ISRCTN94131858 https://doi.org/10.1186/ISRCTN94131858

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

Submission date
30/09/2025

Recruitment status
Recruiting

Registration date
13/10/2025

Overall study status
Ongoing

Last Edited
13/10/2025

Condition category
Circulatory System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

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-sequestrating 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 IInd 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

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-sequestrating 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

Primary study design
Interventional

Study design
Single-centre single-arm open-label study

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 aesthesia, 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 sequestrating 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 ≥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