Scott Prahl

Education

California Institute of Technology	1982	B.S.	Applied Physics
University of Texas at Austin	1988	Ph.D.	Biomedical Engineering

Professional Experience

1988 – 1989	*Research fellow*, Academic Medical Center, Amsterdam
1990 – 1991	*Research fellow*, Massachusetts General Hospital, Boston
1991 – 1993	*Instructor*, Harvard Medical School, Boston
1993 – 2006	*Assistant Professor*, Oregon Graduate Institute, Portland
1993 – 2011	*Senior Research Scientist*, Oregon Medical Laser Center, Portland
1993 – Present	*Research Assistant Professor*, Dermatology, OHSU, Portland
2006 – Present	*Research Assistant Professor*, Biomedical Engineering, OHSU, Portland
2011 – Present	*Visiting Professor*, Electrical & Computer Engineering, PSU, Portland
2012 – 2017	*Associate Professor*, Electrical Engineering & Renewable Energy, OIT, Portland
2017 – Present	*Professor*, Electrical Engineering & Renewable Energy, OIT, Portland

Awards and Other Professional Activities

1995 – 2001	Editorial Board	Lasers in Surgery and Medicine
2001	Distinguished Teaching Award	Oregon Graduate Institute
2003 – 2007	Medical Imaging Study Section (ad hoc)	NIH SBIR/STTR
2007, 2009, 2010	Session chair	SPIE Photonics West
2009 – 2010	Ohio Biomedical Research	National Academy of Science
2009 – 2010	BISH (ad hoc)	NSF
2009 – 2017	External Advisory Board	Beckman Laser Institute
1995 – Present	Physics Chairman	Oregon Academy of Science
2012 – Present	Op-TEC Advisory Board Member	

Refereed Papers

[1] P. A. Patel, J. W. Valvano, J. A. Pearce, S. A. Prahl, and C. R. Denham. A self-heated thermistor technique to measure effective thermal properties from the tissue surface. *J. Biomechanical Engineering*, 109:330–335, 1987.

A microcomputer based instrument to measure effective thermal conductivity and diffusivity at the surface of a tissue has been developed. Self-heated spherical thermistors, partially embedded in an insulator, are used to simultaneously heat tissue and measure the resulting temperature rise. The temperature increase of the thermistor for a given applied power is a function of the combined thermal properties of the insulator, the thermistor, and the tissue. Once the probe is calibrated, the instrument accurately measures the thermal properties of tissue. Conductivity measurements are accurate to 2 percent and diffusivity measurements are accurate to 4 percent. A simplified bioheat equation is used which assumes the effective tissue thermal conductivity is a linear function of perfusion. Since tissue blood flow strongly affects heat transfer, the surface thermistor probe is quite sensitive to perfusion.

[2] S. L. Jacques, C. A. Alter, and S. A. Prahl. Angular dependence of HeNe laser light scattering by human dermis. *Lasers Life Sci.*, 1:309–333, 1987.

A goniometric apparatus is presented for measuring angular dependence of scattering of a HeNe laser beam by *in vitro* human dermis samples of various thicknesses, hydrated to an 85 percent water content. Measurements of the transmitted and reflected light as a function of angle are presented for tissue thicknesses of 20–650 μm. Extrapolation of these angular scattering patters to the limit of an incremental tissue thickness specifies the scattering phase function appropriate for use in the radiative transport equation. The scattering phase function is composed of a forward-directed scattering component (90 percent contribution) characterized as a Henyey-Greenstein function with $g_{HG} = 0.91$, and an additional isotropic component (10 percent contribution, $b = 0.10$). The net value for the average cosine of the scattering phase function, $g = (1 - b)g_{HG}$ is 0.82, which corresponds to an average deflection angle of 35° for a scattering event. The on-axis attenuation of the collimated HeNe laser beam indicates a total attenuation constant of 190 cm^{-1} , composed of an absorption coefficient of 2.7 cm^{-1} and a scattering coefficient of 187 cm^{-1}.

[3] S. L. Jacques and S. A. Prahl. Modeling optical and thermal distributions in tissue during laser irradiation. *Lasers Surg. Med.*, 6:494–503, 1987.

The propagation of light energy in tissues is an important problem in phototherapy, especially with the increased use of lasers as light sources. Often a slight difference in delivered energy separates a useless, efficacious, or disastrous treatment. Methods are presented for experimental characterization of the optical properties of a tissue and computational prediction of the distribution of light energy within a tissue. A standard integrating sphere spectrophotometer measured the total transmission, T_t , total reflectance, R_t , and the on-axis transmission, T_a , for incident collimated light that propagated through the dermis of albino mouse skin, over the visible spectrum. The diffusion approximation solution to the one-dimensional (1-D) optical transport equation computed the expected T_t and R_t for different combinations of absorbance, k, scattering, s, and anisotropy, g , and by iterative comparison of the measured and computed T_t and R_t values converged to the intrinsic tissue parameters. For example, mouse dermis presented optical parameters of 2.8 cm^{-1}, 239 cm^{-1}, and 0.74 for k, s, and g, respectively, at 488 nm wavelength. These values were used in the model to simulate the optical propagation of the 488 nm line of an argon laser through mouse skin *in vivo*. A 1-D Green's function thermal diffusion model computed the temperature distribution within the tissue at different times during laser irradiation. In vitro experiments showed that the threshold temperature range for coagulation was 60–70°C, and the kinetics were first order, with a temperature-dependent rate constant that obeyed an Arrhenius relation (molar entropy 276 cal/mol°K, molar enthalpy 102 kcal/mol). The model simulation agreed with the corresponding *in vivo* experiment that a 2 s pulse at 55 W/cm ^{2} irradiance will achieve coagulation of the skin.

[4] G. Yoon, S. A. Prahl, and A. J. Welch. Accuracies of the diffusion approximation and its similarity relations for laser irradiated biological media. *Appl. Opt.*, 28:2250–2255, 1989.

The accuracy of the diffusion approximation is compared with more accurate solutions for describing light interaction with biological tissues. Generally the diffusion approximation underestimates the light distribution in the surface region, and, for high albedos, it significantly underestimates the fluence rate. This difference is only a few percent for albedos of less than 0.5 due to the dominance of collimated light. As the anisotropy of scattering increases, deviations increase. In general, fluxes can be computed more accurately with the diffusion approximation than fluence rates. For anisotropic scattering, better results can be obtained by simple transforms of optical coefficients using the similarity relations. The similarity relations improve flux calculations, but computed fluence rates have substantial errors for high albedos and the large index of refraction differences at the surface.

[5] M. Keijzer, S. L. Jacques, S. A. Prahl, and A. J. Welch. Light distributions in artery tissue: Monte Carlo simulations for finite-diameter laser beams. *Lasers Surg. Med.*, 9:148–154, 1989.

Finite-width light distributions in arterial tissue during Argon laser irradiation (476 nm) are simulated using the Monte Carlo method. Edge effects caused by radial diffusion of the light extend ±1.5 mm inward from the perimeter of a uniform incident beam. For beam diameters exceeding 3 mm the light distribution along the central axis can be described by the one-dimensional solution for an infinitely wide beam. The overlapping edge effects for beam diameters smaller than 3 mm reduce the penetration of the irradiance in the tissue. The beam profile influences the light distribution significantly. The fluence rates near the surface for a Gaussian beam are two times higher on the central axis and decrease faster radially than for a flat profile. The diverging light from a fiber penetrates tissue in a manner similar to collimated light.

[6] C. J. M. Moes, M. J. C. van Gemert, W. M. Star, J. P. A. Marijnissen, and S. A. Prahl. Measurements and calculations of the energy fluence rate in a scattering and absorbing phantom at 633 nm. *Appl. Opt.*, 28:2292–2296, 1989.

We have studied the influence of absorption, scattering, and refractive index of a phantom medium in conjunction with various beam diameters on the penetration depth of light at 633 nm. We used mixtures of Intralipid 10% (scattering medium) and Evans blue (absorbing medium). Measurements were performed in media with a scattering coefficient of 1/mm, an anisotropy factor of 0.71, absorption coefficients of 0.0013, 0.01, and 0.05/mm, and a refractive index of 1.33. The experimental results were compared with an analytical solution of the fluence rate based on diffusion theory. We found good agreement (deviations of <10%) between theory and experiment for incident beam diameters between 10 and 60 mm.

[7] M. R. Prince, G. M. LaMuraglia, C. E. Seidlitz, S. A. Prahl, C. A. Athanasoulis, and R. Birngruber. Ball-tipped fibers for laser angioplasty with the pulsed-dye laser. *IEEE J. Quantum Electron.*, 26:2297–2304, 1990.

A method of introducing high-intensity laser radiation into arteries has been developed and tested in amputated human limbs. The device consists of a small-diameter, flexible, quartz optical fiber which tapers to a large-diameter, smooth, rounded-ball tip. The smooth-ball tip minimizes the chance of mechanical dissection or perforation of the vessel wall. The spot size can be varied over a large range by varying the fiber input coupling, taper length, and numerical aperture. With 480nm radiation, which is preferentially absorbed by atherosclerotic plaque and thrombus, at $8\,\mu$s pulse durations, the device effectively recanalized occluded human peripheral arteries creating a 2–3mm diameter channel. The radiant exposure required to recanalize arteries (85 J/cm^2) was higher than the ablation threshold for plaque (56 J/cm^2) but well below the fluence required to ablate normal artery and perforate (226 J/cm^2). Time-delayed, flash photography shows the formation of a large vapor bubble with each ablative pulse, which suggests that laser recanalization can involve not only ablating plaque but also an expanding effect similar to balloon angioplasty. These data demonstrate that a tapered ball-tipped fiber can deliver the high-intensity 480nm radiation for selective ablation of plaque and that this device can effectively recanalize symptomatic peripheral artery occlusions.

[8] W. F. Cheong, S. A. Prahl, and A. J. Welch. A review of the optical properties of biological tissues. *IEEE J. Quantum Electron.*, 26:2166–2185, 1990.

The known optical properties (absorption, scattering, total attenuation, effective attenuation, and/or anisotropy coefficients) of various biological tissues at a variety of wavelengths are reviewed. The theoretical foundations for most experimental approaches are outlined. Relations between Kubelka-Munk parameters and transport coefficients are listed. The optical properties of aorta, liver, and muscle at 633 nm are discussed in detail. An extensive bibliography is provided.

[9] E. L. Koschmieder and S. A. Prahl. Surface tension driven Bénard convection in small containers. *J. Fluid Mechanics*, 215:571–583, 1990.

The onset and the form of surface-tension-driven convection in three different small circular and one small square container has been studied experimentally. In the smallest circular container, with increasing aspect ratio, the pattern consisted of first a circular roll and then segments of a circle outlined by different numbers of azimuthal nodal lines, with up to six segments. Simple solutions in the square container were the one-cellular pattern and a pattern consisting of four square cells. Unexpected solutions formed when the number of the cells in the square container was not a square number. When the aspect ratio permitted two cells, two triangular cells were observed. With space for three cells, one square cell and two wedge-shaped cells formed. The onset of convection in all fluid layers was characterized by a steep increase of the critical Marangoni number with decreasing aspect ratio.

[10] H. J. van Staveren, C. J. M. Moes, J. van Marle, S. A. Prahl, and M. J. C. van Gemert. Light scattering in Intralipid-10% in the wavelength range of 400–1100 nm. *Appl. Opt.*, 31:4507–4514, 1991.

The absorption, scattering , and anisotropy coefficients of the fat emulsion Intralipid-10% have been measured at 457.9, 514.5, 632.8, and 1064 nm. The size and shape distributions of the scattering particles in Intralipid-10% were determined by tansmission electron microscopy. Mie theory calculations performed by using the particle size distribution yielded values for the scattering and anisotropy coefficients from 400 to 1100 nm. The agreement with experiemntal values is better than 6%.

[11] J. W. Pickering, C. J. M. Moes, H. J. C. M. Sterenborg, S. A. Prahl, and M. J. C. van Gemert. Two integrating sphere with an intervening scattering sample. *J. Opt. Soc. Am. A*, 9:621–631, 1992.

Two integrating spheres placed so that the exit port of one and the entry port of the other are adjacent, with only a sample intervening, will allow the simultaneous determination of the reflectance and transmittance of the sample. Such a geometry allows measurements to be made as the sample undergoes some external stimulation, such as heat, pressure, or a chemical change. To determine the sample reflectance and transmittance from the measured values of irradiance within each sphere requires the calculation of the exchange of light through the sample between the spheres. First the power collected by a detector situated in the wall of an integrating sphere is calculated as a function of the area and reflectance of the wall, holes, sample, and detector for both diffuse and collimated light incident on the sample, and for a sample located at either the exit port (reflectance) or the entry port (transmittance) of the sphere. Next, using the single sphere equations, the effect of the multiple exchange of light between two integrating spheres, arranged so that the sample is placed between them, is calculated. In all cases of two integrating spheres the power detected is greater than or equal to that for the single sphere and depends on both the reflection and transmission properties of the sample. Additionally, the effect of a baffle placed between the sample and detector or of a non-isotropic detector is to reduce the power detected.

[12] S. A. Prahl, I. A. Vitkin, U. Bruggemann, B. C. Wilson, and R. R. Anderson. Determination of optical properties of turbid media using pulsed photothermal radiometry. *Phys. Med. Biol.*, 37:1203–1217, 1992.

Pulsed photothermal radiometry (PPTR) measures blackbody radiation emitted by a sample after absorption of an optical pulse. Three techniques for obtaining the absorption coefficient of absorbing-only, semi-infinite samples are examined and shown to give comparable results. An analytic theory for the time dependence of the PPTR signal in semi-infinite scattering and absorbing media has been derived and tested in a series of controlled gel phantoms. This theory, based on the diffusion approximation of the radiative transport equation, is shown to model the time course of the detected signal accurately. Furthermore, when the incident fluence is known, the theory can be used in a non-linear, two-parameter fitting algorithm to determine the absorption and reduced scattering coefficients of a turbid sample with an accuracy of 10–15% for transport albedos ranging from 0.42–0.88.

[13] J. W. Pickering, S. A. Prahl, N. van Wieringen, J. F. Beek, H. J. C. M. Sterenborg, and M. J. C. van Gemert. Double-integrating-sphere system for measuring the optical properties of tissue. *Appl. Opt.*, 32:399–410, 1993.

A system is described and evaluated for the simultaneous measurement of the intrinsic optical properties of tissue, the scattering coefficient, absorption coefficient, and anisotropy factor. This system synthesizes the theory of two integrating spheres and an intervening scattering sample with the inverse adding-doubling algorithm, which employs the adding-doubling solution of the radiative transfer equation to determine the optical properties from the measurement of the light flux within each sphere and of the unscattered transmission. The optical properties may be determined simultaneously, which allows for measurements to be made while the sample undergoes heating, chemical change, or some other external stimulus. An experimental validation of the system with tissue phantoms resulted in the determination of the optical properties with $<5\%$ deviation when the optical density was between 1 and 10 and the albedo was between 0.4 and 0.95.

[14] S. A. Prahl, M. J. C. van Gemert, and A. J. Welch. Determining the optical properties of turbid media by using the adding-doubling method. *Appl. Opt.*, 32:559–568, 1993.

A method is described for finding the optical properties (scattering, absorption, and scattering anisotropy) of a slab of turbid material using total reflection, unscattered transmission and total transmission measurements. This method is applicable to homogeneous turbid slabs with any optical thickness, albedo, or phase function. The slab may have a different index of refraction from its surroundings and may or may not be bounded by glass. The optical properties are obtained by iterating an adding-doubling solution of the radiative transport equation until the calculated values of the reflection and transmission match the measured ones. Exhaustive numerical tests show that the intrinsic error of the method is less than 3% when four quadrature points are used.

[15] I. A. Vitkin, B. C. Wilson, R. R. Anderson, and S. A. Prahl. Pulsed photothermal radiometry in optically transparent media containing discrete optical absorbers. *Phys. Med. Biol.*, 39:1721–1744, 1994.

A description of heat transport by conduction and radiation in inhomogeneous materials following absorption of a brief optical pulse is presented, and investigated experimentally using pulsed photothermal radiometry (PPTR). The model indicates that the role of radiation as an intra-medium heat transfer modality increases with increasing temperatures and decreasing infrared (IR) absorption of the medium. However, for the range of conditions analyzed in this study, conductive transfer dominates. Thus the inclusion of radiation does not significantly perturb the internal temperature profile although it does influence the radiometric emission from the sample, and hence the PPTR signal.

[16] D. D. Royston, R. S. Poston, and S. A. Prahl. Optical properties of scattering and absorbing materials used in the development of optical phantoms at 1064 nm. *J. Biomedical Optics*, 1:110–116, 1996.

Optical phantoms have been developed to simulate the distribution of visible light in tissue. These phantoms can then be used to evaluate the performance of optical fiber delivery and/or radiometric detecting systems. This paper describes the development of an optical phantom for the Nd:YAG laser wavelength of 1064 nm and the absorption coefficient, scattering coefficient, and anisotropy of the media used in its development.

[17] U. S. Sathyam, A. Shearin, E. A. Chasteney, and S. A. Prahl. Threshold and ablation efficiency studies of microsecond ablation of gelatin under water. *Lasers Surg. Med.*, 19:397–406, 1996.

Background and Objective: Laser Thrombolysis is the selective ablation of thrombus occluding vessels by microsecond pulsed laser irradiation. To achieve efficient ablation of thrombus, the optimal wavelength, spot size, and pulse energy need to be determined.

Study Design/Materials and Methods: A gelatin-based thrombus model confined in 3 mm inner diameter tubes was ablated under water using a 1 μs pulsed dye laser. Wavelength studies were conducted by varying the absorption of the gelatin between 10–2000 cm^{-1} corresponding to the waveband between 400–600 nm on the absorption spectrum of thrombus. A unique spectrophotometric method was developed to measure the ablated mass. An acoustic method was used to measure ablation thresholds under water as a function of absorption.

Results: The mass removed per pulse per unit energy was nearly equal over an absorption range of 100–1000 cm^{-1} at pulse energies above threshold. Mass removal increased linearly with pulse energy but did not have a direct relationship with radiant exposure. Ablation thresholds indicate that the gelatin needed to be heated only to 100°C for ablation to commence. Ablation masses measured were an order of magnitude higher than those predicted by thermal ablation models.

Conclusions: The results suggest that any wavelength between 410–590 nm can be used for effective thrombolysis. The ablation efficiency depends on the total energy delivered rather than the radiant exposure. The high ablation efficiencies suggest a dominance of the mechanical action of vapor bubbles over thermal ablation in the ablation process.

[18] H. Shangguan, L. W. Casperson, A. Shearin, K. W. Gregory, and S. A. Prahl. Drug delivery with microsecond laser pulses into gelatin. *Appl. Opt.*, 35:3347–3357, 1996.

Photoacoustic drug delivery is a technique for localized drug delivery by laser-induced hydrodynamic pressure following cavitation bubble expansion and collapse. Photoacoustic drug delivery was investigated on gelatin-based thrombus models with planar and cylindrical geometries by use of one microsecond laser pulses. Solutions of a hydrophobic dye in mineral oil permitted monitoring of delivered colored oil into clear gelatin-based thrombus models. Cavitation bubble development and photoacoustic drug delivery were visualized with flash photography. This study demonstrated that cavitation is the governing mechanism for photoacoustic drug delivery, and the deepest penetration of colored oil in gels followed the bubble collapse. Spatial distribution measurements revealed that colored oil could be driven a few millimeters into the gels in both axial and radial directions, and the penetration was less than 500 μm when the gelatin structure was not fractured.

[19] H. Shangguan, L. W. Casperson, and S. A. Prahl. Microsecond laser ablation of thrombus and gelatin under clear liquids: Contact vs non-contact. *IEEE J. Selected Topics Quantum Electron.*, 2:818–825, 1996.

Laser thrombolysis is a procedure for removing blood clots in occluded arteries using pulsed laser energy. The laser light is delivered through an optical fiber to the thrombus. The ablation process is profoundly affected by whether the optical fiber tip is inside a catheter or is in contact with the thrombus. This study measured ablation efficiency of one microsecond laser pulses to remove porcine clot confined in a silicone tube. The cavitation process was investigated by visualizing laser-induced bubble formation on gelatin targets with flash photography and measuring the acoustic transients with a pressure transducer. The laser spot size did not affect the mass of material removed. The efficiency of the contact ablation was at least three times greater than that of the non-contact ablation. Finally, the mass removed was closely correlated with the measured bubble expansion pressure.

[20] U. S. Sathyam and S. A. Prahl. Limitations in measurement of subsurface temperatures using pulsed photothermal radiometry. *J. Biomed. Opt.*, 2:251–261, 1997.

A pulsed photothermal technique to calculate internal temperatures from non-contact surface temperature measurements is presented. The inversion process is based on approximating the integral equation describing the thermal interaction with a matrix equation. The matrix equation is then solved using singular value decomposition. The method was evaluated using computer simulations and experiments with tissue phantoms and skin. The algorithm predicted internal temperatures within 10% for homogeneous samples down to a depth of about 500 μm. It did not predict internal temperatures accurately for inhomogeneous samples, but yielded fairly accurate estimates of the depths of subsurface absorbers and conserved energy.

The uncertainty in the calculated depth of the absorber increased with depth. Currently this technique can probe depths to 500 μm.

[21] E. N. La Joie, A. D. Barofsky, K. W. Gregory, and S. A. Prahl. Patch welding with a pulsed diode laser and indocyanine green. *Laser Med. Sci.*, 12:49–54, 1997.

Laser tissue welding is a sutureless method of wound closure that has been used successfully in nerve, skin, and arterial anastomoses. We welded an elastin-based biomaterial patch to the intimal surface of porcine aorta. The aorta was stained with indocyanine green dye to efficiently absorb the 808nm diode laser light. Laser welding with a pulsed diode laser thermally confines heating to stained portion of tissue, minimizing adjacent tissue damage. Laser welds of stained aorta to biomaterial were attempted by sandwiching the samples between glass slides and applying pressures ranging from 4–20 Ncm^{-2} for 5ms pulse durations and 83 mJ mm^{-2} radiant exposure. We observed bleaching of the indocyanine green by as much as 85% after exposure laser irradiation. Finally, successful welds required 5 Ncm^{-2} of pressure between the elastin biomaterial and aorta.

[22] H. Shangguan, L. W. Casperson, and S. A. Prahl. Pressure impulses during microsecond laser ablation. *Appl. Opt.*, 36:9034–9041, 1997.

The collapse of laser-induced cavitation bubbles creates acoustic transients within the surrounding medium and also pressure impulses to the ablation target and light-delivery fiber during microsecond laser ablation. The impulses are investigated here using time-resolved flash photography, and they are found to occur whether or not the light delivery fiber is in contact with the target. We demonstrate that the impulses depend primarily on the energy stored in the cavitation bubble. They are not directly dependent on the mode of light delivery (contact versus non-contact), and they are also not directly correlated to the other acoustic transients. The pressure impulses do seem to be associated with the bubble-driven jet formation due to the bubble collapse.

[23] H. Shangguan, L. W. Casperson, D. L. Paisley, and S. A. Prahl. Photographic studies of laser-induced bubble formation in absorbing liquids and on submerged targets: Implications for drug delivery with microsecond laser pulses. *Optical Engineering*, 37:2217–2226, 1998.

Pulsed laser ablation of blood clots in a fluid-filled blood vessel is accompanied by an explosive evaporation process. The resulting vapor bubble rapidly expands and collapses to disrupt the thrombus (blood clot). The hydrodynamic pressures following the bubble expansion and collapse can also be used as a driving force to deliver clot-dissolving agents into thrombus for enhancement of laser thrombolysis. Thus, the laser-induced bubble formation plays an important role in the thrombus removal process. We investigate the effects of boundary configurations and materials on bubble formation with time-resolved flash photography and high-speed photography. Potential applications in drug delivery using microsecond laser pulses are then discussed.

[24] H. Shangguan, K. W. Gregory, L. W. Casperson, and S. A. Prahl. Enhanced laser thrombolysis with photomechanical drug delivery: an *In Vitro* study. *Lasers Surg. Med.*, 23:151–160, 1998.

BACKGROUND AND OBJECTIVE: Current techniques for laser thrombolysis are limited because they can not completely clear thrombotic occlusions in arteries, typically leaving residual thrombus on the walls of the artery. The objective of this study was to investigate the possibility of using photomechanical drug delivery to enhance laser thrombolysis by delivering drugs into mural thrombus during laser thrombolysis. STUDY DESIGN/MATERIALS AND

METHODS: Three experimental protocols were performed *in vitro* to quantitatively compare the effectiveness of thrombolysis by 1) constant infusion of drug, 2) laser thrombolysis, and 3) photomechanical drug delivery. A fiber-optic flushing catheter delivered drug (a solution of 1 μm fluorescent microspheres) and light (a 1 μs pulsed dye laser) into a gelatin-based thrombus model. The process of laser-thrombus interaction was visualized using flash photography and the laser-induced pressure waves were measured using an acoustic transducer. RESULTS: Lumen sizes generated by mechanically manipulating the catheter through the thrombus were smaller than those generated by laser ablation. The microspheres could be driven several hundred microns into the mural thrombus. CONCLUSION: Photomechanical drug delivery has potential for enhancement of laser thrombolysis. Two mechanisms seem to be involved in photomechanical drug delivery: 1) mural deposition of the drug at the ablation site and 2) increased exposure of the thrombus surface area to the drug.

[25] J. A. Viator, S. L. Jacques, and S. A. Prahl. Depth profiling of absorbing soft materials using photoacoustic methods. *IEEE Journal of Selected Topics in Quantum Electronics*, 5:989–996, 1999.

A Q-switched, frequency doubled, Nd:YAG laser coupled to an optical parametric oscillator generated 4.75 ns laser pulses at 726 nm to create subsurface acoustic waves in India ink solutions, India ink acrylamide gels, and in flat segments of elastin biomaterial stained with India ink. The acoustic waves traveled through the target and were detected by a piezoelectric transducer. The waveforms were converted to measurements of initial laser induced pressure and temperature as functions of depth in the material. An algorithm based on Beer's Law was developed and applied to the acoustic signals to extract information about the absorption coefficient as a function of depth in the samples.

[26] J. A. Viator and S. A. Prahl. Laser thrombolysis using long pulse frequency-doubled Nd:YAG lasers. *Lasers in Surgery and Medicine*, 25:379–388, 1999.

Background and Objective: Laser thrombolysis is a means for clearing blood clots in occluded arteries. Many researchers have studied the mechanisms of clot ablation and research clinicians have used the technique to treat myocardial infarction using a number of different laser systems. Specifically, a 1 μs pulsed dye laser has been used clinically to remove blood clots in coronary arteries. As a comparative study, the ablation characteristics of lasers with pulse durations in the ranges 50–150 μs and 2–10 ms are investigated. Two frequency-doubled Nd:YAG lasers at 532 nm were used in this study. Ablation threshold and ablation efficiency of gel phantoms and thrombus using these two lasers were measured and compared to the results of the pulsed dye laser. The pulsed dye laser in this study operated at 522 nm.

Study Design/Materials and Methods: Gelatin samples with 150 cm^{-1} absorption coefficient at 532 nm and animal clot were confined to 3 mm silicone tubes to measure ablation parameters. Additional samples with 150 cm^{-1} absorption coefficient at 522 nm were prepared for use with the pulsed dye laser. A fluorescence technique and photographic bubble detection were used to determine ablation threshold. A spectrophotometric technique was used to determine ablation efficiency.

Results: The ablation threshold of the gel phantoms for all three lasers was determined to be 17$\pm$2 mJ/mm^2. Ablation efficiency for the gel phantoms was 1.7$\pm$0.1 μg/mJ. Clot had an ablation efficiency of 2.9$\pm$1.0 μg/mJ.

Conclusions: Ablation threshold and efficiency are independent of laser pulse duration for 1 μs, 50–150 μs, and 2–10 ms pulses ($p<0.05$).

[27] T. P. Moffitt and S. A. Prahl. Sized-fiber reflectometry for measuring local optical properties. *IEEE JSTQE*, 7:952–958, 2001.

Sized-fiber spectroscopy describes a device and method for measuring absorption and reduced scattering properties of tissue using optical fibers with different diameters. The particular device used in this paper consists of two fibers with diameters of 200 and 600 μm. Each fiber emits and collects its own backscattered light. Backscattered light measurements for solutions with absorption coefficients of 0.1–2.0 cm^{-1} and reduced scattering coefficients of 5–50 cm^{-1} demonstrate that the device is most sensitive for the highest scattering materials. Monte Carlo simulations indicate the device is insensitive to the fiber illumination distribution and that the light returning to the fiber is nearly uniform over all directions. Finally, experiments and Monte Carlo simulations of the sized-fiber device indicate that 50% of the signal arises from roughly 1.2 and 1.9 reduced mean free paths for the 200 and 600 μm fibers respectively.

[28] J. A. Viator, G. Au, G. Paltauf, S. L. Jacques, S. A. Prahl, H. Ren, Z. Chen, and J. Stuart Nelson. Clinical testing of a photoacoustic probe for port wine stain depth determination. *Lasers in Surgery and Medicine*, 30:141–148, 2002.

Background and Objective: Successful laser treatment of port wine stain (PWS) birthmarks requires knowledge of lesion geometry. Laser parameters, such as pulse dura- tion, wavelength, and radiant exposure, and other treat- ment parameters, such as cryogen spurt duration, need to be optimized according to epidermal melanin content and lesion depth. We designed, constructed, and clinically tested a photoacoustic probe for PWS depth determination.

Study Design / Materials and Methods: Energy from a frequency-doubled, Nd:YAG laser (λ=532 nm, τ_p=4 nanoseconds) was coupled into two 1,500 mm optical šbers štted into an acrylic handpiece containing a piezoelectric acoustic detector. Laser light induced photoacoustic waves in tissue phantoms and a patient's PWS. The photoacoustic propagation time was used to calculate the depth of the embedded absorbers and PWS lesion.

Results: Calculated chromophore depths in tissue phan- toms were within 10% of the actual depths of the phantoms. PWS depths were calculated as the sum of the epidermal thickness, determined by optical coherence tomography (OCT), and the epidermal-to-PWS thickness, determined photoacoustically. PWS depths were all in the range of 310$\pm$570 mm. The experimentally determined PWS depths were within 20% of those measured by optical Doppler tomography (ODT).

Conclusions: PWS lesion depth can be determined by a photoacoustic method that utilizes acoustic propagation time

[29] A. D. Janis, L. A. Buckley, A. N. Nyara, S. A. Prahl, and K. W. Gregory. A reconstituted in vitro clot model for evaluating laser thrombolysis. *J. Thrombosis and Thrombolysis*, 13:167–175, 2002.

BACKGROUND/OBJECTIVE: Laser thrombolysis is the selective removal of thrombus from occluded blood vessels using laser energy. A reconstituted clot model with reproducible optical absorption properties was developed to evaluate the effect of various laser parameters on thrombus removal rate.

STUDY DESIGN/MATERIALS AND METHODS: Reconstituted clots were made with known fibrinogen concentrations and hematocrits. Ex vivo clots were collected from ten swine. Four red gelatin phantoms were prepared. Mass removal rates and ablation efficiencies were determined using a 577 nm, 1 microsecond pulsed dye laser. The ablation efficiencies of the three clot models were compared at an energy of 25 mJ and a repetition rate of 4 Hz. In addition, the reconstituted clot model was ablated as pulse energy and repetition rate were varied with average power held constant at 100 mW.

RESULTS: The mean ablation efficiency for ex vivo clots ranged from 0.4±0.1 to 3.4±0.7 μg/mJ/pulse, with significant differences between groups (ANOVA $p < 0.05$). Reconstituted clots of varied fibrinogen content had ablation efficiencies of 1.5±0.2 to 1.6±0.3 microg/mJ/pulse at this energy and repetition rate. Gelatin ablation efficiency was inversely proportional to protein content and ranged from 0.5±0.3 to 2.0±0.7 μg/mJ/pulse. Reconstituted clot mass removal rates (in μg/s) were clinically similar for settings ranging from 13 mJ at 8 Hz to 33 mJ at 3 Hz.

CONCLUSIONS: The reconstituted model clot is a reproducible and biologically relevant thrombolysis target. Ex vivo clot lacks reproducibility between individuals and gelatin phantoms lack clinical relevance. At a constant average power, varying laser parameters did not affect mass removal rates to a clinically significant degree.

[30] T. P. Moffitt, D. Baker, S. J. Kirkpatrick, and S. A. Prahl. Mechanical properties of coagulated albumin and failure mechanisms of liver repaired using an argon beam coagulator with albumin. *J. Biomedical Materials Research (Applied Biomaterials)*, 63:722–728, 2002.

Hemostasis in the traumatized liver has been achieved by thermally denaturing albumin topically applied. In this paper, the mechanical properties of liver and denatured albumin (solder) were measured and the failure methods of liver repaired with albumin were identified. The ultimate tensile strength and Young's modulus was measured for healthy liver (N=20) and thermally damaged liver (N=20). The ultimate tensile strength and Young's modulus was measured for three concentrations of coagulated albumin (25, 38 and 53%) in a single layer and for two layers of denatured 38% albumin. Failure under tension of argon beam coagulator soldered liver on the parenchymal surface (N=30) with 38% albumin in two layers had a 70% occurrence for tearing at a mean stress of 39 kPa and a 23% occurrence for shearing at a mean stress of 7 kPa. Liver repaired on the interior surface (N=11) failed in tension by tearing (64%) at a mean stress of 34 kPa and by shearing (36%) at a mean stress of 6 kPa. Argon beam coagulator soldering with 38% albumin took 6 s/cm^2 for two layers of solder and gave the best balance of usability, strength, and matching of mechanical properties with those of the liver.

[31] G. Paltauf, J. A. Viator, S. A. Prahl, and S. L. Jacques. Iterative reconstruction method for three-dimensional optoacoustic imaging. *Journal of Acoustic Society of America*, 112:1536–1544, 2002.

Optoacoustic imaging is based on the generation of thermoelastic stress waves by heating an optically heterogeneous medium with a short laser pulse. The stress waves contain information about the distribution of structures with preferential optical absorption. Detection of the waves with an array of broadband ultrasound detectors at the surface of the medium and applying a back projection algorithm is used to create a map of absorbed energy inside the medium. With conventional reconstruction methods a large number of detector elements and filtering of the signals are necessary to reduce back projection artifacts. As an alternative this study proposes an iterative procedure. The algorithm is designed to minimize the error between measured signals and signals calculated from the reconstructed image. In experiments using broadband optical ultrasound detectors and in simulations the algorithm was used to obtain three-dimensional images of multiple optoacoustic sources. With signals from a planar array of 3 x 3 detector elements a significant improvement was observed after about 10 iterations compared to the simple radial back projection. Compared to conventional methods using filtered back projection, the iterative method is computationally more intensive but requires less time and instrumentation for signal acquisition.

[32] Ronald F. Wolf, Hua Xie, John Petty, Jeff S. Teach, and Scott A. Prahl. Argon ion beam hemostasis with albumin following liver resection. *Am. J. Surg.*, 183:584–587, 2002.

Background: Bleeding is common after liver resection and establishing hemostasis with sutures or argon beam coagulation can be difficult. In our laboratory, concentrated albumin applied to the liver surface before argon beam coagulation improves sealing of the resected surface of the liver, including closure of blood vessels and ducts not generally seen with standard argon beam coagulation.

Methods: Domestic swine underwent heparinization, then laparotomy and wedge resection of the left medial segment of the liver, using finger fracture technique. Blood vessels and ducts 5 mm or greater were ligated. For achieving hemostasis, the animals were randomized to either a control group using argon beam coagulation alone ($N = 15$) or an albumin group using argon beam coagulation with concentrated 38% albumin ($N = 13$). After initial hemostasis, the resected liver surfaces were packed for 3 minutes. Repeated applications of argon beam coagulation with or without albumin were performed as needed, followed by 3 minutes of repacking, until complete hemostasis was achieved. Liver functions and blood counts were examined four days postoperatively.

Results: The albumin group was less likely to require repeat applications of argon beam coagulation than control animals (mean 0.5 vs. 1.5 times, $p = 0.006$). The total time of argon beam coagulation was significantly shorter in the albumin group (mean 90 vs. 154 seconds, $p = 0.001$).

Conclusion: Adding albumin to the liver surface substantially increases the durability of the repaired surface and reduces the time needed to achieve stable hemostasis when compared to standard argon beam coagulation. Further investigations using this technique are warranted.

[33] H. Xie, B. S. Shaffer, S. A. Prahl, and K. W. Gregory. Intraluminal albumin stent assisted laser welding for ureteral anastomosis. *Laser Surg. Med.*, 31:225–229, 2002.

Background and Objectives: The success of laser tissue welding or soldering depends on optimal laser settings, solder material, and tissue type and geometry. To develop a practical laser welding technique for ureteral repair, an intraluminal albumin stent was designed to enhance the welding effects on ureteral end to end anastomosis.

Study Design / Materials and Methods: In vitro porcine ureters were anastomosed using an albumin stent alone, the albumin stent plus a solder, and the solder alone. All welding was performed with an 810 nm diode laser with either a continuous wave (1 watt, CW) or two pulse modes (2 watts, 3.3 Hz; 1 watt, 5 Hz). Laser parameters, tensile strength (TS) and burst pressure (BP) of the ureteral anastomosis, and tissue thermal injury were measured.

Results: In the 2 watts pulse mode, BP in the albumin stent plus solder group (mean 185 mmHg) and the stent only group (mean 133 mmHg) were significantly higher than the

solder only group (mean 77 mmHg, $p < 0.05$). Laser ureteral anastomosis with the stent plus solder group at 1 watt CW and 2 watt pulse laser modes yielded the highest TS (mean 97, 82 grams) and BP (mean 183, 185 mmHg). Among the three modes, the 1 watt pulse delivered the lowest energy and yielded the lowest TS and BP in ureteral anastomosis. There was no significant difference in the thermal damage to the tissue among the modes and groups.

Conclusions: Using the albumin stent increased the reliability of ureter end to end laser anastomosis. Further studies will be warranted in vivo and other tubular organs as well.

[34] Paulo R. Bargo, Scott A. Prahl, and Steven L. Jacques. Optical properties effects upon the collection efficiency of optical fibers in different probe configurations. *IEEE J. Selected Topics Quantum Electron.*, 9:314–321, 2003.

When optical fiber are used for delivery and collection of light, two major factors affect the measurement of collected light: (1) the light transport in the medium from the source to the detection fiber, and (2) the light coupling to the optical fiber which depends on the angular distribution of photons entering the fiber. This paper studies the latter factor, describing how the efficiency of the coupling depends on the optical properties of the sample. The coupling dependence on optical properties is verified by comparing experimental data to a simple diffusion model and to a Monte Carlo corrected diffusion model. Mean square errors were 7.9% and 1.4% were for the diffusion and the Monte Carlo corrected model respectively. The efficiency of coupling was shown to be highly dependent on the numerical aperture (NA) of the optical fiber. However, for lower scattering, such as in soft tissues, the efficiency of coupling could vary 2–3 fold from that predicted by fiber NA. The collection efficiency can be used as a practical guide for choosing optical fiber based systems for biomedical applications.

[35] Jessica C. Ramella-Roman, Paulo R. Bargo, Scott A. Prahl, and Steven L. Jacques. Evaluation of spherical particle sizes with an asymmetric illumination microscope. *IEEE J. Selected Topics Quantum Electron.*, 9:301–306, 2003.

A polarized microscope system is used to perform goniometric measurements of light scattered by small particles. The light incident angle on a sample of monodispersed latex micro spheres is increased sequentially and a microscope objective lens collects scattered light from the samples. Light is only collected at angles greater than the objective lens numerical aperture, so that only light scattered by the spheres is collected. The experimental results were modeled with a Mie theory-based algorithm. Experiments conducted with micro spheres of diameter 1.03 μm, 2.03 μm and 6.4 μm show that, by decreasing the objective lens numerical aperture from N.A.=0.55 to N.A.=0.0548, a more distinguishable scattering pattern is detectable. From these highly shaped curves, we found that the size of a sphere of nominal diameter 2.03 μm was $2.11 \pm 0.06\mu$m and a 6.4 μm sphere was $6.34 \pm 0.07\mu$m.

[36] Yin-Chu Chen, Sean J. Kirkpatrick, and Scott A. Prahl. Measurement of changes in concentrations of biological solutions using a Rayleigh interferometer. In V. V. Tuchin, editor, *SPIE Saratov Fall Meeting 2002: Optical Technologies in Biophysics & Medicine IV*, volume 5068, pages 273–283, 2003.

A Rayleigh interferometer was constructed to measure changes of concentrations in the biological solutions. With the stability tests, our Rayleigh interferometer system showed its insensitivity to environment vibrations and with the second compensating cuvette, effects on the refractive index changes other than the concentration changes of molecules in the sample solution could be compensated. A thin glass plate was inserted in the beam path and rotated to vary the optical path length to test the sensitivity of the system. With this glass plate, the detectable optical path differences of the system was $\Delta(n\ell) = 7\,\mathrm{nm}$. Finally, the concentration of sucrose solutions were varied to change the refractive index. The refractive index changes by 1.43×10^{-4} for each gram of sucrose per liter at 20°C. With our system, the sensitivity to sucrose solution was 7mg/L. Based on this sensitivity this interferometric system can be used to detect concentrations of albumin solutions as low as 0.6 mg/mL.

[37] H. Xie, B. S. Shaffer, S. A. Prahl, and K. W. Gregory. Laser ureteral anastomosis using intraluminal albumin stent in a porcine model. *Lasers Surg Med*, 32:294–8, 2003.

BACKGROUND AND OBJECTIVES: We compared ureteral anastomosis using a laser and intraluminal albumin stent with both conventional suturing and laser soldering techniques. STUDY DESIGN/MATERIALS AND METHODS: Twelve pigs underwent bilateral ureteral anastomoses ($N = 24$) using one of the three anastomotic methods: (1) laser welding with intraluminal albumin stent ($N = 11$); (2) with albumin solder ($N = 8$); and (3) conventional suturing ($N = 5$). Operative parameters, leakage rate, intrapelvic perfusion pressure, urography, and histology of the anastomoses were examined. RESULTS: Operative time for ureteral anastomosis in the stent and solder groups were significantly shorter than the suture group (means 370 s and 360 vs. 710 s, both $p = 0.02$). Leakage rate of the anastomoses was lower in the stent group (9%, 1/11) as compared to the solder group (25%, 2/8). The Whitaker test showed that the intrapelvic perfusion pressure elevated gradually after anastomosis and significantly increased at 4 weeks postoperatively in all three methods. Various degrees of hydronephrosis were also noticed in three groups after 4 weeks of surgery. CONCLUSIONS: Use of the intraluminal albumin stent increased the reliability of laser welding for ureteral anastomosis. The clinical significance of using this technique should be investigated further.

[38] Stefan A. Carp, Scott A. Prahl, and Vasan Venugopalan. Radiative transport in the δ-P$_1$ approximation: Accuracy of fluence rate and optical penetration depth predictions in turbid semi-infinite media. *Journal of Biomedical Optics*, 9:632–647, 2004.

Using the δ-P1 approximation to the Boltzmann transport equation we have developed analytic solutions for the fluence rate produced by planar (1-D) and Gaussian beam (2-D) irradiation of a homogeneous, turbid, semi-infinite medium. To assess the performance of these solutions we compare the predictions for the fluence rate and two metrics of the optical penetration depth with Monte Carlo simulations. We provide results under both refractive-index matched and mismatched conditions for optical properties where the ratio of reduced scattering to absorption lies in the range $0 \le (\mu_s'/\mu_a) \le 10^4$.

For planar irradiation, the δ-P$_1$ approximation provides fluence rate profiles accurate to ±16% over the full range of optical properties for depths up to 6 transport mean free paths (l*). Metrics for optical penetration depth are predicted with an accuracy of ±4%. For Gaussian irradiation using beam radii $r_0 \ge 3l^*$, the accuracy of the fluence rate predictions is no worse than the planar irradiation case. For smaller beam radii, the predictions degrade significantly. Specifically for media with $(\mu_s'/\mu_a) = 1$ irradiated with a beam radius of $r_0 = l^*$, the error in the fluence rate approaches 100%. Nevertheless, the accuracy of the optical penetration depth predictions remains excellent for Gaussian beam irradiation, and degrades to only ±20% for $r_0 = l^*$. These results show that for a given set of optical properties (μ_s'/μ_a), the optical penetration depth decreases with a reduction in the beam diameter. Graphs are provided to indicate the optical and geometrical conditions under which one must replace the δ-P$_1$ results for planar irradiation with those for Gaussian beam irradiation to maintain accurate dosimetry predictions.

[39] Yin-Chu Chen, J. J. Brazier, M. Yan, and Scott A. Prahl. Fluorescence-based optical sensor design for molecularly imprinted polymers. *Sensors and Actuators B: Chemical*, 102:107–116, 2004.

Many studies have attempted to integrate an optical fibers or waveguides with molecularly imprinted polymer (MIP) as the sensing element; however, little work has been done on the fluorescence analysis of such sensing system. Two major factors affect the sensitivity of the fluorescence sensing system: 1) fluorescence collecting efficiency of the optical sensing system and 2) the strength of the analyte fluorescence signals. In this research, first, anthracene imprinted polyurethane films were fabricated and tested with their rebinding. Our imprinted polymers showed the rebinding to the imprinted polymers was six times more than to the non-imprinted polymers, which agreed with many of the published studies. Second, the optical properties of MIP were characterized quantitatively to provide the background knowledge to the theoretical analysis. It is shown that the background absorption coefficients increased while the solvent inside the polymer was evaporated. The absorption coefficient was determined to be $15 \pm 1\, cm^{-1}$ at the excitation (358 nm) wavelength of anthracene and $3.5 \pm 0.8\, cm^{-1}$ at emission (404 nm) wavelength in day one.

Finally, a theoretical model for the fluorescence output efficiency of a fluorescence-based molecularly imprinted polymer sensing system was reported and verified experimentally.

The theoretical model showed that the fluorescence signal increases with thickness and saturates at some point. Higher concentration of fluorophores tends to saturate earlier. The model also shows how the background absorption coefficients affect the output efficiency. This analysis provides an optimization strategy for sensor design. If the fluorescence output efficiency needs to be greater than 0.005% to be detectable by the fluorometer, and if the system wants to detect at least 1 ppm anthracene (or say $\mu_a^f = 0.063\,\mathrm{cm}^{-1}$) with 0.1 mm thick polymer sensing layer, the background absorption of the polymer needs to be smaller than $0.2\,\mathrm{cm}^{-1}$ if assuming the quantum yield of the analyte = 1 and assuming the polymer doesn't fluorese the same wavelength as the analyte.

[40] Jessica C. Ramella-Roman, Kenneth Lee, Scott A. Prahl, and Steven L. Jacques. Design, testing, and clinical studies of a handheld polarized light camera. *Journal of Biomedical Optics*, 9:1305–1310, 2004.

Polarized light imaging has been used to detect the borders of skin cancer and facilitate assessment of cancer boundaries. A design for an inexpensive handheld polarized camera is presented and clinical images acquired with this prototype are shown. The camera is built with two universal serial bus (USB) color video cameras, a polarizing beamsplitter cube, and a 4× objective lens. Illumination is provided by three white LEDs and a sheet polarizer. Horizontal and vertical linearly polarized reflected images are processed at 7 frames/s and a resulting polarized image is displayed on screen. We compare the performances of cheap USB camera and a 16-bit electronically cooled camera. Dark noise and image repeatability are compared. In both cases, the 16-bit camera outperforms the USB cameras. Despite these limitations, the results obtained with this USB prototype are very satisfactory. Examples of polarized images of lesions taken prior to surgery are presented.

[41] Zhen Ren, Anthony Funary, H. Xie, Kathryn A. Lagerquist, Allen Burke, Scott A. Prahl, and Kenton W. Gregory. Optimal dye concentration and irradiance for laser-assisted vascular anastomosis. *Journal of Clinical Laser Medicine & Surgery*, 22:81–86, 2004.

Objective: This investigation was done in order to find optimal indocyanine green (ICG) concentration and energy irradiance in laser vascular welding. *Background Data:* Many studies have shown that laser tissue welding with albumin solder/ICG may be an effective technique in surgical reconstruction. However, there are few report regarding optimal laser settings and concentrations of ICG within the albumin solder in laser-assisted vascular anastomosis. *Methods:* Porcine carotid artery strips ($N = 120$) were welded end-to-end by diode laser with 50% albumin solder with 0.01, 0.1, and 1.0 mM ICG and at irradiances of 27.7, 56.7, and 76.9 W/cm^2, respectively. Temperature was measured by inserting thermocouples outside and inside the vessel. Tensile strength and histology were studied. *Results:* Temperature and strength of the anastomosis significantly decreased (all $p < 0.05$) with increasing ICG concentration at 56.7 W/cm^2. Histological study showed minimal thermal injury limited to adventitia and no appreciable difference between all groups. *Conclusions:* ICG concentration within solder is the most important factor affecting both vascular temperature and tensile strength. The optimal balance between strength and minimal thermal injury may be achieve primarily at 56.7 W/cm^2 and 0.01 mM ICG.

[42] H. Xie, R. F. Wolf, A. P. Burke, S. B. Gustafson, K. W. Gregory, and S. A. Prahl. Concentrated albumin as a biological glue for hemorrhage control on hepatic resection with argon beam coagulation. *J Biomed Mater Res*, 71B:84–9, 2004.

Topically applied concentrated albumin with argon beam coagulation (ABCA) has been shown to be more effective at achieving hemostasis than using argon beam coagulation alone (ABC) in a liver injury model. This study investigated the host response to the concentrated albumin after argon beam coagulation. Complete hemostasis was achieved using ABCA ($N = 10$) or ABC ($N = 10$) on a nonanatomic liver resection in a heparinized porcine model. The repairs were evaluated grossly and microscopically at postoperative periods of 30 and 90 days. We found no evidence of biliary leakage, rebleeding, or intraabdominal infection. Blood analysis indicated liver chemistry indices were within normal range after ABC and ABCA treatments. The histopathology showed that the postoperative healing response was similar in both groups: a moderate chronic inflammatory response as part of an on-going normal healing process. All repairs were encapsulated by fibrous tissue. There was no difference in the postsurgical adhesion scores for the ABCA (mean 3.4) and ABC (mean 3.8). It was concluded that use of the concentrated albumin as biological glue in conjunction with argon beam coagulation is a safe and efficient procedure for controlling hepatic hemorrhage in surgery. Further studies are warranted to investigate the clinical significance of this technique.

[43] P. R. Bargo, S. A. Prahl, T. T. Goodell, R. A. Sleven, G. Koval, G. Blair, and S. L. Jacques. In vivo determination of optical properties of normal and tumor tissue with white light reflectance and an empirical light transport model during endoscopy. *J. Biomedical Optics*, 10:034018–1–034018–15, 2005.

Determination of tissue optical properties is fundamental for application of light in either therapeutical or diagnostics procedures. In the present work we implemented a spatially resolved steady-state diffuse reflectance method where only two fibers (one source and one detector) spaced 2.5 mm apart are used for the determination of the optical properties. The method relies on the spectral characteristics of the tissue chromophores (water, dry tissue and blood) and the assumption of a simple wavelength dependent expression for the determination of the reduced scattering coefficient. Because of the probe dimensions the method is suited for endoscopic measurements. The method was validated against more traditional models, such as the diffusion theory combined with adding doubling for in vitro measurements of bovine muscle. Mean and standard deviation of the absorption coefficient and the reduced scattering coefficient at 630 nm for normal mucosa were $0.87 \pm 0.22\,\mathrm{cm}^{-1}$ and $7.8 \pm 2.3\,\mathrm{cm}^{-1}$, respectively. Cancerous mucosa had values $1.87 \pm 1.10\,\mathrm{cm}^{-1}$ and $8.4 \pm 2.3\,\mathrm{cm}^{-1}$, respectively. These values are similar to data presented by other authors. Blood perfusion was the main variable accounting for differences in the absorption coefficient between the studied tissues.

[44] J. C. Ramella-Roman, S. A. Prahl, and S. L. Jacques. Three Monte Carlo programs of polarized light transport into scattering media: part I. *Optics Express*, 13:4420–4438, 2005.

Propagation of light into scattering media is a complex problem that can be modeled using statistical methods such as Monte Carlo. Few Monte Carlo programs have so far included the information regarding the status of polarization of the photon before and after every scattering event. Different approaches have been followed and limited numerical values have been made available to the general public. In this paper, three different ways to build a Monte Carlo program for light propagation with polarization are given. Different groups have used the first two methods; the third method is original. Comparison in between Monte Carlo runs and Adding Doubling program yielded less than 1% error.

[45] J. C. Ramella-Roman, S. A. Prahl, and S. L. Jacques. Three Monte Carlo programs of polarized light transport into scattering media: part II. *Optics Express*, 13:10392–10405, 2005.

Three Monte Carlo programs were developed which keep track of the status of polarization of light traveling through mono-disperse solutions of micro-spheres. These programs were described in detail in our previous article [Optics Express, 13, 4420–4438, 2005]. In this paper the simulations were used to model a series of experiments conducted in transmission and reflection. Furthermore the codes were expanded to model light propagating through poly-disperse solutions of micro-spheres. Several particle size distributions were tested and results were successfully compared to Adding Doubling calculations. The influence of anisotropy on the depolarization of light traveling through multiply scattering media was also studied, and we found that for both mono-disperse and poly-disperse solutions, anisotropy is the dominating factor in linear depolarization.

[46] Yin-Chu Chen, Jack L. Ferracane, and Scott A. Prahl. A pilot study of a simple photon migration model for predicting depth of cure in dental composite. *Dental Materials*, 21:1075–1086, 2005.

Objectives: The purpose of this study was to build a photo migration model to calculate the radiant exposure (irradiance · time) in dental composite and to relate the radiant exposure with extent of cure using polymer kinetics models.

Methods: A composite (Z100) cylinder (21 mm diameter by 15 mm deep) was cured with tungsten–halogen lamp emitting $600\,\mathrm{mW/cm}^2$, 1 mm above the composite for 60 seconds. For each of the 2×1 mm grids along the longitudinal cross section (diameter versus depth), the degree of conversion (DC) and hardness (KHN) were measured to construct the curing extent distribution. The inverse adding–doubling method was used to characterize the optical properties of the composite for the Monte Carlo model simulating the photon propagation within the composite cylinder. The calculated radiant exposure (H) distribution along the cross section was related to the curing extent DC/DC_{max} distribution and fitted with two polymer curing kinetics models, the exponential model $DC = DC_{max}[1 - \exp((\ln 0.5)H/H_{dc}^{50\%})]$ and

Racz's model $DC = DC_{max}/[1+(H/H_{dc}^{50\%})^{-2}]$, where $H_{dc}^{50\%}$ is a fitting parameter representing the threshold for the 50% of the maximum curing level.

Results: The absorption and scattering coefficients of uncured composite were higher than that of cured composite at wavelength between 420 to 520 nm. A roughly hemi-sphere distribution of radiant exposure in the Monte Carlo simulation result was comparable with the curing profiles determined by both DC and KHN. The relationship between DC (or KHN) and H agreed with the Racz model ($r^2 = 0.95$) and the exponential model ($r^2 = 0.93$). The $H_{dc}^{50\%}$ was 1.5±0.1, equal for the two models ($p < 0.05$). The estimated radiant exposure threshold for the 80% of the maximum curing level was between 3.8 and 8.8 J/cm^2. The simulation results verify that the radiant exposure extends to a greater depth and width for composite with lower absorption and scattering coefficients.

[47] Yin-Chu Chen, Zheming Wang, Mingdi Yan, and Scott A. Prahl. Fluorescence anisotropy study of molecularly imprinted polymers. *Luminescence*, 21:7–14, 2006.

A molecularly imprinted polymer (MIP) is a biomimetic material that can be used as a biochemical sensing element. We studied the steady-state and time-resolved fluorescence and fluorescence anisotropy of anthracene imprinted polyurethane. We compared MIPs with imprinted analytes present, MIPs with the imprinted analytes extracted, MIPs with rebound analytes, non-imprinted control polymers (non-MIPs), and non-MIPs bound with analytes to understand MIP's binding behavior. MIPs and non-MIPs had similar steady-state fluorescence anisotropy in the range of 0.11–0.24. Anthracene rebound in MIPs and non-MIPs had a fluorescence lifetime τ=0.64 ns and a rotational correlation time ϕ_F=1.2–1.5 ns, both of which were shorter than that of MIPs with imprinted analytes present (τ=2.03 ns and ϕ_F=2.7 ns). The steady-state anisotropy of polymer solutions increased exponentially with polymerization time and might be used to characterize the polymerization extent *in-situ*.

[48] Theodore Moffitt, Yin-Chu Chen, and Scott A. Prahl. Preparation and characterization of polyurethane optical phantoms. *Journal of Biomedical Optics*, 11:041103, 2006.

We describe a method for the preparation of a polyurethane phantom to simulate the optical properties of biologic tissues at two wavelengths in the visible and near infrared spectral range. We characterize the addition of added molecular absorbers with relatively narrow absorption bands (FWHM 32 and 76 nm for Epolight 6084 and 4148 respectively) for independent absorption at 690 nm for absorption up to 5 cm^{-1} and 830 nm for absorptions up to 3 cm^{-1}. Absorption by both dyes is linear in these respective regions and is consistent in polyurethane both before and after curing. The dyes are stable over long durations with no more than 4% change. The absorption of visible light by polyurethane decreases with time and is stable by one year with a drop of 0.03 ± 0.003 cm^{-1} from 500–830 nm. The scattering properties are selected by the addition of TiO_2 particles to the polyurethane which we functionally describe for the 690 and 830 nm wavelengths as related to the weight per volume. We demonstrate that the variation in absorption and scattering properties for large batch fabrication (12 samples) is ±3%. The optical properties of the phantoms has not significantly changed in a period of exceeding one year which makes them suitable for use as a reference standard.

[49] Yin-Chu Chen, Jack L. Ferracane, and Scott A. Prahl. Quantum yield of conversion of the photoinitiator camphorquinone. *Dental Materials*, pages 655–664, 2007.

The primary absorber in dental resins is the photoinitiator, which starts the photo polymerization process. We studied the quantum yield of conversion of camphorquinone (CQ), a blue light photoinitiator, using 3M FreeLight LED and VIP lamps as the light curing units at 5 different irradiances. The molar extinction coefficient, ε_{469}, of CQ was measured to be $46\pm2\,\mathrm{cm}^{-1}/(\mathrm{mol/L})$ at 469 nm. We found that the reciprocity of irradiance and exposure time holds for the conversion of the photoinitiator CQ. That is, irradiance $\times$ the exposure time = radiant exposure is a constant. The relationship between the CQ absorption coefficient and the radiant exposure was the same for the 5 irradiances and fit an exponential function: $\mu_{a469}(H) = \mu_{ao}\exp(-H/H_{\mathrm{threshold}})$, where μ_{ao} is $4.46\pm0.05\,\mathrm{cm}^{-1}$, and $H_{\mathrm{threshold}}=43\pm4\,\mathrm{J/cm}^2$. Combining this exponential relationship with CQ molar extinction coefficient and the absorbed photon energy (i.e., the product of the radiant exposure with the absorption coefficient), we plotted CQ concentration [number of molecules/cm^3] as a function of the accumulated absorbed photons per volume. The slope of the relationship is the quantum yield of the CQ conversion. Therefore, in our formulation (0.7 w% CQ with reducing agents 0.35 w% DMAEMA and 0.05 w% BHT) the quantum yield was solved to be 0.07 ± 0.01 CQ conversion per absorbed photon.

[50] Luis F. J. Schneider, Carmem S. C. Pfeifer, Simonides Consani, Scott A. Prahl, and Jack L. Ferracane. Influence of photoinitiator type on the rate of polymerization, degree of conversion, hardness and yellowing of dental resin composites. *Dental Materials*, 24:1169–1177, 2008.

OBJECTIVES: To evaluate the degree of conversion (DC), maximum rate of polymerization (R_p^{max}), Knoop hardness (KHN) and yellowing (b-value) of resin composites formulated with phenylpropanedione (PPD), camphorquinone (CQ), or CQ/PPD at different concentrations. The hypotheses tested were (i) PPD or CQ/PPD would produce less R_p^{max} and yellowing than CQ alone without affecting DC and KHN, and (ii) R_p^{max}, DC, and KHN would be directly related to the absorbed power density (PD$_{abs}$).

METHODS: CQ/amine, PPD/amine and CQ/PPD/amine were used at low, intermediate and high concentrations in experimental composites. Photoinitiator absorption and halogen-light emission were measured using a spectrophotometer, R_p with differential scanning calorimetry (DSC), DC with DSC and FTIR, KHN with Knoop indentation; and color with a chromameter. The results were analyzed with two-way analysis of variance (ANOVA)/Student-Newman-Keul's test ($p < 0.05$). Correlation tests were carried out between PD$_{abs}$ and each of DC, R_p^{max} and KHN.

RESULTS: The PD$_{abs}$ increased with photoinitiator concentration and PPD samples had the lowest values. In general, maximum DC was comparable at intermediate concentration, while R_p^{max} and KHN required higher concentrations. DC was similar for all photoinitiators, but R_p^{max} was lower with PPD and CQ/PPD. PPD produced the lowest KHN. Yellowing increased with photoinitiator concentration.scmc PPD did not reduce yellowing at intermediate and/or high concentrations, compared to CQ-formulations. PD$_{abs}$ showed significant correlations with DC, R_p^{max} and KHN.

CONCLUSION: PPD or CQ/PPD reduced R_p^{max} in experimental composites without affecting the DC. The use of PPD did not reduce yellowing, but reduced KHN. DC, R_p^{max} and KHN were dependent on PD$_{abs}$.

[51] David G. Fischer, Scott A. Prahl, and Donald D. Duncan. Monte Carlo modeling of spatial coherence: free-space diffraction. *J. Opt. Soc. Am. A*, 25:2571–2581, 2008.

We present a Monte Carlo method for propagating partially coherent fields through complex deterministic optical systems. A Gaussian copula is used to synthesize a random source with an arbitrary spatial coherence function. Physical optics and Monte Carlo predictions of the first and second order statistics of the field are shown for coherent and partially coherent

sources for free-space propagation, imaging using a binary Fresnel zone plate, and propagation through a limiting aperture. Excellent agreement between the physical optics and Monte Carlo predictions is demonstrated in all cases. Convergence criteria are presented for judging the quality of the Monte Carlo predictions.

[52] Scott A. Prahl, David G. Fischer, and Donald D. Duncan. A Monte Carlo Green's function for the propagation of partially coherent light. *J. Opt. Soc. Am. A*, 26:1533–1543, 2009.

We present a Monte Carlo-derived Green's function for the propagation of partially spatially coherent fields. This Green's function, which is derived by sampling Huygens-Fresnel wavelets, can be used to propagate fields through an optical system and to compute first- and second-order field statistics directly. The concept is illustrated for a cylindrical $f/1$ imaging system. A Gaussian copula is used to synthesize realizations of a Gaussian Schell-model field in the pupil plane. Physical optics and Monte Carlo predictions are made for the first- and second-order statistics of the field in the vicinity of the focal plane for a variety of source coherence conditions. Excellent agreement between the physical optics and Monte Carlo predictions is demonstrated in all cases. This formalism can be generally employed to treat the interaction of partially coherent fields with diffracting structures.

[53] Amanda Dayton, Laurel Soot, Ronald Wolf, Christina Gougoutas-Fox, and Scott A. Prahl. Light guided lumpectomy: Device. *J. Biomed. Opt.*, 15(6):061706, 2010.

We describe the development, design, fabrication and testing of an optical wire to assist in the surgical removal of small tumors during breast-conserving surgery. We modified a standard localization wire by adding a 200 micron optical alongside it: the resulting optical wire fit through an 18 gauge needle for insertion in the breast. The optical wire was anchored in the tumor by a radiologist under ultrasonic and mammographic guidance. At surgery, the tip was illuminated with an eye-safe, red, HeNe laser and the resulting glowball in the breast tissue surrounded the tumor. The surgeon readily visualized the glowball in the operating room. This glowball provided sufficient feedback to the surgeon that it was used to find the lesion and as a guide during tumor resection. Light guided lumpectomy was a simple enhancement to traditional wire localization that could enhance the current standard of care for small, non-palpable breast tumors.

[54] Genevieve R. Mueller, Paul D. Hansen, Ronald F. Wolf, Ken W. Gregory, and Scott A. Prahl. Hemostasis after liver resection improves after single application of albumin and argon beam coagulation. *J Gastrointest Surg*, 14(11):1764–1769, 2010.

Background: Bleeding from the liver surface is common after hepatic resection. Animal studies have demonstrated superiority of argon beam coagulation (ABC) and 38resection when compared to ABC alone. There are no data addressing the combination of albumin and argon beam coagulation (ABCA) applied to the bleeding liver after resection in humans. The aim of this study was to evaluate the safety and efficacy of ABCA on hemostasis when applied to the surface of the liver remnant post hepatic resection.

Methods: Ten patients underwent liver resection and were treated with ABCA immediately after the liver was divided. The liver surface was coated with albumin and ABC applied simultaneously, the liver was covered with gauze for 3 minutes and ABCA was repeated if necessary. Number of rebleeding episodes requiring re-application of ABCA, time of ABCA application, overall blood loss, and liver functions were monitored. Patients were followed for at least 6 months.

Results: Nine of 10 patients required a single application of ABCA, and one patient required 2 treatments. Average time of ABC use was 5±3 minutes. Median blood loss was 230 ml. Liver functions returned to near normal within 4 days of resection.

Conclusions: ABCA performed well with respect to hemostatic properties, much like previous observations in animal studies. Further clinical trials are justified using this technique.

[55] Amanda Dayton, Laurel Soot, Ronald Wolf, Christina Gougoutas-Fox, and Scott A. Prahl. Light guided lumpectomy: First clinical experience. *J. Biophotonics*, 4:752–758, 2011.

Background and Objectives: Despite numerous advances, lumpectomies remain a technically challenging procedure and margin status is critical its success. Positive margins following lumpectomy usually lead to a second surgery to clear the margins. This not only increases morbidity but also prolongs the course of treatment and creates additional cost. A visible, spherical glowball of light centered on the lesion may not only be able to assist in locating the lesion but also in resecting it with uniform margins.

Methods: Eight patients underwent a light guided lumpectomy. Subjects with non-palpable breast lesions undergoing lumpectomy for breast malignancy with radiographic measurable disease were included in the study. Instead of a bare Kopans wire, an optical wire was designed that incorporated a Kopans wire with an optical fiber.

Results: The optical wires were placed in the same manner as a Kopans wire. During the light-guided lumpectomies, the optical fiber was illuminated and emitted a sphere of light surrounding the lesion. This light was used to localize and resect the lesion. Seven of eight light guided lumpectomies resulted in negative margins.

Conclusions: This procedure may result in a decrease in positive margins and in more uniformly spherical specimens. This could result in fewer procedures, reduced cost, and better cosmesis.

[56] Jessica C. Ramella-Roman, Amritha Nayak, and Scott A. Prahl. A spectroscopic sensitive polarimeter for biomedical applications. *J. of Biomedical Optics*, 16:047001, 2011.

We present the design and calibration of a spectroscopic sensitive polarimeter. The polarimeter can measure the full Stokes vector in the wavelength range 550–750 nm with 1 nm resolution and consists of a fiber-based spectrophotometer, a white LED light source, two liquid crystal retarders, and one polarizer. Calibration of the system is achieved with a scheme that does not require knowledge of the polarizing elements' orientation or retardation. Six intensity spectra are required to calculate the full spectrum Stokes vector. Error in the polarimeter is less than 5 percent. We report the Stokes vectors for light transmitted through non-scattering polarizing elements as well as a measurement of the depolarizing properties of chicken muscle at several wavelengths.

[57] Donald D. Duncan, David G. Fischer, Amanda Dayton, and Scott A. Prahl. Quantitative Carré differential interference contrast microscopy to assess phase and amplitude. *J. Opt. Soc. Am. A*, 28:1297–1306, 2011.

We present a method of using an un-modified differential interference contrast microscope to acquire quantitative information on scatter and absorption of thin tissue samples. A simple calibration process is discussed that uses a standard optical wedge. Subsequently we present a phase-stepping procedure for acquiring phase gradient information exclusive of absorption effects. The procedure results in two-dimensional maps of the local angular (polar and azimuthal)

ray deviation. We demonstrate the calibration process, discuss details of the phase-stepping algorithm, and present representative results for a porcine skin sample.

[58] Luis Felipe J. Schneider, Larissa Maria A. Cavalcante, Scott A. Prahl, Carmem S. Pfeifer, and Jack L. Ferracane. Curing efficiency of dental resin composites formulated with camphorquinone or trimethylbenzoyl-diphenyl-phosphine oxide. *Dental Materials*, 28:392–397, 2012.

Objectives. Since photoinitiator systems for dental resins based on camphorquinone (CQ) present color disadvantages, trimethylbenzoyl-diphenyl-phosphine oxide (TPO) has been proposed as an alternative. However, there are remaining considerations about its curing efficiency. The aims of the present investigation were: to characterize the relationship between the photoinitiator absorption spectra and the light spectrum emitted from a QTH light (absorbed power density, PD_{abs}); to evaluate the kinetics of polymerization, and the depth of cure for filled dimethacrylate resins formulated with different photoinitiator systems.

Methods. CQ + EDMAB (control); TPO and TPO + EDMAB were used in 50:50 Bis-GMA/TEGDMA resins. Photoinitiator absorption and QTH-light emission were evaluated using a spectrophotometer and kinetics of polymerization with differential scanning calorimetry (DSC) ($n = 3$). Depth of cure was analyzed by the scraping method ($n = 5$), as recommended by ISO4049. One-way ANOVA/Tukey's ($p < 0.05$) was used to analyze the results from DSC.

Results. CQ presented higher PD_{abs} than TPO (364 and 223 mW/cm^3, respectively). The DSC revealed that TPO and TPO + EDMAB produced a faster reaction than CQ + EDMAB. Composite formulated with CQ + EDMAB produced higher depth of cure (6.3±0.4) than those with TPO (4.3±0.1) or TPO + EDMAB (4.2±0.3).

Conclusions. Although CQ presented higher PD_{abs} than TPO, formulations containing TPO exhibited higher reactivity than that with CQ. On the other hand, materials formulated with TPO demonstrated lower depth of cure than that with CQ. Therefore, its use as an alternative photoinitiator requires further investigation, with higher concentrations. observations in animal studies. Further clinical trials are justified using this technique.

[59] Reid McCargar, Hua Xie, Kirk Price, and Scott A. Prahl. In vitro mechanical assessments of laser-welded vascular anastomoses using water as the chromophore and dissolvable extruded albumin stents. *Lasers in Surgery and Medicine*, 44:330–338, 2012.

We present a clinically-relevant method for producing and sterilizing dissolvable albumin stents to provide intralumenal support in vascular anastomosis, and a method for photothermally welding vessels using a 1.9 μm diode laser with albumin solder and water as the chromophore. The axial tensile strength and burst pressure of welded vessels were tested in-vitro. Optimized weld parameters yielded tensile strengths of 4.4±1.2 N and burst pressures of 400±180 mmHg with stay sutures (95%CL). It was concluded that stay sutures would be necessary in vivo due to degradation of the tensile strength with exposure to moisture. Stent dissolution was monitored with UV absorbance measurements in PBS, which produced similar results when compared to measurements by weight in blood ($P = 0.99$). Sterilization by 25 kGy γ-irradiation did not cause significant changes ($P > 0.6$) in stent solubility, which was primarily volume and geometry-dependent. Under simulated intravascular flow conditions, 3 mm stents dissolved completely with 2.7±1.3 mL/mg (95%CL).

[60] Scott A. Prahl, Amanda Dayton, Kyle Juedes, Erik J. Sánchez, Rafael López Páez, and Donald D. Duncan. Experimental validation of phase using Nomarski microscopy with an extended Fried algorithm. *J. Opt. Soc. Am. A*, 29:2104–2109, 2012.

Reconstruction of an image (or shape or wavefront) from measurements of the derivatives of the image in two orthogonal directions is a common problem. We demonstrate how a particular reconstructor, commonly referred to as the Fried algorithm, can be used with megapixel derivative images to recover the original image. Large datasets are handled by breaking the derivative images into smaller tiles, applying the Fried algorithm and stitching the tiles back together. The performance of the algorithm is demonstrated using differential interference contrast microscopy on a known test object.

Patents

[1] R. R. Anderson, N. Bhatta, S. Prahl, and P. J. Dwyer. Laser illuminator. *United States Patent. No. 5,527,308*, 1996.

An illuminator including a differential optical radiator and a laser fiber disposed within the differential optical radiator. The differential optical radiator includes a first region that has a first level of reflectivity and a first level of transmissivity and a second region that has a second, higher level of reflectivity and a second, lower level of transmissivity. The first and second regions are positioned such and their reflectivities and transmissivities are chosen such that the radiator produces a substantially uniform pattern of illumination from the first and second regions. In another embodiment, the illuminator includes an expandable radiator and a laser fiber disposed within the expandable radiator. The reflectivity of the expandable radiator is such that the illumination at the outer surface of the expandable radiator is substantially uniform.

[2] L. A. Buckley, S. A. Prahl, and S. L. Jacques. Method and apparatus for determination of psoralen concentrations in biological tissues. *United States Patent. No. 5,522,868*, 1996.

Levels of psoralen concentration in a biological detection target are determined so that an appropriate UVA light dose of PUVA therapy can be delivered to a biological treatment target. The appropriate therapy is determined by the product of the UVA light dose and psoralen concentration level. After determination of a baseline optical autofluoresence signal from the detection target, a first dosage of psoralen (preferably 8-methoxypsoralen [8-MOP]) is administered. Thereafter, the detection target is irradiated under the same conditions as the pre-psoralen irradiation. Then, the optical return from the psoralen-treated detection target is analyzed. A computer (86) compares the pre-psoralen optical return and psoralen-treated optical return to calculate a real time determination of the concentration level of psoralen in the treatment target. Then, then knowing the precise psoralen concentration level, a UV dosage level required to achieve the desired PUVA therapy can be precisely determined and applied to the treatment target. In some embodiments, the detection target is the treatment target and in vivo real time psoralen concentration is determined. Various forms of applicators (52, 452, 552, 652, 752) are provided for differing types of targets. Each applicator is mounted on an optical fiber bundle (54). In some embodiments, the same optical fiber bundle (54) is employed to transmit the irradiation and optical return signals in the psoralen concentration determination, as well as to transmit the UVA for the PUVA therapy.

[3] S. A. Prahl and S. L. Jacques. Multiple diameter fiber optic device and process of using the same. *United States Patent. No. 6,014,204*, 1998.

A multiple diameter fiber optic device comprises one or more optical fibers that are used to irradiate light onto a tissue and to detect light back-scattered by the tissue wherein each fiber is used for both irradiation and detection. In the case of multiple fibers, the fibers typically are bundled together at the probe end of the bundle. The diameters and/or numerical apertures of the one or more fibers are selected to provide different sampling volumes within the tissue. More specifically, the diameter and/or numerical apertures of the one or more fibers are chosen to emphasize differences in light penetration into the tissue such that the diameter and/or numerical aperture of each fiber is related to the scattering and absorption path lengths in the tissue.

[4] Scott Prahl and Amanda Dayton. Optical wire illuminator. *United States Provisional Patent Application*, 2009.

The invention is for an optical wire lumpectomy (OWL) system. This system has three components: an optical wire, an optical fiber, and a light source. The optical wire is a replacement for the Kopans wire commonly used for wire-localized breast lumpectomies. The optical wire consists of a metallic hook, a translucent plastic tube, a crimping ring to retain the hook in the tube. A metallic wire is inserted into the tube to provide rigidity. Before surgery, the optical wire is placed by a radiologist with x-ray or ultrasonic guidance in exactly the same manner as a traditional Kopans wire. At surgery, the metallic wire is removed and an optical fiber is inserted into the optical wire. The optical fiber is coupled to a light source to create a glowball of light around a breast lesion. The glowball helps the surgeon find and remove the lesion.

[5] Y. Wadia and S. A. Prahl. Biocompatible denatured albumin lamina. *United States Patent. No. RE 43,134*, 2012.

The present invention provides a denatured albumin lamina, useful for repairing lesions on solid visceral organs. The lamina comprises human serum albumin, formed into a thin, pliant sheet and denatured. The denatured lamina can be sterilized and stored until used. As well, it can be impregnated with a variety of bioagents. A method for repairing a lesion on a solid visceral organ includes applying an energy-absorbing proteinaceous material to a lesion site on the solid visceral organ lesion; irradiating the proteinaceous material with energy sufficient to fuse the energy-absorbing material at least partially to the lesion site; applying a biocompatible denatured albumin lamina onto the proteinaceous material on the lesion site; and irradiating the biocompatible albumin lamina and the proteinaceous material with energy sufficient to fuse the biocompatible albumin lamina to the proteinaceous material and/or the lesion site. A laser solder can be deployed beneath the lamina to aid in welding it to the organ surface using laser light energy.

Supervised Theses

[1] Amanda Dayton. *Light-Guided Lumpectomy: Visual and Frequency Domain Localization of Breast Lesions.* PhD thesis, Oregon Health & Science University, 2013.

In the U.S. in 1996, the last year the National Survey of Ambulatory Surgery was completed, 341,000 outpatient lumpectomies were performed. Positive margins following lumpectomy in approximately 30%, of procedures, the patient usually undergoes a second surgery to clear the margins. The long term goal of this work was to develop a simple, practical tool to improve the outcome of lumpectomy surgeries. An optical wire was developed to make the breast tissue surrounding a lesion glow red by placing a light source within the lesion.It was hypothesized that light guided lumpectomies could result in a decrease in positive margins, fewer procedures, reduced cost, and better cos- metic outcomes. The goals of the work presented here were to develop an optical wire, clinically evaluate the feasibility of light guided lumpectomies, and to quantitatively determine the distance from the tissue surface to a light source within.

An optical wire was designed with a 3 m optical fiber axially attached to a standard localization wire. After placement of the wire, the lumpectomy could be performed using standard methods but with the additional assistance of being able to see a red glow-ball of light surrounding the lesion. A small clinical study of light guided lumpectomy in 8 patients was conducted. During surgery, a glow-ball of red light provided immediate visualization at the end of the optical wire which the surgeon was able use to estimate proximity to the wire tip. Seven of the eight lumpectomies resulted in negative margins upon pathology review. Use of the optical wire resulted in good clinical outcomes, but it was re-designed to be more comfortable for the patient and easier to use.

The intensity of the visible light during lumpectomy was variable and not a reliable indicator of distance from the light source. In addition to a visual guide, the operating surgeon also wanted to know exactly how far the dissection plane was from the lesion. It was hypothesized that the distance could be determined using the light emitted from the optical wire with frequency domain measurements. In scattering media, sinusoidally modulated light becomes demodulated and a phase lag develops between the source and the propagating wave. A multi detector probe is proposed to be used in conjunction with light-guided lumpectomy to give the operating surgeon a quick measurement of distance within the breast without a-priori knowledge of the tissue optical properties. An expected relative error of 1% from the proposed method was determined.

A fiber coupled optical system was assembled to modulate the intensity of a red laser diode with a network analyzer. The detected signal was compared to the source and a phase lag between the two was measured. As expected, the phase lag measured through optical phantoms was found to be in agreement with the diffusion theory approximation and found to be linear as a function of distance from the source with a deviation from linearity of 0.1 deg/mm. Three prophylactic mastectomy specimens were also tested after surgery and before examination by pathology. During the investigations, an optical fiber was inserted stereotactically through a needle and the phase lag from the edge of the tissue to the fiber tip was measured with another optical fiber. The phase lag was used to determine the distance between the fibers. Optical measurements of the distance between source and detector were within 15% of the actual value.

[2] Theodore Paul Moffitt. *Light Transport in Polymers for Optical Sensing and Photopolymerization.* PhD thesis, Oregon Health & Science University, 2005.

Fiber optics can facilitate a non-invasive means of tissue biopsy through optical inspection in small volumes to differentiate between normal and diseased tissue. Optical fibers provide a non-complex means to deliver and collect reflected light allowing for the determination of the absorption and scattering properties. These optical properties correlate with the chemical and structural state of the tissue. The arrangement of the emission and collection fibers dictates the volume of tissue that is optically sampled. Fiber-optic probes that sample the smallest possible volume by emitting and collecting their own backscattered light are investigated.

Two complimentary studies are presented that are necessary to provide the tools to evaluate the behavior of fiber-optic probes. First, a method to fabricate optically stable phantoms is investigated. The optical properties of the phantoms are defined at two wavelengths. Linear relations are given for the concentration of dyes and TiO_2 scattering agent that predict the absorption and scattering properties of the finished phantoms with less than 4% error. The phantoms are demonstrated to be stable over a period exceeding one year. Second, a combined inverse adding-doubling and Monte Carlo model is presented to evaluate the optical properties of the phantoms using integrating sphere measurements. The combined IAD/MC model is demonstrated to accurately determine optical properties of homogenous optically turbid samples with a reasonable precision using multiple sample thicknesses and sample port sizes for both single and double sphere experiments. The scattering is predicted with 1% error and absorption error is 2–4%. The nomenclature for integrating sphere measurements is simplified and rationalized using the concept of sphere gain to express the results. Explicit directions for determining sphere parameters were shown. Formulas were given that work for diffuse incidence or collimated incidence or any combination thereof.

A new kind of fiber optic probe, a sized-fiber reflectometry device is presented and investigated. Experimental studies are performed using phantoms with known absorption and scattering properties. A Monte Carlo model is developed to simulate the device behavior to evaluate effects due to absorption scattering, scattering anisotropy, and optical sampling volume. The model is validated by comparison to experimental results. Both experiments and Monte Carlo simulations of the sized-fiber device indicate that 50% of the signal arises from roughly 1.2 and 1.9 reduced mean free paths for the 200 and 600 μm fibers respectively and that in general larger fibers sample deeper optically. Specular reflectance is shown to act as a noise source comparable in magnitude to the diffuse reflection signal for perpendicularly polished fibers and can be rejected with bevel-tipped fibers. The measurement variability decreases 6 fold to 4.5% on *in vivo* skin with a 200 micron fiber with the beveled-tip fiber and to 2.2% for a 1000 micron fiber with the beveled-tip fiber. The absorption and scattering sensitivity is presented for a bevel- tipped sized fiber device using a Monte Carlo generated grid to invert optical properties from the measured diffuse reflectance. The scattering coefficient could be predicted with an error of $1.5 \pm 0.2\%$ over the entire range of absorption and scattering properties. A second two-fiber probe design is investigated that uses two identical diameter fibers with only a single source fiber and both fibers collecting reflected light. The inversion of absorption and the reduced scattering is investigated using a heuristically determined closed form relationship from device simulations. The scattering coefficient could be predicted with a mean error of $\pm 4.3\%$. Typical error for absorption coefficient determination is shown to be between 50-100% for absorption less than $2\,\mathrm{cm}^{-1}$. The poor resolution of absorption is related to the mean optical path for collected light which typically is less than 2 mm for tissue.

A clinical study is presented using a dual 400 micron fiber probe to distinguish oral pigmented lesions caused by either melanin or dental amalgam. Two methods of discrimination were investigated. The first method used the spectral features of melanin in the 640–720 nm wavelength band. The pigmented lesions containing melanin exhibited a higher change in reflectance with respect to wavelength over this band in comparison to amalgam tattoos or non-pigmented sites. The sensitivity and specificity for identifying melanotic lesions from amalgam tattoo was 98% and 92% respectively. The second method of discriminating amalgam tattoo, melanin pigment and non-pigmented sites uses discriminant function analysis on uniformly spaced wavelength bands of reflectance to simulate spectrally filtered reflected light. The sensitivity and specificity was 94% and 100% respectively for classifying melanin pigmented sites.

[3] Yin-Chu Chen. *Light Transport in Polymers for Optical Sensing and Photopolymerization.* PhD thesis, Oregon Health & Science University, 2005.

This thesis studied light-polymer interaction in fluorescent-based molecularly imprinted polymer (MIP) sensors and photopolymerized dental composites. Through the optical property characterization of the polymers and the light transport modeling in the polymers, an optical MIP sensor design strategy and an optimal photo-cured system for dental composites may be explored.

A MIP is a biomimetic sensing element that is robust and stable in a harsh environment and cheap to produce when compared to immunoassay methods. This thesis investigated the sensitivity factors of MIP sensors consisting of highly cross-linked polyurethane containing anthracene binding sites. Two types of transducers were designed and examined with respect to their fluorescence collection efficiency. The optical properties of MIPs, the fluorescence quantum yield of anthracene in MIPs, and the fluorescence anisotropy property of anthracene and polyurethane were studied. Polyurethane would be an effective waveguide but the high background absorption in the spectrometric regions of interest was a serious problem for sensor sensitivity. The MIP rebinding capacity measured by bath batch was about one micromole/g and was six times more than that of non-imprinted polymers. The fluorescence anisotropy study suggests that anthracene rebinds with MIPs tightly and closely. The detection limit of the MIP sensor was about 15 ppm of anthracene, which is about 0.1 μM/g.

Photocured composites are commonly used as dental restoratives. Due to the large variety of composite formulations and curing-unit types, it is difficult to test the light curing efficiency of all possible combinations. This thesis sought to provide guidelines for optimization of a photopolymerized system based on the light transport model. The quantum yield of photoinitiator conversion and the composite's dynamic optical properties (as curing) were measured.

The photoinitiator conversion (as well as the composite's optical properties, or the composite extent of cure) as a function of radiant exposure was found to fit an exponential model and obey a reciprocity rule for irradiance and illumination time. A dynamic Monte Carlo model to predict the radiant exposure distribution in a medium with dynamic optical properties was constructed and validated. This model will improve understanding of how composite formulations and the spectrum and power of curing units affect curing efficiency.

[4] J. A. Viator. *Characterization of photoacoustic sources in tissue using time domain measurements.* PhD thesis, Oregon Graduate Institute of Science and Technology, 2001.

Photoacoustic phenomenon in tissue and tissue phantoms is investigated with the particular goal of discrimination of diseased and healthy tissue.

Propagation of broadband photoacoustic sources in tissue phantoms is studied with emphasis on attenuation, dispersion, and diffraction. Attenuation of photoacoustic waves induced by a circular laser spot on an absorber/air interface is modeled by the on-axis approximation of the acoustic field of a baffled piston source. Dispersion is studied in a diffraction free situation, where the disk of irradiation was created by a 5 mm laser spot on a $200\,\mathrm{cm}^{-1}$ solution. The genesis of diffraction in an absorbing solution was displayed by showing the merging of a boundary wave with a plane wave from a circular laser spot on an absorbing solution.

Depth profiling of absorbing tissue phantoms and stained tissue was shown using a photoacoustic method. Acrylamide gels with layers of different optical absorption and stained elastin biomaterials were irradiated with stress confined laser pulses. The resulting acoustic waves were detected with a lithium niobate wideband acoustic transducer and processed in an algorithm to determine absorption coefficient as a function of depth.

Spherical photoacoustic sources were generated in optically clear and turbid tissue phantoms. Propagation time and acoustic pulse duration were used to determine location and size, respectively. The photoacoustic sources were imaged using a multiplicative backprojection scheme. Image sources from acoustic boundaries were detected and dipole sources were detected and imaged.

Finally, an endoscopic photoacoustic probe was designed, built, and tested for use in determining treatment depth after palliative photodynamic therapy of esophageal cancer. The probe was less than 2.5 mm in diameter and consisted of a side firing $600\,\mu$m optical fiber to deliver laser energy and a $890\,\mu$m diameter, side viewing piezoelectric detector. The sensitivity of the probe was determined. The probe was also tested on coagulated and non–coagulated liver, *ex vivo* and on normally perfused and underperfused human skin, *in vivo*.

[5] H. Shangguan. *Local Drug Delivery with Microsecond Laser Pulses:* In vitro *Studies*. PhD thesis, Portland State University, 1996.

Photomechanical drug delivery is a technique for localized drug delivery using laser-induced hydrodynamic pressure following cavitation bubble expansion and collapse. This dissertation presents *in vitro* studies of photomechanical drug delivery. The main goals were investigate the possibility of photomechanical drug delivery as a new means of localized drug delivery to thrombus for enhancement of laser thrombolysis and to address some of the questions regarding the physical processes during photomechanical drug delivery.

A parametric study was performed to characterize laser-induced cavitation phenomena that take place in absorbing liquids or on soft targets using time-resolved flash photography, high-speed shadowgraphy, particle image velocimetry. The laser-induced cavitation bubble dynamics depended where the bubble was formed. The bubble expansion and collapse could cause the surrounding flow motion at a speed of up to 12 m/s. A theoretical model was used to estimate the bubble volumes formed in absorbing liquids. This model assumed vaporization of the entire disk of absorbing liquids under a delivery fiber, rather than vaporization of a fraction of the disk. Good agreement was found between the model and experimental results.

Photomechanical drug delivery into soft materials (gelatin or thrombus) were studied using solutions of oil and dye or $1\,\mu$m fluorescent microspheres. The drug could be driven into thrombus several hundred micrometers and even few millimeters in both axial and radial directions when the gelatin structures were fractured. The results of using thrombus phantoms

were comparable to those obtained using porcine clots. The cavitation bubble formation is the governing mechanism for photomechanical drug delivery.

The ablation process is profoundly affected by whether the optical fiber tip is inside a catheter or is in contact with the thrombus when the laser light is delivered through an optical fiber to the thrombus. The contact ablation efficiency of porcine clot was at least three times greater than the non-contact ablation efficiency. The mass ablated was correlated with the expansion pressure of the cavitation bubble. The fluorescent microspheres penetrated the mural clot the same distance for both ablation methods. The kinetic energy generation depended on the total delivered energy regardless of the light delivery methods.

[6] K. S. Kumar. Spectroscopy of indocyanine green photodegradation. Master's thesis, Oregon Graduate Institute of Science and Technology, 1996.

In laser tissue welding, indocyanine green (ICG) is topically applied at the weld site to enhance light absorption and to minimize collateral damage. The uptake of ICG by tissues is variable, and photobleaches when exposed to high radiant exposures. To understand these processes, the intimal surface of porcine aorta stained with ICG was exposed to multiple pulses from an 804 nm pulsed diode laser. ICG concentration was varied from 0.8–6.45 mM. Radiant exposures between 20–70 $\mathrm{mJ/mm^2}$ were used with a spot size of 36 $\mathrm{mm^2}$ and a 5 ms pulse duration. After each laser pulse diffusely reflected light from 450–850 nm was obtained from the irradiated spot with an optical fiber based spectrometer. Temperatures were measured during the laser pulse. ICG penetration depth in aorta and the depth of damage were measured. Despite uniform visual appearance, ICG uptake varies by a factor of three at different spots on the same aorta. ICG bleaching is manifested by the shift in absorption peak from 530 nm to 640 nm. The decrease in absorption with successive pulses is an additive effect and follows a power law. The rate of decrease varies linearly with incident energy and may be independent of the concentration of ICG. Temperatures were almost constant with successive pulses. ICG is absorbed into aorta to a depth of 25 μm but the 804 nm light penetrates to $\sim$15 μm. Strong fluorescence of irradiated samples suggest that some molecular reorganization of ICG occurs.

[7] U. S. Sathyam. *Laser Thrombolysis: Basic Ablation Studies.* PhD thesis, Oregon Graduate Institute of Science and Technology, 1996.

Laser thrombolysis is a procedure that is being developed to treat cardiovascular disease and stroke by removing clots occluding arteries of the heart and the brain. This thesis presents studies of pulsed ablation phenomena that take place during during laser thrombolysis. The main goals were to optimize laser parameters for efficient ablation, and to investigate the ablation mechanism. Most of the studies described here used a gel-based clot model, and selected results were verified using porcine clot.

A parametric study was performed to identify the optimal wavelength, spot size, pulse energies, and repetition rate for maximum material removal. The minimum radiant exposures to achieve ablation at any wavelength were measured. The results suggest that most visible wavelengths were equally efficient at removing material at radiant exposures above threshold. Larger catheters are likely to ablate more efficiently. Ablation was initiated at surface temperatures just above 100°C. A vapor bubble was formed during ablation. The vapor bubbles expanded and collapsed within 500 μs after the laser pulse. Less than 5% of the total pulse energy is coupled into the bubble energy. A large part of the delivered energy is unaccounted for and is likely released partly as acoustic transients from the vapor expansion and partly wasted as

heat. When the ablation process was studied within the cylindrical confines of a tube, dilation of the vessel due to bubble expansion was observed at clinically relevant energies.

The thesis concludes by summarizing the relevance of the gel results to the implementation of laser thrombolysis. It proposes optimal laser parameters for the design of a next generation laser system; a doubled Nd:YAG laser is suggested. It also suggests that the current laser and delivery systems may not be able to completely remove large clot burden that is sometimes encountered in heart attacks. However, laser thrombolysis may emerge as a favored treatment for strokes where the occlusion is generally smaller and rapid recanalization is of paramount importance. A final hypothesis is that laser thrombolysis should be done at radiant exposures close to threshold to minimize any damaging effects of the bubble dynamics on the vessel wall.

[8] S. D. Pearson. Mechanical strength studies of steady-state thermal and pulsed laser tissue welding. Master's thesis, Oregon Graduate Institute of Science and Technology, 1996.

Laser tissue welding is the process of binding two tissues together using laser irradiation with a mechanism that is still poorly understood. This study examined the mechanism of laser welding by determining the effects of heat and pulsed diode laser light on tissue. This includes yield strength tests, steady-state thermal contraction/expansion tests, and waterbath and laser welding experiments.

Yield strength measurements indicated that porcine aorta and intestine have great variations in yield due to structural and thickness variability. Waterbath heating experiments demonstrated that initial heating had little effect on average yield strength, while laser yield tests indicated a 20% decrease in average yield strength. Also, yield strength was inversely proportional to number of pulses: i.e., the more pulses fired, the lower the yield strength.

Porcine aorta, intestine and elastin biomaterial react differently to immersion in hot water. Porcine intestine contracted at an exponential rate of $0.6\pm0.1\,\mathrm{s}^{-1}$ above a threshold temperature of 77 ± 1°C. Aorta contracted at two different rates, the first at a rate of $0.07\pm0.03\,\mathrm{s}^{-1}$ above a threshold temperature of 65 ± 5°C and the second at a slightly increasing linear rate of 0.0005 ± 0.0001/s°C. The elastin biomaterial actually elongated with increasing temperature at a linear rate of 0.036 ± 0.006/s°C. Laser contraction was performed on porcine aorta and intestine stained with 6.5 mM ICG. Results show contraction occurred only after 10 pulses at irradiances above 75 mJ/mm^2, and maximized at 2–3 mm.

Waterbath welds were performed on all five combinations of intestine, aorta, and heterograft at temperatures from 50–80°C and times in the range of 3–15 minutes. All welds peaked at temperatures of 70–75°C, and all intestine type welds peaked at 10 minutes. The others have time peaks beyond the times used in these studies.

Laser welds were attempted on all waterbath weld types with success in all types except aorta-aorta welds. Laser weld strengths peaked at staining concentrations of 1.6 mM, irradiances of 42 mJ/cm^2, and high pulse numbers (above 10 pulses). Peak laser weld strengths were 30–100% of waterbath weld strengths.

Mechanical strength tests provided a basis for thermal effects on tissue strength. Thermal contraction/expansion studies produced different mechanisms for thermal changes in each tissue type. The waterbath and laser welding studies provided a basis for the strongest welds possible between each tissue type, as well as two viable methods to produce tissue welds. The welding

tests also lead to separate mechanisms for welding due to large differences in peak welding times and temperatures.

[9] S. D. Robinson. Measurement of 8-methoxypsoralen concentration using fluorescence. Master's thesis, Oregon Graduate Institute of Science and Technology, 1995.

A new method of measuring the level of 8-methoxypsoralen in blood serum was developed for the reasons of speed, accuracy, and cost. This new method uses laser induced fluorescence of the psoralen to determine the concentration in serum. The fluorescence is analyzed with an optical multichannel analyzer coupled to an intensified photodiode array detector. Research was first attempted on samples with ethanol as the solvent to confirm that the method would work. Sample concentrations of 8-methoxypsoralen in serum are determined by comparing the fluorescence signal obtained from previously known concentrations. Levels down to 200 ng per milliliter of serum can be measured with this technique.

[10] E. N. La Joie. Tissue welding: Studies of pulsed diode laser interaction with ICG stained porcine aorta and elastin-based biomaterial. Master's thesis, Oregon Graduate Institute of Science and Technology, 1995.

Laser tissue welding is a sutureless method of wound closure that has been used successfully in nerve, skin, and arterial anastomoses. After heating generated by laser exposure, a glue is formed between tissue edges that forms a weld upon cooling. The advantages of laser welding over traditional wound closure are no foreign body reaction and less scar formation. However, traditional methods of laser welding have a minimal surface area of tissue to weld, such as in anastomoses. Also, excess heating occurs with the use of traditional surgical CW lasers such as the Argon and CO_2. These studies used an artificial biomaterial made mostly of elastin and fibrin to weld to porcine aorta, which allowed greater surface area for welding and measurement of optical properties of the weld site. Also, a pulsed diode laser was used to maintain thermal confinement and therefore minimize excess heating.

Steady state thermal experiments indicated that the elastin-based biomaterial was thermally stable up to 100°C. Welds between biomaterial and aorta were successful between 65–80°C with pressures of $5\,\mathrm{N/cm^2}$ for immersions of 5 minutes.

Photosensitive dyes with high absorption at the laser wavelength are added to the weld site to increase heating and to minimize thermal damage to surrounding unstained tissue. The intimal surface of porcine aorta was stained with indocyanine green dye to efficiently absorb 808 nm diode laser light. A 5 mg/ml solution of indocyanine green dissolved in water penetrated $200\,\mu$m into the intimal side of porcine aorta.

Transmission measurements of stained aorta were made using radiant exposures of 6–129 $\mathrm{mJ/cm^2}$ and using pulse durations of 0.5–5 ms. Transmission increases and reaches a maximum of 80–85% with successive pulses for radiant exposures greater than $\sim$25 $\mathrm{mJ/cm^2}$, indicating that the absorption coefficient, and therefore heating, of stained tissue decreases with repetitive pulses.

Thermal measurements of the surface of stained aorta using a photothermal radiometer were made for radiant exposures of 38–120 $\mathrm{mJ/cm^2}$. Temperature rises of 10–100°C were measured after one pulse. Thermal measurements of samples from different aortas, each stained with new solutions of ICG, showed the wide variability in the heating of tissue, and therefore the variability in concentration of ICG for different samples.

Simultaneous transmission and thermal measurements were made of stained aorta to eliminate sample variability and to compare the absorption coefficients calculated from each measurement. As in previous transmission measurements, transmission increased over pulses, indicating a decrease in absorption. However, the surface temperature, and therefore the absorption coefficient remained constant over repetitive pulses. It was postulated that ICG was undergoing a photochemical change with repeated exposure to laser light. This change was thought to be a change in effective depth of the ICG since the penetration depth of ICG was the only hard to measure quantity in our calculations. The effective depth of stain is inversely proportional to the fourth root of the pulse number.

Laser welds of stained aorta to biomaterial were attempted by sandwiching the samples between glass slides and applying pressures ranging from 4–20 $\mathrm{N/cm^2}$ for 5 ms pulse durations and 86 $\mathrm{mJ/cm^2}$ radiant exposure. Welds were successful for pressures above 11 $\mathrm{N/cm^2}$.

[11] S. A. Prahl. *Light Transport in Tissue.* PhD thesis, University of Texas at Austin, 1988.

Two numerical solutions for radiative transport in tissue are presented: the Monte Carlo and the adding-doubling methods. Both methods are appropriate for tissues with internal reflection at boundaries and anisotropic scattering patterns. The adding-doubling method yields accurate solutions in one-dimension. The slower Monte Carlo method is the only exact solution available for finite beam irradiance of tissue. Convolution formulas for calculation of fluence rates for circularly symmetric flat and Gaussian irradiances using the Monte Carlo impulse response are presented.

Book Chapters

[1] S. A. Prahl. Pulsed photothermal radiometry of inhomogeneous tissue. In A. Mandelis and P. Hess, editors, *Progress in Photothermal and Photoacoustic Science and Technology Series: Life and Earth Sciences*, volume 3, pages 516–438. SPIE Optical Engineering Press, 1997.

This chapter describes a technique for extracting an internal thermal profile using measurements of the surface temperature. The method is applicable to materials and tissues with uniform thermal properties and non-uniform optical properties. The technique is based on singular value decomposition and works reasonably well down to depths of about 500 μm. The uncertainty in the location of the internal temperature layers grows linearly with the depth of the layer. The inversion algorithm is tested using computer simulations and experiments on colored glass. Analysis of *in vivo* data from a tanning experiment on human skin is presented to show the potential of the technique.

[2] S. A. Prahl. The adding-doubling method. In A. J. Welch and M. J. C. van Gemert, editors, *Optical-Thermal Response of Laser Irradiated Tissue*, chapter 5, pages 101–129. Plenum Press, 1995.

This chapter describes the adding-doubling method for solving the radiative transport equation. The advantages and disadvantages of the method are presented, followed by sections describing its theory and computer implementation. A detailed example is given with intermediate numerical results. Accurate tables with values of reflection and transmission for slabs of varying thicknesses with mismatched boundaries are given.

[3] S. A. Prahl. The diffusion approximation in three dimensions. In A. J. Welch and M. J. C. van Gemert, editors, *Optical-Thermal Response of Laser Irradiated Tissue*, chapter 7, pages 207–231. Plenum Press, 1995.

The diffusion approximation of the radiative transport equation is used extensively because closed-form analytical solutions can be obtained. The previous chapter gave closed-form solutions to the one-dimensional diffusion equation. In this chapter, the classic searchlight problem of a finite beam of light normally incident on a slab or semi-infinite medium will be solved in the time-independent diffusion approximation. The solution follows naturally once the Green's function for the problem is known, and so the Green's function subject to homogeneous Robin boundary conditions will be given for semi-infinite and slab geometries. The diffuse radiant fluence rates are then found for impulse, flat (constant), and Gaussian shaped finite beam irradiances.

How do Green's functions help solve the problem of a finite beam incident on a turbid medium? As unscattered light propagates through the medium, it is scattered and becomes diffuse. This initial scattering event acts as a source of diffuse light. The Green's function describes the distribution resulting from a point source of diffuse light. Since the unscattered light decays exponentially with increasing depth in the slab, the Green's function for an irradiation point on the surface may be obtained by convolving the Green's function with the proper exponential function. Again using superposition, the response for an arbitrary source distribution is obtained by adding the contributions of all point irradiances. This description is not quite complete because it neglects the contribution from boundary conditions, however the analytic derivation in this chapter is complete.

The solutions for the searchlight problem are expressed as definite integrals or infinite series. There are a number of possible ways of obtaining solutions to the diffusion equation. Green's functions for a slab geometry [Reynolds 1976] have been known for some time. Somewhat surprisingly, the Green's function for a semi-infinite medium is not readily available in the literature and is included for completeness. The solutions for the semi-infinite and slab geometries are extended to include exponentially attenuating line sources. Finally, we present equations for calculating the internal fluence rates for finite beam irradiances (flat top and Gaussian) on slab and semi-infinite media with inhomogeneous Robin boundary conditions.

To avoid the usually complicated expressions that arise in solutions for a semi-infinite geometry, some authors use monopole and dipole methods. Both techniques generate solutions that satisfy the diffusion equation at the expense of satisfying the boundary conditions. The solutions and compromises inherent in using the dipole and monopole techniques are briefly discussed.

[4] M. J. C. van Gemert, S. A. Prahl, and A. J. Welch. Lichtausbreitung und Streuung in trüben Medien. In G. Müller and H. P. Berlien, editors, *Angewandte Lasermedizin: Lehr- und Handbuch für Praxis und Klinik*, chapter II–3.1.2, pages 1–10. ecomed verlagsgesellshaft mbH, München, 1989.

Wäre Gewebe ein ausschließlich lichtabsorbierendes und nicht lichtstreuendes Medium, so könnte die räumliche Lichtverteilung bei einer Laserbestrahlung mit Hilfe einer einfachen exponentiellen Dämpfung beschrieben werden. In diesem Fall wäre Dosimetrie einfach. Wir wissen jedoch, daßGewebe ein trübes Medium ist und Licht streut. Vernachlässigt man die Streuung des Lichtes, so weicht die angenommene Lichtverteilung im Gewebe wesentlich von der wirklichen Lichtverteilung ab. Direkt unter der Oberfläche kann die auf das Gewebe fallende Lichtintensität infolge von Streuprozessen im Inneren erhöht werden, so daßmehr Licht für Absorption verfügbar ist. Besonders in einem Wellenlängenbereich, in dem das Material wenig absorbiert (bei vielen Geweben zwischen 600 nm und 1500 nm), kann infolge von Streuprozessen die auftreffende Lichtintensität um einen Faktor 2 bis 3 zunehmen. In Hohlraumorganen, wie z.B. der Harnblase, kann die auf das Gewebe fallende Lichtintensität noch weiter ansteigen (Faktor 4 bis 7). Streuung erhöht auch seitlich des einfallenden Lichtstrahls die verfügbare Lichtintensität. Wie wesentlich Streuprozesse bei der Lichtausbreitung (im Gewebe) sind, hängt ab von Streusowie Absorptionseigenschaften, dem Brechungsindex des Gewebes und dem Durchmesser des Laserstrahls. Der Sinn de Kapitels ist es, den Einflußder Streuung auf die Lichtverteilung im Gewebe zu demonstrieren. Die Diskussion soll sich im wesentlichen auf Abbildungen konzentrieren und weniger eine mathematische Beschreibung der Probleme darstellen; dennoch werden einige mathematische Definitionen angegeben.

Innerhalb des Wellenlängenbereichs der klinischen Lasermedizin (etwa 193 nm bis 10600 nm) kann der Absorptionskoeffizient des Gewebes stark variieren, wobei der Streukoeffizient monoton mit steigender Wellenlänge abnimmt. Das Verhältnis der Koeffizienten ändert sich ebenfalls wesentlich mit der Wellenlänge des Laserlichts. Abb. 1 zeigt ein Beispiel der Abhängigkeit der Absorption und Streuung von der Wellenlänge in vaskulärem Gewebe. Abb. 1c stellt die Albedo (das Verhältnis aus Streukoeffizienten zur Summe von Streu- und Absorptionskoffizient) von vaskulärem Gewebe über der Wellenlänge dar.

Conference Proceedings

[1] P. A. Patel, J. W. Valvano, S. A. Prahl, and C. R. Denham. A self-heated thermistor technique to measure blood flow from the tissue surface. In *ASME Winter Annual Meeting*, volume HTD 61, pages 11–16, Anaheim, CA, 1986.

A microcomputer based instrument to measure thermal conductivity, thermal diffusivity and perfusion at the surface of a tissue has been developed. Self-heated spherical thermistors, partially embedded in an insulator, are used to simultaneously deliver thermal energy to the biological tissue and to measure the resulting temperature rise. The temperature increase of the thermistor for a given applied power is a function of the combined thermal properties of the insulator, the thermistor and the tissue. Once the probe is calibrated, the instrument accurately measures the thermal properties of tissue. Conductivity measurements are accurate to better than 2% and diffusivity measurements are accurate to better than 4%. The surface thermistor probe is quite sensitive to perfusion.

[2] P. A. Patel, J. W. Valvano, and S. A. Prahl. Perfusion measurement by a surface thermal probe. In *IEEE/Ninth Annual Conference of the Engineering in Medicine and Biology Society*, pages 28–29, Boston, MA, 1987. IEEE.

The purpose of this paper is to demonstrate the sensitivity of a surface thermal probe for the measurement of tissue persfuion. Measurements using isolated and *in vivo* rat livers show that the surface thermal prove is sensitive to the perfusion. Thermographic images of the liver surface have been taken of both the isolated rat liver as well as the *in vivo* rat liver. The thermographic images can be used to evaluate the spatial distribution of perfusion at the tissue surface. Perfusion is found to be nonuniform in the isolated rat liver and uniform in the *in vivo* rat liver.

[3] J. W. Valvano, S. A. Prahl, J. C. Chan, and J. A. Pearce. Thermal camera imaging to measure tissue blood flow. In *Sixth Southern Biomedical Engineering Conference*, Dallas, TX, 1987 abstract only.

A thermal washout technique is capable of measuring perfusion from the tissue surface. A cold applicator is held on the tissue for 60 seconds. During this time the tissue surface is cooled. The applicator is removed, and a thermal camera is used to monitor the rewarming of the tissue surface. Since blood flow significantly affects local heat transfer, this technique is quite senstive. Tissue with a high perfusion can sink more heat, hence will have a smaller initial temperature change and a faster recovery back to baseline.

[4] J. C. Chan, J. W. Valvano, J. A. Pearce, L. J. Hayes, and S. A. Prahl. Thermal camera imaging to measure perfusion from the tissue surface. In J. W. Clark, P. I. Horner, A. R. Smith, and K. Strum, editors, *Phys. Med. Biol.*, volume 33, page 408, San Antonio, TX, 1988 abstract only.

A thermal washout technique is being developed which measures perfusion form the tissue surface. This perfusion measurement is similar to other indicator washout techniques. The basic approach is to apply a heat source to the surface of a tissue for exactly 60 seconds. The heat source is then removed and the temperature recovery is monitored with a calibrated thermal camera. Blood flow significantly affects local heat transfer making this technique quite sensitive. Highly perfused tissue will absorb more heat and, hence will have a smaller temperature increase and a faster recovery back to baseline.

The finite element numerical method is used to model the heat transfer problem with realistic geometries and boundary conditions. The relationship between the actual perfusion and the measured temperature response is determined using both analytical and numerical techniques. It is important that the boundary and initial conditions be carefully controlled and monitored during both the warming and cooling phases. *In vivo* experiments with alcohol fixed canine kidneys demonstrate the feasibility of the technique. The disturbing factors include: uncertainty of the temperature measurement, uncertainty of the time measurement, baseline temperature gradients, and perfusion gradients.

[5] G. L. LeCarpentier, S. Rastegar, A. J. Welch, S. A. Prahl, and H. Hussein. Comparative analysis of laser ablation of plaque using direct laser irradiation and a metal contact probe. In J. W. Clark, P. I. Horner, A. R. Smith, and K. Strum, editors, *Phys. Med. Biol.*, volume 33, page 17, San Antonio, TX, 1988 abstract only.

The purpose of this research was to establish the theoretical temperature distribution and ablation characteristics in atherosclerotic plaque resulting from both direct argon laser irradiation and the application of a metal contact probe. The plaque was assumed to be a single-layered homogeneous medium, and the laser light distribution within the tissue was calculated using a delta-Eddington approximation. One dimensional temperature distributions and ablation depths were calculated using an immobolized finite element method. Thermal and optical properties of the tissue were assumed to remain constant. Ablation front positions and temperature profiles at times prior to ablation, at the onset of ablation, and during the ablation process were calculated for both modalities. Additionally, ablation velocities were calculated as a function of both tissue water content and heat flux transmitted through the metal probe tip. For the typical operating conditions used, calculated values agreed qualitatively with experimental results. Temperature calculations after the onset of ablation indicated high sub-surface temperature rises beyond the surface threshold temperature for the direct irradiation case but monotonically decreasing profiles for the metal probe. However, deeper within the tissue, calculated temperatures appeared to be higher for the probe than for direct irradiation.

[6] S. A. Prahl, W. F. Cheong, G. Yoon, and A. J. Welch. Optical properties of human aorta during low power argon laser irradiation. In *SPIE Proceedings of Laser Interaction with Tissue*, volume 908, pages 29–33, 1988.

The optical properties of human aorta were measured during low power argon laser irradiation ($\sim$100 mW/mm^2). The delta-Eddington optical model was iterated to determine the optical properties. The results indicated that the transport albedo was nearly constant (0.96) until the onset of tissue charring, after which it decreased quickly. The optical depth gradually declined (after an abrupt initial increase) until tissue charring when it dropped sharply. The anisotropy dropped initially and increased linearly with time of exposure.

[7] S. A. Prahl, M. Keijzer, S. L. Jacques, and A. J. Welch. A Monte Carlo model of light propagation in tissue. In G. J. Müller and D. H. Sliney, editors, *SPIE Proceedings of Dosimetry of Laser Radiation in Medicine and Biology*, volume IS 5, pages 102–111, 1989.

The Monte Carlo method is rapidly becoming the model of choice for simulating light transport in tissue. This paper provides all the details necessary for implementation of a Monte Carlo program. Variance reduction schemes that improve the efficiency of the Monte Carlo method are discussed. Analytic expressions facilitating convolution calculations for finite flat and Gaussian beams are included. Useful validation benchmarks are presented.

[8] S. L. Jacques, L. Buckley, S. Prahl, and K. Gregory. Quantifying psoralen in tissues by fluorescence: Dosimetry for psoralen administration followed by ultraviolet A irradiation (Puva) to block restenosis. In G. S. Abela, editor, *SPIE Proceedings of Diagnostic and Therapeutic Cardiovascular Interventions IV*, volume 2130, pages 82–88, 1994.

PUVA therapy may prove effective in preventing restenosis of vessels following balloon angioplasty to open vessels narrowed by atherosclerosis. The technique relies on the ability of PUVA (psoralen administration followed by ultraviolet A irradiation) to cause crosslinks and monoadducts that prevent cellular proliferation without causing cell death. Such PUVA treatment has been successful in controlling cutaneous cell proliferation of psoriasis. The efficacy of PUVA treatment depends on the drug concentration and the light dose. The amount of light delivered is easily modified to adapt to variations in the drug concentration if the drug levels in the vessel wall are known. This paper demonstrates the feasibility of assaying psoralen levels in tissues and in serum samples using psoralen fluorescence as an indictor.

[9] E. N. La Joie, A. D. Barofsky, K. W. Gregory, and S. A. Prahl. Welding artificial biomaterial with a pulsed diode laser and indocyanine green. In R. R. Anderson, editor, *SPIE Proceedings of Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems V*, volume 2395, pages 508–516, 1995.

Laser tissue welding is a sutureless method of wound closure that has been used successfully in nerve, skin, and arterial anastomoses. We welded an elastin-based biomaterial that elicits minimal foreign body reaction to the intimal surface of porcine aorta. The aorta was stained with indocyanine green dye to efficiently absorb the 808 nm diode laser light. Laser welding with a pulsed diode laser thermally confines heating to stained portion of tissue, minimizing adjacent tissue damage. Laser welds of stained aorta to biomaterial were attempted by sandwiching the samples between glass slides and applying pressures ranging from 4–20 N/cm^2 for 5 ms pulse durations and 83 mJ/mm^2 radiant exposure. Welds were successful for pressure above 5 N/cm^2. Transmission measurements of stained aorta were made using radiant exposures of 6–129 mJ/mm^2 using pulse durations of 0.5–5 ms. Transmission increases and reaches a maximum of 80–85% with successive pulses for radiant exposure greater than 26 mJ/mm^2 for a spot size of 9 mm^2 and 13 mJ/mm^2 for a spot size of 36 mm^2.

[10] H. Shangguan, L. W. Casperson, A. Shearin, K. W. Gregory, and S. A. Prahl. Photoacoustic drug delivery: The effect of laser parameters on spatial distribution of delivered drug. In S. L. Jacques, editor, *SPIE Proceedings of Laser-Tissue Interaction VI*, volume 2391, pages 394–402, 1995.

Photoacoustic drug delivery is a technique for delivering drugs to localized areas by timing laser-induced pressure transients to coincide with a bolus of drug. This study explores the effects of target material, laser energy, absorption coefficient, fiber size, repetition rate, and number of pulses on the spatial distribution of delivered drug. A microsecond flash-lamp pumped dye laser delivered 30–100 mJ pulses through optical fibers with diameters of 300–1000 μm. Vapor bubbles were created 1–5 mm above clear gelatin targets submerged in mineral oil containing a hydrophobic dye (D&C Red #17). The absorption coefficient of the oil-dye solution was varied from 50–300 cm^{-1}. Spatially unconfined geometry was investigated. We have found that while the dye can be driven a few millimeters into the gels in both the axial and radial directions, the penetration was less than 500 μm when the gel surface remained macroscopically undamaged. Increasing the distance between the fiber tip and target, or decreasing the pulse energy reduced the extend of the delivery.

[11] U. S. Sathyam, A. Shearin, and S. A. Prahl. The effect of spotsize, pulse energy, and repetition rate on microsecond ablation of gelatin under water. In S. L. Jacques, editor, *SPIE Proceedings of Laser-Tissue Interaction VI*, volume 2391, pages 336–344, 1995.

The efficiency of laser ablation of thrombus depends on spot size, pulse energy and repetition rate. A 1 μs pulsed dye laser (504 nm) was used to ablate a gelatin-based thrombus model containing an absorbing dye under water. The gelatin was confined in 3 mm inner diameter tubes and pulse energies of 25–100 mJ were delivered via 300, 600, and 1000 μm core diameter fibers. The experiments were conducted at pulse repetition rates of 3 Hz and 10 Hz. The amount of gelatin removed was measured using a spectrophotometric method and ablation efficiency was defined as mass removed per pulse per unit energy. Flash photography was used to visualize the ablation process in 1 cm cuvettes. Results: More material was removed using bigger fibers in the 3 mm tubes at similar pulse energies. The amount of gelatin removed per pulse increased linearly with pulse energy. There was no significant change in the amount removed at pulse repetition rates of 3 Hz and 10 Hz. In the 1 cm cuvettes, the ablation mass was roughly the same with both the 300 μm and 1000 μm fibers. Flash photography of the ablation process in 1 cm cuvettes showed that less than 1% of the laser energy went into formation of a vapor bubble. The mass removed increased roughly linearly with bubble energy. Conclusions: Ablation mass increases linearly with pulse energy, but does not have a direct relationship with radiant exposure. It is independent of the repetition rate under 10 Hz.

[12] S. A. Prahl. Charts for rapid estimation of spatial and temporal distribution of temperature following laser irradiation. In S. L. Jacques, editor, *SPIE Proceedings of Laser-Tissue Interaction VI*, volume 2391, pages 499–511, 1995.

A recurring problem in laser applications is estimating the thermal response of target tissues to laser irradiation. This typically involves using an optical model to determine the distribution of absorbed laser energy and then using a thermal model to establish the temperature during and after laser irradiation. To avoid such modelling and yet allow one to obtain fast, accurate estimates of temperature, a series of charts for laser irradiation of semi-infinite homogeneous media with adiabatic boundaries is presented. These charts were created using analytic solutions of the temperature for absorbing-only media with simple pulsed source geometries. Through the use of non-dimensional parameters, these charts allow one to make rapid estimates of the spatial and temporal thermal distributions following laser irradiation for arbitrary pulse durations and absorption coefficients.

[13] H. Shangguan, L. W. Casperson, A. Shearin, and S. A. Prahl. Investigation of cavitation bubble dynamics using particle image velocimetry: Implications for photoacoustic drug delivery. In R. R. Anderson and A. Katzir, editors, *SPIE Proceedings of Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems VI*, volume 2671, pages 104–115, 1996.

Photoacoustic drug delivery is a technique for delivering drugs to localized areas in the body. In cardiovascular applications, it uses a laser pulse to generate a cavitation bubble in a blood vessel due to the absorption of laser energy by targets (e.g., blood clots) or surrounding liquids (e.g., blood or injected saline). The hydrodynamic pressure arising from the expansion and collapse of the cavitation bubble can force the drug into the clots and tissue wall tissue. Time-resolved particle image velocimetry was used to investigate the flow of liquids during the expansion and collapse of cavitation bubbles near a soft boundary. A gelatin-based thrombus model was used to simulate the blood clot present during laser thrombolysis. An argon laser chopped by an acousto-optic modulator was used for illumination and photography was achieved using a

CCD camera. The implications of this phenomenon on practical photoacoustic drug delivery implementation are discussed.

[14] U. S. Sathyam, A. Shearin, and S. A. Prahl. Visualization of microsecond laser ablation of porcine clot and gelatin under a clear liquid. In R. R. Anderson and A. Katzir, editors, *SPIE Proceedings of Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems VI*, volume 2671, pages 28–35, 1996.

Laser thrombolysis uses microsecond laser pulses to remove thrombus-blocked arteries in the heart and the brain. Rapidly expanding and collapsing vapor bubbles are formed upon absorption of the laser energy by the thrombus. The goal of this study was to visualize the process of ablation and assess the effects of pulse repetition rate. The differences between contact versus non-contact of the laser delivery device with the thrombus were also investigated. Initial experiments were conducted with a gel-based clot model confined in 3 mm inner diameter silicone tubes. Subsequent experiments used 24 hour old porcine blood clots. Laser pulses of 50 mJ pulse energy were delivered via a quartz fiber contained in a flushing catheter. Pulse repetition rates of 1 Hz, 3 Hz, and 6 Hz were used. Wavelengths of 506 nm and 577 nm were used to ablate clot. Bubble action was captured by flash photography using a CCD camera and recorded on video. The amount of material removed was measured using a spectrophotometric technique. Bubble action was similar on clot and the clot model. No significant differences in bubble action or mass removal were observed at the three pulse repetition rates and the two wavelengths. Contact between the catheter and the clot did not result in a pistoning effect of the catheter at the pulse energy used.

[15] E. J. Chapyak, R. P. Godwin, S. A. Prahl, and H. Shangguan. Comparison of numerical simulations and laboratory studies of laser thrombolysis. In R. R. Anderson, K. E. Bartels, L. S. Bass, K. W. Gregory, D. M. Harris, H. Lui, R. S. Malek, G. J. Mueller, M. M. Pankratov, A. P. Perlmutter, H. Reidenbach, L. P. Tate, and G. M. Watson, editors, *SPIE Proceedings of Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems VII*, volume 2970, pages 28–34, 1997.

We compare Los Alamos numerical simulations with Oregon Medical Laser Center laser deposition experiments conducted with gelatin thrombus surrogates specifically chosen for relevance to clinical laser thrombolysis. Initial idealized calculations suggest that a surprisingly large fraction of the absorbed laser energy appears as acoustic radiation. We build on these results here by investigating geometrical affects, material property variations, and sources of dissipation including viscosity and plastic flow, as well as acoustic radiation, in an effort to explain flow effects observed in the experiments. In particular, strong jetting is observed in the simulations when the gelatin is given a kinematic viscosity in excess of approximately $1.0\,\mathrm{cm}^2/\mathrm{s}$. Jetting is clearly evident in the experiments.

[16] H. Shangguan, L. W. Casperson, A. Shearin, D. L. Paisley, and S. A. Prahl. Effects of material properties on laser-induced bubble formation in absorbing liquids and on submerged targets. In D. L. Paisley and A. M. Frank, editors, *Proceedings of the 22nd International Congress on High-Speed Photography and Photonics*, volume 2869, pages 783–791, 1997.

Pulsed laser ablation of blood clots in a fluid-filled blood vessel is accomplished by an explosive evaporation process. The resulting vapor bubble rapidly expands and collapses to disrupt the thrombus (blood clot). The hydrodynamic pressures following the bubble expansion and collapse can also be used as a driving force to deliver clot-dissolving agents into thrombus for enhancement of laser thrombolysis. Thus, the laser-induced bubble formation plays an important role in the thrombus removal process. In this study the effects of material properties on laser-induced cavitation bubbles formed in liquids and on submerged targets have been visualized with a microsecond strobe or high speed framing camera.

[17] B. S. Amurthur, J. A. Viator, and S. A. Prahl. Acoustic cavitation events during microsecond irradiation of aqueous solutions. In R. R. Anderson et al., editors, *SPIE Proceedings of Diagnostic and Therapeutic Cardiovascular Interventions VII*, volume 2970, pages 4–9, 1997.

Previous experimental studies have investigated photospallation in tissue ablation during laser irradiation with nanosecond laser pulses. However, sub-threshold cavitation effects during laser ablation with microsecond pulses have not been reported. The primary focus of our study is to analyze laser induced acoustic transient generation during microsecond ablation of aqueous solutions at temperatures much below 100 degrees centigrade. Simultaneous imaging using laser flash photography confirmed formation of bubbles at temperature rise of 11 degrees centigrade. We used a simple model to analyze the effect of stress confinement in the given operating conditions. The implications of this study in the context of tissue ablation has been discussed.

[18] H. Shangguan, L. W. Casperson, K. W. Gregory, and S. A. Prahl. Penetration of fluorescent particles in gelatin during laser thrombolysis. In R. R. Anderson, K. E. Bartels, L. S. Bass, K. W. Gregory, D. M. Harris, H. Lui, R. S. Malek, G. J. Mueller, M. M. Pankratov, A. P. Perlmutter, H. Reidenbach, L. P. Tate, and G. M. Watson, editors, *SPIE Proceedings of Diagnostic and Therapeutic Cardiovascular Interventions VII*, volume 2970, pages 10–18, 1997.

The use of pulsed laser energy to clear arteries obstructed by thrombus (blood clot) and plaque has emerged as a promising method for the treatment of cardiovascular diseases such as myocardial infarction and stroke. Current techniques for laser thrombolysis are limited because they cannot completely clear the clot in arteries, especially where a large volume clot is presented. Mural clot is a potent stimulus for reocclusion. We suggest that the combination of laser thrombolysis and localized intramural delivery of clot-dissolving drugs during the procedure may be a solution to this limitation. Ninety pulses of 30–70 mJ were delivered onto gelatin-based thrombus model with a flushing catheter. A solution of 1 μm fluorescent particles as a drug model was injected at a rate of 4 mL/min in coincidence with the laser delivery. The controls were performed by injecting drug after laser thrombolysis. We measured the penetration of the particles in gelatin and the sizes of the lumen and stained areas. The results of this study demonstrated the possibility of enhancing laser thrombolysis by delivering drugs into thrombus. It was found that the particles could be driven several hundred micron in gelatin, and the lumen areas would be increased up to 25% if the areas were dissolved by the drugs.

[19] S. A. Prahl and S. D. Pearson. Rate process models for thermal laser welding. In S. L. Jacques, editor, *SPIE Proceedings of Laser-Tissue Interaction VIII*, volume 2975, pages 245–252, 1997.

Laser tissue welding is a thermal process for binding two tissues together. Optical and thermal models exist that allow the temperatures of laser irradiated tissues to be calculated. However, a rate process model is required to relate the estimated time-temperature histories to weld strengths. This paper proposes a rate process model based on a broad range of parametric welding experiments. Aorta, intestine, and digested carotid arteries were patch welded at constant pressure using either constant temperature (3–15 min at 60–80°C) or pulsed laser heating (5 ms, 3 Hz, 5–30 pulses).

[20] U. S. Sathyam, A. Shearin, and S. A. Prahl. Basic ablation phenomena during laser thrombolysis. In R. R. Anderson et al., editors, *SPIE Proceedings of Diagnostic and Therapeutic*

Cardiovascular Interventions VII, volume 2970, pages 19–27, 1997.

This paper presents studies of pulsed ablation phenomena that take place during laser thrombolysis. The main goals were to optimize laser parameters for efficient ablation, and to investigate the ablation mechanism. Most of the studies described here used a gel-based clot model, and selected results were verified using porcine clot.

[21] U. S. Sathyam and S. A. Prahl. Limitations in measurement of subsurface temperatures using pulsed photothermal radiometry. *J. Biomed. Opt.*, 2:251–261, 1997.

A pulsed photothermal technique to calculate internal temperatures from non-contact surface temperature measurements is presented. The inversion process is based on approximating the integral equation describing the thermal interaction with a matrix equation. The matrix equation is then solved using singular value decomposition. The method was evaluated using computer simulations and experiments with tissue phantoms and skin. The algorithm predicted internal temperatures within 10% for homogeneous samples down to a depth of about 500 μm. It did not predict internal temperatures accurately for inhomogeneous samples, but yielded fairly accurate estimates of the depths of subsurface absorbers and conserved energy. The uncertainty in the calculated depth of the absorber increased with depth. Currently this technique can probe depths to 500 μm.

[22] Steven L. Jacques, Andrew D. Barofsky, HanQun Shangguan, Scott A. Prahl, and Kenton W. Gregory. Laser welding of biomaterials stained with indocyanine green to tissues. In Steven L. Jacques, editor, *SPIE Proceedings of Laser-Tissue Interaction VIII*, volume 2975, pages 54–61, 1997.

This paper considers some issues pertinent to laser welding of elastin-based biomaterials to tissues using a pulsed diode laser (10 ms pulse) and indocyanine green (ICG) as an absorbing chromophore to localize laser heating to the "weld surface," the elastin/tissue interface where welding occurs. Experiments involved laser welding of elastin heterografts to the intimal surface of the carotid artery (in vitro, porcine) as a $\sim 4 \times 5\,\mathrm{mm}^2$ spot weld, then determining the breaking strength when the two tissues were pulled in a direction parallel to the plane of the spot weld while submerged in water. The questions answered are:

What is the peak temperature required for welding elastin heterograft to the intimal surface of carotid artery? ANSWER: ∼300°C threshold, ∼600° C for maximum strength. This estimate is based on optical measurements of dye accumulation in stain layer and measurements of thickness of stain layer via fluorescence microscope examination.

What is the dependence of weld strength on the laser exposure? ANSWER: Breaking force $g = \mathrm{Max}(1 - \exp(-(E_p - E_{th})/U_{67})$, where Max is the maximum strength achievable by laser welding, expressed as the breaking force in g when elastin heterograft and tissue are pulled. E_p is the laser pulse energy. E_{th} is the apparent threshold laser pulse energy that will break the weld. U_{67} is the laser energy above threshold which achieves 67% of Max. Max was about 15 g for the $\sim$20 mm^2 weld area of our experiments. E_{th} was 0.8 J, U_{67} was 1.44 J.

Does weld strength depend on hydration conditions? ANSWER: Not on the amount of excess unbound water. There was no significant difference in weld strength between welding dripping wet tissues vs well blotted tissues.

What difference is there between irradiating the weld surface through the biomaterial vs through the tissue, when the biomaterial is partially stained with ICG? ANSWER: There is a difference if the stain layer is heavily stained. Irradiation through the tissue allows direct irradiation on the weld surface which achieves the highest peak temperatures for the least laser pulse energy. Irradiation through the elastin heterograft causes direct irradiation of the rear surface of the stain layer, within the biomaterial and away from the weld surface, and thermal diffusion must bring the heat to the weld surface. This difference occurs only when the absorption by the stain layer is sufficiently high that little laser energy directly reaches the weld surface.

[23] M.-A. Descalle, S. L. Jacques, S. A. Prahl, T. L. Laing, and W. R. Martin. Measurements of ligament and cartilage optical properties at 351 nm, 365 nm, and in the visible range(440 to 800 nm). In Guy P. Delacretaz, Lars O. Svaasand, Rudolf W. Steiner, Roberto Pini, and Guilhem Godlewski, editors, *SPIE Proceedings of Laser-Tissue Interaction, Tissue Optics, and Laser Welding III*, volume 3195, pages 280–286, 1998.

To further evaluate the potential for intra-articular phototherapy, the optical properties of normal porcine ligament and cartilage were determined *in vitro*. The diffuser reflectance, R_d, was measured with an integrating sphere at 351, 365 nm and in the range 440–800 nm. The lateral spread of light introduced by a 400 mm optical fiber was measured and analyzed to yield the optical penetration depth δ. The two measurements, R_d and δ yielded the absorption coefficient μ_a and the reduced scattering $\mu_s' = \mu_s(1-g)$ at 351, 365 nm and in the range 440–800 nm.

[24] R. P. Godwin, E. J. Chapyak, S. A. Prahl, and H. Shangguan. Laser mass-ablation efficiency measurements indicate bubble-driven dynamics dominate laser thrombolysis. In R. R. Anderson, K. E. Bartels, L. S. Bass, C. G. Garrett, K. W. Gregory, H. Lui, R. S. Malek, A. P. Perlmutter, L. Reinisch, P. J. Smalley, L. P. Tate, S. L. Thomsen, and G. M. Watson, editors, *SPIE Proceedings of Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems VIII*, volume 3245, pages 4–11, 1998.

Mass removal experiments have been performed at the Oregon Medical Laser Center with 10 to 100 mJ one microsecond laser pulses at optical wavelengths. Above the energy threshold for bubble formation, the laser mass ablation efficiency (μg/mJ) for removal of gel surrogate thrombus is nearly constant for a given experimental geometry and gel absorption coefficient. The efficiency in 'contact' experiments, in which the optical fiber delivering the energy is in close proximity to the absorbing gel, is approximately three times that of 'non-contact' experiments, in which the optical fiber is approximately 1 mm from the gel. Mass removal occurs hundreds of microseconds after the laser deposition. Experimental data and numerical simulations are consistent with the hypothesis that jet formation during bubble collapse plays a dominant role in mass removal. This hypothesis suggests a model in which the mass removed scales linearly with the maximum bubble volume and explains the distinctive features, including the magnitude, of the mass removal.

[25] S. A. Prahl and S. L. Jacques. Sized-fiber array spectroscopy. In S. L. Jacques, editor, *SPIE Proceedings of Laser-Tissue Interaction IX*, volume 3254, pages 348–352, 1998.

Sized-fiber array spectroscopy describes a device and method for measuring absorption and reduced scattering properties of tissue. The device consists of two or more optical fibers with different diameters (comparable to the optical path length in the tissue) that are used to measure the amount of light backscattered into each fiber. Each fiber is used for both irradiation and detection. Only one fiber emits and collects light at a given time. This paper presents Monte Carlo simulations of the sized-fiber device to indicate the behavior of a device with 50 and 1000 μm fiber sizes. Experimental results are presented for a device constructed with 400 and a 600 μm fibers that demonstrate the accuracy of the device in measuring the scattering coefficient of 10%-Intralipid samples over a reduced scattering coefficient range of 1–50 cm^{-1}.

[26] H. Shangguan, S. A. Prahl, S. L. Jacques, L. W. Casperson, and K. W. Gregory. Pressure effects on soft tissues monitored by changes in tissue optical properties. In S. L. Jacques, editor, *SPIE Proceedings of Laser-Tissue Interaction IX*, volume 3254, pages 366–371, 1998.

For pulsed laser tissue welding, an appropriate pressure needs to be applied to the tissues to achieve successful welds. In this study, we investigated the influences of pressure on in vitro optical properties of elastin biomaterial. The optical properties were measured as a function of pressure with a double integrating-sphere system. A He-Ne laser (633 nm) was used for all measurements. Each sample was sandwiched between microscope slides and then compressed with a spring-loaded apparatus. Transmittance and diffuse reflectance of each sample were measured under a pressure (0–1.5 $\mathrm{kg/cm}^2$ and then released to 0). Absorption and reduced scattering coefficients were calculated using the inverse doubling method from the measured transmittance and reflectance values. Results from this study demonstrated: (1) The overall transmittance increased while the reflectance decreased as the tissue thicknesses were reduced up to 72% and the tissue weights were decreased about 40%, (2) The absorption and scattering coefficients increased with increasing the pressure, and (3) The pressure effects on the tissue optical properties were irreversible. Possible mechanisms responsible for the changes in the tissue optical properties were also investigated by changing tissue thicknesses or weights (through dehydration). This study implies that changes in tissue thickness and water content are important factors that affect tissue optical properties in different ways.

[27] H. Shangguan, L. W. Casperson, D. L. Paisley, and S. A. Prahl. Photographic studies of laser-induced bubble formation in absorbing liquids and on submerged targets: Implications for drug delivery with microsecond laser pulses. *Optical Engineering*, 37:2217–2226, 1998.

Pulsed laser ablation of blood clots in a fluid-filled blood vessel is accompanied by an explosive evaporation process. The resulting vapor bubble rapidly expands and collapses to disrupt the thrombus (blood clot). The hydrodynamic pressures following the bubble expansion and collapse can also be used as a driving force to deliver clot-dissolving agents into thrombus for enhancement of laser thrombolysis. Thus, the laser-induced bubble formation plays an important role in the thrombus removal process. We investigate the effects of boundary configurations and materials on bubble formation with time-resolved flash photography and high-speed photography. Potential applications in drug delivery using microsecond laser pulses are then discussed.

[28] J. A. Viator, S. L. Jacques, and S. A. Prahl. Generating subsurface acoustic waves in indocyanine green stained elastin biomaterial using a Q-switched laser. In S. L. Jacques, editor, *SPIE Proceedings of Laser-Tissue Interaction IX*, volume 3254, pages 104–111, 1998.

A Q-switched frequency-doubled Nd-YAG laser coupled to an optical parametric oscillator generated 4.75 ns 800 nm laser pulses to create a subsurface acoustic wave in planar indocyanine green gel samples and flat segments of elastin biomaterial stained with indocyanine green. The acoustic waves traveled through the target and were detected by a piezoelectric transducer. The waveforms were converted to measurements of pressure (and temperature) as a function of depth in the material. An algorithm was developed and applied to the acoustic signals to extract information about the absorption coefficient as a function of depth in the samples.

[29] J. A. Viator and S. A. Prahl. Laser thrombolysis using a millisecond frequency-doubled Nd:YAG laser. In S. L. Jacques, editor, *SPIE Proceedings of Laser-Tissue Interaction IX*,

volume 3254, pages 287–291, 1998.

A frequency-doubled Nd:YAG laser at 532 nm with pulse durations of 2, 5, and 10 ms was used to ablate blood clot phantoms. The clot phantoms were prepared with 3.5% (175 Bloom) gel and Direct Red 81 dye to have an absorption coefficient of $150\,\text{cm}^{-1}$. Ablation thresholds were determined by a fluorescent technique using flash photography to detect the gel surface. The threshold was $15\pm2\,\text{mJ/mm}^2$ and corresponded to calculated temperatures of 80 ± 10°C. Ablation efficiency experiments were conducted at 20 mJ. Ablation efficiencies were approximately $1.7\pm0.1\,\mu$g/mJ for the millisecond pulses and were comparable to previously published efficiencies for ablation of clot with a 1 microsecond pulsed dye laser.

[30] J. A. Viator and S. A. Prahl. Photoacoustic imaging of gelatin phantoms using matched field processing. In S. L. Jacques, G. J. Müller, A. Roggan, and D. H. Sliney, editors, *SPIE Proceedings of Laser-Tissue Interaction X*, volume 3601, pages 276–283, 1999.

Matched Field Processing (MFP) has been used in the ocean acoustics community to localize acoustic sources by correlating experimental data with a modelled field based on a solution to the acoustic wave equation. Here we attempt to adapt the method of MFP to localize an acoustic source in a tissue phantom made from an acrylamide gel. An acrylamide gel in a cylindrical geometry was formed with a small optically absorbing sphere embedded within it. A Q-switched, frequency- doubled Nd:YAG laser operating at 532 nm coupled to an optical parametric oscillator (OPO) tuned to 726 nm was used to irradiate the absorbing sphere. The pulse duration was 4.75 ns and the absorption coefficient of the absorbing sphere was $15\,\text{cm}^{-1}$. The stress confined laser energy resulted in an acoustic pulse radiating from the absorbing sphere. A piezoelectric transducer was used to detect the pulses at various locations on the gel. By vertically translating the transducer a virtual hydrophone array was constructed. The acoustic field was modeled using normal mode methods. A simulation was performed using the normal mode model as virtual data which was then correlated with the normal mode model itself. Finally, the experimental acoustic array data was correlated to the normal mode model.

[31] H. Xie, B. S. Schafer, S. A. Prahl, and K. W. Gregory. Sutureless end-to-end ureteral anastomosis using a new albumin stent and diode laser. In Q. Luo, B. Chance, L. V. Wang, and S. L. Jacques, editors, *1999 International Conference on Biomedical Optics*, volume 3683, pages 398–406, 1999.

Sutureless end to end ureteral anastomoses was successfully constructed in acute and chronic experiments. A photothermal sensitive hydrolyzable (PSH) albumin stent played roles as solder and intraluminal supporter to adhesion and position the anastomosed ureter by end to end fashion. The anastomosis seam was lased with 810 nm diode laser energy supplied through hand-held 600 micron noncontact optical fiber. A continuous 1 watt wave of power was applied for laser anastomosis. Integrity, welding strength, bursting pressures of anastomosis and histological reaction, and radiological phenomena were compared to those of anastomoses constructed using a liquidity soldering technique. The acute results of two methods were equivalent at welding strengths, but the liquid soldering showed more energy consumption. At chronic study, the radiological and histological studies were performed to evaluate the complications of the anastomosis. Excellent heating and varied degrees of complications were observed. We conclude that PSH stent showed great promise for ureteral anastomosis using laser welding.

[32] T. P. Moffitt and S. A. Prahl. In-vivo sized-fiber spectroscopy. In R. R. Alfano, editor, *SPIE Proceedings on Optical Biopsy III*, volume 3917, pages 225–231, 2000.

Sized-fiber array spectroscopy describes a device for measuring the absorption and reduced scattering properties of tissue. The device consists of two fibers with different diameters that measure the amount of light back-scattered into each fiber. Only one fiber emits and collects light at a time. Recent innovations allow for spatially limited measurement diffuse reflectance over a wavelength range of 500–800 nm. Reflection spectra of in vitro an din vivo porcine tissue are presented for a device with 200 and 600 micrometers fibers to demonstrate its performance.

[33] J. A. Viator, G. Paltauf, S. L. Jacques, and S. A. Prahl. Localization of spherical photoacoustic sources in acrylamide gels using time domain measurements. In A. A. Oraevsky, editor, *SPIE Proceedings of Biomedical Optoacoustics*, volume 3916, pages 89–99, 2000.

Photoacoustic imaging may be used to detect tumor masses in biological tissue. In particular, time of flight measurements of the photoacoustic waves may indicate tumor location. Here we use time of flight information to localize spherical photoacoustic sources in tissue phantoms. A Q- switched, frequency-doubled Nd:YAG laser operating at 532nm with a pulse duration of 5 ns irradiated absorbing spheres 2 mm in diameter. The spheres were in mineral oil or turbid acrylamide blocks. A PVDF acoustic transducer was built and used to detect the acoustic waves. The position of the detector was translated so that the time of flight information from two acoustic waveforms from the source could be correlated by a convolution algorithm. This convolution result in a 2D map indicating the position of the source. Source location was indicated to within 5 percent of the true location for acoustic propagation distances of 20 mm. An image source is also indicated when the true source was in proximity to a reflecting boundary.

[34] Y. Wadia, H. Xie, M. Kajitani, and S. A. Prahl. Liver repair and hemorrhage control using laser soldering of liquid albumin in a porcine model. In R. Rox Anderson et al., editors, *SPIE Proceedings of Lasers in Surgery*, volume 3907, pages 74–81, 2000.

The purpose of this study was to evaluate laser soldering using liquid albumin for welding liver lacerations and sealing raw surfaces created by segmental resection of a lobe. Major liver trauma has a high mortality due to immediate exsanguination and a delayed morbidity and mortality from septicemia, peritonitis, biliary fistulae and delayed secondary hemorrhage. Eight laceration injuries (6×2 cm deep) and eight non-anatomical resection injuries (raw surface 6×2 cm) were repaired. An 805 nm laser was used to weld 53% liquid albumin-ICG solder to the liver surface, reinforcing it with a free autologous omental scaffold. The animals were heparinized to simulate coagulation failure and hepatic inflow occlusion was used for vascular control. For both laceration and resection injuries, eight soldering repairs each were evaluated at three hours. A single suture repair of each type was evaluated at three hours. All 16 laser mediated liver repairs were accompanied by minimal blood loss as compared to the suture controls. No dehiscence, hemorrhage or bile leakage was seen in any of the laser repairs after three hours. In conclusion laser fusion repair of the liver is a quick and reliable technique to gain hemostasis on the cut surface as well as weld lacerations.

[35] H. Xie, B. S. Schafer, S. A. Prahl, and K. W. Gregory. Laser welding with an albumin stent: Experimental ureteral end-to-end anastomosis. In R. Rox Anderson et al., editors, *SPIE Proceedings of Lasers in Surgery*, volume 3907, pages 215–220, 2000.

Porcine ureters were anastomosed using an albumin stent and diode laser in vitro. The albumin stent provided precise apposition for an end to end anastomosis and enhanced welding strength. The anastomosis seam was lasered with an 810 nm diode laser using continuous wave and pulse light through a hand-held 600 micrometer noncontact optical fiber. Tensile strength, burst pressures, operative times, total energy and thermal damaged were measured in this study. The results demonstrated that using an albumin stent to laser weld ureteral anastomoses produces strong weld strengths. The liquid albumin solder also provided satisfactory welding strength. There were no significant differences of tissue thermal damage between the albumin stent alone, liquid solder alone and both combination groups. Thermal damage to tissue depended on laser setting and energy. This study determined the appropriate laser setting parameters to perform in vivo ureteral end to end anastomosis.

[36] G. Paltauf, J. A. Viator, S. A. Prahl, and S. L. Jacques. Iterative reconstruction method for three-dimensional optoacoustic imaging. In Alexander A. Oraevsky, editor, *SPIE Proceedings of Biomedical Optoacoustics*, volume 4256, pages 138–146, 2001.

Three-dimensional optoacoustic imaging uses detection of laser-generated thermoelastic waves with an ultrasound sensor array. Integrated acoustic signals (velocity potentials) are back projected into the source volume to give a map of absorbed laser energy. Since the number of array elements and the receiving solid angle are limited, radial back projection produces artifacts such as back projection arcs. To solve this problem, we developed in this study an iterative method for image reconstruction. A first image estimate was generated by simple radial back projection. A model for signal generation from a volume containing arbitrary optoacoustic sources was then used to calculate acoustic wave propagation from this estimate. Calculated signals at the array elements were compared with the measured signals and the difference was used to improve the image. In simulations and experiments we used the algorithm to obtain three-dimensional images of multiple optoacoustic sources. With signals from an array of 3 x 3 detector elements a significant improvement was observed after about 10 iterations compared to the simple radial back projection. Although computationally more intensive, iterative reconstruction can minimize the time and instrumentation for signal acquisition because a small number of array elements already gives a good quality optoacoustic image.

[37] S. A. Prahl, T. Denison, and E. N. La Joie. Laser repair of liver. In R. R. Anderson et al., editors, *SPIE Proceedings of Lasers in Surgery: Advanced Characterization, Therapeutics and Systems XI*, volume 4244, pages 215–219, 2001.

Laser repair of liver using albumin is a promising method for treating liver trauma. Concentrated human serum albumin is applied to a liver laceration and then denatured using a laser. These repairs were pulled with a material tester to measure the ultimate strength of the laser repair. We show that the ultimate strength of the liver repairs tends to increase with delivered laser energy, that the mode of delivery (pulsed versus continuous) does not matter, that the repair strength correlates with the area of denatured albumin, and that strong welds cause about 1.5 mm of thermal damage.

[38] J. A. Viator, G. Paltauf, S. L. Jacques, and S. A. Prahl. Design and testing of an endoscopic photoacoustic probe for determining treatment depth after photodynamic therapy of esophageal cancer. In A. A. Oraevsky, editor, *SPIE Proceedings of Biomedical Optoacoustics II*, volume 4256, pages 16–27, 2001.

An endoscopic photoacoustic probe is designed and tested for use in PDT treatment of esophageal cancer. The probe, measuring less than 2.5 mm in diameter, was designed to fit within the lumen of an endoscope that will be inserted into an esophagus after PDT. PDT treatment results in a blanched, necrotic layer of cancerous tissue over a healthy, deeper layer of perfused tissue. The photoacoustic probe was designed to use acoustic propagation time to determine the thickness of the blanched surface of the esophagus, which corresponds to treatment depth. A side-firing 600 micrometers fiber delivered 532 nm laser light to induce acoustic waves in the perfused layer of the esophagus beneath the blanched (treated) layer. A PVDF transducer detected the induced acoustic waves and transmitted the signal to an oscilloscope. The probe was tested on clear and turbid tissue phantom layers over an optically absorbing dye solution.

[39] H. Xie, L. A. Buckley, S. A. Prahl, B. S. Schafer, and K. W. Gregory. Thermal damage control of dye-assisted laser tissue welding: Effect of dye concentration. In R. R. Anderson et al., editors, *SPIE Proceedings of Lasers in Surgery: Advanced Characterization, Therapeutics and Systems XI*, volume 4244, pages 189–192, 2001.

Successful laser-assisted tissue welding was implemented to provide proper weld strength with minimized tissue thermal injury. We investigated and compared the weld strengths and morphologic changes in porcine small intestinal submucose (SIS) and porcine ureteral tissues with various concentration of indocyanine green (ICG) and with a solid albumin sheet. The study showed that the tissues were welded at lower ICG concentration (0.05 mM) with minimized tissue thermal damage using an 800 nm wavelength diode laser.

[40] P. R. Bargo, S. A. Prahl, and S. L. Jacques. Collection efficiency of a single optical fiber in turbid media for reflectance spectroscopy. In *OSA Biomedical Topical Meetings*, pages 604–606, Washington, D.C., 2002. Optical Society of America.

The effect of optical properties on the optical fiber collection efficiency in turbid media was studied experimentally and modelled by Monte Carlo simulations. An anaytic expression was obtained to estimate the collection efficiency.

[41] Jennifer J. Brazier, Mingdi Yan, S. A. Prahl, and Yin-Chu Chen. Molecularly imprinted polymers used as optical waveguides for the detection of fluorescent analytes. In K. J. Shea, M. J. Roberts, and M. Yan, editors, *Materials Research Society Proceedings of Molecularly Imprinted Materials-Sensor and Other Devices*, volume 723, pages 115–120, 2002.

This article demonstrates the novel approach of fabricating molecularly imprinted polymers (MIPs) as fiber optic waveguides for the detection of fluorescent analytes. Combining a polyurethane system and the soft lithography technique of micromolding in capillaries (MIMIC), polymer waveguiedes of 50 μm and 100 μm dimensions were patterned onto a silicon substrate. Laser coupling into small waveguide segments has been verified visually. Binding experiments using the waveguides are currently being explored. Some preliminary binding studies have been performed, however, for smaller freestanding filaments of sizes consistent with conventionally prepared MIP particles. Using fluorimetry measurements, templated fibers of 20 μm dimension preferentially bound the analyte molecules by a factor of 1.5 compared to control polymers.

[42] A. D. Janis, K. W. Gregory, S. J. Kirkpatrick, and S. A. Prahl. Effects of in vitro target compression modulus on laser thrombolytic ablation rate. In *SPIE Proceedings on Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems XII*, volume 4609, pages 419–429, 2002.

Laser thrombolysis (LT) is under investigation as a safe and rapid therapy for arterial recanalization in acute embolic stroke. Clot formation is a complex process affected by many factors that lead to differences in strength and hemoglobin concentration in samples formed from whole blood. The strength of thrombus formed in vivo also varies with age. Laser thrombolysis experiments were performed using a 577 nm 1μsec pulsed dye laser at an energy of approximately 25 mJ and a repetition rate of 4 Hz. Laser ablation and confined compression

modulus were measured with three in vitro clot models: gelatin, static clot, and reconstituted clot. Laser ablation studies demonstrate that LT ablation efficiency (in μg/mJ/pulse) is not significantly affected by differences in the confined compression modulus of clot. This agrees with previous studies using dye and gelatin. These results provide support for the effective use of this laser thrombolysis system for the removal of clots of varied age and strength.

[43] T. P. Moffitt and S. A. Prahl. Determining the reduced scattering of skin in vivo using sized-fiber reflectometry. In *SPIE Proceedings on Optical Biopsy IV*, volume 4613, pages 254–263, 2002.

Sized-fiber reflectometry describes a device and method for measuring absorption and reduced scattering of tissue using optical fibers with different diameters. The device used in this paper consists of two fibers with diameters of 200 and 600 micron. Each fiber emits and collects its own backscattered light. Monte Carlo simulations tabulating the diffuse reflectance collected by 200 and 600 micron fibers in a semi-infinite homogenous media are presented for an absorption, μ_a range of 0.2–30 cm^{-1} and a reduced scattering, μ_s' range of 10–200 cm^{-1}. The diffuse reflectance collected by a 600 micron fiber may be approximated by a linear relation to the 200 micron fiber. An empirical relation is derived relating the reduced scattering coefficient to the diffuse reflectance collected with 200 and 600 micron fibers. The sensitivity of the relation is determined for changes in each fiber measurement. Finally, *in vivo* diffuse reflection measurements and reduced scattering coefficient of skin are presented using the aforementioned fiber sizes with a wavelength range of 400–800 nm.

[44] T. P. Moffitt, D. A. Baker, S. J. Kirkpatrick, and S. A. Prahl. Mechanical properties of repaired liver using an argon beam coagulator with albumin. In *SPIE Proceedings on Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems XII*, volume 4609, pages 178–185, 2002.

A new method for tissue soldering using an argon ion beam coagulator (ABC) and human serum albumin is presented. The ABC is widely used in surgery and provides a fast and precise means of achieving hemostasis. In this paper, the mechanical properties of liver and denatured albumin (solder) were measured and the failure methods of liver repaired with albumin were identified. The ultimate tensile strength was measured for healthy liver (N=37) and thermally damaged liver (N=32). The ultimate tensile strength was measured for three concentrations of coagulated albumin (25, 38 and 53%) in a single layer and for two layers of denatured 38% albumin. Failure under tension of argon beam coagulator soldered liver on the parenchymal surface (N=30) with 38% albumin in two layers had a 70% occurrence for tearing at a mean stress of 39 kPa and a 23% occurrence for shearing at a mean stress of 7 kPa. Liver repaired on the interior surface (N=11) failed in tension by tearing (64%) at a mean stress of 34 kPa and by shearing (36%) at a mean stress of 6 kPa. Argon beam coagulator soldering with 38% albumin took 6 $\mathrm{s/cm}^2$ for two layers of solder and gave the best balance of usability and strength.

[45] S. A. Prahl. Simple and accurate approximations for reflectance from a semi-infinite turbid medium. In *OSA Biomedical Topical Meetings*, pages 613–614, Washington, D.C., 2002. Optical Society of America.

Rational polynomial approximations are given for the total reflection from a semi-infinite turbid medium for normal collimated irradiance. These approximations have an error of less than 0.01 for any albedo or anisotropy.

[46] S. A. Prahl. Semi-analytic model for fiber-based fluorescence measurements. In *OSA Biomedical Topical Meetings*, pages 717–718, Washington, D.C., 2002. Optical Society of America.

A semi-analytic model is presented for calculating the fraction of fluorescent light returning to an optical fiber (which also delivers the excitation light). The model depends upon the observation that the collected light has been scattered only a few times.

[47] H. Xie, R. Wolf, J. Petty, A. Burke, J. S. Teach, K. W. Gregory, and S. A. Prahl. Hemostasis after partial hepatectomy using argon beam coagulation and a concentrated albumin. In *SPIE Proceedings of Lasers in Surgery: Advanced Characterization, Therapeutics and Systems XII*, volume 4609, pages 186–194, 2002.

Background: The argon beam coagulator (ABC) is frequently used to control bleeding on parenchymatous organs during surgery. The purpose of this study was to assess whether it improves the efficacy of hemostasis of using the argon beam coagulation with a concentrated human albumin at partial hepatectomy.

Methods: Thirty-two domestic swine were randomized and treated with either conventional argon beam coagulation alone (ABC, N=16) or the argon beam coagulation in association with a concentrated human albumin (ABCA, $N = 16$) following by wedge resection of left median lobe of the liver using a digital fracture technique. Postoperative followup was up to 90 days for acute parameters and chronic bio-compatibility studies.

Results: The ABCA group required fewer repeat applications of argon beam coagulation than ABC alone group (mean 0.5 vs. 1.5, $p = 0.007$). The total blood loss of ABCA was significantly less than ABC group (mean 3.83 vs. 8.29, $p = 0.049$). The post-operative reaction was similar to the both groups, which shows a chronic inflammation response as part of the ongoing normal healing process.

Conclusions: We demonstrated that the ABCA is more effective and reliable than ABC alone in hemostasis of hepatic injury. Clinical trials of using the ABCA for solid organs injury repair are warranted.

[48] Yin-Chu Chen, Sean J. Kirkpatrick, and Scott A. Prahl. Measurement of changes in concentrations of biological solutions using a Rayleigh interferometer. In V. V. Tuchin, editor, *SPIE Saratov Fall Meeting 2002: Optical Technologies in Biophysics & Medicine IV*, volume 5068, pages 273–283, 2003.

A Rayleigh interferometer was constructed to measure changes of concentrations in the biological solutions. With the stability tests, our Rayleigh interferometer system showed its insensitivity to environment vibrations and with the second compensating cuvette, effects on the refractive index changes other than the concentration changes of molecules in the sample solution could be compensated. A thin glass plate was inserted in the beam path and rotated to vary the optical path length to test the sensitivity of the system. With this glass plate, the detectable optical path differences of the system was $\Delta(n\ell) = 7\,\text{nm}$. Finally, the concentration of sucrose solutions were varied to change the refractive index. The refractive index changes by 1.43×10^{-4} for each gram of sucrose per liter at 20°C. With our system, the sensitivity to sucrose solution was 7mg/L. Based on this sensitivity this interferometric system can be used to detect concentrations of albumin solutions as low as 0.6 mg/mL.

[49] Jessica C. Ramella-Roman, Kenneth Lee, Scott A. Prahl, and Steven L. Jacques. Polarized light imaging with a handheld camera. In Valery V. Tuchin, editor, *SPIE Saratov Fall Meeting 2002: Optical Technologies in Biophysics and Medicine IV*, volume 5068, 2003.

Polarized light imaging can facilitate clinical mapping of skin cancer margins and can poten-

tially guide clinical excision. A real-time hand-held polarized-light system was built to image skin lesions in the clinic. The system consisted of two 8-bit CCD cameras (Camera 1 and Camera 2) mounted on the camera assembly and illuminated the patient's skin. Light was polarized parallel to the source-patient-camera plane. The light, reflected from the patient, was collected with an objective lens mounted on the beam splitter and divided into a horizontal (H) and vertical (V) component. The H component was collected by Camera 1, and the V component was collected by Camera 2. A new image was generated based on the polarization ratio $(H - V)/(H + V)$ and displayed. This image was sensitive to the superficial skin layer and some early clinical examples are presented.

[50] Theodore P. Moffitt and Scott A. Prahl. The specular reflection problem with a single fiber for emission and collection. In Valery V. Tuchin, editor, *SPIE Saratov Fall Meeting 2002: Optical Technologies in Biophysics and Medicine IV*, volume 5068, 2003.

A single fiber may be employed to emit and collect light from a optically diffusing medium such as biological tissues. However, the light collected by the fiber consists of two components: diffusely scattered light from within the tissue and specularly reflected light from the surfaces. Only the diffuse reflection contains the desired information regarding the optical absorption and scattering properties of the tissue, but the specular component is comparable in magnitude to the diffuse reflection with visible light. The refractive index mismatch between the fiber and tissue account for a portion of the specular reflection. However, imperfect contact of the fiber with the surface of tissue creates additional boundaries and thus additional specular reflections. Experiments are performed with a 200 micron diameter fiber and a 632.8 nm He-Ne source to characterize the specular reflection collected through the same fiber using water as a coupling medium. The angular collection efficiency is measured for a fiber in contact with the surface on a glass substrate (specular reflection only) and an epoxy resin tissue phantom (specular and diffuse reflection components). Next, the collection efficiency is measured for a separation between the fiber and the samples for perpendicular illumination to the surface, 14 degrees, and 25 degrees from normal. Imperfect contact is demonstrated to vary the amount of specular reflection collected using a single fiber where changes in angle greater than 4 degrees or a separation between the fiber and the surface in excess of 400 micron caused a minimum of 7 percent reduction of the collected specular reflection.

[51] Zhen Ren, Anthony Furnary, Hua Xie, Kathryn A. Lagerquist, Allen Burke, Scott A. Prahl, and Kenton W. Gregory. Optimal dye concentration and power density for laser-assisted vascular anatomosis (lava). In Lawrence S. Bass, Nikiforos Kollias, Reza S. Malek, Abraham Katzir, Udayan K. Shah, Brian J. F. Wong, Eugene A. Trowers, Timothy A. Woodward, Werner T. W. de Riese, David S. Robinson, Hans-Dieter Reidenbach, Keith D. Paulsen, and Kenton W. Gregory, editors, *SPIE Proceedings of Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems XIII*, volume 4949, pages 186–193, 2003.

Laser tissue welding with albumin solder/indocyanine green (ICG) dye is an effective technique in surgical reconstruction. This study was carried out in vitro to find optimal ICG concentration and power density (PD) in laser assisted vascular anastomosis (LAVA). Fresh porcine carotid arteries incised into vascular strips ($N = 120$) were welded by diode laser in end-to-end with 50% albumin solder of 0.01, 0.1, and 1.0 mM ICG and at power density of 27.7, 56.7, and 76.9 W/cm^2. Direct temperature was measured by inserting thermocouples outside and inside vessel. Tensile strength was tested immediately and histological study was performed. Temperature (both outside and inside vessel) significantly gradually decreasd ($p < 0.01$) with the increasing of ICG concentration at PD 56.7 W/cm^2. Tensile strength significantly gradually decreased ($p < 0.01$) with increasing of ICG concentration at PD 56.7 W/cm^2. Histological study showed minimal thermal injury limited to adventitia of vessels and no appreciable difference in all groups. We find that ICG concentration within solder is most important factor affecting both tissue temperature and tensile strength during laser vessel welding. The optimal balance between stronger strength and minimal thermal injury of vessel may be achieved primarily by using PD 56.7 W/cm^2 at 0.01 mM ICG within solder during LAVA.

[52] Hua Xie, Ronald F. Wolf, Jeffery S. Teach, Allen Burke, Kenton W. Gregory, and Scott A. Prahl. Concentrated albumin for hemorrhage control on hepatic resection with argon ion beam coagulation: A long-term evaluation in a porcine model. In *2003 Annual Meeting Transactions*. Society for Biomaterials, 2003.

Hemorrhage from injuries of solid organs, such as liver, spleen and kidney is commonly difficult to control using conventional suture or electrocautery. In our laboratory, a 38applied to liver resection to seal the active bleeding surface of the liver. This study investigated the long-term host response to the concentrated albumin used in the liver repairs.

[53] Yin-Chu Chen and Scott A. Prahl. Quantum yield of conversion of the dental photoinitiator camphorquinone. In V. V. Tuchin, editor, *SPIE Saratov Fall Meeting 2004: Optical Technologies in Biophysics & Medicine VI*, volume 5771, pages 256–266, 2005.

The primary absorber in dental resins is the photoinitiator, which start the photo polymerization process. We studied the quantum yield of conversion of camphorquinone (CQ), a blue light photoinitiator, using 3M FreeLight LED lamp as the light curing unit. The molar extinction coefficient, ε_{469} of CQ was measured to be 46±2 cm^{-1}/(mol/L) at 469 nm. The absorption coefficient change to the radiant exposure was measured at three different irradiances. The relationship between the CQ absorption coefficient and curing lamp radiant exposure was the same for different irradiances and fit an exponential function: $\mu_{a469}(H) = \mu_{a0}\exp(-H/H_{\text{threshold}})$, where μ_{a0} is 4.46±0.05 cm^{-1}, and $H_{\text{threshold}} = 43 \pm 4$ J/cm^2. Combining this exponential relationship with CQ molar extinction coefficient and the absorbed photon energy (i.e., the product of the radiant exposure with the absorption coefficient), we plotted CQ concentration [number of molecules/cm^3] as a function of the accumulated absorbed photons per volume. The slope of the relationship is the quantum yield of the CQ conversion. Therefore, in our formulation (0.7 w% CQ with reducing agents 0.35 w% DMAEMA and 0.05 w% BHT) the quantum yield was solved to be 0.07±0.01 CQ conversion per absorbed photon.

[54] Yin-Chu Chen, J. J. Brazier, M. Yan, and Scott A. Prahl. Evaluation of molecularly imprinted polyurethane as an optical waveguide for PAH sensing. In Saif Islam and Achyut K. Dutta, editors, *SPIE Proceedings in Nanosensing: Materials and Devices Symposium*, volume 5593, pages 513–520, 2004.

We developed a numerical model for the fluorescence output efficiency of a molecularly imprinted polymer (MIP) waveguide sensing system. A polyurethane waveguide imprinted with a polycyclic aromatic hydrocarbon (PAH) molecule was fabricated using micromolding in capillaries. The coupling of light into a 5 mm long MIP segment was verified by comparing the output transmission signals of a deuterium lamp from the MIP waveguide collected by an optical fiber with the background lamp signals collected by the same optical fiber. It was found that polyurethane MIP was an effective waveguide but absorbed much shorter wavelengths, especially in the UV region, thereby the transmission of light appeared orange/red in color. The high background absorption of polyurethane in the spectrometric regions of interest was found to be a critical problem for sensor sensitivity. Our numerical model shows that the fluorescence

output is only 2×10^{-6} of the input excitation for 25 mM anthracene for a 5 mm polyurethane waveguide. A 10 fold decrease of background absorption will increase the fluorescence output 250 times.

[55] Theodore P. Moffitt and Scott A. Prahl. Implementation of a real-time differential pathlength spectrometer system. In V. V. Tuchin, editor, *SPIE Saratov Fall Meeting 2004: Optical Technologies in Biophysics & Medicine VI*, volume 5771, pages 267–275, 2005.

We report on the development of an optical-fiber-based diagnostic instrument to determine the local optical properties of a turbid media. The system relies on making differential diffuse reflection measurements. We present a method to correct for the variations in the spectral characteristics of the two spectrometers. We also introduce a novel method to evaluate the differential reflectance by encoding a relative wavelength sensitivity constant into the signal processing to account for differences in the spectral sensitivity between spectrometers. This method allows us to record differential reflectance without needing to make additional reference measurements before an experiment to account for spectral variation of the lamp.

[56] Yin-Chu Chen, Jack L. Ferracane, and Scott A. Prahl. A dynamic Monte Carlo model for predicting radiant exposure distribution in dental composites: model development and verifications. In Peter Rechmann and Daniel Fried, editors, *Lasers in Dentistry XI*, volume 5687, pages 90–101, 2005.

Photo-cured dental composites are widely used in dental practices to restore teeth due to the esthetic appearance of the composites and the ability to cure in situ. However, their complex optical characteristics make it difficult to understand the light transport within the composites and to predict the depth of cure. Our previous work showed that the absorption and scattering coefficients of the composite changed after the composite was cured. The static Monte Carlo simulation showed that the penetration of radiant exposures differed significantly for cured and uncured optical properties. This means that a dynamic model is required for accurate prediction of radiant exposure in the composites. The purpose of this study was to develop and verify a dynamic Monte Carlo (DMC) model simulating light propagation in dental composites that have dynamic optical properties while photons are absorbed. The composite was divided into many small cubes, each of which had its own scattering and absorption coefficients. As light passed through the composite, the light was scattered and absorbed. The amount of light absorbed in each cube was calculated using Beer's Law and was used to determine the next optical properties in that cube. Finally, the predicted total reflectance and transmittance as well as the optical property during curing were verified numerically and experimentally. Our results showed that the model predicted values agreed with the theoretical values within 1% difference. The DMC model results are comparable with experimental results within 5% differences.

[57] P. Wu, L. Lucchesi, J. Guo, S. A. Prahl, and K. Gregory. Development of in vitro adhesion test for chitosan bandages. In *Society for Biomaterials 30th Annual Meeting Transactions*, 2005.

Chitosan, a hydrophilic biopolymer derived by N-deacetylation of chitin, is a major component of crustacean shells such as crab, shrimp, and crawfish. Chitosan is biocompatible, biodegradable, bioadhesive non-toxic, and induces hemostasis, which makes it a desirable material for biomedical applications. Chitosan bandages are being developed as wound dressings for severely bleeding injuries. The bandages need to adhere to the wound site to effectively control hemorrhages. The objective of this study is to develop a simple and quick in vitro test to evaluate the adhesion property of chitosan bandages.

[58] Amanda L. Dayton and Scott A. Prahl. Turbid-polyurethane phantom for microscopy. In R. J. Nordstrom, editor, *SPIE Proceedings on Design and Performance Validation of Phantoms Used in Conjunction with Optical Measurements of Tissue*, volume 6870, pages 687006–1–687006–7, 2008.

Calibration standards are needed for measurements of tissues in reflectance mode confocal microscopy. We have created a three dimensional turbid polyurethane phantom with a grid of inclusions. The grid had a 10-fold increase in absorption compared to the bulk of the phantom and the same scattering properties. India ink was used as an absorber for the bulk of the phantom, and Epolin 5532 (absorption peak at 500 nm) was used in the grid. Titanium dioxide particles were used as scatterers. The optical properties of the constructed phantoms were characterized with difiuse reflectance and transmission measurements followed by an inverse adding doubling method. At 488 nm the total attenuation coeffcient was $40.6\pm0.3\,\mathrm{cm}^{-1}$ in the grid and $32.5\pm0.3\,\mathrm{cm}^{-1}$ in the bulk of the phantom. The phantom was imaged with reflectance mode confocal microscopy. Image analysis using the Beer-Lambert-Bouguer Law was performed. In the low absorbing bulk of the phantom the total attenuation coeffcient was estimated accurately, however in the high absorbing grid, the total attenuation coeffcient was underestimated by image analysis techniques.

[59] Amanda L. Dayton and Scott A. Prahl. Optical wire guided lumpectomy. In Israel Gannot, editor, *SPIE Proceedings on Optical Fibers and Sensors for Medical Diagnostics and Treatment Applications IX*, volume 7173, pages 71730M–1–71730M–8, 2009.

In practice, complete removal of the tumor during a lumpectomy is difficult to accomplish. Published rates of positive margins, range from 10% to 50%. A spherical lumpectomy specimen with tumor directly in the middle must be obtained more frequently. The proposed optical technique may provide a practical means by which all surgeons may achieve such a resection. It has been shown that the intensity of light sources can be sinusoidally modulated and will predictably become demodulated upon propagation through a scattering medium.

In this work, the modulated light within the medium was collected by optical fiber(s) fixed distance(s) from the source and used to measure the optical properties of the area. The optical properties were then used to calculate the distance the light had traveled through the medium. The fiber was coupled to an 830 nm diode laser that was modulated at 100, 200 and 300 MHz. A handheld optical probe collected the modulated light and a network analyzer measured the phase lag. This data was used to calculate the distance the light traveled from the emitting fiber tip to the probe. An optical phantom as well as a prophylactic mastectomy specimen were used to explore the feasibility of the system.

The optical properties were $\mu_a = 0.004\,\mathrm{mm}^{-1}$ and $\mu_s' = 0.38\,\mathrm{mm}^{-1}$ in the phantom. The optical properties for the tissue were $\mu_a = 0.005\,\mathrm{mm}^{-1}$ and $\mu_s' = 0.20\,\mathrm{mm}^{-1}$. The prediction of distance from the source was within 4 mm of the actual distance at 30 mm in the phantom and within 3 mm of the actual distance at 25 mm in the tissue. The feasibility of a frequency domain system that makes measurements of local optical properties then extrapolates those optical properties to make measurements of distance with a separate probe was demonstrated.

[60] Ville T. J. Keränen, Anssi J. Mäkynen, Scott A. Prahl, and Matti Törmänen. A scattering measurement system to determine the optical characteristics of industrial suspensions. *Pro-*

ceedings of the International Instrumentation and Measurement Technology Conference, 2009. I2MTC '09. IEEE, pages 570–573, 2009.

A scattering measurement system to determine the optical characteristics of industrial suspensions in the wavelength range 430–700 nm was realized. The suspensions were mixtures of water and solid matter; the optical characteristics measured were the absorption coefficient, the scattering coefficient and the anisotropy. The measurement system comprised two integrating spheres of 203 mm diameter, a light source and a multichannel optical power meter. Different lasers and a halogen lamp were used as light sources. Optical power was measured with a spectrophotometer or a conventional power meter.

[61] Scott A. Prahl, Donald D. Duncan, and David G. Fischer. Monte Carlo propagation of spatial coherence. In Adam Wax and Vadim Backman, editors, *SPIE Proceedings on Biomedical Applications of Light Scattering III*, volume 7187, pages 71870G–1–71870G–8, 2009.

The propagation of light through complex structures, such as biological tissue, is a poorly understood phenomenon. Current practice typically ignores the coherence of the optical field. Propagation is treated by Monte Carlo implementation of the radiative transport equation, in which the field is taken to be incoherent and is described solely by the first-order statistical moment of the intensity. Although recent Monte Carlo studies have explored the evolution of polarization using a Stokes vector description, these efforts, too are single-point statistical characterizations and thus ignore the wave nature of light. As a result, the manner in which propagation affects coherence and polarization cannot be predicted.

In this paper, we demonstrate a Monte Carlo approach for propagating partially coherent fields through complicated deterministic optical systems. Random sources with arbitrary spatial coherence properties are generated using a Gaussian copula. Physical optics and Monte Carlo predictions of the first and second order statistics of the field are shown for coherent and partially coherent sources for a variety of imaging and non-imaging configurations. Excellent agreement between the physical optics and Monte Carlo predictions is demonstrated in all cases. Finally, we discuss convergence criteria for judging the quality of the Monte Carlo predictions.

Ultimately, this formalism will be utilized to determine certain properties of a given optical system from measurements of the spatial coherence of the field at an output plane. Although our specific interests lie in biomedical imaging applications, it is expected that this work will find application to important radiometric problems as well.

[62] Amanda Dayton, Niloy Choudhury, and Scott A. Prahl. Light guided lumpectomy: Is continuous wave or frequency domain more accurate. In Israel Gannot, editor, *SPIE Proceedings on Biomedical Applications of Light Scattering IV*, volume 7573, 2010.

Improving the success of lumpectomies would reduce the number of procedures, cost, and morbidity. A light source could be placed in a lesion to assist in finding and removing the lesion. A quantitive measurement of the distance between such a light source and a detector would further aid in the procedure by providing surgeons with easy to use intra-operative guidance to the lesion.

Two methods, continuous wave and frequency domain (FD), of accomplishing this measurement were directly compared. Within one radio frequency experimental system, the amplitude at 15 MHz was taken to represent the continuous wave signal and the phase at 100 MHz was taken to represent the frequency domain signal. For the continuous wave method, data at source detector separation distances of 20, 30 & 50 mm were used to predict other distances of 10, 20, 30, 40, & 50 mm. Data at source detector separation distances of 20 & 40 mm was used to predict distances for the frequency domain method.

When the difference between the predicted distance and the actual distance was compared to zero the continuous wave method was significantly different (student's t-test, $p = 0.03$) while the FD method was not statistically different from zero (student's t-test, $p > 0.05$). The frequency domain method was more accurate at predicting the source detector separation distance between 10 & 50 mm. This FD method of measuring distance may be useful in locating and removing lesions during lumpectomy procedures.

[63] Amanda Dayton, Niloy Choudhury, and Scott A. Prahl. Measuring distance through turbid media: A simple frequency domain approach. In Tuan Vo-Dinh, Warren S. Grundfest, and Anita Mahadevan-Jansen, editors, *SPIE Proceedings on Advanced Biomedical and Clinical Diagnostic Systems VIII*, volume 7555, 2010.

In both industry and medicine there is no optical technique to measure distance through light scattering media. Such a technique may be useful for localizing embedded structures, or may be a non-contact method of measuring turbid media. The limits of a frequency domain based technique were explored in three polyurethane optical phantoms.

We have demonstrated a simple method to measure the distance between an intensity modulated light source and detector in turbid media based on the proportionality of the phase lag to the distance. The limits of the technique were evident for distances less than 5 mm, particularly when $\mu_s' < 0.1\,\mathrm{mm}^{-1}$ and distances greater than 55 mm for the phantoms studied. This method may prove useful in industry and medicine as a non destructive way measure distance through light scattering media.

[64] Donald D. Duncan, David G. Fischer, Mehran Daneshbod, and Scott A. Prahl. Tissue structural organization: measurement, interpretation, and modeling. In Adam Wax and Vadim Backman, editors, *SPIE Proceedings on Dynamics and Fluctuations in Biomedical Photonics VII*, volume 7563, 2010.

Analysis of the first and second order statistical properties of light is powerful means of establishing the properties of a medium with which the light has interacted. In turn, the first and second order statistical properties of the medium dictate the manner in which light interacts with the medium. The former is the inverse problem and the latter is the forward problem. Towards an understanding of the propagation of light through complex structures, such as biological tissue, one might choose to explore either the inverse or the forward problem. Fundamental to the problem, however, is a physical parametric model that relates the two halves; a model that allows prediction of the measured effect or prediction of the parameters based on measurements. This is the objective of our study.

As a means of characterizing the first and second order properties of tissue, we discuss measurements using differential interference contrast microscopy and a phase-stepping Mach-Zehnder interferometer. First and second order properties are characterized respectively in terms of scatter phase functions and spatial power spectral densities Results are shown for a number of representative tissue types. To explore the utility of such parametric tissue models, we report preliminary efforts at quantifying the effects of partial spatial coherence. These measurements are made on various biological media using a spatial light modulator within the Mach-Zehnder interferometer.

[65] Donald D. Duncan, David G. Fischer, Mehran Daneshbod, and Scott A. Prahl. Differential interference contrast microscopy for the quantitative assessment of tissue organization. In Jose-Angel Conchello, Carol J. Cogswell, Tony Wilson, and Thomas G. Brown, editors, *SPIE Proceedings on Three-Dimensional and Multidimensional Microscopy: Image Acquisition and Processing XVII*, number 7570-0C, 2010.

The propagation of light through complex structures, such as biological tissue, is a poorly understood phenomenon. Typically the tissue is envisioned as an effective medium, and Monte Carlo techniques are used to solve the radiative transport equation. In such an approach the medium is characterized in terms of a limited number of physical scatter and absorption parameters, but is otherwise considered homogeneous. For exploration of propagation phenomena such as spatial coherence, however, a physical model of the tissue medium having a multiscale structure is required.

We present a particularly simple means of establishing such a multiscale tissue characterization based on measurements using a differential interference contrast (DIC) microscope. This characterization is in terms of spatially resolved maps of the (polar and azimuthal) angular ray deviations. With such data, tissues can be characterized in terms of their first and second order scatter properties. We discuss a simple means of calibrating a DIC microscope, the measurement procedure and quantitative interpretation of the ensuing data, and give example characterizations for a number of different tissue types. These characterizations are in terms of the scatter phase function and the spatial power spectral density.

[66] Donald D. Duncan, Scott A. Prahl, Amanda Dayton, and David G. Fischer. Quantification of tissue organizational structure using DIC microscopy. In Valery V. Tuchin, editor, *Saratov Fall Meeting, Joint Workshop on Microscopic and Low-Coherence Methods in Biomedical and Non-Biomedical Applications III*, 2010.

Characterization of the multiscale scatter properties is essential for an understanding of the underlying structural organization of biological tissues. Such characterizations will lead to improved diagnoses and new imaging concepts. We present a particularly simple means of performing the requisite scatter measurements with a differential interference contrast microscope. The resulting characterization is in terms of spatially resolved maps of the (polar and azimuthal) angular ray deviations of the scattered light. With such data, tissues can be characterized in terms of their first and second order scatter properties. We discuss a simple means of calibrating a DIC microscope, the measurement procedure and quantitative interpretation of the ensuing data. First and second order statistics are presented for a variety of tissue types.

[67] Zeinab Eskandarian, Scott Prahl, and Alexandre Douplik. Theoretical and experimental estimation of anisotropy factor for mixed scatterers. In Valery V. Tuchin, editor, *Saratov Fall Meeting, Joint Workshop on Microscopic and Low-Coherence Methods in Biomedical and Non-Biomedical Applications III*, 2010 abstract only.

We compare the anisotropy factor of mixed scatterers using simple theoretical model with direct experimental validation. Two different mixtures of microspheres were used. The scattering anisotropy, absorption and scattering coefficients for monodisperse samples were derived from unscattered light transmission, and total transmission and total diffuse reflection using the Inverse Adding-Doubling method. The monodisperse samples were mixed in different ratios and the optical properties of the mixtures were found. By comparing the analytical Mie theory values for the optical properties with the experimental results, we can estimate the limits of applicability of the proposed model for the scattering anisotropy.

[68] Ville T. Keränen, Amanda L. Dayton, and Scott A. Prahl. Polyurethane phantoms with homogeneous and nearly homogeneous optical properties. In R. J. Nordstrom, editor, *SPIE Proceedings on Design and Performance Validation of Phantoms used in Conjunction with Optical Measurement of Tissue*, volume 7567D, pages 1–4, 2010.

Phantoms with controlled optical properties are often used for calibration and standardization. The phantoms are typically prepared by adding absorbers and scatterers to a clear host material. It is usually assumed that the scatterers and absorbers are uniformly dispersed within the medium. To explore the effects of this assumption, we prepared paired sets of polyurethane phantoms (both with identical masses of absorber, india ink and scatterer, titanium dioxide). Polyurethane phantoms were made by mixing two polyurethane parts (a and b) together and letting them to cure in the polypropylene container. The mixture was degassed before curing to ensure sample without bubbles. The optical properties were controlled by mixing titanium dioxide or india ink into polyurethane part (a or b) before blending the parts together. By changing the mixing sequence, we could change the aggregation of the scattering and absorption particles. Each set had one sample with homogeneously dispersed scatterers and absorbers, and a second sample with slightly aggregated scatterers or absorbers. We found that the measured transmittance could easily vary by a factor of twenty. The estimated optical properties (using the inverse adding-doubling method) indicate that when aggregation is present, the optical properties are no longer proportional to the concentrations of absorbers or scatterers.

[69] Scott A. Prahl, Donald D. Duncan, and David G. Fischer. Monte Carlo propagation of spatial coherence. In Adam Wax and Vadim Backman, editors, *SPIE Proceedings on Biomedical Applications of Light Scattering IV*, volume 7187, pages 75730D–1–6, 2010.

The propagation of light through complex structures, such as biological tissue, is a poorly understood phenomenon. Current practice typically ignores the coherence of the optical field. Propagation is treated by Monte Carlo implementation of the radiative transport equation, in which the field is taken to be incoherent and is described solely by the first-order statistical moment of the intensity. Although recent Monte Carlo studies have explored the evolution of polarization using a Stokes vector description, these efforts, too are single-point statistical characterizations and thus ignore the wave nature of light. As a result, the manner in which propagation affects coherence and polarization cannot be predicted.

In this paper, we demonstrate a Monte Carlo approach for propagating partially coherent fields through complicated deterministic optical systems. Random sources with arbitrary spatial coherence properties are generated using a Gaussian copula. Physical optics and Monte Carlo predictions of the first and second order statistics of the field are shown for coherent and partially coherent sources for a variety of imaging and non-imaging configurations. Excellent agreement between the physical optics and Monte Carlo predictions is demonstrated in all cases. Finally, we discuss convergence criteria for judging the quality of the Monte Carlo predictions.

Ultimately, this formalism will be utilized to determine certain properties of a given optical system from measurements of the spatial coherence of the field at an output plane. Although our specific interests lie in biomedical imaging applications, it is expected that this work will find application to important radiometric problems as well.

[70] L. F. Schneider, L. M. Cavalcante, S. A. Prahl, and J. Ferracane. Trimethylbenzoyl-diphenylphosphine oxide as photoinitiator in dental resins and composites. In *IADR/AADR/CADR 88th General Session*, volume 89A, 2010 abstract only.

Objectives: Since photoinitiator systems for dental resins based on camphorquinone (CQ) present color disadvantages, trimethylbenzoyl-diphenyl-phosphine oxide (TPO) could be a substitute. However, there are remaining considerations about its curing efficiency. The aims of the present investigation were: to characterize the relationship between the photoinitiator absorption spectra and the light spectrum emitted from a QTH light (Absorbed power density, PD_{abs}); and to evaluate the kinetics of polymerization and the degree of conversion (DC) at different depths for unfilled and filled dimethacrylate resins.

Methods: CQ+EDMAB (control); TPO and TPO+EDMAB were used in 50:50 Bis-GMA/TEGDMA resins. Photoinitiator absorption and QTH-light emission were evaluated using a spectrophotometer, kinetics of polymerization with differential scanning calorimetry (DSC), and DC at top and bottom surfaces of 2 mm thick discs via FTIR ($n = 3$). One way ANOVA/Tukey's ($p < 0.05$) was used to analyze the results from DSC and two-way ANOVA/Tukey's ($p < 0.05$) for those from FTIR.

Results: CQ presented higher PD_{abs} than TPO (364 and 223 mW/cm^3, respectively). The DSC revealed that TPO and TPO+EDMAB produced a faster reaction than CQ+EDMAB. There were no differences for DC among the photoinitiators for unfilled materials, whereas only the combination TPO+EBMAB was able to produce similar DC as CQ+EDMAB for filled materials.

Group tested	DC(%) and R_P^{max} (%/s) by DSC		DC(%) by FTIR in unfilled resins		DC(%) by FTIR i	
	DC	R_P^{max}	Surface	2 mm depth	Surface	2 m
CQ+EDMAB	59 ± 1^b	3.8 ± 0.0^b	70 ± 2	73 ± 4	54 ± 1^a	5
TPO	62 ± 1^a	6.0 ± 0.2^a	70 ± 3	69 ± 1	48 ± 2^b	4
TPO+EDMAB	64 ± 2^a	6.6 ± 0.4^a	72 ± 2	70 ± 3	56 ± 2^a	5

Different lower case letters in each column means statistically significant differences.

Conclusions: CQ presented higher PD_{abs} than TPO, but TPO exhibited higher reactivity. DC was similar for unfilled resins. For composites, TPO alone produced lower DC, but the combination TPO+EDBMA produced similar DC as CQ+EDMAB at the surface and 2 mm deep.

[71] Harry Davis, Scott A. Prahl, and Jack L. Ferracane. Reciprocity in dental resins and composites. In *IADR/AADR/CADR 89th General Session*, volume 90A, 2011, poster.

Reciprosity, i.e. equal cure based on equal radiant exposure (mJ/cm^2) independent of exposure time/irradiance, has in general been shown to hold for dental composites, but with limitations. Objective: To develop depth of cure profiles to determine the limits of reciprosity for experimental dental composites having varied monomer content, photoinitiator type, and filler shape. Methods: Composites were produced with Bis-GMA:TEGDMA of 50:50, 70:30, and 90:10 with camphoroquinone (CQ)/EDMAB (1:2) or PPD (1:2; 50:50 mixture); and 62 wt% spherical or irregular 0.4 μm silanated glass. The same radiant exposure (5730 mJ/cm^2) was used to cure composites (15 mm diameter x 10 mm deep) using a Demi light (10 mm tip; Kerr) at (573 mW/cm^2) for 10 seconds and comparing with the same light transmitting through neutral density filters (72 mW/cm^2) for 80 seconds. The relatively low radiant exposure was chosen to accentuate the differences between the composites. After 24 hours, the specimens were bisected with a diamond saw and polished. Knoop Hardness (KHN) measurements were made (100 g; 15 seconds) in equidistant 1 mm squares across the width and depth (n=3/group). Regression was used to determine reciprosity (slope near 1.0 for plot of KHN

10s vs 80s). Results: Reciprosity was evident for the 70:30 and 90:10 resins (see figure-left) at nearly all measurable depths. Reciprosity only held for the 50:50 resin with CQ at 4 mm, but up to 3 mm with PPD (see figure-right). When reciprosity did not hold, longer exposure time tended to produce increased hardness at greater depths. Overall, reciprocity was less evident for composites with irregular compared to spherical fillers. Conclusions: Reciprosity was a function of monomer composition, being most evident for composites of higher viscosity (i.e. more bis-GMA), especially with spherical fillers. Longer exposure with lower irradiance was more effective for achieving depth of cure. Supported by NIH/NIDCR 1R21DE016758

[72] Scott A. Prahl, Chelsea Y. Chen, Ville Keränen, and Jack L. Ferracane. Dynamic optical properties of dental composites. In *IADR/AADR/CADR 89th General Session*, volume 90A, 2011, abstract only.

Depth of cure of composites is a function of light transport through the material as it polymerizes. Objectives: To measure the scattering and absorption properties of unfilled resins and composites during photo-activated curing. Methods: The composite was 50:50 weight ratio of BIS-GMA:TEGDMA mixed with 25 wt% strontium glass (avg. 2 micron). The total reflection and total transmission spectra of unfilled resin and composite samples (1 mm thick × 25 mm diameter) were measured during light curing (150mW/cm^2 for varied times). The composites were prepared with six different concentrations (0, 0.044, 0.058, 0.088, 0.116, and 0.175 wt%) of camphorquinone (CQ). The refractive index of the unfilled resins with four equivalent CQ concentrations was measured during curing with an Abbe refractometer. Results: The absorption spectrum of uncured composite matched the absorption spectrum of CQ in unfilled resin. Uncured composite with and without CQ had the same scattering coefficient spectrum. The extinction coefficient of CQ in composite was 4:5±0.1mm^{-1}/(mol/L), equal to that of CQ in unfilled resin. The absorption and scattering coefficients at 469 nm of composites with five different CQ concentrations decayed exponentially as a function of radiant exposure (figure). The refractive index increased with radiant exposure; Mie scattering calculations suggest that the index of refraction changes are responsible for scattering changes in the composite. Conclusion: The optical properties of a composite affect the light distribution within the composite during curing. Changes in absorption are caused by changes in CQ absorption. Changes in scattering are directly attributable to index of refraction changes of the resin during curing. Supported by NIH/NIDCR Grant 1R21-DE016758.

[73] Scott A. Prahl. Using light to quantitatively monitor composites during photocuring. In *European Chapter of the Tissue Engineering and Regenerative Medicine International Society*, 2011, abstract only.

Introduction: Photocured polymers are widely used in dental applications and as tissue engineering constructs. The physical and mechanical properties of the composite change during curing; the appearance of the composite also changes. This talk summarizes insights gained into the photopolymerization process by quantitatively monitoring appearance.

Methods: The composite were 50:50 weight ratio of BIS-GMA:TEGDMA mixed with various sizes of strontium glass as filler and different concentrations (0–0.175 wt%) of camphorquinone (CQ). The curing irradiance was 100–400 mW/cm2. Total reflection and total transmission spectra of filled and unfilled 1 mm thick composite samples were measured before and after curing. Total transmittance was measured every 50 ms from 400–900 nm during curing. The refractive index of the unfilled resins was also measured during curing using an Abbé refractometer. Before and after reflectance and transmittance values were converted to scattering and absorption properties using the inverse adding-doubling technique. Transmission data during curing was analyzed by using red light to monitor changes in scattering and blue light to assess changes in absorption.

Results: The absorption spectrum of uncured composite measured matched the absorption spectrum of CQ in unfilled resin. Uncured composite with and without CQ had the same scattering coefficient spectrum. The absorption and scattering coefficient at 469 nm of composites with five different CQ concentrations decayed exponentially as a function of radiant exposure. The refractive index increased with radiant exposure.

Conclusion: The optical properties of a composite affect the light distribution within the composite during curing. Changes is absorption are caused by changes in CQ absorption. Mie scattering calculation indicate that scattering changes are directly attributable to index of refraction changes of the resin during curing.

[74] J. A. Delgado Atencio, S. A. Prahl, S. Vázquez y Montiel, M. Cunill Rodríguez, F. Gutierrez Delgado, and J. Castro Ramos. Theoretical analysis and experimental validation of a two-fiber probe for biomedical spectroscopy applications. In *International Commission for Optics 22 General Congress*, 2011, poster.

The goal of the present work is to characterize theoretically and experimentally a simple two-fiber optic probe for spectroscopy applications in turbid biological media such as human skin. First, we perform a review of the wavelength dependence of optical parameters of this tissue. The validity of the diffusion approximation is evaluated for a simple model of skin in term of the restriction that scattering should dominate over absorption. The spectral bands where the diffusion theory fails are found for this model. Second, radially-resolved diffuse reflectance is compared using both Monte Carlo and the diffusion techniques. The optimal source-detector distance that minimizes errors is identified. In addition, a two-fiber optic probe was built and characterized to record spectra from in-vivo skin and phantoms mimicking some interesting real situation and in-vivo spectra from volunteers are used to evaluate an algorithm to extract intrinsic tissue optical properties. The derived optical properties are presented.

[75] B. Morales Cruzado, S. A. Prahl, J. A. Delgado Atencio, and S. Vázquez y Montiel. Validation of GA-MCML algorithm against IAD program. In *International Commission for Optics 22 General Congress*, 2011, poster.

Determining optical properties of turbid media has been performed by many research groups using a technique based on iteratively solving the radiative transport equation using the adding doubling technique (IAD). We present a new, alternative method, GA-MCML, for determining optical properties based on a Monte Carlo technique for radiative transport (MCML) guided by a genetics algorithm. The Monte Carlo method is more flexible than the adding-doubling technique and can be adapted to a wider range of sample geometries. The genetic algorithm is a robust search technique that is well-adapted to avoding the local minima in this optimization problem. GA-MCML, has been implemented by modifying the MCML source code to account for two common experimental problems: light losses due to the finite sample size and non-linear integrating sphere effects using Moffitt's equations. GA-MCML was validated by comparing with IAD method for data acquired at 632.8 nm on a set of phantoms using a single integrating sphere system. The GA-MCML results were equivalent to the IAD technique.

[76] M. Cunill Rodríguez, J. A. Delgado Atencio, S. Vázquez y Montiel, B. Morales Cruzado, S. A. Prahl, and J. Castro Ramos. Theoretical-experimental analysis of a video reflectometry setup.

In *International Commission for Optics 22 General Congress*, 2011, poster.

Video Reflectometry is a relatively simple technique to determine of the optical properties of biological tissues. The video image captures the spatially resolved diffuse reflectance, $R_d(r)$, generated by a narrow light beam normally incident on the surface of the tissue. The video system uses a CCD camera in combination with optical density filters that allows recording of the reflectance signal over a large dynamic range. In this paper, we describe the theoretical framework for evaluating experimental measurements using Monte Carlo simulations. The influence of various factors on the derived optical properties is presented. The specific factors explored are (1) mis-focusing of the camera on the surface, (2) tilting of incident beam, (3) finite beam diameter. We present experimental results of the performance of the system on using Teflon disks as optical standards. Finally, we report on the effect of the reading direction of CCD pixels on the profile of diffuse reflection curves.

[77] Scott A. Prahl, Rafael López Páez, Erik J. Sánchez, Kyle Juedes, and Donald D. Duncan. Quantitative retrieval of phase information using differential interference contrast microscopy. *Proceedings of the Oregon Academy of Science*, 71, 2012 abstract only.

Differential interference contrast (DIC) microscopy uses a Nomarski prism to split the illumination light into two orthogonally polarized beams that are displaced (sheared) relative to one other. A second Nomarski prism recombines the two beams after the light passes through the objective. The DIC image is directly related to the spatial derivative of the phase of light passing through image. The derivative of the phase can be quantitatively recovered from a series of phase-stepped DIC images [1]. In this talk, we extend the process to recover the original phase of the object. By using derivative images in two orthogonal shear directions, the Fried technique enables reconstruction of the phase over a small 32x32 pixel tile. Stitching together multiple tiles allows the phase to be recovered over the entire image. We demonstrate the method by processing DIC images of a sample with known phase properties. [1] Duncan et al., JOSA:A, 28, 1297-1306 (2011).