

Response to Diaphragmatic Pacing in Subjects with Pompe Disease

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STATISTICAL ANALYSIS PLAN

Testing:

Pulmonary Function: Spirometry, maximal respiratory pressures, and occlusion pressure ($P_{0.1}$, a Clinical estimate of drive) will be completed per American Thoracic Society guidelines. Pacing will be turned off during these tests. In addition, the breathing pattern (breath flows, volumes, timing, end-tidal CO_2) will be calculated continuously while testing on MV support, during pacing, and for 1 hour after pacing. These measures will be obtained when patients are able to come to the testing site, or when the study team is able to travel to the patient's local area.

Ventilator Weaning: To evaluate weaning effects of diaphragm pacing, the duration of ventilator-free breathing (timing, volume, minute ventilation) will be recorded remotely. We will query each subject's ventilator data chip when possible to track weaning.

Electrophysiology: We will compute root mean square (RMS) of the spontaneous (unpaced) diaphragm EMG during resting MV, unassisted breathing and MIP tests. The implanted intramuscular electrodes permit us to conduct quantitative, longitudinal electrophysiological tests of phrenic motor function previously only feasible in animals; these *exploratory tests* include power spectral analysis and spike sorting to identify active motor units.

Data Interpretation: Outcomes for both aims are largely quantitative and continuous. Sample distributions and summary statistics will be calculated for each outcome and represented with box plots. Data transformation of non-linear distributions will be done if needed. Within-session measurements, when possible, will be evaluated using repeated measures ANOVA, with volume, rate, and ventilation as primary outcomes. Between-session outcomes of interest include off ventilator function (**primary outcome measure**) and breathing pattern/ventilation. These will be quantified with repeated measures ANOVA.

Expected Outcomes: Completion of this project will generate needed information concerning the rate, extent and duration of functional gains with diaphragm pacing. Within-session measurements will elucidate baseline diaphragm/phrenic function in MV-dependent adults with Pompe, and provide needed insights concerning neuromuscular modulation by diaphragm pacing. Between-session measurements will yield important data concerning the efficacy of diaphragm pacing to restore phrenic function and to reduce MV dependence over time.