Development and Implementation of an Objective, Non-invasive, Behaviorally Relevant Metric for Laser Eye Injuries

Principal Investigator: MARTINSEN, GARY L
Institution Receiving Award: T.R.U.E. RESEARCH FOUNDATION
Program: PRMRP
Proposal Number: PR012306
Funding Mechanism:
Partnering Awards:
Award Amount: $756,250.00

TECHNICAL ABSTRACT

Background: Battlefield and accidental laser-induced retinal injuries can produce significant retinal scarring and permanent visual loss. Despite the increasing risk to military personnel, there is still no coherent, empirically driven evaluation and treatment regimen for retinal injuries from lasers. Ongoing protocols at the U.S. Army Walter Reed Army Institute of Research are evaluating a number of pharmaceuticals for their treatment efficacy. Although previous work has shown functional losses and recovery after lesions, there are no established functional metric or endpoints developed specifically for these protocols. Developing a reliable test of retinal function is a critical step in the development of a treatment for laser retinal injuries. Behavioral measures and electrophysiological measurements of the electrical response of the retina are an important, objective measure of function and a critical requirement to evaluate future treatment modalities.

Objective: The objective of this study is to determine whether the current multifocal electroretinogram (MERG) is sufficiently sensitive to provide an objective, noninvasive metric for the effects of localized retinal laser injury that correlates with perceptual deficits in the same eye and whether the MERG can quantitatively assess the natural time course of recovery from retinal laser injury as measured by both optical coherence tomography (OCT) images and behaviorally assessed visual acuity and contrast sensitivity.

Specific Aims and Study Design: The primary questions this work attempts to address are, (1) How deep a "hole" must there be in the response profile of the MERG for it to be detectable, i.e., a signal within noise detection problem? (2) Can we predict acuity from MERG deficit and vice versa as a function of time post-laser exposure? To answer these, the study is composed of three experiments. The goal of Experiment 1 is to determine approximately the sensitivity of an enhanced MERG to militarily relevant laser damage and to determine the lesion level, energy dose, and laser type (CW or Q-switched) for the subsequent experiments. The goal of Experiment 2 is to identify the relationship between morphological indexes of retinal damage and MERG patterns with a known behavioral endpoint (acuity/contrast sensitivity). The results will be correlated with the imaging techniques and with each other. The goal of the final experiment is to further refine and extend the sensitivity of the MERG metric to extramacular pathologies by extracting a more precise ED50 dose for MERG and OCT changes by placing more lesions. After recording the MERG maps, FA and OCT images for each of the new lesions, the animal will be euthanized and the lesions recovered via standard histological methods.

Relevance: There is a critical need for functional assessments of laser retinal injury. This work will transition directly to the current and future clinical treatment protocols. The morphological and functional endpoints demonstrated in this and in conjunction with future clinical studies will elucidate the retinal tissue savings with various pharmaceuticals. Reproducible, functional assessments of the post-lesion retina would dramatically enhance the capability of the ongoing efforts to provide retinal therapeutics on the battlefield.