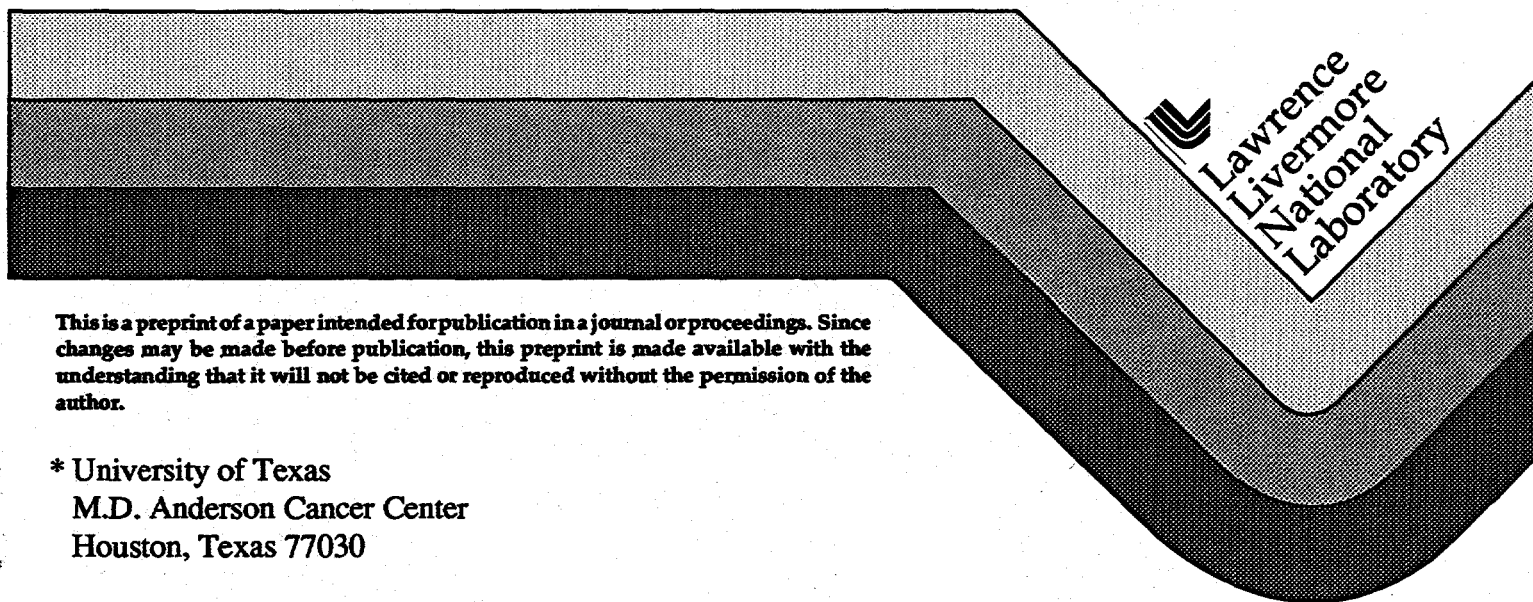


Modeling of Endovascular Patch Welding Using the Computer Program LATIS

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ABSTRACT

A new computer program, LATIS, being developed at Lawrence Livermore National Laboratory is used to study the effect of pulsed laser irradiation on endovascular patch welding. Various physical and biophysical effects are included in these simulations: laser light scattering and absorption, tissue heating and heat conduction, vascular cooling, and tissue thermal damage. The geometry of a patch being held against the inner vessel wall (500 μm inner diameter) by a balloon is considered. The system is exposed to light pulsed from an optical fiber inside the balloon. A minimum in the depth of damage into the vessel wall is found. The minimum damage zone is about the thickness of the patch material that is heated by the laser. The more ordered the tissue the thinner the minimum zone of damage. The pulse length which minimizes the zone of damage is found to be the time for energy to diffuse across the layer. The delay time between the pulses is determined by the time for the heated layer to cool down. An optimal pulse length exists which minimizes the total time needed to weld the patch to the wall while keeping the thickness of the damaged tissue to less than 100 μm . For the case that is considered, a patch dyed with light absorbing ICG on the side next to the vessel (thickness of the dyed layer is 60 μm), the best protocol is found to be 65-200 ms pulses applied over 2 min.

Keywords: laser, welding, soldering, endovascular, patch, stent, simulation

2. INTRODUCTION

There is general interest in endovascularly welding patches or stents to close aneurysms, to reinforce vessel walls,¹ and to cover the vessel wall after angioplasty or metal stent deployment. These patches need to be attached to the wall by some means. A possibility is tissue welding or soldering.² To accomplish this, the inside of the vessel wall needs to be heated to a high enough temperature for a long enough time to cause the proteins to unfold, to expose the polar parts of their molecular structure, and then to have those polar parts form hydrogen bonds with the proteins in the patch. A layer no thicker than 100 μm should be "damaged" so that the tissue does not necrose.³ The use of pulsed radiation to control this zone of damage has been suggested.⁴ This paper explores via computer simulation the feasibility of doing it in a realistic situation.

The concept of tissue damage has been quantified in various ways. Properties such as birefringence,⁵ tissue necrosis, tissue whitening, light scattering and contraction⁶ have been used as a metric. The results have indicated a reaction process that can be modeled (to first order) as a single rate process with an energy of activation that varies between 20 to 40 meV depending on how ordered the tissue is. The reaction rate is given by the Arrhenius expression:

$$k(T) = \frac{k_B T}{h} \exp(-\Delta H / RT + \Delta S / R), \quad (1)$$

where ΔH is the enthalpy of reaction and ΔS is the entropy of reaction. The temperature dependence of the reaction rates for various types of tissue are shown in Fig. 1. Notice that the more ordered the tissue the higher the energy barrier that must be surmounted. These measures of damage are assumed to be correlated to the protein unfolding that is necessary for tissue bonding to occur. We emphasize that this is an assumption that should be investigated. It is also an assumption that tissue bonding is a single rate process. It has already been determined that there are at least two rates that contribute to changes in birefringence.⁵ In addition it should be noted that according to this model some tissues will become damaged in 3 hrs at body

temperature. Since this is obviously not true, there has to be a repair process or other correction to the damage rate which takes the net rate to zero at body temperature.

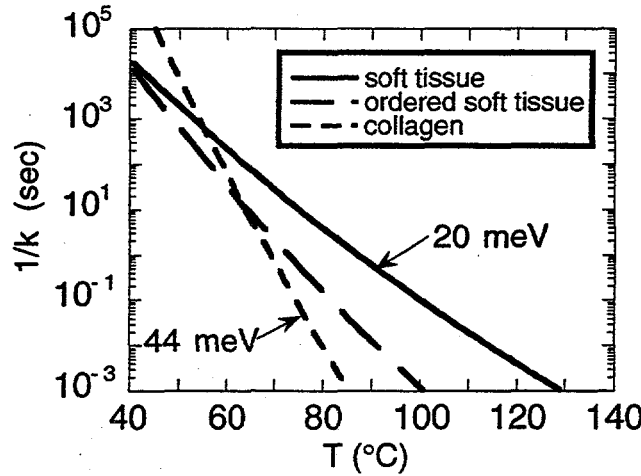


Fig. 1. Tissue damage timescale ($1/k$) vs. temperature.

The concept that pulsed energy delivery can lead to a controlled zone of damage is based on the exponential nonlinearity of the reaction rate shown in Eq. (1). If one delivers energy to a volume on a time scale that is greater than or equal to the time for energy to thermally diffuse across the layer, then the temperature will decay as L^{-d} where d is the dimensionality of volume over which the heat is spreading and L is the scale length of the volume. For thermal diffusion it is well known that $L \sim t^{1/2}$, where t is the time since the energy was deposited. The number of undamaged protein molecules N_u evolves according to the equation

$$\frac{dN_u}{dt} = -k(T) N_u, \quad (2)$$

Therefore the number of undamaged molecules evolves as $N_{tot} \exp(-\Omega)$ where N_{tot} is the initial number of protein molecules and $\Omega = \int k dt$. What we now wish to find is how the damage index Ω scales with L . This scaling is given by

$$\Omega = \int k dt \propto L^{2-d} e^{-(L/L_0)^d} \quad (3)$$

where L_0 is a constant, the factor L^2 is contributed by $\int dt$ and the factor $L^{-d} e^{-(L/L_0)^d}$ is contributed by the reaction rate. Notice that for large enough length scales, Ω always tends to zero because of the exponential factor. For the small length scales of interest, not enough damage can be done with one pulse. Therefore multiple pulses must be applied to accumulate the damage. The pulses must be separated by enough time – the average temperature must be kept low enough so that the tissue will not become damaged over the course of the treatment.

3. SIMULATION METHOD

A new computer code, LATIS (an acronym for LAsEr TISsue) is being developed at Lawrence Livermore National Laboratory. It is based on our past experience in constructing large computer programs that integrate many physical processes such as: laser propagation, laser energy deposition, hydrodynamics, atomic physics, radiation absorption, radiation emission, and radiation transport. Our final product in the past has been a simulation tool that can predict the results of laser interactions with plasmas. The new code LATIS is meant to be an analogous tool for laser tissue interactions. The physical processes that have been incorporated in LATIS and tested are: laser light scattering and absorption, tissue heating and heat conduction, vascular cooling of the surrounding tissue, and tissue thermal damage. Other physics such as

hydrodynamics, diffusive photon transport, evaporative cooling, and radiative cooling are coupled into the code but have not been tested. Planned additions are condensed history Monte Carlo photon transport, elastic wave propagation, material failure, water diffusion, and 3D geometries.

The laser light is propagated via a Monte Carlo transport scheme. The total census of photons is kept a constant, 1000 for the simulations presented in the paper. The photons are split or killed to keep the census number a constant. The scattering is done at random with a Henyey-Greenstein angular distribution.⁷ This distribution is based on the assumption that the size of the scatterers is of order the wavelength of the light (Mie scattering theory). It was originally used to model the scattering of light by interstellar dust. The distribution is determined by two parameters: the scattering coefficient μ_s and the average value of the cosine of the scattering angle g . The weight of the photons is decreased as they are absorbed consistent with the absorption coefficient μ_a . The weight is decreased down to a user specified value, 10^{-2} for our case, at which time the photon is killed. The photons are refracted at the zone (cell) boundaries and both refracted and reflected at region boundaries. This is consistent with the discontinuous change in material properties between different regions and the continuous change in properties of a single material within a region. As a first approximation for the effect of surface roughness the photons are reflected into a 2π solid angle (in contrast to a specular reflection) at a specified probability (1% for our simulations).

The energy that is taken out of the photons due to the absorption is deposited into the tissue's thermal energy. The energy is then allowed to diffuse with a zone dependent heat conductivity that can be different along the two directions that define the orientation of the grid. For our simulations we used an isotropic heat conduction.

Tissue damage is accumulated on a zone by zone basis as the local reaction rate $k(T)$ is summed to give the damage integral Ω . The tissue scattering is modified by the damage, changing from the undamaged value μ_{su} to the damaged value μ_{sd} according to the formula

$$\mu_s N_{tot} = \mu_{su} N_u + \mu_{sd} N_d, \quad (4)$$

where $N_d = N_{tot} - N_u$ and is the number of damaged protein molecules. This allows a soft tissue to whiten as chicken does as it is cooked – the scattering increasing by a factor of seven as the protein collects into clumps. For a structural protein such as collagen the opposite happens – the fibers are melted together as it is damaged, turning it into a jello with scattering that is ten times less than in its undamaged state.

The bulk vascular cooling of the tissue is modeled by an energy source term Q_v given by

$$Q_v = A(T) (T_{body} - T) e^{-\Omega}, \quad (5)$$

where T_{body} is the body temperature and $A(T)$ is a temperature dependent prefactor set to give a cooling time consistent with a blood perfusion rate of 40 ml/100 gm/sec at body temperature. It is multiplied by a factor of four for temperatures above 42°C due to a physical dilation of the capillaries. The exact behavior is shown in Fig. 2. The factor $e^{-\Omega}$ in Eq. (5) shuts off the cooling as the tissue is damaged.

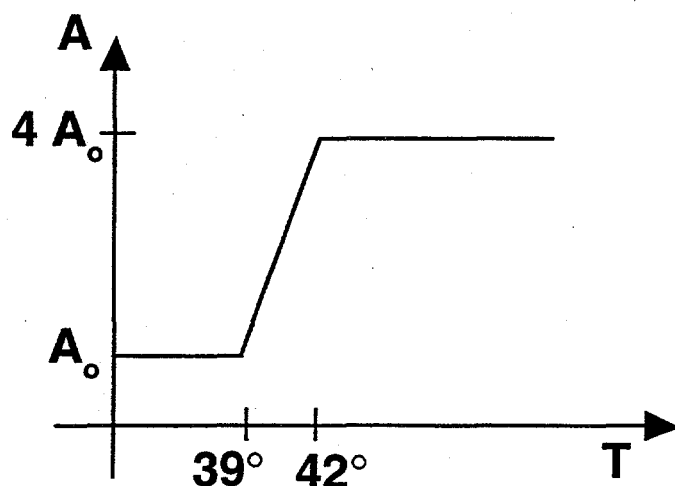


Fig. 2. Increase in the vascular cooling rate due to capillary dilation at elevated temperatures.

4. RESULTS

A series of simulations were done using the geometry shown in Fig. 3. For all regions of the simulation a density of 1 gm/cc and a heat capacity of 4.18 J/gm $^\circ$ K is used. The other important parameters are shown in Table I. Vascular cooling is only applied to the surrounding tissue. The properties used for the balloon, saline, and fiber were taken from an engineering handbook.⁸ The tissue parameters are generic numbers for soft tissue and visible light. The absorption coefficient of the gel+ICG layer was adjusted so that 1/10 of the laser energy would be absorbed in it. This was done to deposit as much energy as possible at the tissue side of the layer. The laser intensity had the profile shown in Fig. 4. It consisted of a train of square pulses of length Δt separated by a delay τ . The energy in the pulse is adjusted so that the maximum temperature at the end of the pulse is 100 $^\circ$ C. Only one pulse is modeled giving a damage integral Ω_1 . The damage of N pulses is assumed to be additive so that $\Omega = N\Omega_1$. The number of pulses was chosen so that the maximum Ω in the tissue is 10. The additivity of the damage is not a strictly valid assumption. There is a nonlinear feedback through the effect of the thermal damage on the scattering coefficient. This effect will be the subject of subsequent investigations.

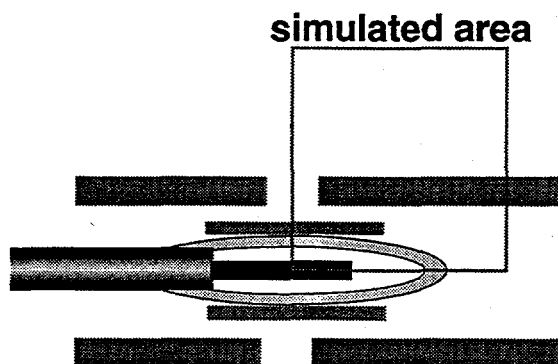


Fig. 3a. Geometry that is simulated. Shown is the simulation area. This area is symmetric about the left vertical line. There is an azimuthal symmetry about the line $r=0$ (lower horizontal line).

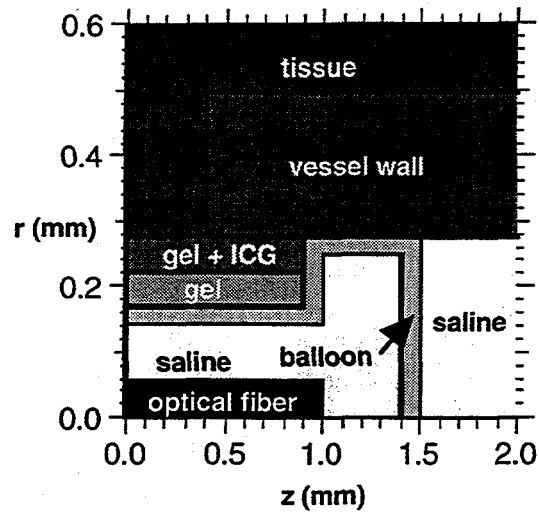


Fig. 3b. Area that is simulated.

	μ_a (cm^{-1})	μ_{su} (cm^{-1})	μ_{sd} (cm^{-1})	n	damage model	κ (W/m $^{\circ}$ K)
vessel	0.3	5.0	35.0	1.37	soft tissue or ordered soft tissue	0.609
gel + ICG	10.0	10.0	1.0	1.37	collagen	0.609
gel	0.01	10	1.0	1.37	collagen	0.609
balloon		clear		1.45	none	0.170
saline		clear		1.33	none	0.609
fiber		clear		1.5	none	0.609
tissue	0.3	5.0	35.0	1.37	soft tissue or ordered soft tissue	0.609

Table I. Parameters used in the simulation.

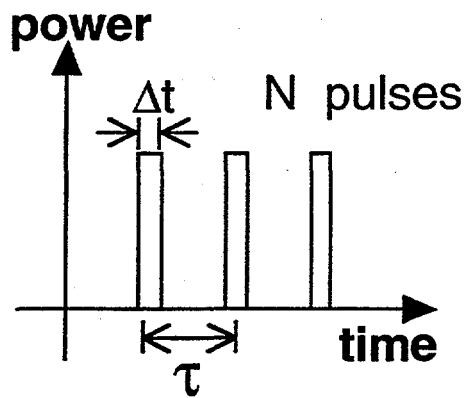
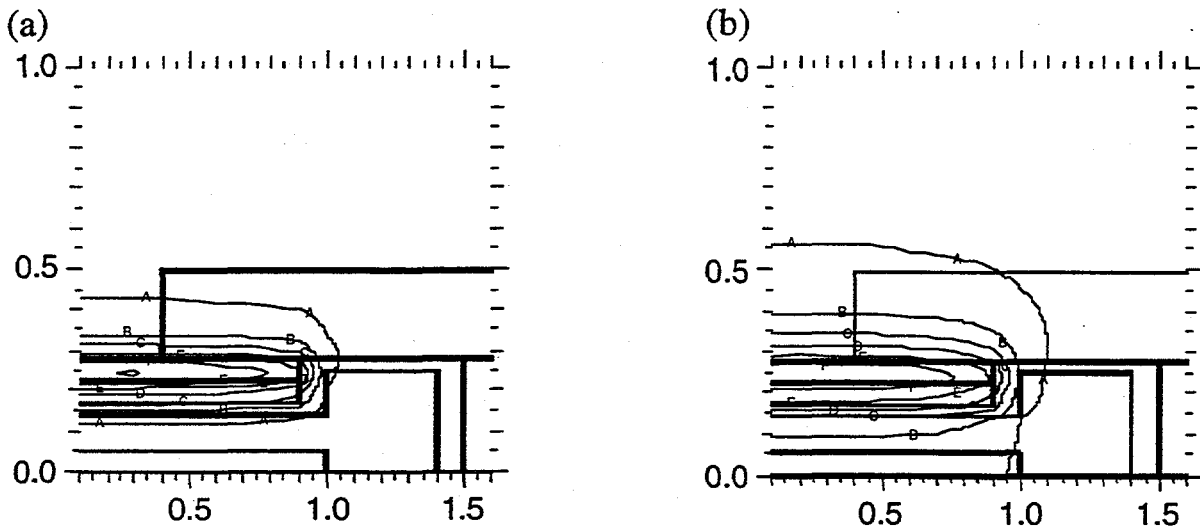


Fig. 4. Laser pulse profile.

The results of these simulations are shown in Figs. 5 and 6. Due to the exponential character of the damage rate, the edge of the damage zones are sharper than the temperature profiles. Notice that the extent of the temperature diffusion increases monotonically with increasing pulse length as expected. In contrast, the zone of damage shows a minimum for 60 ms pulses. This is more clearly shown in Fig. 7 where the thickness of the damage zone is plotted as a function of the pulse length. The thickness is defined as the radial distance from the outside edge of the patch to the point at which $N_d / N_{tot} = 0.5$. The bars indicate the value to which the damage thickness asymptotes for very short pulses. The minimum is due to the nonlinear character of the damage rate. Although the diffusion operator is linear and the contributions of the early part of the pulse to the temperature add to the contributions of the later part of the pulse, the damage rate amplifies the contribution of the later part making its shorter length scale dominant. This amplification is larger for the ordered soft tissue leading to a smaller minimum value for the depth of damage.



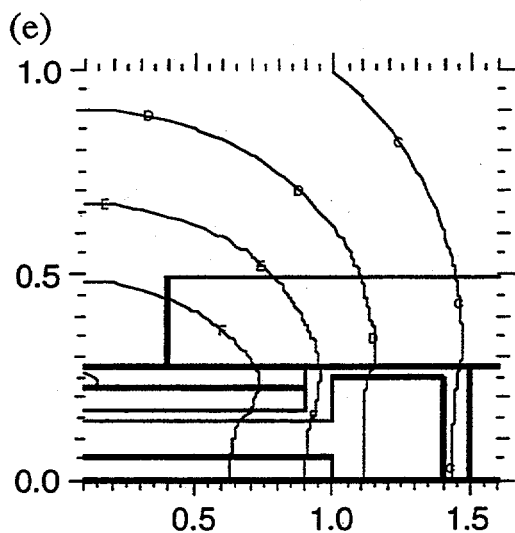
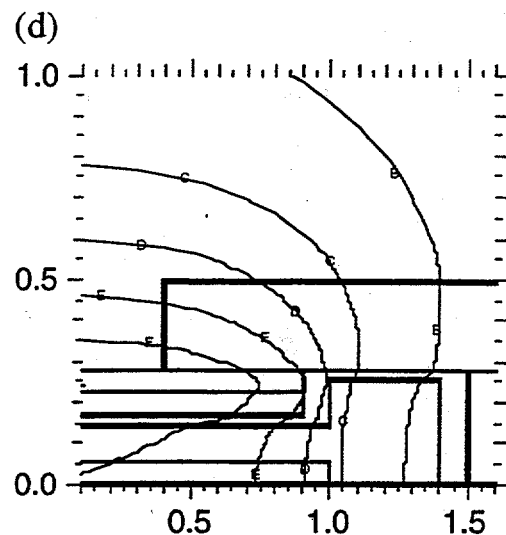
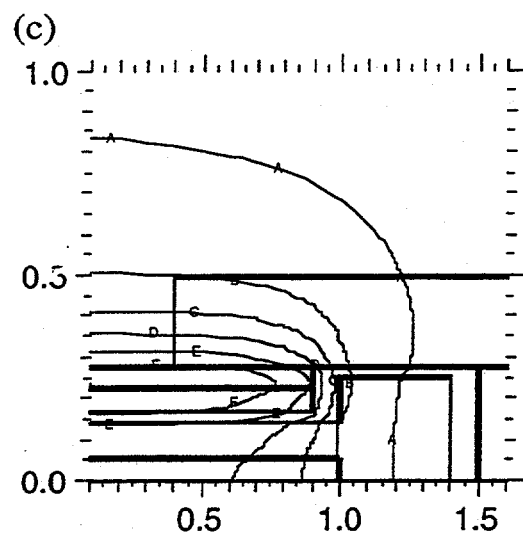
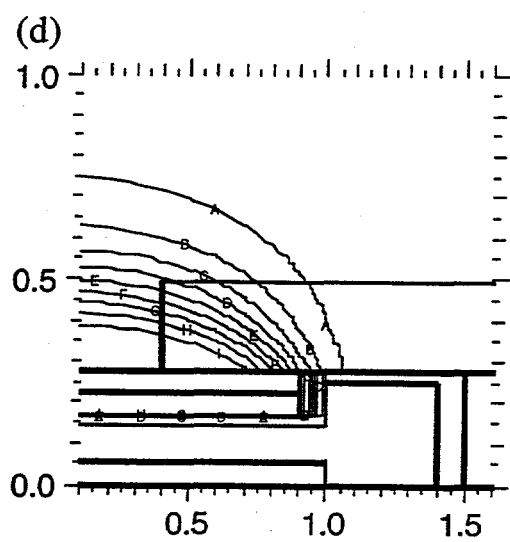
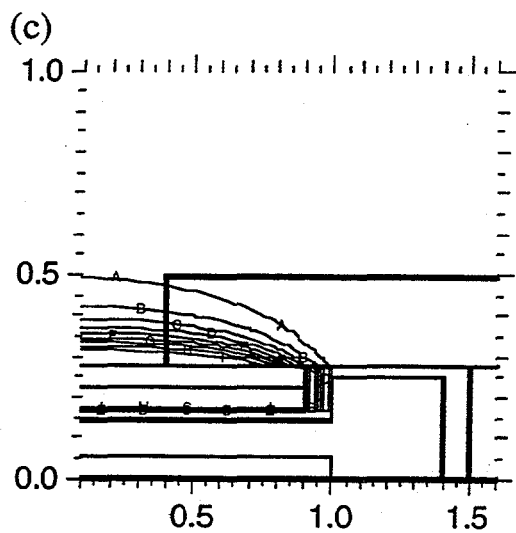
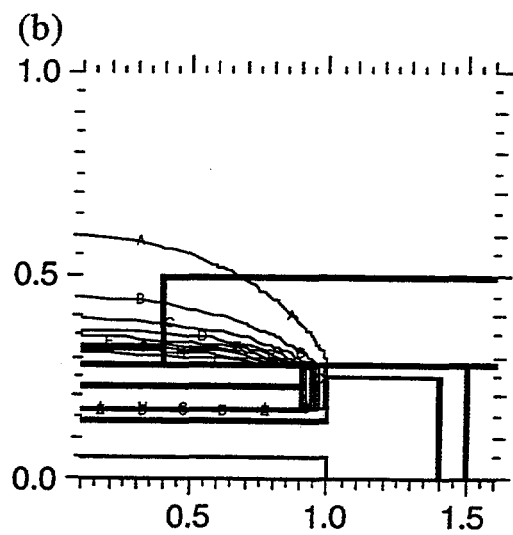
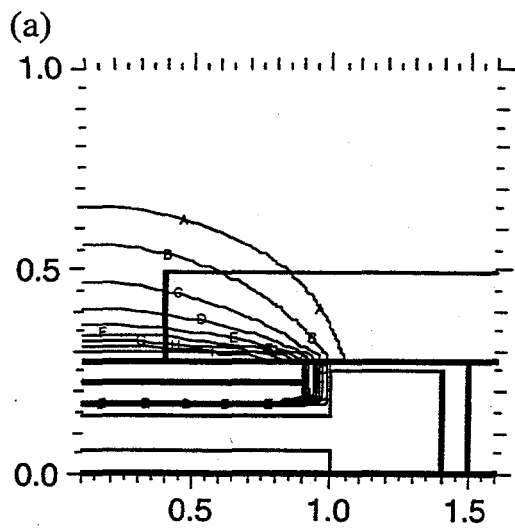


Fig. 5. Temperature profiles at the end of the pulse for different pulse lengths ($a = 20$ ms, $b = 60$ ms, $c = 200$ ms, $d = 600$ ms, $e = 2000$ ms). The contour levels are: $A = 40^{\circ}\text{C}$, $B = 50^{\circ}\text{C}$, $C = 60^{\circ}\text{C}$, $D = 70^{\circ}\text{C}$, $E = 80^{\circ}\text{C}$, $F = 90^{\circ}\text{C}$, $G = 100^{\circ}\text{C}$. The vertical axis is radial and the horizontal axis is axial with distances labeled in mm.



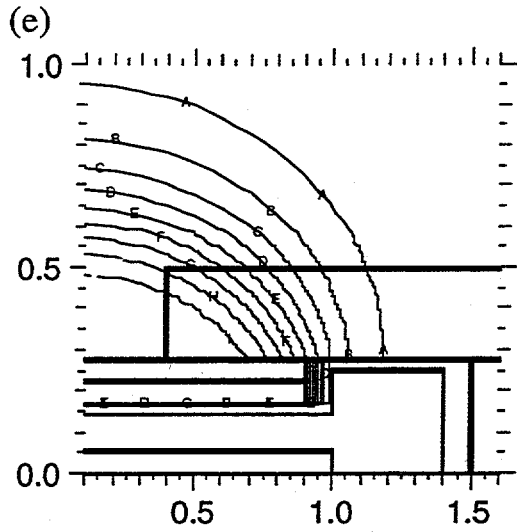


Fig. 6. Amount of damaged tissue at the end of the pulse train (a = 20 ms, 2035 pulses; b = 60 ms, 442 pulses; c = 200 ms, 65 pulses; d = 600 ms, 8 pulses; e = 2000 ms, 2 pulses). The contour levels are for N_d / N_{tot} : A = 0.1, B = 0.2, C = 0.3, D = 0.4, E = 0.5, F = 0.6, G = 0.7, H = 0.8, I = 0.9. The vertical axis is radial and the horizontal axis is axial with distances labeled in mm.

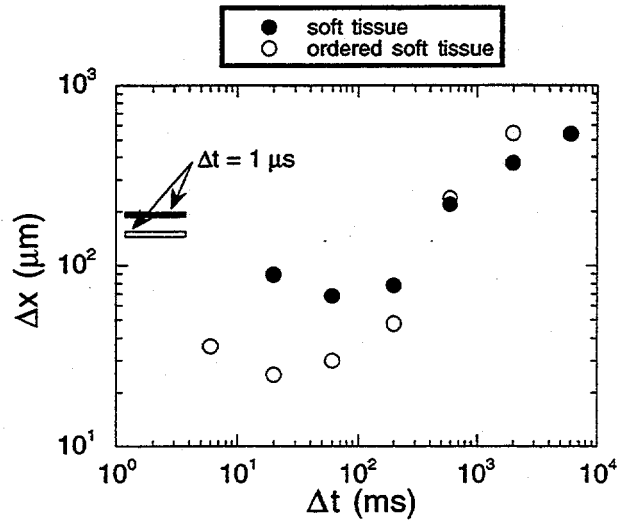


Fig. 7. Depth of damage zone vs. pulse width.

The pulse delay τ is determined by continuing the simulation out to long times. The condition that we take is that the temperature rise from N pulses at the total treatment time $N\tau$ should be less than $\Delta T = 3^\circ\text{C}$, that is

$$\left[T_{\max}(t = N\tau) - T_{\text{body}} \right] N = \Delta T . \quad (6)$$

An example is shown in Fig. 8. A summary of the results of the simulations for soft tissue is given in Table II. Note that there is an optimal $\Delta t=200$ ms which minimizes $N\tau$ while keeping $\Delta x < 100 \mu\text{m}$.

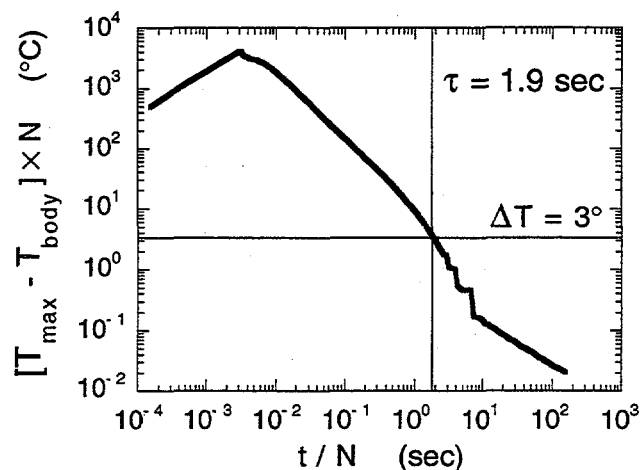


Fig. 8. Average temperature rise vs. pulse delay ($\Delta t = 200$ ms).

Δt (ms)	N	τ (sec)	$N\tau$ (min)	Δx (μm)
20	2035	1.7	57	89
60	442	0.54	4.0	68
200	65	1.9	2.1	78
600	8	15	2.0	220
2000	2	33	1.1	371
6000	1	47	0.8	540

Table I. Parameters used in the simulation.

5. DISCUSSIONS AND CONCLUSIONS

It is possible to control the zone of damage by use of pulsed laser irradiation. The minimum size of this zone is determined by the thickness of the layer over which the laser energy is deposited. The delay between pulses is determined by the time it takes the tissue to cool down. For a $60 \mu\text{m}$ thick collagen layer dyed with ICG, one can limit the zone of damage to $80 \mu\text{m}$ by applying 65-200 ms pulses over the course of 2 min. This treatment protocol minimizes the treatment time while keeping the zone of damage to less than $100 \mu\text{m}$ in thickness.

6. ACKNOWLEDGMENTS

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