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## Title page

### **Title:**

**"adaptatiVe Endovascular strategy to the CloT MRI in large intracranial vessel Occlusion" (VECTOR): study protocol of a randomized control trial**

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**Trial registration**

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**Sponsor:** University Hospital of Nantes(France) is equipped to undertake the Study under its own responsibility and under the direction of Coordinator Investigator and Sponsor.

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**Roles and responsibilities of sponsor, company and coordinating investigator are detailed in supplementary data.**

**Conflicting interests: None**

## **ABSTRACT**

A correlation between the susceptibility vessel sign (SVS) and red thrombi has been identified in MRI. We hypothesized that the Embotrap allow better retrieving of SVS+ thrombi. The Adaptative Endovascular strategy to the CloT MRI in large intracranial vessel Occlusion (VECTOR) trial is a multicenter, prospective and randomized study designed to compare a first line strategy combining Embotrap added to contact aspiration (CA) versus CA alone in patients with SVS+ occlusions.

## **ABBREVIATIONS**

AIS: acute ischemic stroke

ASTER: The contact Aspiration vs STENT Retriever for successful revascularization

CA: contact aspiration

CT: computed tomography

eCRF: electronic case-report form

EVT: endovascular therapy

ICA: internal carotid artery

IV t-PA : intravenous tissue-type plasminogen activator infusion

MRI: magnetic resonance imaging

mRS: modified Rankin scale

NIHSS: national institute of health stroke scale

RBC: red blood cells

SVS: susceptibility vessel sign

THRACE: THRombectomy des Artères CERébrales

TICI: Thrombolysis In Cerebral Infarction

VECTOR: adaptatiVe Endovascular strategy to the CloT MRI in large intracranial vessel Occlusion

## **INTRODUCTION**

The primary goal of acute ischemic stroke (AIS) treatment is to open the occluded artery with intravenous tissue-type plasminogen activator infusion (IV t-PA) and/or endovascular therapy (EVT)[1,2]. A pre-treatment knowledge about clot composition might be pertinent since predominance of red blood cells (RBC) affects the efficacy of IV thrombolysis and mechanical thrombectomy (MT) [3–5].

Thrombus imaging approaching the RBC content could be helpful to plan a treatment strategy in order to maximize the rate of early successful reperfusion[6,7]. Two studies identified a correlation between the susceptibility vessel sign (SVS) and the RBC composition[8,9]. The SVS on T2\* sequence is defined as a hypo-intense signal exceeding the diameter of the contralateral artery located at the site of the thrombus[10]. Also, several studies have demonstrated SVS to be a negative predictor of early reperfusion after IV t-PA and an incentive to EVT[11–16]. In the ASTER trial, the presence of SVS impacted the success rate of the EVT strategy. In the SVS (+) sub-population, patients treated with stent retrievers achieved higher rates of complete reperfusion within fewer passes compared to contact aspiration (CA), which translated into a better functional outcome[17]. Furthermore, based on the ASTER and THROMbectomie des Artères CERébrales (THRACE) trial populations, a higher rate of favorable clinical outcome at 3 months was recently found in SVS (+) patients treated with stent retriever as a first line strategy[16].

The VECTOR trial is a multicenter, prospective, randomized, open-label study with blinded evaluation (PROBE design). We aim to compare, in case of SVS+ occlusions, a first line Embotrap added to CA combined strategy versus a CA alone strategy (*figure 1*).

## **METHODS**

### Primary hypothesis

The hypothesis is that the Embotrap, thanks to its dedicated design, will help to the stabilization of friable clots and allow better retrieving of SVS + thrombi in a lower number of passes. The primary objective is to show the superiority of first-line combined Embotrap and CA strategy compared to first-line CA alone strategy to increase the near to complete reperfusion (eTICI 2c/3) after  $\leq 3$  passes) in patients with acute ischemic stroke from anterior circulation and SVS positive intracranial occlusion on MRI.

### Secondary hypothesis

First-line combined EMBOTRAP II and CA strategy improves clinical outcomes in patients with anterior AIS and SVS positive intracranial occlusion on MRI compared to first line CA alone strategy.

### Selection criteria

Patients greater than 18 years of age who have a clinical diagnosis of AIS from a large anterior circulation cerebral vessel occlusion involving the termination of the internal carotid artery (ICA), the first (M1) or the horizontal second segment of the middle cerebral artery (M2) and a clear SVS facing the occlusion according to the definition of *Rovira et al.* in a 1.5T MRI with T2 \*sequence could be randomized allocation of treatment options [10]. Patients could be treated previously with intravenous thrombolysis.

### Randomization

Patients will be randomized in two parallel groups (1:1): one group will receive endovascular intervention with first-line CA alone whereas the other group will receive the EMBOTRAP II and CA combined treatment. To assure a centralized real-time randomization procedure, a web-based randomization will be performed using the electronic case-report form (eCRF) system. Minimization criteria will be the following: neuroradiology center, age ( $\leq 80$  versus  $> 80$  years), prior use of IV thrombolysis and occlusion site (isolated middle cerebral artery versus middle cerebral artery/internal carotid artery).

### Blinding

Blinding the study of SVS and procedure is not possible because all patients will be SVS+ and technical aspects of mechanical thrombectomy will be on the images. However, to avoid bias in study results, two imaging core labs will be determined: one for procedure related data and one for neuroimaging secondary end-points. In addition, the modified Rankin Scale score at 90 days will be assessed by trained research nurses unaware of the study group assignments.

### Embotrap device

The EmboTrap revascularization device (Cerenovus) is a nitinol dual layer stent retriever, engineered with large inlet windows, and a distal capture zone for removing clots and restoring blood flow in patients with AIS related to large vessel occlusion[18].

### Interventions

The experimental treatment is the combined CA/Embotrap approach into with a large bore balloon guide catheter placed into the cervical ICA. This combined thrombectomy technique will be performed using the "ARTS" technique which requires complete removal outside the patient of the distal aspiration catheter and retriever stent at each pass. Before starting aspiration in the suction catheter, the micro catheter used to hoist the retriever stent will be completely removed from the patient ("bare wire" technique) to ensure maximum suction volume in the catheter.

The control treatment is the contact aspiration strategy alone with a large-bore balloon guide catheter placed into the cervical ICA. The aspiration catheter will be connected to a continuous

aspiration from the dedicated aspiration pump during 3 min and then tension is applied to pull out the aspiration catheter.

The randomized treatment will be repeated until successful reperfusion (Thrombolysis In Cerebral Infarction; eTICI 2c/3) is achieved or the procedure terminated. At least three attempts must be performed before changing strategy for other adjunctive devices.

### Sample size

526 patients will be included in the study. We calculated that 229 patients per arm (458 in total) is needed to detect this effect size, by assuming primary endpoint rate of 35% in control arm. To anticipate 15% of patients with spontaneous recanalization or catheterization failure, 263 patients per arm (a total of 526) will be included

### Outcome measures

The primary endpoint of VECTOR is the near to complete reperfusion (eTICI 2c/3) rate after  $\leq 3$  passes on immediate post-treatment angiogram[19]. The secondary outcomes include the safety related to standard of care procedure (rate of symptomatic and asymptomatic intracerebral haemorrhage at MRI or CT scan 24h after thrombectomy, rate of all-cause mortality at 90 days and rate of periprocedural complications), the clinical efficacy (change in national institute of health stroke scale (NIHSS) from baseline to 24 hours (delta NIHSS)) and the rate of functional independence defined as a modified Rankin scale (mRS) 0-2 at 90 days.

### Data management

Data collection for each person participating in the research will be performed with an electronic case report form (eCRF). The trial will be monitored by a Data Review Committee (DRC) which will be responsible for reviewing the data of the clinical trial for the duration of the study and undertake to take part and observe data confidentiality. The members of the DRC will be selected collectively by the coordinator and the sponsor.

### Duration of the trial

Each patient will be followed for at least 3 months after mechanical thrombectomy. We plan a 12-month recruitment phase. The study should be completed within 15 months including analysis.

### Statistical analyses

Statistical analyses will be independently performed by the Biostatistics Department of University of Lille. For data analysis, statisticians and investigators will be aware of the experimental arm allocation. Under the intention-to-treat principle, all patients who are randomized are included in the analysis.

### Ethical considerations

The ethical review board of the Centre Hospitalier de l'Université de Nantes approved the protocol. If the state of consciousness of the patient does not allow consent to be obtained, and because of this therapeutic urgency, the consent of a trustworthy person will be looked for, without causing delay in the management of the patient. Should this not be possible, the doctor will include the patient according to the protocol of inclusion in an emergency situation. When the patient has regained a sufficient state of consciousness, his/her consent to the pursuit of the research and to the treatment of the collected information will be asked for.

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**FIGURES**

**Figure 1: Study flow chart.**

