Statistical Analysis Plan

Efficacy of Combined Dynamic Stabilometry and Transcranial Direct Current Stimulation in the Early Recovery Period of Ischemic Stroke in Patients With Hemiparesis: a Single-Center Randomized Sham-Controlled 2×2 Factorial Trial (STAB-tDCS)

1. Administrative Information

Item	Details
Protocol ID	SamSMU-BEC-322-2026 (Bioethics Committee approval, Protocol No. 322, May 15, 2026)
Registry	ClinicalTrials.gov, NCT number pending
Protocol version	Version 1.0, April 15, 2026
SAP version and date	Version 1.0, October 26, 2026 (finalized before enrollment of the first participant)
Principal Investigator	A.V. Zakharov, MD, PhD, Research Institute of Neurosciences, Samara State Medical University
SAP author / statistician	A.D. Adelshin
Software	R (version 4.x) and/or IBM SPSS Statistics

The SAP will be finalized and signed before database lock and unblinding. Any later changes will be dated and justified in a SAP amendment.

2. Objectives and Hypotheses

Primary objective. To evaluate the effect of dynamic stabilometry with biofeedback and of anodal tDCS, alone and in combination, on postural balance measured by the Berg Balance Scale (BBS) at Day 12.

Primary hypotheses (two-sided, 2×2 factorial):

1. Main effect of stabilometry: adjusted Day 12 BBS differs between dynamic (groups A + B) and static (groups C + D) stabilometry.
2. Main effect of tDCS: adjusted Day 12 BBS differs between active (groups A + C) and sham (groups B + D) tDCS.
3. Interaction: the effect of dynamic stabilometry depends on tDCS type (synergy); tested as the stabilometry × tDCS term.

Secondary objectives. To evaluate effects on functional independence (FIM), fall risk (MFS), ambulation (HAI), global disability (mRS), mobility (RMI), neurological deficit (NIHSS), muscle strength (MRC) and spasticity (MAS) at Days 6 and 12, and to evaluate safety.

3. Design, Randomization and Sample Size

Design. Prospective, single-center, pilot randomized controlled trial with a 2×2 factorial design: Factor 1 — stabilometry (dynamic vs static, locked platform); Factor 2 — tDCS (active anodal vs sham). Four groups: A (dynamic + active), B (dynamic + sham), C (static + active), D (static + sham). All groups receive standard rehabilitation of equal volume. Assessments: Day 0 (baseline), Day 6 (interim), Day 12 (end of course).

Randomization. Allocation 1:1:1:1, permuted blocks of 8, stratified by age (<65 / ≥65 years) and side of the lesion (left / right hemisphere). Allocation concealment by sealed opaque envelopes or centralized web-based randomization.

Blinding. Participants are blinded to stimulation type; outcome assessors are blinded to group allocation. The statistician will analyze data with coded group labels until the primary analysis is complete.

Sample size. The calculation is based on the primary outcome (Day 12 BBS) and the main-effect comparisons of the factorial design (60 vs 60 participants per factor level). Assumptions: expected between-level difference ΔBBS = 6 points, SD = 10 (Cohen's d = 0.6), two-sided α = 0.05.

Participants per comparison arm	Power (two-sample t-test, d = 0.6)
36	71%
45	80%
51 (60 with 15% dropout)	85%
60 (no dropout)	90%

A total of 120 participants (30 per group) gives about 85% power for each main effect after 15% dropout. Adjustment for baseline BBS in ANCOVA is expected to increase power further. The study is not powered for the interaction or for pairwise between-group comparisons; these are interpreted as exploratory.

4. Analysis Populations and Outcomes

Population	Definition	Used for
Intention-to-treat (ITT)	All randomized participants, analyzed in the group to which they were allocated	Primary and secondary efficacy analyses
Per-protocol (PP)	ITT participants who completed ≥ 8 of 10 sessions, had the Day 12 assessment and no major protocol deviation	Sensitivity analysis
Safety	All participants who received at least one session, analyzed by treatment actually received	Adverse events

Outcome	Scale range and direction	Type	Time points
Primary: Berg Balance Scale (BBS)	0–56, higher = better balance	Continuous	Day 0, Day 12
BBS (interim)	0–56, higher = better	Continuous	Day 6
Functional Independence Measure (FIM)	18–126, higher = more independent	Continuous	Day 0, 6, 12
Morse Fall Scale (MFS)	0–125, higher = higher fall risk	Continuous	Day 0, 6, 12
Hauser Ambulation Index (HAI)	0–9, higher = worse ambulation	Ordinal	Day 0, 6, 12
modified Rankin Scale (mRS)	0–6, higher = more disability	Ordinal	Day 0, 6, 12
Rivermead Mobility Index (RMI)	0–15, higher = better mobility	Continuous (discrete)	Day 0, 6, 12
NIH Stroke Scale (NIHSS)	0–42, higher = more severe deficit	Continuous (discrete)	Day 0, 6, 12
MRC muscle strength (paretic limbs, sum score)	0–5 per muscle group, higher = stronger	Continuous	Day 0, 6, 12
Modified Ashworth Scale (MAS)	0–4, higher = more spasticity	Ordinal	Day 0, 6, 12
Adverse events	Count and proportion of participants	Binary / count	Day 0 to Day 12

5. Statistical Methods

5.1 General principles

- All tests are two-sided, $\alpha = 0.05$; estimates are reported with 95% confidence intervals.
- Continuous variables: mean ± SD or median [IQR] depending on distribution (Shapiro–Wilk test, Q–Q plots). Categorical variables: n (%).
- Baseline characteristics are summarized by group without significance testing (CONSORT 2010).
- A CONSORT flow diagram reports screening, randomization, allocation, follow-up and analysis numbers.

5.2 Primary analysis

ANCOVA on Day 12 BBS in the ITT population:

$$\mathrm{BBS}_{12} = \beta_0 + \beta_1\,\mathrm{BBS}_{0} + \beta_2\,\mathrm{Stab} + \beta_3\,\mathrm{tDCS} + \beta_4\,(\mathrm{Stab}\times\mathrm{tDCS}) + \beta_5\,\mathrm{Age}_{\geq 65} + \beta_6\,\mathrm{Side} + \varepsilon$$

- Stab: dynamic = 1, static = 0; tDCS: active = 1, sham = 0; stratification factors (age group, lesion side) are included as covariates.
- The interaction term (β4) is tested first. If $p \geq 0.05$, main effects are estimated from the model without the interaction term; if $p < 0.05$, simple effects of each factor are reported at each level of the other factor.
- Results: adjusted mean differences with 95% CI, partial η^2, and Cohen's d.
- Model assumptions (normality and homoscedasticity of residuals, homogeneity of regression slopes) are checked. If violated, robust (HC3) standard errors or rank-based ANCOVA are used.

5.3 Secondary analyses

- **Pairwise group comparisons** (A vs B, A vs C, A vs D) from the same ANCOVA, with Holm correction; exploratory.
- **Trajectories over Day 0, 6, 12:** linear mixed-effects model (generalization of mixed ANOVA) with fixed effects of time, stabilometry, tDCS and their interactions, stratification factors, and a random intercept per participant; Kenward–Roger degrees of freedom.
- **Continuous secondary outcomes** (FIM, MFS, RMI, NIHSS, MRC): ANCOVA on Day 12 values adjusted for baseline, as for the primary outcome.
- **Ordinal outcomes** (mRS, HAI, MAS): proportional odds logistic regression adjusted for baseline score and stratification factors (common odds ratio with 95% CI); if the proportional odds assumption fails, the aligned rank transform ANOVA is used.
- Secondary outcomes are exploratory; p-values are reported without adjustment for multiplicity and interpreted with caution.

5.4 Safety analysis

Adverse events (e.g., skin irritation, headache, dizziness, falls, seizures) are summarized by group as number of events and number (%) of participants with at least one event, by severity and relatedness. Groups are compared with Fisher's exact test.

5.5 Interim analysis

No interim efficacy analysis is planned. No Data Monitoring Committee is established; serious adverse events are reviewed by the Principal Investigator as they occur.

6. Missing Data, Sensitivity Analyses and Subgroups

Missing data. The primary ITT analysis uses multiple imputation by chained equations (20 imputed datasets) under the missing-at-random assumption. The imputation model includes group, stratification factors, baseline and Day 6 scores. Estimates are pooled using Rubin's rules. Reasons for dropout are reported by group.

Sensitivity analyses for the primary outcome:

1. Complete-case analysis.
2. Per-protocol analysis.
3. Linear mixed-effects model using all available Day 0, 6 and 12 data without imputation.

Exploratory subgroups (interaction tests, not powered): age (<65 / ≥65 years), side of the lesion (left / right), time since stroke onset (≤ 30 days / > 30 days).

7. Deviations From the Protocol Text

Protocol (Version 1.0)	SAP	Reason
Primary ANCOVA adjusted for baseline FMA	Adjusted for baseline BBS	FMA is not collected; BBS is the outcome used for the sample size calculation
BBS described as a secondary endpoint	BBS is the primary outcome	Consistency with the sample size calculation and trial registration
n = 36 per group; n ≥ 30 per group after 15% dropout	120 participants; power based on factorial main effects (60 vs 60)	The protocol arithmetic does not account for dropout correctly; the factorial design uses pooled comparisons
Analysis populations, missing data handling and ordinal outcomes not specified	Specified in Sections 4–6	Required detail for a pre-specified analysis

8. Approval

Principal Investigator _____ /signature/ _____ A.V. Zakharov · Date: _____

Statistician _____ /signature/ _____ P.A. Adelshin · Date: _____