Exhibit R-2, RDT&E Budget Item Justification Fiscal Year (FY) 2005 Budget Submission	Date: February 2004
APPROPRIATION/BUDGET ACTIVITY RDT&E, D BA2	R-1 ITEM NOMENCLATURE Medical Free Electron Laser PE 0602227D8Z

COST ($ in Millions)	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Total PE Cost	11.609	18.518	9.668	9.850	10.072	10.078	10.090
Medical Free Electron Laser/P483, Subtotal Cost	11.609	18.518	9.668	9.850	10.072	10.078	10.090

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, and new medical imaging modalities. Uniquely, laser applications will be clinically tested in medical centers, leading to Food and Drug Administration (FDA) approval. There is high potential dual use for 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 in FY 2004 under new center grants, with the primary focus of the work remaining on the development of militarily relevant laser medicine applications.

(U) Overall management plans for FY 2004 include strengthening the interactions of the new 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.

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B. Program Change Summary:

	FY 2003	FY 2004	FY 2005
Previous President's Budget	0	9.494	9.694
Current FY 2005 President's Budget	11.609	18.518	9.668
Total Adjustments	-11.609	-9.024	-.026
Congressional program reductions	-0.103	-0.182	
Congressional rescissions			
Congressional increases	11.712	9.206	
Reprogrammings			
SBIR/STTR Transfer			
Other			-0.026

C. Other Program Funding Summary: Not Applicable

D. Execution
Laboratories/Centers

Beckman Laser Institute, University of California-Irvine, Irvine, CA
Duke University, Durham, NC
Stanford University Picosecond FEL Center, Stanford, CA
Vanderbilt University FEL Center for Research, Nashville, TN
Wellman Laboratories, Massachusetts General Hospital, Boston, MA

Exhibit R-2a, RDT&E Project Justification Fiscal Year (FY) 2005 Budget Submission			Date: February 2004
Appropriation/Budget Activity RDT&E, D BA 2	PROGRAM ELEMENT: Medical Free Electron Laser, PE 0602227D8Z		Project Name and Number Medical Free Electron Laser, P483

Cost ($ in millions)	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Project/Thrust Cost	11.609	18.518	9.668	9.850	10.072	10.078	10.090

A. Mission Description and Budget Item 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 materials research.

(U) Overall management plans for FY 2004 include strengthening the interactions of the new grantee institutions with military medical research facilities to improve both the content of the grant programs and the implementation of new techniques in military medicine.

(Cost in $ Millions)	FY 2003	FY 2004	FY 2005
Imaging Technology	2.314	4.438	1.864

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 detectors 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 using a hand-held laparoscopic probe for imaging. A similar probe can also be used in conjunction with many standard diagnostic scopes in other areas of medical practice, such as injuries to the trachea and respiratory tract. Work on improving the resolution of OCT images is also being done, with resolutions down to 1 um shown to be possible with short pulse lasers. A tunable, monochromatic x-ray system has been developed using the electron beam of an RF 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 are being studied to characterize important biomolecules and processes tagged with microparticles or molecular biosensors. The potential of the use of near-field IR microscopy in cellular imaging is also being examined. Plans for 2004 include work on improving the contrast and depth of OCT imaging with emphasis on its use in burn injury, development of new ultrasmall fiber optic endoscopy systems, continued development of monochromatic x-ray and Pulsed Photothermal Radiometry applications, new applications of Near Field Optical Microscopy, and other IR microscopy techniques.

(Cost in $ Millions)	FY 2003	FY 2004	FY 2005
Laser Surgery Methods	1.233	3.047	1.065

FELs are being used in experimental surgery studies and human surgical cases. An FEL has been used in the surgical removal of a human brain surface tumor, and additional surgical applications are on-going. Experimental surgery studies are developing techniques for precision surgical requirements such as optic nerve fenestration 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 under this program has also led to the observation of laser effects on chondrocyte regeneration, critical for effective treatment of arthritic degeneration. 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 for 2004 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. New efforts will examine the application of laser-based imaging to orthopedic repair of cartilage.

(Cost in $ Millions)	FY 2003	FY 2004	FY 2005
General Clinical Medicine Techniques	**2.501**	2.902	1.994

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 the effect of using this technique for the treatment of difficult infections such as tuberculosis are being initiated. Other photosensitive compounds attached to cells have been shown to be able to modulate cellular activity. For example, chondrocytes, activated by light sensitive molecules, have been able to 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, which may provide the possibility of controlling 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 is now being tested for effectiveness in nerve and tendon repair, and repair of damage to the trachia. In 2004, 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.

(Cost in $ Millions)	FY 2003	FY 2004	FY 2005
Laser/Tissue Interactions and Wound Healing Studies	**1.287**	2.620	1.110

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 will provide 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 follow the processes of fibronectin growth and wound closure. Vasodialation, which is an important factor in wound healing, has also been shown to be sensitive to the application of UVA and blue light *in vivo*. Studies examining the effect on wound healing of this phenomenon and its enhancement by norepinephrin, a known vasoconstrictor, are also underway. Studies on laser ablation and the subsequent healing processes will continue in 2004, with a continuing 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.

(Cost in $ Millions)	FY 2003	FY 2004	FY 2005
Physical and Materials Science Research	0.610	0.767	0.515

Research on the improvement of the performance and reliability of the FELs is a continual 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 macromolecules, on the dynamics of various surface-based processes, and on the nature, formation and deposition processes of thin films. Continued work on spectroscopy methods, surface-based processes, and the nature and formation of thin films are planned for 2004.

(Cost in $ Millions)	FY 2003	FY 2004	FY 2005
Laser Operations Support	3.664	4.744	3.120

A major upgrade in the components of the Duke University FEL system was completed, greatly improving the efficiency and overall capability of the system for research. A total of more than 5,000 hours of beam time has been provided for the use of various scientists at the three FEL facilities combined. Plans for 2004 include continued efforts to improve FEL performance and reliability, and to supply increased beam time for use by investigators in all of the disciplines noted above.