Exhibit R-2a, RDT&E Project Justification								Date: February 2003
Appropriation/Budget Activity RDT&E, D BA 2				Project Name and Number Medical Free Electron Laser, PE 0602227D8Z				
Cost ($ in millions)	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006[1]	FY 2007	FY 2008	FY 2009
Medical Free Electron Laser/P483	19.660	11.897	9.494	9.694	9.879	10.089	10.081	10.079

A. Mission Description and Budget Item Justification:

(U) The MFEL program seeks to develop advanced, laser-based applications for military medicine and electronic materials research. 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) The majority of this program is focused on developing advanced procedures 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. Laser applications will be clinically tested in unique program 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 repair, and neurosurgery. Current work on the existing programs will continue through FY2003, with the primary focus of the work remaining on the development of militarily relevant laser medicine applications.

(U) A small part of this program is focused on electronic materials research. In this research, the high energy FEL beam is exploited for improved processing applications including more effective microstructure, surface cleaning and modification of transport properties of microelectronic substrates.

(U) Overall management plans for FY2003 include conducting a full and open recompetition for the program, with the goal of having new grants or contracts in place for the start of FY 2004.

B. Accomplishments/Planned Program

	FY 2002	FY 2003	FY 2004	FY 2005
Imaging Technology	3.780	2.232	1.825	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. 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. The potential of the use of near-field IR microscopy in cellular imaging is also being examined. Plans for 2003 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.

	FY 2002	FY 2003	FY 2004	FY 2005
Laser Surgery Methods	2.160	1.275	1.043	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 surface tumor, and additional surgical applications are on-going. Experimental surgery studies are developing techniques for precision surgical requirements such as optic nerve fenestration repair 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 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 development of an effective animal model for study of corneal healing after laser vision correction surgery. Subsequent work using this model has described important steps to minimize the scarring which can adversely affect vision correction efforts. Plans for 2003 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.

	FY 2002	FY 2003	FY 2004	FY 2005
General Clinical Medicine Techniques	4.097	2.419	1.978	2.020

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* were completely healed following treatment with photosensitive compounds. Studies on the effect of this technique on *Staphylococcus* organisms are ongoing. 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 collage explants. Similarly, light absorbing nanoparticles have been shown to affect various properties of cells, including their permiability, which may provide for 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 has now been shown to be effective in closure of skin graft wounds, gingival grafts, and in tendon repair. In 2003, studies will continue on developing new photosensitizers and methods for their delivery, and their use in treating infections of selected microorganisms and for controlling various cellular activities.

	FY 2002	FY 2003	FY 2004	FY 2005
Laser/Tissue Interactions and Wound Healing Studies	2.251	1.329	1.087	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 are currently underway 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 2003, with a new 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.

	FY 2002	FY 2003	FY 2004	FY 2005
Physical and Materials Science Research	1.044	0.616	0.504	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 and formation of thin films. Continued work on spectroscopy methods, surfaced-based processes, and the nature and formation of thin films are planned for 2003.

	FY 2002	FY 2003	FY 2004	FY 2005
Laser Operations Support	6.328	3.738	3.056	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 2003 include continued efforts to improve FEL performance, and to supply increased beam time for use by investigators in al of the disciplines noted above.

C. Other Program Funding Summary: N/A.
D. Acquisition Strategy. N/A
E. Major Performers:

Beckman Laser Institute; University of California, Irvine; Irvine, CA; Michael Berns, Ph.D., Principal Investigator. Award Date – August 2000.
This work investigates the mechanisms of laser interactions with molecules, cells, and tissues to better address medical problems of importance to military and general populations. Areas include (a) invasive and non-invasive detection of tissue pathology, (b) design and construction of optical systems for diagnostic techniques, (c) laser effects on biochemical and structural changes in cells and tissues.
Duke University, Center for FEL Research; Durham, NC; Glenn S. Edwards, Ph.D., Principal Investigator. Award Date – September 2000
This work involves the development of new accelerator-based light source capabilities for investigations in biological and biomedical science, and the application of IR and UV FEL technology to a broad program of medical and surgical research, and studies in cell biology and biological physics. Work is focused on (a) development of neurosurgical techniques, (b) laser surgical methods and healing in corneal tissue, (c) mechanisms of laser-induced tissue ablation and generalized wound healing, and (d) the development of new, more reliable, higher intensity light sources in both the UV and IR.
Vanderbilt University, Free-Electron Laser Center for Research; Nashville, TN; David W. Piston, Ph.D., Principal Investigator. Award Date – May 2001
The goal of this work is to increase the applicability of infrared (IR) laser light for studies in the medical and biological sciences. Work has focused on (a) surgical applications of FEL in neurosurgery and ophthalmology, (b) research on the mechanisms of tissue cutting processes using specific IR wavelengths, (c) spectroscopy studies of biological macromolecules, and (d) the development of a new technique and instrument for generation of monochromatic x-rays.
Wellman Laboratories, Massachusetts General Hospital, Boston, MA; John A. Parrish, MD, Principal Investigator. Award Date – January 2000.
The goal of this work is to develop clinically important biomedical applications of FEL technology. Studies by this group are focused on (a) the development of photovasodilation as a potential method for light stimulated wound healing and possible reversal of tissue ischemia, (b) photodynamic inactivation of pathogenic microorganisms, (c) development of methods for the use of Optical Coherence Tomography imaging in diagnostic applications and of laser-based *in vivo* hemocytometry equipment, (d) development of photochemical tissue bonding materials and techniques, and (e) studies on laser interactions with subcellular components for modulation of cellular processes.
Stanford University Picosecond FEL Center; Stanford, CA; H. Alan Schwettman, Ph.D., Principal Investigator. Award Date – August 2000.
The work of this program is directed toward the development of instrumental capabilities based on the FEL and other lasers for use in medical and biomedical science research. Areas of focus include (a) improvement of IR FEL reliability and capability, (b) development of single-cell broad-band FTIR spectroscopy for investigation of subcellular activities, (c) studies on the mechanisms of tissue ablation from single picosecond laser pulses, and (d) the use of scanning near-field IR microscopy in cells and tissues.

An additional 10 small programs are accomplished in government laboratories, FFRDCs, and other universities which support the work of the major performers in laser physics and materials science areas, and in the development of clinical applications of new findings.