A RANDOMIZED SHAM-CONTROLLED STUDY OF HOME-DELIVERED NON-INVASIVE NEUROSTIMULATION FOR MIGRAINE [IRB#19008-01, NCT03874351]

STATISTICAL ANALYSIS PLAN

(UPDATE 1.29.20)

Analysis Plan (Update 1.29.20)

Participants will be randomized within randomly selected blocks of sizes 2, 4, and 6. The randomization list will be generated by an investigator not otherwise associated with the administration of treatment or collection of data.

All patient characteristics and outcomes will be evaluated for distribution. For all bivariate tests, the appropriate parametric or non-parametric test will be selected based on distribution. Patient characteristics will be described and bivariate tests will evaluate any differences across treatment group (active tDCS vs. sham tDCS). Primary and secondary outcomes at baseline will be described and bivariate tests will evaluate any differences across group. Bivariate tests will evaluate differences in attrition, patient satisfaction, adverse events (including all adverse events, serious adverse events, and adverse events attributed to the treatment), and quality of blinding across group.

All outcomes will be described using data visualization. Differences in outcome between the active tDCS and sham tDCS groups will be evaluated in both intent-to-treat and completer analysis using non-parametric statistics as appropriate (see Table below). Intent-to-treat analysis will impute missing values using all available data. Differences in outcome between people with chronic (15 or more headache days/month) vs. episodic migraine, with and without medication overuse (e.g., using a MSM on 10 or more days per month during the baseline period), and with high and low levels of patient compliance will also be evaluated using the appropriate non-parametric statistic.

Alpha will be set at 0.05, two-tailed, for all analyses. SPSS v. 25.0 and R will be used for all analyses.

Primary Outcome	Description	Tentative Analysis Type
Change in migraine day/30 day	Median change in the number of migraine days per 30 day period, from M0 to M2.	Mann-Whitney U
Secondary Outcomes		
Responders	% of participants who report a 50% reduction in migraine days, from M0 to M2.	Fisher's Exact Test
Change in headache attack/30 days	Median change in number of attacks per 30 day period, from M0 to M2.	Mann-Whitney U
Change in acute medication use	Median change in number of days on which an acute medication was used from M0 to M2.	Mann-Whitney U
Change in headache attack intensity	Median change in NRS from headache days in a 30 day period from M0 to M2.	Mann-Whitney U

Change in Migraine-Specific Quality of Life – Total, and 3 subscales	Median change in MSQ score from M0 to M2	Mann-Whitney U
Change in Hamilton Depression Scale	Median change in Ham-D score from M0 to M2	Mann-Whitney U
Tolerability	Side effects AEs Total AEs related in any degree to the treatment	Mann Whitney Us
Satisfaction	% of participants who report being satisfied with the treatment	Fisher's Exact Test