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Authors

Wong, BJF
Milner, TE
Kim, HK
[et al.](#)

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Characterization of Temperature-Dependent Biophysical Properties During Laser Mediated Cartilage Reshaping

Brian J. F. Wong, Thomas E. Milner, Hong K. Kim, Sergey A. Telenkov, Clifford F. Chew, Emil N. Sobol, and J. Stuart Nelson

Abstract—Laser radiation can be used to reshape cartilage tissue into new morphologic configurations. When a critical temperature is attained, mechanically deformed cartilage becomes malleable and may be reshaped into new geometric configurations that harden as the tissue cools. This temperature-dependent process results in mechanical stress relaxation and is characteristic of a phase transformation. The principal advantages of using laser radiation for the generation of thermal energy in tissue are precise control of both the space-time temperature distribution and time-dependent thermal denaturation kinetics. In this study, we illustrate the utility of laser mediated cartilage reshaping in *ex vivo* porcine model of reconstructive nasal and laryngeal surgery, and attempt to determine the temperature range in which accelerated stress relaxation occurs during laser mediated cartilage reshaping. Optimization of the reshaping process requires identification of the temperature dependence of this phase transformation and its relationship to observed changes in cartilage optical (diffuse scattering), mechanical (internal stress), and thermodynamic properties (heat capacity). Light scattering, infrared radiometry, and modulated differential scanning calorimetry were used to measure temperature-dependent changes in the biophysical properties of cartilage tissue during fast (laser mediated) and slow heating (conventional calorimetric heating). Our studies using MDSC and laser probe techniques have identified changes in tissue thermodynamic and optical properties suggestive of a phase transformation occurring near 60 °C. Clinically, reshaped cartilage tissue can be used to recreate the underlying cartilaginous framework of structures in the head and neck such as the ear, larynx, trachea, and nose.

Index Terms—Cartilage, cartilage reshaping, infrared radiometry, light scattering, Nd:YAG laser, orthopedic surgery, otolaryngology, phase transformations, plastic surgery, reconstructive surgery, stress relaxation.

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B. J. F. Wong is with the Beckman Laser Institute and Medical Clinic, University of California at Irvine, Irvine, CA 92612 USA. He is also with the Department of Otolaryngology-Head and Neck Surgery, University of California at Irvine, Orange, CA 92668 USA.

H. K. Kim, C. F. Chew, and J. S. Nelson are with the Beckman Laser Institute and Medical Clinic, University of California at Irvine, Irvine, CA 92612 USA.

C. F. Chew is with the Beckman Laser Institute and Medical Clinic and the Department of Otolaryngology—Head and Neck Surgery, University of California at Irvine, Irvine, CA 92612 USA.

T. E. Milner and S. A. Telenkov are with the Biomedical Engineering Program, Department of Electrical and Computer Engineering, College of Engineering, University of Texas at Austin, Austin, TX 78712-1084 USA.

E. N. Sobol is with the Department Of Advanced Laser Technologies, Center for Technological Lasers, Russian Academy of Sciences 2, Pionerskaya Troitsk, Moscow Region 142092, Russia.

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I. INTRODUCTION

THE INTERACTION of coherent light with tissue may result in a variety of effects depending on the laser wavelength, pulse duration, irradiance, tissue thermal and optical properties [1]. In industry, photothermal, photomechanical, and photochemical effects are used for ablative and nonablative applications in many areas such as semiconductor, alloy, ceramic, and polymer processing. While industrial nonablative laser applications are commonplace, lasers have been used predominantly in medicine to ablate and destroy tissue. Few nonablative medical applications of lasers have been developed. Laser mediated reshaping of cartilage is a novel nonablative application. Thermally mediated alterations in cartilage biophysical properties during laser irradiation strongly suggest the occurrence of a phase transformation. *Phase transformations* are energy dependent changes in the molecular structure of matter which, during laser mediated cartilage reshaping, are manifest by alterations in the biophysical properties of the tissue matrix. The modification of solids during laser radiation proceeds through phase transformations whose progress is governed mainly by heat and mass transfer processes. To illustrate this technique in a model of nasal reconstruction, we characterize the temperature dependence of alterations in cartilage optical, thermal, and mechanical properties accompanying laser mediated reshaping.

The plastic deformation of cartilage via laser-mediated stress-relaxation was introduced by Sobol and colleagues in 1993 following observation that laser irradiation of cartilage specimens under mechanical deformation resulted in permanent reshaping [2]–[8] without carbonization or ablation. Light and electron microscopic studies showed intact chondrocyte structure, preservation of fibrillar matrix components, normal cytoskeletal structure and evidence of limited tissue damage [9]. In a later study, temperature sensitive tensiometric measurements of internal stress suggested that marked stress relaxation occurs when tissue temperature reached approximately 60 °C–70 °C [10]. To illustrate laser mediated cartilage reshaping, a flat cartilage specimen was cut in the approximate shape of a lower lateral nasal cartilage [Fig. 1(a)], and reshaped using optical feedback control [Fig. 1(b)] [11]. A

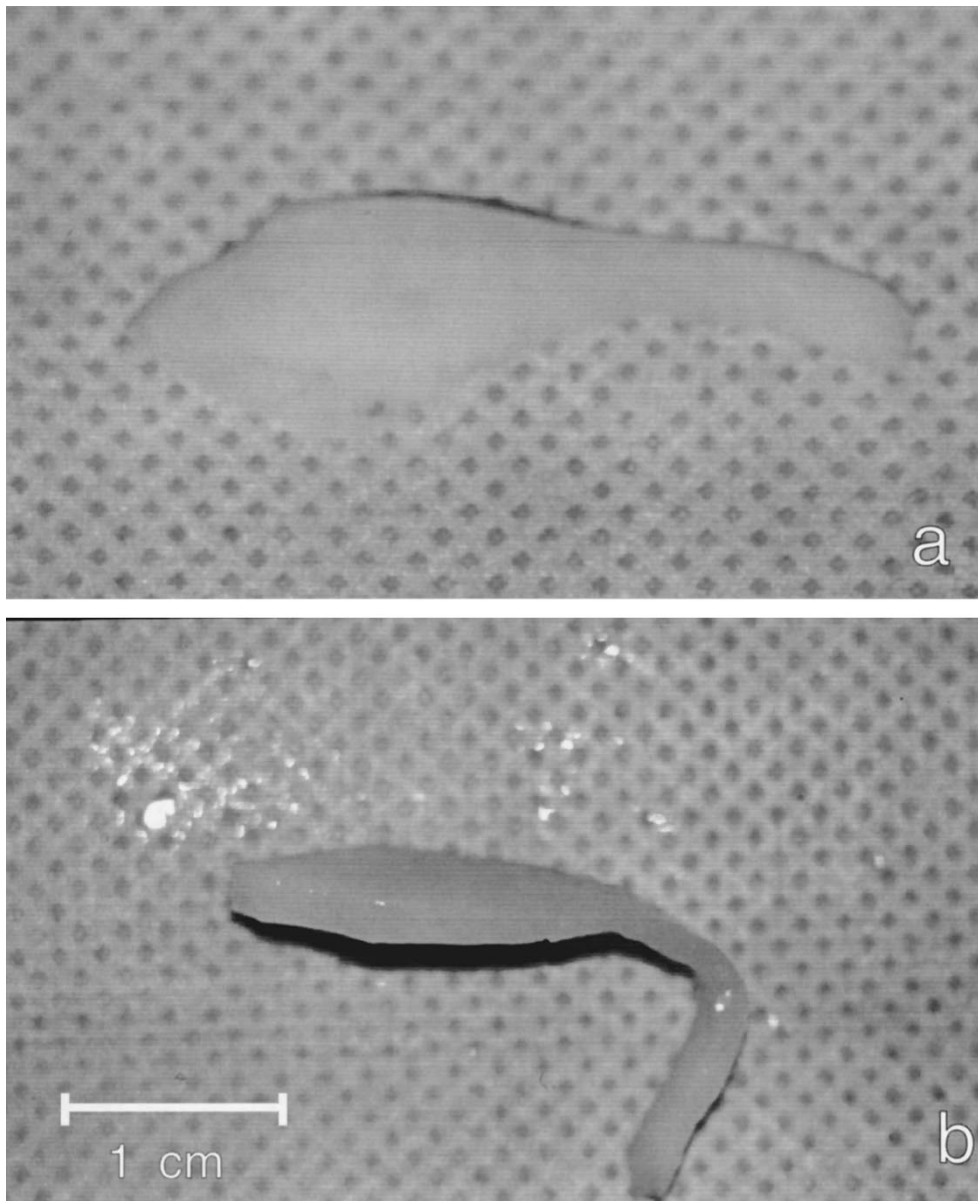


Fig. 1. Simulated lower lateral cartilage fashioned from porcine septum before (a) and after (b) laser mediated reshaping.

curved specimen was created without carving, cross-hatch incisions, or morselization.

While the underlying molecular basis for thermal mediated stress relaxation remains incompletely understood, the mechanism of action is thought to involve: 1) a temperature-dependent bound to free water transition in the cartilage matrix; 2) selective collagen or proteoglycan denaturation; 3) local mineralization of proteoglycan subunits by free cations (chiefly Ca^{++}); and 4) reorganization of van der Waals bonds and weak interactions within the proteoglycan macromolecules. Laser induced temperature increase can be used to reshape autologous donor cartilage grafts into mechanically stable shapes and may potentially be used to reconstruct complex anatomic structures such as the external ear without significant loss or waste of harvested tissue. The reshaping process is reversible and adaptable for use in minimally invasive procedures. In contrast to traditional

reconstructive surgical techniques, no suturing, carving, or morselization is required to relieve or balance the elastic forces within the cartilage.

To date, only three *in vivo* laser mediated cartilage reshaping studies have been performed and none of these investigations monitored changes in tissue temperature, optical properties, or internal stress nor was a feedback control system used to modulate laser dosimetry. Wang *et al.* successfully reshaped crushed canine tracheal cartilage via an endoscopic approach using a pulsed Nd:YAG laser ($\lambda = 1.44 \mu\text{m}$), but the cartilage and its overlying mucosa were simultaneously irradiated [12], [13]. Sobol and colleagues created complex deformations in the external ears of domestic pigs using Ho:YAG laser ($\lambda = 2.12 \mu\text{m}$) radiation delivered percutaneously with a fiberoptic cable [14]. In Greece, a small number of patients underwent laser mediated nasal septoplasty for airway obstruction using a CO_2 laser ($\lambda = 10.6 \mu\text{m}$) but the results of this study

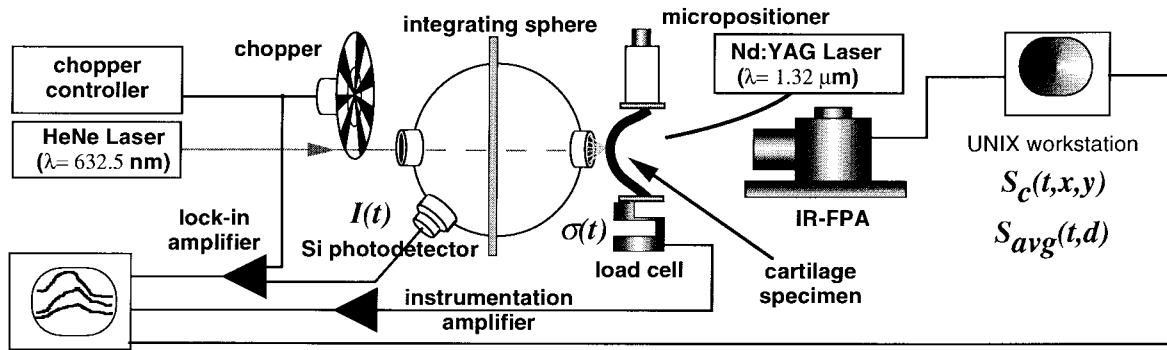


Fig. 2. Schematic of instrumentation used for measurement of integrated back scattered light intensity $I(t)$, internal stress $\sigma(t)$, and radiometric surface temperature $S_{avg}(t, x, y)$.

were mixed and difficult to interpret (E. Sobol, personal communication, 1996). While clinical trials to test cartilage reshaping are ongoing in Greece and Russia, neither the biophysical basis for the reshaping phenomena is known, nor has the procedure been performed *in vivo* using a feedback control system to minimize thermal injury.

The principal advantages of using laser radiation for the generation of thermal energy in tissue are precise control of both the space-time temperature distribution and time-dependent thermal denaturation kinetics. Optimization of the reshaping process requires identification of the temperature dependence of this phase transformation and its relationship to observed changes in cartilage optical, mechanical, and thermodynamic properties. In this study, we illustrate the utility of laser mediated cartilage reshaping in an *ex vivo* model of reconstructive nasal surgery using porcine nasal septum, and characterize the temperature range in which accelerated stress relaxation occurs. Photothermal radiometry is used to examine the spatial distribution of temperature during the laser radiation of cartilage and correlated with simultaneous measurements of tissue optical and mechanical properties. Diffuse light scattering and calorimetric techniques are used to determine the temperature dependence of changes in tissue properties.

II. MATERIALS AND METHODS

Although a function of time-dependent heating, the critical temperature at which accelerated stress relaxation (reshaping) occurs is about 65 °C in laser irradiated cartilage. Three different experiments were completed to characterize changes in optical, mechanical, and thermal properties in cartilage at different heating conditions.

A. Optical, Mechanical, and Thermal Properties During Laser Irradiation

Using a modification of previous experimental setups [10], [11], [15], *integrated backscattered light intensity* [$I(t)$] from a probe HeNe laser ($\lambda = 632.5$ nm, 5 mW, Melles Griot, Irvine, CA), *internal stress* [$\sigma(t)$], and *radiometric surface temperature* [$S_c(t, x, y)$] were recorded from a cartilage specimen (23 × 10 × 2 mm) undergoing compressive deformation during irradiation (9 s) with a Nd:YAG laser ($\lambda = 1.32$ μm , 50-Hz

PRR, NewStar Lasers, Auburn, CA). Laser spot size (5 mm) was estimated by measuring the burn diameter of irradiated thermal paper (Zap-It, Kentek, Pittsfield, NH). Laser irradiance (4 W, 20.4 W/cm²) was measured using a pyroelectric optical power meter (Model 10A-P, Ophir, Jerusalem, Israel). As described previously, fresh porcine septal cartilage was obtained immediately following euthanasia from a local abattoir (Clougherty Packing Company, Vernon, CA) and prepared [10].

Backscattered HeNe laser light (*probe laser*) incident on the opposing surface of the irradiated cartilage specimen was collected in an integrating sphere (6", Labsphere, North Sutton, NH) and measured using a silicon photodetector and preamplifier (Model 2001, New Focus, Mountain View, CA) to obtain integrated back scattered light intensity $I(t)$ (a.u.) (Fig. 2). The HeNe beam was incident at the center of the Nd:YAG laser spot on the specimen. HeNe laser light intensity was amplitude modulated (10 kHz) with a mechanical chopper (Ithaco, Ithaca, NY) and synchronously detected by a lock-in amplifier (Model SR 850, $\tau = 30$ ms, Stanford Research Systems, Sunnyvale, CA).

Cartilage specimens were maintained in mechanical compression between an aluminum plate attached to a calibrated single-axis micropositioner (Model M-461, Newport Corp, Irvine, CA) and a thin beam load cell (0.25% full scale combined error, Model LCL-113G, Omega Engineering Inc. Stamford, CT) coupled to an aluminum mounting plate (Fig. 2). The internal stress [$\sigma(t)$] (a.u.) across the cartilage specimen was adjusted by translating the micropositioner.

To improve on our previous investigations using a single element thermal detector [10], [11], [16], an infrared focal plane array (IR-FPA) (Galileo Model, InSb, 3–5 μm sensitivity, Amber Engineering, Goleta, CA) was used to measure the spatial and temporal distributions of surface temperature [$S_c(t, x, y)$] [17] in cartilage specimens following laser exposure [17]. The IR-FPA was operated in a 256 × 256 pixel region readout with a lateral resolution of 30 μm /pixel. Photothermal radiometry relies on the measurement of blackbody radiant emission resulting from temperature increase created by absorption of incident laser radiation. Infrared radiation from the specimen surface is a function of tissue emissivity and temperature, and is described by the Planck blackbody spectrum; the detected signal contains information concerning the optical and thermal

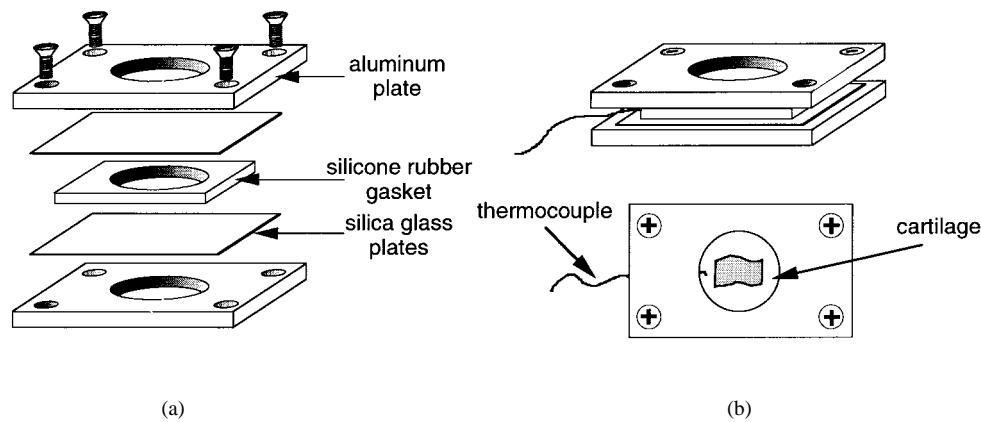


Fig. 3. Rose chamber schematic. (a) Disassembled. (b) Assembled.

properties of the tissue. Image acquisition by the IR-FPA camera was triggered simultaneously with laser irradiation using an InGaAs photoreceiver (Model 2011, New Focus, Mountain View, CA) and a sequence of 100 consecutive frames was stored in memory for subsequent processing. Camera optics provided an imaging field-of-view of $8 \times 8 \text{ mm}^2$ which was larger than the laser irradiation spot diameter (approximately 5 mm diameter). Using software visualization utilities (AVS, Waltham MA) on a UNIX workstation platform (Digital Equipment Corporation, Maynard, MA), the average radiometric temperature $[S_{\text{avg}}(t, d)]$ was calculated within a fixed circular region centered on a variable diameter (d) laser spot (i.e., $d = 0.4, 3.2, \text{ or } 6.4 \text{ mm}$).

B. Rose Chamber Light Scattering Measurements

One feature of laser mediated heating is that the resultant temperature distribution is nonuniform due to evaporative cooling and an inhomogeneous light distribution (irradiance decreases with tissue depth), resulting in asynchronous changes in tissue properties throughout the specimen. Radiometric measurements of temperature (e.g., $S_c(t, x, y)$) detect only the infrared emissions from the most superficial layers of the tissue (6–20 μm). In contrast, $I(t)$ and $\sigma(t)$ are bulk measures of changes in all regions of the specimen undergoing laser irradiation. To eliminate effects due to spatial nonhomogeneity, $I(t)$ and $\sigma(t)$ should be measured during spatially homogeneous heating of the cartilage specimen.

To create a uniform temperature distribution and eliminate the effect of dehydration/desiccation, $I(t)$ was measured in porcine nasal septal cartilage heated within a Rose chamber [15, which is a sealed, sterile structure (containing tissue specimens and saline) created by “sandwiching” an impermeable silicone rubber gasket between two large silica microscope slides held in place with aluminum plates fastened at the corners with screws (Fig. 3). A thermocouple was inserted through a small hole in the silicone gasket into the chamber and maintained at a position in close approximation to the cartilage.

The tip of a teflon insulated Type E thermocouple (Chromega-Constantan, 0.005" wire diameter, 5TC-TT-E-36-36 with cold junction compensator, M60/1290, MCJ Series, Omega Co., Stamford, CT) was inserted through the

silicone gasket into the chamber in close proximity to the cartilage. The voltage at the cold junction compensator was amplified and low-pass filtered (Stanford Research Systems, SRS 650, Sunnyvale, CA) and displayed on a digital storage oscilloscope (Textronik DSA 601, Beaverton, OR). Calibration was performed using a mercury thermometer in a water bath slowly heated from 20 °C to 100 °C. The response of the thermocouple was linear over the range of 20 °C–100 °C. The assembled chamber was placed on a laboratory hot plate and slowly heated to a preset endpoint temperature. Back-scattered light was measured using a modification of the instrumentation and apparatus illustrated in Fig. 2. A nonuniform temperature distribution or thermal gradient within the chamber were reduced by the slow rate of heating, high thermal conductivity and relatively large mass of the aluminum mounting plates. Fresh cartilage tissue specimens were heated to endpoint temperatures varying from 50 °C to 75 °C while $I(t)$ and chamber temperature were recorded. To assess the irreversible nature of this process (*under slow heating conditions*), a previously heated specimen was reheated following storage in saline for 24 h at 5 °C.

C. Modulated Differential Scanning Calorimetry

Differential scanning calorimetry (DSC) is a conventional thermal analysis technique used to measure temperature and heat flow associated with transitions in materials as a function temperature and time [18]. Modulated differential scanning calorimetry (MDSC) is used primarily to analyze complex transitions (i.e., enthalpic relaxations, crystallization events, glass transitions) in polymers and other organic compounds, and differs from conventional DSC in that a sinusoidal heating curve is superimposed on the conventional linear heating used in DSC. Deconvolution of the resultant heat flow profile during cyclic heating allows determination of total heat flow (as obtained in conventional DSC), reversible heat flow (directly proportional to specimen heat capacity c_p), and nonreversible heat flow (kinetic or volatile components). Disc shaped cartilage specimens (5 mm diameter, approximately 0.5 mm in thickness, mass 15.3 mg) were placed in the calorimeter (Model 2920, TA Instruments, New Castle, DE), and brought to thermal equilibrium at 25 °C. Calorimeter temperature was increased at a baseline rate of 5.5 °C/min superimposed

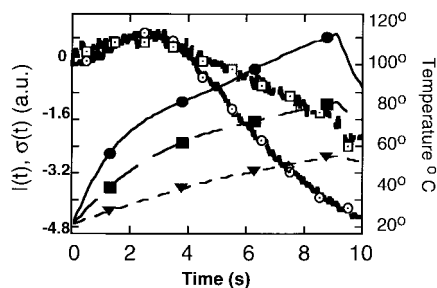


Fig. 4. Simultaneous measurement of $I(t)$, $\sigma(t)$, and $S_{\text{avg}}(t, d)$ for $d = (0.4, 3.2, \text{ and } 6.4 \text{ mm})$. An infrared focal plane array (IR-FPA) was used to acquire surface temperature measurement. (\circ — $I(t)$, \square — $\sigma(t)$, \bullet — 0.4 mm , \blacksquare — 3.2 mm , \blacktriangledown — 6.4 mm).

with a sinusoidal heating profile (60-s period, amplitude of $0.7965 \text{ }^\circ\text{C}$).

III. RESULTS

A. Optical, Mechanical, and Thermal Properties During Laser Irradiation

Integrated backscattered light intensity [$I(t)$], internal stress [$\sigma(t)$], and average radiometric temperature [$S_{\text{avg}}(t, d)$] are depicted during 9 s of laser irradiation (Fig. 4). Several observations on $S_{\text{avg}}(t, d)$ and its relationship to region of interest diameter d are notable. As the diameter [d] of the region of interest is increased, the peak temperature decreases as expected. For large values of d (e.g., $d = 6.4 \text{ mm}$), a nearly linear temperature rise during irradiation is observed. For small values of d (e.g., $d = 0.4 \text{ mm}$), a slope change in $S_{\text{avg}}(t, d)$ is observed (at $65 \text{ }^\circ\text{C}$ – $70 \text{ }^\circ\text{C}$ and 3 s), accompanied by characteristic changes (peaks) in $I(t)$ and $\sigma(t)$ which is in agreement with our previous studies [16].

Both $I(t)$ and $\sigma(t)$ initially increase and then peak (at 2–3 s) during sustained laser irradiation. The transient increase in $\sigma(t)$ during the onset of laser irradiation likely represents the thermo-elastic expansion of water (or collagen) in the irradiated tissue volume during heating. This initial increase is followed immediately by stress relaxation (decrease in $\sigma(t)$ over time). The synchronous changes between the peaks for $I(t)$ and $\sigma(t)$ along with the slope change in $S_{\text{avg}}(t, d = 0.4 \text{ mm})$ indicate an alteration in both the thermal and optical properties of the cartilage matrix, consistent with the occurrence of a phase transformation. These findings are in agreement with our previous results [10], [11], [16], [19], [20]. At $65 \text{ }^\circ\text{C}$ proteins, collagen in particular, undergoes denaturation [21]. Inasmuch as the maxima of light scattering and internal stress curves are nearly coincident, $I(t)$ (or similar optical measurements) may be used as a feedback control signal to optimize the process of laser-mediated reshaping, as previously demonstrated [11].

B. Rose Chamber Light Scattering Measurements

$I(t)$ was observed to increase initially and then peak when the chamber temperature reached $55 \text{ }^\circ\text{C}$ (Fig. 5); this pattern was strikingly similar to observations in laser irradiated tissue albeit at a different temperature transition range (Fig. 4).

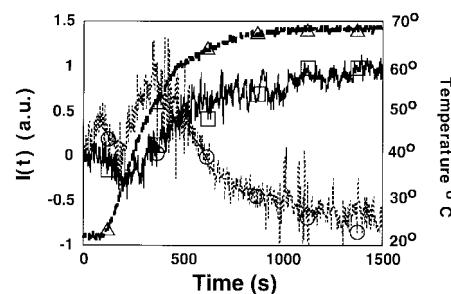


Fig. 5. Integrated backscattered light intensity $I(t)$ as a function of temperature within a Rose Chamber. A fresh cartilage specimen was slowly heated to $70 \text{ }^\circ\text{C}$; $I(t)$ peaks at approximately $55 \text{ }^\circ\text{C}$. Same specimen was then immersed in saline solution for 24 h at $5 \text{ }^\circ\text{C}$, and reheated in Rose Chamber to an endpoint temperature of $70 \text{ }^\circ\text{C}$. (\circ — $I(t)$ fresh cartilage, \square — $I(t)$ reheated cartilage, \triangle — Rose Chamber temperature).

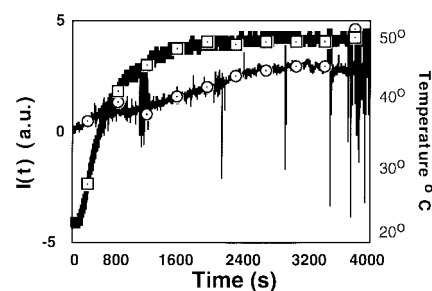


Fig. 6. Rose Chamber endpoint temperature set to $50 \text{ }^\circ\text{C}$. $I(t)$ does not peak when chamber temperature does not exceed a critical value (approximately $55 \text{ }^\circ\text{C}$, not illustrated). When endpoint temperatures are below the threshold, no peak in $I(t)$ is observed and a plateau is reached despite prolonged heating. (\circ — $I(t)$, \square — Rose Chamber temperature).

To assess the reversibility of these findings, the experiment was then repeated on the specimen after it was removed from the chamber and stored in saline for 24 h at $5 \text{ }^\circ\text{C}$. The peak in $I(t)$ disappeared, and only an increase and plateau were observed (Fig. 5). These findings suggest that the temperature-dependent phase transformation is acutely irreversible under conditions of slow uniform heating. This process was also dependent on the endpoint temperature; when set to $50 \text{ }^\circ\text{C}$, $I(t)$ was observed to increase and plateau, despite prolonged heating (Fig. 6).

C. Modulated Differential Scanning Calorimetry

Total heat flow (mW), reversible heat flow, and nonreversible heat flow were determined as a function of temperature (Fig. 7). Note the difference in scales for the Y axes; the reversible heat flow was a relatively small component of the total heat flow and would be difficult to measure using conventional DSC. Reversible heat flow into the cartilage specimen increased until approximately $70 \text{ }^\circ\text{C}$ (chamber temperature), and then began to decrease, directly reflecting changes in cartilage heat capacity c_p . Irreversible heat flow represents energy used primarily to volatilize water. MDSC measurements suggest a critical transition temperature region near $70 \text{ }^\circ\text{C}$, which is further evidence of a phase transformation occurring in cartilage within this temperature range. The peak in reversible heat flow at about $70 \text{ }^\circ\text{C}$ is consistent with

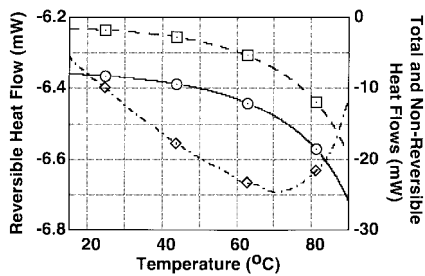


Fig. 7. Modulated differential scanning calorimetric measurements of cartilage. Total heat flow, reversible heat flow, and nonreversible heat flow measurements were obtained as a function of temperature. Note that reversible heat flow (heat flow into the cartilage specimen) reaches a peak at approximately 70°C. (—○— total heat flow, -◇- - reversible heat flow, -□- - nonreversing heat flow).

temperature-dependent changes in the optical and mechanical properties of the specimen as observed in laser and Rose chamber experiments.

IV. DISCUSSION

Native cartilage tissue undergoes shape change and warping as a result of surgical manipulation. Gillies noted that if a cartilage specimen is carved on one side with sparing of the perichondrial soft tissue on the opposite side, the graft would curve with concavity on the perichondrial surface [22]. He, therefore, recommended that the perichondrial soft tissue be removed prior to implantation. Gibson *et al.* studied a 30-year clinical series of autogenous cartilage grafts used in nasal reconstruction, and observed warping even in cases where perichondrium was entirely removed. He developed the concept of “balanced cross sections” and formulated the fundamental principles that are still used today to minimize warping in cartilage tissue grafts during reconstructive surgery [23]. In 1967, Fry demonstrated the dependence of this phenomenon on both the proteoglycans and collagen in the tissue, and introduced the concept of “interlocked stresses” [24], [25]. These early studies focused on the prevention of unwanted shape change in cartilage during grafting. In practice, head and neck surgical reconstructive procedures often require the opposite effect in that cartilage must be fashioned into curvilinear shapes. The development objective in laser mediated reshaping is to create a desired curvature without cutting, scoring, or morselizing the specimen.

Collectively, the alterations in $\sigma(t)$, $I(t)$, and $S_{\text{avg}}(t, d)$ observed during laser heating, $I(t)$ measured in Rose chamber studies, and heat flow measured during MDSC investigations, suggest the cartilage is undergoing a phase transformation [5]. Each experiment reflects the same pattern of increase, plateau or peak, and then decrease in the measured physical property whether optical, thermodynamic (heat flow), or mechanical in nature. The critical transition temperature for the resultant change in a specific physical property varies with the time-dependent temperature profile created by different heating methods. Slow heating results in a lower critical transition temperature $\sim 55^\circ\text{C}$ (such as in Rose chamber) in contrast to rapid heating (e.g., laser mediated) $\sim 65^\circ\text{C}$. Our observations are consistent with rate-process models of tissue denaturation [26].

Light scattering experiments provide insight into several possible mechanisms underlying the reshaping process. When surface temperature reaches about 65°C , a stationary region in the fractional change in integrated back scattered light intensity signal ($dI(t)/dt = 0$) is observed. Sobol and co-workers have suggested that the change in light scattering properties of cartilage may be due to the formation of isolated regions of water movement with anomalous refractive index values leading to an increase in back scattered light intensity [4]. Over time as the tissue is heated, additional regions undergo this change in refractive index and eventually coalesce resulting in a decrease in the overall scattered light signal. At the molecular level, they have suggested that water in the cartilage is undergoing transition from a bound state (to proteoglycans or collagen) to a free or mobile state. This bound-to free transition is temperature dependent. Hence, during laser heating, water moves through the cartilage matrix, and charged moieties on the proteoglycans are no longer shielded by water molecules.

In a cartilage specimen under mechanical stress, cooling results in the reformation of weak bonds (hydrogen, polar bonds) between proteoglycan groups and water, and new stable shapes are formed. Alternatively, the process of stress relaxation may involve partial denaturation of collagen or other protein subsystems. A slope change in $S_{\text{avg}}(t, d)$ occurs at about 65°C that is synchronous with changes in $I(t)$ where $dI(t)/dt = 0$, and this change in the heating rate at the surface suggests an alteration in cartilage thermal properties. At 65°C proteins, collagen in particular, begin to denature [21].

From IR-FPA measurements, our primary observation is that size of the region of interest over which temperature is averaged, must be significantly smaller than the size of the laser spot. For example, use of $S_{\text{avg}}(t, d = 6.4 \text{ mm})$ will significantly underestimate peak temperatures of the center of the laser spot (Fig. 3). Given that future clinical devices may be constructed using low-cost thermopile detectors for temperature feedback control; significant underestimation of surface temperature may occur. The observation of a slope change in $S_{\text{avg}}(t, d)$ at 65°C when temperature is averaged over small regions of interest (i.e., 0.4 mm) suggest a temperature-dependent change in cartilage thermal properties, but in the absence of an analytic model for heat conduction in cartilage, one is unable to determine whether this observation is due solely to intrinsic changes in tissue thermodynamic properties, or a partial consequence of axial and radial heat conduction.

In laser mediated cartilage reshaping, thick (1.5–4 mm) tissue specimens are heated to at least 65°C , though it is unclear as to whether the temperature distribution as a function of depth is uniform. Uniform heating could be accomplished using nonlaser sources (ultrasonic, conventional oven, microwave) but the relatively slow heating times associated with these devices would result in marked tissue desiccation and possibly nonspecific thermal injury. To examine precise temperature-dependent changes in light scattering as a function of temperature, we heated cartilage in saline within a Rose chamber. While these conditions provide substantially slower and spatially uniform heating, these studies indicate a uni-

form temperature profile may be induced in cartilage without specimen dehydration.

In Fig. 5, $I(t)$ reaches a peak and subsequently decreases at approximately 55 °C. When the specimen is stored in saline for 24 h at 5 °C and the experiment is repeated, the peak in $I(t)$ disappears. While, this experimental arrangement differs from our previous configurations (performed in air, heated with a laser, and under mechanical stress versus water heating at a slow rate without mechanical stress), results of these studies suggest: 1) a critical transition temperature exists near 55 °C under conditions of slow heating; and 2) changes in the optical properties in cartilage tissue are irreversible following prolonged exposure at this temperature under slow heating conditions. Notably, when the Rose chamber endpoint temperature is set to 50 °C, $I(t)$ is observed to increase and plateau, despite prolonged heating (Fig. 6).

Temperature-dependent changes in cartilage were studied using modulated differential scanning calorimetry (MDSC). MDSC provides an important tool; key features include: 1) ability to analyze properly complex transitions (i.e., enthalpic relaxations, crystallization events, glass transitions); 2) high sensitivity; and 3) high resolution in contrast to conventional differential scanning calorimetry. Fig. 7 illustrates total, nonreversible, and reversible heat flow as a function of temperature. At about 70 °C, reversible heat flow (heat flow into the specimen) reaches a maximum and subsequently decreases. MDSC studies were performed under conditions in which the volatile components of cartilage evaporated (non reversible heat flow), and hence reversible heat flow measurements reflect only changes in the matrix components of cartilage. The presence of a peak in reversible heat flow at about 70 °C is in agreement with temperature-dependent changes in the optical and mechanical properties we have observed as noted above in both laser (*fast heating*) and Rose chamber (*slow heating*) experiments.

V. CONCLUSION

Congenital malformation, trauma, and ablative oncologic surgery can result in loss or severe disruption of the underlying structural framework for the upper airway and aesthetic facial features. Conventional reconstructive techniques require the grafting of autologous cartilage and may involve carving, suturing, and/or morselization to recreate the shape of the absent tissue and, as a consequence, abundant normal healthy cartilage tissue is often discarded. Because only a limited cartilage mass is available from a harvest site, practice of conventional reconstructive techniques is frequently problematic, and aggressive harvest may lead to donor site morbidity. Because laser mediated reshaping is a cartilage conserving technique with the potential for reversibility, the method may advance reconstructive surgery in the head and neck. Otoplasty, tip rhinoplasty, and tracheal deformities could be performed using minimally invasive cartilage delivery techniques combined with laser irradiation.

For safe and efficacious clinical implementation, the underlying molecular mechanisms accompanying laser mediated reshaping must be understood, and an effective feedback

control system for laser irradiation must be developed. Stress relaxation in cartilage is a time and temperature-dependent process; alterations in tissue properties (optical, mechanical, thermal) are a function of the temperature profile of the specimen during heating and the total heating time. Our overall goal is to determine the biophysical changes in cartilage during laser mediated reshaping and develop methods to perform the procedure safely. Clinical implementation of reshaping requires characterization of the temperature-dependent changes cartilage undergoes during laser irradiation, understanding of light and heat transport in cartilage, knowledge of the relationship between the tissue thermo-optical response and chondrocyte viability, and finally design of a feedback controlled system incorporating dynamic measurements of tissue temperature and biophysical alterations.

Although significant progress has been made in understanding the reshaping process, several fundamental questions concerning the phase transformations and thermo-optical response accompanying laser mediated cartilage reshaping need to be addressed before proceeding with extended clinical trials. These and related questions are the focus out of current research and will be reported in the future.

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Brian J. F. Wong received the B.S. degree in biomedical and electrical engineering from the University of Southern California, Los Angeles, CA, in 1985, and the M.D. degree from The Johns Hopkins University, Baltimore, MD, in 1990. He has also completed graduate study in the Department of Engineering Science at Oxford University, Oxford, U.K., from 1985 to 1986.

He is an Assistant Professor in the Department of Otolaryngology—Head and Neck Surgery at the University of California—Irvine and at the Beckman

Laser Institute. He is a board-certified head and neck surgeon with fellowship training in facial plastic surgery. His research interests are in laser-tissue interactions and applications to head and neck plastic and reconstructive surgery.

In 1998, Dr. Wong received the Sir Harold Delf Gillies from the American and Academy of Facial Plastic and Reconstructive Surgery Award.

Thomas E. Milner, for photograph and biography, see this issue, p. 1066.

Hong K. Kim received the B.S. degree from the University of California at Irvine in 1997.

He has been a research assistant at the Beckman Laser Institute and Medical Clinic since 1996. He presently is serving in the United States Peace Corps in Ghana, West Africa. He intends to pursue a career in public health and medicine.



Sergey A. Telenkov received the Ph.D. degree in laser physics from Moscow State University, Russia, in 1993.

He joined Wayne State University, Detroit, MI in 1994 where he developed an infrared imaging technique for evaluation of composite materials and polymers. He was a Postdoctoral Researcher at Beckman Laser Institute and Medical Clinic, University of California at Irvine and currently he is a Post-Doctoral Fellow with Biomedical Engineering Program, The University of Texas at Austin. His

research activity is focused on laser-tissue interactions and application of infrared imaging technique for noncontact characterization of biological materials. He is interested in development of numerical algorithms for image processing and tomographic image reconstruction.



Clifford F. Chew received the B.S. degree in chemistry from Stanford University, Stanford, CA, in 1991 and the M.D. degree from the University of California at Irvine in 1995.

He is a Research Associate at the Beckman Laser Institute and presently completing residency training in Otolaryngology—Head and Neck Surgery. His interest include tracheal reconstruction and laser applications in head and neck surgery.

Emil N. Sobol received the M.S., Ph.D., and D.Sc. degrees in the physics of solids and materials science from the Moscow Institute of Steel and Alloys, Russia, in 1972, 1976, and 1994.

He is the group leader of the Research Center for Technological Lasers at the Russian Academy of Sciences, Troitsk. He was an Assistant Professor at the Moscow Institute of Steel and Alloys from 1987–1989. He is the author *Phase Transformations and Ablation in Laser-Treated Solids* (New York: Wiley, 1995) and over 145 scientific papers. His current scientific interests are in laser-biomaterial interaction, and in laser applications in medicine. In 1994, he received the Theodore Maiman Award for the outstanding paper in laser application in biology and medicine at the Symposium on Biomedical Optics, Los Angeles, and was awarded a Kapitza Fellowship from the Royal Society, U.K., in 1995–1996. In 1998, he began collaborative research at the Vanderbilt University FEL Center.

J. Stuart Nelson, for photograph and biography, see this issue, p. 1066.