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LLNL-TR-747869

Lasers for Surgery and Photodynamic Therapy Final Report CRADA No. TC-0437-93

R. Beach, T. F. Deutsch

March 15, 2018

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Lasers for Surgery and Photodynamic Therapy

Final Report
CRADA No. TC-0437-93

Date: 1/20/97 Revision: 1

A. Parties

The project is a relationship between the Lawrence Livermore National Laboratory (LLNL) and The Wellman Laboratory of Photomedicine.

University of California
Lawrence Livermore National Laboratory
P.O. Box 808, L-795
Livermore, CA 94551

The Wellman Laboratory of Photomedicine
Massachusetts General Hospital
Boston, MA 02114

B. Project Scope

This proposed project is designed to apply the combined resources and expertise of the Lawrence Livermore National Laboratory (LLNL) and the Wellman Laboratories of Photomedicine (WL) to develop several new diode laser systems for use in photodynamic therapy (PDT) and to develop diode-pumped solid state infrared lasers for surgery. The use of laser light-activated photosensitive dyes in the treatment and diagnosis of disease is developing rapidly. Current PDT relies on the use of large, expensive, and inefficient argon-ion laser pumped dye lasers as sources. The recent advances in the technology of diode lasers emitted in the 620-700 nm region offers an opportunity to make source technology for PDT more reliable, compact, and efficient. This project will develop visible diode lasers and control system for photodynamic therapy, and infrared diode pumped solid-state lasers for applications to surgery.

Testing and evaluation of the laser systems will be performed at WL using cells, tissue in vitro, animal models, and ultimately human subjects in clinical trials. Once clinical testing is complete, commercialization will be pursued through WL ties to the medical laser industry.

Several efforts within this proposed program are of interest to a number of other potential LLNL funding sources. In particular, several of the diode pumped solid-state devices share some commonalty with work being proposed in conjunction with the Beckman Laser Institute and Medical Clinic. A further example is the commonalty with LLNL existing and proposed efforts in coupling high average power diode arrays into fiber optic delivery systems.

C. Technical

The proposed compact advanced laser systems require the development of both diode and diode-pumped solid state laser systems and their integration into compact, clinically-useful control and delivery systems. LLNL will be responsible for the development of the laser system, including integration into clinically useful packages. WL will be responsible for all pre-clinical and clinical testing and evaluation. This proposed research program is broken into two major efforts.

1. *Diode laser systems for photodynamic therapy.* Diode laser systems offer the opportunity for more reliable and ultimately less expensive source technology for Photodynamic therapy (PDT). Recent experimental evidence suggest that PDT with mechanically-chopped CW radiation can produce different tissue effects than can be achieved with continuous wave radiation. Diode lasers are ideally suitable for performing pulsed format experiments to further investigate delivery format effects. The first phase of this task will apply diode lasers to the evaluation of new photosensitizers. This phase will use diode-based systems delivering 0.25-1.0 W at 695, 657, and 675 nm together with cells or animal models of tumor systems. The second phase will develop high-power (5-10 W) multi-diode laser systems for use in clinical trials of the photosensitizer BPD, which are in progress at WL. These trials will be greatly enhanced by the development of a multi-diode system using fibers for delivery of 695 nm light. Each system will consist of an integrated laser package consisting of the diode sources, modulatable power supply, thermal management system, and lensing system suitable for delivery to a WL supplied delivery system. WL will use the systems to study the effect of CW versus pulsed format delivery on the effectiveness of treatment.

The attached manuscript "Applications of microlens - Conditioned Laser Diode Arrays" contains a detailed description of the technical approach used in the delivered fiber-coupled PDT units.

2. *Diode-pumped solid-state lasers for surgery.* The use of solid-state lasers for surgery has been investigated at WL using pulsed solid-state lasers. These experiments suggest that since 1.9 mm radiation is strongly absorbed by water in tissue but can be transmitted by commercial quartz fiber optics. lasers emitting at this wavelength are useful for cutting and coagulation of tissue. As little as 1 W of power can be useful for some applications, such as sinus surgery. This task will focus on the development of a 1.9 mm diode pumped solid-state laser delivering up to 10 W CW that can be coupled to a fiber delivery system. During phase 1 of this task, a prototypical system delivering 0.25-1 W of optical power will be developed by LLNL and used by WL in pre-clinical and clinical testing.

The attached manuscript "High average power Tm:YAG diode-pumped solid-state laser" contains a detailed description of the technical approach used in the delivered lasers.

D. Partner Contribution

Diode-laser systems for photodynamic therapy (PDT)

Diode-laser systems offer the opportunity of more reliable and ultimately less expensive source technology for PDT. In addition, recent experiments suggest that PDT with mechanically-chopped CW radiation can produce different tissue effects than the same total light dose delivered as continuous wave radiation. Diode lasers are ideally suited for performing experiments of this kind, since they can be modulated to produce a variety of on/off schedules that would be difficult to implement with mechanical shutters.

This task centers on the development and testing of three diode laser systems, operating at wavelengths of 695, 675, and 657 nm. The development and testing efforts are broken into two phases. During phase 1,0.25-1 W diode systems will be developed and tested. During phase 2, diode array systems delivering up to 10 W will be developed and tested. LLNL is responsible for the development of the integrated laser diode systems. Each system will consist of an integrated laser package consisting of the diode sources, modulatable power supply, thermal management system, and lensing system suitable for delivery to a WL supplied delivery system (possibly a 600 mm multimode fiber). WL will be responsible for the application of these systems to the investigation of several photosensitizers (BPD, Chlorine e_6, CASPc, PPIX, etc.) for study of PDT in animal models.

WL will use the systems to study the effect of CW versus pulsed format delivery on the effectiveness of treatment. Clinical trials of the photosensitizer BPD are now being conducted at WL in conjunction with clinical protocol development by Lederle Laboratories of American Cyanamid. Current treatment protocols specify the use of a dye laser pumped by an argon-ion laser to provide 695 nm radiation, but can be modified with the consent of Lederle to allow use of a 695 nm diode laser system. Ultimately the treatment system should consist of five independently controllable diode lasers, each providing 2 W of optical power out of a 600 mm multimode fiber.

Wl will be responsible for obtaining approval for modification of the clinical protocols, and for pre-clinical and clinical testing of the new laser system. Should animal trials of pulsed format delivery of the laser light be encouraging, WL will investigate the possibility of incorporating this format into the clinical trials; such a change will require FDA approval, as well as the consent of Lederle.

Diode-pumped 1.9 mm solid-state lasers for surgery.

The use of solid-state lasers for surgery has been investigated at WL using the pulsed 1.9 mm Co:MgF_2 laser as well as pulsed 2.1 mm Ho:YAG laser. These experiments have suggested that a diode-pumped 1.9 mm solid state laser capable of operation in the chopped CW mode would have a number of applications in cutting and coagulation. Powers as low as 1 W delivered by a 600 mm multimode fiber may be useful in sinus and lacrimal duct surgery. This task will focus on the development of a 1.9 mm diode-pumped solid-state laser delivering up to 10 W CW that can be coupled to a fiber delivery system. The system must be capable of pulse-width adjustment from 10 ms to CW operation. The candidate system will be a diode pumped Tm:YAG laser. LLNL will be responsible for the development of the laser system, including procurement of diode material and processing and packaging at LLNL. WL will be responsible for application and testing of the device in vitro and in a pre-clinical and clinical setting.

This task is broken into two phases. During phase 1 a prototypical system, delivering up to 1 W of optical power, will be developed by LLNL used by WL in preliminary testing. During phase 2, a diode-pumped solid state laser system, with optical output power of 5-10 W will be developed by LLNL and used in the comprehensive pre-clinical and clinical testing.

E. Documents/Reference List

A. Publications

1. R.J. Beach, M.A. Emanuel, B.L. Freitas, J.A. Skidmore, N.W. Carlson, W.J. Benett, and R.W. Solarz, "Applications of Microlens-Conditioned Laser Diode Arrays," SPIE Vol. 2383 p. 283-297 (1995)
2. R.J. Beach, S.B. Sutton, J.A. Skidmore, and M.A. Emanuel, "High power 2 micron wing-pumped Tm:YAG laser," Advanced Solid State Lasers Technical Digest p. 249-252 (1995)
3. E.C. Honea, R.J. Beach, S.B. Sutton, J.A. Speth, S.C. Mitchell, J.A. Skidmore, M.A. Emanuel, and S.A. Payne, "High average power Tm:YAG diode-pumped solid-state laser," UCRL-JC-125109 Preprint, submitted to IEEE Journal of Quantum Electronics

B. Patents and disclosures:

1. "High efficiency 2 micrometer laser utilyzing wing-pumped Tm3+ and a laser diode array end-pumping architecture," by R.J. Beach, CIL-9691 LLNL patent application filed October 2, 1996.
2. "Fiber optic coupling of a microlens conditioned, stacked semiconductor laser diode array," by R.J. Beach, W.J. Benett, and S.T. Mills, CIL-9614 LLNL patent application filed February 1996.

F. Acknowledgment

Participant's signature of the final report indicates the following:

1) The Participant has reviewed the final report and concurs with the statements made therein.
2) The Participant agrees that any modifications or changes from the initial proposal were discussed and agreed to during the term of the project.
3) The Participant certifies that all reports either completed or in process are listed and all subject inventions and the associated intellectual property protection measures attributable to the project have been disclosed or are included on a list attached to this report.
4) The Participant certifies that if real property was exchanged during the agreement, all has either been returned to the initial custodian or transferred permanently.
5) The Participant certifies that proprietary information has been returned or destroyed by LLNL.

Thomas F. Deutsch — Date	Raymond Beach — Date
Wellman Laboratory of Photo Medicine	Lawrence Livermore National Laboratory

Attachment I – Final Abstract
Attachment II – Project Accomplishments Summary
Attachment III – Final Quarterly Report

Lasers for Surgery & Photodynamic Therapy

Attachment I
Abstract
CRADA No. TC-0437-93

Date: Revision: 1

Brief Description:
Lawrence Livermore National Laboratory and the Wellman Laboratories of Photomedicine worked together to develop revolutionary laser systems for use in photodynamic therapy (a cancer therapy) and laser surgery. These dual-use medical/laser applications were made possible by two Lawrence Livermore technologies, micro-channel cooling of laser diodes and a high-performance micro lens. The Wellman Laboratories are considering the new laser technology for several types of cancer surgery: colon, middle ear, gynecological, and esophageal. The same technology will improve photodynamic laser therapy, in which photosensitizers are introduced into the body where they selectively accumulate in cancerous areas; lasers tuned to specific wavelengths then irradiate the tissue. This therapy is used to treat recurrences of breast cancer after a mastectomy and skin tumors; the new system may also be an alternative treatment for psoriasis. These new medical laser systems address two major national concerns: economic competitiveness and the rising costs of medical treatment.
Because of reliability problems with 630 nm diode laser arrays a fiber coupled unit at 950 nm was substituted for the originally called for unit at 630 nm. In total 3 fiber coupled units were delivered to Wellman: one at ~675 nm, one at ~ 690 nm, and the final substitute unit at ~950nm. The 2 micron Tm:YAG laser performed better than the originally call for 10 W cw device and was capable of delivering greater than 20 W cw. Detailed descriptions of both types of hardware, the fiber coupled units and the 2 micron Tm:YAG unit can be found in the publications which are attached to the final report.

Industrial Partner:
Wellman Laboratories of Photomedicine in Boston, Mass., are a part of the Department of Dermatology at Massachusetts General Hospital, a major teaching hospital affiliated with Harvard Medical School

Purpose:
Collaboratively design, construct, integrate, and test new prototype laser-based medical systems.

Benefit to Industry:
Accelerate the introduction of lasers into cost-effective applications within the medical community, one system for use in photodynamic therapy and the second for laser surgery.

Benefit to DOE/LLNL:
Improved diode pumped solid state lasers, the laser of choice in commercial and military applications: diode source improvements for laser fusion, laser isotope separation plants, remote sensing, and biological activity.

Time Period:
Three years, starting September 17, 1993

LLNL Contact:
Ray Beach, (510) 423-8986

Lasers for Surgery & Photodynamic Therapy

Project Accomplishments Summary (Attachment II)
CRADA No. TC-0437-93

Date: Revision:

A. Parties

The project is a relationship between the Lawrence Livermore National Laboratory (LLNL) and The Wellman Institute of Photomedicine

University of California
Lawrence Livermore National Laboratory
7000 East Avenue, L-795
Livermore, CA 94550

The Wellman Laboratory of Photomedicine
Massachusetts General Hospital
Boston, Massachusetts 02114

B. Background

While parts of the medical community are aware of new developments in laser sources, the cost of laser diodes has frequently prevented the demonstration of the usefulness of these devices in medicine, both for diagnosis and treatment. Recent Lawrence Livermore National Laboratory (LLNL) advancements in diode packaging for high average power now offer the potential for these sources to be cost effective in medical treatment and diagnosis systems. Wellman Laboratories of Photomedicine (WL) is one of the leading centers in the work in the development of medical applications of lasers and light. WL is actively engaged in the development of PDT for both cancer and non-cancer applications, as well as in the development of surgical applications of new solid-state lasers. The ultimate goal of this project is the transfer of LLNL technology in both diode lasers and diode-pumped solid-state lasers to WL for application to PDT and to surgery. To this end, LLNL proposes to work jointly with WL to accomplish two principle tasks:

1. Diode laser systems for photodynamic therapy.

2. Diode-pumped 1.9 μm solid-state lasers for surgery.

This effort is targeted toward two TACT areas of emphasis: Microelectronics and Photonics, and Advance Manufacturing and Precision Engineering. To accomplish the goals of this proposed effort requires development of advanced manufacturing techniques for both the laser diode pump source and the solid state laser. This effort will improve domestic diode fabrication and packaging technology. Additionally, the application of laser technology to biomedical treatment involves precision measurements and precision engineering.

Several efforts within this proposed program are of interest to a number of other potential LLNL funding sources. In particular, several of the diode pumped solid-state devices share some commonalty with work being proposed in conjunction with the Beckman Laser and Medical Clinic. A further example of commonalty are the LLNL current and proposed efforts regarding coupling of high average power diode arrays into fiber optic delivery systems.

C. Description

1. Technical Rationale

This project is designed to take advantage of the combined resources and expertise at LLNL and WL to produce new laser systems for PDT and for surgery. The requirements for the new laser systems have been developed by WL based on experiments with PDT and with the use of infrared lasers, such as Er:YAG and Ho:YAG, for cutting and coagulation of tissue.

One key requirement is that the laser sources must be amenable to compact and thermally efficient packaging. This focuses interest on the application of semiconductor diode laser technology. Required improvements in this area will be based on the extensive LLNL expertise and experience in processing and fabrication of diode lasers, and high average power thermal management using microchannel cooler packaging technology, as well as LLNL expertise in solid-state laser technology. WL's expertise in development and use of PDT and in the investigation of new infrared lasers is pivotal for the evaluation of the new laser systems.

2. Work Plan

This project is broken into two key tasks:

1. Diode-laser systems for photodynamic therapy.
2. Diode-pumped 1.9 μm solid-state lasers for surgery.

Each task is divided into two parts to reflect the varied experience and expertise of LLNL and WL. LLNL will assume lead responsibility for development of the proposed laser systems. The primary LLNL deliverable for each task will be a single laser system that can be coupled to a fiber delivery system. WL will be responsible for application and testing of the laser systems in the pre-clinical (in vitro and animal model) and clinical (human studies) environment.

Diode-laser systems for photodynamic therapy (PDT)

Diode-laser systems offer the opportunity of more reliable and ultimately less expensive source technology for PDT. In addition, recent experiments suggest that PDT with mechanically-chopped CW radiation can produce different tissue effect than the same total light dose delivered as continuous wave radiation. Diode lasers are ideally suited for performing experiments of this kind, since they can be modulated to produce a variety of on/off schedules that would be difficult to implement with mechanical shutters.

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D. Expected Economic Impact

Economic competitiveness and the rising costs of medical treatment are two of the major issues confronting our nation. One of the more promising fields in the treatment of human cancer employs photosensitive dyes. The use of these dyes to absorb laser light allows the selective destruction of cancerous tissue. Improvements in system reliability and treatment procedure that can be afforded by the introduction of diode laser sources offers the potential for reducing the cost of treatment as well as improving the effectiveness of this treatment procedure. This should allow more widespread treatment as well as treatment at reduced cost.

E. Benefits to DOE

Diode pumped solid state lasers are rapidly becoming the laser of choice in many commercial and military systems. It is anticipated that the demand for these systems will only increase in the future as diode costs and performance improves. The proposed work in the program will extend existing LLNL developed diode processing and packaging technology from largely military based systems to more directly commercial endeavors. The resulting diode source improvements will directly translate to current as well as future DOE and DP efforts. An example is the impact that low-cost diode lasers will have on laser fusion economic viability, as well as future laser isotope separation plants where diode pumped solid state lasers are a candidate for replacing copper vapor lasers. Additionally, the Department of Energy has a long-standing involvement in advanced biomedical technology. To this point, however, DOE developed diode laser technology has not been applied to the biomedical technology area. This effort leverages the investment made in diode technology to the historical DOE involvement in biomedical research.

F. Industry Area

Solid-state lasers, and in particular, diode pumped systems are receiving increasingly more attention with regards to commercial applications in precision manufacturing and medicine. Numerous foreign companies (such as Sony and Panasonic) are actively engaged in the development of diode pumped laser systems. The U.S. still maintains a competitive advantage in the field of diode packaging for high average power. The work proposed in this research effort enhances the U.S. position by making improvement in packaging technology, as well as implementing a path for domestic commercialization.

G. LLNL Point of Contact for Project Information

Ray Beach, L-441, P.O. Box 808; LLNL, Livermore, CA 94550 (510) 423-8986

H. Company Size and Point(s) of Contact

The Wellman Research Laboratories of Photomedicine were founded in 1978 and are a division of the Department of Dermatology at the Massachusetts General Hospital, a major teaching hospital of the Harvard Medical School. John A. Parrish, M.D., is the Director of the Laboratories and the Cutaneous Biology Research Center, Chairperson of the Department of Dermatology Service at the Harvard Medical School, and Chief of the Dermatology Service at the Massachusetts General Hospital. Lynn A. Drake, M.D., is Director of Policy and Planning of the Wellman Laboratories.

The Wellman Laboratories employ approximately 85 full-time investigators, clinical research fellows, students, and technical and support personnel. Multidisciplinary approaches to problems are possible because the investigators have expertise in many areas including cutaneous photobiology, dermatology, photochemistry, spectroscopy, tissue optics laser technology, experimental pathology, immunology, biophysics, cardiology, and gastroenterology. The laboratories also benefit greatly from interaction with the Massachusetts Institute of Technology Health Sciences and Technology Program (MIT/HST), and collaborations with individual scientists at MIT, Harvard, and other research institutions.

The more fundamental work occurs in 11,000 square feet of space in three contiguous buildings. Research on pre-clinical laser applications takes place in a specially-designed complex of laboratories next to the surgical research laboratories which includes an additional 5,000 square feet dedicated to laser laboratories, a procedure room, and engineering support facilities.

The laboratory staff is divided into seven teams:

Biomedical Laser Applications
R.R. Anderson, M.D.
Norman S. Nishioka, M.D.

Physics
Thomas F. Deutsch, Ph.D.
Apostolos G. Doukas, Ph.D.

Photopathology
Thomas J. Flotte, M.D.

Photobiochemistry
Tayyaba Hasan, Ph.D.
Irene E. Kochevar, Ph.D.

RELEASE OF INFORMATION

I have reviewed the attached Project Accomplishment Summary prepared by Lawrence Livermore National Laboratory and agree that the information about our CRADA may be released for external distribution.

Thomas F. Deutsch — 2/26/98
Date

Thomas F. Deutsch
Wellman Laboratory of Photo Medicine

RELEASE OF INFORMATION

I certify that all information contained in this report is accurate and releasable to the best of my knowledge.

Karena McKinley

Karena McKinley, Director
Industrial Partnerships
and Commercialization

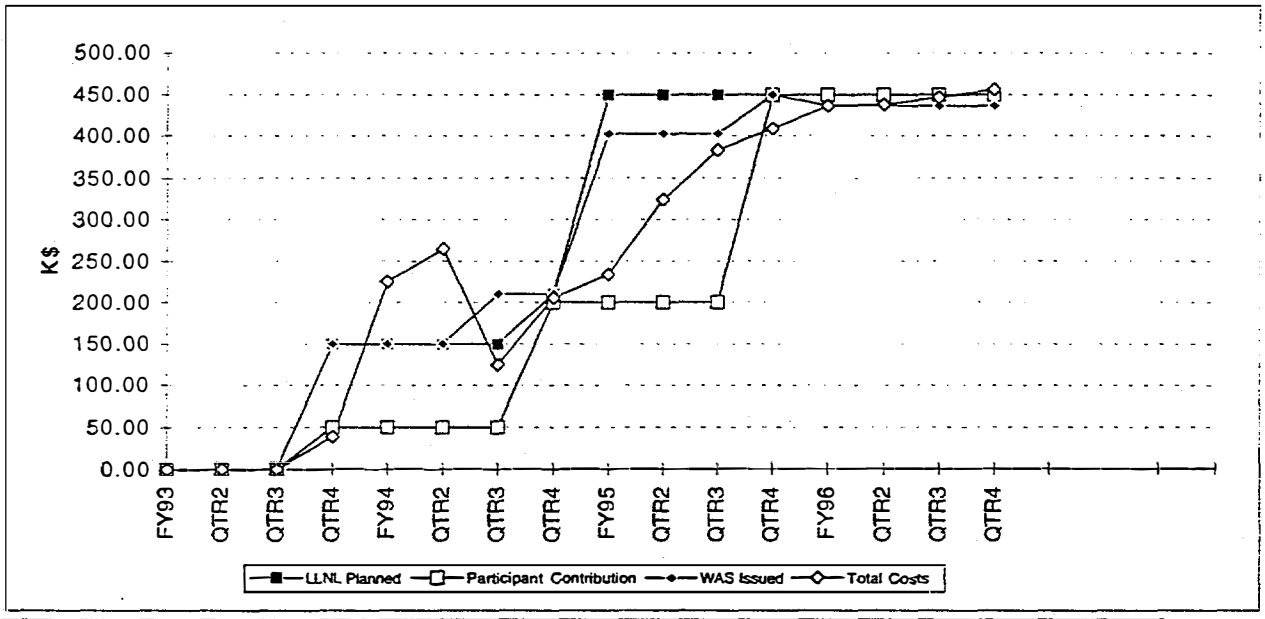
10/7/98
Date

Lawrence Livermore National Laboratory
Attachment III

Title:	Lasers for Surgery & Photodynamic Therapy	Reporting Period:	07/01/95 - 09/30/96
Participant:	Wellman Laboratory of Photo Medicine	Date CRADA Executed:	#######
DOE TTI No.:	93-LLNL-004-XX	DOE Approval Date:	#######
CRADA No.:	TC-0437-93	Scheduled Ending Date:	#######
TACT:	BIO	Project Completed:	#######
Account Numbers	4722-50 & 51	B & R Code ($):	DP0301
Account Closed:	#######		35DP03

Approved Funding Profile ($K)

	FY93	FY94	FY95	FY96	FYOUT	Total
LLNL Planned	150	60	240	0	0	450
Participant In-Kind	50	150	250	0	0	450
Paticipant Funds-In	0	0	0	0	0	0
WAS DP0301	150	60	240	-14	0	437
WAS 35DP03	0	0	0	0	0	0
Total Costs	38	167	203	48	0	456



DP0301	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sep	FYTD	456
FY93	0	0	0	0	0	0	0	0	0	0	0	38	38	
FY94	33	53	100	112	-99	26	-21	19	-137	-11	102	-11	167	
FY95	1	15	13	28	25	38	29	10	20	4	15	6	203	
FY96	1	18	9	0	0	1	2	6	1	0	4	6	48	
FYOUT	0	0	0	0	0	0	0	0	0	0	0	0	0	

35DP03	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sep	FYTD	0
FY93	0	0	0	0	0	0	0	0	0	0	0	0	0	
FY94	0	0	0	0	0	0	0	0	0	0	0	0	0	
FY95	0	0	0	0	0	0	0	0	0	0	0	0	0	
FY96	0	0	0	0	0	0	0	0	0	0	0	0	0	
FYOUT	0	0	0	0	0	0	0	0	0	0	0	0	0	

STAFF w/phone:

Lab PI: Ray Beach (510) 422-6218 — Participant: Thomas F. Deutsch (617) 726-6167

Resource Manager: Bonnie Zucca (510) 423-9516

DOE OAK: Jerry Scheinberg (510) 637-1653 — DOE HQ: John Uecke (202)586-5431

Reporting Period: 07/01/95 - 09/30/96
DOE TTI No.: 93-LLNL-004-XX
CRADA No.: TC-0437-93

Milestones and Deliverables:

List the complete set of milestones for all phases of the CRADA. Continue on a separate page if necessary.
Report any changes from the original CRADA or previous quarterly report on the CRADA Change Form.

	Completion Date: Scheduled	Actual
1. Please see attached report from Ray Beach		
2. Developed high power 690 nm laser diodes	06/94	06/94
3. Developed fiber coupling hardware	06/94	06/94
4. Demonstrated 1.5 W cw Tm:YAG 2 µm laser	05/94	05/94
5. Demonstrated >10 W cw from 690 nm PDT unit	08/94	08/94
6. Demonstrated > 5 W cw from 2 micron Tm:YAG	09/94	09/94
7. Completed 690 nm PDT laser diode packages	11/94	11/94
8. Completed 675 nm PDT laser diode packages	12/94	12/94
9. Final design drawings on PDT head hardware are complete	12/94	12/94
10. Tested 950 nm laser diode bars which are being substituted for 630 nm bars (see CRADA change report)	12/94	12/94
11. Completed engineering modifications to Tm:YAG cooling circuit	11/94	11/94
12. Specified and ordered final diode assembly and Tm:YAG rod for surgical laser	12/94	12/94
13. Delivered 20 W cw 2 micron Tm:YAG laser with utility system	12/95	07/96

Verification of participants' in-kind contribution was made in accordance with LLNL policy. Explain basis of verification:

Please initial: YES X NO ____

Telephone conversations with Thomas Deutsch at Wellman

I believe that the participants in-kind contribution was consistent with that agreed upon in the CRADA because the participant met the milestones that were described in the contract.

List any subject inventions by either party (include IL# for LLNL inventions), additional background intellectual property, patents applied for, software copyrights, publications, awards, licenses granted or reportable economic impacts

1. "High efficiency 2 micrometer laser utilyzing wing-pumped Tm3+ and a laser diode array end-pumping architecture," by R.J. Beach, CIL-9691 LLNL patent application filed October 2, 1996.
2. "Fiber optic coupling of a microlens conditioned, stacked semiconductor laser diode array," by R.J. Beach, W.J. Benett, and S.T. Mills, CIL-9614 LLNL patent application filed February 1996.

Verification that all equipment and proprietary information has been returned to the initial owner or permanently transferred

Please initial: YES X NO ____

Accomplishments

Describe Technical/Non-Technical lessons learned and other observations.
Summarize causes/justification of deviations from original scope of work.

See Final Report.

Reviewed by CRADA project Program Manager: _____ Date: _____

Reviewed by Karena McKinley, Director, LLNL/IP&C: Karena McKinley Date: 10/7/98

Direct questions regarding this Report to IP&C Resource Manager, Carol Asher, at (510) 422-7618