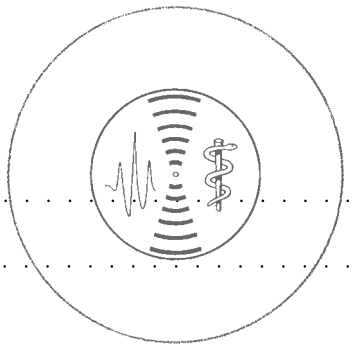
Rochester Center for Biomedical Ultrasound
1999 Annual Report



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From the Directors

From Director Kevin J. Parker:

The words "breakthrough" and "innovation" are widely used in the trade journals. There are occasions where some truly outstanding landmarks in research are reported, and I'm delighted to point to the work summarized this year and in the last annual report by Dr. Charles Francis and his colleagues in the Rochester Center for Biomedical Ultrasound (RCBU). Dr. Francis and his team have reported some remarkable synergistic effects of therapeutic ultrasound with selected chemical agents, and the results could impact some of the most difficult to treat cases of blood clots, strokes, and even heart attacks. Last year's RCBU annual report contained summaries of their demonstration of the combined effects of therapeutic ultrasound with urokinase to dissolve blood clots.

This year's report on page 4 summarizes some *in-vivo* experiments on a rabbit model where low frequency ultrasound in combination with streptokinase, can actually restore significant blood flow and reverse the ischemic appearance of muscle following arteral ligation. The continuing progress of this research and the uncovering of underlying mechanisms could lead to a major impact on the recovery of millions of patients who lose function due to accidental blockage of blood flow to critical organs.

From other RCBU laboratories, additional new devices such as echogenic needles and catheters, new contrast agent techniques, transducer array innovations, and three-dimensional (3D) techniques are emerging and are being exploited for improved patient care.

The RCBU has, over the years, been a steady generating source of fundamental concepts and innovations. Many of today's most exciting developments — contrast agents and in nonlinear techniques — have a scientific history that includes benchmark experiments at the University of Rochester. This year's RCBU annual report documents continued progress across broad fronts, from the fundamentals of tissue-ultrasound interactions, to therapeutic actions, to advanced diagnostic techniques. We welcome your comments on any of the enclosed reports.

From Associate Director Deborah J. Rubens:

As the 20th century came to a close and it was time to reflect on the Ultrasound Unit's 1999 activities, it was clear that ultrasound was entering the 21st century with continued growth in increased patient volumes and with new direction for ultrasound imaging.

Ultrasound procedures saw an increase of 12.5 percent over 1998 volumes. To meet the growing demand for ultrasound studies, two additional sonographers were hired and an evening shift was instituted.

The Ultrasound Unit was reaccredited by the Intersocietal Commission for the Accreditation of Vascular laboratories (ICAVL), for extracranial cerebrovascular, peripheral venous, and visceral vascular testing. We are pleased to have again met the high standards set forth by the ICAVL and will continue to meet, if not exceed, them during this three-year reaccredidation (1999-2002).

In July, we were awarded a three-year National Institutes of Health grant for "3D Sonoelastography Imaging for Prostate Cancer." The goal of this research is to develop real-time, 3D transrectal ultrasound sonoelastography that will lead to advances in the diagnosis, guided biopsy, volume measurements, and management of prostate cancer.

We welcomed Arthur C. Fleischer, M.D., Professor of Radiology and Radiological Sciences, and of OB/GYN, and Chief of Diagnostic Sonography at Vanderbilt University Medical Center, to the University in August. Dr. Fleischer's most recent article at the time, "Quantified Color Doppler Sonography of Tumor Vascularity in an Animal Model" was published in the *Journal of Ultrasound in Medicine* in August 1999, and his lecture entitled "Sonographic Depiction of Tumor Vascularity and Flow" was well attended.

The brachytherapy program continues to increase, attracting patients from all regions of upstate New York. The PIPER (Prostate Implant Planning for Endocavitary Radiation) program headed by the team of Drs. Edward Messing, Ralph Brasacchio, Yan Yu, John Strang, and Deborah Rubens, realized a 25 percent increase over 1998 figures for successful implantation of prostate cancer patients. In conjunction with the program, Dr. Strang

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presented the paper and poster (co-authored by Drs. Rubens, Yu, Brasacchio, and Messing) titled "Real-Time Sonographic Determination of Pubic Arch Interference for Brachytherapy: More Cost Effective and Accurate than CT," at the Radiological Society of North America's (RSNA) 85th Scientific Assembly and Annual Meeting in November. The poster subsequently received a *cum laude* award for scientific exhibit from the RSNA.

In addition to screening for sickle cell patients at risk for stroke, transcranial Doppler monitoring protocols were adopted by the Neurovascular Surgery Service and have been successfully implemented to follow post-operative patients with subarachnoid hemorrhage.

The liver study to determine the ability of contrast agents to alter measured blood flow velocities in liver transplant patients was presented by Drs. Strang and Rubens at the American Institute of Ultrasound in Medicine's (AIUM) 43rd Annual Convention in March. In addition, as a leading site in the previous year's national contrast agent studies, the University of Rochester was chosen along with Yale, University of Michigan, and Penn State-Hershey to pilot a contrast agent study for renal artery stenosis. We will be performing future studies on patients with indeterminate renal or hepatic lesions on CT or MR; and a transcranial Doppler-imaging study is planned for the fall of 2000, under the direction of Dr. Susan Voci.

I have been invited to serve as a member of the Diagnostic Radiology Study Section Center for Scientific Review, for the term beginning July 1, 2000, and ending June 30, 2004. This represents a major commitment of professional time and energy as well as a unique opportunity to contribute to the national biomedical research effort. Study sections review grant applications submitted to the National Institutes of Health, make recommendations on the applications to the appropriate NIH national advisory council or board, and survey the status of research in their fields of science.

We look forward to the changes, challenges, and commitments expected during the beginning of a new century.

About the Center

The Rochester Center for Biomedical Ultrasound (RCBU) at the University of Rochester was created in 1986 to unite professionals from the medical, engineering, and applied-science communities. The Center started with about 30 members and now has over 110 members, with several visiting scientists from locations around the world.

The Center provides a unique environment where professionals can join together to investigate the use of very high frequency sound waves in medical diagnosis along with other ultrasound-related endeavors.

The inside-back page of this report shows the diverse departments involved in collaborative ultrasound research.

The Center's objectives include:

Research interaction — including joint laboratories, technical discussion in formal meetings and communication through a Center newsletter. In addition, interactions with industry, government, and foundations provide an assessment of the needs of the field and encourage mutually beneficial research programs and fellowships.

Education — including graduate-level courses in biomedical ultrasound and closely related fields, specialized short courses open to the international community, and post-doctorate collaborations with bioimaging areas within the University.

The University of Rochester has a long history of leadership and innovation in biomedical ultrasound. For more than two decades, there has been steady progress in the quality of images of organs within the body which are reconstructed from the echoes of very short pulses of ultrasound.

In the late 1960s, Center Member Raymond Gramiak led a team that became the first to report use of an ultrasound contrast agent. At that time, agitated liquids were injected via a catheter while performing an ultrasound of the heart and great vessels. A dramatic increase in echoes was produced from the highly reflective air bubbles contained within the injected solution.

Work has progressed through the years in this and other areas. Current projects include: nonlinear acoustics, contrast agents, three-dimensional (3D) sonoelastography, ultrasound and MRI fusion, scattering, bioeffects, advanced imaging systems, and other areas.

Research

Low Frequency, Low Intensity Ultrasound on Fibrinolysis and Vascular Tone

Research has focused on the effects of low frequency, low intensity ultrasound on fibrinolysis and vascular tone. Ultrasound accelerates fibrinolysis, but unacceptable tissue heating can occur and penetration is limited at frequencies commonly used of 500 kHz and higher.

We showed previously that 40 kHz ultrasound at low intensity accelerates enzymatic fibrinolysis *in vitro* with little heating and good tissue penetration. We have now extended these studies to examine the effects of 40 kHz ultrasound on thrombolysis and also on tissue perfusion in a rabbit model.

Treatment was administered with either 40 kHz ultrasound alone at 0.75 W/cm^2, streptokinase alone, or the combination of both ultrasound and streptokinase. Ultrasound alone resulted in no significant increase in arterial flow, and streptokinase increased flow minimally. Thrombolysis was much greater with the combination, increasing flow to 83 percent of the baseline, pre-thrombosis flow after 120 minutes. Ultrasound also reversed the ischemic appearance of non-perfused muscle in the absence of thrombolysis and with no arterial flow, and this was further investigated by measuring muscle perfusion and tissue pH. After thrombosis, tissue perfusion decreased from 13.7 $\pm$ 0.2 U to 6.6 $\pm$ 0.8 U and then declined further to 4.5 $\pm$ 0.4 U after 240 minutes. Ultrasound improved perfusion to 10.6 $\pm$ 0.5 U and 12.1 $\pm$ 0.5 U after 30 and 60 minutes. This effect was reversible and declined to pre-treatment values after ultrasound was discontinued. Similarly, tissue pH declined from normal to 7.05 $\pm$ 0.02 after thrombosis and to 6.9 $\pm$ 0.03 at 240 minutes. Ultrasound improved pH to 7.34 $\pm$ 0.03 after 60 minutes, and this was also reversible with recurrent acidosis after discontinuation. Ultrasound-induced improvement in tissue perfusion and pH also occurred following femoral artery ligation indicating that thrombolysis did cause these effects.

We have concluded that 40 kHz ultrasound at low intensity markedly accelerates fibrinolysis and also improves tissue perfusion and reverses acidosis, effects that would be beneficial in treatment of acute thrombosis.

Charles Francis
Valentina Suchkova

Non-Thermal, Ultrasound-Induced Cellular Effects and Inertial Cavitation Activity

The project's specific aims are: (1) to elucidate the effects of acoustically activated microbubbles on cells, tissues, and relevant models; and (2) to determine physical mechanisms by which acoustically activated bubbles affect cells and tissues. The project's main working hypothesis is that non-thermal, ultrasound-induced cellular effects are due primarily to inertial cavitation activity. In the course of a year, three hypotheses were tested. A mini review on gene transfection and drug delivery was also prepared, and a new avenue of investigation dealing with ultrasound-induced heat and its relation to teratogenicity in rats was initiated.

Hypothesis Number 1. The *a priori* hypotheses guiding this research were that erosion of the monolayers would: (1) arise due to insonation treatment, (2) arise as a consequence of cavitation activity and, thus, increase with increasing peak negative pressure (P^-) at constant center frequency, and decrease with increasing center frequency at constant P^-, (3) be increased significantly by the presence of a microbubble contrast agent, and (4) have some dependence on monolayer orientation, although it was not clear *a priori* whether the surface located at the site of ultrasound entrance into the exposure vessel (hereafter called the "proximal" orientation of the monolayer) or the surface at the site of ultrasound exit from the vessel (the "distal" orientation) would have the greater sensitivity to damage. The erosion of cells from fibroblast monolayers simulating the vascular endothelium by 20 μs pulses of ultrasound at 500 Hz PRF was studied in relation to the peak negative acoustic pressure (P^-; 0.0-2.5 MPa), ultrasound frequency(1.0, 2.1 or 3.5 MHz), orientation of the monolayer (*i.e.,* simulating the sites of ultrasound entry/exit from a blood vessel) and the presence or absence of a microbubble contrast agent (3 Vol percent Albunex®). Under the most severe exposure conditions used, most of the affected cells appeared to have been lysed; however, a substantial number of viable cells were dislodged from the monolayer surface. The results are consistent with a cavitation-related mechanism of induction and generally supported the hypotheses.

Hypotheses Number 2. This project tested the hypothesis that human erythrocytes, being larger than bovine erythrocytes, would be the more sensitive to

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sonolysis induced by inertial cavitation. The rationale behind this hypothesis was an earlier demonstration that among sized populations of erythrocytes, an inverse relation existed between erythrocyte volume and mechanically-induced shear forces in the surrounding medium; viz, the larger the cell, the less shear force required to rupture the cell's membrane. At low erythrocyte densities (*i.e.,* ~5 percent hematocrit) the hypothesis was supported; at high cell densities(*i.e.,* ~35 percent hematocrit) it was not supported. The data are consistent with an ultrasound-induced symmetric implosion of affected gas nuclei as causing the effect at low cell densities; under such conditions there is ample spacing among cells for ultrasound-induced symmetric growth and collapse of gas nuclei and the concomitant production of radially-expanding shock waves (which lyse the cells); at high cell densities there is not sufficient spacing among cells for ultrasound-induced symmetric growth and collapse of bubbles and an alternative mechanism, possibly asymmetric bubble collapse, becomes operational.

Hypotheses Number 3. The hypothesis tested in this project was that the amount of ultrasound-induced hemolysis of whole human blood *in vitro* would be greater with Optison (OPT), a "second generation" contrast agent containing perfluoropropane, relative to that obtained with Albunex(ALX), a "first generation" agent containing air. The data supported the hypothesis; in general, the hemolytic yields for the ultrasound regimens involving the infusion of OPT were considerably greater than those obtained with ALX; over three acoustic frequencies (1.0, 2.2 and 3.4 MHz) each including five differing acoustic amplitudes (P^-; 2.59 - 0.38 MPa) and involving the same five blood donors, the overall OPT:ALX ratio (n=15), was 2.53 $\pm$0.21 (sem). Corroborative support for the hypothesis was also provided by a 20 MHz passive cavitation detector system in which at each of three frequencies (1.0, 2.2 and 3.4 MHz) the rms and peak-to-peak outputs for the OPT regimens were significantly greater than those of the corresponding ALX regimens.

Morton W. Miller

Tumor Volume Estimation Using 3D Sonoelastography

Vibration amplitude sonoelastography differentiates between hard tumors and normal tissue by detecting the relative vibration amplitude between the regions of tissue. Low frequency shear waves (less than 0.1 mm displacement and 1 KHz frequency) are propagated through the tissue, while real-time Doppler techniques are used to image the resulting vibration pattern. A discrete hard inhomogeneity, such as a tumor, will produce a localized disturbance in the vibration pattern which forms the basis for tumor detection. A 3D image of the vibration pattern in the tissue is produced by assembling sequential tomographic slices. Segmentation techniques can then be applied to determine the shape and extent of the tumor.

In order to establish the accuracy of this technique a tissue mimicking phantom containing a stiff lesion was imaged using both 3D sonoelastography and 3D MRI. Segmentation techniques were applied to both data sets. A tumor volume was obtained in the known location of the lesion for both modalities. The images were then registered using a correlation technique. Visual comparison of equivalent 2D slices in both data sets show that the MRI and the sonoelastography renderings of the tumor agree as to the location of the tumor. The MRI image produced a better rendering of the smooth outline of the ellipsoidal lesion. The tumor volume was calculated in both modalities and the tumor volume estimate from the sonoelastogram measured 85 percent of the MRI tumor volume.

Lawrence S. Taylor, Brian Porter, Deborah J. Rubens, and Kevin J. Parker

Three Dimensional Frameless Fusion of Ultrasound Liver Volumes

We have derived a "frameless fusion" technique to integrate volumetric images using internal vasculature as the fiducial markers. With this technique we demonstrate the feasibility of ultrasound (ultrasound to ultrasound) liver image fusion using internal vascular landmarks. Ultrasound volumes obtained from different dates and scan planes were compared for fusion error.

Oblique axial grayscale and power Doppler images were obtained from a single volunteer with a 5-8 MHz curvilinear transducer (GE Logiq 700MR) attached to a motorized, hand-held track. The ultrasound volumes include scans from varying orientations on a single day and six weeks later. Ultrasound volumes (8x14x8 cm) were segmented to extract and reconstruct the portal vein structure as 1 mm cubed voxels. The vessel volumes were then rendered with commercial 3D software and correlated as a rigid body by a semi-automated, in-house program. Volume registration was judged by alignment of diaphragm (six or more measurements averaged) and vessel in walls on six slices at 25-75 percent through the volume (10 measures averaged).

The displacement between two landmarks on two volumes is denoted as "d". The results for same-day fused volumes are: Vessel d: = 2.2 mm (range 1.5-4 mm) at 5-9 cm depth; Diaphragm d: = 4.1mm (range 1.1-6.3 mm) at 15 cm depth. The results for six-week interval fused volumes are: Vessel d: = 1.8 mm (range 0.9-4.5 mm) at 4-9 cm depth; Diaphragm d: = 2.7 mm (range 0.4-6.1 mm) at 14 cm depth.

Ultrasound volume fusion can be performed segmenting portal veins as an internal fiducial, independent of acquisition orientation, change in patient position or breathhold. Volumes can be acquired over time and compared, with an average 2 mm error centrally and 3-4 mm at the far field, similar to that on same-day acquisition. Image processing using morphing, or gray scale segmentation instead of Doppler may further improve these results. Ultimately, real-time ultrasound volume fusion may permit monitoring of hepatic lesions for radiation and/or chemotherapy.

Future work will include improvements to the data acquisition system by using DC magnetic positioning for freehand scanning.

Brian Porter, Deborah J. Rubens, and Kevin J. Parker

Ultrasound Interaction with Unilamellar Vesicles at the Phospholipid Phase Transition: Perturbation by Phospholipid Side Chain Substitution with Deuterium

The ultrasonic absorption, $\alpha\lambda$, as a function of temperature and frequency was determined in large unilamellar vesicles (LUVs) in which specific phospholipid side chains were deuterated. Deuteration significantly altered the temperature and frequency dependence of $\alpha\lambda$. The frequency change was especially marked, with decreased frequency and broadening of the ultrasound relaxation, even with only minor changes in the phase transition temperature. Deuteration decreased the T_m and enthalpy of the lipid phase transition, as shown by differential scanning calorimetry, whereas electron spin resonance showed that at and above the lipid phase transition, no differences in the mobility as a function of temperature were observed. These results show that the observed increase in ultrasonic absorption in LUVs at the phospholipid phase transition arises from the interaction of ultrasound with the hydrophobic side chains, probably coupling with structural reorganization of small domains of molecules, a process which is maximized at the phase transition temperature.

Reef Philip D. II, Morse, L. D. Ma, R. L. Magin, and Floyd Dunn (Honorary RCBU Member)

Application of a Marked Regularity Model to the Evaluation of Scattering from a Fractal Liver Model

The spatial distribution characteristics of scattering sites generated by a three-dimensional fractal model of the hepatic portal vasculature were analyzed utilizing a framework referred to as the regularity model. In particular, a one-dimensional regularity model yields parameters which describe the mean and variance of the interscatter distance distributions produced by the fractal liver model. The regularity parameters derived from the fractal liver model are shown to correlate roughly with the estimated regularity parameters that can be used to describe a variety of cumulative distribution functions associated with first order statistics observed from ultrasonic backscatter signals obtained in tissue. As such, this may be viewed as an indication of the validity of scattering sets obtained with the fractal liver model. It also provides some insight into how variations of the fractal liver model characteristics, such as branching ratios and scattering strength distributions, can affect the statistical characteristics of the simulated backscatter signals derived from it.

Daniel B. Phillips, Robert M. Cramblitt [1], Kevin J. Parker
[1] SVS R \& D Systems, Inc. Albuquerque, NM

A New Simulation Model for Non-Linear Ultrasound Propagation

Finite amplitude sound propagation undergoes nonlinear distortion due to continuous path interaction with the propagation medium. This distortion tends to defocus the beam causing significant lateral and contrast resolution degradation.

Fundamental understanding of this interaction requires appropriate development of computational models that accurately predict the nonlinear interaction - development of media-borne harmonics - as well as produce an ultrasound image - introduction of transducer effects, interface transitions, and innovative image processing to extract harmonics. Most computational models of ultrasound propagation assume axial symmetry for computational expediency.

A new end-to-end model, NUPROP, is being investigated that incorporates non-axially symmetric geometries and simplified transducer responses to accurately predict ultrasound RF signals for image reconstruction. Innovative frequency modulated sinusoidal input produce significant image quality improvement in moderate to high noise environments. B-Scan image simulations were demonstrated for single frequency and frequency modulated sinusoidal input signals. Statistical analyses of single frequency and frequency modulated sinusoidal input signals research is under review.

Kevin W. Ayer
Navalgund Rao

Novel Tissue Imaging Technique with Contrast Agents

The diagnosis and treatment of many diseases depends on imaging techniques. Among the imaging techniques available the ultrasound technique is relatively inexpensive, non-invasive, and reliable — especially in the studies of the heart and the liver.

Recently, microbubble-based ultrasound contrast agents have attracted the attention of many researchers. The principle of such contrast agents is that the microbubbles are effective scatterers of ultrasound energy due to the differences of their mechanical properties as compared with soft tissue. For perfusion imaging after an intravenous injection of a dose of ultrasound contrast agent, the presence of microbubbles indicate blood flow to the region of interest; hence possible tissue death or presence of lesion. Because the dynamic equation governing the motion of the bubble is nonlinear, it has been hypothesized that the nonlinearity of these bubbles might provide increased contrast enhancement. One proposed technique, called harmonic imaging, simply uses electronic filters to detect the second harmonic frequency. Some animal studies and even human studies are being reported. It has been realized that the nonlinear effect of the tissue response must be considered in these studies.

The goal of our research is to test a novel ultrasound imaging technique which exploits the acoustic nonlinearity of biological tissue and the microbubbles used as ultrasound contrast agents. The hypothesis is that the ultrasound scattering signal from the microbubbles in ultrasound contrast agents contains unique time signatures and this signal can be used to improve tissue imaging such as tissue perfusion studies and the boundary definition of 2D imaging by increasing the differentiation between the blood pool and the surrounding tissue. The theoretical aspect of the interaction of ultrasound with bubbles when surrounded by soft tissue will be addressed. The transient response of the microbubbles to the probing ultrasound energy will be studied. If born out, this technique will have a major impact on the diagnosis and therapy of coronary disease, and the detection of tumor in the liver. Specific aims of the project include: 1. Study the dynamics of microbubbles present in bubble-based ultrasound contrast agents, their interaction with ultrasound when they are surrounded by soft tissue, such as the myocardium or the liver; and derive optimal ultrasound parameters for the purpose of nonlinear image enhancement. 2. Modify an existing prototype nonlinear imaging apparatus and test the device using *in-vitro* flow models. 3. Test the nonlinear imaging technique as an *in-vivo* animal model.

Karl Q. Schwarz and Xucai Chen

Bioeffects of Positive and Negative Pressures in Tissues with Contrast Agents

In previous work, we have shown that tissues containing gas-based ultrasound contrast agents can be particularly susceptible to damage from exposure to pulsed ultrasound or lithotripter fields. The threshold for hemolysis in mice *in vivo* is ~2 MPa negative pressure for exposures at 1 MHz (10 ms pulse, 100 Hz PRF) when ~0.1 mL of the contrast agent Albunex™ is present in the blood. Without Albunex™ there was no detectable hemolysis for exposures up to 10 Pa peak positive pressure. Injection of Albunex™ during exposure of mice to a piezoelectric lithotripter field with amplitude of only 2 MPa, produced hemorrhages in most soft tissues, including fat, muscle, mesentery, intestine, kidney, stomach, bladder and seminal vesicle. However, without contrast agents present in the blood, many of these tissues (excluding lung and intestine) show only minimal damage at exposures with a piezoelectric lithotripter at amplitudes of 40 MPa. In addition, Albunex™ increased the sensitivity of some tissues exposed to low amplitude lithotripter fields for several hours after the initial injection.

Recently, we tested the hypothesis that cavitation is the mechanism for hemorrhage in tissues containing contrast agents by determining the extent of hemorrhage in mice exposed to either positive pressure pulses or negative pressure pulses. According to classical cavitation theory, the inertial collapse pressure of a bubble exposed to a negative pulse is much greater than that exposed to a positive pulse. The Wolf electrohydraulic lithotripter was used to obtain an essentially purely positive pressure pulse and a negative pulse was obtained by reflecting the positive pulse off a water/air surface and blocking the direct pulse. Mice were infused with ~0.1 mL of Albunex™ and then exposed to either 100 positive pressure pulses or 100 negative pressure pulses. When Albunex™ was present, the mean length of intestinal hemorrhage was ~20 times greater for exposure to negative pulses than positive pulses. The area of surface hemorrhage on the kidney was ~10 times greater with negative pressures than with positive pressures. In addition, damage to other tissues, such as the skin, muscle, mesentery and fat, was also significantly greater for exposure to negative pressure pulses than positive pulses. This result, provides further evidence that ultrasound-induced hemorrhage in tissues containing contrast agents *in vivo* arises from inertial cavitation.

Diane Dalecki, Carol H. Raeman, Sally Z. Child, Sheryl M. Gracewski, and Edwin L. Carstensen

Response of Lung to Low Frequency Sound

The biological effects of low frequency underwater sound are most pronounced in and near tissues that contain resonant gas bodies. Murine lung provides an excellent illustration of the response of gas bodies *in vivo* to low frequency sound. Supported by the Office of Naval Research, our laboratory is investigating the effects of low frequency (audible) sound on biological tissues.

Through several different avenues of investigation, we have shown that murine lung responds to low frequency acoustic fields as a resonant structure. Acoustic fields at frequencies of 100–500 Hz were generated using an open, inertial impedance calibration system capable of producing pressure amplitudes on the order of 190 dB re 1 μPa. Through measurements of acoustic scattering near murine lung, we demonstrated that the response of lung to low frequency sound fields can be described by a linear theory of a bubble in water. A pronounced resonance in the total acoustic field was observed at ~335 Hz for adult mice. At resonance, the total acoustic field measured near the chest was ~13 dB greater than without the animal in the exposure vessel. Similar measurements of acoustic scattering with young mice and rats indicated that the resonance frequency of lung scales approximately inversely with the cube root of body weight.

Measurements of the displacement amplitudes of lung in response to low frequency sound were also measured for adult mice and rats using an ultrasonic pulse-echo ranging technique. The resonance phenomena observed through measurements of displacement amplitude were consistent with observations of acoustic scattering described above. Maximum displacement amplitudes measured in murine lung were on the order of 0.1 mm.

The selective sensitivity of lung to damage at the resonance frequency is also consistent with the response of lung as a resonant structure. For exposures of mice at frequencies near lung resonance, the area of lung damage increased with increasing pressure amplitude. At amplitudes well above threshold, nearly the entire lung was damaged, air was present in the pleural cavity, and areas of liver located near the lung were damaged. Effects on the liver are an indirect effect of the oscillation of the lung rather than a direct action of the sound on the liver. Thresholds for lung and liver damage are lowest for exposures at the resonance frequency of the lung. For adult mice exposed at the resonance frequency, the threshold for lung and liver hemorrhage is ~184 dB re 1 μPa (*i.e.*, 1600 Pa). This threshold is at least two orders of magnitude lower than thresholds for lung hemorrhage observed previously from exposure to pulsed ultrasound over the 0.05–5 MHz frequency range or from exposure to lithotripter fields.

Diane Dalecki, Carol H. Raeman, Sally Z. Child, Christopher Cox, David Penney, Stephen McAleavey, and Edwin L. Carstensen

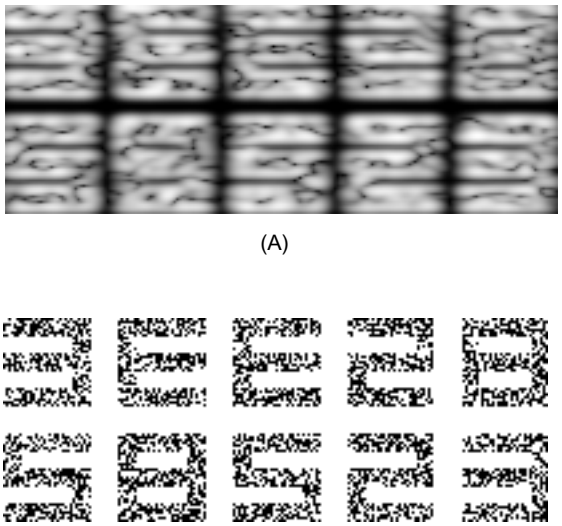
Characterization of a Thin-Film Phantom for Contrast and Resolution Measurements

This research involves the characterization of a unique thin-film ultrasound phantom.

The phantom consists of a film with controllable acoustic properties immersed in an ultrasonically transparent material. The placement of scattering sites on the film creates an image when scanned with a clinical instrument. The backscatter from a halftoned region as a function of halftone density is presented for white and blue noise halftoning. Simulations and measurements were found to be in agreement with a theory for scattering from a dense concentration of point targets. The results indicate a maximum contrast of 19dB may be achieved with the material selected, and contrast may be controlled over a 10dB range. A suitable character set for testing the MTF of a clinical instrument has been selected. A study using simulated ultrasound images was conducted demonstrating the suitability of the character set and suggesting future modifications. The resolution of a medical ultrasound imaging system was determined using a wire phantom and thin-film techniques.

The results were found to be consistent with one another, with the thin-film phantom indicating a lower resolution due to its lower overall contrast. Reduced contrast in the thin-film lead to a further reduction in the measured resolution.

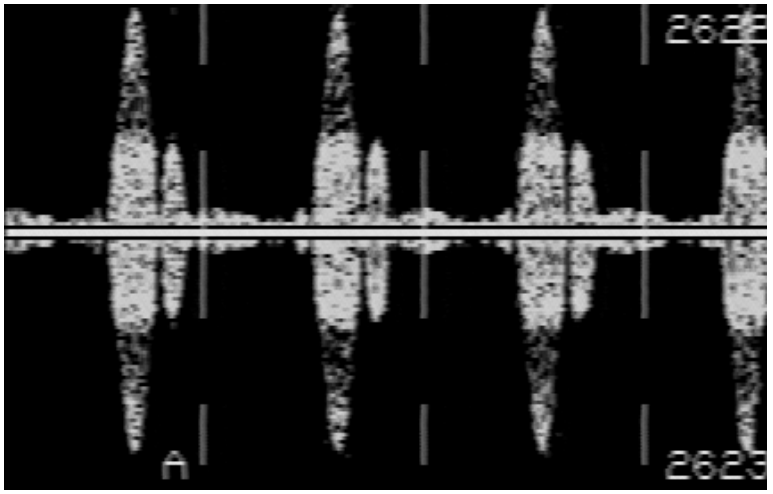
Stephen A. McAleavey, Robert G. Naum, and Kevin J. Parker



(A)

(B)

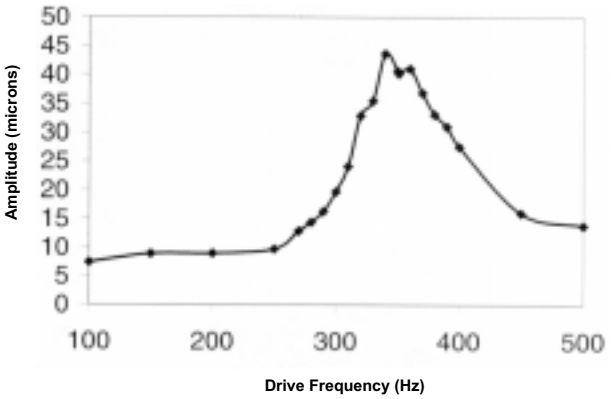
A Thin-Film Phantom halftone pattern (A) and a simulated ultrasound scan of the pattern (B).



A PW Doppler display of a synthesized arterial signal generated with the Thin-Film Phantom. The Doppler display was created by a Quantum QAD-1 scanner. The target was a Thin-Film Phantom vibrated by a time varying noise source designed to simulate arterial flow.

Measurements of Lung Vibration in Response to Low Frequency Sound

The amplitude of vibration of lung in response to low-frequency (100-500 Hz) sound was measured in mice and rats *in vivo*. Low frequency sound fields were generated in an inertial water column driven at its base with an electromagnetic transducer. Estimates of vibration amplitude of the lung were obtained by calculating the variations in the round-trip delay of pulsed wideband ultrasound bursts. The relative time delays were calculated by determining the maximum of the cross-correlation of the first echo with subsequent echoes. The ultrasound bursts were emitted at a rate of 1-5 kHz, allowing 10 displacement estimates to be calculated per cycle of lung oscillation. The mean resonance frequencies obtained through measurements of vibration amplitude were ~330 Hz for mice and ~189 Hz for rats. The maximum observed displacements were on the order of 0.1 mm. The resonance observed through measurements of displacement amplitude was equivalent to that obtained through acoustic scattering measurements and consistent with observations of lung hemorrhage.



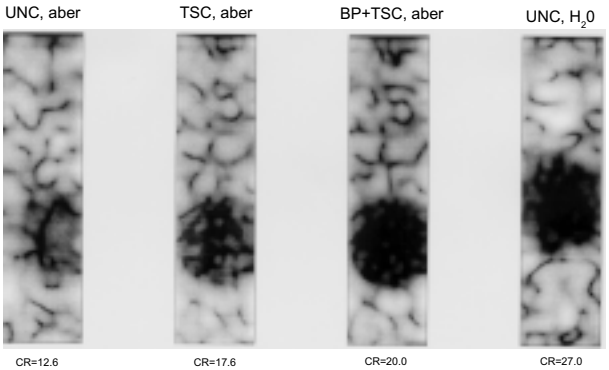
Plot of amplitude of murine lung vibration as a function of frequency. Resonance at ~ 330 Hz is clearly visible.

Stephen McAleavey, Carol H. Raeman, Kevin J. Parker, and Diane Dalecki

A Two-Dimensional Array System for Studies of Ultrasonic Imaging with Aberration Correction

A 2D array system is described for pulse-echo studies of aberration correction. The transducer array is an 80x80 array with a center frequency of 3.0 MHz and a -6 dB bandwidth of 56 percent. At the center frequency, each element has a physical size of 1.04 wavelength and spacing of 1.2 wavelength. A multiplexer accesses any contiguous 128 elements for transmission and any contiguous 16 elements for simultaneous reception. Transmit electronics have independently programmable waveforms. Each receive channel includes a 20 MHz, 12-bit A/D converter, and a time varied gain programmable over 40 dB. Transmit and receive apertures up to the size of the array are formed synthetically. A method that iteratively predistorts transmit waveforms to produce a transmit focus compensated for aberration has been implemented. Point-spread functions have been measured for propagation through a water path and through a tissue-mimicking aberration path. Pulse-echo images have been formed through a water path, through a tissue-mimicking aberrator, and through the aberrator using aberration correction that consists of time-shift compensation in the transmit-receive aperture or backpropagation followed by time-shift compensation. The system is useful for pulse-echo measurements of aberration, development of adaptive focussing techniques, and formation of high-resolution ultrasonic images using aberration correction.

Robert C. Waag, Daniel B. Phillips, Carsten G. Draeger, Makoto Tabei, James C. Lacefield, and Feng Lin



Field: 10 mm x 2.67 mm. Range: 50 mm - 60 mm. Focus: 55 mm.
Dynamic Range: 35 dB. Tx/Rx f/#: 1.7/1.2 (aber), 1.5/1.2 (H_2O)
Aberrating path: 35 mm. Water path: 35 mm. Surface of random medium: 35 mm.

A *k*-space Method for Large-Scale Models of Wave Propagation in Tissue

Large-scale simulation of ultrasonic pulse propagation in inhomogeneous tissue is important for study of ultrasound-tissue interaction as well as for development of new imaging methods. Typical scales of interest span hundreds of wavelengths; most current 2D methods, such as finite-difference and finite-element methods, are unable to compute propagation on this scale with the efficiency needed for imaging studies. Furthermore, for most available methods of simulating ultrasonic propagation, large-scale 3D computations of ultrasonic scattering are infeasible. Some of these difficulties have been overcome by previous pseudospectral and k-space methods, which allow substantial portions of the necessary computations to be executed using fast Fourier transforms. This research presents a new *k*-space method that has advantages of both past *k*-space methods and pseudospectral methods. In this method, the spatial differential equations are solved by a simple Fourier transform method and temporal iteration is performed using a *k-t* space propagator. The applicability of the *k*-space method to large-scale soft-tissue modeling is shown by simulating propagation through several tissue-mimicking cylinders as well as a model chest wall cross section. Numerical results indicate that this method is accurate for large-scale soft-tissue computations, with much greater efficiency than that of an analogous leapfrog pseudospectral method or a 2-4 finite difference time-domain method. However, numerical results also indicate that the *k*-space method is less accurate than the finite-difference method for a high-contrast scatterer with bone-like properties, although qualitatively reasonable results can still be obtained by the *k*-space method with high efficiency. Possible extensions to the method, including 3D computations and inclusion of absorption effects, are discussed.

Laurent P. Souriau, T. Douglas Mast, Dong-Lai Liu, Adrian I. Nachman, and Robert C. Waag

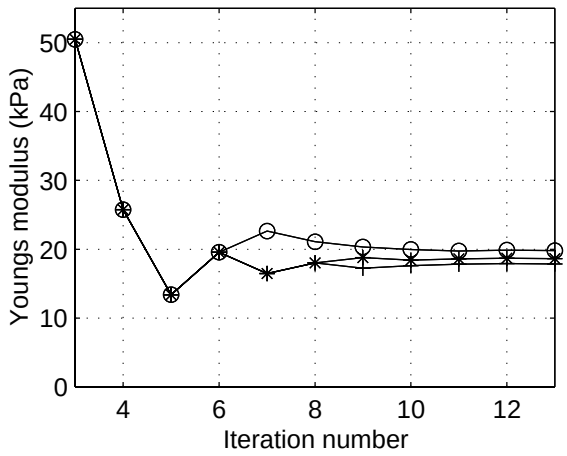
Simulation of Ultrasonic Pulse Propagtion, Distortion, and Attenuation in the Human Chest Wall

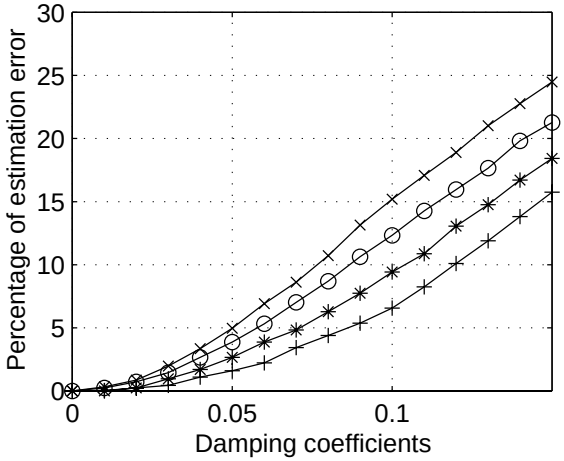
A finite-difference time-domain model for ultrasonic pulse propagation through soft tissue has been extended to incorporate absorption effects as well as longitudinal-wave propagation in cartilage and bone. This extended model has been used to simulate ultrasonic propagation through anatomically detailed representations of chest wall structure. The inhomogeneous chest wall tissue is represented by 2D maps determined by staining chest wall cross sections to distinguish between tissue types, digitally scanning the stained cross sections, and mapping each pixel of the scanned images to fat, muscle, connective tissue, cartilage, or bone. Each pixel of the tissue map is then assigned a sound speed, density, and absorption value determined from published measurements and assumed to be representative of the local tissue type. Computational results for energy level fluctuations and arrival time fluctuations show qualitative agreement with measurements performed on the same specimens, but show significantly less waveform distortion than measurements. Visualization of simulated tissue-ultrasound interactions in the chest wall shows possible mechanisms for image aberration in echocardiography, including effects associated with reflection and diffraction caused by rib structures. A comparison of distortion effects for varying pulse center frequencies shows that, for soft tissue paths through the chest wall, energy level and waveform distortion increase markedly with rising ultrasonic frequency and that arrival-time fluctuations increase to a lesser degree.

T. Douglas Mast, Laura M. Hinkelman, Leon A. Metlay, Michael J. Orr, and Robert C. Waag

Quantitative Sonoelastography — Results in Soft Tissue Phantoms and Human Muscle

A systems approach has been developed to quantitatively reconstruct the shear elastic modulus from ultrasound image sequences of low-frequency induced vibrations. Our approach integrates a mesh-based speckle tracking algorithm and an FEM-based method of elastic reconstruction into a single construct. Central to the method is a deformable rectilinear mesh with node points that are assigned to regions with high feature content, building on a method developed by former Center member Fai Yeung. Vibration amplitude and phase vectors are obtained by applying a least-squares estimator to the 2D frame-to-frame displacements of the nodes. An iterative forward finite element-based elastic modulus reconstruction algorithm is then applied to the same mesh structure. Given the measured vibration vectors in an homogeneous region of interest (ROI) and assumed values of Poisson's ratio and the damping coefficient, the elastic modulus can be determined. Sensitivity to the assumed values was assessed using finite element simulations of vibration propagation, as illustrated below, left. Regardless of the accuracy of the assumed Poisson's ratio, the Young's elastic modulus converged to the actual value of 20 kPa that was used in the simulation. The sensitivity to the assumed damping coefficient, which is representative of viscosity, however, becomes increasingly significant as the frequency of vibration increases below, right). Additional simulations were used to assess the effect of image noise on reconstructed elasticity. Finite element simulations of vibrational motion in a two-layer mathematical phantom were used, to which Gaussian noise that was 5 percent of





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Research

Sonographic Investigation of Flow Patterns in the Perfused Human Placenta and Their Modulation by Vasoactive Agents with Enhanced Visualization by the Ultrasound Contrast Agent Albunex®

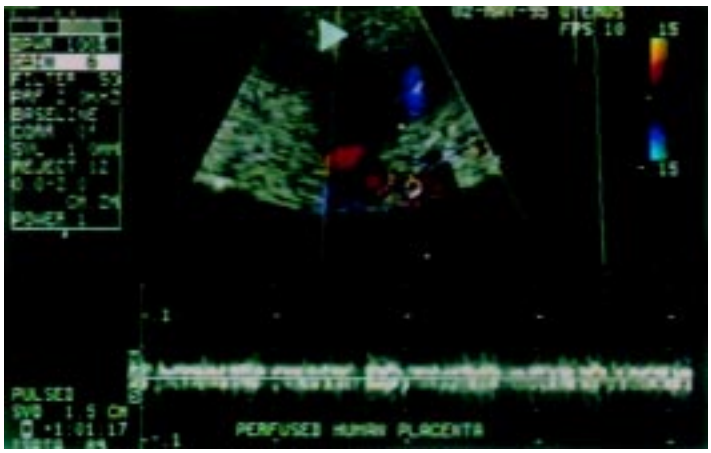
Purpose. Our objective was to demonstrate sonographic-ally the flow distribution in the circulation of human placentae as well as the sensitivity of the human fetal capillary bed to vasoconstriction and dilatation.

Methods. Five human full-term placental lobules were obtained following delivery and maintained *in vitro* with fetal and maternal flow. The cotyledon was selected and connected (using 5-French umbilical catheters) to a maternal and a fetal pump. Commercial ultrasound scanners were used for imaging. Albunex® (1 ml bolus) was administered to the fetal "artery" to monitor patterns of flow. U46619 (1 ml, 10^{-6} M; a thromboxane agonist and potent vasoconstrictor) and/or nitroglycerin (a potent vasodilator) were added to the fetal artery.

Results. Following the addition of U46619, mean "fetal pressures" rapidly rose from 23.2 $\pm$ 0.8 to 118 $\pm$ 2.9 mm Hg (mean + standard error of mean; $p < 0.001$); venous flow rates decreased. As demonstrated by color Doppler imaging, flow markedly changed from a pattern of general distribution throughout the lobule to flow only near the chorionic plate. Color persistence was 94.4 $\pm$ 6.5 seconds with Albunex® after nitroglycerin and 39.8 $\pm$ 3.4 seconds with Albunex® after injection of U46619 ($p < 0.001$). Nitroglycerin had no effect when injected by itself but returned "constricted" flow to a "normal" pattern when injected after U46619.

Conclusion. The contrast medium Albunex® improved visualization of the fetal circulation throughout the lobule. Flow in the human placental capillary bed can be regionally manipulated throughout the placental lobule by vasomodulators and monitored by Albunex®-enhanced sonographic examination.

Jacques S. Abramowicz, Daniel B. Phillips, Lynn N. Jessee, Harold Levene, Kevin J. Parker, and Richard K. Miller



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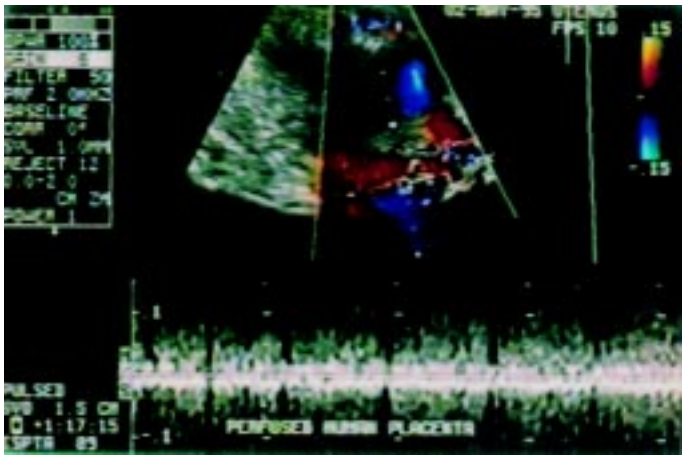
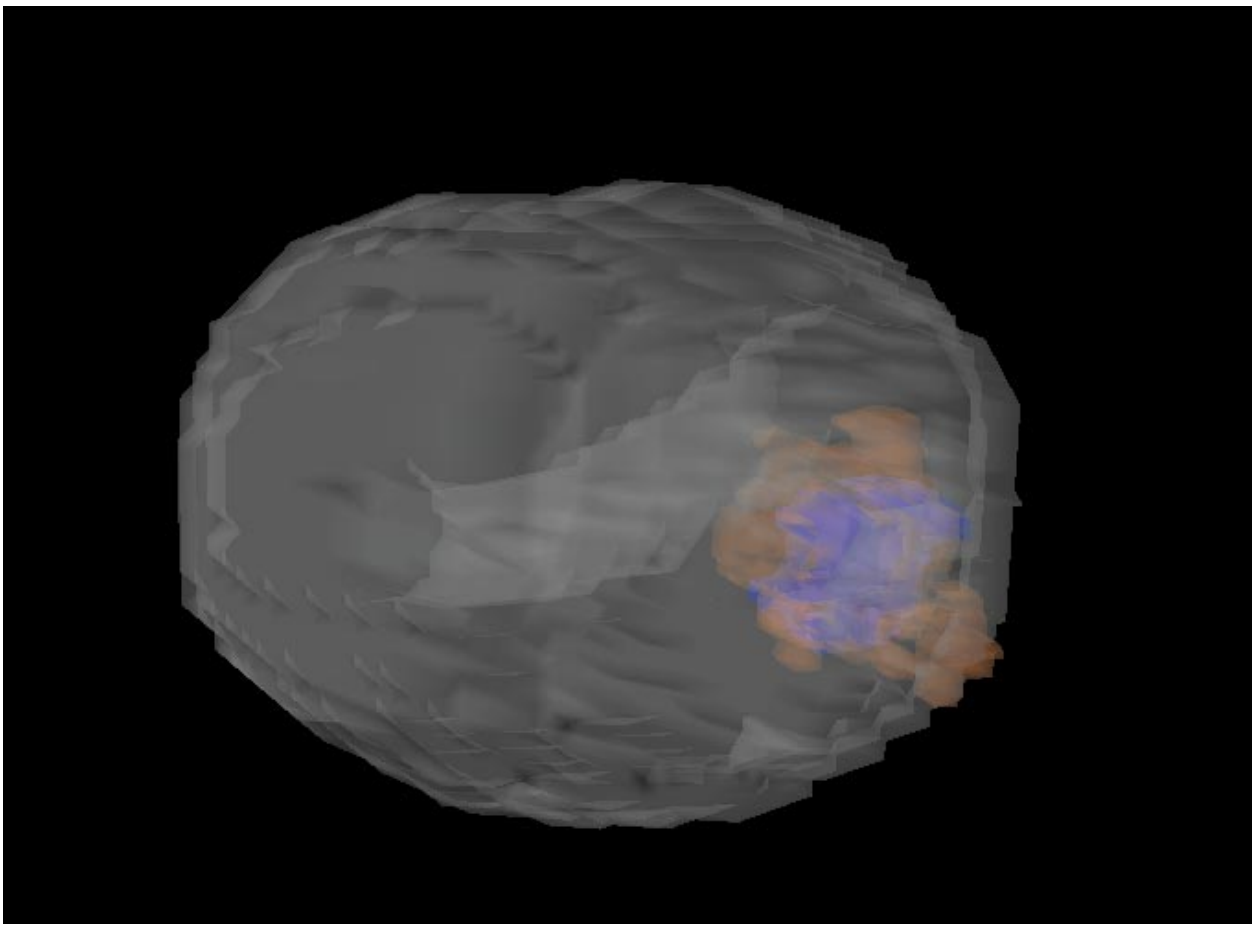


B

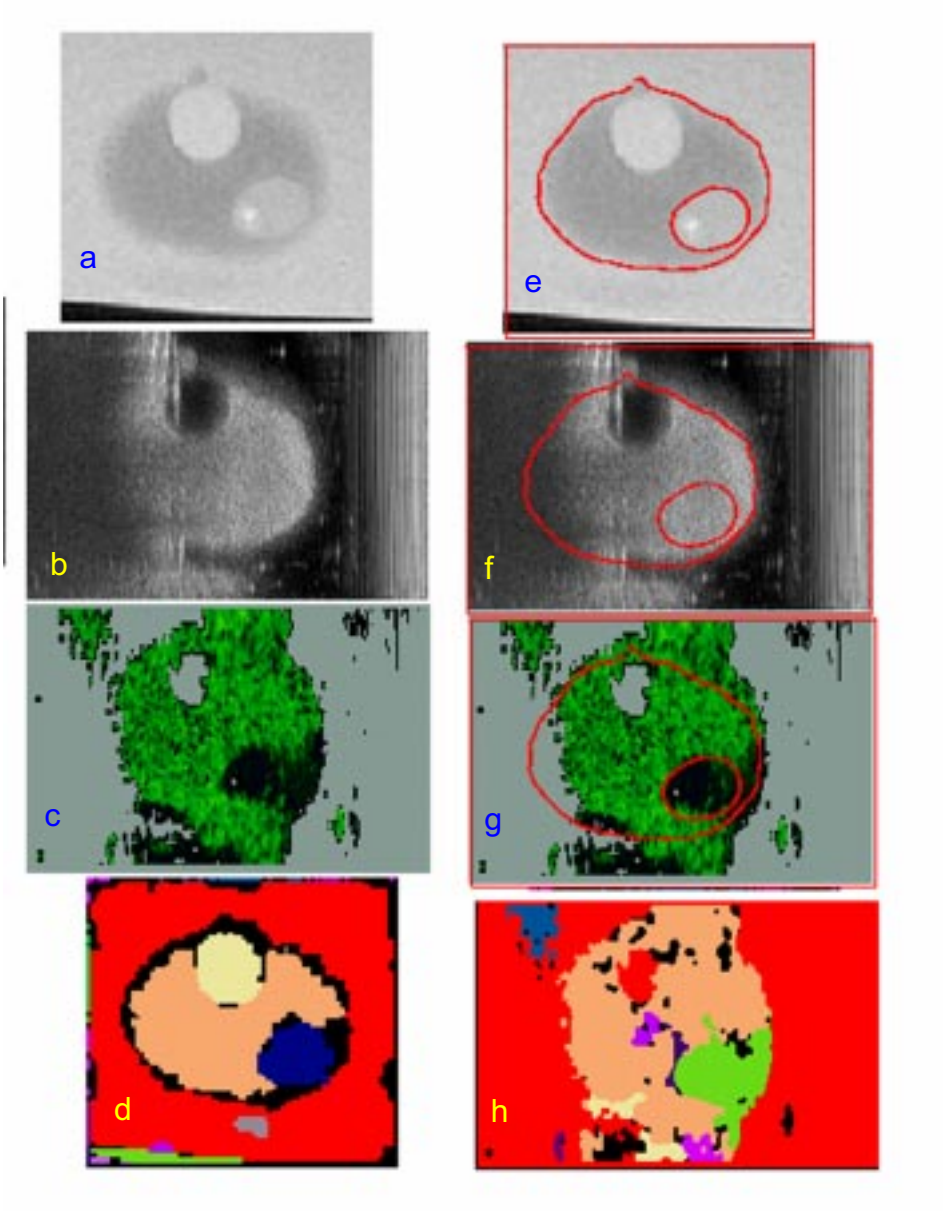
Modulation of flow. (A) Injection of Albunex® after addition of U46619. Note absence of flow in the decidual plate region (arrowhead). (B) After addition of nitroglycerin. Flow is generalized.

Research



See page 5 for related article

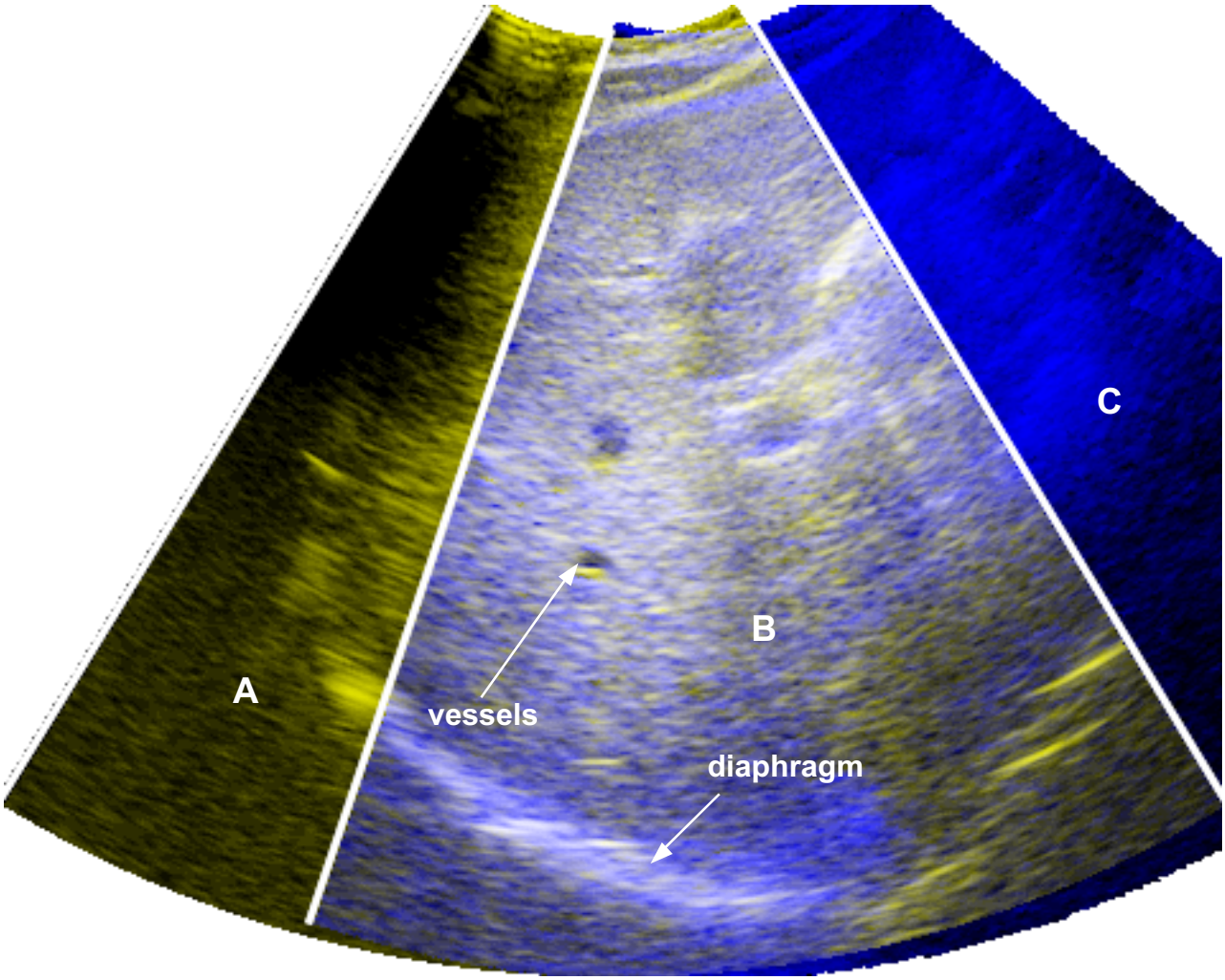
3D rendering of MR and ultrasound data from the prostate phantom. The MR segmentation of the gland is shown as a surface rendering in transparent gray to serve as a geometrical reference for the tumor. The MR segmentation of the tumor is shown in blue, the segmented tumor from the sonoelastography image is orange. The urethra is visible as a transparent tube running from one the apex to the base of the gland.



See related article on page 5.

2D MRI and ultrasound images of the phantom in a region containing the tumor. (a) MR image: the gland is visible as the darker gray tone against the brighter background. The bright, nearly circular region, anterior in the image, is the urethra and the light grey ellipse, posterior and right in the image, is the tumor. (b) Same image as in (a), but the gland surface and tumor boundary have been outlined in red. (c) b-scan image of the phantom at approximately the same image plane as the MR image in (a). The scanning transducer was located on the right of the image during acquisition. The outline of the gland is visible but the edge of the gland distal to the transducer is blurred. The urethra is quite visible as a black circular region. (d) Same image as (c), except the red lines outlining the MR image were translated to verify the regions of interest imaged are comparable. Note that the outline of the tumor from the MR image is located over an isoechoic region of b-scan. (e) Sonoelastography image of the same region of interest taken while vibrating at 296 Hz. The bright green indicates areas of high vibration and the dark green areas of low vibration. The urethra is visible as an area of no vibration. (f) Sonoelastography image with boundaries from the MR image added. The MR tumor outline aligns well with the area of low vibration in the image except for the dark region that spreads out near the right edge of the gland. The color Doppler signal shows consider blooming beyond the true edge of the gland, especially in the lateral direction of the scanning beam (up and down in the image). (g) Segmentation of the MR grayscale image. The tumor is segmented as purple in the image, the urethra is yellow. (h) Segmentation of the sonoelastography image. The tumor is segmented as lime green, the urethra as the background orange brown.

Research



Fusion image shows the fixed data in Regions A and B; and the second data set in Regions B and C. Region B contains overlapping grayscale data from both volumes. Arrows indicate the location of the diaphragm and vessels.

See page 6 for related article

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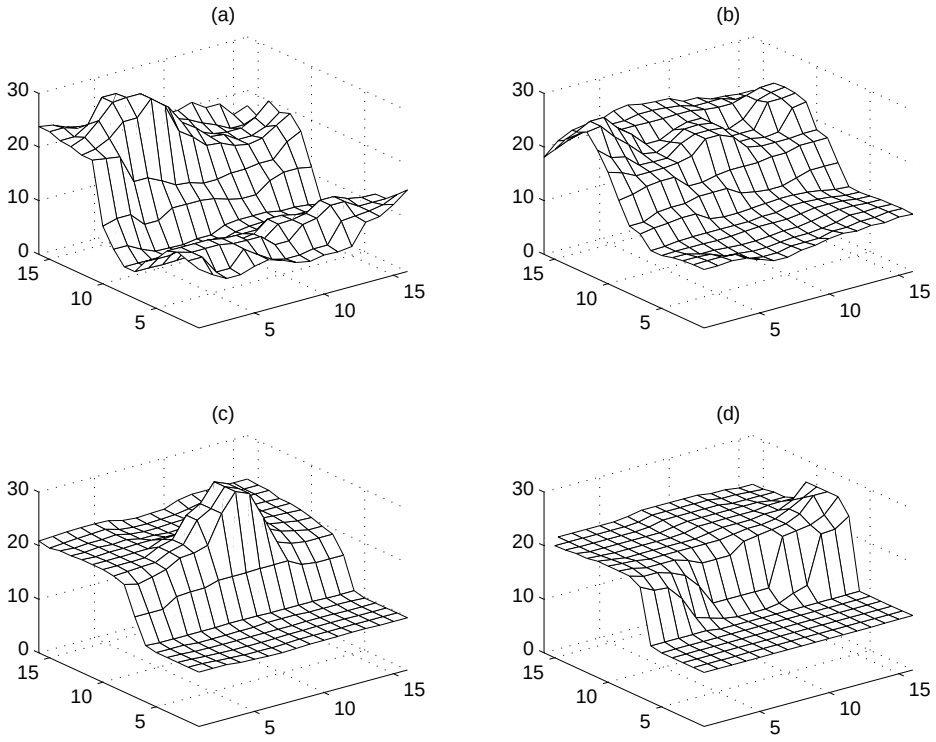
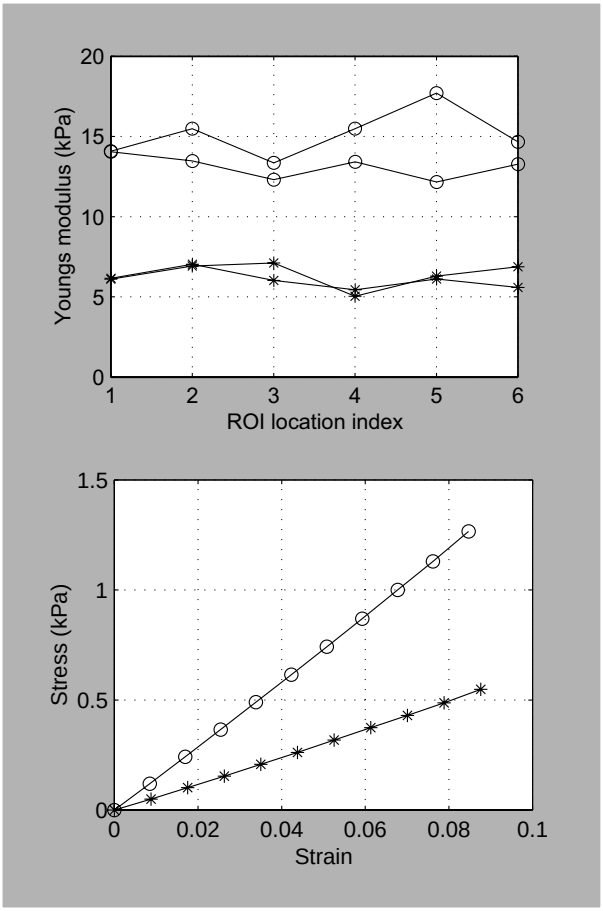
the maximum vibration amplitude was added. The results obtained at four different frequencies are shown right. Although regional variations in reconstructed elasticity were noted, average elasticity in each of the homogeneous regions was highly accurate when regions that crossed the boundary between layers were discounted.



In order to assess the accuracy of the approach in real world situations, a series of experiments was performed using B-scan ultrasonic image sequences from homogeneous and layered gel-based physical phantoms. Images of vibration amplitude and phase in the axial and lateral directions were obtained by applying the speckle tracking method and the least-squares estimator to image sequences.

The iterative forward approach was used to estimate Young's moduli at different locations in the specimens. A 2 cm X 2 cm ROI was used. The results, shown (right, top), were compared to independent measurements of Young's moduli made on small circular cylindrical samples that were fabricated at the same time as the phantoms. Young's modulus was calculated from the slope of the stress-strain curve under static deformation, as shown (right, bottom). The values so measured differed from those obtained from sonoelastography by 10.4 percent in the homogeneous phantom, and by 11.9 percent and 10.5 percent, in the soft and hard regions of the layered phantom, respectively. Quantitative sonoelastography is also being studied in the quadriceps muscle groups of healthy volunteers. Although independent verification is not possible, comparisons among and within subjects should facilitate assessment of the method's reliability. It is expected that our approach will allow the visualization of changes in the viscoelastic properties of muscle in response to exercise.



Dongshan Fu, Stephen Levinson, Sheryl Gracewski, and Kevin Parker

AcouStick: A Tracked A-Mode Ultrasonography System for Registration in Image-Guided Surgery

Objective: Registration of preoperative images such as CT or MR with the physical space occupied by the patient during surgery is a fundamental step in image-guided surgery. Image-to-physical (IP) registration is commonly performed using stereotactic frame systems, points, and surfaces. Point-based registration can be accomplished using external anatomic landmarks, skin-affixed markers, and bone-implanted markers. Surface-based registration is generally accomplished using the air-skin interface. In this study we describe a system for noninvasively determining cranial surface points using an optically tracked A-mode ultrasound transducer. These points can be used to perform surface-based IP registration of 3-D head images.

Methods: We use a heavily damped, spherically focused, 10 MHz A-mode ultrasound immersion transducer. The nominal element size is 6 mm and the focal length in water is 19 mm. The transducer is driven with an ultrasonic pulser/receiver. The output is connected to a 12-bit, 80 MHz analog-to-digital (A/D) data acquisition board. The transducer is optically tracked using an Optotrak 3020 system (Northern Digital, Inc.). An adjustable, water-filled, plastic offset is attached to the transducer. The tip is normally set at about 15 mm from the transducer face so that the transducer focal point is approximately at the cranial surface. Twenty infrared light-emitting diodes are mounted on a plastic cylindrical housing. Echo locations are determined using the Hilbert transform. The AcouStick is essentially a tracked probe with a variable length tip. Cranial surface positions p are calculated as $p = p_0 + dn_p$, where p_0 is the position of the transducer, $d = ut/2$ is the distance from the transducer to the bone-tissue interface, u is the speed of sound in tissue (we use 1540 m/s), t is the time interval between the initial sound pulse and the bone-tissue echo, and n_p is the unit vector along the direction of the ultrasound beam. Calibration for this system is the process of determining p_0 and n_p. Our method is variation of the invariant point method commonly used for calibrating ball-tipped probes. To estimate the AcouStick point localization error, we measured the position of 25 steel balls arranged in a 5 ¥ 5 grid on an acrylic plate in a water bath. We used the AcouStick system to collect cranial surface points on a plastic skull phantom covered with a layer of gelatin. We also used the system to collect cranial surface points on three volunteers and one patient.

Results: The cranial surface point localization error of this system is less than 0.5 mm. The target registration error (TRE) of the cranial surface-based registration for the skull phantom was computed by using as a reference gold standard the point-based registration obtained with eight bone-implanted markers. The mean TRE for a 150-surface-point registration is 1.0 mm, and ranges between 1.0 and 1.7 mm for six 25-surface-point registrations. Visual inspection of the volunteer and patient ultrasound-determined cranial surface points suggests than most of the points are within one or two voxels (1 to 2 mm) of the inner surface of the subcutaneous fat in the volunteer MR images or the outer cranial surface in the patient CT image.

Conclusions: Our preliminary results suggest that accurate, noninvasive, IP registration of head images may be possible using an optically tracked A-mode ultrasound-based system.

This paper was presented at *MICCAI 1999* and appears in the conference proceedings: CR Maurer Jr, RP Gaston, DLG Hill, MJ Gleeson, MG Taylor, MR Fenlon, PJ Edwards, DJ Hawkes. AcouStick: A tracked A-mode ultrasonography system for registration in image-guided surgery. In: CJ Taylor, ACF Colchester, eds. *Medical Image Computing and Computer-Assisted Intervention (MICCAI) 1999*. Berlin: Springer-Verlag, 1999, pp. 953-962. (Cambridge, UK, Sep 19-22, 1999.) A manuscript has been submitted to *Medical Physics*. A patent application was filed with the USPTO: WA Bass, RL Galloway Jr, CR Maurer Jr, RJ Maciunas. Apparatus for bone surface-based registration of physical space with tomographic images for guiding a probe relative to anatomical sites on the image. U.S. Patent Application Serial No. 09/255,254. (Filed Feb 22, 1999.)

Calvin R. Maurer, Jr.

People, Promotions, and Awards

Andrew Brayman left the University of Rochester to work with Larry Crum at the Applied Research Laboratory at the University of Washington in Seattle.

Xucai Chen and **Karl Schwarz** received a National Institutes of Health (NIH) three-year grant in the amount of $477,642 for "Novel Tissue Imaging Technique with Contrast Agent."

Diane Dalecki was named Vice-Chair of the AIUM Bioeffects Committee.

Floyd Dunn was named a Life Fellow of the Institute of Electrical and Electronics Engineers (IEEE).

Charles Francis received an American Heart Association Grant-in-Aide for Ultrasound Enhanced Thrombolysis.

Maria Helguera received the Ph.D. degree from Rochester Institute of Technology in May 1999. Her thesis was titled "Non-Rayleigh Ultrasonic Characterization of Tissue Scattering Microstructure via a Multibandwidth Probing Technique." Dr. Navalgund Rao was her thesis advisor.

James C. Lacefield, Ph.D., a research associate working with **Robert C. Waag** in the Ultrasound Research Laboratory at the University of Rochester, applied for the Acoustical Society (ASA) of America Hunt Fellowship for the year 2000. The fellowship is awarded annually by the ASA only when the applicant as well as the environment in which the applicant is working are both outstanding. Dr. Lacefield received notification prior the printing of this publication that he was the recipient of this distinguished award.

Stephen McAleavey received Second Place, Student Paper on Biomedical Ultrasound/Bioresponse to Vibration at the 138th Meeting of the Acoustical Society of America in Columbus, Ohio, for "Measurements of Lung Vibration to Low Frequency Sound" (co-authored with Carol H. Raeman, Diane Dalecki, and Kevin J. Parker).

An NIH Merit Award Grant for Biophysical Bases of Pulsed Ultrasound Bioeffects" for **Morton W. Miller** was renewed for an additional three years. An NIH Grant "Ultrasound-induced Hyperthermic Teratogenicity", initially awarded to Andrew Brayman, was transferred to Morton W. Miller.

Kevin Parker received the Joseph Holmes Pioneer Award from the AIUM for his contributions to ultrasound.

Deborah Rubens was invited to serve as a member of the Diagnostic Radiology Study Section Center for Scientific Review for the term beginning July 1, 2000, and ending June 30, 2004. Study sections review grant applications submitted to the NIH, make recommendations on the applications to the appropriate NIH national advisory council or board, and survey the status of research in their fields of science.

The **University of Rochester Ultrasound Unit** was reaccredited by the Intersocietal Commission for the Accreditation of Vascular Laboratories (ICAVL), for extracranial cerebrovascular, peripheral venous, and visceral vascular testing for the period 1999-2002.

Center Profile

Center Profile: Calvin R. Maurer, Ph.D.

The University of Rochester welcomed Calvin R. Maurer, Jr., Ph.D. in December 1998. Dr. Maurer is an Assistant Professor in the Departments of Neurological Surgery, Radiation Oncology, and Biomedical Engineering and Director of the Image-Guided Surgery Research Laboratory in the Department of Neurosurgery.

Dr. Maurer is working with Robert Maciunas, M.D., Professor and Chair, Department of Neurological Surgery, to develop new image-guided neurosurgery techniques. One project is an investigation of the use of non-rigid image-to-image registration methods to register individual patient images to an atlas or reference image for planning functional procedures such as placement of a thalamic stimulator to treat movement disorders. Another project, being performed in collaboration with Chris Brown, Ph.D., Professor, Department of Computer Science, is the development of an augmented reality system for neurosurgical planning.

Several of Dr. Maurer's projects are pertinent to the Rochester Center for Biomedical Ultrasound. He is developing methods of using ultrasound to determine cranial surface points noninvasively for bone-surface-based image-to-physical registration. In September 1999, at the *Medical Image Computing and Computer-Assisted Surgery* conference in Cambridge, U.K., he presented a method and results using an optically tracked A-mode ultrasound probe. He hopes to develop a similar method using B-mode ultrasound, and to validate both methods with clinical data. In collaboration with a group in London, he is developing a new method of calibrating optically or magnetically tracked B-mode ultrasound probes, which is a necessary step for compounding free-hand tracked 2D ultrasound images into 3D images. Working with Cargill Alleyne, Assistant Professor, Department of Neurological Surgery, he plans to track transcranial Doppler (TCD) ultrasound images to create 3D TCD images, and to register these images with CT, CTA, MR, and MRA images. And he is interested in correcting for intraoperative brain deformation by non-rigidly deforming preoperative MR images to intraoperative 3D ultrasound images formed by free-hand tracking and compounding.

Dr. Maurer received the B.S.E. degree in Chemical Engineering, *magna cum laude*, from Princeton University and the M.S. and Ph.D. degrees in Biomedical Engineering from Vanderbilt University. His initial research interest was quantitative physiology. At Princeton, he wrote a senior thesis about diffusion modeling of tumor growth. At Vanderbilt, he initially studied cardiac physiology and wrote several papers about the dependence of heart chamber dimensions and dynamics on chamber demands and myocardial properties, and the evaluation of myocardial properties from image and pressure data for chronic conditions. From 1985 to 1987, he was a Research Assistant in the Department of Biomedical Engineering at Vanderbilt. He wrote a master's thesis under the direction of Thomas Harris about using water extraction and pulmonary diffusing capacity as methods of measuring pulmonary microvascular surface area, and wrote a paper comparing propanediol and urea as markers of lung vascular injury. From 1988 to 1989, he was a Research Engineer in the Department of Pediatric Cardiology at Vanderbilt, where he wrote software for calculating left and right atrial and ventricular volumes from biplane cineangiocardiograms, wrote software for calculating left-ventricular diastolic function indices from M-mode echocardiograms, and mathematically modeled the force-interval relationship in heart muscle using a calcium three-compartment model.

In 1990, Dr. Maurer switched to his current research interests in medical imaging and image processing, with a particular emphasis on image registration and image-guided therapy. From 1990 to 1995, he was a Research Engineer in the Departments of Biomedical Engineering and Neurological Surgery at Vanderbilt. During this time he integrated the use of nuclear medicine scans into a frame-based neurosurgical planning system, developed new user interface tools for a radiosurgery planning system, and helped develop the Acustar neurosurgical navigation system. He wrote a dissertation under the direction of J. Michael Fitzpatrick about the registration of multimodal 3D medical images using points and surfaces. In 1996 he was a Research Fellow in the Department of Neurosurgery and in 1997 he was an Adjunct Assistant Professor in the Department of Computer Science at Vanderbilt. During this time he studied intraoperative brain deformation, the use of fMRI for neurosurgical planning, and new image registration methods.

For the two years prior to his appointment at the University, Dr. Maurer was a Research Fellow in the Computational Imaging Science Group for the Division of Radiological Sciences and Medical Engineering at Guy's Hospital, King's College London, London, U.K. In London, he continued to study intraoperative brain deformation using intraoperative MRI images, investigated the validation of fMRI using electrophysiology measurements, contributed to the development of an augmented reality surgical microscope system, and started the ultrasound work mentioned above.

Dr. Maurer has received a National Institutes of Health Research Fellowship and is a member of *Tau Beta Pi* and *Sigma Xi*. He is a member of the Association for Computing Machinery, The Institute of Electrical and Electronics Engineers, The International Society for Optical Engineering, and the Biomedical Engineering Society. He has authored more than twenty journal papers, two book chapters, forty conference papers, and three patents (see patent pending, page 27).

Publications

Selected Publications

Abramowicz JS, Lewis V
"Hysterosalpingography of the Myometrium"
Anderson J (ed): *Gynecological Imaging*. Churchill Livingston, London, 1999.

Abramowicz JS, Phillips DB, Jessee LN, Levene H, Parker KJ, Miller RK
"A Sonographic Investigation of Flow Patterns in the Perfused Human Placenta and Their Modulation by Vasoactive Agents with Enhanced Visualization by an Ultrasound Contrast Agent (Albunex®).
J Clin Ultrasound, 27:513-522, 1999.

Brayman A, Coppage ML, Vaidya S, and Miller MW
"Transient Poration and Cell Surface Receptor Removal from Human Lymphocytes *In Vitro* by 1 MHz Ultrasound"
Ultrasound Med Biol 25(6):999-1008, 1999.

Brayman A, Lizotte LM, and Miller MW
"Erosion of Artificial Endothelia *In Vitro* by Pulsed Ultrasound: Acoustic Pressure, Frequency, Membrane Orientation and Microbubble Contrast Agent Dependence.
Ultrasound Med Biol 25(8):1305-20, 1999.

Brayman A. and Miller MW
"Sonolysis of Albunex®-supplemented, 40% Hematocrit Human Erythrocytes by Pulsed 1-MHz Ultrasound: Pulse Number, Pulse Duration and Exposure Vessel Rotation Dependence"
Ultrasound Med Biol 25(2):307-14, 1999.

Carstensen EL, Dalecki D, Gracewski SM, Christopher T
"Nonlinear Propagation and the Output Indices"
J. Ultrasound Med. 18:69-80;1999.

Chen X, Schwarz KQ, Phillips D, Steinmetz S, Schlief R
" A Mathematical Model for the Assessment of Hemodynamic Parameters Using Quantitative Contrast Echocardiography"
IEEE Trans. Biomed. Eng. 45:754-765 (1998).

Cramblitt RM and Parker KJ
"Generation of Non-Rayleigh Speckle Distributions Using Marked Regularity Models,"
IEEETransactions on Ultrasonics, Ferroelectrics, and Frequency Control, 46(**4**) 867-874, July 1999.

Dalecki D, Child SZ, Raeman CH, Cox C
"Hemorrhage in Murine Fetuses Exposed to Pulsed Ultrasound"
Ultrasound Med. Biol. 25:1139-1144; 1999.

Dalecki D, Child SZ, Raeman CH, Gildner CD
"Lung Hemorrhage from Exposure to Low Frequency Ultrasound"
J. Ultrasound Med. 18:S145; 1999.

Dalecki D, Raeman CH, Child CZ, Carstensen EL
"Lung Response to Low Frequency Underwater Sound"
J. Acoust. Soc. Am. 106:2165; 1999.

Fu D, Levinson SF, Gracewski SM, and Parker KJ
"Solution of the Inverse Problem in Sonoelastography Using an Iterative Forward Approach," 24th International Symposium on Ultrasonic Imaging and Tissue Characterization Proceedings, pp.61-62, 1999.

Fu D, Levinson SF, Gracewski SM, and Parker KJ
"Noninvasive Quantative Reconstruction of Tissue Elasticity Using an Iterative Forward Approach," , *Physics in Medicine and Biology*, special issue, 2000.

Fultz PJ, Jacobs CV, Gottlieb RH, Rubens DJ, Totterman SMS, Meyers S, Angel C, Del Priore G, Warshal DP, Hall WJ, Zou KH, Shapiro DE
"Ovarian Cancer: Comparison of Observer Performance for Four Methods of Interpreting CT Scans"
Radiology: 212, 401-410, 1999.

Gottlieb RH
"Around-the-Clock-Services: Quality-of-Care Issues"
AJR, 172: 7, 1999.

Gottlieb RH, Widjaja J, Mehra S, Robinette WB
"Clinically Important Pulmonary Emboli: Does Calf Vein US Alter Outcomes?"
Radiology, 211: 25-29, 1999.

Gottlieb RH, Voci SL, Cholewinski SP, Robinette WB, Rubens DJ, O'Mara RE, Orloff MS, Johansson M, Bronsther OL
"Urine Leaks in Renal Transplant Patients: Diagnostic Usefulness of Sonography and Renography"
Clinical Imaging: 23, 35-39, 1999.

Gottlieb RH, Widjaja J
"Clinical Outcomes of Untreated Symptomatic Patients with Negative Findings on Sonography of the Thigh for Deep Vein Thrombosis: Our experience and a review of the literature"
AJR, 172: 1601-1604, 1999.

Gottlieb RH, Widjaja J, Tian L, Rubens DJ, Voci SL
"Performance of Calf Ultrasound in Detecting Deep Venous Thrombosis in Symptomatic Patients: Our Experience and Review of the Literature"
JCU, in press, 1999.

Gottlieb RH, Zusman E, Hartley DF, Rubens DJ, Voci SL, Robinette WB, Melendez L, Morris T, Ojha S, Chengazi V, Ertuk E, Messing E
"Effect of Angiotensin Converting Enzyme Inhibition on the Doppler Waveform in Dogs with Renal Artery Stenosis"
J Ultrasound Med: 18, 481-487, 1999.

Hollenberg G, Adams M, Weinberg E
"Ultrasound and Color Doppler Ultrasound of Acute and Subacute Achilles Tendon Ruptures, A Pictorial Review"
Emergency Radiology, 5(**5**): 317-323, 1999.

Lewis V, Abramowicz JS
"Hysterosalpingography of the Endometrium"
Anderson J (ed): *Gynecological Imaging*. Churchill Livingston, London, 1999.

Lewis V, Abramowicz JS
"Hysterosalpingography of the FallopianTubes"
Anderson J (ed): *Gynecological Imaging*. Churchill Livingston,London, 1999.

Mast TD, Metlay LA, Orr MJ, Waag RC
"Simulation of Ultrasonic Pulse Propagation, Distortion, and Attenuation in the Human Chest Wall
J. Acoust. Soc. Am. 106(6), December 1999

McAleavey S, Phillips D, and Parker KJ
"Industrial Flow Techniques,"
Wiley Encyclopedia of Electrical and Electronics Engineering, Volume 7 (Ed: J. G. Webster, John Wiley & Sons, Inc.), 1999.

McAleavey SA, Raeman CH, Parker KJ, Dalecki D
"Measurements of Lung Vibration in Response to Low Frequency Sound"
J. Acoust.Soc.Am. 106:2165; 1999.

Messing EM, Zhang JB, Rubens DJ, Brasacchio RA, Strang JG, Soni A, Schell MC, Okunieff PG, and Yu Y
"Intraoperative Optimized Inverse Planning for Prostate Brachytherapy: Early Experience"
Int. J. Radiation Oncology Biol. Phys. 44(**4**): 801-808, 1999.

Miller MW, Brayman AA, Abramowicz JS
"Obstetric Ultrasound: A Biophysical Consideration of Patient Safety. The "Rules" Have Changed"
Am J Obstet Gynecol, 179:241-54,1998.

Miller MW
"Gene Transfection and Drug Delivery"
Commemorative Millennium Supplement of *Ultrasound Med Biol* (in press), 1999.

Morse PD, Ma LD, Magin RL, and Dunn F
"Ultrasound Interaction with Large Unilamellar Vesicles at the Phospholipid Phase Transition: Perturbation by Phospholipid Side Chain Substitution with Deuterium"
Chem. Phys. Lipids, in press.

Porter B, Rubens D and Parker KJ
"Soft Tissue Volume Fusion of U.S. and MRI,"
IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control: 46 (**6**), cover image, November 1999.

Rubens DJ, Gottlieb RH, Fultz PJ
"Role of Color Doppler Imaging in Interventional Sonography"
JCU, 27(**5**), June 1999.

Sandborg M, Abramowicz JS, Lewis V
"Plain Radiography and Fluoroscopy"
Anderson J (ed): *Gynecological Imaging*. Churchill Livingston, London, 1999.

Schwarz KQ, Chen X, Steinmetz S
"Methods for Quantifying Ultrasound Backscatter and 2D Video Intensity: Implications for Contrast Enhanced Sonography"
J. Am. Soc. Echo. 11(2):155-168 (1998).

Souriau LP, Mast TD, Liu D-L, Nachman AI, and Waag RC
"A *k*-space Method for Large-Scale Models of Wave Propagation in Tissue"
IEEE Trans. UFFC, submitted

Taylor LS, Porter B, Rubens D, and Parker KJ
"3D Sonoelastography for Prostate Tumor Imaging," Proceedings of the International ICSC Congress on Computational Intelligence: Methods and Applications (CIMA'99) RIT Rochester, NY: 468-472. June 1999.

Voci SL, Gottlieb RH
"Doppler Respiratory Patterns in the Femoral Veins with Pelvic Vein Obstruction,"
Clinical Imaging, 1999.

Wang M and Parker KJ
"Properties of Jointly Blue Noise Masks and Applications to Color,"
Journal of Imaging Science & Technology, special issue, 2000.

Yu Y, Zhang JB, Brasacchio RA, Okunieff PG, Rubens DJ, Strang JG, Soni A, Messing EM
"Automated Treatment Planning Engine for Prostate Seed Implant Brachytherapy"
Int J. Radiat Oncol Bio Phys: 43(4), 647-652, 1999.

Zhu W and Parker KJ
"Color Filter Arrays Based on Mutually Exclusive Blue Noise Patterns,"
Journal of Visual Communication and Image Representation 10, 245-267, 1999.

Selected Presentations

Abramowicz J
"Doppler Ultrasound in Obstetrics: Luxury or Necessity?"
International Society of Ultrasound in Obstetrics and Gynecology, Buenos Aires, Argentina, 1999.

Abramowicz J
"Abnormal Fetal Growth: Can it Really be Diagnosed by Ultrasound?"
International Society of Ultrasound in Obstetrics and Gynecology, Buenos Aires, Argentina, 1999.

Abramowicz J
"MI and TI, or the ABCs of Ultrasound Bioeffects: What Does it Mean to the End User?"
International Society of Ultrasound in Obstetrics and Gynecology, Buenos Aires, Argentina, 1999.

Abramowicz J
"New Technologies in Ultrasound: the Dawn of a New Era?"
International Society of Ultrasound in Obstetrics and Gynecology, Buenos Aires, Argentina, 1999.

Abramowicz J
"Prenatal Diagnosis of Fetal Anomalies.....Then What?"
International Society of Ultrasound in Obstetrics and Gynecology, Buenos Aires, Argentina, 1999.

Gottlieb RH, Voci SL, Rubens DJ, Fultz PJ
“Can Ultrasound be Trusted in the Calf in Patients with Lower Extremity Signs, and/or Symptoms?”
43rd AIUM Annual Convention, San Antonio, TX, March 14-17, 1999.

Gottlieb RH, Widjaja J, Voci SL, Rubens DJ, Robinette WB
“Performance of Ultrasound in Detecting Isloated Calf Deep Venous Thrombosis in Symptomatic Patients: A Meta-Analysis.”
American Roentgen Ray Society 99th Annual Meeting New Orleans, LA, May 9-14, 1999.

1999 RCBU Meetings

“Smart Endotracheal Tube” Jack Mottley, Ph.D., Electrical and Computer Engineering, University of Rochester, January, 12, 1999.

“Diagnostic Ultrasound During Pregnancy: Effects of New Standards on Tissue Heating and their Relevance to Hyperthermic Teratogenicity,” Morton W. Miller, Ph.D., Obstetrics and Gynecology, University of Rochester (co-authored with Wesley L. Nyborg, William C. Dewey, Marshall L. Edwards, Jacques Abramowicz, and Andrew Brayman), July 13, 1999.

“Sonographic Depiction of Tumor Vascularity and Flow,” Arthur C. Fleischer, M.D., Radiology and Radiological Sciences/Obstetrics & Gynecology, Vanderbilt University Medical Center, August 10, 1999.

“Multifeature Tissue Analysis Procedures for Breast Cancer Classification,” S. Kaisar Alam, Ph.D., Riverside Research Institute (New York, NY), presentation co-authored with Fredric L. Lizzi, Ernest J. Feleppa, Tian Liu, and Andy Kalisz, September 7, 1999.

“Extraction of Propagating Waves in Cine Images from Magnetic Resonance Elastography,” James Smith, Ph.D., Senior Research Engineer, Measurement Systems Design, Corning, Inc., November 9, 1999.

"Myocardial Perfusion Imaging. An Interactive Discussion," Karl Schwarz, M.D., Cardiology, University of Rochester, December 14, 1999.

Levinson, SF, Parker KJ, Fu Dongshan
"Solution of the Inverse Problem in Sonoelastography Using an Iterative Forward Approach"
24th International Symposium on Ultrasonic Imaging and Tissue Characterization, pp.61-62, 1999.

Parker KJ
"Smart Piezoelectric Devices"
Center for Future Health Forum, January 1999.

Porter B, Rubens DJ, Robinette W, and Parker KJ
"Imaging Techniques for 3D Rendering of Liver Vasculature"
AIUM, San Antonio,1999.

Porter B, Rubens DJ, and Parker KJ
"Three-Dimensional Frameless Fusion of Ultrasound Liver Volumes"
IEEE Int'l. Ultrasonics Symposium, Lake Tahoe, NV, October 18-21, 1999.

Porter B, Rubens DJ and Parker KJ
"Ultrasound 3D Imaging Techniques for Frameless Fusion"
24th Int'l Symposium on Ultrasonic Imaging & Tissue Characterization, Arlington, VA, 1999.

Porter B, Rubens DJ and Parker KJ
"Three-Dimensional Frameless Fusion of Power Doppler Ultrasound Liver Volumes"
RSNA, Chicago, 1999.

Rubens DJ, Strang JG, Hameed T
"Effect of a Microbubble Contrast Agent (DMP-115, DuPont Merck) on Measurement of Blood Velocity"
43rd AIUM Annual Convention, San Antonio, TX, March 14-17, 1999.

Strang JG, Rubens DJ, Yu Y, Brasacchio RA, Messing EM
"Real-Time Sonographic Determination of Pubic Arch Interference for Brachytherapy: More Cost-Effective and Accurate than CT"
RSNA 85th Scientific Assembly and Annual Meeting, Chicago, IL, November 28-December 3, 1999.

Taylor LS, Porter B, Rubens D, and Parker KJ
"Tumor Volume Estimation Using3D Sonoelastography,"
24th International symposium on Ultrasonic Imaging and Tissue Characterization Arlington, VA June 2-4 1999.

Voci SL, Gottlieb RH, Mehta AL, Fultz PJ
"Delayed Computed Tomographic Characterization of Renal Cell Carcinoma: Preliminary Experience"
ARRS, 99th Annual Meeting, New Orleans, LA, May 1999.

Wang M and Parker KJ
"Properties of Blue Noise Patterns"
ICIP, September 1999.

Wang M and Parker KJ
"Properties of Jointly Blue Noise Masks and Application on Color Halftoning"
7th Color Imaging Conference, IS&T, Scottsdale, AZ, November 1999.

Waag RC, Phillips DB, Draeger CG, Tabei M, Lacefield JC, and Lin F
"A Two-Dimensional Array System for Studies of Ultrasonic Imaging with Aberration Correction"
Paper 2aBB1, 138th Meeting, Acoust. Soc. Am., Columbus, OH, November 1-5, 1999.

Yu Y, Cheng G, Liu H, Zhang JB, Rubens DJ, Strang JG, Brasacchio R, Schell MC, Okunieff P, Messing E
"Advances in Image-Guided Prostate Brachytherapy"
Int'l. Conf. of Medical Imaging, Medical Physics and Precision Radiation Therapy, Guangzhou, China, October 4-6, 1999.

Selected Courses at the University of Rochester

Acoustic Waves (ECE433). Acoustic wave motion, energy, and momentum. Transmission through infinite media and reflection from surfaces. Radiation from points, spheres, and pistons. Scattering in regularly and randomly organized media. Plane waves in uniform media and scattering by turbulence.

Digital Signal Processing (ECE446). Review of discrete-time linear systems and random processes, Z-transforms, difference equations, discrete Fourier analysis, circular convolutions, FFT algorithms, and optimum discrete-time filtering based on second-order satistical properties.

Image Processing (ECE447). Elements of image processing systems. Image model and imaging geometry. Image sampling and quantization. Two-dimensional Fourier transform and discrete Fourier and cosine transform. Image-compression models and information theory basics. Error-free and lossy image compression. Image enhancements and filtering. Image degradation models and image restoration techniques. Image segmentation and applications. VLSI design and implementation of image processing algorithms. Image analysis and computer-vision basics.

Pattern Recognition (ECE448). Statistical methods in pattern recognition. Bayes decision theory, hypothesis testing, linear classifiers, parameter estimation, feature selection, supervised and unsupervised learning/clustering. Applications from image recognition and image understanding. Hough transform. Texture modeling and image segmentation methods. Neural networks for pattern recognition.

Digital Video Processing (ECE449). Fundamentals of digital-video representation, filtering, and compression. Topics include popular algorithms for 2D and 3D motion estimation, object tracking, frame-rate conversion, deinterlacing, image enhancement, and the emerging international standards for image and video compression. Applications to digital TV, multimedia, video conferencing, videophone and mobile-image communications, advanced image-compression techniques such as entropy coding, subband coding, and object-based coding.

Biomedical Ultrasound (ECE451). The fields and materials basis for applications of high-frequency sound in diagnosis, therapy, and surgery. Macromolecular relaxation mechanisms for the absorption of sound, finite amplitude effects, sound propagation in tissue, scattering and interfacial phenomena, acoustic cavitation, thermal and nonthermal biological effects of ultrasound, and radiation diathermy.

Medical Imaging — Theory and Implementation (ECE452). Fundamentals of x-ray, ultrasound, and magnetic resonance imaging and instrumentation. Special attention is given to Fourier transform relations and reconstruction algorithms of x-ray, ultrasonic tomography, and magentic resonance imaging.

Reduction and Analysis of Noisy Data (ECE477). The basic ideas of sampling, statistics, inference, and deduction from noisy data. Basic properties of various distributions, testing of hypotheses, statistical inference, analysis of variance, regression analysis, curve-fitting and non-parametric statistics. Problems and examples drawn from situations of interest in such areas as biomedical ultrasound materials testing. Major emphasis on appropriate use of statistical measures.

Continuum Mechanics (ECE444). The mechanics of continuous media. Introduction to tensors. Study of stress and strain. Constitutive laws for solids and fluids. Balance of mass, momentum, angular momentum, and energy. Entropy production.

Wave Propagation in Elastic Media (ME 446). Physical phenomena (reflection, dispersion) and mathematical techniques (Green's function, Fourier analysis, stationary phase) are studied for waves on strings. Concepts are then used to study waves on infinite, semi-infinite, and layered structures and waves in layers and cylinders.

All courses are not offered each semester. Some courses have prerequisites. See official University of Rochester bulletin for exact course information.

Patents and Software

The RCBU is working on novel concepts in ultrasound research on a continuous basis. A collection of patents and software programs that originated at the Center are summarized on the next few pages. For more information, technology transfer arrangements, or licensing agreements for a specific patent contact the Center office, the University of Rochester Technology Transfer office at (716) 275-3998, or as otherwise indicated.

System for Model-Based Compression of Speckle Images

Ultrasound images contain speckle. These high-spatial patterns are ill suited for compression using conventional techniques, particularly by JPEG, which is designed for photographic images with regions of smooth or negligible intensity variations. Conventional compression techniques fail to provide high quality reproductions with high-compression ratios. This combination is desirable for telemedicine and other applications where the available bandwidth or storage constraints create a need for high quality and high compression of ultrasound images. U.S. Patent No. 5,734,754 issued March 31, 1998, describes a system for compression of speckle images.

Linear and Nonlinear Acoustic Field Propagation Software

A computational model for the nonlinear propagation of acoustic beams has been developed. The physical effects of diffraction, absorption, dispersion, nonlinearity, and planar reflection and refraction are accounted for in an accurate and efficient manner. Descriptions of the novel algorithms accounting for these physical effects have been presented in a series of publications. The model has been compared successfully with theoretical and experimental results. The model has also been used to make predictions about the *in-vivo* performance of biomedical ultrasonic imaging devices and lithotripters. Finally, the model is currently being extended to consider non-axially symmetric source propagation in phase-aberrate media.

Blue Noise Mask

Medical images are sometimes printed on devices that have limited output states. For example, laser printers can render black or white but not shades of gray. Halftone methods render gray as patterns of black and white dots. The Blue Noise Mask is a halftone screen method for digital or photographic rendering of images. The Blue Noise Mask produces the fatest possible rendering of medical images with an artifact-free halftone pattern. The fax transmission of medical images can also be made faster and with higher quality by utilizing the Blue Noise Mask and new tonefac algorithm. The Blue Noise Mask invention received numerous patents, including: U.S. Patent Nos. 5,708,518; 5,726,772; 5,111,310; 5,477,305; and 5,543, 941. This patented technology has been accepted by over 15 U.S. companies and organizations including: Hewlett-Packard, Tektronix, and Research Corporation Technologies. For further information contact Eugene Cochran, Research Corporation Technologies, at (520) 748-4461.

Thin-Film Phantoms and Phantom Systems

Phantoms for testing and measuring the performance of ultrasonic imaging systems have regions of precisely controlled scattering or echogenicity which contain subresolvable scatterers. The phantoms can reveal the combined influences of all the stages in the imaging chain in terms of modulations transfer function, and resolution limits as well as other artifacts and defects in the system such as aliasing and frequency response which cannot be evaluated with conventional ultrasound phantoms. Halftone masks may be used to produce regions of precisely controlled subresolvable scatterers to be used for gray-scale evaluation of the imaging system by producing speckle images of different echogenicity. The thin-film sheets are thinner than the thickness of the ultrasonic beam and enable propagation of the beam in the plane of the sheets to the patterns which may be located at different depths. The sheets may be made of piezoelectric material having electrodes across which varying electrical signals are applied to displace the sheets, thereby stimulating movement of objects for Doppler measurements. U.S. Patent No. 5,756,875 was granted on May 26, 1998, to co-inventors Daniel B. Phillips and Kevin J. Parker.

Patents

An Inexpensive Wide-Bandwidth Hydrophone for Lithotripsy Research

Probing the acoustic field of extracorporeal lithotripters places several demands upon conventional hydrophones. 'Needle' hydrophones, while better able than 'membrane' hydrophones to withstand the cavitation-related damage inherent in lithotripter measurements, nevertheless lack their superior high-frequency response. Even the most popular of membrane hydrophones do not have sufficient sensitivity at high frequencies to resolve the rapid risetimes (1-20 ns) of waveforms which may occur at a lithotripter focus. To overcome these limitations, we have developed a membrane-type hydrophone which costs hundreds (not thousands) of dollars and has disposable active elements which can be replaced easily when damaged. These elements, of 6-mm-thick PVDF copolymer film, incorporate an electrode pattern which assures identical sensitivity from one element to the next, obviating the need for recalibration after replacement of the element. On-board conditioning electronics increase the effective bandwidth of the hydrophone to over 125 MHz and provide clipping of the undesirable electromagnetically induced transients of spark-discharge lithotripters. For further information, contact Carr Everbach at (215) 328-8079.

Apparatus for Bone Suface-Based Registration

A novel technique has been developed that could be used for neurosurgical and other applications. The device is entitled "Apparatus for Bone Surface-Based Registration of Physical Space with Tomographic Images for Guiding a Probe Relative to Anatomical Sites on the Image." The co-inventors of this technique are from Vanderbilt University and the University of Rochester: W. A. Bass, R. L. Galloway, Jr., C. R. Maurer, Jr., and R. J. Maciunas. U.S. Patent Application Serial No. 09/255,254 was filed February 22, 1999.

The Acoustic Filter

A system for reducing post-cardiopulmonary bypass encephalopathy due to microembolization of the brain of a patient with gaseous microbubbles (less than 40 microns in diameter). This invention is recommended for use during open-heart surgery with a cardiopulmonary bypass machine by passing a stream of blood from the patient through an ultrasonic traveling wave which propagates across the stream without reflection and sweeps the blood clean of the microbubbles without inducing blood-cell trauma. The blood passes through a chamber between an input port and a filtrate exit port. The microbubbles are carried by the traveling wave to a waste exit port in the chamber downstream of the input port. To prevent establishment of resonance conditions, reflections, and traveling waves, the chamber may be submerged in a liquid bath and a body of acoustically absorbed material disposed at an end of the chamber opposite to the end into which the ultrasonic beam is projected. U.S. Patent No. 5,334,136 has been issued to co-inventors Karl Schwarz, Richard Meltzer, and Charles Church. For more information, contact Karl Schwarz (716) 275-2381 or <Karl_Schwarz@URMC.rochester.edu>.

Multiple Function Infant Monitor

Piezoelectric polymer sheets made of PVDF, placed on the floor of the crib can output voltage that provides information about the heart and breathing rates of an infant in a crib. Using external detection and conditioning wtih the PVDF sheet, we have constructed a low-cost PVDF infant health monitor. The monitor can alert parents, with the aid of a remote alarm, to a declining heart and/or respiration rate indicative of the onset of sudden infant death syndrome. U.S. Patent No. 5,479, 932 has been issued for this invention. For more information, contact Carr Everbach (215) 328-8079.

Sonoelasticity Imaging Estimators

Sonoelasticity imaging is a novel method for assessing the stiffness, or elastic constants, of tissues. This combination of externally applied vibration and new Doppler imaging techniques was pioneered at the University of Rochester by Robert M. Lerner and Kevin J. Parker in 1986, following earlier work by Dr. Lerner on stiffness and compressibility of phantom materials and basic Doppler studies by Dr. Jarle Holen and colleagues. Since sonoelasticity imaging reveals patterns of vibrations within tissues, stiff tumors which may not be accessible to palpation can be imaged regardless of subtle changes in echogenicity. U.S. Patent No. 5,086,775, concerning time and frequency domain estimators for sonoelasticity imaging has been issued to co-inventors Ron Huang, Robert Lerner, and Kevin Parker.

Modal Analysis for Breast-Tissue Imaging

Beyond "sonoelasticity imaging" lies the realm of quantitative analysis of the low-frequency mechanical properties of tissues such as breast, prostate, liver, and other organs. Concepts such as modal patterns, shear-wave propagation, and eigenfrequencies can be combined with sonoelasticity imaging to charcterize tissue and assist in identification of abnormalities. U.S. Patent No. 5,009,848 concerning the method and apparatus for such analyses has been issued to co-inventors Ron Huang, Robert Lerner, and Kevin Parker.

Butterfly Search Technique

We have developed a novel, robust, and accurate blood-velocity estimation technique that is implemented by elementary digital signal processing without any transforms, correlation searches, SAD searches, matched filters or other intensive operations. In this technique, echoes from repeated firings of a transducer are resampled along a set of predetermined trajectories of constant velocity. These are called butterfly lines because of the intersection and crossing of the set of different trajectories at some reference range. The slope of the trajectory on which the sampled signals satisfy a predetermined criterion appropriate for the type of signal in question provides an estimate of the velocity of the target. The search for this trajectory is called Butterfly Search and is carried out efficiently in a parallel-processing scheme. The estimation can be based on the RF echo, its envelope, or its quadrature components. The Butterfly Search on quadrature components has shown outstanding noise immunity, even with relative few successive scan lines, and was found to out perform all the common time domain and Doppler techniques in simulations with strong noise. The Butterfly Search can overcome many disadvantages faced by the present-day techniques, such as the stringent tradeoff criterion between imaging resolution and velocity resolution implicit in Doppler techniques, and the need for computations. U.S. Patent No. 5,419, 331 has been issued to co-inventors Kaisar Alam and Kevin Parker.

'Smart' Endotracheal Tube

This invention relates to airway management devices for use in medical emergencies and more particularly to an endotracheal tube apparatus that generates a signal to ensure proper placement of the tube in a patient's trachea.

A flexible tube extends from the patient's oral or nasal cavity to a distal end within the trachea. A first ultrasound transducer connected to the tube near its distal end is in intimate contact with the forward inner wall of the patient's trachea at substantially its midpoint. A second ultrasound transducer is disposed in intimate contact with the forward outer skin surface of the patient's neck. Either the first or the second transducer can be a transmitter of an ultrasound signal provided by ultrasound transducer excitation, to which it is electrically connected. The other transducer serves as a receiver, which is connected to ultrasound detector situated externally to the patient.

Also, a process for monitoring the position of an endotracheal tube inserted in a patient utilizes an apparatus comprised of a flexible tube extending from the patient's oral or nasal cavity to a distal end and the first ultrasound transducer connected to the tube near its distal end. The first transducer is placed into contact with the forward inner wall of the trachea at substantially its midpoint, and a second ultrasound transducer is placed in intimate contact with the forward outer skin surface of the patient's neck at a position at least partially overlying the position of the first transmitter.

U. S. Patent No. 5,785,051 was issued July 29, 1998, to co-inventors Jack Mottley and Randy Lipscher for this invention.