The objective of our program has been to investigate the mechanisms of short and ultrashort pulse laser retinal injury and to develop and apply new diagnostics for the assessment of retinal injury. A key focus of our effort during this program has been to develop and apply optical coherence tomography (OCT) to investigate the morphology of retinal laser injury. OCT is a new noninvasive optical diagnostic technique for micron scale cross sectional imaging, which can permit the noninvasive imaging of retinal microstructure in situ. Working in collaboration with investigators at Brooks AFB, we have applied OCT to study lesion structure, development, and healing response from laser retinal injury. An increased understanding of the mechanisms of laser retinal injury is relevant to the development of laser safety standards as well as the development and improvement of clinical laser therapies for ocular disease.
2. Objectives

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3. and 4. Status of Effort and Accomplishments / New Findings

Noninvasive Imaging of Retinal Structure using Optical Coherence Tomography

Optical Coherence Tomography is a new medical imaging technique which was developed by our laboratory working in collaboration with MIT Lincoln Laboratory and the New England Eye Center. OCT can perform noninvasive micron scale cross sectional imaging in biological systems. OCT operates in a manner somewhat similar to ultrasound B mode scanning, except that imaging is performed using light rather than sound waves. One of the central components of this program has been the development of OCT technology for the noninvasive imaging of retinal structure and retinal laser lesions. The system that
we developed used 800 nm probe light and achieved an axial resolution of 15 microns. This technology is enabling for a wide range of investigations ranging from studies of laser retinal injury to the diagnosis and clinical management of retinal diseases.

**In-Vivo Imaging of the Evolution of Retinal Laser Lesions using Optical Coherence Tomography**

We have performed the first studies which use OCT to image in vivo retinal lesions produced by different laser retinal exposure parameters. This investigation was performed in collaboration a multidisciplinary team consisting of investigators from the Armstrong Laboratory at Brooks Air Force Base (specializing in laser retinal injury, safety standards, and veterinary medicine), the Laser Medical Center of Lubeck Germany (specializing in mechanisms of laser injury), and Duke University (clinical ophthalmology). In preliminary studies performed at MIT, we developed an OCT system for retinal tomography and image recording and analysis. This system was transported on site to the Armstrong Laboratory at Brooks Air Force Base where laser exposures were performed.

Laser retinal lesions from several complementary laser sources were investigated. In order to study thermally mediated laser lesions, similar to those used clinically, Argon laser exposures in the 100 ms range were investigated. Short and ultrashort pulse effects were examined using exposures in the nanosecond, picosecond, and femtosecond regime with pulse durations as short as 90 fs. A key advantage of optical coherence tomography is that it permits the in situ imaging of retinal lesion morphology in real time. Thus, although OCT does not have as high resolution as histopathology, it can permit repeated imaging of lesions both during their formation and healing.

Studies were performed to image lesions immediately following exposure to track their acute development. In addition, imaging was performed at repeated time intervals post exposure in order to track healing response. Tomographic images of lesions at different time intervals were displayed sequentially to make a movie of lesion development and healing. Retinal images from OCT were also correlated with more conventional endpoints of retinal injury including ophthalmoscopic examination and fluorescein angiography. Detailed histological studies were performed on selected lesions and OCT images were correlated with histopathology. This served the dual purpose of giving accurate histopathological information on the lesion morphology as well as defining a baseline for interpreting structures which were observed in OCT images. This study represents was first investigation of retinal injury using OCT and provided the first in vivo view of the microstructure, development, and healing of retinal laser lesions.

**Noninvasive Imaging for Cataract Evaluation using OCT**

In addition to studies of retinal structure and retinal injury, we have also applied optical coherence tomography for the examination of structures in the anterior eye. Working in collaboration with investigators at the Armstrong Laboratory of Brooks Air Force Base,
we have demonstrated the use of OCT for the noninvasive assessment of cataracts. These studies were performed using geriatric rhesus monkeys from the Brooks Air Force Base Delayed Effects Colony (DEC). Eighteen rhesus monkeys from the DEC and one four year old control rhesus were imaged using OCT, and subsequently evaluated by slit-lamp examination. OCT images were produced and compared to the current and previous cataract grading exams. OCT provided additional information on all opacities (central and peripheral) and provided the information in a log reflective scale format to aid in assessing the extent of the cataract. Studies showed good correlation of OCT images with conventional slit lamp examination and clinical grading of cataracts. In addition OCT provided a detailed map of the structure and morphology for corneal opacities. These studies have the potential for leading to a method for objectively and quantitatively assessing cataract progression. Given the prevalence of cataracts, this concept may be of importance for clinical health care management.

5. Personnel Supported and Associated with Effort

Prof. James G. Fujimoto (Professor, Dept. of Electrical Engineering and Computer Science, MIT)

Dr. Brett Bouma (Postdoctoral Associate, Dept. of Electrical Engineering and Computer Science, MIT)

Stephen Boppart (MD/PhD student Dept. of Electrical Engineering and Computer Science, MIT and Harvard-MIT, Division of Health Sciences and Technology)

Michael Hee (MD/PhD student Dept. of Electrical Engineering and Computer Science, MIT and Harvard-MIT, Division of Health Sciences and Technology)

Collaborators

Dr. William P. Roach (formerly at Armstrong Lab, Brooks AFB, TX)

Dr. Benjamin Rockwell (Armstrong Lab, Brooks AFB, TX)

Dr. Clarance P. Cain, Gary D. Noojin (TASC, San Antonio, TX)

Dr. Cheryl D. DiCarlo (formerly at Occupational and Environmental Health Directorate, Brooks AFB, TX)

Dr. Cynthia A. Toth (Professor, Duke Eye Center, Durham, NC)

Dr. Donald A. Gagliano (U.S. Army Medical Research Directorate, Brooks AFB, San Antonio, TX)

Dr. Reginald Birngruber (Director, Medizinisches Laserzentrum, Lubeck, Germany)

Eric A. Swanson (Assistant Group Leader, MIT Lincoln Laboratory, Lexington, MA)
6. Publications


7. Interactions / Transitions:

7a. Participation / Presentations at Conferences


23. C. Wong, M. R. Hee, C. A. Puliafito, J. S. Duker, E. Reichel, B. Rutledge, J. S. Schuman, E. A. Swanson, and J. G. Fujimoto, "Imaging of macular degeneration and choroidal neovascularization with optical coherence tomography (OCT)," Technical Digest of the Annual Meeting of the Association for Research in Vision and


7b and 7c. Consultative and advisory functions / Transitions

(a) Collaborative studies at the Armstrong Laboratory of Brooks Air Force, Optical Radiation Division (Drs. W.P. Roach, B. Rockwell) investigated the structure and evolution of short pulse retinal injury using OCT. Other collaborators included the Occupational and Environmental Health Directorate (Dr. Cheryl DiCarlo), TASC (Drs. C. Cain and G. Noojin), Duke Eye Center, University Medical School (Dr. C. Toth) and the Laser Medical Center of Lubeck Germany (Dr. R. Birngruber).

(b) Collaborative studies with the Occupational and Environmental Health Directorate (Dr. Cheryl DiCarlo) and the U.S. Army Medical Research Detachment of Brooks AFB (Dr. D. Gagliano) investigated the grading and imaging of cataracts using OCT.

(c) Collaborative studies with 1995 MIT Lincoln Laboratory (E. Swanson) investigated the development of new OCT technology.

(d) Collaborative studies with the New England Eye Center of the Tufts University School of Medicine (Dr. Carmen Puliafito) investigated the imaging of the normal retina and macular disease in clinical subjects.
8. New discoveries, inventions, patent disclosures

None.

9. Awards, honors

P.I. James G. Fujimoto was General Co-Chair for the Quantum Electronics and Lasers Science Conference, June 1996, Anaheim, CA; Program Co-Chair for the Ultrafast Phenomena conference, May 1996, San Diego, CA; Program Chair for the Optical Imaging and Photon Migration Conference, March 1996, Orlando, FL. He was also elected Fellow of the Optical Society of America (1995) and the IEEE (1995).