

# Evaluating whether highly calcified stenoses of arteries supplying the brain can be safely treated percutaneously using ultrasound stone-crushing technique

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## Plain English summary of protocol

### Background and study aims

Highly calcific ('stone-like') carotid stenoses (HCCS) remain a significant challenge for endovascular management, and open surgery is usually considered the treatment of choice. However, a significant proportion of patients who require treatment are elderly and may be too frail for surgery; such patients could likely benefit from minimally invasive (percutaneous) treatment. Recent technology developments enable using ultrasound energy, applied from a modified angioplasty balloon (transiently placed in the artery), to crack the rigid, 'stone-like' atherosclerotic calcifications. This approach is similar to cracking, for instance, kidney stones with ultrasound energy. The novel technology, called intravascular lithotripsy (IVL), is today typically used to crack highly calcific atherosclerotic stenoses of the heart or arteries in the legs – but not yet routinely in the arteries supplying the brain. This study evaluates the use of IVL, in combination with plaque-sequestering carotid stents, to treat highly calcific stenoses of arteries supplying the brain.

### Who can participate?

Consecutive patients aged 18 years and over with HCCS scheduled for carotid revascularization as a means of primary or secondary stroke prevention as per Neurovascular Team recommendation.

### What does the study involve?

The study involves the use of IVL and routinely available plaque containing carotid stents to treat, under routine cerebral protection, highly calcified arteries supplying the brains. The IVL technique is not new in management highly calcific atherosclerosis as it is commonly used in coronary and ilio-femoral arteries.

### What are the possible benefits and risks of participating?

One fundamental benefit is that the use of endovascular treatment rather than open surgery. However, IVL like any endovascular treatment may be associated with formation of embolic

particles. For this reason, the study involves routine use of double (proximal and distal) cerebral protection that has been shown in the pilot series to effectively prevent cerebral embolism.

Where is the study run from?

The study is run from –and in– Saint John Paul II Hospital (Poland), a hospital routinely performing carotid artery revascularization (both endovascular and surgical).

When is the study starting and how long is it expected to run for?

February 2025 to December 2028

Who is funding the study?

The study is initiated and run by the investigators (investigator-initiated study), and it is funded by Jagiellonian University Medical College (Poland)

Who is the main contact?

Prof. Piotr Musialek, p.musialek@szpitaljp2.krakow.pl

## Contact information

### Type(s)

Public, Scientific, Principal investigator

### Contact name

Prof Piotr Musialek

### ORCID ID

<https://orcid.org/0000-0001-9300-4833>

### Contact details

Pradnicka 80

Krakow

Poland

31-202

+48 (0)126142111

p.musialek@szpitaljp2.krakow.pl

## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Protocol serial number

1072.6120.286.2018

## Study information

### Scientific Title

A novel PARADIGM in highly calcified carotid stenoses endovascular management: intravascular lithotripsy and CGuard MicroNet covered stent: the PARADIGM–IVL study

## Acronym

PARADIGM-IVL

## Study objectives

To evaluate the feasibility, safety and efficacy of endovascular management of highly calcific carotid stenoses in symptomatic and increased-stroke-risk asymptomatic patients using intravascular lithotripsy and plaque-sequestering carotid stent.

## Ethics approval required

Ethics approval required

## Ethics approval(s)

approved 25/10/2024, Jagiellonian University Ethics Committee (Skawinska 8, Kraków, 31-066, Poland; +48 (0)12 433 27 43; komisja\_bioetyczna@uj-cm.krakow.pl), ref: 1072.6120.286.2018\_10.2024

## Study design

Single-centre single-arm open-label study

## Primary study design

Interventional

## Study type(s)

Treatment, Safety, Efficacy

## Health condition(s) or problem(s) studied

Symptomatic and increased stroke risk asymptomatic, highly calcific carotid stenoses deemed for endovascular revascularization

## Interventions

In local anaesthesia, after common femoral artery puncture and 9F sheath insertion, a diagnostic catheter is placed in target site common carotid artery, and the target lesion is fully visualized. The diagnostic catheter is then changed into proximal cerebral protection catheter (either Flowgate or MoMa). Distal embolic protection filter (any type) is delivered through the lesion to the internal carotid artery under cerebral protection. After cerebral protection is established initial predilatation is performed by stiff, non-compliant balloon(s). Intravascular lithotripsy (IVL) using coronary or peripheral ShockWave balloons is performed afterwards as per instruction for use, delivering maximally tolerated number of calcium cacking deliveries as per catheter specifications. This is usually followed by another a larger non-compliant balloon to further optimize lesion preparation.

Then a high-radial-force, MicroNet covered (plaque sequestering CGuard stent) is implanted. Finally non-compliant balloon postdilations is performed (in case of diameter(s) greater than 6 mm, a larger semi-compliant balloon(s) such as 7-8 mm can be used. In case of proximal protection intolerance (signs of cerebral ischemia) the flow is restored and procedure is continued under distal protection. Intravascular ultrasound is performed at the end of the procedure to document the stent expansion and apposition, visualize any in-stent material and document lumen reconstruction.

## Intervention Type

Device

## Phase

Phase II/III

## Drug/device/biological/vaccine name(s)

Intravascular Lithotripsy + CGuard MicroNet covered stent

## Primary outcome(s)

Combined (hierarchical) clinical endpoint of death, stroke, myocardial infarction verified at 30-day Duplex Ultrasound (DUS) outpatient visit or telephone visit by 30 days

## Key secondary outcome(s)

1. Death verified at 30-day DUS outpatient or telephone visit by 30 days
2. Stroke verified at 30-day DUS outpatient or telephone visit by 30 days
3. Myocardial infarction by 30 days according to the 4th universal myocardial infarction definition
4. Combined (hierarchical) clinical endpoint of death, stroke, myocardial infarction, periprocedurally defined as within 48 hours from the procedure or before hospital discharge, whichever comes first
5. Death peri-procedurally measured using the discharge letter from the index hospitalization
6. Stroke peri-procedurally measured using the discharge letter from the index hospitalization
7. Myocardial infarction peri-procedurally (according to the 4th universal myocardial infarction definition) measured using discharge letter from index hospitalization
8. Technical success defined as the effective delivery of IVL, carotid stent and residual stenosis at the time of the index procedure
9. Clinical success defined as technical success without clinical events - no death, stroke, myocardial infarction at from the time of the index procedure until discharge
10. Procedure failure (rate of conversion to open surgery, i.e. number of patients referred to surgery with attempted precutaneous procedure) at the time of scheduled index procedure, surgery may be postponed to a different hospitalization
11. Residual stenosis >30% (assessed by angiography and duplex ultrasound, DUS) at the time of index procedure (angiography), and hospitalization (DUS)
12. Stent thrombosis within 30 days (assessed by DUS, angiography, verified at the 30-day DUS outpatient visit)
13. Proportion of patients treated endovascularly (in relation to open surgery) at the time of scheduled index procedure, surgery may be postponed to a different hospitalization
14. Rate of conversion to open surgery (proportion of procedure conversion to open surgery with attempted precutaneous procedure) at the time of the scheduled index procedure, surgery may be postponed to a different hospitalization

## Completion date

31/12/2028

## Eligibility

### Key inclusion criteria

1. Presence of carotid stenosis requiring revascularization:
  - 1.1. Symptomatic stenosis >50% (within 6 months: stroke, transient cerebral ischemia, amaurosis fugax, retinal stroke).
  - 1.2. Asymptomatic stenosis >70-80% with high-risk features (plaque irregularity, thrombus containment, ulceration, containment of large lipid core; evidence of plaque progression)
2. Heavy calcification of carotid stenosis in duplex ultrasound and confirmed in angiography according to HCCS score [Mazurek CCI]

3. Subject deemed medically eligible for intravascular management, per institutional guidelines and clinical judgment

4. Age  $\geq$ 18 years, no upper age limit

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

99 years

**Sex**

All

**Key exclusion criteria**

Lack of the patient agreement for endovascular carotid revascularization or any study related procedure

**Date of first enrolment**

17/02/2025

**Date of final enrolment**

31/12/2028

**Locations**

**Countries of recruitment**

Poland

**Study participating centre**

Saint John Paul IInd Hospital

Pradnicka Str. 80

Kraków

Poland

31-202

**Sponsor information**

**Organisation**

Jagiellonian University Medical College

**Funder(s)****Funder type**

Government

**Funder Name**

Wydział Lekarski, Uniwersytet Jagielloński Collegium Medicum

**Alternative Name(s)**

Faculty of Medicine, Jagiellonian University Medical College, WL, UJCM, WL CM UJ

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Universities (academic only)

**Location**

Poland

**Results and Publications****Individual participant data (IPD) sharing plan**

Anonymised data will be shared upon reasonable request submitted to the PIs.

**IPD sharing plan summary**

Available on request