The Physical Response of Soft Musculoskeletal Tissues to Short Pulsed Laser Irradiation

by

Marta Lyselle Dark

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The University of Virginia, 1992

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Submitted to the Department of Physics on May 14, 1999 in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy in Physics

ABSTRACT

An experimental study was performed to determine the physical properties of knee meniscus using a low energy laser technique. Following irradiation by a 10 ns laser pulse, tissue undergoes thermoelastic expansion in response to laser-induced stresses. The stresses evolve, propagating through the tissue. If they exceed the material’s strength, ablation occurs—the material ruptures. Below ablation threshold, the material remains in an expanded state until thermal relaxation occurs. We use numerical methods to solve the 3-D thermoelastic wave equation for a hydrated sample. In addition to thermoelastic expansion, expansion due to the formation of cavitation bubbles within the tissue was modeled. Cavitation occurs when tensile stresses rupture fluid.

The laser-induced response of a gelatin phantom was measured with a Michelson interferometer and compared with predictions. Using gelatin as a tissue model provided a consistent experimental model of meniscus. Meniscus, like all biological tissue, is highly heterogeneous. By adapting the time dependent numerical solution of the wave equation, the measurement of physical properties of a hydrated sample became possible. The thermoelastic model depends on sound speed, Poisson’s ratio, thermal expansion coefficient, and optical penetration depth. Once the behavior of gelatin was understood, human knee meniscus was studied. The thermoelastic model and experiment, allows measurement of physical properties of meniscus. Also, a numerical model of cavitation based on Rayleigh’s equations was developed. By comparing experiment and theory in menicus and water, we determined properties important to cavitation: threshold pressure, bubble density, surface tension and nucleation size.

Finally, histology was compared with experiment. The presence and amount of cavitation displacement was correlated with the condition of meniscus. Physical properties can be used to diagnose degenerative cartilage. This research has increased understanding of the interaction of short laser pulses with cartilage tissue, and measured significant physical properties of knee meniscus with a minimally invasive laser technique.

Thesis Supervisor: Michael S. Feld
Title: Professor of Physics
To Sallie Louise Hall Scales, the only grandmother I had the opportunity to know, without whom neither I, nor this thesis, would be possible.

We miss you Nana.

April 30, 1910 – April 15, 1999
Acknowledgements

My MIT experience began with two sentences spoken by Dr. James Turner (MIT ’71) to me at Metropolitan AME Church in Washington, DC. As I remember, he simply said, “Go ahead and apply. You can get in.” So I applied, and was thrilled when my brother Cedric read my letter of acceptance over the phone. How naïve! I am ecstatic to be finishing this chapter of my life. My years at MIT were the most difficult years of my life. However, I survived and wish to thank many people for their roles in helping me survive and succeed.

First, I would like to acknowledge my research advisor, Michael Feld. He provided the laboratory, the research, the funding and the support that allowed me to mature as a scientist. Irving Itzkan and Lev Perelman both contributed immensely to this research from beginning to end: experiment, theory, and analysis. Ramachandra Dasari supported my goals throughout my years here. Douglas Albagli taught me about lab research first hand, and authored the thesis that laid the foundation for my work. Dr. Jonathan Schaffer contributed his orthopedic expertise and meniscus samples. Dr. Maryann Fitzmaurice performed the histology. My committee members gave helpful suggestions and were “nice guys”: Saul Rappaport, Toyo Tanaka, and Nicolaas Bloembergen.

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One good thing MIT has given me has been the opportunity to make friends with some wonderful people. The Physics Education Office was a place to go for solace. Peggy Berkovitz and Pat Solakoff have always been sympathetic. I treasure my friends who have since graduated and moved on to better things: Caterina Riconda, Pamela Blakeslee, and Gillian Reynolds. Anat Shiloach lived with me for five years and listened kindly to my whining throughout. Ibo Matthews helped me pass part I of the general exams and challenged me during his years here. Many others encouraged me at different points in seven years of “mood swings”: Robbin, Kimani, Nicole, Kaz, Grum, Tehani, Bill, Jermane, Alison, Lyndie, Yool, and Tica. Finally I wish to acknowledge Sandra Brown, without whose friendship I would have gone insane, cried alone, drank myself stupid many times, and possibly stepped in front of a bus.

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<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Cavitation bubble radius, μm</td>
</tr>
<tr>
<td>α</td>
<td>Normalized bubble radius, unitless</td>
</tr>
<tr>
<td>β</td>
<td>Thermal expansion coefficient, K⁻¹</td>
</tr>
<tr>
<td>c_L</td>
<td>Longitudinal sound speed, m/s</td>
</tr>
<tr>
<td>c_T</td>
<td>Transverse sound speed, m/s</td>
</tr>
<tr>
<td>C_v</td>
<td>Heat capacity at constant volume, J/g-K</td>
</tr>
<tr>
<td>D</td>
<td>Optical penetration depth, μm</td>
</tr>
<tr>
<td>Δ</td>
<td>Grid cell size in numerical modeling, μm</td>
</tr>
<tr>
<td>Δt</td>
<td>Time step in numerical modeling, ns</td>
</tr>
<tr>
<td>E</td>
<td>Young’s modulus</td>
</tr>
<tr>
<td>ε</td>
<td>Energy density, J/m³</td>
</tr>
<tr>
<td>Φ</td>
<td>Laser fluence (energy/beam area), mJ/mm²</td>
</tr>
<tr>
<td>g₀</td>
<td>Geometrical correction factor, unitless</td>
</tr>
<tr>
<td>γ</td>
<td>Surface tension per unit area, kg/s</td>
</tr>
<tr>
<td>Γ</td>
<td>Grüneisen coefficient</td>
</tr>
<tr>
<td>I</td>
<td>Intensity, W/m²</td>
</tr>
<tr>
<td>κ</td>
<td>Thermal diffusion coefficient, mm²/s</td>
</tr>
<tr>
<td>λ</td>
<td>Laser wavelength, nm</td>
</tr>
<tr>
<td>μₐ</td>
<td>Absorption coefficient, mm⁻¹</td>
</tr>
<tr>
<td>μₛ</td>
<td>Reduced scattering coefficient, mm⁻¹</td>
</tr>
<tr>
<td>n</td>
<td>Bubble density, μm⁻³</td>
</tr>
<tr>
<td>ν</td>
<td>Poisson’s ratio, unitless</td>
</tr>
<tr>
<td>P</td>
<td>Pressure, atm</td>
</tr>
<tr>
<td>p_th</td>
<td>Threshold pressure, atm</td>
</tr>
<tr>
<td>r</td>
<td>Radial coordinate, μm</td>
</tr>
<tr>
<td>R</td>
<td>Aspect ratio, unitless</td>
</tr>
<tr>
<td>ρ</td>
<td>Mass density, g/cm³</td>
</tr>
<tr>
<td>R₀</td>
<td>Initial radius of cavitation bubble, nucleation site size, nm</td>
</tr>
<tr>
<td>S</td>
<td>Surface displacement, nm</td>
</tr>
<tr>
<td>S₀</td>
<td>Equilibrium surface displacement, nm</td>
</tr>
<tr>
<td>σₖ</td>
<td>Stress tensor, atm</td>
</tr>
<tr>
<td>t</td>
<td>Time coordinate, ns</td>
</tr>
<tr>
<td>tセル</td>
<td>Collapse time of a cavitation bubble, ns</td>
</tr>
<tr>
<td>T</td>
<td>Temperature, K</td>
</tr>
<tr>
<td>τₑ</td>
<td>Inertial confinement time, ns</td>
</tr>
<tr>
<td>τₚ</td>
<td>Duration of laser pulse, ns</td>
</tr>
<tr>
<td>uᵢ</td>
<td>Thermoelastic displacement vector, μm</td>
</tr>
<tr>
<td>V_TOT</td>
<td>Sum of of cavitation bubble volumes, μm³</td>
</tr>
<tr>
<td>w</td>
<td>Radius of laser beam, μm</td>
</tr>
<tr>
<td>z</td>
<td>Axial coordinate, nm</td>
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</table>
Chapter 1
Introduction

The laser is currently used as a surgical tool in many medical fields, including ophthalmology, dermatology, and dentistry. These applications often involve the cutting and removal of biological tissue, called laser ablation. Lasers are used to sculpt the corneal surface in order to improve the vision of nearsighted patients in a technique called photorefractive keratectomy. Cosmetic applications of infrared wavelength lasers in dermatology include tattoo and wrinkle removal. A laser based dentist’s drill, although more expensive than current mechanical drills, has advantages such as reduced noise and less apprehension for patients.

Attempts at using lasers such as the carbon dioxide and Nd:YAG lasers for tissue removal purposes in orthopedic surgery were not as successful. Lasers have not become popular in orthopedics as in other medical specialties. It appears that the laser has no advantage over current orthopedic tools used for cutting bone and cartilage tissue. However, laser light may prove useful in diagnosing mechanical properties of orthopedic tissues. A useful apparatus for orthopedic surgeons would be a device that distinguishes between normal and degenerate cartilage. Such a device might provide orthopedic surgeons with an instrument of precision that determines which sections of cartilage to remove and which to leave intact. An important step in deciding whether or not lasers can be used as diagnostic tools is to determine the behavior of these tissues when irradiated with laser light.

The purpose of this work is to develop a minimally invasive method, and then use it to determine physical properties of human meniscus, a fibrocartilage of the knee joint, by studying its thermomechanical response to nanosecond laser pulses. As part of this work certain mechanical, optical, and thermal properties of meniscus were measured. A histological study of meniscus was performed as well. Physical properties were compared with experimental and theoretical results in order to determine possible correlations between laser-induced response and tissue pathology. A medical goal of this thesis was to determine if a method based on interferometric monitoring of a tissue’s surface can be used as a diagnostic for orthopedics.
1.1 Literature Review

1.1.1 Lasers in orthopedics

Lasers have found many uses in a variety of medical specialties, such as ophthalmology, dermatology, and urology. However, laser applications in orthopedics have been quite limited. The use of the carbon dioxide and neodymium: yttrium-aluminum-garnet (Nd:YAG) lasers in the early 1980's as cutting tools for arthroscopic surgery resulted in little success. The efficiency of current mechanical instruments utilized in orthopedic surgery has prevented the adoption of lasers in this specialty. However, scientific studies continue to illuminate this field of laser use, and the possibilities for diagnosis and treatment of orthopedic disorders remain.

Investigations of laser effects in cartilage have focused mainly on laser ablation of these tissues, because lasers were considered a treatment tool. Orthopedic laser studies have used mainly four lasers: carbon dioxide (CO₂), neodymium: yttrium-aluminum-garnet (Nd:YAG), holmium:YAG (Ho:YAG), and erbium:YAG (Er:YAG). The wavelengths of these lasers are 10.6 μm, 1.06 μm, 2.1 μm and 2.94 μm, respectively.

Sherk et al found an average zone of meniscal tissue damage of 447 μm following irradiation with a continuous wave CO₂ laser (power = 20 W). The ablated surface also showed carbon char. [Sherk et al, 1995] Whipple et al performed electron microscopy following CO₂ laser irradiation (λ=10.6 μm) to find laser-induced effects not visible with staining and light microscopy. Areas of fifteen human menisci were ablated (beam diameter = 2 mm and power = 10, 20, and 30 W), and the tissue surrounding the ablated surface was observed at distances from 0 to 300 μm. Individual collagen fibers were no longer visible at 42,000x magnification, and cellular changes ranged from disruption cell membranes to complete cell disruption. [Whipple et al, 1987]

Buchelt et al investigated Ho:YAG and Er:YAG ablation of meniscus and intervertebral disc. The Ho:YAG (λ=2.12 μm, τₚ=250 μs) laser beam was delivered to excised tissue samples by a quartz fiber of core diameter 800 μm. An ablation threshold was found to be 18 J/cm², but smoke formation and tissue shrinkage occurred. Ho:YAG ablation caused thermal damage around the ablated crater from 120 to 240 μm. The damage was
carbonized debris, tissue necrosis, and disruption of collagen fibers. One interesting result of Ho:YAG ablation was shrinking of the tissue, particularly during irradiation of nucleus pulposus. The Er:YAG beam was delivered to the meniscus surface via lenses and mirrors (diameter = 500 μm). The Er:YAG ablation resulted in a damaged region of 20 to 60 μm, with coagulation and the loss of the fibrillar appearance of collagen. The ablation threshold for the Er:YAG laser was 1 J/cm². [Buchelt et al, 1992]

Buchelt et al compared excimer and CO2 ablation of meniscus. A XeCl excimer laser (λ=308 nm, τp=130 ns) was delivered with a 600 mm diameter fiber. The ablation process was characterized by no charring or smoke formation. A blue fluorescence emission was observed during irradiation. A 5 to 10 μm zone of thermal coagulation bordered the ablation crater. CO2 irradiation resulted in smoke formation, tissue shrinkage and large areas of charred tissue. [Buchelt et al, 1991] Typical surgical lasers operating in the infrared cause thermal damage that would not happen using standard surgical tools, and lasers do not appear to be an advantageous method of removing orthopedic tissues. However, Buchelt et al suggested that the Ho:YAG laser may be useful to treat protruding discs. [Buchelt et al, 1992]

Prodoehl et al also studied excimer laser ablation of meniscus and femoral articular cartilage. The XeCl excimer laser (λ=308 nm, τp=135 ns) was used to perforate cartilage samples. This research found a 10 to 50 μm zone of tissue damage surrounding the ablated crater. Cell clusters less than one cell diameter away from the ablated area had clearly intact nuclei. They assume that ablation by XeCl laser was primarily non-thermal and preferable to lasers that produce thermal ablation, although the degree of damage from propagating acoustic waves was unknown. [Prodoehl et al, 1994]

Akai et al used a rat knee model to study effects of low intensity irradiation (λ = 810 nm, Ga-Al-As semiconductor laser) on bone and cartilage during joint immobilization. Immobilized joints lost bone density in the tibia and femur, and laser irradiation showed no stimulatory effect. However, articular cartilage maintained stiffness with laser energies of 40 and 60 mJ, when compared with immobilized joints that received no irradiation. [Akai et al, 1997] Although laser removal of orthopedic tissues has unwanted thermal effects, low energy irradiation may be useful for its stimulatory effect on cartilage.
1.1.2 Gelatin Phantoms

Researchers commonly use gelatin-based models to investigate laser effects on soft biological tissue. Gels provide a simple, controllable medium in which to perform basic studies of the laser-tissue interaction. Dyes, both organic and inorganic, are typically added to absorb a particular laser wavelength. Rastegar et al made agar gel phantoms containing black india ink to study ablation using an argon laser. They measured an “ablation velocity”, defined as the sample thickness divided by the time needed to drill through the sample. [Rastegar et al, 1988] Sathyam et al used a gelatin containing Direct Red 81 as an absorber to model arterial clots in vessels. Using 1 μsec pulses of 577 nm light, these researchers irradiated bulk samples of gel under water, and cylindrical forms (inner diameter = 3 mm, l = 1-2 cm) of gel in tubes. Measurements of ablation thresholds and efficiencies were obtained. They determined from their gelatin phantom experiments that laser wavelengths between 410-590 nm were most suitable for removing blood clots. [Sathyam et, 1996] Oraevsky et al used 5% collagen gels containing with potassium chromate to study laser ablation at temperatures below 100° C. These researchers used gelatin as a model medium with optical and thermomechanical properties that simulate soft biological tissue. [Oraevsky et al 1996] The majority of these studies are performed in order to study the process of gelatin removal by laser pulses, i.e. laser ablation. Gelatin is a standard experimental model used to model the effects of laser light, particularly pulsed lasers, on tissue.

1.1.3 Laser-induced bubble formation and cavitation

It has been well established in the literature that laser pulses can be used to create vapor and cavitation bubbles in aqueous solutions. There are several mechanisms, which depend on the pulse duration, boundary conditions and incident energy density. Slow vaporization occurs for long pulses at laser energies generating temperatures in excess of 100° C. In this case vapor bubbles form, and liquid is ejected during the laser pulse. For short pulses at similar fluences, explosive vaporization occurs and material is ejected late into the pulse or after the pulse ends. For pigmented microparticles in an aqueous suspension, short pulses are absorbed, and the particles’ temperature greatly exceeds that of the surrounding

Cavitation is also associated with laser-induced plasma formation in liquids. In this case, a cavitation bubble will form following the expansion of plasma created at the laser beam’s focus. [Juhasz et al, 1994; Noack et al, 1998] Finally, for short pulses and energy densities below the vaporization threshold, the tensile stress component of a propagating bipolar acoustic wave causes the rupture of the liquid medium. It is this type of cavitation caused by pressure reductions that is most relevant to the studies of this thesis.

Paltauf et al [1992] used schlieren photography to observe the ablation of an aqueous dye solution following irradiation by 8 ns pulses. The beam diameter, 2 mm, is greater than the absorption depth, D = 530 µm; thus, the stress waves propagate primarily in the direction normal to the surface. They observe cavitation in the liquid in the region under tensile stress. The transition from compression to tension produces a high gradient in refractive index and appears as a dark bar on the photographs, and the bubbles’ shadows appear as dark spots.

Paltauf and Schmidt-Kloiber [1996] used 20 % gelatin in an aqueous solution of distilled water and orange G, and studied the dynamics of microcavities in water and gel caused by Q-switched Nd:YAG pulses (second harmonic, λ = 532 nm, τp = 8 ns). In these experiments, the diameter of the irradiated area is much larger than the optical penetration depth (diameter/depth ≈ 6–8). Stress waves propagate in a direction normal to the surface. Paltauf and Schmidt-Kloiber focused a cw He-Ne beam into a glass sample cell to 50 microns. The beam was directed to a photodiode. Formation of a bubble caused a transient decrease in the photodiode signal. Using this method, they could obtain qualitative measurements of bubble radius versus time curves at low laser fluences where no coalescence of bubbles took place. They measured bubble lifetimes of 3 µs and maximum radii of 10 microns in water for a fluence of 0.7 J/cm². In gelatin for a fluence of 5 J/cm², they measured lifetimes of 10 µs and radii of 25 microns. These findings are significant to this study because we wish to study the formation of cavitation bubbles under similar conditions: nanosecond laser pulses, hydrated samples, low laser fluences ~ 1 J/cm².

A second group of researchers used the flash photography technique to observe the
ablation of aqueous dye and gelatin by a 14 ns Nd:YAG pulse (third harmonic, $\lambda = 355$ nm). [Oraevsky et al, 1996] In aqueous potassium chromate, which was added to provide UV absorption, they observed the growth, coalescence, and collapse of cavitation bubbles. They suggest that the minimum value of tensile stress for cavitation to occur is 8 to 14 bars, which corresponds to temperature increases of 4 to 6° C in aqueous solutions. The basic characteristics of these experiments are similar to our own: nanosecond duration pulses, liquid or liquid containing samples, and sub-vaporization energies. Therefore, it is quite reasonable, based on these observations, to expect that cavitation will be significant to the experiments of this work.

1.2 Previous Work at MIT

Earlier work studying the fundamental mechanisms of pulsed laser ablation of biological tissue was begun by Dr. Douglas Albagli and is described in his Ph.D. thesis [Albagli, 1994]. His work consisted of a theoretical and experimental study of the ablation process in homogeneous solid materials: glass, acrylic, and bone. A summary of the results, which are important to this thesis, follows. These results, obtained by Dr. Albagli and our colleagues at the Spectroscopy Laboratory, were summarized in the Proceedings of the National Academy of Sciences. [Itzkan et al, 1995]

This previous work in hard tissues is important because it provides a theoretical and experimental foundation for the work of this thesis, which deals mainly with soft tissues. In studying the effects of a nanosecond laser pulse on cartilage, a biological tissue of high water content, it is important to note that this interaction is primarily a thermomechanical one. When the pulse duration is shorter than both the acoustic relaxation time and thermal diffusion time, ($\tau_p < D/c_L$, $\kappa/D^2$; $D =$ optical penetration depth, $c_L =$ longitudinal sound speed, $\kappa =$ thermal diffusion coefficient) photomechanical processes dominate the laser-tissue interaction. A material absorbs a laser pulse, and the resulting temperature distribution creates internal stresses, which propagate as acoustic waves. The material responds through thermoelastic deformation. This deformation can be described by the thermoelastic wave equation, which is discussed in the following section.
This work established that the ablation of solid materials by short laser pulses is a photomechanical phenomenon. The current work is not concerned with the ablation of cartilage, but with its physical properties and its response to pulsed laser light at sub-ablation energies. Because laser-induced thermoelastic deformation occurs in cartilage, we describe the significant results in the following sections. The Michelson based interferometer is briefly discussed in Section 1.2.2. It is the experimental technique used in this thesis and will be described in detail in Chapter 3.

1.2.1 Theory

For ablation using short pulsed lasers, it was suggested that photomechanical effects play the most significant role. It is presumed that the material will fail wherever the induced tensile stresses exceed the tensile strength, since most materials are weaker in tension than in compression. For the lasers and wavelengths used in ablating biological tissue, the optical absorption depth is usually comparable to the transverse laser dimension (beam diameter), and a three dimensional model was necessary. The fully time dependent three-dimensional equations were solved, which predict that significant tensile stresses are created on the surface, precisely where ablation is observed to occur.

When a material absorbs and is heated by laser energy, the resulting non-uniform temperature distribution causes internal forces, which lead to thermoelastic deformation. This deformation in a solid body is determined by the thermoelastic wave equation [Landau and Lifshitz, 1986]:

$$
\rho \frac{\partial^2 \mathbf{u}}{\partial t^2} - \frac{E}{2(1+\nu)} \nabla^2 \mathbf{u} - \frac{E}{2(1+\nu)(1-2\nu)} \nabla(\nabla \cdot \mathbf{u}) = \frac{-E\beta}{3(1-2\nu)} \nabla T,
$$

subject to the appropriate initial and boundary conditions, where \(\mathbf{u}\) is the displacement vector, \(\rho\) is the density, \(E\) is Young's modulus, \(\nu\) is Poisson's ratio, \(\beta\) is the thermal expansion coefficient and \(T_L\) is the laser-induced temperature increase above a uniform ambient level. Equation 1.1 is Newton's second law with mass (density) times acceleration set equal to the internal elastic forces plus the force generated by the thermal gradient. The laser-induced stresses can be determined from the displacement vector using the stress-strain relation.

For sub-threshold laser fluences, the problem can be divided into four regimes,
governed by 1) inertial confinement, 2) a transient regime, 3) a quasi steady-state equilibrium, and 4) relaxation by thermal conduction. In the first regime, the absorption of the short laser pulse is essentially a delta function in time. Since nothing has had time to move, the initial stresses can be found from the stress-strain relation by setting all displacements and their first derivatives equal to zero. These stresses serve as the initial conditions for the second regime. In the second, or transient regime, the material reconfigures itself to return the net force to zero. This lasts for a period of time approximately equal to L/c, where c is a speed of sound in the material and L is a characteristic length. A fully time-dependent numerical solution was developed that integrates the thermoelastic wave equation to find the transient stresses and resulting strains. [Itzkan et al, 1995]

In the third, or quasi steady-state regime, the system reaches equilibrium and the net force in any direction is zero. However, individual stress components are not zero and can be appreciable. Even though the transients have ceased, quasi steady-state thermoelastic stresses exist due to the persistence of the non-uniform temperature distribution. In the fourth, or thermal relaxation regime, stresses decay to zero as thermal conduction causes the temperature distribution to become uniform.

Two important results came from the numerical solution. The theoretically predicted movement on axis at the surface (z=0, r=0) is a unique measure of the important optical and mechanical properties of the material. Features in the surface expansion versus time curve allow determination of \( c_L \), the longitudinal speed of sound, \( \nu \), the Poisson ratio, the optical penetration depth, \( D \), the ratio of the expansion coefficient to the heat capacity, \( \beta/C_v \), and the stresses can be calculated from the now known parameters and displacements. By measuring the time dependent displacement at \( z=0 \) and \( r=0 \) at sub-threshold fluences, we could determine all the physical parameters and stresses of the material under study.

The second significant result was that substantial tensile stresses are generated directly on the surface (\( z=0 \)), where ablation is observed to occur. The numerical model showed the time evolution of the radial stress on the surface as a function of radial position during the transient regime. The stress oscillates between compression and tension, and the tensile stresses are nearly 50% of the initial peak compressive stress. The numerical solution revealed that important tensile stresses also persist into the quasi steady-state regime. The quasi steady-
state circumferential stress contained a large tensile component on the surface just outside the irradiated area for a "top-hat" initial temperature distribution. The confined hot material attempts to force the cold surrounding material outward. Even though the quasi steady-state stresses were smaller than the transient stresses they persist for eight orders of magnitude longer in time. It is the large tensile stresses that rupture the material at laser-induced temperatures well below vaporization.

1.2.2 Experiment: Interferometry of homogeneous solid samples

The experimental apparatus consisted of an interferometric surface monitoring probe and an intense pump laser to provide the thermal input pulse. [Schaffer et al, 1995] A detailed schematic of the apparatus will be found in chapter 3. The pump beam is a 7.5 ns, frequency tripled, Q-switched Nd:YAG laser operating at a wavelength of 355 nm. The beam passes through a 3 mm aperture and is then demagnified and reimaged onto a spot on the target surface whose diameter can be varied from approximately 750 μm to 1 mm. The interferometer can measure the laser induced surface movement of a target material with a spatial resolution of ≈ 4 nm and a temporal resolution of ≈ 3 ns. The laser-induced thermoelastic expansion is measured by a Michelson interferometer, which uses a He-Ne probe laser: the sample is the end mirror in one arm, and a rotating corner cube prism is included in the reference arm. The diameter of the probe is approximately 50 μm. This apparatus allows the direction as well as the speed to be measured; thus, the surface position as a function of time can be determined. Experimental data were collected for several materials, including an acrylic (acrylite FF, Cyro) and glass filters (GG 375 and BG 18, Schott). Bovine tibial cortical bone was scraped of excess soft tissue, and polished to obtain a smooth surface for better light reflection of the helium-neon beam.

The surface displacement of acrylic increased linearly with laser fluence Φ, but the temporal features remained constant. These features include an exponential surface rise to the quasi-steady state value and two small contractions that correspond with longitudinal and transverse acoustic waves propagating from the beam's edge to the centered helium-neon probe. All the features previously described agreed very well with the theory. The measured
quasi steady-state displacement versus fluence for acrylic and glass were linear as expected. For glass, the agreement with theory was excellent, even to ablation threshold $\Phi \sim 30 \text{ mJ/mm}^2$.

We studied the onset of ablation in cortical bone, a tissue whose behavior is similar to that of acrylic. Although there was general agreement between the measured and predicted displacement, the predicted contractions were “washed out.” For a turbid media such as bone, scattering within the target will change the temperature distribution and blur the sharp temperature gradient at the radial edge of the laser beam. The agreement between theory and experiment was greatly improved when scattering effects were considered.

In the apparatus, the probe beam can be translated across the sample’s surface relative to the pump beam, so that it can be positioned at different radii. Off-center monitoring also allowed us to observe the behavior of the rim during ablation. Although the surface was destroyed once ablation occurred and material was ejected, we monitored the surface outside the irradiated area to determine when ablation occurred. Ablation of bone occurred approximately 350 ns after the laser pulse. There was an abrupt departure from the theoretical curve, the surface at the rim experienced a large contraction to a position 200 nm below the original surface position, followed by a slow recoil expansion for several microseconds to the limit to which we monitored time in this measurement. This experiment was repeated for acrylic and surface damage was observed under a microscope. The appearance of surface damage always corresponded with the large negative surface motion of the rim.

1.2.3 Summary

In order to understand the photomechanical model of ablation, both a theoretical model and experimental apparatus were developed in this laboratory. We developed a three dimensional model that is appropriate for the wavelengths and absorption depths involved in ablation of hard tissue, i.e. bone. A numerical technique was developed to find a time dependent solution in the earlier regimes. The numerical model predicts the propagation of tensile stresses through the irradiated volume. A Michelson based interferometer was developed with nanosecond, nanometer resolution. The interferometer was used to verify the theoretical model and measure physical properties of bone, acrylic, and glass at sub-threshold
fluences. Ablation of bone occurred for laser-induced temperatures of 20°C, but the associated stresses were ~ 400 bars. These results support the conclusion that the mechanism of ablation is photomechanical when the pulse duration is smaller than the inertial confinement time, \( \tau_p < \tau_{ic} \approx D / c_L \). This previous work provides a foundation for the study of the physical response of cartilage tissue to pulsed laser irradiation. The Michelson interferometer needed modifications in order to make careful investigation of meniscus possible. Laser-induced elastic deformations of cartilage, a soft tissue containing \( \sim 70\% \) water, were qualitatively different from those of hard tissue; only one small contraction was observed. The prediction of propagating tensile stresses suggests that the formation of cavitation bubbles in cartilage and water may occur. Cavitation, a physical phenomenon not present in hard tissue, further alters the surface expansion of the tissue. The dynamics of cavitation bubbles, as applicable to the laser-meniscus interaction, will be investigated in this work.

1.3 Objectives, Outline, and Accomplishments of This Work

The primary objective of this thesis is to understand the physical response of knee meniscus, a soft hydrated tissue, to sub-ablation nanosecond laser pulses. We will also extract mechanical, optical, and thermal properties of meniscus without damaging it. In order to reach such an objective, it was first necessary to review the biological structure and function of meniscus within the knee joint. Chapter 2 details the structure of cartilage, a hydrated tissue composed of water in an extracellular matrix with a sparse number of cells. To understand the laser light distribution, the optical properties of meniscus at 355 nanometers were measured. The optical properties of tissue are reviewed in Chapter 2, and the measurements on meniscus are described.

Chapter 3 describes the initial interferometry of meniscus following a ten nanosecond laser pulse. These experiments observed interesting laser-induced behavior of meniscus and led to the questions that this thesis attempts to answer. The interferometer is explained in further detail. Interferometric monitoring of meniscus samples revealed the inhomogenous nature of the tissue and its varied responses. The variability of meniscus samples led to the development of a gelatin phantom. Physical properties of the gelatin phantom are detailed in Chapter 3.
Analytical and numerical solutions to the thermoelastic wave equation were developed in this laboratory as described above. Chapter 4 reviews the theory of elasticity and the one-dimensional analytical solution to the thermoelastic wave equation. The one-dimensional solution describes how tensile stresses develop and propagate in a tissue with an air-tissue boundary condition. The numerical solution to the thermoelastic wave equation is described as well. It was necessary to adapt this model, adequate for describing solid materials like bone, for mainly water samples such as meniscus, gelatin, and water. We discuss modeling of thermoelastic waves in a liquid in Chapter 4.

In Chapter 5, experimental results from the interferometric apparatus are compared with predictions of the numerical model in the sub-cavitation regime. From experiments performed in gelatin, saline, water, and meniscus, the thermoelastic response of a hydrated sample to a nanosecond laser pulse was well characterized. Physical properties of the samples were determined from the comparisons of experiment and theory.

A numerical model based on Rayleigh’s equation of motion for a bubble was developed in order to describe the growth and collapse of cavitation bubbles in tissue following a laser pulse. Chapter 6 describes the formulation of this numerical model. The transient pressure induced by the laser pulse develops a tensile component that is responsible for rupturing the liquid and causing cavitation. Bubbles open as the tensile wave propagates, creating local reductions in pressure. The numerical model calculates the size of these bubbles and sums their contributions to find the excess surface displacement that they cause in a sample. Using the interferometric surface monitoring apparatus, predictions of the model were compared with experiment in meniscus, water, and saline in this chapter. Cavitation is indeed responsible for excess expansion in water and water containing samples, not predicted by the thermoelastic theory.

The histology of meniscus is described in Chapter 7. The meniscus samples were sent for a light microscopy assessment following laser irradiation to determine the pre-existing condition of the tissue. Comparison between the experimental results and the tissue’s condition was made to find correlations. Conclusions and suggestions for future work stemming from this thesis are given in Chapter 8.
Chapter 2
Cartilage: Function, Structure, and Physical Properties

2.1 Overview

If we are to understand the response of cartilage to nanosecond laser pulses, we must understand the tissue itself in detail. We wish to know the microscopic and macroscopic structure of knee cartilage, information that is discussed in the orthopedic literature. Knowing what constituents make up cartilage, we gain further understanding of how light will interact with this biological tissue. It is important to know the optical properties of cartilage, because we are interested in its response to a short pulse of laser light. Since these studies are few in the literature, experimental measurements of the optical properties of meniscus were performed. Knowledge of meniscus properties guided the development of gelatin as an experimental model, and a theoretical model of a hydrated tissue’s response to a laser pulse.

In order to build a physical model of the laser-induced response of cartilage, it is necessary to understand its structure and physical properties. In Section 2.2, a review of the orthopedic literature describes the physiology of the knee joint and the important function that cartilage serves for a weight-bearing biped. Section 2.3 details the macroscopic and microscopic structure of cartilage, specifically meniscal cartilage. Most importantly, we learn that meniscus is mainly an acellular network of collagen fibers, with water composing 70-75% of its mass. It is essential to consider the water content in order to guide any modeling of meniscus. The changes in structure due to aging and disease, mainly arthritis, are also described in this section. Section 2.4 reviews studies of meniscus mechanical and optical properties. The Kubelka-Munk theory of diffuse irradiance, which is appropriate for a scattering, inhomogeneous sample such as biological tissue, is described. From this theory and spectrophotometer measurements, the optical absorption and scattering properties of meniscus was determined. Section 2.4 gives these optical properties of meniscal samples at \( \lambda = 355 \text{ nm} \), the wavelength of interest to this work.
2.2 The Function of Cartilage in The Knee Joint

Joints are an important part of the musculoskeletal system, as the point of connection between two bones. Joints that move freely are called diarthroidal or synovial joints, and some examples are found in the knee, elbow, and fingers. The knee is an important diarthroidal joint, allowing people to function in their daily lives, but causing enormous pain, inconvenience, and morbidity when the knee cartilage is dysfunctional, often due to injury related tears or osteoarthritic changes. Arthroscopic surgery is the technique used to repair damage in knee cartilage. In arthroscopy, surgeons make two incisions, one to insert a camera and one to insert surgical instruments. They flush any loose debris out of the joint with saline and/or remove loose flaps of cartilage around a tear. The final option for knee problems is a total joint replacement, and this surgery is quite common. According to the Center for Disease Control, in 1995 there were 314,000 total knee replacement surgeries in patients 65 years and older in the United States.

All diarthroidal joints have some common features. They are enclosed in a fibrous capsule, called the joint capsule. The inner surfaces of the capsule are lined with the synovium, a tissue which secretes the synovial fluid and provides nutrients to the cartilage in the joint. The bone ends (tibial and femoral surfaces in the knee) which make up the joint are covered with a layer of hydrated soft tissue called articular cartilage. In a diarthroidal joint, the synovial fluid, articular cartilage and supporting bone form the nearly frictionless, locomotive structures of the body. [Mow et al, 1992] Figure 2-1 shows an exposed knee joint as Dr. Jonathan Schaffer begins a total knee replacement.

In addition to articular cartilage on the tibial and femoral surfaces, the knee joint contains the medial and lateral menisci; two hydrated wedges of fibrocartilaginous tissue. Menisci have several biomechanical functions in the knee joint. They transmit loads applied to the joint, converting compression to circumferential tensile stress. During compressional loading, i.e. walking, the femoral condyle presses on the menisci, causing them to be radially displaced. This radial displacement transforms into circumferential tensile stress because the menisci are attached circumferentially by ligaments. Menisci absorb shock, provide stability, and lubricate the joint. [Ghosh and Taylor, 1987; MacConaill, 1931; Brantigan and Voshell, 1941; Shrive, 1978]
Figure 2-1. Exposed knee joint of patient undergoing total knee joint replacement. The femoral head is visible, and the yellowed surfaces are articular cartilage covering the bone surface.
2.3 Cartilage Structure

Meniscus is a crescent shaped tissue with a wedge shaped cross section, located between the tibial plateau and the femoral condyle (see Figure 2-2). It is attached to the tibia by the fibers of the extension of the anterior cruciate and the posterior cruciate ligaments. [Ghosh and Taylor, 1987] Meniscal tissue is a hydrated fibrous matrix, containing a small number of fibrochondrocyte type cells. Its fibrous extracellular matrix is composed mainly of collagen fibers with water comprising 70-75% of its total wet weight. The dry weight consists of approximately 75% collagen, 8-13% non-collagen proteins, and 1% hexosamine. The collagen fibers dominate the structure and mechanical properties of meniscus. Proteoglycans, which compose about 3% of the dry meniscus, are significant to the function of meniscus as well, adding compressive strength. [Adams et al, 1992]

Articular cartilage, or hyaline cartilage, in the knee joint is a few millimeters thick from the articular surface to the subchondral bone. It is glassy smooth and appears Bluish white, but degenerative cartilage loses this appearance. As articular cartilage ages, it appears yellowed and rough, and water content gradually decreases. Water content in osteoarthritic cartilage is higher than in normal cartilage. Water contributes from 60-85% of the total wet weight of hyaline cartilage. [Mow et al, 1990] Of the dry weight, collagen makes up about 60%; proteoglycans, 25-35%; and non-collagenous proteins and glycoproteins, 15-20%. Table 2-1 compares the composition of meniscal and articular cartilage. [Buckwalter and Mankin, 1997]

<table>
<thead>
<tr>
<th></th>
<th>Meniscal cartilage</th>
<th>Articular cartilage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Water</strong></td>
<td>70-75</td>
<td>60-85</td>
</tr>
<tr>
<td><strong>Dry weight composition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Collagen</strong></td>
<td>75</td>
<td>60</td>
</tr>
<tr>
<td><strong>Proteoglycans</strong></td>
<td>3</td>
<td>20-30</td>
</tr>
<tr>
<td><strong>Non-collagen proteins</strong></td>
<td>8-13</td>
<td>15-20</td>
</tr>
</tbody>
</table>
Figure 2-2. Schematic of the knee joint, showing cross sections of the menisci which sit between the heads of the tibia and femur. Adapted from [Bullough. 1992].
2.3.1 Collagen

The collagen molecule is a right-handed triple helix. Each chain, called an alpha (α) chain, is made up of a sequence of amino acids. In collagen, one of every three amino acids is glycine. Thus, collagen is characterized by an X-Y-Z triplet structure, where X denotes the glycyl residue. Glycine and proline are common amino acids in a triplet sequence. Figure 2-3 shows the chemical structure of a typical triplet sequence. Three α chains coil around each other to form the triple helix of collagen. Inter-chain hydrogen bonds and covalent cross-links support the triple helix. [Yannas, 1972]

![Triplet structure of collagen, glycine-proline-Z. Glycine has a hydrogen atom attached to the center carbon, and proline has CH₂ attached to the center carbon.](image)

The collagen within meniscus is composed of many molecular types of collagen. Types II, III, V, and VI are present in small amounts. Type I collagen is the most prevalent, accounting for more than 90% of the collagen present. Meniscus consists of coarse fiber bundles of type I collagen, while articular cartilage is dominated by finer type II collagen. [Fithian et al, 1990]

In the surface layer of meniscus, the collagen fibers are randomly oriented. Deeper into the tissue, fibers are circumferentially oriented in large bundles of 50-150 μm. A few radially oriented fibers are also present in the deep zone, serving to tie the large circumferential fibers together and adding shear strength. [Fithian et al, 1990]

2.3.2 Proteoglycans

Proteoglycans are present in both articular cartilage and meniscus, comprising less than 3% of the dry weight of meniscus and 20-30% of the dry weight of articular cartilage.
Proteoglycans are macromolecules made of one or more glycosaminoglycan chains (GAG's) that are covalently bound to a protein core. In cartilage, there are two classes of proteoglycans: large, high buoyant density proteoglycans and small, low buoyant density proteoglycans. The large proteoglycan forms when many chondroitin sulfate and keratan sulfate chains attach to a protein core. An aggregate is formed when 100-200 of the proteoglycan units bind to a chain of hyaluronic acid. The aggregates are large, hydrophilic structures that help to hold water in the tissue. The small proteoglycans have one or two GAG chains. They are called decorin or biglycan, respectively. [Adams et al, 1992]

The chondroitin sulfate has a sulfate (SO$_4$) and a carboxyl group (COOH) for each disaccharide unit. The keratan sulfate averages one SO$_4$ group per disaccharide. The SO$_4$ and COOH groups become ionized, exerting strong negative-negative charge repulsive forces. These electrostatic interactions are a fundamental cause of cartilage swelling and increase compressive strength of articular cartilage and meniscus. [Mow et al, 1992]

Proteoglycans may have an important role in maintaining the high water content of meniscus. The glycosaminoglycans contain many negatively charged sulfate ions, SO$_3^-$, and the tissue has a higher ion concentration than surrounding fluid. Water is thus forced into the meniscus by osmosis. [Mow et al, 1990] Electrolytes such as sodium, chloride, potassium and calcium are present in the fluid. Interactions between GAG sulfate ions and positively charged ions in the water may also help hold the water in the extracellular matrix. [Linn and Sokoloff, 1965; Myers et al, 1988] Proteoglycans may also affect the mechanical properties of meniscus in two additional ways. First, they form a reinforced fiber network with the
collagen fibers. Second, they may create a pre-stressed state of the collagen network. [Adams et al, 1992]

2.3.3 Cells

Meniscus is sparsely populated with cells called fibrochondrocytes. These cells are elongated in the surface layer of meniscus, and rounded in the deeper layers. Surrounding the fibrochondrocytes is a distinct “territorial matrix” of collagen fibrils, in which there is no cell-to-cell contact. The orientation of the fibrils is circumferential, providing a meshwork that surrounds the cell’s boundary. Immediately next to the cell is a layer of finer fibrils that may appear amorphous. [Adams et al, 1992] The function of these cells is to synthesize the fiber matrix and repair tears. However, meniscus has a limited ability to repair itself, as the bulk of the tissue is avascular. Approximately 20% of the outer surface area of the menisci is vascularized with capillaries at age 40. This has decreased from 50% of the outer region having capillaries in the newborn [Ghosh and Taylor, 1987].

Chondrocytes are present in articular cartilage, making up approximately 1% of the volume of adult human articular cartilage. Again, these chondrocytes do not make cell to cell contact, and are surrounded by extracellular matrix. The chondrocytes receive nutrients from the synovial fluid, which must pass through the synovium and the cartilage matrix before reaching the cells. In children, these cells produce new tissue to expand and remodel a growing articular surface. In adults, they replace degraded macromolecules by synthesizing collagen, proteoglycans, and non-collagenous proteins. [Buckwalter and Mankin, 1997]

2.3.4 Pathology of meniscus

The major disease that affects cartilage of the knee joint is arthritis (joint inflammation). Osteoarthritis is the most common type. Cartilage erodes from wear, eventually bones rub against each other, causing pain. Major risk factors for osteoarthritis in the knee are aging, obesity, and previous injuries. Rheumatoid arthritis has a greater affinity for small joints such as in the hand, wrist, or foot, but can affect the knee. Antibodies and antigens act in rheumatoid arthritis to alter the synovial fluid. Enzymes are formed which attack articular cartilage, meniscus, and soft subchondral bone in the joint. Rheumatoid
arthritis can irreversibly change the structure and function of a weight bearing joint, such as the knee, so that other degenerative changes occur. Gout is another type of arthritis where uric acid is deposited in joints and may crystallize. Cartilage and meniscus affected by gout would contain these crystal deposits.

Changes in knee meniscus composition accompanying osteoarthritis and rheumatoid arthritis are well documented in medical literature. As with aging, similar changes occur in the proteins of osteoarthritic joint menisci: collagen content decreases and levels of non-collagen proteins increase. Collagen content also decreases in joints affected by rheumatoid arthritis. [Ghosh et al., 1975] Data from menisci obtained from osteoarthritic joints were interpreted to indicate increases in proteoglycans at sites with degenerative change. In menisci affected by rheumatoid arthritis, proteoglycan content decreases. [Ghosh and Taylor, 1987] The water content of degenerative meniscus is higher when compared to control samples of matching age. [Herwig et al, 1984]

As meniscus and articular cartilage age, changes in its composition occur that are similar to the changes due to osteoarthritis. Collagen concentration from birth to the age of 30 years and remains generally unchanged until the age of 70 years. In the eighth decade, collagen content of meniscus begins to decline. The non-collagen proteins of the extracellular matrix show more significant changes with age. Meniscus of newborns contains 22% non-collagen proteins, which decreases to 8% between the ages of 30 and 70. After 70 years, these proteins increase to 12%. Differences due to aging were found in the proportions of glysaminoglycan types in the meniscus proteoglycans. The proportions of keratan sulfate relative to chondroitin sulfate on the proteoglycan monomer increased. The increase in keratan sulfate occurs in older articular cartilage as well. [McNicol and Roughley, 1980]

2.4 Physical Properties

Studies of meniscus mechanical properties are typically concerned with measurements of static strength and elastic moduli of the bulk tissue. These results are summarized here. A study of optical properties of meniscus by Vangness et al is reviewed in this section. Because the optical properties of meniscus are not well studied, a spectrophotometric analysis of meniscus samples was performed for this thesis. These results and the methods of determining
optical absorption and scattering coefficients in tissue are described. The results of a near infrared Raman spectroscopic study of meniscus are also included here.

2.4.1 Mechanical properties of meniscus

In Fithian et al, the compressional strengths of bovine cartilage are given. Compression studies were taken perpendicular to the tibial surface, and the results were 0.79 and 0.42 MPa for articular and meniscal cartilage, respectively. The higher compressional strength of articular cartilage as expected, given its higher concentration of proteoglycans, which resist compressional loads, (see section 2.3.2). The mean Young’s tensile moduli are given for human menisci by region. For the medial meniscus, Young’s moduli are 159.6, 93.2, and 110.2 MPa in the anterior, central, and posterior sections. For the lateral meniscus, Young’s moduli are 159.1, 228.8, and 294.1 MPa in the anterior, central, and posterior sections. [Fithian et, 1990]

The tensile strength properties within meniscus are complex due to its structural organization. The surface zone is weaker under tension than the deeper zones (60 MPa, 200 MPa), and this is attributed to surface collagen fibers being randomly oriented while fibers are circumferentially oriented deeper in the tissue. [Mow et al, 1992a]

2.4.2 Optical properties of tissue

Knee meniscus, like most other human biological tissues, is a turbid medium where scattering effects dominate absorption properties. Light propagation in meniscus can be described using the diffusion approximation to transport theory. These methods will be used in the following sections to calculate optical properties of meniscal tissue.

One study of meniscus optical properties was found in the literature, and is briefly described here. A spectrophotometric analysis of human meniscus was performed by Vangsness et al [1995] from wavelengths of 300 to 2500 nm. Similar absorption curves were noted for tissue from different zones (anterior, middle and posterior). Absorption peaks were found consistently at 300 nm, 2940 nm, and 2500 nm, with a smaller peak at 1440 nm. The absorption peak at 300 nm was attributed to collagen protein absorption of UV wavelengths. The remaining peaks observed were characteristic of water absorption in the infrared.
Measurements of the transmission and reflection properties of meniscal tissue were performed in order to determine optical penetration depth, which is necessary to understand the light distribution in meniscus (at incident wavelength $\lambda = 355$ nm specifically). The measurements of diffuse reflectance, $R$, and transmission, $T$, were obtained using a Shimadzu dual beam spectrophotometer equipped with an integrating sphere apparatus. The device uses barium sulfate plates as reflectance standards and integrates the light inside the chamber using a sphere of diameter $= 60$ mm. The spectrophotometer range of wavelengths is from 200 to 700 nm. Samples from the meniscus surface were prepared using a microtome. Tissue samples were placed between quartz slides for the integrating sphere measurements. The sample thickness of approximately 50 microns was chosen, and measured using a microscope to focus on top and bottom surfaces. The error in measuring the thickness is $\pm 20$ $\mu$m. The references by [Izatt, 1991] and [Cheong, 1990] detail the method of calculating optical properties of biological tissue from reflectance, transmission, ($R$ and $T$) and the sample’s thickness.

Kubelka-Munk theory

The Kubelka-Munk theory is a one-dimensional model of the propagation of diffuse irradiance through an isotropic slab with no reflection at the boundaries. [Kubelka, 1948] The light distribution is modeled as two diffuse counter-propagating light fluxes: $F_+$ and $F_-$. The slab has thickness $t$, with absorption coefficient $k$ and a scattering coefficient $s$. There are two directions of propagation in the slab, and the change in flux over a distance $dz$ can be described as follows:

$$\frac{dF_+}{dz} = -(k + s) \cdot F_+ + s \cdot F_-$$  $$\frac{dF_-}{dz} = (k + s) \cdot F_- + s \cdot F_+. \tag{2.1}$$

The flux is assumed to follow an exponential distribution with coefficient $\alpha$:

$$F_+ = C_1 \exp(-\alpha z); \quad F_- = C_2 \exp(+\alpha z). \tag{2.2}$$

By substituting equation 2.4 into equation 2.3 and solving for the coefficient $\alpha$ gives

$$\alpha = \sqrt{k(2s)} \cdot \tag{2.3}$$

The equations for $k$ and $s$ can be written in terms of the measured reflection and transmission coefficients $R$ and $T$ by using intermediate variables of $a$ and $b$. 30
\[ a = \frac{1 + R^2 - T^2}{2R} \]  
\[ b = \sqrt{a^2 - 1} \]  

Then, \( k \) and \( s \) can be written by the following equations:

\[ s = \frac{1}{b \cdot t} \ln \left( \frac{1 - R(a - b)}{T} \right) \]  
\[ k = s (a-1). \]

Some researchers have correlated the Kubelka-Munk coefficients \( s \) and \( k \) with the optical transport coefficients \( \mu_a, \mu_s, \) and \( g \) [Cheong et al., 1990; van Gemert and Star, 1987]. Van Gemert and Star provide a plot of the coefficients \( \eta \) and \( \chi \) which relate \( s \) and \( k \) to the transport properties:

\[ \mu_a = \eta \cdot k \]  
\[ \mu_s = \mu_s (1 - g) = \chi \cdot s \]

Thus, the reduced scattering and absorption coefficients can then be obtained from measured reflection and transmission. A linear approximation to the van Gemert and Star result, valid to within ~5%, for \( 0 \leq k/s \leq 2 \) is

\[ \chi \approx 1.333 + 0.245 \cdot \frac{k}{s} \]  
\[ \eta \approx 0.5 + 0.05 \cdot \frac{k}{s} . \]

The absorption and reduced scattering coefficients \( (\mu_a, \mu_s') \) were found by this method for a sample of meniscus. Figure 2-6 shows the values of these coefficients versus wavelength.

**Diffusion theory of light transport and penetration depth**

The theoretical basis of this work presumes that a non-uniform temperature distribution resulting from absorption of a laser pulse causes internal forces, which lead to thermoelastic deformation. The initial light distribution can be approximated by an exponential function of depth in the tissue \( (z > 0) \), with a radial profile dependent on the laser profile. Thus, the intensity of the light distribution will be

\[ I(r,z) \equiv I_0 L(r) \exp(-z / D) , \]
where L is the beam’s radial profile and D is the optical penetration depth. To find D and describe the propagation of photons in medium that scatters and absorbs, such as tissue, diffusion theory as an approximate solution to the transport equation is typically used. For a slab of thickness t, the intensity of a beam incident at the air-medium boundary attenuates with an effective attenuation coefficient \( \mu_{\text{eff}} = \sqrt[3]{3 \mu_a \left( \mu_a + \mu_s' \right)} \). [Star, 1995] The optical property needed to determine the initial light distribution is the optical penetration depth, D, defined by transport theory to be

\[
D = \frac{1}{\mu_{\text{eff}}} = \frac{1}{\sqrt[3]{3 \mu_a \left( \mu_a + \mu_s' \right)}}.
\]

Thus, the optical penetration depth of a tissue sample with known thickness can be calculated from measurements of diffuse reflectance and transmission.

The values of optical penetration depth, absorption and reduced scattering coefficients at the incident wavelength (\( \lambda = 355 \) nm) are given in Table 2-4. The mean penetration depth (± st. deviation) for meniscus is \( \overline{D}_{\lambda=355} = 250 \pm 38 \mu m \). This measurement will be useful to compare with penetration depths of meniscus obtained from fitting measured surface displacements of meniscus with the thermoelastic model predictions (Chapters 4,5). From the spectrophotometer results we can expect the penetration depth of meniscus samples to be between 200 and 280 microns.

In the numerical models of chapters 4 and 6, the initial temperature distribution directly follows the light intensity profile (eq. 2-12) and \( T(r,z) = T_0 \cdot L(r) \cdot \exp(-z/D) \). For a transparent medium with little to no scattering, such as water, the penetration depth is the inverse of the absorption coefficient \( D = 1/\mu_a \). In a turbid media such as tissue, the light is subject to both absorption and scattering; and penetration depth should be calculated using equation 2.13. We can approximate the three-dimensional temperature distribution in knee meniscus that attenuates with an effective penetration depth to be

\[
T(z) = \frac{I_0 \tau_p}{\rho C_v D} e^{-\gamma_D} = T_0 e^{-\gamma_D},
\]

where \( C_v \) is heat capacity (constant volume) and \( \rho \) is density. Laser-induced temperature is
\[ T_0 = \frac{\Phi}{\rho C_v D}. \]  

where \( \Phi \) is the laser fluence (energy/area).

Table 2-4. Absorption and reduced scattering coefficients, penetration depth of meniscus at \( \lambda = 355 \) nm.

<table>
<thead>
<tr>
<th>Sample</th>
<th>( \mu_s (\text{mm}^{-1}) )</th>
<th>( \mu_s' (\text{mm}^{-1}) )</th>
<th>D (( \mu \text{m} ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>039-19-82-6</td>
<td>0.86</td>
<td>4.0</td>
<td>281 ( \pm 30 )</td>
</tr>
<tr>
<td>010-70-78-8</td>
<td>0.84</td>
<td>5.0</td>
<td>261 ( \pm 30 )</td>
</tr>
<tr>
<td>002-02-40-8</td>
<td>1.7</td>
<td>2.7</td>
<td>208 ( \pm 30 )</td>
</tr>
</tbody>
</table>

2.4.3 Near infrared Raman spectroscopy of meniscus

The main constituents of meniscal tissue were described in Section 2.2. In this section the near infrared Raman spectra of meniscus is described in order to provide a method of comparison between meniscus and gelatin phantoms. Type I collagen is the main component of the dry weight of meniscus, as described in Section 2.2. Thus, we expect protein groups will dominate the Raman spectrum of meniscus.

Scattering occurs when electrons of a molecule oscillate due to an applied electromagnetic wave. Most of the light is scattered at the incident frequency, called Rayleigh scattering, but a fraction of the scattered light differs in frequency from the incident light. This type of scattering is called Raman scattering. Either the molecule absorbs some of the photon’s energy, or the molecule gives energy to the photon. The probability of scattering light at frequency \( \nu_{\text{scattered}} \) is large if two conditions are met. First, the scattered frequency is

\[ \nu_{\text{scattered}} = \nu_{\text{incident}} \pm \Delta E / h \]  

where \( \Delta E \) is the energy of a transition between states of the molecule. The transition moment between the two states must be large, and is defined as

\[ \alpha_f = \int \psi_t \alpha \psi_f \, d\tau \]  

where \( \alpha \) is the polarizability operator and \( \psi_t \) and \( \psi_f \) are the state functions. If a molecular vibration changes the polarizability of the molecule, then the transition is called Raman
active. Near IR Raman spectra of a human meniscus sample is shown in Figure 2-5. These experiments were performed with an excitation wavelength of 830 nm and power of 50 mW. [Hanlon et al. 1999] To remove the broadband fluorescence background, the raw spectrum was fit to a polynomial (4th order) and background subtracted. Because the polynomial is scaled to spectrum peaks, subtracting the background can result in negative Raman intensities.

The spectrum is dominated by Raman bands of functional groups found in all proteins. These groups include amide I at 1666 cm⁻¹, amide III near 1260 cm⁻¹, and the CH₂ bending mode at 1453 cm⁻¹. The strong peaks at 857 and 940 cm⁻¹ are attributed to proline and hydroxyproline. The weaker bands at 1006 and 820 cm⁻¹ are attributed to phenylalanine and tryptophan, respectively. A small peak at 1059 cm⁻¹ is attributed to the sulfate groups in the proteoglycans. As expected, the Raman spectrum of meniscus consists of vibrations in protein groups, and we can compare it with gelatin spectra in order to determine any biochemical differences.

Figure 2-5. Near infrared spectrum of human meniscus.
Table 2-3. Near IR Raman peaks of human meniscal tissue

<table>
<thead>
<tr>
<th>Raman peak (cm$^{-1}$)</th>
<th>Band assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1666</td>
<td>amide I</td>
</tr>
<tr>
<td>1453</td>
<td>CH$_2$ bending</td>
</tr>
<tr>
<td>1271</td>
<td>amide III</td>
</tr>
<tr>
<td>1249</td>
<td>amide III</td>
</tr>
<tr>
<td>1059</td>
<td>sulfate (glysaminoglycans)</td>
</tr>
<tr>
<td>1006</td>
<td>phenylalanine</td>
</tr>
<tr>
<td>940</td>
<td>proline, hydroxyproline</td>
</tr>
<tr>
<td>857</td>
<td>proline, hydroxyproline</td>
</tr>
<tr>
<td>820</td>
<td>tryptophan</td>
</tr>
</tbody>
</table>

Figure 2-6. Absorption and reduced scattering coefficients of meniscus as a function of wavelength.
2.5 Conclusions

Meniscus is a fibrous cartilage of importance to the knee joint. It is a tissue composed mostly of water (70-75%). Therefore, we must consider that the water contained in meniscus dominates its physical response to pulsed laser light. Collagen, composing most of the dry weight, is significant because it is the primary absorber of near-ultraviolet photons. Using diffusion approximations to transport theory, we can use an effective penetration depth as the optical parameter that defines the light and temperature distribution properties in meniscus, a biological tissue that will scatter photons. Experimental studies of water and collagen gels will be an important method to further understanding the physical response of meniscus to a laser pulse.
Chapter 3
Interferometric Surface Monitoring of Hydrated Samples

Interferometric surface monitoring is an experimental technique with precise temporal and spatial resolution. This technique is an excellent method by which to probe the response of a target to a short laser pulse. It has distinct advantages over the more commonly used acoustic transducer. The transducer is often used in pulsed laser experiments on tissue. It is placed on the target surface opposite from the surface that is irradiated. The transducer measures a laser-induced stress wave after it has propagated through a sample. One can study opto-acoustic properties, but attenuation of the wave must be taken into account. Interferometric surface monitoring measures the velocity of an expanding surface and allows us to infer the target's physical properties that relate to its laser-induced motion.

The initial interferometric experiments on knee meniscus suggested some interesting questions. First, knee meniscus was found to exhibit two types of responses. In some instances meniscus responded linearly with fluence, but its curve shape was different from that of previously studied homogeneous, hard samples (plastic, bone). Only one of the two peaks, which are due to waves from the beam boundary reaching the centered probe, was observed. In other instances, meniscus displacements were qualitatively similar to that of water. These samples displayed an overshoot of microsecond duration before reaching equilibrium. The overshoot was not predicted by theory and its shape and duration varied with laser fluence. The two responses occurred in different samples; as well as in different locations within one meniscus. We want to understand why the elastic behavior of meniscus (and other soft tissues) is different from that of homogeneous solids. We also want to understand the physics behind the microsecond overshoots and the morphological condition of tissue that gives rise to this behavior. In addition, knowledge of the laser-induced physical response and the physiological condition of a particular meniscus sample may suggest a laser-based method of diagnosis.
The heterogeneity of knee meniscus led to the creation of gelatin tissue phantoms. Once we understood the elastic and non-elastic regimes in gelatin, we could then apply these principles to knee meniscus. This chapter describes the interferometric technique and its initial experimental results on meniscal tissue. Section 3.4 details the development of a gelatin phantom and the methods by which we prepare it. Some physical properties of gelatin from the literature, which are useful to this work, are tabulated in section 3.4. Section 3.5 gives the optical properties of the gelatin model at wavelength $\lambda = 355$ nm, the wavelength of interest.

3.1 Description of Interferometric Surface Monitoring Technique

This section describes the pump-probe technique first developed by this research group that was briefly discussed in Section 1.2. [Albagli, 1994] This technique can measure laser induced surface expansion of a sample with spatial resolution $\approx 4$ nanometers and temporal resolution $\approx 3$ nanoseconds. A schematic of the experiment is shown in Figure 3-1. When a tissue sample absorbs a short laser pulse, a non-zero temperature distribution is created (Section 2.4). Because the temperature is introduced on such a short time scale, the sample is inertially confined. Volume is constant, and pressure or stress builds up in the sample. The stresses then propagate as acoustic waves, and the sample undergoes thermoelastic expansion.

This technique is based on a Michelson interferometer that uses a rotating prism as the end mirror in the reference arm and the tissue surface as the end mirror in the other arm. The interferometric surface monitoring technique measures both speed and direction of the tissue movement. Therefore, surface displacement as a function of time can be resolved.

3.1.1 Pump Laser System

The pump light in this experiment (i.e. the light of sufficient intensity to cause measurable thermoelastic motion by the target) is supplied by a frequency tripled Q-switched Nd:YAG laser (wavelength $= 354.7$ nm, pulse duration $= 7.5$ ns, beam diameter
A 3 mm aperture is used to pass the more uniform center of the beam, blocking the Gaussian edges. A 25 cm lens is used to re-image and demagnify the beam at the aperture onto a 1 mm spot on the target surface (concentric with the 50 μm diameter interferometric probe beam) with a top-hat radial profile. The laser energy is controlled via a half-wave plate and Glan polarizing prism. The energy per pulse arriving at the tissue surface is between 0.5 and 12 mJ.

Since all quantitative measurements will depend on the fluence of the incident pump beam, careful considerations must be given to its measurement. In particular, under typical experimental conditions, one cannot obtain a smooth top-hat radial profile from a Q-switched, frequency tripled Nd:YAG pulse. Two steps were taken to address this problem. First, a passive beam homogenizer was developed and built.

Through an arrangement of mirrors and three 50/50 beamsplitters, the laser pulse is split into eight separate beams. The eight different path lengths through the homogenizer are all of different lengths by at least the coherence length of the laser, in order to avoid large intensity fluctuations due to interference effects that would occur after recombination. In our case, the path length difference was chosen to be at least 5 cm, while the coherence length of the laser is estimated to be 5 mm. The laser beam is split into eight beams and recombined into two. The light entering the final two paths consists of four pulses. Due to the rotations set up in two of the four paths, the four pulses of light entering the last two paths will be spatially averaged.

The light in these two paths is directed to cross at an aperture, and is then demagnified and reimaged onto the target surface. The overlap of these two beams is adjusted to give the most uniform spatial profile, as measured on the laser beam analyzer. In addition to this beam averaging, a portion of the beam is directed to a laser beam analyzer (Big Sky Software) which stores the energy profile of the pulse in a 240 by 240 array. The beam analyzer measures beam diameter and energy of each pulse. [Albagli, 1994]
Figure 3-1. Schematic of Michelson based interferometric surface monitoring experiment.
3.1.2 Interferometric Probe System

In the interferometric surface monitoring apparatus, light from a continuous wave helium-neon laser is electronically shuttered to a 6 millisecond pulse duration and passed through a 50/50 beamsplitter in a Michelson interferometer (see figure 3-1). In the sample arm, a 5 cm lens focuses the light onto the target. The target is adjusted to be perpendicular to the incoming beam, so that the small fraction of light reflected from the air-target interface is recollimated by the lens and returned to the 50/50 beamsplitter.

In the reference arm of the interferometer, the light passes through a 10 cm lens and a moving corner cube, before coming to a focus on a reflecting mirror. The mirror is adjusted so that the light returns to the corner cube, is recollimated by the lens and travels back toward the beamsplitter. A neutral density filter is placed in the reference arm, further reducing the reflected light, in order to compensate for lower specular reflection in the sample arm. The corner cube prism has the property that a beam incident on it will be reflected parallel (and displaced) to the incoming beam. This property is independent of the angle of incidence. When the corner cube is used along with a flat mirror, as in this experiment, a light beam can be reflected back onto itself (collinear but traveling in the opposite direction) regardless of the angle of incidence. By placing the corner cube on a rotating wheel (f = 10 Hz), the corner cube will rotate into position every 100 ms. For a small portion of this rotation (θ = +/- 2 degrees), the corner cube’s tangential velocity will remain essentially constant, and this retro-reflecting optical system will maintain alignment.

The path length of the reference arm is changed at a constant rate, creating an interference fringe pattern. Since the motion of the sample produces a modulation in this fringe pattern, a demodulation of this pattern allows one to determine both the direction and the speed of the sample surface. The light from both arms of the interferometer is combined by the beamsplitter and directed towards a photomultiplier tube sensitive to red wavelengths (Hamamatsu, R928). An interference filter centered at 632.8 nm is used to filter out any stray light. The signal from the photomultiplier tube is captured and digitized at a rate of 1 gigasample/second by a digital oscilloscope (Tektronix, model 601A) and transferred to a computer for analysis.
Experimental data is taken for a time interval of 10 µs, during which the angular position of the corner cube is \( \theta = +/- 0.02 \) degrees and the tangential velocity \( (v_{cc}) \) is 2.78 m/s. Figure 3-2 shows the sinusoidal voltage pattern created by interference fringe pattern of the light. The increased period of the sinusoidal fringes immediately following the laser pulse (at 2000 ns) demonstrates the modulation of the fringes.

![Graph showing AMPLITUDE (mV) vs TIME (ns) for interference fringes in saline, laser pulse occurs at t = 2000 ns.]

Since the path length in the reference arm changes at a rate four times greater than the corner cube velocity, the half-period of the reference interference pattern is:

\[
P_r = \frac{\lambda/2}{4v_{cc}} = 28.5 \text{ ns},
\]

(3.1)

where \( \lambda \) is the wavelength of the helium-neon laser (632.8 nm). If the target in the sample arm moves as a function of time, then the interference half-period \( (P_i) \) will change:

\[
P_i = \frac{\lambda/2}{(4v_{cc} - 2v_s)},
\]

(3.2)

where \( v_s \) is the average velocity of the sample over the half-period (the direction of \( v_s \) is defined as positive for motion towards the beamsplitter). The corner cube velocity is multiplied by an additional factor of two because the light only strikes the corner cube twice but the sample only once. The surface movement of the sample \( (S_s) \) during the
period can be found by multiplying the sample velocity, $v_s$, and the observed half-period, $P_i$ (Eq. 3-2):

$$S_s = \frac{\lambda}{4} \left( \frac{P_i}{P_r} - 1 \right).$$

(3.3)

A positive value of $S_s$ indicates motion towards the beamsplitter. Thus, the surface motion of the sample can be determined each half-period (28.5 ns) and the complete motion can be found by summing. The intrinsic time resolution of the experiment is determined by the 2-3 ns rise time of the PMT, and not the time interval over which the half-period is found.

All timing in the experiment is controlled by two pulse generators (Stanford Research Systems, DG535) which trigger the Nd:YAG laser, electronic shutter, laser beam analyzer, and digital oscilloscope. A pin diode, attached to the rotating wheel, triggers the pulse generators when the corner cube has moved into position. Data is collected for a 10 μs period, with the laser pulse firing exactly 2 μs into this period (with a jitter of +/- 2 ns). The reference half-period ($P_r$) is determined from the first 2 μs of interference fringes (stationary target). The laser-induced thermoelastic motion of the sample over the next 8 μs is then determined from the remaining interference fringes and equation 3.3.

In order to determine the spatial resolution of this technique, the surface movement as a function of time of a stationary sample has been calculated from the fringe pattern and is shown in figure 3-3. The sample is stationary, and any calculated motion is a measure of the system’s spatial resolution. The data in figure 3-3 shows no movement with a standard deviation of ± 4 nm. The scatter in the data is related to the error in measuring the interference period due to the random noise on the voltage pattern. This noise has contributions from both shot noise (there are only 3000 photoelectrons) and background electronic noise.
3.1.3 System Improvements

When using the interferometric surface monitoring system with meniscus, it became apparent that the specular reflection of the meniscal surface was much lower in comparison to previous targets of acrylic, glass, water, and polished cortical bone. In order to increase the interference signal, the 5 mW helium-neon laser was replaced by a 35 mW helium neon laser (Melles Griot, 05-LHP-926). The shutter exposure was decreased from 6 to 4 ms to reduce the HeNe power hitting the tissue. Figure 3-4 shows surface displacement of two meniscus samples measured by the 5 mW and 35 mW lasers. Originally, meniscus displacement was measured with an accuracy of ±10 nanometers. The addition of the 35 mW probe laser allows measurement of meniscus displacement with an improved accuracy of ±4 nanometers. The 5 mW data is offset by 50 nanometers to aid visual comparison. Adding this higher power helium-neon laser significantly improved signal in meniscus. Originally, it was necessary to average data from at least 3 laser “shots” to obtain data with reasonable noise levels. With the new laser, we can now obtain single shot data in knee meniscus. The HeNe beam

To ensure that the photomultiplier tube was detecting only the helium-neon probe light, a HeNe line filter was placed in front of the PMT. The line filter blocks any stray light from the pump laser (λ=355 nm) from entering the detector. In addition, any fluorescence from the 355 nm excitation of organic samples will be blocked. Fluorescence was apparent in the PMT signal and visually, when using aqueous dyes.
Figure 3-4 Surface displacement of meniscus samples shows improved spatial resolution with addition of the 35 mW HeNe probe laser.

such as sodium salt fluorescein and rhodamine 6G. This filter has a transmission value of 85% at 633 nm, and a 10.5 nm bandwidth at half maximum (Andover, 633/12/25D).

3.2 Initial Results on Human Meniscus

Initial interferometry on meniscal tissue samples showed a range of behavior dependent on the sample, and variations within one sample dependent on the site. Figure 3-5 shows two different patients’ menisci that were irradiated with similar fluences. Sample 1 has an overshoot of approximately 250 nm that grows and collapses in 2 μs. Sample 2 displays significantly less expansion in both the overshoot and quasi-steady state equilibrium. Neither of the samples’ expansion resembles that of hard tissue. The presence of the 2 μs duration overshoot is not predicted by the theory for homogeneous solids (see Section 1.2).

Figure 3-6 shows the laser-induced surface expansion of meniscus at two different sample sites on the surface. The quasi-steady state value is the same, but the second site has a large overshoot lasting approximately 3.5 μs. Thus, meniscal tissue is a highly heterogeneous sample. Not only does meniscus differ from patient to patient, but also it can differ significantly within one sample. Therefore, we must treat each sample site as an independent one. To develop the correct theoretical model of thermoelastic expansion in soft tissue, it became necessary to develop a controllable, reproducible gelatin phantom, which has less variability than meniscal tissue.
Figure 3-5 Different meniscus samples display dramatically different physical responses to the same laser fluence.

Figure 3-6. A meniscus sample shows dramatically different responses to identical laser fluences.
3.3 Aqueous Samples

Because meniscus is a soft tissue composed of 75% water, de-ionized water and phosphate buffered saline were used as experimental samples. Primuline was added to decrease the penetration depth at $\lambda = 355$ nm to an order of magnitude of $10^2$ microns. Transmission was measured in a spectrophotometer in order to determine the penetration depth, $D$. Quartz cells of 100 micron path length were used for this measurement. Using the following equation, penetration depth can be calculated

$$T = T_0 e^{-\frac{x}{D}},$$

(3.4)

where $x$ is 100 microns and $T_0$ is the transmission of the quartz cell when empty. In the case of aqueous dye, scattering is negligible and penetration depth is the inverse of the absorption coefficient ($D = 1/\mu_a$).

3.4 Development of a Gelatin Phantom

In order to further understand the physical response of meniscus to a nanosecond laser pulse, it became evident that a gelatin phantom would be useful as a controllable experimental model. Meniscus samples exhibit variations from patient to patient, as well as by location within a given sample. The often rough surface of meniscus reduces specular reflection of the helium-neon beam and decreases the amplitude of the interference fringes. Also, the number of spots on the meniscus surface for which we can obtain an interferometric signal is limited. Typically, the surface reflection decreases after a few laser shots, and the interference fringes are lost.

It would be highly useful to have an experimental sample that possesses a smooth, highly reflective surface. This sample must be similar in composition as meniscus; i.e. it must be composed of mostly water, with collagen comprising most of the dry weight. A sample within which the water content could be changed would be useful, since increased water content indicates degenerative changes in cartilage. In addition, a sample in which optical penetration depth could be adjusted would be ideal. Gelatin is such a sample.

Gelatin samples are composed of water bound to collagen fibrils with low level structure. Gelatin is advantageous because it consists of collagen and water; however,
gelatin does not have the highly organized, large collagen fibers as in meniscus. Chemical dyes can be added to gelatin to increase its light absorption at a particular wavelength. Of course, care must be taken to choose a molecule that does not affect the gelatin cross-links. With these considerations, a gelatin phantom for laser-tissue interaction studies was developed.

3.4.1 Preparation of gel phantom

The phantom was prepared from bovine skin gelatin (Sigma, Type B, 75 bloom, Saint Louis) by adding gelatin powder to de-ionized water heated to 40° C. The solution was kept at 40° C throughout the mixing process, and continuously stirred by a magnetic stir bar. Once enough gelatin was added for the appropriate concentration (by mass—\( x = \frac{m_{\text{gel}}}{m_{\text{gel}} + m_{\text{water}}} \)), the solution was poured into cylindrical forms (volume ≈ 8.5 cm³) and kept at 4° C until use. Gels were allowed approximately 24 hours to set before being used as samples. Samples older than 5 days were discarded, in order to minimize error due to evaporation of water from the gelatin, which occurs over time.

Gelatin samples were used in order to study the laser response as a function of water content. Samples were made with a protein content as low as 3%. At these lower concentrations, the optical penetration depth at \( \lambda = 355 \text{ nm} \) is large because the amount of absorbing protein molecules has decreased. To enhance absorption and approximate the penetration depth of meniscus at the pump laser wavelength, several dyes were tested. Initially, potassium chromate (K₂CrO₄) was used due to its strong absorption; a small amount of potassium chromate was needed for an appropriate penetration depth (0.8 g/l H₂O for D = 350 µm). However, it has been noted in the literature that chromate salts interact with carboxyl groups to reduce gelatin swelling in water and increase its melting point, hardening the gel [Mees and James, 1967]. Thus, in later work, primuline (C₂₁H₂₄N₄O₃S₃Na) became the absorbing dye of choice (Sigma/Aldrich, 20686-5). Table 3-1 lists the concentration of primuline in de-ionized water needed to obtain useful values of penetration depth at \( \lambda = 355 \text{ nm} \). In chapter 4, we consider the presence of primuline as a second light absorber.
Table 3-1 Optical penetration depth at $\lambda = 355$ nm of primuline solution

<table>
<thead>
<tr>
<th>concentration (g / 1 H$_2$O)</th>
<th>optical penetration depth (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.47</td>
<td>200</td>
</tr>
<tr>
<td>0.28</td>
<td>360</td>
</tr>
</tbody>
</table>

3.4.2 Physical properties of gelatin

Some physical properties of gelatin, which are useful to this work, are found in the literature. The density of pure gelatin is given as $1.27$ g/cm$^3$ and using this value the density of gel phantoms, $\rho$, can be calculated knowing percent by mass of gelatin, $x$, in the sample

$$\rho = x\rho_{gel} + (1-x)\rho_{water}.$$ \hspace{1cm} (3.5)

where $x$ is $m_{gel}/(m_{gel} + m_{water})$. The mass density of water is $\rho_{water}=1.00$ g/cm$^3$. Heat capacity of gelatin for temperatures from 0 to 25° C was obtained from data given in Physical Properties of Tissue [Duck, 1990].

In figure 3-7, the value heat capacity, $C_V$, of gelatin as a function of concentration is plotted [Duck, 1990]. A linear fit was made for gelatin of concentrations less than 30%. The following equation gives heat capacity in units of J g$^{-1}$ K$^{-1}$:

$$C_V = -0.0178 \cdot (% gel) + 4.176$$ \hspace{1cm} (3.6)

Table 3-2 Physical properties of gelatin as a function of concentration

<table>
<thead>
<tr>
<th>Concentration (%)</th>
<th>$C_V$ (J g$^{-1}$ K$^{-1}$)</th>
<th>$\rho$ (g cm$^{-3}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>4.09</td>
<td>1.01</td>
</tr>
<tr>
<td>10</td>
<td>4.00</td>
<td>1.03</td>
</tr>
<tr>
<td>15</td>
<td>3.91</td>
<td>1.04</td>
</tr>
<tr>
<td>20</td>
<td>3.82</td>
<td>1.05</td>
</tr>
<tr>
<td>25</td>
<td>3.73</td>
<td>1.07</td>
</tr>
<tr>
<td>Gel with primuline (0.5 g/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.1</td>
<td>4.01</td>
<td>1.02</td>
</tr>
<tr>
<td>17</td>
<td>3.87</td>
<td>1.05</td>
</tr>
</tbody>
</table>
Heat capacity is a physical property necessary for calculating the thermal expansion coefficient from the measurements of quasi-steady state displacement.

![Graph showing heat capacity vs gel concentration](image)

**Figure 3-7.** Heat capacity of gelatin versus concentration. A linear fit to the lower concentration data points (filled diamonds) gives eq. 3.6. Open squares denote $C_v$ at high gel concentrations.

### 3.5 Optical Properties of a Gelatin Phantom

The optical penetration depth of gelatin samples was measured using a dual beam spectrophotometer (Shimadzu) at wavelength $\lambda = 355$ nm. Gelatin was cast in quartz spectrophotometer cells of path length 100 microns. The gelatin was placed in a refrigerator at 4° C for a minimum of 24 hours. The samples were returned to room temperature for spectrophotometer measurements. A possible source of error is the circumstance that some gelatin may leak out of the etched part of the cell onto the edges. The path length will then be larger by about 30 microns, and measurements of penetration depth will be too small. This uncertainty of the sample thickness is a source of up to 30% error. Table 3-3 lists the values of penetration depth for gelatin.
3.5.1 Near Infrared Raman Spectroscopy of a Gelatin Phantom

Near IR Raman spectra of gelatin samples (no primuline) are shown in Figures 3-8 and 3-9. These experiments used the same 830 nm excitation as did the meniscus spectra, with a power of 75 mW. The spectra for 15% and 25% gelatin samples are virtually identical, the only difference being the higher intensities of the higher concentration sample (25%). The spectra are dominated by Raman bands of functional groups found in all proteins. For the 15% gelatin, these groups include amide I at 1668 cm\(^{-1}\), amide III near 1251 cm\(^{-1}\), and the CH\(_2\) bending mode at 1453 cm\(^{-1}\). For the 25% gelatin sample, these peaks were found at 1665, 1249, and 1451 cm\(^{-1}\), respectively. The peaks near 870 and 922 cm\(^{-1}\) are attributed to proline and hydroxyproline; they are near 860 and 930 cm\(^{-1}\) in the 25% gelatin sample. The narrow bands at 1003 and 816 cm\(^{-1}\) are attributed to phenylalanine and tryptophan, respectively; 1003 and 814 cm\(^{-1}\) for the 25% sample. The high intensity, narrow peak at 980 (981) cm\(^{-1}\) is attributed to the presence of sulfate. The bands and their wavenumbers are listed for both concentrations in Table 3-4. These Raman spectra of gelatin and meniscus (Section 2.4) demonstrate the biochemical similarities between a collagen gel phantom and meniscus.

<table>
<thead>
<tr>
<th>Gel (%)</th>
<th>D (microns)</th>
<th>Gel (%) with 0.5 g/l primuline</th>
<th>D (microns)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>570 ± 60</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>15</td>
<td>440 ± 60</td>
<td>15</td>
<td>160 ± 40</td>
</tr>
<tr>
<td>20</td>
<td>360 ± 90</td>
<td>20</td>
<td>190 ± 60</td>
</tr>
<tr>
<td>25</td>
<td>330 ± 30</td>
<td>25</td>
<td>190 ± 60</td>
</tr>
</tbody>
</table>
Figure 3-8. Raman spectrum of 25% gelatin.

Figure 3-9. Raman spectrum of 15% gelatin.
Chapter 4
Analytical and Numerical Solutions of the Thermoelastic Wave Equation

In order to evaluate the physical response of cartilage and gelatin phantoms to a nanosecond laser pulse, a quantitative model must be developed. The theory of elasticity is the foundation of these models, based on the solution to the thermoelastic wave equation. A time dependent solution of the thermoelastic wave equation has been obtained for laser-induced heating of a hydrated sample in a one-dimensional geometry. This solution shows that the sample will undergo thermoelastic expansion and the surface will reach a new equilibrium position. The time constant of this expansion is governed by the ratio of the 1/e depth of laser light absorption to the speed of sound in the sample.

The predictions of this one-dimensional model also show that the laser-induced stress distribution, which begins as compressive stress, evolves into a traveling bipolar wave with tensile and compressive components. The presence of tensile stresses is necessary to explain experimental observations of cavitation in meniscus, water and gelatin. The three-dimensional numerical solution, which is used to predict thermoelastic expansion of hydrated solids, is also described in this chapter. The numerical solution can be used to calculate the laser-induced pressure distribution, which we will use in Chapter 6 to create cavitation bubbles as a function of time.

4.1 Theory of Elasticity

This review of the theory of elasticity comes from the text by Landau and Lifshitz [Landau and Lifshitz, 1986].

4.1.1 The strain tensor

Cauchy and Poisson established the basic equations of elasticity theory in the 1820’s. The mechanics of solid objects form the content of the theory of elasticity. Under the application of forces, a solid object deforms. We will let $x_i$ and $x'_i$ be the coordinates of a point in the solid, before and after deformation. The displacement of this point due to the deformation is called the displacement vector:
\[ u_i = x'_i - x_i . \] \hspace{1cm} (4.1)

Under a deformation, the distances between two points change. Before and after the deformation, distances between the points are

\[ dl = \sqrt{(dx'_1 + dx'_2 + dx'_3)} , \hspace{1cm} dl' = \sqrt{(dx'_1^2 + dx'_2^2 + dx'_3^2)} . \] \hspace{1cm} (4.2)

Using

\[ du_i = \frac{\partial u_i}{\partial x_k} dx_k , \] \hspace{1cm} (4.3)

the distance between two points after deformation can be written as

\[ dl'^2 = dl^2 + 2 \frac{\partial u_i}{\partial x_k} dx_i dx_k + \frac{\partial u_i}{\partial x_k} \frac{\partial u_i}{\partial x_l} dx_k dx_l , \] \hspace{1cm} (4.4)

where repeated indices indicate summation. The second term on the right can also be written as

\[ 2 \frac{\partial u_i}{\partial x_k} dx_i dx_k = \left( \frac{\partial u_i}{\partial x_k} + \frac{\partial u_k}{\partial x_i} \right) dx_i dx_k , \] \hspace{1cm} (4.5)

and \( dl'^2 \) can take the form

\[ dl'^2 = dl^2 + 2u_{ik} dx_i dx_k , \] \hspace{1cm} (4.6)

where \( u_{ik} \) is the strain tensor defined as

\[ u_{ik} = \frac{1}{2} \left( \frac{\partial u_i}{\partial x_k} + \frac{\partial u_k}{\partial x_i} + \frac{\partial u_i}{\partial x_l} \frac{\partial u_l}{\partial x_k} \right) . \] \hspace{1cm} (4.7)

The sum of the diagonal components is the relative volume change.

4.1.2 The stress tensor

The total force on a small volume of the body can be written as a volume integral

\[ \int F_i dV \] where \( F_i \) is a vector. The force per unit volume vector, \( F_i \), can be written as the divergence of a rank two tensor, and using the divergence theorem the volume integral becomes a surface integral,

\[ F_i = \frac{\partial \sigma_{ik}}{\partial x_k} \quad \text{and} \quad \int F_i dV = \int \frac{\partial \sigma_{ik}}{\partial x_k} dV = \oint \sigma_{ik} df_k \] \hspace{1cm} (4.8)

where \( \sigma_{ik} \) is the stress tensor. Thus, \( \sigma_{ik} df_k \) gives the \( i \)th component of force on a surface element \( df \).
The stress tensor for a body under uniform (hydrostatic) compression is simple to describe. A pressure, $p$, of constant magnitude acts on every unit surface area of the body, and is directed along the normal vector inward. The force acting on a surface element is $-p dV$. In terms of the stress tensor, this force is $\sigma_{ik} dV$. Writing $-p dV = -p \delta_{ik} dV$, the stress tensor for hydrostatic compression is

$$\sigma_{ik} = -p \delta_{ik}. \tag{4.9}$$

Therefore, the non-zero diagonal components of the stress tensor equal the pressure.

4.1.3 Relationship of the stress and strain tensors

The change of internal energy of a deformed body is

$$dE = T dS - dW,$$ \hspace{1cm} (4.10)

for a reversible process, where $T dS$ is the heat added to a unit volume and $dW$ is the work done by internal stresses. Total work done is of course force (eq. 4-8) multiplied by displacement, and integrating over volume gives

$$\int \delta W dV = \int \frac{\partial \sigma_{ik}}{\partial \xi_k} \delta u_i dV. \tag{4.11}$$

Integrating by parts and using the strain tensor defined in equation 4.7 gives

$$\delta W = -\sigma_{ik} \delta u_i. \tag{4.12}$$

Using the Helmholtz free energy equation, $F = E - TS$, and equations 4.10 and 4.12 yields

$$dF = -S dT + \sigma_{ik} du_i, \quad \text{and} \quad \sigma_{ik} = \left( \frac{\partial F}{\partial u_i} \right)_T. \tag{4.13}$$

Thus, if the free energy, $F = F(u_i)$, is known, then the relationship between the stress and strain tensors can be found.

Consider the deformation of a solid object with no external forces present, but accompanied by a temperature change. The undeformed state is the state of the object at a given temperature $T_a$. If the body is at a temperature $T$, where $T - T_a \neq 0$, then the object will be deformed due to thermal expansion. We expand the free energy, $F(T)$, in powers of $u_i$. The free energy is a scalar; thus, every term in the expansion must be a scalar also. From the components of the tensor $u_i$, only the sum $u_i$ of the diagonal components forms a linear scalar quantity. For a small temperature change, we assume that this linear term is proportional to the temperature difference. The coefficient of this term is written as $-K\beta$, and the first two terms of the free energy are
\[ F(T) = F_o(T) - K\beta (T-T_a) u_{ll} . \quad (4.14) \]

There are two second-order terms because two independent scalars can be formed from a symmetric rank 2 tensor. The free energy then becomes
\[ F(T) = F_o(T) - K\beta (T-T_a) u_{ll} + \frac{1}{2} \lambda u_{ll}^2 + \mu u_{ik}^2 \quad (4.15) \]

where \( \lambda \) and \( \mu \) are constants called the Lamé coefficients.

If the trace of the strain tensor is zero, then the volume of the object does not change, only its shape is altered. This type of deformation is "pure shear." The opposite case, called "hydrostatic compression," occurs for a volume change with no shape change of the object. The strain tensor for this type of deformation is \( u_{ik} = \text{constant} \cdot \delta_{ik} \).

Any deformation can be expressed as a sum of a pure shear and a hydrostatic compression, and the following identity is used,
\[ u_{ik} = (u_{ik} - \frac{1}{3} \delta_{ik} u_{ll}) + \frac{1}{3} \delta_{ik} u_{ll} . \quad (4.16) \]

where the first term on the right is pure shear and the second is hydrostatic compression. The free energy becomes
\[ F(T) = F_o(T) - K\beta (T-T_a) u_{ll} + \mu (u_{ik} - \frac{1}{3} \delta_{ik} u_{ll} )^2 + \frac{1}{2} Ku_{ll}^2 \quad (4.17) \]

The quantities \( K \) and \( \mu \) are the bulk modulus and shear modulus respectively. By differentiating \( F(T) \) with respect to \( u_{ik} \), we determine the stress tensor:
\[ \sigma_{ik} = Ku_{ll} \delta_{ik} - K\beta (T-T_a) \delta_{ik} + 2 \mu (u_{ik} - \frac{1}{3} \delta_{ik} u_{ll} ) . \quad (4.18) \]

The stress tensor can also be expressed using the constants \( E \) and \( \nu \), which are Young's modulus and Poisson's ratio:
\[ E = \frac{9K\mu}{3K + \mu} \quad \text{and} \quad \nu = \frac{3K-2\mu}{2(3K+\mu)} . \quad (4.19) \]

Poisson's ratio is the ratio of transverse compression to longitudinal extension and varies between 0 and 0.5. Thus, the stress tensor can be written as
\[ \sigma_{ik} = \frac{E}{1+\nu} \left( u_{ik} + \frac{\nu}{1-2\nu} u_{ll} \delta_{ik} \right) - \frac{E\beta T_L}{3(1-2\nu)} \delta_{ik} , \quad (4.20) \]

where the temperature increase \( T - T_a \) is replaced by \( T_L \), the laser-induced temperature increase. In component form using cylindrical coordinates (our problem has axial symmetry), equation 4.20 becomes
\[ \sigma_{rr} = \sigma_{zz} = \frac{E}{(1+\nu)} u_{rr} ; \]

\[ \sigma_{rr} = M \left[ (1-\nu)u_{rr} + \nu(u_{rr} + u_{zz} ) - \frac{1+\nu}{3} \beta T(r,z) \right] ; \]  \hspace{1cm} \text{(4.21)}

\[ \sigma_{zz} = M \left[ (1-\nu)u_{zz} + \nu(u_{rr} + u_{zz} ) - \frac{1+\nu}{3} \beta T(r,z) \right] ; \]

\[ \sigma_{\phi\phi} = M \left[ (1-\nu)u_{\phi\phi} + \nu(u_{rr} + u_{zz} ) - \frac{1+\nu}{3} \beta T(r,z) \right] ; \text{ and } M = \frac{E}{(1+\nu)(1-2\nu)}. \]

The strain tensor for small strains and axial symmetry is given by the following: [Landau and Lifshitz, 1986]

\[ u_{zz} = \frac{\partial u_z}{\partial z} ; \hspace{1cm} u_{rr} = \frac{\partial u_r}{\partial r} ; \]

\[ u_{rr} = \frac{1}{2} \left( \frac{\partial u_z}{\partial r} + \frac{\partial u_r}{\partial z} \right) ; \hspace{1cm} u_{\phi\phi} = \frac{u_r}{r} . \]  \hspace{1cm} \text{(4.22)}

The stress tensor in cylindrical coordinates is used to determine a three-dimensional solution to the problem of laser-induced deformation.

4.1.4 Thermoelastic wave equation

The equations of motion can be determined from Newton’s first law, \( F = ma \). The internal stress force is set equal to the product of acceleration and density

\[ \rho \frac{\partial^2 u_i}{\partial t^2} = \frac{\partial \sigma_{ik}}{\partial x_k} . \]  \hspace{1cm} \text{(4.23)}

Substituting the expression of the stress tensor from eq. 4.21 into this expression gives

\[ \rho \frac{\partial^2 u_i}{\partial t^2} = \frac{E}{1+\nu} \left( \frac{\partial u_{ik}}{\partial x_k} + \frac{\nu}{1-2\nu} \frac{\partial u_{ii}}{\partial x_i} \right) - \frac{E\beta}{3(1-2\nu)} \frac{\partial T_i}{\partial x_i} . \]  \hspace{1cm} \text{(4.24)}

Substituting in the strain tensor (eq. 4.7) results in the equation:
\[
\rho \frac{\partial^2 u_i}{\partial t^2} = \frac{E}{1 + \nu} \left( \frac{1}{2} \frac{\partial^2 u_i}{\partial x_i^2} + \frac{1}{2} \frac{\partial^2 u_k}{\partial x_i \partial x_k} + \frac{\nu}{1 - 2\nu} \frac{\partial^2 u_i}{\partial x_j \partial x_j} \right) - \frac{E\beta}{3(1 - 2\nu)} \frac{\partial T_i}{\partial x_i} \tag{4.25}
\]

This can be simplified to

\[
\rho \frac{\partial^2 u_i}{\partial t^2} = \frac{E}{2(1 + \nu)} \frac{\partial^2 u_i}{\partial x_i^2} + \frac{E}{2(1 + \nu)(1 - 2\nu)} \frac{\partial^3 u_i}{\partial x_i \partial x_j \partial x_j} - \frac{E\beta}{3(1 - 2\nu)} \frac{\partial T_i}{\partial x_i} \tag{4.26}
\]

which in vector notation is

\[
\rho \frac{\partial^2 \vec{u}}{\partial t^2} = \frac{E}{2(1 + \nu)} \nabla^2 \vec{u} + \frac{E}{2(1 + \nu)(1 - 2\nu)} \nabla(\nabla \cdot \vec{u}) - \frac{E\beta}{3(1 - 2\nu)} \nabla T_i. \tag{4.27}
\]

The deformation of a solid as a function of time is described by the displacement vector that satisfies eq. 4.27.

4.2 One Dimensional Solution to the Thermoelastic Wave Equation

A derivation of the one-dimensional solution to the thermoelastic wave equation is given in this section. [Albagli, 1994]

4.2.1 One dimensional solution

The thermoelastic wave equation (eq. 4.27) describes the thermoelastic response of a solid material to a temperature distribution. The gradient of the temperature distribution drives the wave equation. In this work, the absorption of a nanosecond laser pulse causes a non-zero temperature distribution. We eventually want a time dependent, three-dimensional solution for a hydrated sample. However, a one-dimensional solution can be found analytically and will be a useful starting point when adding the effect of the growth and collapse of cavitation bubbles.

For a one-dimensional solution, we consider a semi-infinite tissue slab with a boundary at \( z = 0 \), where the air-tissue interface exists. A laser beam of infinite extent strikes the tissue and is absorbed with an exponentially decreasing light profile, of penetration depth \( D \) (Section 2.4.2). In the one-dimensional geometry, displacement occurs only in the \( z \) direction and is strictly \( z \) dependent. Using \( T_1 = T_0 \exp(-z/D) \), the one-dimensional wave equation (eq. 4.27) is
\[ \rho \frac{\partial^2 u_z}{\partial t^2} = c_l^2 \frac{\partial^2 u_z}{\partial z^2} + \frac{E \beta T_0}{3D \rho (1-2\nu)} e^{-\gamma_D} \quad \text{where} \quad c_l^2 = \frac{E(1-\nu)}{\rho(1+\nu)(1-2\nu)}. \quad (4.28) \]

Trying a solution of the form \( u_z(z,t) = \Phi(z,t) + A(z) \), and substituting this into the wave equation (eq. 4.28) yields

\[ \frac{\partial^2 \Phi}{\partial t^2} - c_l^2 \frac{\partial^2 A}{\partial z^2} + \frac{E \beta T_0}{3D \rho (1-2\nu)} e^{-\gamma_D} = 0. \quad (4.29) \]

By equating the right hand side of eq. 4.29 to zero and integrating gives

\[ A(z) = \frac{-\beta T_0 D}{a} e^{-\frac{z}{D}} + b_1 z + b_2 \quad \text{where} \quad a = \frac{3(1-\nu)}{1+\nu}. \quad (4.30) \]

The homogeneous solution of the wave equation (left hand side of eq. 4.29 set equal to zero) is

\[ \Psi(z,t) = (a_1 e^{-k_1 z} + a_2 e^{k_2 z})(a_3 e^{-k_3 c_l t} + a_4 e^{k_4 c_l t}) \quad (4.31) \]

The general solution for displacement is the sum of the particular and homogeneous solutions, and we divide the problem into two regions: \( z \leq c_L t \), and \( z \geq c_L t \). For the displacement to go to zero at infinity, and to be bounded for all \( z \), we keep the following terms:

\[ u_z = \frac{-\alpha T_0 D}{a} e^{-\frac{z}{D}} + b_1 e^{-k_1 (z-c_L t)} + b_2 e^{k_1 (z-c_L t)} \quad \text{for} \quad z \leq c_L t \quad (4.32) \]

\[ u_z = \frac{-\alpha T_0 D}{a} e^{-\frac{z}{D}} + b_3 e^{-k_2 (z+c_L t)} + b_4 e^{k_2 (z+c_L t)} \quad \text{for} \quad z \geq c_L t. \]

4.2.2 Application of initial and boundary conditions

The initial condition is that displacement is initially zero, \( u_z(z,t=0) = 0 \). The boundary condition is that the \( zz \) component of the stress tensor must be zero at the boundary, \( \sigma_{zz}(z=0) = 0 \). From eq. 4.21, this can be written as

\[ \left| \frac{\partial u_z}{\partial z} \right|_{z=0} = \frac{\beta T_0}{a}. \quad (4.33) \]

By applying the boundary condition to eq. 4.32 and using the condition that displacement must be continuous over the boundary of the two regions, \( z = c_L t \), we obtain
\[
\frac{\alpha T_0 D}{2a} \left[ e^{-2kz} + 1 - 2e^{\frac{-z}{b}} \right] = b_0 e^{\frac{2z}{b}} + b_4 - \frac{\alpha T_0 D}{a} e^{\frac{-z}{b}}. 
\]

The final form of displacement is as follows:

\[
 u_z = \frac{\beta T_0 D}{6} \frac{1+\nu}{1-\nu} \left[ e^{\frac{-z+c_{lt}}{D}} + e^{\frac{-z-c_{lt}}{D}} - 2e^{\frac{-z}{b}} \right] \quad \text{for } z \leq c_L t 
\]

\[
 u_z = \frac{\beta T_0 D}{6} \frac{1+\nu}{1-\nu} \left[ e^{\frac{-z+c_{lt}}{D}} + e^{\frac{-z-c_{lt}}{D}} - 2e^{\frac{-z}{b}} \right] \quad \text{for } z \geq c_L t 
\]

The movement of the surface has a simple form, found by setting \( z = 0 \) in eq. 4.35,

\[
 S(t) = \frac{S_0}{3} \frac{1+\nu}{1-\nu} \left[ 1 - \exp \left( \frac{-c_{lt}}{D} \right) \right], \quad \text{where } S_0 = \beta T_0 D. 
\]

Displacement follows an exponential rise to a steady-state equilibrium (figure 4-1). From the rise we can determine the slope, \( c_L/D \), and from the equilibrium displacement, we can determine \( \beta \). At \( t=0 \) the displacement is zero. At long times, the equilibrium displacement is \( S(t \to \infty) = \frac{S_0(1+\nu)}{3(1-\nu)} \). However, the curve shape (figure 4-1), based on a one-dimensional model, is inadequate for predicting the surface displacement of meniscus

![Figure 4-1](image)

Figure 4-1. One-dimensional surface displacement as a function of time:
physical constants are \( c_L = 1500 \text{ m/s} \), \( D = 300 \text{ \mu m} \), \( \nu = 0.5 \), and \( S_0 = 100 \text{ nm} \).
(seen in Chapter 2), water, or gelatin, when the beam radius and penetration depth (w and D) are comparable.

The stress can be determined from the expression for displacement. Axial stress in one dimension is obtained by substituting the expression for displacement (eq. 4.35 and 4.36) into the stress term (eq. 4.21). Initially, the stress is an exponentially decaying function proportional to the initial temperature distribution. Stress begins as entirely compressive. As the stress distribution propagates, it develops into a traveling bipolar wave shown in Figure 4-2. The stress distribution consists of the sum of two identical traveling waves propagating in opposite directions. When the wave propagating in the positive z direction (towards the surface) reaches the surface, it reflects completely and becomes tensile stress. The existence of this tensile component will become important when we discuss the growth and collapse of cavitation bubbles resulting from the existence of tensile stress.

Figure 4-2. The axial stress distribution, initially compressive, evolves into a traveling bipolar wave.
4.3 Three Dimensional Numerical Solution

A discussion of the three-dimensional, fully time dependent numerical solution to the thermoelastic wave equation for homogeneous, solid materials is given here. [Albagli, 1994] This model is applicable to hydrated solids with some modifications, which will be discussed in the following sections.

4.3.1 Basic equations

The purpose of the calculation is to determine the deformation as a function of time of a hydrated solid caused by a laser-induced temperature distribution. Cylindrical coordinates are used because the geometry of the problem has axial symmetry. We assume the laser light has a pulse length \( \tau_p \), a rounded top-hat radial profile of radius \( w \), and is absorbed exponentially by the target with penetration depth \( D \). The laser-induced temperature distribution is

\[
T(r, z, t) = T_0 \frac{t}{\tau_p} \exp\left(-\frac{z}{D}\right)f(r) \quad \text{for } t \leq \tau
\]

\[
T(r, z, t) = T_0 \exp\left(-\frac{z}{D}\right)f(r) \quad \text{for } t > \tau
\]

where \( f(r) \) is a function that describes the radial light distribution. The radial distribution can be described by a "rounded top-hat" function, where a cosine function is used on the edges. With this type of distribution, difficulties with numerical modeling near the sharp edges of the top-hat are avoided. The radial distribution of light is as follows:

\[
f(r) = 1 \quad \text{for } r \leq r_1
\]

\[
f(r) = \frac{1}{2} \left\{ 1 + \cos\left(\frac{\pi}{k} (r - r_3)\right) \right\} \quad \text{for } r_1 < r \leq r_2
\]

\[
f(r) = 0 \quad \text{for } r > r_2,
\]

where \( r_1, r_2, r_3, \) and \( k \) are selected to keep energy the same as in a top-hat of radius \( w \), and to smooth the edges of the profile. For \( w = 510 \, \mu m \), the values of the constants are \( r_1 = 450 \, \mu m \), \( r_2 = 530 \, \mu m \), \( r_3 = 460 \, \mu m \), and \( k = 77 \, \mu m \).

The equations of motion for a deformation in cylindrical coordinates are as follows:
\[ \rho \frac{\partial^2 u_r}{\partial t^2} = \frac{\partial \sigma_{rr}}{\partial r} + \frac{\partial \sigma_{rz}}{\partial z} + \frac{\sigma_{rr} - \sigma_{\phi\phi}}{r}, \quad (4.40) \]

\[ \rho \frac{\partial^2 u_z}{\partial t^2} = \frac{\partial \sigma_{rz}}{\partial z} + \frac{\partial \sigma_{zz}}{\partial r} + \frac{\sigma_{rr}}{r}. \quad (4.41) \]

Each of the equations of motion can be written as two first order differential equations:

\[ \frac{\partial u_r}{\partial t} = v_r, \quad (4.42) \]

\[ \frac{\partial v_r}{\partial t} = \frac{1}{\rho} \left[ \frac{\partial \sigma_{rr}}{\partial r} + \frac{\partial \sigma_{rz}}{\partial z} + \frac{\sigma_{rr} - \sigma_{\phi\phi}}{r} \right], \quad (4.43) \]

\[ \frac{\partial u_z}{\partial t} = v_z, \quad (4.44) \]

\[ \frac{\partial v_z}{\partial t} = \frac{1}{\rho} \left[ \frac{\partial \sigma_{rz}}{\partial z} + \frac{\partial \sigma_{zz}}{\partial r} + \frac{\sigma_{rr}}{r} \right], \quad (4.45) \]

where \( v_r \) and \( v_z \) are velocities in the radial and axial directions respectively.

### 4.3.2 Heat conduction considerations for two absorbers

In order to account for the presence of two UV (\( \lambda=355 \) nm) absorbers in gelatin phantoms with dye (section 3.4), a correction for heat conduction was needed. We make the assumption that for a mix of protein and primuline, each absorbs some amount of the laser energy, increasing the respective temperatures. Through heat conduction, energy is transferred, until the material reaches an equilibrium temperature. To model this effect the heat conduction equation was used,

\[ \frac{\partial T}{\partial t} = \frac{k}{\rho C_V} \nabla^2 T = \frac{S}{\rho C_V}, \quad (4.46) \]

where \( S \) is the source term in units of energy per unit volume and time, \( C_V \) is heat capacity, and \( k \) is the thermal conductivity. The source term arises from the initial temperature difference between the two absorbers, and can be written as

\[ S = \frac{\rho C_V}{\tau} (T_2 - T_1), \quad (4.47) \]

where \( \tau \) is the time for the system to equilibrate. Because the system reaches a quasi-
steady state equilibrium in the order of 1 µs, and thermal diffusion for tissue occurs on the time scale of 100 ms, we can assume the process is adiabatic. Thus, the spatial derivative term is zero, and the equations for temperature of the system become

\[
\frac{\partial T_1}{\partial t} = \frac{T_2 - T_1}{\tau}, \quad \frac{\partial T_2}{\partial t} = \frac{T_1 - T_2}{\tau}.
\]  

(4.48)

Solving these two equations for \(T_1\) and \(T_2\) gives

\[
2T_1 = a\exp(-2\sqrt{\tau}) + b, \quad -2T_2 = a\exp(-2\sqrt{\tau}) - b,
\]  

(4.49)

where the initial condition gives \(a\) and \(b\) as

\[
a = T_1^{(0)} - T_2^{(0)}, \quad b = T_1^{(0)} + T_2^{(0)}.
\]  

(4.50)

Thus, the temperature that drives expansion is no longer a delta function in time, and using equation 4.38, it becomes

\[
T(r, z, t) = \frac{1}{\tau} T_0 \left[ 1 + (2x - 1)\exp\left(-2\sqrt{\tau}\right) \right] \left[ \exp\left(-\frac{z}{D}\right)f(r) \right] \text{ for } t > \tau_p
\]  

(4.51)

where \(x\) is the initial amount of temperature that goes into thermal expansion. This temperature function is used strictly for samples of gelatin doped with primuline.

4.3.3 Adams-Bashforth time stepping method

The velocities given in eqs. 4.43 and 4.45 can be found numerically using the Adams-Bashforth method [Potter, 1977]. Using this method,

\[
v_r(t + \Delta t) = v_r(t) - \left( \frac{3}{2} + \varepsilon \right)G_r(t) + \left( \frac{1}{2} + \varepsilon \right)G_r(t - \Delta t),
\]  

(4.52)

\[
v_z(t + \Delta t) = v_z(t) - \left( \frac{3}{2} + \varepsilon \right)G_z(t) + \left( \frac{1}{2} + \varepsilon \right)G_z(t - \Delta t),
\]  

(4.53)

where \(\Delta t\) is the time step, \(\varepsilon\) is a constant and

\[
G_r = \Delta t \left[ \frac{\partial A_r}{\partial r} + \frac{\partial B_r}{\partial z} + \frac{A_r - C_\phi}{r} \right],
\]  

(4.54)

\[
G_z = \Delta t \left[ \frac{\partial A_z}{\partial r} + \frac{\partial B_z}{\partial z} + \frac{A_z}{r} \right].
\]  

(4.55)

The stress functions \(A, B,\) and \(C\) are defined as follows:
\[ A_r = -\frac{\sigma_{rr}}{\rho}, \quad A_z = -\frac{\sigma_{zz}}{\rho}, \]
\[ B_z = -\frac{\sigma_{rz}}{\rho}, \quad B_r = -\frac{\sigma_{rr}}{\rho}, \]
\[ C_\phi = -\frac{\sigma_{r\phi}}{\rho}. \]

(4.56)

For a liquid that does not support shear stress, we set these terms equal to zero. Thus, 
\( \sigma_{rz} = \sigma_{zz} = 0. \) The stress functions can be written, using eqs. 4.21 and 4.56, and \( c_L^2 \) (defined in eq. 4.28)
\[ A_r = -c_L^2 \left[ \frac{\partial u_r}{\partial r} + \frac{\nu}{1-\nu} \left( \frac{u_r}{r} + \frac{\partial u_r}{\partial z} \right) - \frac{1+\nu}{3(1-\nu)} \beta T(r,z) \right], \]
\[ B_z = -c_L^2 \left[ \frac{\partial u_z}{\partial z} + \frac{\nu}{1-\nu} \left( \frac{\partial u_r}{\partial r} + \frac{u_r}{r} \right) - \frac{1+\nu}{3(1-\nu)} \beta T(r,z) \right], \]
\[ C_\phi = -c_L^2 \left[ \frac{u_r}{r} + \frac{\nu}{1-\nu} \left( \frac{\partial u_r}{\partial r} + \frac{\partial u_z}{\partial z} \right) - \frac{1+\nu}{3(1-\nu)} \beta T(r,z) \right], \]
\[ A_z = B_r = 0. \]

(4.57)

Radial and axial acceleration (multiplied by the time step \( \Delta t \)) can then be written as
\[ G_r = \Delta t \left[ \frac{\partial A_r}{\partial r} + \frac{A_r - C_\phi}{r} \right] \]
\[ G_z = \Delta t \left[ \frac{\partial B_z}{\partial z} \right] \]
\[ (4.58) \]
\[ (4.59) \]

This method of calculation is stable provided that [Potter, 1977]
\[ \Delta t < \frac{\Delta}{\nu_{\text{max}}} \]
\[ (4.60) \]

where \( \Delta \) is the grid cell size (typically 10 microns) and \( \nu_{\text{max}} \) is the maximum velocity of propagation within the grid. The constant, \( \varepsilon \), of eqs. 4.52 and 4.53 is defined as
\[ \varepsilon = \frac{1}{4} \left( \frac{\Delta v_{\text{max}}}{\Delta} \right)^2 + \frac{1}{2} \left( \frac{\Delta v_{\text{max}}}{\Delta} \right)^4 \] (4.61)

For this problem, \( v_{\text{max}} \) is the longitudinal speed of sound and \( \Delta t = 0.15 \Delta / c_L \).

The initial conditions of the problem are such that the displacement and velocity are zero everywhere. After the first time step (usually 1 ns), the laser pulse has deposited some energy in the tissue and a non-uniform light and temperature distribution now exists. The stress equations (eq. 4.57) define the stresses produced by this temperature distribution. These stresses and their first order spatial derivatives are used to calculate \( G_r \) and \( G_z \) from eqs. 4.58 and 4.59. From \( G_r \) and \( G_z \), the velocity components can be calculated using eqs. 4.52 and 4.53. The displacement components are then calculated by integrating eqs. 4.42 and 4.44:

\[ u_r(t + \Delta t) = u_r(t) + \Delta t \cdot v_r(t + \Delta t) \] (4.62)

\[ u_z(t + \Delta t) = u_z(t) + \Delta t \cdot v_z(t + \Delta t) \] (4.63)

4.3.4 Boundary conditions

To integrate the differential equations of the previous section, one must define the boundary conditions of the problem. Boundaries exist on the air-tissue interface (\( z = 0 \)), the cylinder axis (\( r = 0 \)), and the artificial boundaries (\( z = z_{\text{max}}, r = r_{\text{max}} \)).

The boundary between the target and a second substance (air) has special characteristics. The boundary condition of a free surface (at \( z = 0 \)) is [Landau and Lifshitz, 1986]

\[ \sigma_z \big|_{z=0} = 0 \Rightarrow B_z \big|_{z=0} = 0 . \] (4.64)

The stress functions \( A_r \) and \( C_\phi \) (eq. 4.57) both contain a term that is proportional to the first derivative of \( u_z \) in the \( z \)-direction. This derivative is an unknown quantity at \( z = 0 \). To find \( A_r \) and \( C_\phi \) on the surface, we use the \( B_z \) equation (eq. 4.57) and solve for the first term on the right, knowing that \( B_z = 0 \). Substituting this expression into the \( A_r \) and \( C_\phi \) equations, gives expressions which only contain derivatives in the radial direction. These equations can then be calculated on the boundary, \( z = 0 \). There is not a physical boundary condition on the radial axis (\( r = 0 \)), but several terms are inversely proportional.
to radial position (4.57, 4.58). Here, the terms are calculated close to the radial axis (at a grid position \( r \leq \Delta \)) and extrapolated back to \( r = 0 \).

To calculate a numerical solution, we choose maximum values of \( r \) and \( z \) within the semi-infinite target, and artificial boundaries are created. At these boundaries (\( r = r_{\text{max}}, \) and \( z = z_{\text{max}} \)) the displacements \( u_r \) and \( u_z \) are fixed at zero. These artificial boundaries will reflect any acoustic waves that reach them back towards the initial region of interaction. Any reflected waves from these boundaries are unphysical, so we choose \( r_{\text{max}} \) and \( z_{\text{max}} \) to be large enough so that these artifacts will not occur during the time interval for which we run the computer code.

4.3.5 Adaptations for a liquid

For a liquid that does not support shear stress, we set the shear stress terms (\( \sigma_{rz}, \sigma_{zr} \)) equal to zero. The new radial and axial accelerations are given by equations 4-58 and 4-59. This assumption will be applied to a hydrated solid, such as water, gelatin, and cartilage. Water, being incompressible, has a shear modulus \( \mu = 0 \) (eq. 4.19); thus Poisson's ratio goes to \( \nu \rightarrow 1/2 \) and Young's modulus to \( E \rightarrow 0 \). It would appear that these limits would cause zero divisions (eqs. 4.21, 4.28). But for \( \mu = 0 \), \( E/(1-2\nu) \) goes to the limit \( 3K \), where \( K \) is bulk modulus. To avoid this problem in the numerical code we rewrite equation 4.21 using longitudinal sound speed (eq. 4.57), which becomes \( c_L^2 = K/\rho \). The transverse speed of sound, \( c_T \), is zero for \( \nu = 0.5 \):

\[
c_T^2 = c_L^2 (1 - 2\nu) / 2(1 - \nu).
\]  
(4.65)

A zero value of transverse speed of sound does not cause any difficulties. We will see that these considerations predict a displacement versus time curve shape that is appropriate for our experimental results in hydrated samples (Chapter 5).

4.3.6 Time dependent surface expansion

The interferometer described in Chapter 3 measures displacement of the target's surface as a function of time. By comparing experimental measurement of displacement to the predictions of the numerical model, we can determine some physical properties of
the target material. Figure 4-2 shows the three-dimensional, time dependent displacement predicted by the numerical model for a hydrated sample. The peak at 330 ns corresponds with the time needed for longitudinal acoustic waves from the beam edge, the "hot-cold" boundary, to reach the center. From this peak, knowing beam radius, \( w \), we can determine longitudinal sound speed, \( c_{L} \). From the rising slope and \( c_{L} \), we can find \( D \), penetration depth at \( \lambda = 355 \) nm. The surface then falls to its quasi-steady state equilibrium value, which gives us \( \beta / C_{V} \), the ratio of thermal expansion coefficient to heat capacity (Section 4.4). We also see that the second peak, which results from transverse waves reaching the centered probe and occurs in hard samples, is missing since transverse waves do not occur in a liquid.

![Displacement vs Time Graph](image)

Figure 4-3. The three-dimensional surface displacement as a function of time: \( w = 510 \ \mu m \), \( c_{L} = 1500 \ m/s \), \( D = 300 \ \mu m \), \( v = 0.5 \).

4.4 Quasi-Steady State Equilibrium Displacement

Given the optical and mechanical properties of a material, the initial and quasi-steady state stresses can be calculated using previous equations. We can also derive an analytical expression for equilibrium displacement. Since the properties of biological tissue are not often known, an analytical expression would be helpful in determining physical properties of tissue.

Albagli [1994] calculated the steady state axial surface displacement for a top-hat radial profile from the following equation for displacement (\( z = 0 \) on the surface):
\[ u_z = -\frac{1 + \nu}{3(1 - \nu)} D\beta T_0 \int_0^\infty \left[ \frac{(1 - 2\nu + yz')}{(y + 1)} e^{-\frac{y}{y' + 1}} + \frac{ye^{-\frac{y}{y' + 1}} - e^{-\frac{y}{y' + 1}}}{(y^2 - 1)} \right] RJ_1(Ry) J_0(yr') dy. \quad (4.66) \]

The axial surface displacement becomes

\[ u_z = -S_3 g_0(R, r'), \quad (4.67) \]

where the negative sign represents motion towards the incoming light, and

\[ S_3 = \frac{2(1 + \nu)}{3} D\beta T_0 \quad \text{and} \quad g_0(R) = \int_0^\infty \frac{RJ_1(Ry)}{y + 1} \, dy. \quad (4.68) \]

\( J_1 \) is a first order Bessel function and \( n \) is a laser profile correction factor (very close to 1). For a temperature rise of \( T_0 \sim 10^6 \)C and penetration depth \( D \sim 200 \) \( \mu \)m, the equilibrium displacement is approximately 200 nanometers. Also, \( S_3 \) is proportional to \( D\beta T_0 \), the equilibrium displacement, \( S_0 \), from the one-dimensional model. The function \( g_0(R) \) is a geometrical correction factor and demonstrates the significance of the aspect ratio \( (R = w/D) \). For large \( R \), this factor approaches 1, and it goes to zero for small \( R \). For meniscus, where \( R \sim 1-2 \), the value of the correction factor is roughly 0.5, a significant departure from the one-dimensional model. In terms of laser fluence (eq. 2.15), equilibrium displacement becomes

\[ S_0 = \frac{2(1 + \nu)}{3} \frac{\beta}{\rho C_v} g_0(R) \Phi. \quad (4.69) \]

4.5 Conclusions

In this chapter the theoretical basis of this work was established. Based on solutions to the thermoelastic wave equation, the laser-induced stress distribution and resulting strains can be predicted. For hydrated samples, there are significant differences from solids that must be considered. First, we account for the incompressibility of the liquid and set Poisson’s ratio to 0.5. We account for the fact that shear stress is not supported in a liquid by eliminating shear stress terms from the numerical solution. Finally, we know that transverse waves do not occur in a liquid medium, and the transverse sound speed is zero. The predictions of the three-dimensional numerical solution will be compared with experimental results to determine physical properties of a soft tissue, meniscus. Also, it is important to note that within the sample, tensile stresses will develop; which are necessary for cavitation to occur.
Chapter 5
Elastic Behavior of Hydrated Samples: Experiment versus Theory

To understand the behavior of meniscus below cavitation threshold, we studied the behavior of less complex samples: water, saline, and gelatin. The experimental results obtained on these samples are compared with theoretical predictions in this chapter. We want to understand the time dependent behavior of these hydrated samples, and use the numerical model based on the thermoelastic wave equation described in Chapter 4 to predict the laser-induced response. From comparisons of experiment with theory, we obtain physical properties of the sample: longitudinal sound speed \( (c_l) \), and optical penetration depth \( (D) \). In addition, the measured quasi-steady state equilibrium value can be used to calculate the thermal expansion coefficient \( (\beta) \). Thermal expansion coefficients are tabulated for water, saline, and gelatin. The same analysis method is used to determine sound speed and penetration depth in meniscus samples. The measured quasi-steady state equilibrium displacement can be used to calculate the ratio of thermal expansion to heat capacity \( (\beta/C_v) \) in meniscus. Sound speed, penetration depth and thermal properties \( (\beta/C_v) \) are tabulated for several meniscus samples. In Chapter 7, we will use histology assessments to determine if these physical properties of meniscus correlates with the tissue’s condition.

5.1 Experiment versus Theory in Gelatin

5.1.1 Displacement versus time

Figure 5-1 shows the typical displacement of a 25 % gelatin sample for a range of sub-threshold fluences (energy per unit area). For a 10 ns pulse of 8.9 mJ/mm², the gelatin displays a fast rise to 252 nm followed by a decay to a quasi-steady state equilibrium of 200 nm. As seen in Figure 5-2, the shape of the curve is identical for a range of fluences. In these normalized curves, the quasi-steady state (QSS) equilibrium is normalized to 1. As expected, the amplitude of the expansion of gelatin scales linearly with laser fluence.
Figure 5-1. Surface displacement of 25% gelatin as a function of time.

Figure 5-2. Normalized surface displacement of figure 5-1 data (25% gelatin) as a function of time; experimental versus theoretical values normalized to a QSS value of 1.
We use the numerical model described in chapter 4 (section 4.3) to find the best fit to the time dependent features, by varying only two parameters: longitudinal speed of sound \((c_L)\) and penetration depth \((D)\). The transverse speed of sound \((\text{eq. 4.65})\) equals zero since the Poisson ratio \((\nu)\) is 0.5 for hydrated samples (section 4.3.5). As we will see below, that second peak due to transverse waves, seen in hard tissue, is missing from experimental results in a hydrated sample. The time dependent behavior is governed only by longitudinal sound speed and penetration depth. The thermal expansion coefficient \((\beta)\) and heat capacity \((C_v)\) determine the overall magnitude of displacement.

In figure 5-2, the theoretical prediction is plotted along with experimental data for three fluences normalized to a QSS value of 1. The best fit is made using the parameters \(D = 450 \, \mu m\) and \(c_L = 1480 \, m/s\). For these experiments, the beam radius \((w)\) was measured to be \(510 \, \mu m\) (\(\pm\ 5 \, \mu m\)). The goodness of the fit was tested by using the chi-squared deviation [Barlow, 1989], which was calculated for data points in the first 1.5 \(\mu s\) interval following the laser pulse \((2 \, \mu s \leq t \leq 3.5 \, \mu s)\). The formula describing \(\chi^2\) follows:

\[
\chi^2 = \sum_{i=1}^{N} \frac{(u_i^{\text{exp}} - u_i^{\text{th}})^2}{N\sigma_i^2}.
\]  

(5.1)

where \(u_i^{\text{exp}}\) is the measured surface displacement, \(u_i^{\text{th}}\) is the predicted displacement, and \(\sigma_i\) is the error in the measurement (\(\pm\ 5 \, nm\)). The surface reaches quasi-steady state equilibrium displacement approximately 1 \(\mu s\) following the laser pulse, data points beyond 3.5 \(\mu s\) will have reached the QSS equilibrium value. Considering data points after 3.5 \(\mu s\) does not help determine the best values of \(c_L\) and \(D\), because the time dependent features (set by \(c_L\) and \(D\)) have already occurred.

If the prediction correctly describes the data then the difference between measurement and prediction should be roughly the same size as the measurement error, \(\sigma_i\). Thus, the sum of squares divided by error should be approximately \(N\), and \(\chi^2\) approximately 1. For the 25% gelatin data with fluences 2.8, 5.2, 6.5, and 8.9 \(mJ/mm^2\), the deviations are 0.51, 1.3, 3.7, and 11.5 respectively. To find the best fit, we compare chi-squared deviations using different predictions (changing \(c_L\) and \(D\)) and choose values that give fits with the lowest \(\chi^2\).
Figure 5-3. Normalized surface displacement of 20% gelatin.

Figure 5-4. Normalized surface displacement of 15% gelatin. At the highest fluence, 7.8 mJ/mm², measured expansion clearly exceeds the theoretical prediction.
For a 20% gelatin sample (figure 5-3), the expansion reaches a peak at 2339 ns, and for a beam radius of 0.51 mm, the corresponding sound speed is $c_L = 1510$ m/s. The best fit is made using $D = 500 \, \mu m$ and $c_L = 1500$ m/s. For fluences of 2.7, 4.7, and 8.8 mJ/mm$^2$, the chi squared deviations are 0.23, 0.87, and 2.6 respectively. As seen in figure 5-3, theory agrees quite well with experiment. For a 15% gelatin sample (figure 5-4), the best fit is made using $D = 550 \, \mu m$ and $c_L = 1300$ m/s. For the lower fluences, 3.8 and 4.1 mJ/mm$^2$, the deviations are 0.53 and 0.72. At the higher fluences (6.3 and 7.8 mJ/mm$^2$), the surface is overshooting the exponential rise before approaching equilibrium displacement. For these fluences, 6.3 and 7.8 mJ/mm$^2$, $\chi^2$ is much larger: 11.2 and 57.4 respectively. In the 15% gelatin sample excess displacements are beginning at lower laser fluences when compared to the 20 and 25% gelatin samples. We can infer that this excess displacement, due to the onset of cavitation, will increase with the water content and laser fluence.

5.1.2 Equilibrium displacement

The analytical expression that defines the quasi-steady state equilibrium displacement is the following (eq. 4.69):

$$S_0 = \frac{2}{3}(1+\nu) \frac{\beta}{\rho C_V} g_0(R) \Phi$$  \hspace{1cm} (5.2)

From this equation and measured equilibrium displacement, the thermal expansion coefficient can be found since $C_V$ and $\rho$ for gelatin are known (Ch. 3). Using the interferometer, we measured the quasi-steady state equilibrium of gelatin as a function of protein concentration. Figure 5-5 shows equilibrium displacement values as a function of fluence for two gelatin samples (20%). Table 5-1 gives the slope of the equilibrium displacement versus fluence data ($S_0 / \Phi$). The values of density and heat capacity for gelatin are given in Table 3-2. The Poisson’s ratio is $\nu = 0.5$ (Section 4.3.5). The geometrical correction factor $g_0(R)$ is found from eq. 4.68. Aspect ratio $R = w/D$ is known from the beam radius and penetration depth obtained from the initial rise. The thermal expansion coefficient is given as a function of gelatin concentration in Table 5-2.
Table 5-1 Slope of quasi-steady state displacement data for gelatin

<table>
<thead>
<tr>
<th>Gel wt %</th>
<th>Mean ± S.D. $S_o / \Phi$ (nm-mm$^2$/mJ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>6.85 ± 1.4</td>
</tr>
<tr>
<td>15</td>
<td>13.2 ± 3.3</td>
</tr>
<tr>
<td>20</td>
<td>17.3 ± 0.6</td>
</tr>
<tr>
<td>25</td>
<td>20.6 ± 0.2</td>
</tr>
</tbody>
</table>

Table 5-2. Thermal expansion coefficient and ratio to heat capacity of gelatin

<table>
<thead>
<tr>
<th>Gel wt %</th>
<th>$\beta$ (K$^{-1}$)</th>
<th>$\beta/C_v$ (g/J)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>$0.64 \times 10^{-4}$</td>
<td>$1.6 \times 10^{-5}$</td>
</tr>
<tr>
<td>15</td>
<td>$1.2 \times 10^{-4}$</td>
<td>$3.1 \times 10^{-5}$</td>
</tr>
<tr>
<td>20</td>
<td>$1.4 \times 10^{-4}$</td>
<td>$3.7 \times 10^{-5}$</td>
</tr>
<tr>
<td>25</td>
<td>$1.8 \times 10^{-4}$</td>
<td>$4.8 \times 10^{-5}$</td>
</tr>
</tbody>
</table>

Figure 5-5. Quasi-steady state equilibrium displacement of 20% gelatin. Equilibrium displacement is linear with laser fluence.
5.1.3 Gelatin with primuline

To make lower gelatin concentration samples, it is necessary to add a dye which absorbs UV photons ($\lambda = 355$ nm). As for gelatin samples of section 5.1.1, we compare the measured surface displacement with theoretical predictions.

Using 9% gelatin samples doped with primuline (Section 3.4), we observe the same general curve shape. The best fit to the data was made using values of $D = 300$ $\mu$m and $c_L = 1600$ m/s. Figure 5-6 shows data normalized to a quasi-steady state value of 1. However, these experiments did not agree quite as well with theory when compared to the undoped gelatin. The effect of having two absorbers present, primuline and protein molecules, was modeled using the heat conduction equation (Section 4.3.2). Using an initial temperature modified by heat conduction (eq. 4.51) improved the fits to experiment significantly. Thus, the effect of heat conduction is significant in gelatin with primuline.

The numerical model with heat conduction for two absorbers has four parameters to fit the time dependent behavior. In addition to the speed of sound and penetration depth, we must choose the initial amount of laser energy that goes into expansion ($f$) and the time constant that characterizes heat conduction ($\tau$). For a 17% gel sample with primuline, the best fit to the time dependent behavior was made using the following values: $D = 300$ $\mu$m, $c_L = 1650$ m/s, $f = 0.56$, and $\tau = 280$ ns. At the highest fluence of 8.7 mJ/mm$^2$, the surface displacement has begun to overshoot the predicted displacement and reaches equilibrium at 2750 ns. For the 9% gel sample, the best fit to the time dependent behavior was made using $D = 300$ $\mu$m, $c_L = 1600$ m/s, $f = 0.56$, and $\tau = 280$ ns (see figure 5-6). At a higher fluence of 6.0 mJ/mm$^2$, the expansion clearly exceeds the predicted behavior, reaching equilibrium at 2850 ns. For a 5% gel sample, the best fit to the time dependent behavior ($\Phi = 1.8$ mJ/mm$^2$) was made using $D = 200$ $\mu$m, $c_L = 1600$ m/s, $f = 0.56$, and $\tau = 280$ ns (see figure 5-7). Higher fluences show large overshoots due to cavitation. At a fluence of 4.3 mJ/mm$^2$, a large overshoot lasting 2.2 $\mu$s occurs. As with undoped gelatin, we observe that the onset of cavitation has a lower fluence threshold for lower concentration (and therefore weaker) gelatin.
Figure 5-6. Normalized surface displacement of 9% gelatin with primuline added. The solid line represents the theory including heat conduction.

Figure 5-7. Normalized surface displacement of 5% gelatin. The theoretical prediction including heat conduction is applicable to the lowest fluence (1.8mJ/mm²). Large excess displacement occurs for the higher fluence values.
Table 5-3 lists the thermal expansion coefficient of primuline-doped gelatin as well as primuline in aqueous solution (either de-ionized water or saline as the solvent). The values of thermal expansion coefficient obtained from experiment are reasonable for a gelatin phantom; the values are of the same order of magnitude as soft tissue but greater than that of water. For example, the thermal expansion of bovine muscle is $3.75 \times 10^{-4} \text{K}^{-1}$ for 5-30° C. [Duck. 1990]

<table>
<thead>
<tr>
<th>Table 5-3 Thermal expansion of primuline in gel and in aqueous solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S_0/\Phi$ (nm-mm$^2$ / mJ)</td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>De-ionized H$_2$O</td>
</tr>
<tr>
<td>Saline</td>
</tr>
<tr>
<td>3x saline</td>
</tr>
<tr>
<td>Gelatin 5 %</td>
</tr>
<tr>
<td>9 %</td>
</tr>
<tr>
<td>17 %</td>
</tr>
</tbody>
</table>

The numerical model (with a correction for heat conduction between two absorbers) describes the time dependent surface motion of gelatin with primuline for different fluences. The timing of the peak corresponds to a sound speed of $c_L$=1650 m/s for 17% gel and 1600 m/s for 9%. Both of these values are within 10% of the longitudinal sound speed in water. The penetration depth obtained from the initial slope is D = 300 μm. The onset of cavitation in gelatin is clear as the deviation of experiment from the numerical prediction becomes large.

5.2 Experiment versus Theory in Water and Saline

As described in Chapter 2, meniscus contains approximately 70-75% water. Water, a well-characterized liquid, provides us with an experimental sample whose physical properties are known. By understanding the interaction of ten nanosecond laser pulses with water, we can further our understanding of meniscus. In this vein, we
performed experiments on de-ionized water and phosphate buffered saline. Saline may be useful to compare to the synovial fluid contained in meniscus, as it also contains salt ions. As described in Chapter 3, primuline was added to both water and saline for absorption of the 355 nm photons. The penetration depths of these samples were measured; thus, only \( c_L \) was obtained from the fit of experiment to theory.

5.2.1 Displacement versus time

Figure 5-8 shows the typical surface displacement of de-ionized water as a function of time. At the lower fluence values the time dependent behavior resembles that of gelatin. As laser fluence is increased, the water surface displays additional displacements of microsecond duration. Thus, the lower fluence data were compared with theory to determine sound speed and penetration depth values as in gelatin (Section 5.1.1). The penetration depths of primuline doped water, saline and high salt saline (mass of salts added is three times that for normal saline) were measured to be 350, 340, and 380 \( \mu \)m respectively.

For the de-ionized water data, the best fit was made using a sound speed of \( c_L = 1550 \) m/s and penetration depth was set to 350 \( \mu \)m. For the saline data, a fit to the low fluence data was not possible due to excess surface displacement. Figure 5-9 shows the normalized displacement of primuline doped saline compared to a theoretical prediction using \( D=340 \ \mu \)m and \( c_L=1500 \) m/s.

5.2.2 Equilibrium displacement

Using equation 5.2 and the measured equilibrium displacement, the thermal expansion coefficient of de-ionized water was determined. The measured slope of equilibrium displacement as a function of fluence data for de-ionized water is 27.1 nm-mm\(^2\)/mJ. The density of this sample, is 1.0003 g/cm\(^3\). Using the value of heat capacity of water, \( C_v = 4.18 \) J/g K, and a geometric correction factor, \( g_o(R) = 0.544 \), we find the thermal expansion coefficient to be \( \beta = 2.08 \times 10^4 \) K\(^{-1}\). Our measurement agrees with the value of water, \( 208 \times 10^6 \) K\(^{-1}\) at 293 K. [Zemansky, 1957] Thus the small amount of
Figure 5-8. Surface displacement of de-ionized water for different laser fluences.

Figure 5-9. Normalized surface displacement of phosphate buffered saline. Low fluence data show large overshoots of the thermoelastic predictions.
primuline, necessary for 355 nm absorption, does not change the thermal properties of the liquid.

Identically, the thermal expansion coefficient of saline is determined. The slope from the equilibrium displacement data for saline is 38.4 nm-mm²/mJ. The mass density of saline with primuline is \( \rho = 1.01 \text{ g/cm}^3 \). The heat capacity at constant volume of saline is estimated to be that of seawater (1 atm pressure, \( T = 20^\circ \text{ C} \), 1 % salinity) 4.10 J/g-K [Siedler, 1986]. From these values, the measured thermal expansion coefficient is \( \beta = 2.82 \times 10^{-4} \text{ K}^{-1} \) (see Table 5-3). The thermal expansion coefficient of seawater is given in the literature as \( \beta = 2.25 \times 10^{-4} \text{ K}^{-1} \) [Siedler, 1986]. As expected, the addition of salts to water increases its thermal expansion, and we observe a higher value of thermal expansion coefficient in saline.

For 3x saline, the slope of equilibrium displacement data is 37.9 nm-mm²/mJ. The mass density of this mixture is \( \rho = 1.03 \text{ g/cm}^3 \). The heat capacity at constant volume of 3x saline is estimated to be that of seawater (\( P = 1 \text{ atm} \), \( T = 20^\circ \text{ C} \), 3 % salinity), 3.98 J/g-K [Siedler, 1986]. From these values, the measured thermal expansion coefficient is \( \beta = 2.90 \times 10^{-4} \text{ K}^{-1} \) (see Table 5-3).

5.3 Experiment versus Theory in Meniscus

Meniscus was obtained from patients undergoing total knee replacement surgery. The samples were placed in normal saline for transport to the laboratory. They were then placed in a refrigerator at 4°C and kept until use, which was within 24-30 hours. Following irradiation, they were marked with tissue marking dye (Bradley Products, Bloomington, MN), fixed in 10% formalin and sent for a histological assessment.

5.3.1 Displacement versus time

The surface displacement curve shape of meniscus following a 10 ns laser pulse is similar to that of high concentration gelatin (20, 25% gel). The sample rises exponentially, and then reaches a peak that corresponds to acoustic waves from the beam width reaching the center (where the HeNe probe is located. The sample surface then decays to a quasi-steady state equilibrium, at which the sample will remain until thermal
diffusion occurs.

A typical meniscus sample displays an exponential rise to a peak at 2332 ns, 332 ns following the laser pulse (figure 5-10). The surface then approaches its QSS equilibrium value of 90 nm. The best fit to this data (see figure 5-11) using the numerical model of section 4.3 was made using a sound speed of \( c_L = 1600 \, \text{m/s} \) and penetration depth \( D = 280 \, \mu \text{m} \). For fluences of 1.1, 1.5, and 2.9 mJ/mm\(^2\), \( \chi^2 \) is 0.30, 0.92, and 1.6 respectively. These chi-squared values are quite good and should again indicate when the thermoelastic model is no longer sufficient to describe the data. Therefore, large deviations signify excess surface displacement due to the onset of cavitation.

Figure 5-12 shows the normalized displacement of a second meniscus sample. The surface reaches a peak approximately 330 ns following the laser pulse. These fluence values were fit by a sound speed of \( c_L = 1550 \, \text{m/s} \) and penetration depth \( D = 260 \, \mu \text{m} \). This sample shows that displacement in the higher fluences, 7.6 and 8.1 mJ/mm\(^2\), slightly exceeds the predicted displacement during the decay from peak to equilibrium. The chi-squared deviations for this sample are 0.90, 1.4, 6.8, 8.4 for fluence values of 2.4, 5.2, 7.6, and 8.1 mJ/mm\(^2\). The higher values at \( \Phi=7.6 \) and 8.1 mJ/mm\(^2\) arise from excess displacement.

Deviations are slightly higher in meniscus when compared with gelatin data (Section 5.1.1), but this is due to decreased spatial resolution. However, the thermoelastic model is appropriate for predicting the complete motion of meniscus at sub-threshold and/or near threshold fluences. Table 5-4 lists the thermoelastic fit parameters for meniscus samples. The mean longitudinal sound speed of meniscus is \( \bar{c}_L = 1650 \, \text{m/s} \) and the mean penetration depth (at \( \lambda=355 \, \text{nm} \)) is \( \bar{D} = 252 \, \mu \text{m} \). This value of penetration depth agrees within 1% of the mean value of penetration depth as measured by a spectrophotometer (Chapter 2).
Figure 5-10. Typical surface displacement of meniscus.

Figure 5-11. Normalized surface displacement of meniscus and predicted displacement shows good agreement for $c_L=1600$ m/s and $D=280$ μm.
5.3.2 Equilibrium displacement

As discussed in section 5.1.2 we can use the quasi-steady state equilibrium displacement to determine certain physical properties of an irradiated sample. Table 5-5 lists the slope of equilibrium displacement versus fluence data for several meniscus samples. Figure 5-13 shows the equilibrium displacement versus fluence at four different sites on a meniscus sample. Using equation 5.3, the measured equilibrium displacement can be utilized to determine the ratio of thermal expansion coefficient and heat capacity at constant volume ($\beta/C_v$) in knee meniscus. Again, for a hydrated sample such as meniscus, Poisson’s ratio is $\nu = 0.5$. The geometrical correction factor $g_o(R)$ is determined from equation 4.68. The aspect ratio $R = w/D$ is known from the pump beam radius and the value of penetration depth obtained from the time dependent behavior. These values of $\beta/C_v$ are comparable with those of gelatin (no primuline) in Table 5-2.
Figure 5-12. Normalized displacement of meniscus.

Figure 5-13. Quasi-steady state equilibrium displacement of meniscus versus fluence for four samples.
Table 5-4 Longitudinal sound speed and penetration depth ($\lambda = 355$ nm) of meniscus

<table>
<thead>
<tr>
<th>Sample</th>
<th>$c_l$ (m/s)</th>
<th>D (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-15 1</td>
<td>1620</td>
<td>260</td>
</tr>
<tr>
<td>8-15 2</td>
<td>1600</td>
<td>280</td>
</tr>
<tr>
<td>8-15 3</td>
<td>1600</td>
<td>270</td>
</tr>
<tr>
<td>8-15 4</td>
<td>1630</td>
<td>260</td>
</tr>
<tr>
<td>8-15 5</td>
<td>1580</td>
<td>270</td>
</tr>
<tr>
<td>11-7 1</td>
<td>1600</td>
<td>280</td>
</tr>
<tr>
<td>12-19 1</td>
<td>1680</td>
<td>220</td>
</tr>
<tr>
<td>12-19 2</td>
<td>1750</td>
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</tr>
<tr>
<td>12-19 3</td>
<td>1700</td>
<td>240</td>
</tr>
<tr>
<td>12-19 4</td>
<td>1850</td>
<td>250</td>
</tr>
<tr>
<td>12-19 5</td>
<td>1750</td>
<td>250</td>
</tr>
<tr>
<td>1-9 1</td>
<td>1650</td>
<td>240</td>
</tr>
<tr>
<td>1-9 2</td>
<td>1700</td>
<td>240</td>
</tr>
<tr>
<td>1-9 3</td>
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<td>220</td>
</tr>
<tr>
<td>1-9 4</td>
<td>1650</td>
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<td>260</td>
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<tr>
<td>2-20 1</td>
<td>1560</td>
<td>260</td>
</tr>
<tr>
<td>2-20 2</td>
<td>1600</td>
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</tr>
<tr>
<td>Standard deviation</td>
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</tbody>
</table>
Table 5-5 Slope of equilibrium displacement data for meniscus

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<th>$S_0/\Phi$ (nm-mm²/mJ)</th>
<th>$g_0(R)$</th>
<th>$\beta/C_v$ (x10⁻⁴)</th>
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<tr>
<td>2-20 3</td>
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<tr>
<td>2-20 6</td>
<td>25.4</td>
<td>0.627</td>
<td>4.4</td>
</tr>
</tbody>
</table>
5.4 Conclusions

Interferometric surface monitoring is an experimental technique that measures surface expansion of a material following irradiation by a nanosecond laser pulse. Gelatin provided a consistent experimental model of a soft biological tissue, with which to compare the predictions for a hydrated sample based on the thermoelastic wave equation.

However, one must consider the introduction of artificial dye for 355 nm laser light absorption and its effects on the gelatin. In these experiments, primuline acted as a second light absorber. Therefore, in order to approximate meniscus, which has only one absorber, collagen, we will consider undoped gelatin and aqueous dye samples to be more useful for further experiments.

By comparing measured surface expansion and theoretical predictions, one can obtain the longitudinal sound speed, optical penetration depth, and thermal expansion coefficient of hydrated samples. These properties of knee meniscus are not well studied in the literature. This method measured the longitudinal speed of sound and optical penetration depth at 355 nm of meniscus. In addition, thermal properties, in the form of the ratio of thermal expansion coefficient to heat capacity $\beta/C_v$, were determined from equilibrium surface expansion measurements. These results should contribute to the general knowledge of physical properties of meniscus tissue, because the physical properties of meniscus are not well established.
Chapter 6
Cavitation in Hydrated Samples

6.1 Overview of Cavitation

Laser-induced cavitation in tissue is a phenomenon that occurs when laser pulses interact with tissues of high water content. As seen from the review of the literature on the laser-tissue interaction in Chapter 1, bubble formation in liquids occurs for a range of wavelengths, pulse lengths, and energy densities. However, true cavitation results from pressure reductions within a liquid.

Cavitation has been under study by scientists for most of the twentieth century. It became important to marine engineers who dealt with the erosion of propellers and hydraulic turbines. Cavitation “pitting” occurs when these cavities collapse against a solid surface, as they pass from negative to positive pressure zones. Lord Rayleigh contributed greatly to the understanding of cavity behavior in 1917 with his article “On the Pressure Developed in a Liquid During the Collapse of a Spherical Cavity”. [Lord Rayleigh, 1917] He quoted the treatment by Besant (1859) of an empty cavity in an incompressible fluid, and solved the problem through energy conservation, finding that pressure can rise greatly inside a collapsing cavity. Through his calculation, Rayleigh explained the ability of water bubbles to cause “pitting” in material with static yield strengths of $10^5$-$10^6$ psi. [Birkhoff and Zarantonello. 1957]

In this work, cavitation bubbles are opened by the propagating acoustic waves following the laser pulse. Laser-induced cavitation bubbles in water behind the tensile wave have been observed experimentally by Paltauf et al. [Paltauf et al. 1992] Our research group inferred that laser-induced cavitation bubbles formed within meniscus, a soft tissue, using the interferometric measurements of the surface expansion. [Schaffer et al, 1995] Similar observations of cavitation bubbles in water were made by Oraevsky et al [1996]. via strobe photography.

We have developed a numerical model that calculates the size of a bubble’s growth and collapse based on Rayleigh’s equation of motion for a bubble. The transient changes in pressure due to the propagating laser-induced stress wave cause cavitation in a
liquid. A distribution of bubbles develops as a function of time and space. Our interferometer is a tool that measures the motion of a tissue’s surface due to thermal expansion and due to the growth of cavitation bubbles. In this chapter, experimental results in aqueous solution (water, saline) and meniscus are compared with this theoretical model based on the equation of motion for a spherical bubble. Cavitation occurs when tensile stress in a fluid exceeds its tensile strength and causes it to rupture. The static tensile strength of very pure water is given to be anywhere from 10 to 200 atmospheres. [Knapp et al., 1970] The presence of impurities will lower the tensile strength of water. In meniscus, cavitation of the tissue’s fluid could occur in areas where the extracellular matrix is either weakened or not present. Therefore, by studying the cavitation behavior of meniscus, we can infer information about its mechanical properties.

6.2 Spherical Bubble Dynamics

6.2.1 Bubble Equation of Motion

The derivation of the bubble equation of motion is taken from the text by Birkhoff and Zarantonello. [Birkhoff and Zarantonello, 1957] The problem to be considered is that of a spherical bubble of radius \( a(t) \), in a liquid of density \( \rho \). The liquid is incompressible. At a distance \( r \) from the center of the bubble (see figure 6-1) the radial velocity, \( \frac{dr}{dt} \), satisfies

\[
\frac{dV}{dt} = 4\pi r^2 \frac{dr}{dt} = f(t) \tag{6.1}
\]

The radial velocity of the bubble surface must also satisfy equation (6.1):

\[
\frac{dV_s}{dt} = 4\pi a^2 \frac{da}{dt} = f(t) \tag{6.2}
\]

because the liquid is incompressible. Thus, radial velocities satisfy the equation

\[
a^2 \dot{a} = r^2 \dot{r} = f(t), \tag{6.3}
\]

where \( a \) and \( \dot{a}/dt \) are functions of time only. The kinetic energy of the liquid is found by integrating \( dE = (\rho v^2 dt)/2 \) throughout the liquid. The kinetic energy is defined by
\[ E = \frac{1}{2} \rho \int_{a}^{\infty} r^{2} 4\pi r^{2} dr. \]  

(6.4)

Using equation 6.3 to eliminate \(dr/dt\), the kinetic energy becomes

\[ E = 2\pi \rho \int_{a}^{\infty} r^{2} \cdot \frac{dr}{r^{2}} = 2\pi \rho a^{4} \cdot \frac{dr}{r^{2}} = 2\pi \rho a^{2} a^{3}. \]  

(6.5)

![Figure 6-1. Spherical bubble of radius a. in an incompressible fluid of density \(\rho\).](image)

Cavitation usually occurs in a flowing liquid when it flows through a region of negative pressure. In this work, it occurs when the propagating acoustic wave, with a tensile component, passes through a particular region of a liquid. An expression for the bubble’s growth and collapse can be obtained by looking at the work-energy relation

\[ dW = \mathbf{F} \cdot d\mathbf{r} = -P(t) \cdot (4\pi a^{2}) \dot{a} dt, \]  

(6.6)

where \(P(t)\) is the local pressure difference, \(p_{\text{out}} - p_{\text{in}}\). We assume that the size of the bubble is smaller than the scale over which pressure changes. By neglecting surface tension, the energy equation becomes

\[ \frac{dE}{dt} = -4\pi a^{2} \dot{a} P(t). \]  

(6.7)

Using equation 6.5, we obtain the second order differential equation for the bubble radius,

\[ -\frac{P(t)}{\rho} = \frac{3}{2} a \ddot{a} + a \dot{a}. \]  

(6.8)

Given pressure in the liquid, equation 6.8 gives the radius as a function of time. In this chapter, we will calculate the radii of a distribution of bubbles and find the excess displacement of the surface above this distribution of bubbles. If we consider surface tension the equation of motion becomes
\[-\frac{P(t)}{\rho} - \frac{2\gamma}{a} = \frac{1}{2} a^2 + a\ddot{a}, \quad (6.9)\]

where \(\gamma\) is surface tension per unit area. To obtain an analytical solution, the equation must first be simplified; pressure is constant and surface tension is neglected. By setting kinetic energy (eq. 6.5) equal to work done by pressure, we have a simpler differential equation that can be integrated by elliptic integrals or incomplete \(\beta\)-functions. Here, conservation of energy gives

\[
\left(\frac{\dot{a}}{a_{\text{max}}}\right)^2 = K^2 \left[\left(\frac{a_{\text{max}}}{a}\right)^3 - 1\right], \quad K = \sqrt{\frac{2P}{3\rho a_{\text{max}}^2}}. \quad (6.10)
\]

Solving equation 6.10 gives an integral that can be solved with elliptic integrals,

\[
\tau = \int_0^1 \frac{\alpha^2 d\alpha}{\alpha - \alpha^4}, \quad \text{where} \quad \tau = Kt, \quad \alpha = a/a_{\text{max}}. \quad (6.11)
\]

6.2.2 Rayleigh’s Time of Collapse of a Spherical Cavity

Equation 6.8 gives the equation of motion of a bubble generated by a pressure function. We can use a simpler version of this equation to estimate the size of these bubbles from the interferometric data. Lord Rayleigh [1917] first calculated the timescale of collapse of a cavity at rest with radius \(a(0) = a_{\text{max}}\). The pressure at large distances, \(p_\infty\), exceeds the vapor pressure in the bubble by a fixed amount \(P\). The formula that describes the collapse time is as follows:

\[
t_c = 0.915 a_{\text{max}} \sqrt{\frac{\rho}{p_\infty - p_v}} = 0.915 a_{\text{max}} \sqrt{\frac{P}{P}} \quad (6.12)
\]

For a sample of knee meniscus, we calculate the average bubble size by using the time from maximum surface displacement to equilibrium displacement. For a laser pulse of 4.1 mJ/mm\(^2\) (see Figure 6-2), the collapse time is 3140 ns (± 48 ns). With a pressure of 1 atmosphere and density of 1.1 g/cm\(^3\), we calculate an average radius of 33 microns. Bubbles with size on the order of 10 microns is quite reasonable since Paltauf et al resolved cavitation bubbles in water following an 8 ns laser pulse using strobe photography with a 532 nm light source. [Paltauf et al, 1992]
For primuline in de-ionized water ($\Phi = 5.9 \text{ mJ/mm}^2$), the collapse time is 2690 ± 54 ns (time for surface to reach equilibrium following maximum displacement). Using equation 6.10, the average radius of cavitation bubbles in water is 30 microns. Therefore, we continue this study under the hypothesis that cavitation is the cause of excess surface displacement in aqueous solutions and knee meniscus.

![Graph showing surface displacement of knee meniscus](image)

Figure 6-2. Surface displacement of knee meniscus. Collapse time is approximately 3140 nm.

6.3 Numerical Modeling of Cavitation

A numerical model was developed in FORTRAN that integrates the bubble equation of motion, in order to find the radius of a cavity as a function of time. Using the thermoelastic stress components, we obtain pressure at discreet points in space and time. The ultimate goal is to calculate the radii of cavities in an irradiated sample from the pressure distribution. The bubble volumes and the surface expansion they cause can be calculated. The predictions of the model were compared with measured surface expansion and cavitation parameters were obtained for meniscus, gelatin, saline, and de-ionized water.

6.3.1 Basic equations

The model is based on the bubble equation of motion (eq. 6.8), which is normalized to the initial radius of the nucleation site, $R_0$. The assumption made is that cavitation begins at these nucleation sites, or very small free bubbles [Knapp et al. 1970].
We also know from our previous estimate that the maximum size of a bubble, 30 \mu m, is smaller than the length scale over which pressure changes. Pressure differences caused by the acoustic wave occur on a length scale of roughly D \sim 300 \mu m. Using this knowledge, we will use a constant value of pressure over the spatial scale of one bubble diameter. An additional assumption made is that these bubbles do not perturb the propagating acoustic wave. We consider the effect of these empty bubbles on density of the medium. The volume of a bubble is \( \frac{4}{3}\pi r^3 \) or \( 1.1 \times 10^5 \mu m^3 \), and the laser-irradiated volume is \( \pi w^2 D = 2.5 \times 10^8 \mu m^3 \). For a 10% change in density,

\[
\rho' = 0.1 \rho = \left( 1 - N \frac{\frac{4}{3}\pi r^3}{\pi w^2 D} \right) \rho
\]  

(6.13)

2000 bubbles would need to form. From strobe photography of cavitation [Paltauf et al, 1992], we expect the number of bubbles formed to be well under 2000.

In order to avoid dividing by zero, which would occur in the case of a closed bubble (a=0), we choose a new variable \( \alpha \). By dividing both sides of equation 6.8 by \( R_o^2 \), we obtain the following equation:

\[
-\frac{P(t)}{\rho R_o^2} = \frac{3}{2} \dot{\alpha}^2 + \alpha \ddot{\alpha},
\]

(6.14)

where \( \alpha = \frac{a}{R_o} \). We define pressure as a sum of the transient pressure due to the propagating acoustic wave and a cavitation threshold pressure that must be exceeded in order for the bubble to rupture. Therefore, pressure is given by the following equation:

\[
P(t) = P_{TE}(z, t) + P_{th}
\]

(6.15)

The pressure due to thermoelastic stress is related to the diagonal components of the stress tensor (eq. 4.9) by the following equation:

\[
P_{TE} = \frac{\sigma_{rr} + \sigma_{zz} + \sigma_{\phi\phi}}{3}.
\]

(6.16)

We define the velocity divided by initial radius, \( \dot{\alpha} \), in the following equation:

\[
\frac{\dot{\alpha}}{R_o} = \ddot{\alpha} = \beta
\]

(6.17)

The equation of motion becomes
\[ \dot{\beta} = -\frac{1}{\alpha} \left( \frac{P}{\rho R_0^2} + \frac{1}{2} \beta^2 \right), \quad (6.18) \]

and in the case where surface tension is considered the equation of motion is

\[ \dot{\beta} = -\frac{1}{\alpha} \left( \frac{P}{\rho R_0^2} + \frac{2\gamma}{\rho R_0^2 \alpha} + \frac{1}{2} \beta^2 \right). \quad (6.19) \]

**6.3.2 Numerical Modeling**

By integrating the equation of motion twice, we calculate the normalized radius of a bubble. The Adams-Bashforth method is used to numerically integrate equation 6.18 (or eq. 6.19) [Potter, 1977]. Using this method, the equations for velocity and radius become

\[ \beta(t + \Delta t) = \beta(t) - \left( \frac{1}{2} + \varepsilon \right) \dot{\beta}(t) \cdot \Delta t + \left( \frac{1}{2} + \varepsilon \right) \ddot{\beta}(t - \Delta t) \cdot \Delta t, \quad (6.20) \]

\[ \alpha(t + \Delta t) = \alpha(t) - \left( \frac{1}{2} + \varepsilon \right) \beta(t) \cdot \Delta t + \left( \frac{1}{2} + \varepsilon \right) \beta(t - \Delta t) \cdot \Delta t, \quad (6.21) \]

where \( \varepsilon \) is the constant defined by equation 4.61, and \( \Delta t \) is the time step defined in the thermoelastic numerical model (section 4.3.3).

The initial conditions are chosen so that the radius of each bubble, \( a \), is equal to the radius of the nucleation site, \( R_0 \). Thus, the normalized radius \( \alpha \) for all bubbles is initially one, \( \alpha(t=0) = 1 \). All initial velocities and accelerations are set equal to zero. Initial pressure everywhere, \( P(t=0) \), is also set equal to zero. Typically, one bubble exists in each cell of the computer grid. Each bubble is driven by the pressure of that particular cell.

The volume of each bubble is calculated at a time step approximately equal to the time necessary for an acoustic wave to propagate through one grid cell or

\[ \Delta t_{\text{acw}} \leq \frac{\Delta}{c_i}, \quad (6.22) \]

where \( \Delta \), divided by the speed of sound, typically 6 ns for a 10 micron cell and sound speed of water 1.5 \( \mu \text{m/ns} \). By using a \( \Delta t_{\text{acw}} \) larger than \( \Delta t \), we cut down on the number of calculations necessary and minimize the amount computer memory needed. Then, these bubble volumes are used to find the displacement due to cavitation.

As the acoustic wave propagates into the tissue (z direction), bubbles open as the
tensile part of the wave reaches that grid cell. Once a bubble opens, it is added in to compute surface displacement, but only after a specific time delay. This delay accounts for the time necessary for the information to propagate itself back to the surface. It depends on the depth below the surface and the speed of sound in the following manner:

\[ t_{\text{delay}} = \frac{z}{c_s}. \]  

(6.23)

Therefore, after a time of approximately \(2z/c_s\), a bubble volume begins to affect the surface. The total volume, at a discreet time step is calculated by summing the volumes of the bubble in each grid cell:

\[ V_{\text{tot}}(t) = \sum_{j=0}^{n} V_j \left( t - \frac{j\Delta t}{c_s} \right) \]  

(6.24)

where \(j\) is the index of cells in the axial (z) direction. The displacement caused by these bubbles is taken to be the cube root of the total volume. Therefore, surface displacement due to cavitation is simply:

\[ z_{\text{cav}}(t) = \left[ V_{\text{tot}}(t) \right]^{1/3}. \]  

(6.25)

We then introduce a scaling factor, which is the amount the maximum displacement of the numerical result is scaled by to match the experimentally measured maximum surface displacement. By multiplying the nucleation site density by the scaling factor, we obtain a density representative of the actual density of cavitation bubbles within the sample. In the numerical model, the nucleation site density is simply 1 bubble per cell or \(10^{-3}\) bubble/\(\mu\text{m}^3\). Adding the predicted cavitation displacement and the thermoelastic displacement together should give a complete picture of the physical response of a hydrated sample to a nanosecond laser pulse.

6.3.3 Output of Model
Pressure

As discussed above, pressure is related to the components of the stress tensor in a simple way. To determine the results of this calculation, pressure was calculated by the code and plotted as a function of depth within the sample. As expected, the pressure
Figure 6-3. Pressure as calculated by the numerical model as a function of depth (D=300 μm, c_L=1500 m/s).

Figure 6-4. Pressure as calculated by the numerical model as a function of depth (D=300 μm, c_L=1500 m/s).
distribution follows the general behavior of the stress components. Pressure begins by compressing the sample at the initial time, t = 0. The pressure wave propagates and develops a tensile part that grows larger, becoming a bipolar wave when it reaches one penetration depth. Figure 6-3 shows this bipolar wave reaching one depth (z/D = 1) at 200 ns, which is correct for this set of parameters (c_l=1500 m/s, D=300 μm). By 400 ns, the shape has begun to evolve from a bipolar wave to a narrow tensile pulse, which propagates deeper into the tissue (see figures 6-3 and 6-4). We attribute this shape change to three-dimensional effects. In the one-dimensional case (Chapter 4) we would see the bipolar wave propagate and decay exponentially. In figure 6-4, the wave continues to propagate and by 1200 ns, it has reached six penetration depths (z/D = 6), as expected.

Bubble Radius

The simplest case of cavitation is a spherical bubble in an incompressible, infinite medium at a constant pressure, p_w. Equation 6.12 gives the collapse time for a spherical bubble as calculated by Lord Rayleigh. For a periodically, oscillating bubble, one which rebounds elastically after it closes, the collapse time is a half-period. Thus, the simplest bubble shape is a half-ellipse. Keeping this fact in mind for comparison purposes, we use the numerical model to calculate the growth of bubbles. Figure 6-5 shows the growth of cavitation bubbles as calculated by the model. For a set of physical parameters (c_l=1500 m/s, D=300 μm, R_0=20 nm, p_w=0), bubble radii are given at chosen depths within the sample. These depths are z = 10, 20, 300 and 2990 microns below the surface, or grid cell j = 1, 2, 30, and 299 respectively. Near the surface bubbles are smaller and short lived, reaching a maximum radius of 1 μm and lasting for about 1 μs. At z = 300 μm or one penetration depth, the tensile stress reaches its largest value; thus, the bubbles are the largest at z/D =1. Near the bottom of the computer grid, once the magnitude of tensile stress has decayed, bubbles continue to open, but are again small and short lived. Once each bubble closes, the model prevents it from opening again. Figure 6-5 also shows that bubbles close faster than they open. This result is as expected since the tensile part of the acoustic wave is followed by a compressive component before stress becomes zero.
Figure 6-5. Radius of bubbles as a function of time \((c_L=1500 \text{ m/s, } D=300 \mu \text{m, } R_0=20 \text{ nm, } p_m=0)\).

Figure 6-6. Typical surface displacement of water as a function of time. An overshoot of about 3.5 \(\mu\text{s} \) occurs at the highest fluence \((8.4 \text{ mJ/mm}^2\)).
6.4 Cavitation: Experiment versus Theory

A comparison of the theoretically predicted and measured expansion due to cavitation is given in this section. Experimental results were obtained for de-ionized water, saline, and human knee meniscus. De-ionized water and saline samples contained primuline in order to increase absorption of 355 nm light to a value comparable to that of meniscus. In section 6.4.1, we will compare theory with experiment in water and saline. In section 6.4.2, we will compare theory with experiment in gelatin. In section 6.4.3, we will compare experimental results in meniscal tissue with theoretical predictions.

6.4.1 Cavitation in water and saline

De-ionized water

We begin our study of cavitation by studying de-ionized water. Figure 6-6 shows the typical surface displacement of de-ionized water as a function of time, for a range of fluences. For a laser fluence of 8.4 mJ/mm², the cavitation overshoot reaches a peak displacement of 580 nm and persists for about 3.5 μs. We run our numerical model with a chosen set of thermoelastic properties, changing three parameters to obtain the best fit to the time dependent shape of the overshoot. The thermoelastic properties described in Chapter 5 are as follows: density, longitudinal sound speed, penetration depth, and Poisson’s ratio. For water, these properties are well known. For saline, these properties are also well known, except for the longitudinal sound speed; however, we can expect the sound speed of saline to be within 10% of that of water. Table 6-1 lists the values of the thermoelastic properties for both water and saline.

The three cavitation parameters are threshold pressure, nucleation site size, and surface tension per area (pₜ, R₀, and γ). We scale the maximum displacement of the theoretical curve so that it equals the maximum displacement of the experimental result. This fourth parameter multiplied by 10⁻³ μm⁻³ (nucleation site density) will give us the density of bubbles (n) within the sample.

For a de-ionized water sample, we first fix the values of the physical properties needed for the thermoelastic model. Once the thermoelastic parameters are set, we then
Table 6-1. Physical properties of water and saline obtained from comparison of experimental results to theoretical predictions.

<table>
<thead>
<tr>
<th>Physical properties</th>
<th>Water (Φ=5.1 mJ/mm²)</th>
<th>Saline (Φ=5.0 mJ/mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density ρ (g/cm³)</td>
<td>1.00</td>
<td>1.01</td>
</tr>
<tr>
<td>Sound speed c_L (m/s)</td>
<td>1500</td>
<td>1650</td>
</tr>
<tr>
<td>Penetration depth D (µm)</td>
<td>350</td>
<td>340</td>
</tr>
<tr>
<td>Poisson’s ratio ν</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Threshold pressure p_th (atm)</td>
<td>0.70</td>
<td>0.27</td>
</tr>
<tr>
<td>Nucleation site R₀ (nm)</td>
<td>50</td>
<td>2</td>
</tr>
<tr>
<td>Bubble density n (µm³)</td>
<td>1.5 x 10⁻⁶</td>
<td>1.1 x 10⁻⁶</td>
</tr>
<tr>
<td>Surface tension γ (kg/s²)</td>
<td>0.002</td>
<td>0</td>
</tr>
</tbody>
</table>

adjust the cavitation parameters described above to find the best theoretical prediction of cavitation displacement. A good prediction was made using the following parameters: p_th = 0.70 atm, R₀ = 50 nm, and γ = 0.002 kg/s².

Saline

Compared to deionized water, phosphate buffered saline displays much more surface motion due to cavitation Figure 6-7 shows typical surface displacement of saline for different laser fluences. Following the method detailed above, the numerical cavitation code was run to generate the best predicted surface displacement. The best prediction was made using these values: p_th = 0.27 atm, R₀ = 2 nm, and γ = 0.

Discussion

Figure 6-8 shows the surface motion of de-ionized water and saline, experiment and theory. Both fluence and optical penetration depth are similar (see Table 6-1); thus any differences in behavior attributed to laser fluence or geometry of the light distribution are minimized. The most significant differences between saline and water occur in the threshold pressure and nucleation site size parameters. We know that the addition of impurities to pure water decreases its resistance to cavitation. Undissolved gas is the basic
Figure 6-7. Surface displacement of saline shows even larger overshoots than de-ionized water.

Figure 6-8. Excess surface displacement in saline and water is explained by cavitation. The predicted displacement compares reasonably well with experiment.
impurity that reduces a liquid's tensile strength from its high theoretical value to the lower values seen in measurements. [Knapp et al, 1970] The de-ionized water samples have been doped with primuline for laser light absorption; thus, a significant reduction in tensile strength ($\approx 1$ atm) is expected. Studies by Paltauf et al [1992] obtained a threshold value of -7 bars in distilled water doped with copper sulfate.

The effect of impurities is also seen in the lower threshold pressure, $p_\text{th}$, of saline compared to water. Certainly, the presence of salt ions will disrupt the normal hydrogen bonding between water molecules. The positive ions ($\text{Na}^+$, $\text{K}^+$) attract the oxygens and the negative ions ($\text{Cl}^-$) attract the positive, hydrogen end of the water molecules. In our model threshold pressure is the negative pressure needed for a bubble to begin opening; essentially threshold pressure is a measure of the local tensile strength in the liquid.

The larger surface displacement of saline can be attributed to the growth of larger bubbles. As the bubbles grow in size surface tension will play a less significant role. This effect can be seen directly in the surface tension term in the equation of motion (eq. 6.19). The force due to surface tension is inversely proportional to $\alpha$ (unitless bubble radius); thus, as a bubble grows larger the influence of surface tension decreases.

Regarding the density of bubbles that have opened, not much has been discussed in the literature. As discussed previously, Paltauf et al [1992] imaged cavitation bubbles using schlieren photography. From one of the photographs, we can estimate roughly the density of bubbles. In a thin slice of the photo perpendicular to the laser beam ($r=1$ mm), approximately 30 bubbles are seen. This slice represents a disc of irradiated liquid of area $a = \pi r^2 = 3.14$ mm$^2$, and bubbles per unit area is 9.6 mm$^{-2}$. To estimate bubbles per unit volume, we sum over these discs in the depth that the bipolar wave has propagated. In this photograph, the bipolar wave has propagated a distance of $z = c_L \cdot \Delta t = 1.5 \mu$m/ns $\cdot 60$ns $= 900\mu$m. Thus, an estimate of bubble density is $1.1 \times 10^8$ $\mu$m$^{-3}$. The estimate is smaller than the value obtained from our model by two orders of magnitude, but the schlieren photograph certainly undercounts bubbles. Our model gives plausible values for bubble density.

The predicted change in slope of that occurs during the collapse of the surface can be attributed to deep bubbles. The bubbles at the bottom of the computer grid open last,
and their effects reach the surface only after the appropriate time delay. All other bubbles have closed, but these deep bubbles still contribute to the surface. To check this aspect of the model, the bottom grid cells were shut off, while bubbles to a depth of 5 penetration depths \((z=5D)\) were allowed to open normally. By doing this calculation the "tail" was shortened, and the predicted shape more closely resembled the experimental result in de-ionized water.

We must consider that our model is an ideal one, where mechanisms of energy loss are not included. Any attenuation of the acoustic wave as it propagates in the \(z\) direction would decrease pressure and limit growth of deep bubbles. As pressure threshold (tensile strength) of the material increases, the opening of deep bubbles is suppressed; therefore we see the "tail" in saline and not de-ionized water.

An additional computer simulation was performed to determine changes in cavitation displacement as a function of laser fluence. Unlike thermoelastic expansion, expansion due to cavitation is definitely not a linear effect, and it was essential to see how the model compared with experiment for changes in laser fluence. No other parameters were changed. For both de-ionized water and saline, the theoretical model predicted changes in surface motion as a function of laser fluence that agree qualitatively with experiment. Changes in the magnitude of surface displacement, as well as duration of the cavitation overshoot, compared reasonably well with experimental observations. This simulation gave additional credence to this numerical model of cavitation.

### 6.4.2 Cavitation in gelatin

Excess surface expansion due to cavitation also occurred in gelatin samples with low protein content. Figure 6-9 shows the experimentally measured surface expansion of a 5% gelatin sample (doped with primuline) following a laser pulse of fluence \(\Phi=5.1\) mJ/mm\(^2\). The sample surface rises to a peak of 1.2 \(\mu\)m at 3100 ns. The surface falls and reaches equilibrium displacement of 290 nm at about 6000 ns. A good theoretical prediction was made using the following cavitation parameters: \(p_0 = 0.22\) atm, \(R_0 = 75\) nm, and \(\gamma = 9\) g/s\(^2\). The thermoelastic parameters used in the model were \(c_L=2200\) m/s and \(D=140\) \(\mu\)m. The resulting bubble density was \(n = 8.6 \times 10^6\) \(\mu\)m\(^{-3}\).
Although laser fluence is similar to that of water and saline data of the previous section (section 6.4.2), this result cannot be immediately compared with that data. Because penetration depth is smaller by a factor of 2.5, then energy density, \( \varepsilon = \Phi / D \), is larger than in the water data by that same factor. The magnitude of the pressure distribution is approximately

\[
P_0 = \Gamma \varepsilon = \frac{\beta c_L^2}{C_\gamma} \frac{\Phi}{D},
\]

(6.23)

where \( \Gamma = \left( \beta c_L^2 \right) / \left( C_\gamma \right) \) is the Grüneisen coefficient. Assuming heat capacity and thermal expansion of gelatin are dominated by water, only sound speed differs significantly. Thus, maximum pressure in gelatin exceeds that in water by a factor of \((2.5)(2.2/1.5^2)\) or 5.4. By multiplying the pressure threshold in gelatin, 0.22 atm, by this factor, we obtain a value that can be compared with the results in table 6-1. Gelatin has a higher threshold, \( p_{th} = 1.2 \) atm, than de-ionized water. This is a reasonable observation, because we would expect gelatin to be stronger than water under tension. Our cavitation model is appropriate for predicting expansion in gelatin.

### 6.4.3 Cavitation in knee meniscus

Figure 6-2 displayed a meniscus sample with a large amount of excess displacement. Our goal was to determine if cavitation was the source of such motion in knee meniscus and to quantify the cavitation parameters. A comparison of the experimentally measured expansion and theory was made in order to determine the cavitation parameters of meniscus. The results showed excellent agreement with theory. Figure 6-10 shows the experimentally measured surface displacement, the thermoelastic theory, and the complete theoretical curve that includes cavitation effects. The values used for this calculation were the following parameters: \( c_L = 1550 \) m/s, \( D = 300 \) \( \mu \)m, \( p_{th} = 0.048 \) atm, \( R_0 = 20 \) nm, and \( n = 8.7 \times 10^6 \) \( \mu \)m\(^3\). Longitudinal sound speed is within 7\% of the mean value obtained from measurements of 22 meniscus samples (\( c_L = 1651 \pm 70 \) m/s).

The next step was to apply the model to other meniscus samples, those that did
not display such large displacements due to cavitation effects. However, these samples displayed surface expansion that exceeded the predictions of the thermelastic model. The majority of meniscus samples did not feature large overshoots of microsecond duration unlike the sample shown in figure 6-10. These samples tended to reach peak displacement at a time similar to the peak of thermoelastic displacement. But they did display excess expansion. Figure 6-11 shows the expansion of meniscus at three laser fluences; displacement at the highest fluence exceeds the thermoelastic prediction during the 1 μs following the laser pulse. The deviations from thermoelastic predictions, discussed in chapter 5, signified the start of expansion due to cavitation.

6.4.4 Modeling meniscus as a layered structure

From histology of meniscus it is clear that meniscus is not homogeneous, with degenerated layers, normal layers and tears forming structure in the tissue. To model cavitation in such inhomogeneous samples, this layered structure was incorporated into the numerical model in a simple manner. The numerical grid was divided into two layers, each with a different density of nucleation sites. By decreasing the density of nucleation sites of in the lower layer, displacement due to lower bubbles is decreased. The bubbles in the surface layer become more significant. Since the excess expansion typically occurs in the first microsecond following the pulse, we expect the top bubbles to make the more significant effects.

The meniscus samples were fit to the numerical model with four parameters: pressure threshold, surface tension, initial bubble radius, surface layer thickness, and ratio of nucleation site densities \( p_{th}, \gamma, R_0, \Delta Z_s, \) and \( n_2/n_1 \). Figure 6-12 shows displacement of meniscus, the 5.4 mJ/mm\(^2\) fluence data from figure 6-11, experiment and theory. The parameters that gave the best theoretical prediction were \( p_{th} = 1.65 \text{ atm}, \gamma = 0 \text{ g/s}^\alpha, R_0 = 100 \text{ nm}, \Delta Z_s = 100 \mu\text{m}, \) and \( n_2/n_1 = 10^4 \). Figure 6-13 shows the comparison of experiment and theory in another meniscus sample. By adding expansion due to cavitation bubble formation, the model fit the experimental result quite well. The parameters used in the cavitation model were \( p_{th} = 0.64 \text{ atm}, R_0 = 100 \text{ nm}, \Delta Z_s = 80 \mu\text{m}, \) and \( n_2/n_1 = 10^3 \).
Figure 6-9. The surface displacement of 5% gelatin phantom compares well with predicted displacement of the cavitation model.

Figure 6-10. The theoretical prediction of surface displacement due to cavitation bubble formation compares well with experiment. The parameters used in the model are $c_l=1550 \text{ m/s}$, $D=300 \text{ µm}$, $p_{in}=0.05 \text{ atm}$, $R_0=20 \text{ nm}$, and $n=9 \times 10^{-6} \text{ µm}^{-3}$. 
Figure 6-11. Meniscus shows some expansion greater than thermoelastic predictions in the first 500 ns following a laser pulse at $\Phi=5.4 \text{ mJ/mm}^2$.

Figure 6-12. The predictions of the cavitation model fit well with experiment for meniscus, and cavitation results in excess displacement beyond thermoelastic expansion.
Figure 6-13. The predictions of the cavitation model fit well with experiment for meniscus, using the parameters: \( p_{th} = 0.64 \) atm, \( R_0 = 100 \) nm, \( \Delta z_s = 80 \) \( \mu \)m, and \( n_2/n_1 = 10^{-3} \).
Table 6-2 lists the cavitation parameters for samples that displayed any excess displacement. Threshold pressures ranged from 0.5 to 2 atmospheres. One interesting result is that initial bubble radius (nucleation size) does not change greatly. The mean initial radius is $\bar{R}_0 = 93 (\pm 13)$ nm. The surface layer thickness is on the order of 100 microns, and the ratio of densities of nucleation sites in the two layers ranges from $10^{-4} - 10^{-1}$. In more than half of the samples (8/14), the surface tension value was small, $\gamma \leq 3$ g/s$^2$. The mean value from all samples, $\gamma = 3$ g/s$^2$, was used to fit all the meniscus data a second time, with one less free parameter. By adjusting threshold pressure, the fit to experiment was attained. The values of $p_{th}$ with fixed $\gamma$ are listed in Table 6-2.

Table 6-2. Cavitation parameters used for fits to meniscus surface expansion data.

<table>
<thead>
<tr>
<th>Sample</th>
<th>$p_{th}$(atm)</th>
<th>$p_{th}$(atm), $\gamma$(g/s$^2$)</th>
<th>$R_0$ (nm)</th>
<th>$n_1$ (µm$^3$)</th>
<th>$\Delta z_i$(µm)</th>
<th>$n_2/n_1$</th>
</tr>
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<tbody>
<tr>
<td>8-15 5</td>
<td>0.68</td>
<td>0.68, 3</td>
<td>90</td>
<td>$8.0 \times 10^{-7}$</td>
<td>160</td>
<td>$10^{-2}$</td>
</tr>
<tr>
<td>11-7 1</td>
<td>0.4</td>
<td>0.4, 1</td>
<td>100</td>
<td>$8.0 \times 10^{-6}$</td>
<td>1200</td>
<td>0.25</td>
</tr>
<tr>
<td>12-19 1</td>
<td>1.65</td>
<td>1.65, 0</td>
<td>100</td>
<td>$1.5 \times 10^{-6}$</td>
<td>10</td>
<td>$10^{4}$</td>
</tr>
<tr>
<td>12-19 2</td>
<td>1.3</td>
<td>1.2, 5</td>
<td>100</td>
<td>$5.1 \times 10^{-6}$</td>
<td>140</td>
<td>$10^{4}$</td>
</tr>
<tr>
<td>12-19 3</td>
<td>1.23</td>
<td>1.25, 0</td>
<td>100</td>
<td>$1.9 \times 10^{-6}$</td>
<td>80</td>
<td>$10^{4}$</td>
</tr>
<tr>
<td>12-19 4</td>
<td>1.94</td>
<td>1.9, 10</td>
<td>70</td>
<td>$2.4 \times 10^{-6}$</td>
<td>80</td>
<td>$10^{4}$</td>
</tr>
<tr>
<td>12-19 5</td>
<td>1.2</td>
<td>1.2, 5</td>
<td>80</td>
<td>$5.0 \times 10^{-6}$</td>
<td>70</td>
<td>$10^{4}$</td>
</tr>
<tr>
<td>1-9 3</td>
<td>2.0</td>
<td>2.0, 1</td>
<td>100</td>
<td>$4.4 \times 10^{-6}$</td>
<td>70</td>
<td>$10^{4}$</td>
</tr>
<tr>
<td>1-9 4</td>
<td>1.3</td>
<td>1.3, 1</td>
<td>80</td>
<td>$2.2 \times 10^{-6}$</td>
<td>50</td>
<td>$8 \times 10^{-5}$</td>
</tr>
<tr>
<td>1-9 6</td>
<td>1.3</td>
<td>1.3, 1</td>
<td>100</td>
<td>$2.5 \times 10^{-6}$</td>
<td>60</td>
<td>$10^{-3}$</td>
</tr>
<tr>
<td>2-20 2</td>
<td>0.64</td>
<td>0.65, 1</td>
<td>100</td>
<td>$2.6 \times 10^{-6}$</td>
<td>80</td>
<td>$10^{-3}$</td>
</tr>
<tr>
<td>2-20 3</td>
<td>1.35</td>
<td>1.3, 15</td>
<td>110</td>
<td>$2.6 \times 10^{-6}$</td>
<td>110</td>
<td>$10^{-3}$</td>
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<td>2-20 4</td>
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<td>0.5, 10</td>
<td>100</td>
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<td>150</td>
<td>$10^{-3}$</td>
</tr>
<tr>
<td>2-20 6</td>
<td>1.4</td>
<td>1.2, 6</td>
<td>80</td>
<td>$1.8 \times 10^{-6}$</td>
<td>100</td>
<td>$10^{-3}$</td>
</tr>
</tbody>
</table>

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Discussion

As expected, meniscus has a range of values for threshold pressure. This tissue can have essentially no resistance to cavitation as seen in figure 6-10. It can be stronger under pressure decreases, having a threshold pressure of 2 atmospheres. We might expect the changes in threshold depend on the tissue's condition, and this question will be investigated in the following chapter. The nucleation site radius in meniscus samples is approximately $10^2$ nm. Bubble density is similar to that of water and gelatin. Cavitation displacement is sensitive to the surface layer thickness, and this parameter will be a useful one to compare with histological assessments of the samples.

The difference in bubble density within the two layers suggests two possible physical explanation of what is happening in the tissue. Either the acoustic wave is attenuating as it propagates deeper into the tissue or the tissue itself has less nucleation sites in deeper layers of the tissue. There are additional ways to further develop our model of cavitation that will be discussed in chapter 8.

6.4 Conclusions

A numerical model of cavitation based on Rayleigh's equation of motion for a spherical cavity was developed. This numerical model predicts expansion due to cavitation for different hydrated samples: water, saline, gelatin, and knee meniscus. Comparisons of experiment and theory allowed measurement of cavitation related parameters in water, saline, gelatin, and knee meniscus. The threshold for cavitation in water compares with other measurements of laser-induced acoustic cavitation. Bubble densities compare with value estimated from Paltauf et al [1992] strobe photographs of cavitation in water. Threshold pressures were measured in meniscus. The range of values may be a useful parameter to compare with histology in order to determine if diagnosis of degenerative changes is feasible. Even in meniscus where the magnitude of cavitation displacements are quite small, using a layered structure, the model predicts displacement by changing only the ratio of nucleation sites in the two layers.
Chapter 7
Comparison of Meniscus Histology with Experiment and Theory

It would be exciting if the physical response of meniscus to a laser pulse told us something specific about its condition. There are several physical properties obtained from the comparison of experiment and theory developed in the preceding chapters that may reveal something about the condition of meniscus. In this chapter these parameters are compared with histology of those samples. The correlations that were found between the physical properties and condition of meniscus samples are discussed in section 7.2. This analysis is a significant step to determine if interferometry of meniscus following nanosecond laser pulses would be a useful diagnostic technique for orthopedics.

7.1 Histology Assessment of Meniscus

7.1.1 Methods

The meniscus samples were obtained from patients undergoing total knee replacement surgery. They were placed in saline and transported to our laboratory where they were placed in a refrigerator at 4° C. Within a 24 to 30 hour period, the menisci were irradiated. Each site that had an appreciable interferometric signal was used as a data sample. An attempt was made to obtain data at identical values of laser fluence for each sample. Typically, the interference signal decreased after a few (~ 5) laser shots. In other samples, the specular reflection from the surface was low, resulting in decreased interference signal. In these samples, the displacements at low fluences (0.5, 1.5 mJ/mm²) were of the same order as spatial resolution.

Following irradiation, each irradiated site on the meniscus surface was marked with a millimeter diameter colloidal ink dot (Bradley Products, Bloomington, MN). Different colors (black, blue, green, and orange) were used for each sample site. Upon completion of the laser experiment, the meniscus was placed in 10% neutral buffered formalin in order to “fix” the tissue. The formalin cross-links the collagen fibers and replaces the water in the tissue, and preserves it.
The meniscus samples were routinely processed for microscopy. Transverse sections that contained the ink dot were cut and embedded in paraffin. Microtome sections of 4 micron thickness were cut and stained with hematoxylin and eosin (H & E). Approximately 20 H & E stained sections were taken at 50 micron intervals through the ink dot and examined by light microscopy. Dr. Maryann Fitzmaurice examined the meniscus slides. The microscopic study assessed the presence or absence of surface irregularities, degenerative changes, and embedded fragments of bone.

7.1.2 Classification of meniscus samples

The changes in meniscus included foci of myxoid change and fissuring or fracturing of the fibrocartilage. Myxoid change is a degenerative change in which there is an increase in the mucopolysaccharide content of the ground substance of the tissue as compared to normal, which gives it a pale blue-gray (rather than a pink) appearance on H&E stained sections. The degenerative changes were classified as mild if less than 50% of the cross-sectional area under study showed myxoid change. If more than 50% of the cross-sectional area showed the blue-gray color under staining, then the classification was moderate degenerative change. Degenerative changes were considered severe if fissures and fractures were present in addition to myxoid change. The depth below the surface where change in the meniscus began was also measured using an ocular micrometer. Table 7-1 lists the condition of the meniscus samples as determined by a light microscopic assessment. Depth measurements and observed irregularities are also listed in table 7-1.

7.2 Comparison of Condition and Results

Once the histology was completed, the physical properties of meniscus obtained from experiment and theory were compared to histology to determine any correlation. Scatter plots were used to correlate the thermoelastic and cavitation parameters with the diagnostic classes: normal, or mild, moderate and severe degenerative change.
7.2.1 Meniscus classification and physical properties

As described in Chapter 5, the thermoelastic expansion of hydrated samples allows measurement of physical properties of those samples. From the time dependent behavior we obtained longitudinal sound speed and optical penetration depth at the pump laser wavelength (\( \lambda = 355 \) nm). From the quasi-steady state equilibrium displacement of meniscus, we determined the ratio of thermal expansion coefficient to heat capacity (\( \beta/C_V \)). We wish to know if any of these physical parameters are useful to diagnose meniscus condition. Each parameter (\( c_L, D, \beta/C_V \)) was tested to determine any correlation with pathology classification. Only the ratio of thermal expansion coefficient to heat capacity showed a correlation with condition for normal meniscus and moderate and severe degenerative change.

In Chapter 6, comparison of experiment with the cavitation model determined several cavitation properties of meniscus samples. The threshold pressure, nucleation size, and bubble density parameters (\( p_0, R_0, n_1, \gamma \)) were tested to find any diagnostic capability. Two cavitation parameters suggested a slight correlation with meniscus condition. However, the layer thickness parameter (\( \Delta z \)) compared quite well with the histological measurements of depth below surface where compositional changes begin.

7.2.2 Meniscus classification and thermoelastic properties

The thermal expansion-heat capacity ratio did suggest a correlation of the physical properties with condition. Meniscus classified as normal has a higher ratio of thermal expansion to heat capacity than meniscus with moderate and severe degenerative changes. Figure 7-1 shows the thermal expansion-heat capacity ratio grouped by pathological classification. If we select a separation line at \( \beta/C_V = 4.5 \times 10^{-5} \) g/J, values that fall above threshold would be normal, and values below would be either moderately or severely degenerated samples. Using this threshold value, 5 of 5 normal samples and 7 of 8 moderate/severe samples were predicted correctly.

Normal meniscus has a mean \( \beta/C_V \) ratio of \( 5.7 (\pm 1.0) \times 10^{-5} \) g/J. Meniscus with mild degenerative change has mean \( \beta/C_V = 4.5 (\pm 1.3) \times 10^{-5} \) g/J, and moderately
degenerated meniscus has a mean of $3.7 \pm 0.7 \times 10^{-5}$ g/J. The mean $\beta/C_V$ ratio of the severe degenerative samples are $3.4 \pm 1.4 \times 10^{-5}$ g/J. Therefore, as meniscus experiences degenerative changes its thermal expansion decreases. The decrease is a reasonable change since degeneration in meniscus typically means a breakdown of the collagen fiber matrix and increased water content. We would expect the tissue to have decreased elasticity. The differences in this physical value according to tissue classification are small. The standard deviation shows overlap adjacent classifications, but we can distinguish the difference between normal and moderate/severe degenerative changes.

Figure 7-2 shows the longitudinal sound speed measurements grouped by histological classification. The mean sound speed ($\pm$ standard deviation) is $\bar{c}_L = 1650 \pm 70$ m/s. There is no correlation between sound speed and tissue condition. Figure 7-3 shows the optical penetration depth (at $\lambda=355$ nm) grouped by histological classification. The mean value ($\pm$ standard deviation) is $\bar{D} = 253 \pm 17$ $\mu$m. There is also no correlation between penetration depth and tissue condition.

7.2.3 Meniscus pathology and cavitation parameters

A similar study of cavitation parameters showed minor correlations with tissue classification, if any existed. The size of the nucleation site parameter shows no correlation with condition and is plotted in figure 7-4. The bubble density parameter also displays no correlation with the tissue’s condition, and is plotted in figure 7-5. Threshold pressure, plotted in figure 7-6 shows a slight separation between normal samples and those with severe degenerative changes. The normal samples have $p_{th} \geq 1.25$ atm and severe have $p_{th} \leq 1.2$ atm. We expect that the tissue would weaken as it degenerates, and this hypothesis is validated by comparison of threshold pressures in the normal and severe samples. The value of surface tension per unit area plotted in figure 7-7 shows clear separation of normal and severe samples.
Figure 7-1. A plot of the ratio of thermal expansion coefficient to heat capacity of knee meniscus samples show the ability to distinguish normal menisci from menisci with moderate and severe degenerative changes.

Figure 7-2. Longitudinal sound speed grouped by sample histology. The mean sound speed for 23 samples is 1650 m/s with a standard deviation of 70 m/s.
<table>
<thead>
<tr>
<th>Sample</th>
<th>Condition</th>
<th>Depth (µm)</th>
<th>Other observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-15 1</td>
<td>Normal</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>8-15 2</td>
<td>Normal</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>8-15 3</td>
<td>Mild</td>
<td>470</td>
<td></td>
</tr>
<tr>
<td>8-15 4</td>
<td>Normal</td>
<td>-</td>
<td>disrupted surface</td>
</tr>
<tr>
<td>8-15 5</td>
<td>Moderate</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>11-7 1</td>
<td>Mild</td>
<td>1180</td>
<td></td>
</tr>
<tr>
<td>12-19 1</td>
<td>Mild</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>12-19 2</td>
<td>Mild</td>
<td>120</td>
<td></td>
</tr>
<tr>
<td>12-19 3</td>
<td>Normal</td>
<td>-</td>
<td>raised flap at surface, bone fragment</td>
</tr>
<tr>
<td>12-19 4</td>
<td>Mild</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>12-19 5</td>
<td>Mild</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>1-9 1</td>
<td>Moderate</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>1-9 2</td>
<td>Moderate</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>1-9 3</td>
<td>Normal</td>
<td>-</td>
<td>flap at edge of site</td>
</tr>
<tr>
<td>1-9 4</td>
<td>Moderate</td>
<td>380</td>
<td>flap at surface</td>
</tr>
<tr>
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<td>Mild</td>
<td>350</td>
<td>edge defect</td>
</tr>
<tr>
<td>1-9 6</td>
<td>Moderate</td>
<td>50</td>
<td>embedded bone fragment</td>
</tr>
<tr>
<td>1-9 7</td>
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<td>300</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2-20 3</td>
<td>Normal</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>2-20 4</td>
<td>Severe</td>
<td>280</td>
<td>crystal deposits*</td>
</tr>
<tr>
<td>2-20 5</td>
<td>Moderate</td>
<td>320</td>
<td></td>
</tr>
<tr>
<td>2-20 6</td>
<td>Severe</td>
<td>120</td>
<td>bone particles at surface</td>
</tr>
</tbody>
</table>

* crystal deposits were either uric acid (gout) or calcium pyrophosphate (pseudogout)
The model can predict accurately the thickness of the upper layer in which cavitation bubble density is higher. Table 7-2 lists the surface depth parameter Δz_s and the histology measurement of depth below surface where changes begin. Except for two samples, predictions of the cavitation model compare well with the histology measurements of depth. The samples where no depth measurement is given are normal samples, thus no region of the meniscus has degenerative changes. However, 2 of the 3 normal samples have partially detached flaps of tissue at the surface. These flaps are approximately 100 μm thick.

As described in the cavitation model, the upper layer has a higher bubble density than the lower layer. The bubble density is simply larger near the surface. A possible explanation is that the wave attenuates as it propagates deeper into the tissue, causing fewer bubbles to open. Also, we know from orthopedic literature that the surface zone of meniscus is weaker under tensile stress, compared with the deeper tissue (section 2.4.1). [Mow et al, 1992a] Thus, a higher bubble density in the top layer can be understood knowing that the tissue’s structure results in a surface zone that is weaker under tension.

A binary plot of the two parameters which best separate the samples was made. Figure 7-8 shows the Grüneisen coefficient (eq. 6-23), Γ, plotted as a function of surface tension per area, γ. Grüneisen coefficient is obtained by multiplying the β/C_V ratio (figure 7-1) by sound speed squared (figure 7-2), c_L^2, for each sample. In this type of graph it is possible to separate normal/mild from moderate/severe. The moderate degenerative and severe degenerative changes also separate in the plot of Γ versus γ. Choosing a line to separate normal from mild degenerative changes selects 4 of 6 mild degenerative samples correctly. This type of plot shows the best promise for diagnosing meniscus classification.
Figure 7-3. Penetration depth of meniscus shows no correlation with the tissue condition.

Figure 7-4. The radius of the nucleation site shows no correlation with the condition of meniscus tissue.
Table 7-2. Comparison of cavitation model predictions and histology regarding layer depth.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Δzₜ (µm)</th>
<th>Depth dₑ (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-15 5</td>
<td>160</td>
<td>200</td>
</tr>
<tr>
<td>11-7 1</td>
<td>1200</td>
<td>1180</td>
</tr>
<tr>
<td>12-19 1</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>12-19 2</td>
<td>140</td>
<td>120</td>
</tr>
<tr>
<td>12-19 3</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>12-19 4</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td>12-19 5</td>
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<td>50</td>
<td>380</td>
</tr>
<tr>
<td>1-9 6</td>
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<td>50</td>
</tr>
<tr>
<td>2-20 2</td>
<td>80</td>
<td>1240</td>
</tr>
<tr>
<td>2-20 3</td>
<td>120</td>
<td>-</td>
</tr>
<tr>
<td>2-20 4</td>
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<td>280</td>
</tr>
<tr>
<td>2-20 6</td>
<td>100</td>
<td>120</td>
</tr>
</tbody>
</table>

7.3 Conclusions

A light microscopy assessment of meniscus samples determined the varied conditions of the samples. Comparison of histology with thermoelastic behavior revealed the ability of this technique to distinguish between normal and moderate to severely degenerated meniscus samples using equilibrium displacement measurements. By adding the surface tension parameter obtained from the cavitation model, normal and mild degenerative changes are well separated from moderate and severe degenerative changes. The cavitation behavior allows measurement of the depth within the tissue below which the density of cavitation bubbles significantly decreases. This depth compares well with histology measurements of depth from the surface to areas of degenerative change. This measurement most likely represents the thickness of the surface zone of meniscus, where collagen fibers are smaller and randomly oriented causing lower tensile strength compared to deeper tissue.
Figure 7-5. A plot of bubble density versus the tissue condition does not reveal any correlation.

Figure 7-6. Threshold pressure grouped by tissue condition. There is a slight separation between normal and severe samples, as those with severe degenerative change initiate cavitation at a lower threshold pressure.
Figure 7-7. Surface tension per unit area grouped by tissue condition. Normal and severe samples show separation by this parameter.
Figure 7-8. Binary plot of surface tension and Gruneisen coefficient separates normal/mild from moderate and severe degenerative change. Samples with moderate degenerative and severe degenerative changes also separate.
Chapter 8
Conclusions and Future Directions

8.1 Conclusions and Thesis Accomplishments

For the physicist, the way of understanding nature is to hypothesize the simplest possible model and test it. We have done just this in order to understand the response of soft tissue to pulsed laser light, specifically laser-induced cavitation in meniscus, and to determine its physical properties. Our investigation consisted of several components: an interferometric method of measuring laser-induced expansion, a physical model based on thermoelastic expansion and cavitation, meniscus histology, and the usage of tissue simulating materials (water, gelatin). From experimental measurements and the theoretical models, we determined important physical properties of knee meniscus. Some of these values, such as the longitudinal speed of sound and thermal expansion coefficient; can be determined by other experimental methods. Certainly, this method allows measurement of these physical properties on a microscopic scale, as opposed to measuring properties of the bulk. However, other values, particularly the cavitation parameters, are not measurable by any other method.

We have verified that cavitation occurs in hydrated samples, and causes additional displacement of the surface of these targets. The type of cavitation caused by laser-induce pressure reductions in a liquid has been imaged via shadowgraphs in water and in gelatin, [Paltauf et al, 1992, Oraevsky et al. 1996] but not soft tissue. Although we do not observe formation of cavitation bubbles directly, our technique allows surface effects of the bubbles to be measured in water, gelatin, and most importantly, soft tissue.

Light microscopy was used to assess the condition of the cartilage tissue. A preliminary comparison of the physical parameters of meniscus obtained from experiment and theory with the histological classification suggested certain parameters allow us to distinguish between normal meniscus and meniscus with moderate and severe degenerative changes. Cavitation effects proved useful as a way of measuring the depth to degenerative changes within the tissue. Perhaps this measurement also determines the thickness of the surface region of the tissue, where collagen fibers are randomly oriented and smaller compared to the deeper regions. The usage of nanosecond laser pulses as a
low energy probe of soft biological tissue has great potential for scientific applications.

8.2 Implications for Meniscus Diagnosis

In this study, the response of human knee meniscus to a nanosecond laser pulse and its physical properties were studied \textit{in vitro} with an interferometric technique. The results suggest that differences in the thermoelastic expansion and cavitation parameters allow one to distinguish between normal meniscus and menisci with moderate/severe degenerative changes. Two natural questions to ask are (i) whether the technique is feasible for real time diagnosis and (ii) what would be required to make a laser based diagnostic device for arthroscopic surgery.

If all that is desired is the ability to distinguish between normal and moderate/severe degenerative change in meniscus, then this technique could be useful during arthroscopy. A fiber optic delivery system for the pump laser pulse and collection of reflected interferometric probe light would need to be incorporated into an arthroscope. The fiber tip must not contact the tissue surface would change the basic geometry of the problem such that the air-tissue interface would become a glass-tissue interface, and tensile stresses would not develop. All-fiber interferometers currently exist and have been used for optical coherence tomography studies.

A more challenging aspect of this problem would be implementing real time data analysis. This would mean the numerical models would need to be automated so that data acquisition, analysis and diagnosis would require as little input from the surgical team as possible. Creating real time diagnostics out of the numerical models would be a significant task.

8.3 Other Applications

Opto-acoustic Tomography

The interferometric technique described in this thesis has potential usage for opto-acoustic tomography. In the case of meniscus, the technique could be used to locate bone fragments in the tissue. One of the meniscus samples displayed an anomalous surface expansion; histological examination found a fragment of bone (approximately 100 microns) embedded in that particular sample. In articular cartilage, it would be possible
to use the technique to measure its thickness: thus finding locations where the cartilage has worn down. The time needed for acoustic reflection of the propagating wave from the cartilage-bone boundary and sound speed obtained from thermoelastic expansion would allow measurement of the tissue's thickness.

Meniscus repair

One consequence of degenerative change in meniscus is fissuring within the tissue. Another possible application of nanosecond laser pulses is closing such fissures in the tissue. Typically the fractures correspond with the geometry of the collagen fiber network, and run parallel to the cartilage surface. By inducing a strong compressive acoustic wave, these fissures might be permanently closed. Holding the surface fixed, would keep the acoustic wave from developing a tensile component. This could be done by either using a contact fiber tip to deliver the laser pulse in vivo, or placing a piece of glass (transparent to the laser wavelength) on the tissue surface for an in vitro laboratory experiment.

8.4 Further Considerations

Scattering

If further work in this area is attempted, the researcher may want to consider the effects of scattering in the tissue more fully. As discussed in chapter 2, biological tissue is a highly scattering medium, and knee meniscus is no exception. We would expect photons to scatter outside the beam area, effectively increasing the beam radius. Additional numerical modeling of the effects of scattering on the initial light distribution could be performed. Once the scattered light (and temperature) distribution was calculated it could be used to determine laser-induced stresses and displacements more precisely.

Cavitation

The numerical cavitation model could be expanded further by adding other physical effects: bubble rebounds, energy loss, and viscosity. Currently, bubble rebound
in the model is suppressed in order to avoid instabilities. However, bubble rebound is a real phenomenon in cavitation, and observed by Paltauf and Schmidt-Kloiber. [Paltauf and Schmidt-Kloiber, 1996] Our model could also be developed by including energy losses due to work done by expanding the bubbles dW=PdV. The viscous nature of fluid in meniscus as it interacts with the extracellular matrix proteins is discussed in orthopedic literature as it relates to static loading and deformations of the tissue. Viscosity of tissue is another physical phenomenon that might be used to further develop the computational model of cavitation.
Bibliography


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