best image on the basis of prior knowledge of the source and instrument. We are already applying one such technique, known as maximum entropy, to obtain the two-dimensional image from our set of one-dimensional images in GRATIS data. This technique selects the “flattest” image (the one with the least structure) commensurate with a statistical goodness-of-fit indicator based on the known instrument properties. In this case, we assume that the scene nature supplies will not have a lot of rapid variations in counts versus position.

Key Words: gamma rays—gamma-ray arc-minute telescope imaging spectrometer (GRATIS), gamma-ray astronomy, gamma-ray bar imaging telescope (GRABIT), gamma-ray camera, gamma-ray imaging spectrometer (GRIS); special nuclear material (SNM); Strategic Arms Reduction Treaty (START).

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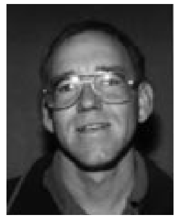
About the Scientist



KLAUS-PETER ZIOCK came to Lawrence Livermore National Laboratory 10 years ago as a post-doctoral scientists in V Division. Since 1988, he has been a staff scientist in V Division’s Laboratory for Experimental Astrophysics. He received his Ph.D. in Physics from Stanford University in 1985 and his B.A. from the University of Virginia in Physics and Chemistry in 1978. His primary area of scientific research is low-energy gamma-ray astrophysics. He has been involved in the development of GRIS, GRABIT, GRATIS, GRB (a gamma-ray burst detector), and SXRP (an x-ray polarimeter).

His numerous publications to date (about 40) are in the area of atomic physics, including high-atomic-number systems, positronium spectroscopy, and instrumentation development for astrophysical research.

Positioning Health Care Technologies for the Needs of the 21st Century

LAST year, expenditures for health care reached about 14% of the U.S. gross domestic product, or a staggering $1 trillion. Many experts agree that the annual bill for health care will grow even larger in the next few years. Moreover, the effects of escalating costs extend beyond the domain of health care per se; they are reflected in added costs of U.S. manufactured products, in labor–management relations, and in many other ways that are not always obvious.

Can the trend be reversed? In some industrial fields, such as electronics, technological innovation is part of an effective strategy to reduce costs without decreasing quality. In marked contrast, investment in technology development accounts for only a tiny fraction of national health care spending, and even medical research and development represents only about 3% of its overall spending. LLNL is marshaling its world-class technology base to help the nation to contain escalating costs for health care.

Over the last decade, a broad spectrum of Livermore research projects has explored new or improved health care technologies that can potentially reduce health care costs. We are developing better imaging systems, such as pulsed x-ray lasers, improved instrumentation and information systems, and advanced sensor and detection systems, such as accelerator mass spectrometry. Other efforts around the Laboratory—often interdisciplinary and involving external collaborators—are already having an impact on the frontiers of research or treatment in maladies such as cancer, heart disease, stroke, diabetes, osteoporosis, and repetitive strain injury as well as in specialties such as ophthalmology, dentistry, and prosthesis design and manufacture.

To coordinate these activities, we established the Center for Healthcare Technologies at LLNL. Its goals are to:

- Continue to pursue the high-quality science and technology efforts that are already directed toward improved health care.
- Become better known in the health care community.
- Propose LLNL initiatives in health care that are more integrated than others’.
- Promote a national focus for federal activities in health care technology.

The Center has an external advisory committee of senior health-care professionals and an internal coordinating and advisory committee. Perhaps most importantly, the Center represents a single point of contact through which interested organizations outside the Laboratory can gain access to the LLNL individuals or groups that are most appropriate for addressing specific health-care needs.

Our current strategy entails three phases of activities, which we have launched in parallel.

In Phase I, we are delivering results on current projects and gaining recognition for our accomplishments in health-care technologies. More than two dozen projects at the Laboratory are currently funded at about $6 million per year. The box illustrates developments from one of our most recent and exciting initiatives—the prevention of hemorrhaging in stroke-damaged blood vessels.

During our first year, we contacted more than 80 medical, industrial, and governmental organizations. We are identifying and coordinating projects that extend LLNL core competency in the multidisciplinary focus of biotechnology, helping to meet future DOE Defense Program requirements and providing cost-effective medical technology at the same time.

In Phase II, we are initiating and participating in larger health-care projects through multidisciplinary teams of collaborators. For example:

- Digital Mammography Systems is a proposed team of military, government, and industrial partners led by an Army medical center. Livermore would be responsible for system integration at 14 sites, for data integrity and archiving, and—with Sandia National Laboratories, Livermore—for new algorithms for computer-assisted diagnosis.
- This year, we have been asked to define and coordinate potential roles for the DOE laboratories in Testbed’95, which will set up a telemedicine system. The Center is a partner in the health-care working group of the National Information Infrastructure Testbed (NIIT), a consortium of telecommunications, computer, and other companies. In September 1994, we participated in a successful, one-day NIIT telemedicine demonstration, Testbed’94, held at the Congressional Office Building in Washington, D.C.

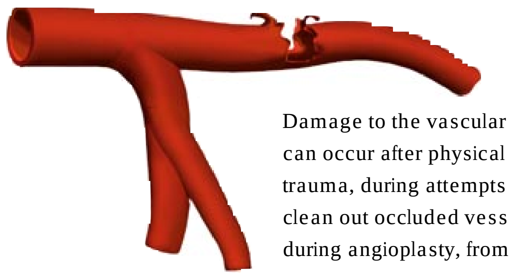
- In a concept paper, we proposed development of minimally invasive medical technology, an area in which the medical industry has great interest and which is now being considered as a government focus area.

Our Phase III activities seek to establish a national strategy for health care technology programs. The focus is on reducing costs without reducing access or quality of service. We have proposed a government organization operating under the National Institutes of Health (NIH). We envision this new agency as a forward-looking, expert organization that pursues the best technical solutions from the best sources combined with the medical expertise of the NIH. We have presented our concepts to the largest health care, medical research, and industrial organizations in the U.S., to Congressional staff members, and to members of the Clinton Administration. *Science and Technology Review* will report on developments and feature important technological advances as they occur.

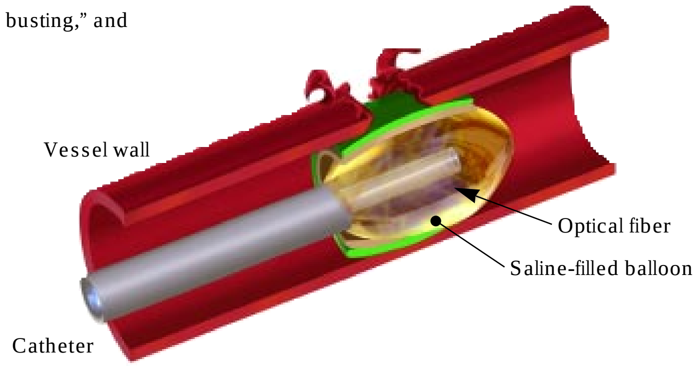
For further information contact J. Patrick Fitch or any member of the Center for Healthcare Technologies (510) 424-4806 (healthcare@llnl.gov).

Patch Welding for Damaged Blood Vessels

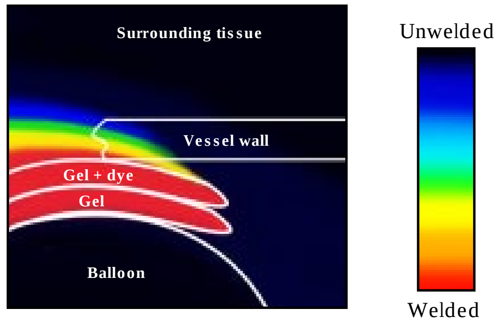
Every year in the U.S., over three million Americans are victims of stroke. The annual cost of care for stroke patients is about $30 billion. When the brain is deprived of oxygen, cell death can begin in a matter of minutes. Now, a change in treatment is coming. To promptly restore blood flow and oxygen supply, we are using a multidisciplinary approach to characterize vessels and occlusions, to do “clot busting,” and to “weld” damaged vessels, as illustrated here.



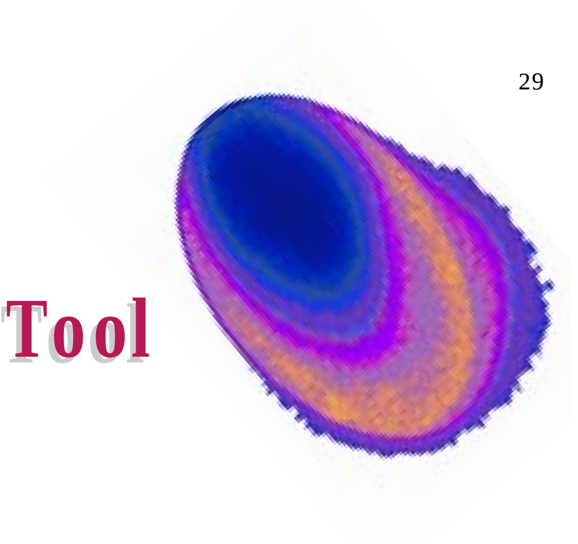
Damage to the vascular wall can occur after physical trauma, during attempts to clean out occluded vessels, during angioplasty, from an aneurysm (a bubble on the vessel wall), or as a consequence of other conditions.



A tiny saline-filled balloon is inflated in the vessel until a biocompatible gel (tan) and the patch or “solder” material (green dye) make contact with the damaged vessel wall. Within the balloon is an optical fiber. Pulsed laser light from the tip of the fiber is absorbed by the dye until the ideal patch-welding temperature is obtained.



In the first six months of this project, we developed a modeling code, LATIS, to control and localize temperature when heating tissue. This code (similar to those used in inertial confinement fusion research) allows us to select the right combination of laser pulse duration, repetition rate, and number of pulses to obtain the ideal temperature (see red zone) for patch welding a blood vessel. At the wavelength we use, about 65 pulses every 200 microseconds are optimal for repairing a vessel without damaging the surrounding soft tissue.



The Short-Pulse Laser: A Safe, Painless Surgical Tool

THE very best surgeons possess exceptional skill and dexterity, but most have not had access to what sounds like the best of high technology tools—a medical laser. Medical lasers have been used successfully in some procedures such as repairing detached retinas, breaking up kidney stones, and removing port wine stain birth marks. However, their remarkable ability to simultaneously cut and cauterize has not caused them to eclipse steel or electrosurgical tools because they have lacked predictable precision with body tissue and have been too large and expensive to be a practical part of medical offices and operating rooms.

Recent advances by Livermore researchers are changing the capabilities of surgical lasers so that they may fulfill their promise to become the “blade of choice,” especially in surgical procedures on organs and tissues that bleed profusely when cut. By applying chirped pulse amplification to solid-state lasers, researchers have built systems that may increase the use of laser surgical techniques in operating rooms. The techniques are expected to revolutionize dentistry and are particularly well-suited to precision microsurgery on corneas, delicate ear bones, and the brain.

Limitations of Earlier Lasers for Surgery

Since their advent about 30 years ago, lasers have been observed to induce damage in transparent solids, such as defect-free dielectrics (electrical insulating materials used during laser beam amplification and as mirrors to direct beams). For pulses longer than a few picoseconds,[*] the generally accepted theory of bulk damage to these materials is that the incident radiation heats electrons (those in an atom’s conduction band, to be exact), and these electrons transfer thermal energy to other electrons and atoms in the lattice. In other words, the dielectric material is damaged by the melting, boiling, and thermal shock that result.

Similarly, a fundamental limitation of past surgical laser systems was the heat caused by the beams—either a continuous beam or one made up of multiple, 1000-ps pulses, or “bursts.” As a result, laser surgery was soon found to be unexpectedly complicated. Lasers affect irradiated tissue through absorption of the light energy, and the absorption is determined largely by the properties of the material being irradiated, such as its color. Consequently, a surgeon might be cutting tissue quite effectively with the laser at the proper specific energy when the beam suddenly hits a different kind of tissue. If the tissue has different absorption properties, the cutting rate and heat generation can suddenly increase or decrease dramatically—by orders of magnitude. Surgeons have had to worry about how much energy the beam deposited and the degree to which the irradiated tissue absorbed or reflected the light. They might irradiate tissue with no apparent effect, only to discover that the light was being reflected or transmitted and absorbed by other tissues and causing undesired burning at these sites.

Indeed, this collateral damage has been a real concern with conventional laser-surgery pulsed systems. For example, laser cutting can significantly heat material some distance from the area being irradiated, causing either desiccation of the material or, if there is water below the surface, explosive vaporization resulting in torn tissue.

There has been a clear need for a tool better than the scalpel, but one that does not require continuous adjustment or present the possibility of catastrophic mishap. Introduced about the same time as lasers, electrosurgical tools, which use radiofrequency waves to interact with tissues, have become the tools of choice for many applications in which lasers proved disappointing. Electrosurgical tools, for example, can simultaneously cut and cauterize; they are also less expensive than lasers, are easier to use, and cut much faster. They are, however, not suited to microsurgery, and they too can cause collateral tissue damage.

Ultrashort Pulses Provide the Answer

Recently, however, laser technology has cleared some hurdles. By applying chirped-pulse amplification to solid-state lasers, Livermore researchers have built systems producing

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[*] One picosecond (ps) = 1 trillionth of a second or 10^{-12} s.

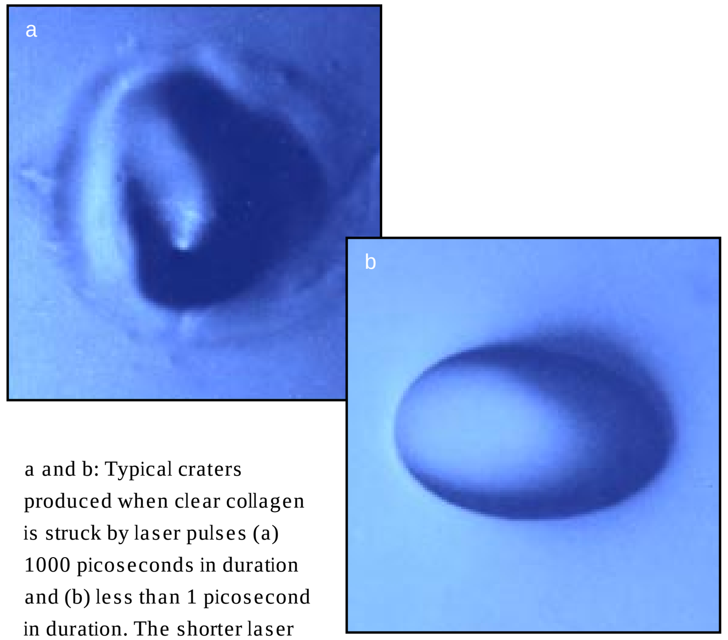
terawatt (10^{12} W) pulses with ultrashort durations—well under a picosecond. (Chirped-pulse amplification is described in some detail in the article on multilayer dielectric gratings in the September 1995 issue of *Science and Technology Review*.) According to theory, subpicosecond durations are far too short for appreciable electron energy to be transferred to surrounding material. As a result, less laser energy is absorbed by the tissue, so material should be able to be removed by subpicosecond pulses with essentially no collateral damage. Theory also predicts that the energy absorption mechanism for ultrashort pulses makes material removal by laser much less sensitive to tissue type than is the case with longer pulses.

To confirm the theoretical promise of ultrashort pulses, we performed a series of experiments on various materials. These extensive experiments, with materials such as fused silica and calcium fluoride, yielded results that agreed well with theory. We then produced “phantom tissues”—materials whose properties mimic the densities and effective atomic numbers of living tissue. We mixed gelatin and water to make collagen gels (collagen is a fibrous protein found in all multicellular animals), and we mixed aqueous solutions of cupric chloride in different concentrations to produce a range of light-absorption properties.

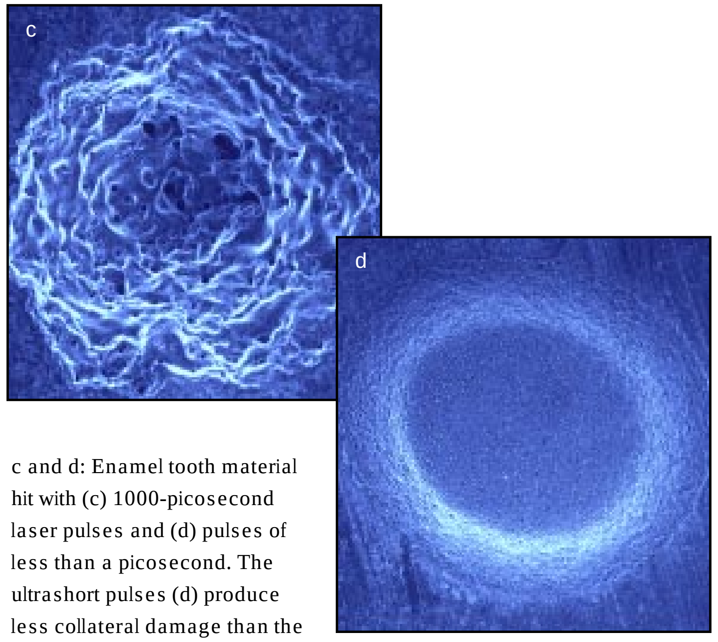
We then performed ablation measurements—measurements of how much material was removed by being “blown off,” or ablated. We used a chirped-pulse amplification laser to obtain pulses of continuously adjustable duration from 0.3 ps to 1000 ps, with a laser spot size of 0.5 mm in diameter (about the size of a period). After irradiating the sample, we inspected it for formation of an ablation crater. The smallest craters we could observe were approximately 1 micrometer in diameter, 500 times smaller than the area the laser had ablated. We determined the ablation threshold for a given pulse width. Then, to determine the ablation efficiency, we measured ablated crater depth and diameter after 10 to 100 laser pulses, recording the energy of each pulse. Now we could predict how the laser was “cutting.”

The figures below show typical craters produced by 1000-ps pulses and by pulses of less than 1 ps in a clear collagen gel (a and b) and in tooth enamel (c and d). Much more thermal damage appears with the longer pulses (a and c). For ultrashort pulses, collateral damage is practically absent, and a clean, smooth crater is produced (b and d).

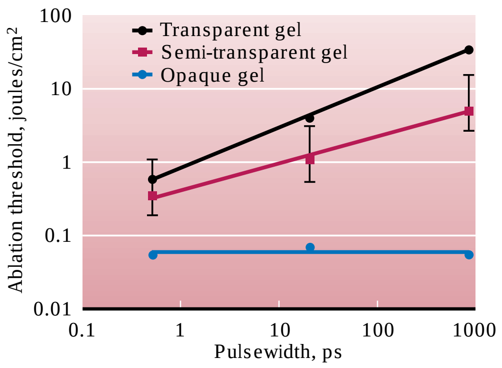
The figure on page 31 presents the results of ablation threshold measurements for collagen gels dyed to have different linear absorptions. The ablation thresholds for collagen gels follow the trends that we predicted. The ablation threshold for clear gels, which are similar to corneas, in the 1000-ps pulse width range (75 joules/cm^2) is about 1000 times higher than the ablation threshold for black gel (0.074 joules/cm^2). In the subpicosecond pulse width range, this difference decreases to only a factor of six. Thus, the ablation thresholds for transparent and nontransparent tissues converge at shorter pulse widths.



a and b: Typical craters produced when clear collagen is struck by laser pulses (a) 1000 picoseconds in duration and (b) less than 1 picosecond in duration. The shorter laser pulses (b) ablate the tissuelike collagen cleanly and precisely and produce less collateral damage than the longer pulses (a).



c and d: Enamel tooth material hit with (c) 1000-picosecond laser pulses and (d) pulses of less than a picosecond. The ultrashort pulses (d) produce less collateral damage than the longer pulses (c).



Short pulses cause highly localized, shallow energy deposits, and each one removes only a thin layer of material (less than 1 micrometer). Varying the number of pulses controls how much material is removed. High repetition rates (greater than 100 Hz) achieve high average removal rates (greater than 1 mm during 10 seconds). This method of tissue ablation has several advantages:

- It is efficient. With decreasing pulse width, the energy density needed to ablate material decreases.
- Minimal collateral damage occurs because ablation is efficient with the short pulse and because the ablated tissue carries away a large fraction of the deposited energy from the laser.
- The ablation threshold and ablation rate vary only slightly as tissue type and state change.
- Ablation depth can be controlled with extreme precision because a small amount of tissue is ablated per pulse and because the number of pulses can be controlled.

With ultrashort laser pulses, the absorption threshold and ablation rate (depth of material removed per pulse) are relatively insensitive to factors such as laser wavelength and tissue state (e.g., structure, hydration, and oxygenation). Because an ultrashort laser pulse (0.005 ps to more than 20 ps) is medically useful by virtue of its duration rather than its wavelength, a variety of lasers operating over a wide range of wavelengths can be used, such as lasers based on dyes, excimers, or solid-state materials. However, solid-state infrared lasers such as those used at the Laboratory offer the advantages of safety and convenience.

Our experimental results are still preliminary; further research is needed to understand what happens to the energy after it is deposited by the laser. How the energy couples to the atoms of the tissue, how the tissue is ablated, how the stress wave is generated, how the stress wave propagates into the tissue, and how the collateral damage occurs all warrant further investigation.

Practical for Surgery

Ultrashort-pulse lasers have an important niche in surgery. The precision ablation of these lasers allows microsurgeons to perform intricate operations, such as drilling holes through small middle ear bones, for which they use microdrills. Likewise in brain surgery, which also puts a premium on accuracy and control and on minimizing thermal collateral damage, a system with a high pulse-repetition rate could allow a surgeon enough speed and control to virtually “sculpt” the tissue.

An added benefit of lasers to surgery is the fact that the pulses can be transmitted by fiber optics. Laser energy can be delivered to many remote locations within the body through fiber-carrying catheters. In the future, instead of making large incisions to gain access to certain organs or cavities, surgeons will use more endoscopic and laproscopic techniques. Fiber-delivered lasers are already being used to break up kidney stones, for example, and are performing better than ultrasound for this purpose.

Ultrashort-pulse laser systems also have great potential in dentistry to replace the dentist’s drill for cavity and root-canal work. The drill produces pain chiefly by heat—the drill gets the tooth very hot—and secondarily by mechanical vibration. We have demonstrated that the ultrashort-pulse lasers produce minimal heat and vibration and virtually no collateral damage to surrounding enamel.

The Laboratory is not alone in developing ultrashort-pulse laser systems. However, the critical step, once their medical utility has been conclusively proven, will be to make them compact and inexpensive. We have been developing the technology to make comparatively compact, easy-to-use high-power optical systems that produce pulses with flexible durations and wavelengths. Essentials for practical use are very high beam quality and reproducibility, in which the Laboratory has long-standing expertise. Using recent advances, we can design high-power, ultrashort-pulse systems small enough to be practical—and affordable—for surgeons and dentists.

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