PROTOCOL TITLE:

Transcutaneous electrical acustimulation in automatic synchronization with breathing for treating functional dyspepsia: A phase I feasibility trial

PRINCIPAL INVESTIGATOR:

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Statistical Design and Power

Basic information
o Number of enrolled subjects: 20
o Sample size: n = 15 (n = 20 accounting for a possible 30% attrition) in the experiment. The sample size calculation is not required, as no efficacy hypothesis is evaluated. The sample size calculation is based on obtaining sufficient pilot clinical data for a power analysis for the follow-on multi-center efficacy study towards obtaining FDA 510(k) de novo clearance. The power analysis is applied using the desired power of 0.8, the desired alpha value of 0.05, and an estimated effect size based on the scores of the symptom questionnaire in the FD patients treated with STEA therapy in an office setting from a previous study.27 Based on these inputs, the sample size calculator suggests n = 10. However, to comply with FDA guidance specifying the minimum number of participants required for the summative usability study as n = 15, the larger number of n = 15 will be used for the experiment. With a 30% attrition estimate, the adjusted sample size for that will be 20.

Randomization
Upon enrollment, the patients will be randomly assigned to a code A-B or a code B-A with equally randomized functional dyspepsia patients. A patient with a code A-B will be treated with AutoSTEA for 4 weeks, followed with a 2-week washout period (to recapture new baseline symptoms) and another 4-week period with sham-stimulation. A patient with a code B-A will be treated with sham stimulation first and then AutoSTEA.

The study coordinator will be responsible for setting up and implementing the randomization scheme.

Statistical Methods
Dr. Michael Kurin and a statistician will perform the statistical analysis. The primary and secondary outcomes will be specified based on the study objectives.
The data will be reviewed for completeness and consistency by flagging any missing data, followed by exploring imputation of missing data for sensitivity analyses (as needed). We will calculate the descriptive statistics for all variables, including mean ± standard deviation for continuous variables and percentages for categorical variables to compare between two treatment phases. For the continuous variables, we will perform the Kolmogorov-Smirnov normality test to confirm the normal distribution. For the data with normal distribution, we will then perform a paired t-test using the data at the first and second clinical visits. For continuous variables that deviate from normality, we will instead perform the two-sided Wilcoxon rank-sum non-parametric test. For categorical variables, we will use the Pearson's $\chi 2$ test to assess between-phase differences. The AE incidence will be evaluated using the lower bound of 95% CI of the Clopper-Pearson exact binomial test (onesided alpha level of 0.05). Success will be defined as 0% incidence of severe AEs and 9% (or lower) incidence of AEs.