OSD RDT&E BUDGET ITEM JUSTIFICATION (R2 Exhibit)

Date: February 2006

APPROPRIATION/ BUDGET ACTIVITY	PE NUMBER AND TITLE
RDT&E/ Defense Wide BA# 2	**0602227D8Z - Medical Free Electron Laser**

Cost ($ in Millions)		FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Total Program Element (PE) Cost		17.575	19.725	10.255	10.567	10.334	10.532	10.765
P483	Medical Free Electron Laser	17.575	19.725	10.255	10.567	10.334	10.532	10.765

A. Mission Description and Budget Item Justification: (U) The Medical Free Electron Laser (MFEL) program seeks to develop advanced, laser-based applications for military medicine. Free electron lasers (FELs) provide unique pulse features and tunable wavelength characteristics that are unavailable in other laser devices. Thus, FELs broaden the experimental options for the development of new laser-based medical technologies.

(U) This program is focused on developing advanced procedures and equipment for rapid diagnosis and treatment of battlefield-related medical problems. Specific applications under investigation include soft tissue repair, hard tissue surgery, therapies for thermal and chemical burns, warfighter vision correction, photochemical treatment of difficult infectious agents, and new medical imaging modalities. Unique, innovative laser applications will be clinically tested in medical centers, leading to Food and Drug Administration (FDA) approval. There is a high potential for dual use in civilian medicine. Thus far, more than 30 clinical procedures have been developed in several medical specialties, including ophthalmology, orthopedics, thermal and chemical burn treatment, and neurosurgery. Work in these areas will continue under the current three-year center grants, with the primary focus of the work remaining on the development of militarily relevant laser medicine applications.

(U) Plans include efforts to strengthen interactions of the grantee institutions with military medical research facilities in order to improve both the content of the grant programs and the implementation of new techniques in military medicine.

B. Program Change Summary	FY 2005	FY 2006	FY 2007
Previous President's Budget (FY 2006)	18.322	9.845	10.096
Current BES/President's Budget (FY 2007)	17.575	19.725	10.255
Total Adjustments	-0.747	9.880	0.159
Congressional Program Reductions		-0.320	
Congressional Rescissions			
Congressional Increases		10.200	
Reprogrammings	-0.212		
SBIR/STTR Transfer	-0.511		
Other	-0.024		0.159

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C. Other Program Funding Summary: Not Applicable.

D. Acquisition Strategy: Not Applicable.

E. Performance Metrics:

FY	Strategic Goals Supported	Existing Baseline	Planned Performance Improvement / Requirement Goal	Actual Performance Improvement	Planned Performance Metric / Methods of Measurement	Actual Performance Metric / Methods of Measurement
07						

Comment: Performance is monitored using instances of successful commercialization of new instruments and techniques; the transfer of new clinical methods to regular clinical use; the number, quality and placement of publications in the open scientific literature; and the numbers and content of patent applications filed.

OSD RDT&E PROJECT JUSTIFICATION (R2a Exhibit)

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RDT&E/ Defense Wide BA# 2	**0602227D8Z - Medical Free Electron Laser**	**P483**

Cost ($ in Millions)		FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
P483	Medical Free Electron Laser	17.575	19.725	10.255	10.567	10.334	10.532	10.765

A. Mission Description and Project Justification: (U) The MFEL Program seeks to develop advanced, laser-based applications for military medicine.
(U) The majority of this program is focused on developing advanced procedures for rapid diagnosis and treatment of battlefield-related medical problems.
(U) A small part of this program is focused on related materials research.
(U) Overall management plans include continued efforts to strengthen the interactions of the grantee institutions with military medical research facilities in order to improve both the content of the grant programs and the implementation of new techniques in military medicine. Increased emphasis will be placed on investigations of potential photochemical treatments of infectious diseases.

B. Accomplishments/Planned Program:

Accomplishment/Planned Program Title	FY 2005	FY 2006	FY 2007
Imaging Technology:	3.951	5.030	2.543

Optical Coherence Tomography (OCT) applications have been developed to assess the clinical status of burns by combining polarization sensitivity for tissue structure and birefringence with Doppler detection to simultaneously measure blood flow in the tissue. Resolution of the extent of the burn can be made to between 2 and 10 um. OCT applications also have been developed for diagnosis and monitoring of surgical repair of orthopedic injuries and injuries to the trachea and respiratory tract using hand-held probes for imaging. Work on improving the resolution and speed of OCT imaging continues, with resolutions down to 1 um shown to be possible with short pulse lasers. Resolution to 3 um has been obtained and an ophthalmic imaging system using this capability has been made, and is in regular clinical use. A 72-fold increase in imaging speed also provides opportunity to detect subtle changes in tissue to improve the management of various injuries. A tunable, monochromatic x-ray system has been developed using the electron beam of a radio frequency accelerator to scatter beams from a terawatt laser, producing the x-rays through an inverse Compton effect. The monochromatic x-ray system provides significantly improved images when compared with standard x-ray sources. Other potential technologies include a Pulsed Photothermal Radiometry technique that can be used to determine changes in the optical properties of the skin and provide diagnostic information on wound management and absorption on the skin of possible chemical agents, and Photon Migration techniques to non-invasively monitor hemodynamic parameters such as oxy/deoxy-hemoglobin ratios. Optical diagnostic methods based on Raman scattering and terahertz spectroscopy are being studied to detect and rapidly characterize important biomolecules of interest. Optical methods are also being used to investigate molecular processes in cells tagged with microparticles, and the specific capabilities of molecular biosensors. The potential use of near-field infrared microscopy in cellular imaging is also being examined. Plans include continuing work on improving the contrast and depth of OCT imaging with emphasis on its use in burn injury, further development of new ultrasmall fiber optic endoscopy systems, commercialization of monochromatic x-ray equipment, new Pulsed Photothermal Radiometry applications, new applications of Near Field Optical Microscopy, and other IR microscopy techniques.

Accomplishment/Planned Program Title	FY 2005	FY 2006	FY 2007
Laser Surgery Methods:	2.576	3.191	1.624

FELs continue to be used in experimental surgery studies in animals and humans. An FEL has been used in the surgical removal of a human brain surface tumor, in optical nerve sheath fenestration. Lasers have also been used for the disruption of kidney stones. Experimental surgery studies continue to develop laser beam delivery endoscopes that meet the precision surgical requirements of optic nerve repair

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and neurosurgical treatment of epileptic foci. Studies examining the most effective laser wave length and pulse duration variables for cutting hard tissue and optimizing post-ablation bone regeneration and healing are also in progress. Studies to determine optimal methods for using lasers for properly shaping collagen materials for use in reconstructive surgery are examining the molecular nature and behavior of the collagen during the reshaping process. Proper shape and shape memory of the material are of critical importance in success of reconstruction efforts. Work in this area of the program has also led to the observation of laser effects on chondrocyte regeneration, critical for effective treatment of arthritic degeneration. Studies to exploit this observation are in progress. An effective animal model for study of corneal healing after laser vision correction surgery has been developed, and subsequent work using this model has described important steps to minimize the scarring which can adversely affect vision correction efforts. Plans include continuing studies in neurological and ophthalmic surgery applications of lasers, as well as continuing work on optimal laser parameters for dermal and hard tissue cutting and subsequent healing. Additional efforts will continue to examine the application of laser-based imaging and laser effects on chondrocyte regeneration for the orthopedic repair of cartilage.

Accomplishment/Planned Program Title	FY 2005	FY 2006	FY 2007
General Clinical Medicine Techniques:	3.271	3.310	1.643

The use of photosensitive materials that can bind to cells, become activated on illumination, and cause a subsequent change in cell activity has been shown to have a number of clinical applications. Photosensitive compounds can be used to tag specific bacteria and lead to virtually complete elimination of the organisms. Antibiotic resistant strains remain vulnerable to such photodynamic therapy. Wounds infected with ordinarily fatal strains of Psuedomonas and various Staphylococcus organisms were completely healed following treatment with photosensitive compounds. Studies on using this technique for the treatment of difficult infections such as Leishmaniasis also have been shown it to be effective. Other photosensitive compounds attached to cells are able to modulate cellular activity. For example, chondrocytes, activated by light sensitive molecules, can initiate complex processes that prevent inflammatory destruction of collagen explants. Similarly, light absorbing nanoparticles have been shown to affect various properties of cells, including their permiability, allowing control of cell processes, as well as improving drug uptake and effectiveness. Photochemical controlled tissue bonding studies have led to the development of materials that provide wound closure that is superior to current mechanical or adhesive methods. The photochemical bonding material was first demonstrated in the closure of the flaps generated during laser vision correction surgery. The material, a sensitizing dye that photochemically crosslinks the tissue surfaces, has been used in repair of blood vessels, the cornea, skin, and has recently been shown to be effective in nerve and tendon repair, and repair of damage to the trachea. Studies will continue on photochemical bonding of tissue, developing new photosensitizers and methods for their delivery, mechanisms for controlling various cellular activities, and the use of photodynamic therapy in treating infections of selected microorganisms.

Accomplishment/Planned Program Title	FY 2005	FY 2006	FY 2007
Laser/Tissue Interactions and Wound Healing Studies	2.502	2.911	1.534

A wide range of studies has examined the interactions of laser energy with tissues, cells and biological macromolecules. Models for laser ablation have been developed and used to examine the course of the post-ablation healing process. Studies using the unique single micropulse capability of the Stanford FEL continue and are providing valuable information on the role of wavelength, pulse structure and pulse sequence in the ablation process on the molecular level. Confocal microscopy with subcellular resolution is being used to study the processes of fibronectin growth and the molecular sequence of wound closure. Vasodialation, an important factor in wound healing, is sensitive to the application of UVA and blue light in vivo, and studies of light effects on wound healing and its enhancement by norepinephrin, a known vasoconstrictor, are continuing. Effective closure of various wounds and blood vessels has been accomplished using photochemical tissue bonding techniques. Studies on laser ablation and the subsequent healing processes will continue, with a focus on determining tissue viability at the wound site, as this is critical for effective wound management. Work on wound closure using photochemical tissue bonding will also be a significant focus. Vasodilation studies for treating ischemic wounds will also be continued.

Accomplishment/Planned Program Title	FY 2005	FY 2006	FY 2007
Physical and Materials Science Research:	0.908	0.645	0.335

Research on the improvement of the performance and reliability of the FELs is a continuing effort. Such work includes the development of new materials for waveguides through which the laser energy may be routed as well as refinements in the existing laser systems. In addition, basic efforts are carried out using laser-based spectroscopy methods, on the structure and nature of biologically important

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macromolecules, on the dynamics of various surface-based processes, and on the nature, formation and deposition processes of complex thin films. Work will continue on spectroscopy methods, surface-based processes, and the nature and formation of thin films.

Accomplishment/Planned Program Title	FY 2005	FY 2006	FY 2007
Laser Operations Support:	4.367	4.638	2.576

A major upgrade in the components of the Duke University FEL system has been completed, greatly improving the efficiency and overall capability of the system for research. Protocols developed for the use of the system are being carried out. More than 5,000 hours of beam time was provided during 2005 for the use of various scientists at the three FEL facilities combined. Plans include continued efforts to improve FEL performance and reliability at each of the FEL sites, and to supply increased beam time for use by investigators in all of the disciplines noted above.

C. Other Program Funding Summary: Not Applicable.

D. Acquisition Strategy: Not Applicable.

E. Major Performers

Category	Name	Location	Type of Work and Description	Award Date
Labs				
	Air Force Office of Scientific Research	Arlington, VA	These funds are provided for technology efforts concerning the application of free electron lasers to combat casualty care-related medical diagnosis and treatment.	12 DEC 2004