MARRS Study: The Millipede AspiRation for Revascularization in Stroke Study

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Title	Millipede AspiRation for Revascularization in Stroke Study
Short Title	MARRS Study
European Sponsor	Perfuze Ltd. Unit 6 Galway Business Park, Dangan Galway, H91 W7CP Ireland
US Sponsor	Perfuze Inc. 61 W Palisades Avenue, Suite 2B, Englewood, New Jersey, 07631 United States
Investigational Device	Millipede System, which consists of: - Millipede 088 Aspiration Catheter - Millipede 070 Aspiration Catheter - Perfuze Aspiration Tube Set
Control Device	N/A – single arm study
Indications for Use	**Millipede Aspiration Catheters** As part of the Millipede System, the Millipede 088 and Millipede 070 Aspiration Catheters are indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset. Patients who are ineligible for intravenous thrombolytic therapy or who fail intravenous thrombolytic therapy are candidates for treatment. **Perfuze Aspiration Tube Set** As part of the Millipede System, the Perfuze Aspiration Tube Set is indicated to connect the Millipede Aspiration Catheters to an aspiration pump.
Study Design	Interventional, open label, single arm, multi center, prospective clinical investigation.
Study Objectives	1. Examine the performance and safety characteristics of the Millipede System when used for revascularization of patients with acute ischemic stroke due to Large Vessel Occlusions (LVOs). 2. Record associated clinical outcomes.
Subject Population	Patients ≥ 18 and ≤ 85 years of age with confirmed acute ischemic stroke secondary to intracranial LVO disease within the internal carotid artery (ICA), M1 and M2 segments of the middle cerebral artery (MCA), basilar artery, or vertebral artery and can be treated within 8 hours of symptom onset.
Number of Subjects	Up to 277 subjects who meet the study eligibility criteria
Number of Investigational Sites	Up to 30 sites in the United States and Europe
Primary Effectiveness Endpoint	Proportion of subjects with successful reperfusion, defined as achieving a modified Thrombolysis in Cerebrovascular Infarction (mTICI) score of 2b or greater, after ≤3 passes with the Millipede System without additional therapy. *At least three passes should be attempted with the Millipede prior to using an additional revascularization therapy. Additional therapy includes the use of another mechanical thrombectomy device, intra-arterial thrombolytics, and intracranial stenting.*

	Devices which are used to support navigation (e.g. intermediate catheters, delivery catheters, guide catheters, sheaths, microcatheters, guidewires) are not considered as additional revascularization therapy.
Primary Safety Outcome	The safety of the Millipede System will be determined through a review of all adverse events (AEs) recorded during the study. *All AEs will be analyzed, with specific attention to the rate of all intracranial hemorrhage (ICH), including symptomatic intracranial hemorrhage (sICH), subarachnoid hemorrhage (SAH), non-hemorrhagic AEs capable of producing neurological deterioration, and death. Total counts and per-patient incidence rates, including 95% confidence intervals, where appropriate, will be reported for all serious adverse events (SAEs), device-related AEs, procedure-related AEs, hemorrhagic AEs, and non-hemorrhagic AEs capable of producing neurological deterioration.*
Secondary Endpoints	1. Proportion of subjects achieving a modified Rankin Scale (mRS) score of ≤ 2 at 90 (±30) days post-procedure. 2. Proportion of subjects with all-cause mortality at 90 (±30) days post-procedure. 3. Incidence of symptomatic intracerebral hemorrhage (sICH) within 24 (-8/+24) hours post-procedure. 4. Incidence of all intracranial hemorrhages, classified according to the Heidelberg Bleeding Classification. 5. Serious Adverse Device Effects (SADEs) up to 90 (±30) days post-procedure, as adjudicated by the CEC. 6. Procedure-Related Serious Adverse Events (PRSAEs) up to 90 (±30) days post-procedure, as adjudicated by the CEC. 7. Embolization to previously uninvolved vascular territory identified on angiography. 8. Proportion of subjects with successful reperfusion, defined as achieving an mTICI score of 2b or greater, at the end of the thrombectomy procedure. 9. Proportion of subjects with complete or near complete reperfusion, defined as achieving an mTICI score of 2c or 3, at the end of the thrombectomy procedure. 10. Proportion of subjects with successful reperfusion (mTICI score ≥ 2b) after the first pass with the Millipede System. 11. Proportion of subjects with complete or near complete reperfusion (mTICI score ≥ 2c) after the first pass with the Millipede System.
Inclusion Criteria	1. Subjects aged ≥ 18 and ≤ 85 years. 2. Pre-stroke mRS score of ≤ 1. 3. Baseline NIHSS score of ≥ 6. 4. A new focal disabling neurologic deficit consistent with acute cerebral ischemia. 5. Evidence of a large vessel occlusion of the intracranial ICA (including T or L occlusions), the M1 or M2 segments of the MCA, the intracranial vertebral artery, or the basilar artery on magnetic resonance angiography (MRA) or computed tomography angiography (CTA). 6. Subject belongs to one of the following subgroups: a. Subject is ineligible for thrombolytic therapy, OR b. Subject is eligible for thrombolytic therapy and thrombolytic therapy was administered without delay and per current practice guidelines. 7. For strokes in the anterior circulation, the following imaging criteria should be met:

	a. Magnetic Resonance Imaging (MRI) criterion: volume of diffusion restriction visually assessed as ≤ 50 mL, or Alberta Stroke Program Early CT Score (ASPECTS) 6-10; OR b. Computed Tomography (CT) criterion: ASPECTS 6-10 on baseline CT or CTA-source images, or volume of significantly lowered relative Cerebral Blood Flow (rCBF) <30% (volume of ≤ 50 mL if CT perfusion is performed). 8. For strokes in the posterior circulation, the following imaging criterion should be met: pcASPECTS score 8 to 10 on baseline CT, CTA-source images, or Diffusion-Weighted Imaging (DWI) MRI. 9. The interventionalist estimates that arterial puncture can be completed within 8 hours of onset/last known well. 10. Informed consent obtained in accordance with the applicable country-specific regulations and as approved by the Institutional Review Board (IRB)/Research Ethics Committee (REC). 11. Angiographic confirmation of a single large vessel occlusion (mTICI of 0-1) of the intracranial ICA (including T or L occlusions), the M1 or M2 segments of the MCA, the intracranial vertebral artery, or the basilar artery that is accessible to the Millipede System. *Note: The Millipede Aspiration Catheters should only be used in vessels that are larger than the outer diameter of the device.* • *Use the Millipede 088 Aspiration Catheter in vessels of diameter >0.108 inches (>2.74 mm).* • *Use the Millipede 070 Aspiration Catheter in vessels of diameter >0.087 inches (>2.21 mm).* *If the baseline angiogram shows that the target occlusion has moved to an excluded location or resolved, or that the target occlusion is not accessible to the investigational device (e.g., due to the presence of an aneurysm, vessel stenosis, carotid disease, arteriovenous malformation, excessive tortuosity or vessel diameter being too small to accommodate the catheter), the subject will be considered an angiographic screen failure and the reasons for ineligibility will be documented on the Consent Log. The Millipede System will not be used, and the subject may be treated with an alternative therapy according to the Investigator's judgement and standard of care.*
Exclusion Criteria	1. Known previous stroke within the past 3 months. 2. Females who are known to be pregnant or breastfeeding. 3. In the Investigator's opinion, any known comorbidity (including COVID-19) that may complicate treatment or prevent improvement or follow-up. 4. Subject currently participating in or has previously participated in another trial involving an investigational device or drug within 30 days of enrollment. 5. Known history of severe contrast allergy. 6. Pre-existing neurological or psychiatric disease that would confound the neurological or functional evaluation. 7. Life expectancy of less than 6 months prior to stroke onset. 8. Known cocaine, methamphetamine, or heroin use at time of treatment. 9. Known history of coagulation factor deficiency or oral anti-coagulant therapy with an International Normalized Ratio (INR) of more than 3.0. 10. Known history of treatment with heparin within 48 hours with a Partial Thromboplastin Time (PTT) more than two times the laboratory normal. 11. Known history of treatment with a direct thrombin inhibitor within 48 hours with a PTT more than 1.5 times the laboratory normal.

	12. Known glucose level< 50 mg/dl (2.78 mmol/L) or > 400 mg/dl (22.20 mmol/L). 13. Known platelet count <50,000/μL. 14. Clinical history, past imaging or clinical judgement suggest that the intracranial occlusion is chronic. 15. For all patients, severe sustained hypertension with Systolic Blood Pressure (SBP) >220 mmHg and/or Diastolic Blood Pressure (DBP) >120 mmHg; for patients treated with thrombolytic therapy, sustained hypertension despite treatment with SBP >185 mmHg and/or DBP > 110 mmHg. 16. Renal failure with serum creatinine ≥3 mg/dL or Glomerular Filtration Rate (GFR) <30 mL/min. 17. Ongoing seizure due to stroke. 18. Initially treated with intra-arterial thrombolytics or a different neurothrombectomy device before use of the Millipede System. 19. Clinical symptoms of bilateral stroke or stroke in multiple territories. 20. Known history of cerebral vasculitis. 21. Evidence of active systemic infection (e.g., septicemia). Exceptions: common cold, hepatitis B virus (HBV), hepatitis C virus (HCV). 22. Any known hemorrhagic or coagulation deficiency. 23. Evidence of current intracranial hemorrhage on imaging. 24. Significant mass effect with midline shift. 25. Known arterial condition in a proximal vessel that requires treatment or prevents access to the site of occlusion or safe recovery of the investigational device (for example, severe stenosis, complete occlusion in the cervical ICA, tandem occlusion). 26. Suspicion or evidence of aortic dissection, septic embolus, or bacterial endocarditis. 27. Evidence of dissection in the extracranial or intracranial cerebral arteries. 28. Excessive arterial tortuosity that may preclude device placement as determined by CTA/ MRA and/or conventional angiography. 29. Evidence of multiple vascular occlusions (e.g., bilateral anterior circulation, anterior/posterior circulation, concurrent occlusions in the anterior cerebral artery (ACA) and MCA, other concurrent ipsilateral occlusions in the same or different territories). 30. CT or MRI showing mass effect or intracranial tumor (apart from small meningioma, ≤ 2 cm in diameter). 31. Known cancer with metastases. 32. Known aneurysm at or near the target treatment segment. 33. Angiographic evidence of known or suspected underlying intracranial vasculopathy or atherosclerotic lesions responsible for the target occlusion.
Follow-up	Subjects will be followed for 90 days post-procedure.
Statistical Analysis	The primary effectiveness endpoint for this study will be tested against a performance goal (PG) derived from adjudicated trial data for similar devices. The primary safety endpoint and secondary efficacy and safety endpoints will not be subject to hypothesis testing but will be examined using confidence intervals to characterize the relevant population parameter.
Determination of Sample Size	The sample size was determined based on the number of subjects needed to demonstrate that the primary effectiveness endpoint was achieved with ≥ 95% power.

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