

Title: Transcranial Infrared Laser Stimulation (TILS) of Prefrontal Cognition in Post-traumatic Stress Disorder (PTSD)

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### Statistical Analysis Plan

TILS/sham-induced changes in HbO<sub>2</sub>, Hb and CCO concentrations from the initial baseline will be calculated using the UCLn algorithm. We will focus on oxidized CCO concentration because it is directly related to the oxygen metabolism at the cellular level. The mean CCO changes during the treatment period will be analyzed with repeated measures ANOVA (analysis of variance), by using treatment type (TILS, sham) as a within-subject variable and sex (male, female) as an independent variable.

An iterative statistical analysis will be implemented to determine whether the  $i$ th TILS treatment ( $i \leq 6$ ) is sufficient to stably up-regulate the veteran's prefrontal activations and functioning, by interrogating the veterans' incremental changes (post-treatment minus pre-treatment) in the prefrontal activations and behavioral scores in the three memory tasks. Specifically, at the  $i$ th iteration, we will include all the data from the  $i$ th to the 6th treatments. Repeated measures ANOVA will be performed on the included data, in which the treatment number ( $i$  to 6) is a within-subject variable and sex is an independent variable. If no significant main effect of treatment number ( $p < 0.05$ , effect size  $> 0.8$ ) is found at the  $i$ th iteration in either the prefrontal hemodynamic activations or the memory task scores, it means the  $i$ th TILS treatment is sufficient to stabilize the veterans' prefrontal activity and the rest treatments are not necessary. Thus, the  $i$ th TILS treatment will be determined as the optimal dosage for treating the veterans with PTSD.