any analgesic requirements for catheter removal. It is likely that removal of the Neurapheresis catheter will have the same pain profile as the removal of lumbar drains so the Investigator may want to consider analgesic coverage per their professional discretion. The steps to removing the catheter are outlined below and are not exclusive of the SOC for spinal catheter removal at each study site. The IFU should also be referenced for more detailed information on catheter removal.

- Stop pump
- Turn flow assembly stopcocks such that the flat aspect of the stop-cock is toward the subject.
- Disengage catheter from the flow assembly stopcock
- Join male and female catheter ends together to form a sterile loop
- Obtain image of final catheter position
- Remove dressings and any sutures or fixation mechanisms used to retain catheter
- Gently pull catheter until it exits the subject
- Hold pressure on site until dressing and/or stitch is applied
- Have Subject lie flat or on their side for 30 minutes
- Watch for signs of headache or Dural CSF leak. If a headache occurs or a blood patch is required to seal a leak, complete an Adverse Event CRF.

Upon removal, follow the steps to return the investigational catheter to the Sponsor. Confer with the MNeuro CFS to ensure proper packaging and documentation for return, in addition to making the appropriate annotations in the study Device Accountability Log.

In the event of a Subject death during Neurapheresis, the Technical Representative will work with the center to obtain the catheter in a timely fashion.

7.6 Post-Neurapheresis Surveillance Schedule

7.6.1 2 Day (±1 day) Follow-up Data

The first surveillance metric will occur at 2 days (±1 day) according to Table 11. It is expected that the Subject will still be in the Neuro ICU at this point. Along with the clinical status and hospital data on the CRF, requirements for this visit include a CT, venous blood sample, GCS and de-identified laboratory and other applicable SOC source documents. Data should be collected from SOC source documents and transferred to the CRFs however, if source documents are not available, completed study worksheets can be signed by the investigator and maintained in the study file as source documents for monitoring.

A protocol required CT is requested at this follow-up to document the status of any subarachnoid blood remaining following Neurapheresis. Care should be taken to obtain the CT at the same

angle as those previously completed to improve the comparability of the data. The CT can be obtained bedside for appropriately equipped investigational sites.

Additionally, a protocol required venous blood sample is to be taken at the 2 day follow-up and sent for analysis. (CBC with Differentials/CMP) with associated laboratory reports provided to the sponsor. As CSF cultures should be followed for 96 hours from the last sample, it is expected that additional CSF analysis laboratory reports would be included with the 2 day follow-up data. Any SOC imaging studies (CTs, TCD, etc.) and associated reports completed since catheter removal should be submitted. The medical record and clinical status should be reviewed for adverse events and reported on the appropriate case report form as applicable. Finally, non-adherence to the visit requirements will result in a protocol deviation.

7.6.2 Neuro ICU Discharge Follow-up Data

Subjects are expected to be discharged on average 10-14 days post aneurysm securement from the Neuro ICU (critical care unit). Discharge may be a change in location (i.e. to a stepdown unit, main hospital floor, rehabilitation facility or home) as dictated by clinical status and institutional SOC. Alternatively, Neuro ICU discharge may be based only on clinical status (i.e. the point at which the subject no longer meets the institutional definition for critical care monitoring). If the date of discharge from clinical status is different than the date of change to physical location, sites are expected to use the earlier of the two dates for the discharge date. Sites are asked to discuss institutional discharge criteria with a sponsor representative to ensure discharge data is collected at the appropriate time.

Data should be collected at the time of discharge and include the following assessments that may not be SOC are required. See Table 11 for detailed requirements; GCS and Modified Rankin Scale (mRS).

As CSF cultures should be followed for 96 hours from the last sample, it is expected that laboratory reports after the 2 day follow-up will be submitted with this discharge follow-up data. Additionally, any SOC imaging studies (CTs, TCD, etc.) and associated reports completed since the last study visit should be submitted. The medical record and clinical status since the last study visit should be reviewed for adverse events and reported on the appropriate case report form as applicable. Finally, non-adherence to the visit requirements will result in a protocol deviation.

7.6.3 30 Day (±3 day) Follow-up Data

The final surveillance metric will occur at 30 days (±3 days) post removal of the Neurapheresis System catheter according to Table 11. It is highly likely that the Subject will not be hospitalized at this follow-up and as such a return to the clinic is recommended to properly perform the required neurological assessments. (GOSE, mRS, Barthel, MoCA). If the subject refuses to or is unable to return, this follow-up may also be completed as able by phone however that should be a last option.

The medical record and clinical status should be reviewed for adverse events and reported on the appropriate case report form as applicable. Finally, non-adherence to the visit requirements will result in a protocol deviation.

Table 4: Data Collection Schedule

Data Items	Screening / Enrollment	Catheter Placement	Neurapheresis Procedure	2-Day Post-Neurapheresis (±1-day)	Discharge from Neuro ICU	30 Days Post-Neurapheresis (±3 days)
Demographics, Medical Hx, SAH Symptomology	√					
Aneurysm data; location, measurements, securement, etc.	√					
Modified Fisher Grade	√					
WFNS	√					
Hunt & Hess	√					
Glasgow Coma Scale (GCS)	√		√¥	√	√	
Peripheral Check			√¥			
Glasgow Outcome Scale Extended (GOSE)						√
Modified Rankin Scale (mRS)					√	√
Barthel Index						√
Montreal Cognitive Assessment (MoCA)						√
Activated Clotting Time Data (if applicable)		√				
Catheter/System data		√	√			
CSF Sampling and Laboratory Reports		√	√	√β	√β	
CBC with Differential/CMP Blood Test and Laboratory Reports	√		√**	√		
Protocol Required CTs Scans		√*	√***	√		
SOC CT Scans	√		√	√	√	
Fluoroscopy or X-ray Image of Catheter		√	√©			
ICP Data (if applicable)			√¥	√	√	
Clinical and Hospital Data e.g., LOS, location, vital signs, complications	√		√	√	√	√
Protocol Deviations	√	√	√	√	√	√
Adverse Events		√	√	√	√	√

* CT is required after aneurysm securement but prior to Neurapheresis initiation and must be assessed to ensure intracranial stability prior to beginning therapy

** Blood sample is required at 36 hrs (± 4hr) and at the end of catheter indwelling or 72 hours (± 4hr) whichever is earlier

*** CT is required at 36 hrs (± 4hr) and at the end of catheter indwelling or 72 hours (± 4hr) whichever is earlier [cannot be bedside CT]

¥ ICP (for subjects with EVD), Lumbar Pressure GCS and peripheral checks are required every 1 hours (± 1hr) during catheter in-dwelling

β Reports for CSF cultures should be followed through 96 hours from the last sample taken prior to catheter removal

© Catheter image to document final catheter placement post-Neurapheresis therapy

8. ADVERSE EVENTS (AEs)

The Study will not track all-cause AEs or AEs related to SOC or the SAH clinical pathway e.g., re-bleed, deep vein thrombosis, skin breakdown etc. Study required event reporting is limited to AEs directly related to the investigational catheter, investigational system or Neurapheresis procedure, or study required element (such as CSF sampling). In cases where the event may have an attributable dual causality i.e., SAH clinical path or the Neurapheresis procedure, the center should report the event.

8.1 Adverse Event Definitions

Adverse Event (AE): Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs in subjects, users or other persons, deemed related to the investigational device (catheter and/or placement accessories), Neurapheresis procedure, or study required element (such as CSF sampling).

Serious Adverse Event (SAE): Adverse event as defined above that

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

Unanticipated Adverse Device Effect (UADE): Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects" (21 CFR§ 812.3(s)).

Unanticipated Adverse Device Effects (UADE) that occur in subjects enrolled in the clinical trial should be reported under the IDE program (812.150) to FDA and all reviewing institutional review boards (IRBs) and investigators within 10 working days after you first receive notice of the adverse effect(s).

8.2 Reportable Adverse Events

The table below outlines the protocol required reportable Adverse Events. Other events should also be reported if they are deemed by the investigator to be related to the investigational catheter, investigational system or Neurapheresis procedure, or study required element (such as CSF sampling).

Table 5: Reportable Adverse Events

Adverse Event	
Spinal headache with or without intervention	Systemic CNS infection/sepsis
Localized insertion site infection	Dural dissection
Meningitis	Paralysis
Brainstem herniation in the absence of re-bleed	Localized pain
Hematoma at insertion site	Peripheral neuropathy
Nausea/vomiting	Death

9. DEVIATIONS FROM THE PROTOCOL

An Investigator must not make any changes to or deviate from the protocol, except to protect the life and physical well-being of a subject in an emergency. An Investigator shall notify the Sponsor and the reviewing IRB of any deviation from the protocol to protect the life or physical well-being of a subject in an emergency, and those deviations which affect the scientific integrity of the clinical investigation. Such notice shall be given as soon as possible, but no later than 5 working days after the emergency occurred, or per prevailing local requirements, if sooner than 5 working days.

All deviations from the protocol, with the reason for the deviation and the date of occurrence, must be documented and reported to the Sponsor using the appropriate case report form. Sites are also required to report deviations to the IRB per local requirements.

Deviations will be reviewed and evaluated on an ongoing basis and, as necessary, appropriate corrective and preventive actions (including notification, center re-training, or discontinuation) will be put into place by the Sponsor.

9.1 Amendments to the Protocol

If a revision to the protocol is necessary which affects the rights, safety or welfare of the Subject or scientific integrity of the data, an amendment by the Sponsor is required. Appropriate approvals of the revised protocol must be obtained prior to implementation. Centers will be notified of any protocol amendment that is to be implemented. Communication from the Sponsor will apprise the center if an enrollment stop is required during the revision processes.

10. DATA ANALYSIS AND MANAGEMENT

The PILLAR-XT Study does not have a hypothesis based statistical endpoint due to the feasibility nature of the investigation. The following analysis populations and definitions will be used to analyze the PILLAR-XT data.

10.1 Analysis Populations

The following analysis populations will be used to perform the endpoint analyses.

Safety Population:
This population includes only subjects that were classified as Attempt to Treat or Treated Subjects and will be used to analyze all pre-defined safety endpoints.

Treated Population:
This population includes only subjects classified as Treated Subjects and will be used to analyze all pre-defined efficacy endpoints, including exploratory endpoints.

10.2 Endpoint Analysis Definitions

Enrollment will be stopped when 30 subjects have been enrolled and treated with Neurapheresis for at least 16 hours, however, this amount of therapy time is not considered a complete treatment as absolute blood clearance would not be expected. This study is expected to generate foundational data for development of the Neurapheresis treatment curve (e.g. time or volume needed to clear blood from the subarachnoid cisterns and lumbar spine).

Primary Endpoints:

1. Mean reduction of cisternal blood via CT post study therapy
    a. Pre, 36 hour and post-Neurapheresis CTs will be evaluated by an independent neuroradiology core laboratory for quantification of blood volume. The core lab will utilize a three (3) member team for independent review of the primary endpoint with agreement of at least two (2) reviewers required.
    b. Mean volumes will be compared using a paired t-test with an alpha level of .05. Pre blood volume will be compared to both the 36-hour and post-Neurapheresis blood volumes separately to support creation of the therapy curve. However, the Pre to Post Neurapheresis comparison will be the primary endpoint measure.
    c. An analysis of variance may be considered based on results from exploratory sub-groups analyses
2. Proportion of subjects with Neurapheresis Catheter, System or Therapy related serious adverse events
    a. Events will be reviewed by an independent medical monitor for relatedness and will be used to calculate this endpoint (Number of subjects with related SAEs/Number of subjects in the Safety Population)

Secondary Safety Endpoints:

- Proportion of subjects with successful catheter placement
    - This only includes the subjects in whom catheter placement was attempted (Number of subjects with catheter attempted/Number of subjects in the Safety Population)
- Proportion of subjects with device or study therapy related adverse events
    - Events will be reviewed by an independent medical monitor for relatedness and will be used to calculate this endpoint (Number of subjects with related AEs/Number of subjects in the Safety Population)
- Proportion of subjects with systemic CNS infection within 5 day of catheter removal
    - In order to be considered a CNS infection, the following must be true; abnormal growth was identified on CSF culture within 5 days of catheter removal, subject has physiologic symptoms of infection and treatment was administered specifically for that infection.
    - CNS infection events will be reviewed by an independent medical monitor for whether or not the event meets the criteria above and will be used to calculate this endpoint (Number of subjects meeting CNS infection definition/Number of subjects in the Safety Population)

Secondary Efficacy endpoints:

- Mean reduction of RBCs and total protein by CSF sample post study therapy
    - This calculation utilizes the pre-Neurapheresis sample (first CSF sample taken either at the time of needle insertion or after catheter placement, whichever laboratory value is greater) as compared to the post-Neurapheresis sample (last CSF sample taken prior to catheter removal)

- Mean length of Neuro ICU stay
  - Mean length of Neuro ICU stay will be calculated by two different methods, one using physical location change, the second using criteria for critical care monitoring.

Exploratory endpoints:

- Proportion of subjects requiring additional CSF management during study therapy or on-going CSF management post study therapy
- Reduction in biomarkers of inflammation as seen in CSF, blood and physiologic manifestations post study therapy
  - Such as cytokines, white blood cell counts, neutrophil/lymphocyte ratio, SIRS
- Proportion of subjects with symptomatic complications from aSAH
  - Such as hydrocephalus, clinical vasospasm and delayed cerebral ischemia
- Analysis of endpoints by the following sub-groups for any groups that have at least 5 subjects that meet the criteria for the group;
  - Age: <45, ≥45-<60, 60 – 70 years
  - Gender: male, female
  - Enrollment Modified Fischer grade: 2, 3, 4
  - Baseline cisternal Hijdra score: ≤15, 16-20, 21-25, 26-30
  - Neurapheresis time: <16hrs, ≥16-32hrs, >32-48hrs, >48hrs
  - Other sub-groups not yet defined

10.3 Data Management

A 21 CFR Part 11 compliant electronic data capture platform will be used for this clinical study and as such, subject clinical data will be entered into the study database by investigational site staff. All changes made to the clinical data will be captured in an audit trail and available for review by MNeuro or its Monitoring representative.

Unique user ID and password will be provided to each database user by MNeuro or the database vendor as determined by contract. Investigators will be required to review and sign off on the data entered for each of their study Subjects. Sites will not have visibility to study data for any other site participating in the study.

Manual and automatic queries will be issued to the site for appropriate response and clarification of data. Site staff will be responsible for resolving all queries generated by the Sponsor and making source documentation available for each change as applicable.

11. MONITORING

A study initiation visit shall be conducted by the Sponsor and/or their representative to ensure but not limited to:

- Current and completed required study documents are on file;
- Training and associated documentation is complete;
- Site staff understand the requirements of this study protocol;
- The site is prepared for study enrollment

MNeuro will provide notification to the site once they have been approved to enroll subjects. IRB approval is a required element for enrollment approval however sites are not authorized to begin enrollment until they receive notification from MNeuro, regardless of having IRB approval in place.

Clinical monitoring will be performed during the study to assess continued compliance with the protocol and applicable regulations. In addition, the Clinical Monitor will verify that study records are adequately maintained, that data are reported in a satisfactory manner with respect to timeliness, adequacy and accuracy, and that the Investigator continues to have sufficient staff and facilities to conduct the study safely and effectively. The Investigator/institution guarantees direct access to original source documents by MNeuro personnel, their designees, and appropriate regulatory authorities. It is important that the Investigator and relevant study personnel are available during on-site monitoring visits or audits and that sufficient time is devoted to the process.

12. SUSPENSION OR EARLY TERMINATION OF THE INVESTIGATION

MNeuro reserves the right to terminate the study at any stage. MNeuro will exercise this right only for valid scientific, safety or administrative reasons and, reasons related to protection of Subjects. Investigators and their associated IRB will be notified in writing in the event of study termination.

Possible reasons for premature study termination include, but are not limited to:

- The occurrence rates of AE/ UADE that present a significant or unreasonable risk to subjects enrolled in the study
- An enrollment rate far below expectation that prejudices the conclusion of the study
- A decision on the part of Minnetronix to suspend or discontinue development of the device or therapy application.

13. COMPLIANCE

13.1 Statement of Compliance

This study will be conducted in accordance with 21CFR§ 812, International Conference on Harmonisation (ICH) E6 Guidelines for Good Clinical Practice (GCP), ethical principles that have their origins in the Declaration of Helsinki, and pertinent individual country laws and regulations. The study shall not begin until the required approval/favorable opinion from the FDA and the IRB has been obtained. Any additional requirements imposed by the IRB shall be followed.

13.2 Independent Medical Monitor

An independent medical monitor will be utilized for review and adjudication of study reported adverse events. The primary focus of adjudication will be whether the event is anticipated and relatedness to study device or procedure. The medical monitor will be provided available information related to each event such as data from case report forms and copies of de-identified source documents including medical records and imaging studies as applicable. Details related to the responsibilities of the Medical Monitor will be documented in a charter.

Medical monitor adjudication data will be provided to the DSMB for review.

13.3 Data Safety Monitoring Board (DSMB)

Following recommendations outlined in guidance documents on data monitoring committees, the Sponsor has chosen to establish a DSMB safety oversight committee for the PILLAR-XT study. Details related to the responsibilities of the DSMB will be documented in a charter.

The DSMB will be responsible for assessing study stopping (enrollment hold) rules related to the occurrence of the following events:

- Brainstem herniation
- Death
- Early termination of Neurapheresis due to neurological decline in subjects presenting as Hunt & Hess IV
- CSF leak due to device failure

Enrollment will be temporarily placed on hold under the following circumstances;

- if there are two separate occurrences of an individual event listed above or;
    - however, if two separate occurrences of the "early termination of Neurapheresis due to neurological decline in subjects presenting as Hunt & Hess IV" is met, only enrollment of Hunt & Hess IV subjects will be placed on hold.
- if one of the events above is determined by the DSMB to be an unanticipated adverse device effect

The Sponsor will perform an investigation of the event(s) and report to appropriate regulatory authorities. Enrollment may be re-initiated following Sponsor, DSMB and regulatory authority approval. Additionally, the DSMB will review any events determined by the medical monitor to be unanticipated adverse device effects.

13.4 Responsibilities

The Investigator is responsible for ensuring complete oversight of the study and, that the study is conducted in accordance with 21 CFR§ 812, the Clinical Study Agreement, the Clinical Protocol, ethical principles that have their origins in the Declaration of Helsinki, any conditions of approval imposed by the reviewing IRB, and prevailing local laws and/or regulations, whichever affords the greater protection to the subject.

The Investigator's responsibilities include, but are not limited to, the following:

- Prior to beginning the study, sign the Investigator Agreement documenting his/her agreement to conduct the study in accordance with the Clinical Protocol
- Provide his/her qualifications and experience to assume responsibility for the proper conduct of the study and that of key members of the center team, signed up-to-date curriculum vitae or other relevant documentation and disclose potential conflicts of interest, including financial, that may interfere with the conduct of the clinical study or interpretation of results
- Ensure that adequate investigation site personnel and facilities are in place and site personnel are trained
- Make no changes in or deviate from this Clinical Protocol, except to protect the life and physical well-being of a subject in an emergency; document and explain any deviation from the approved plan that occurred during the course of the clinical investigation

- Create and maintain source documents throughout the clinical study and ensure their availability with direct access during monitoring visits or audits; ensure that all clinical-investigation-related records are retained per regulatory requirements
- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports
- Record, report, and assess (seriousness and relationship to the device/procedure) every adverse event
- Report to MNeuro, per the protocol requirements, all SAEs and device deficiencies
- Report to MNeuro all UADE's
- Supply Minnetronix with any additional requested information related to the safety reporting of a particular event
- Maintain the device/system accountability logs and control of the device/system, ensuring that the investigational device/system and the accessories are used only by authorized/designated users and in accordance with this Clinical Protocol and the IFU
- Allow the Sponsor or its representative to perform monitoring and auditing activities, and be accessible to the monitor and respond to questions during monitoring visits
- Allow and support regulatory authorities and the IRB when performing auditing activities
- Ensure that informed consent is obtained in accordance with this Clinical Protocol and reviewing IRB requirements
- Provide adequate medical care to a subject during a subject's participation in a clinical study in the case of adverse events, as described in the ICF
- Inform the subject of the nature and possible cause of any adverse events experienced
- Inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required
- Provide the subject with well-defined procedures for possible emergency situations related to the clinical study, and make the necessary arrangements for emergency treatment
- Ensure that clinical medical records are clearly marked to indicate that the subject is enrolled in this clinical study
- Ensure that, if appropriate, subjects enrolled in the clinical investigation are provided with some means of showing their participation in the clinical investigation, together with identification and compliance information for concomitant treatment measures (contact address and telephone numbers shall be provided)
- Inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation
- Ensure that maintenance and calibration of the equipment relevant for the assessment of the clinical investigation is appropriately performed and documented, where applicable.

13.4.1 Investigators Delegation of Authority

When specific tasks are delegated by an Investigator, included but not limited to conducting the informed consent process, the Investigator is responsible for providing appropriate training and documentation thereof, and adequate supervision of those to whom tasks are delegated. The Investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

13.4.2 Investigator Reporting Responsibilities

Table 13 below outlines the Investigators Reporting responsibilities as prescribed in 21 CFR§ 812.150 and required by the sponsor.

Table 6: Investigator Reporting Responsibilities

Event Classification	Communication Method	Communication Timeline
UADE	• Complete AE CRF with all available new and updated information	• Within 5 business days of first becoming aware of the event
SAE	• Complete AE CRF with all available new and updated information	• Within 5 business days of first becoming aware of the event or as per local/regional regulations • Reporting required through the end of the study
	• Provide all relevant source documentation (unidentified) for reported event	• When documentation is available
Adverse Event	Complete AE CRF, which contains such information as date of AE, treatment of AE resolution, assessment of seriousness and relationship to the device	• No later than 10 working days after becoming aware of the information • Reporting required through 30 day follow-up
Withdrawal of IRB approval	Notification to Sponsor	• Within 5 working days
Progress Report	Provide to Sponsor	• Per annum based on date of IRB approval
Non-consent of Subject	Notification to Sponsor	• Sponsor and IRB notification within 5 business days of device being used
Final Report	Provide to Sponsor and IRB	• Within 3 months after study termination or completion of the Investigators part of the investigation.

13.5 Sponsor Responsibilities

MNeuro shall adhere to all Sponsor responsibilities outlined in 21 CFR§ 812.

All information and data sent to MNeuro or its delegate concerning subjects or their participation in this study will be considered confidential. Only authorized MNeuro personnel or a designated representative will have access to these confidential records. Authorized regulatory personnel have the right to inspect and copy all records pertinent to this study. Study data collected during this study may be used by MNeuro for the purposes of this study, publication, and to support future research and/or other business purposes. All data used in the analysis and reporting of this study will be without identifiable reference to specific subject name.

MNeuro will keep subjects' health information confidential in accordance with all applicable laws and regulations. MNeuro may use subjects' health information to conduct this research, as well as for additional purposes, such as overseeing and improving the performance or design of its device, new medical research and proposals for developing new medical products or procedures, and other business purposes.

13.6 Institutional Review Board Approval

Prior to gaining Approval-to-Enroll status, the investigational center will provide to the Sponsor or their delegate documentation verifying that their IRB is registered or that registration has been submitted to the appropriate agency, as applicable according to national/regulatory requirements.

A copy of the written IRB approval of the protocol (or permission to conduct the study), Informed Consent Form and applicable signed agreements, must be received by the sponsor or their delegate before recruitment of subjects into the study. Prior approval must also be obtained for other materials related to subject recruitment or which will be provided to the subject.

Annual IRB renewals will be obtained throughout the duration of the study as required by local/country or IRB requirements. Copies of the Investigator's reports and the IRB continuance of approval must be provided to the sponsor or their delegate.

14. PUBLICATION POLICY

MNeuro shall adhere to the Uniform Requirements of the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org). In order to ensure the public disclosure of study results in a timely manner, while maintaining an unbiased presentation of study outcomes, MNeuro personnel may assist authors and Investigators in publication preparation provided the following guidelines are followed.

- MNeuro involvement in the publication preparation should be discussed with the Coordinating Principal Investigator(s) at the onset of the project
- The First and Senior authors are the primary drivers of decisions regarding publication content, review, approval, and submission. These authors are determined by enrollment status and/or overall contribution to the study. Study non-compliance may be taken into account for authorship determination.

APPENDIX A: PROTOCOL ABBREVIAITONS

Table 7: Protocol Abbreviations

Abbreviation	Term
AE	Adverse Event
CRF	Case Report Form
CFS	Clinical Field Specialist
CSF	Cerebrospinal Fluid
CT	Computed Tomography
CTA	Computed Tomography Angiogram
DSMB	Data Safety Monitoring Board
GCP	Good Clinical Practice
GCS	Glasgow Coma Scale
GOSE	Glasgow Outcome Scale Extended
EVD	External Ventricular Drain
H&H	Hunt and Hess
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICP	Intracranial Pressure
ICU	Intensive Care Unit
IFU	Instructions for Use
IRB	Institutional Review Board
ISO	International Standards Organization
IVH	Intraventricular Hemorrhage
LAR	Legally Authorizes Representative
LOS	Length of Stay
MRA	Magnetic Resonance Angiogram
MRI	Magnetic Resonance Imaging
mRS	Modified Rankin Scale
OTB	Outside-the-body
OTS	Off-The-Shelf
OTW	Over-The-Wire
RBC	Red Blood Cell
SAE	Serious Adverse Event
SAH	Subarachnoid Hemorrhage
SAS	Subarachnoid Space
SNF	Skilled Nursing Facility
SOC	Standard of care
TCD	Transcranial Doppler
TCU	Transitional Care Unit
UADE	Unanticipated Adverse Device Effect
WFNS	World Federation of Neurosurgeons

APPENDIX B: NEUROLOGIC ASSESSMENTS/GRADING INDICIES

Table 8: Glasgow Coma Scale

Activity	Rating	Score
EYE OPENING Never To pain To verbal stimuli Spontaneously	1= Even to supra-orbital pressure 2= Pain from sternum/limb/supra-orbital pressure 3= Non-specific response, not necessarily to command 4= Eyes open, not necessarily aware	
	Eye Score ( )	
MOTOR RESPONSE None Extension Flexor response Withdrawal Localizes pain Obeys commands	1= No response 2= Extension(decerebrate rigidity) 3= Abnormal flexion(discorticate rigidity) 4= Flexion withdrawal 5= Arm attempts to remove supra-orbital/chest pressure 6= Follows simple commands	
	Motor Score ( )	
VERBAL RESPONSE None Incomprehensible Inappropriate Confused Oriented	1= No response 2= Incomprehensible sounds 3= Inappropriate words 4= Disoriented and converses 5= Oriented and converses	
	Verbal Score ( )	
	Total (3-15):	

Table 9: Modified Fisher Grade Classifications

Grade	Appearance of Hemorrhage
0	No SAH, or IVH
1	Thin diffuse or focal SAH, no IVH
2	Thin diffuse or local SAH, with IVH
3	Thick focal or diffuse SAH, no IVH
4	Thick local or diffuse SAH with IVH

Table 10: WFNS Grading System for Subarachnoid Hemorrhage

Glasgow Coma Scale	Motor Deficit	Grade
15	Absent	1
13-14	Absent	2
13-14	Present	3
7-12	Present or Absent	4
3-6	Present or Absent	5

Table 11: Hunt & Hess Scale

Description	Grade
Asymptomatic, mild headache, slight nuchal rigidity	1
Moderate to severe headache, nuchal rigidity, no neurologic deficit other than cranial nerve palsy	2
Drowsiness/confusion, mild focal neurologic deficit	3
Stupor, moderate-sever hemiparesis	4
Coma, decerebrate posturing	5
Grade (1-5)	

Table 12: Glasgow Outcome Scale Extended

Score	Description
1	**DEATH**
2	**VEGETATIVE STATE** Unable to obey commands or say words with only reflex responses but with periods of spontaneous eye opening
3	**SEVERE DISABILITY - Lower** Patient fully dependent for all activities of daily living. Requires assistance to be available constantly. Unable to be left alone at night.
4	**SEVERE DISABILITY - Upper** Can be left alone for up to 8 hours but remains dependent. Unable to use public transport or shop by themselves
5	**MODERATE DISABILITY - Lower** Able to return to work in sheltered workshop or noncompetitive job. Rarely participates in social and leisure activities. Ongoing daily psychological problems (quick temper, anxiety, mood swings, depression)
6	**MODERATE DISABILITY - Upper** Able to return to work but at a reduced capacity. Participates in social and leisure activities less than half as often. Weekly psychological problems.
7	**GOOD RECOVERY - Lower** Return to work. Participates in social and leisure activities a little less and has occasional psychological problems
8	**GOOD RECOVERY - Upper** Full recovery with no current problems relating to the injury
	Total (1-5)_____

Table 13: Modified Rankin Scale

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

Table 14: Peripheral Neurological Assessment

Leg Strength	**Scale**	**Score (0-10)**
RIGHT	+5 Full ROM, Full Strength +4 Full ROM, Less than normal Strength +3–Can raise extremity but not against resistance +2-Can move extremity but not lift it +1-Slight movement 0-No movement	( )
LEFT	+5 Full ROM, Full Strength +4 Full ROM, Less than normal Strength +3–Can raise extremity but not against resistance +2-Can move extremity but not lift it +1-Slight movement 0-No movement	( )
Drift-Leg	**Scale**	**Score (0-2)**
RIGHT	Present: Yes (0) or No (+1)	
LEFT	Present: Yes (0) or No (+1)	
Sensory-Leg	**Scale**	**Score (0-8)**
RIGHT	+2 Intact +1 Decreased to light touch 0 Absent	
LEFT	+2 Intact +1 Decreased to light touch 0 Absent	
Chest	+2 Intact +1 Decreased to light touch 0 Absent	
Umbilicus	+2 Intact +1 Decreased to light touch 0 Absent	
Sensory-Proprioception	**Scale**	**Score (2-4)**
Right Leg	+2 Intact +1 Decreased	
Left Leg	+2 Intact +1 Decreased	
Total Score		**Total Score (2-24)**

Table 15: The Barthel Index

Activity	Score
Feeding 0=unable 5=needs help cutting, spreading butter, etc, or requires modified diet 10=independent	
Bathing 0=dependent 5=independent (or in shower)	
Grooming 0=needs help with personal care 5=independent face/hair/teeth/shaving (implements provided)	
Dressing 0=dependent 5=needs help but can do about half unaided 10=independent (including buttons, zips, laces, etc.)	
Bowels 0=incontinent (or needs to be given enemas) 5=occasional accident 10=continent	
Bladder 0=incontinent, or catheterized and unable to manage alone 5=occasional accident 10=continent	
Toilet Use 0=dependent 5=needs some help, but can do so something alone 10=independent (on and off, dressing, wiping)	
Transfers (Bed to Chair and Back) 0=unable, no siting balance 5=major help (one or two people, physical) can sit 10=minor help (verbal or physical) 15=independent	
Mobility(On Level Surfaces) 0=immobile or < 50 yards 5=wheelchair independent, including coroners, > 50 yards 10=walks with help of one person (verbal or physical) 15=independent (but may use any aid; for example, stick) > 50 yards	
Stairs 0=unable 5=needs help (verbal, physical, carrying aid) 10=independent	
Total (0-100)	