Study title:

Feasibility, Acceptability, and Preliminary Efficacy of Combined Transcranial Direct Current Stimulation and Mindfulness for Pain After Total Knee Arthroplasty

NCT Number: NCT05673720

Statistical analysis plan

October 10th, 2025

Data analysis was performed with R (Vienna, Austria) version 4.1+. Baseline demographic information was summarized using descriptive statistics. The distribution of all variables was examined before any analysis, using appropriate statistical tests like Shapiro's test for normality checking. If the assumption of normality was not met, equivalent non-parametric approaches was employed. Comparison between groups on changes from baseline in clinical variables as well as effect size (Cohen's *d*) calculation were conducted using Wilcoxon rank-sum test for score changes with non-normal distribution, and *t*-test for score changes with normal distribution. Considering the numerous repeated measures and the possibility of imbalances between measures, we conducted an analysis using a generalized mixed effects model to evaluate changes in all outcome measures for both preoperative and postoperative outcomes. Mixed effects models capture more information by offering more flexibility in the presence of missing data and treat time as a continuous variable. Mixed effects models are used for longitudinal observations and are capable of automatically adjusting for baseline differences, accounting for potential confounders (e.g., anxiety) when needed.

For the preoperative period, the analysis looked at differences between preoperative baseline and after 5 sessions with three fixed effects: Condition (Control vs. Treatment), Time (First vs. Last Session) and their interaction Condition*Time to test whether the treatment group showed different patterns of change compared to the control group over time in the preoperative period. For the postoperative period, the analysis looked at differences 1) between Day 1 Post-op vs. Day 5 Post-op, and 2) between Day 1 Post-op vs. 1-month post-op. Our model included three fixed effects: Condition (Control vs. Treatment), Time (Day 1 vs. Day 5 or Day 1 vs.1-month post-op), and their interaction (Condition*Time) to test whether the treatment group showed different patterns of change compared to the control group over time in the postoperative period.

The significance levels (Type-I error probability) for testing the difference between treatment groups over time was 5% and a p-value less than 0.05 was considered statistically significant. However, this level might seem arbitrary in pilot studies and we considered that in this preliminary study, $p < 0.10$ is suggestive (i.e. a trend) of a significant effect that warrants further study. We did not use any Bonferroni corrections for these pair-wise comparisons since a pilot study is usually designed for hypothesis generation instead of hypothesis testing.