Study Protocol

PRO-EMMA — Prospective Outcomes of MMA Embolization

A Prospective Single-center Registry Investigating Endovascular Therapy for Chronic Subdural Hematomas

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Official Title: PRO-EMMA (Prospective Outcomes of MMA Embolization): A Prospective Single-center Registry Investigating Endovascular Therapy for Chronic Subdural Hematomas

NCT Number: TBA

Study Site: Charité – Universitätsmedizin Berlin, Department of Neuroradiology, Campus Mitte

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1. Background and Rationale

Chronic subdural hematoma (cSDH) is a common condition, particularly in older adults. The standard treatment typically consists of surgical decompression (burr-hole craniotomy). However, recurrence rates following surgery alone reach up to 30%.

Middle meningeal artery embolization (MMAE) is a minimally invasive therapy that can significantly reduce the risk of recurrence. Initial randomized controlled trials and meta-analyses demonstrate high efficacy and safety. Nevertheless, prospective, standardized data on patient selection, prognosis, and follow-up remain lacking.

The PRO-EMMA study aims to establish and evaluate a prospective, standardized follow-up protocol.

2. Objectives

Primary: To identify clinical and radiological predictors of good functional outcome (mRS ≤ 2 at 90 days) after MMAE for cSDH.

Secondary:

- Reduction of hematoma volume over time (follow-up CTs)
- Assessment of complications, re-interventions, and mortality
- Validation of a standardized follow-up protocol (CT + clinical/QoL assessments)

Primary Endpoints:

1. **Radiological response** – Change in hematoma volume/thickness at 3 months
2. **Clinical efficacy** – Re-intervention rate and functional outcome (mRS) at 90 days
3. **Clinical safety** – Occurrence of complications

Secondary Endpoints:

- Symptom course over time
- Need for re-hospitalization
- Mortality

Potential Confounders (Core Set):

- Hematoma architecture
- Initial volume/thickness and localization
- Foramen spinosum diameter
- Anticoagulation / antiplatelet therapy
- Extent of embolization (vessel-branch level; embolic agent documented)

3. Study Design

Prospective, single-arm, single-center registry.

Duration: 12 months recruitment.

Target population: 75–150 patients.

4. Eligibility Criteria

Inclusion Criteria:

- CT- or MRI-confirmed chronic subdural hematoma (cSDH)
- Planned or completed MMAE (primary therapy or adjunct to surgical evacuation)
- Age ≥ 18 years
- Written informed consent including agreement to extended follow-up (CT and clinical assessments)

- mRS ≤ 3 at baseline

Exclusion Criteria:

- Acute subdural hematoma requiring emergency neurosurgical intervention
- Known vascular anomalies contraindicating embolization (e.g., high-risk leptomeningeal anastomoses)
- Missing or incomplete baseline clinical and radiological data
- Unavailability for prospective follow-up (e.g., no fixed address, no telephone contact)

5. Study Procedures and Timeline

Treatment phase: MMAE is performed according to clinical routine (standard of care, no modifications).

Study-specific additional assessments:

Clinical and quality-of-life assessments (mRS, GOS-E, EQ-5D-5L, GCS, Markwalder score):

- Pre-interventionally (baseline)
- Day 30 (telephone interview)
- Day 90 (in-person or telephone, within the new cSDH outpatient clinic)
- Day 120 (telephone interview)

Imaging follow-up (cranial CT):

- Within 7 days post-intervention
- At 3 months post-intervention (within the new cSDH outpatient clinic)

Note: *Compared to the currently heterogeneous clinical routine at the Charité, these assessments may result in one additional CT for some patients. The chosen time points are fully consistent with the recommendations of the international ARISE-I consensus, which endorses early follow-up imaging and a 3-month control CT. The use of ionizing radiation in this study has been approved in accordance with the German Radiation Protection Act (Strahlenschutzgesetz) and the applicable regulatory requirements of the Federal Office for Radiation Protection (Bundesamt für Strahlenschutz, BfS).*

6. Data Collection

Clinical: Medical history, GCS, comorbidities, anticoagulation/antiplatelet therapy, symptom course

Radiological: Hematoma volume, architecture, laterality, localization, midline shift, MMA caliber, anatomical MMA variants, foramen spinosum diameter, prior burr-hole trepanation

Procedural: Embolic agent, BE-EMMA score, technical details, embolisate volume, degree of distal penetration, complications

Follow-up: mRS, GOS-E, EQ-5D-5L, GCS, Markwalder score at each time point; re-intervention, recurrence, mortality, symptom course

Documentation is performed in pseudonymized case report forms (CRF; currently Excel-based, with planned migration to REDCap).

7. Data Protection

- Pseudonymization via study-specific ID
- Separate, encrypted assignment list

- Storage exclusively on Charité servers (clinical data: 10 years; CT data: 30 years)
- Access restricted to authorized study personnel only
- Data processing in compliance with DSGVO and BlnDSG

8. Risks and Burden

- Radiation exposure from up to two additional native low-dose CTs (7 days, 3 months) – within diagnostically acceptable dose ranges (ALARA principle)
- Minimal time investment for structured follow-up interviews (telephone or in-person, approximately 10–15 minutes each at days 30, 90, and 120)
- No additional medical interventions or modifications to clinical care
- No further medical risks

9. Benefits

Individual Benefits:

- Close structured follow-up
- Early detection of complications
- Objectified assessment of treatment course

Benefits for Future Patients:

- Validation of a clinically applicable and standardized follow-up protocol
- Improved patient selection and treatment planning in the future
- Contribution to establishing MMAE as a safe and effective therapy in Germany

10. Statistics

Target sample size: 75–150 patients (exploratory).

Descriptive statistics with 95% confidence intervals; bivariate correlation analyses (Pearson or Spearman); logistic regression for predictor analysis. Missing data will be reported but not imputed.

11. Ethics and Legal Framework

- Conducted in accordance with the Declaration of Helsinki, GCP, and DSGVO
- Participation is voluntary and may be withdrawn at any time without consequences for clinical care
- Positive ethics committee vote required prior to study initiation
- Radiation protection approval granted by the Federal Office for Radiation Protection (Bundesamt für Strahlenschutz, BfS) in accordance with the German Radiation Protection Act (Strahlenschutzgesetz)