

# Rochester Center for Biomedical Ultrasound 2003 Annual Report



<b>Contents</b>	<b>Page</b>
From the Directors . . . . .	2
About the Center . . . . .	3
<b>Research</b>	
Biophysical bases of pulsed ultrasound bioeffects and ultrasound-induced hyperthermic teratogenesis . . . . .	4
A generalized Kelvin-Voight viscoelastic constitutive model for soft tissue . . . . .	5
Effects of low frequency ultrasound on lung and intestine. . . . .	6
A study of ultrasound pulse duration and contrast agents on the threshold for cardiac stimulation. . . . .	7
Prognostic value of contrast stress echocardiography in patients with image quality too limited for traditional noncontrast harmonic echocardiography. . . . .	8
Investigation of the response of tissues to underwater sound. . . . .	10
The influence of contrast agent dose on ultrasound-induced arrhythmias . . . . .	11
Simulation of ultrasonic focus aberration and correction through human tissue. . . . .	11
Three-dimensional sonoelastography imaging of HIFU-induced lesions in bovine livers: A preliminary study <i>in vitro</i> . . . . .	12
Sonoelastic imaging of interference patterns for estimation of the shear velocity in homogeneous biomaterials . . . . .	13
People, Promotions, and Awards . . . . .	14
RUBI program. . . . .	14
Second International Conference on the Ultrasound Measurement and Imaging of Tissue Elasticity. . . . .	15
Selected Publications . . . . .	18
Selected Presentations . . . . .	20
Education . . . . .	21
Patents and Software. . . . .	23

# From the Directors

From Director Kevin J. Parker

The Rochester Center for Biomedical Ultrasound (RCBU) was pleased to co-sponsor the Second International Conference on Ultrasonic Measurement and



Imaging of Tissue Elasticity. Held in Corpus Christi, Texas, and gathering investigators from around the world, this event was organized jointly with Dr. Jonathan Ophir of the Ultrasonic Laboratory at the University of Texas Medical School at Houston. Details of the Second International Conference start on Page 15.

Elastography imaging is emerging as a promising and exciting new field with numerous approaches and clinical applications. Plans are underway for the Third

International Conference which is being held in Cumbria, United Kingdom, in October. More details about the upcoming conference can be found at the RCBU website ([www.ece.rochester.edu/users/rcbu/conference](http://www.ece.rochester.edu/users/rcbu/conference)).

The RCBU has, over the years, been a generating source of fundamental concepts and innovations. Many of today's developments — contrast agents and nonlinear techniques — have a scientific history that includes benchmark experiments at the University of Rochester. This year's annual report documents continued progress across broads fronts, from the fundamentals of tissue-ultrasound interactions to three-dimensional imaging.

We welcome your comments on any of the enclosed reports.

*Kevin J. Parker*

From Associate Director Deborah J. Rubens



The OB/GYN Ultrasound Unit continued to update its services in 2003. A new reporting system was installed which allows documentation of more detailed obstetrical anatomy as well as automatic faxing of reports to the referring physicians. Approximately 15,000 obstetric and gynecologic procedures were performed. In addition to diagnostic

sonograms, 500 amniocenteses, 56 chorionic villus samplings, 202 sonohysterograms and 5 fetal blood transfusions were performed. Our sonographers and physicians are completing training to obtain nuchal translucency measurements in the first trimester, as an early screen for fetal abnormalities. We anticipate having two new 4-D capable ultrasound machines within the next year.

The Department of Radiology is pleased to announce the reaccreditation of the Ultrasound unit by American Institute of Ultrasound in Medicine. In addition, the department purchased new ultrasound equipment, a GE LOGIQ9, a GE Logicbook (for use in Interventional Radiology), and two ACUSON Sequoias. The machines are up to date with the latest software including compound imaging, speckle reduction, and voice recognition on the LOGIQ9; and cadence, transmit and spatial compounding, and tissue equalization on the Sequoia. ALI mini PACS has been upgraded to allow dicom storage of cine loops and enhanced communication with Image Cast, which allows viewing of Radiology images throughout the Strong Health network.

Department of Urology: Prostate brachytherapy remained a major focus of urology and ultrasound. Thirty-seven brachytherapy procedures were performed in the operating room (and thus at least 37 preimplant ultrasounds performed for sizing purposes) The PIPER genetic algorithm was used in the vast majority. We eagerly await institution of the robotic brachytherapy project and the continuation of the prostate sonoelasticity study. Additionally, 307 prostatic ultrasounds and biopsies were performed by the Urology department in 2003, the overwhelming majority in the office with no sedation or full anesthesia.

*Deborah Rubens MD*

# About the Center

The 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 around 100 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, 3D sonoelastography, ultrasound and MRI fusion, scattering, bioeffects, therapeutics, advanced imaging systems, and other areas.





## Biophysical bases of pulsed ultrasound bioeffects and ultrasound-induced hyperthermic teratogenesis

by Morton W. Miller

This project concerned mechanical and thermal aspects of ultrasound-induced bioeffects. There were five peer-reviewed papers published in 2003; four of them concerned mechanical aspects, one thermal aspects.

**Mechanical Aspects.** There were two independent experiments testing the hypothesis that cell size was an important physical factor in ultrasound-induced hemolysis. In one study of 15 independent trials, the hemolytic effectiveness of a 1 MHz ultrasound exposure, comparing HIV macrocytic blood *in vitro* [mean corpuscular volume (mcv) = 115 mm<sup>3</sup>] against *in vitro* normal human blood [mcv = 85 mm<sup>3</sup>], was significantly different: 70.5 % hemolysis (HIV macrocytic blood) vs. 64.0 % (normocytic blood); the hemolytic ratio macrocytic/normocytic blood was 1.2. In a second study involving 6 independent trials, normocytic human blood *in vitro* (mcv = 89.5 mm<sup>3</sup>) showed significantly more ultrasound-induced hemolysis (1 MHz) than mouse blood *in vitro* (mcv = 49.0 mm<sup>3</sup>); the sonolytic ratio (human blood/mouse blood) was 1.5. The results of these two reports, involving a wide range of situation specific erythrocytic mcv's, supported the hypothesis.

Two related hypotheses were also tested. In the first, the hypothesis was supported that the amount of dissolved gas, expressed as the partial pressure of oxygen in the suspending medium, would have an effect on the amount of ultrasound-induced hemolysis in blood *in vitro* laced with Alunex®, an air-filled echo contrast agent. Whole human blood *in vitro* with a relatively high O<sub>2</sub> level had statistically significantly more 1 MHz ultrasound-induced hemolysis than blood with a relatively low O<sub>2</sub> level, with sonolytic effectiveness less at 2.2 and 3.5 MHz exposures. Passive cavitation detection (pcd) results, undertaken with Professor E C. Everbach (Swarthmore College,

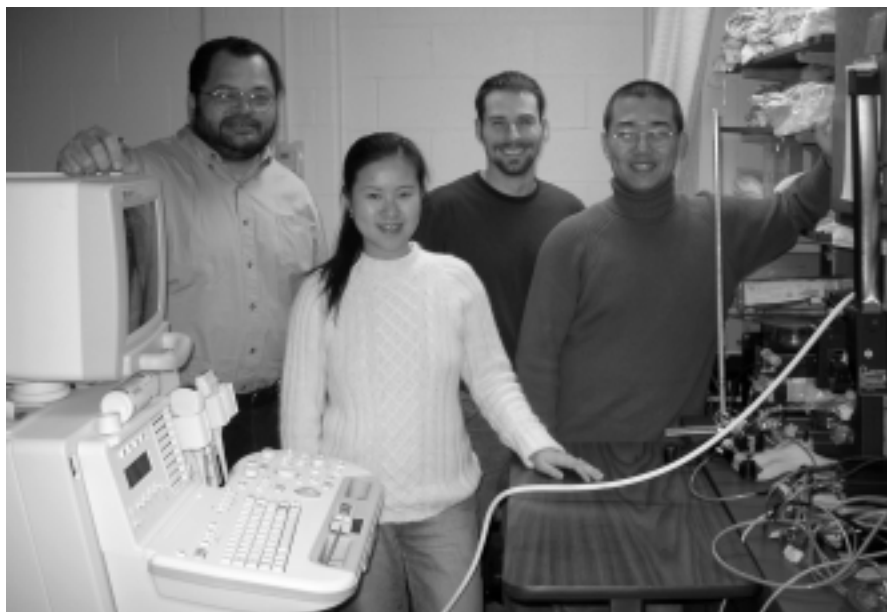
Swarthmore, PA; also a member of RCBU) indicated a linear relationship ( $r^2 = 0.99$ ) for hemolysis up to ~ 70 % and pcd values. In the second, the hypothesis was supported that the presence of an antioxidant (Trolox®) would be more susceptible to ultrasound-induced hemolysis by a cavitation mechanism because of an increased fragility of the erythrocytic membrane. Several years ago, a noted Canadian researcher (Barclay. *Can J Chem* 1993;71:1-16) proposed that the free radical quenching mechanism of antioxidants caused a “kinking” of the cellular membrane, thereby increasing its fragility. First, mechanical fragility tests supported the general hypothesis of increased fragility of whole human blood *in vitro* with Trolox® supplementation. Second, similar statistically significant results were obtained with 1 MHz insonation of whole human blood *in vitro* and Trolox® supplementation vs. non-Trolox supplementation. There was substantially less ultrasound-induced hemolysis at 2.2 and 2.5 MHz regimens. The data supported the hypothesis.

**Thermal Aspects.** An extended commentary was co-authored by Dr. W. C. Dewey (U. California San Francisco) and published in *UMB* (2003; 29:1653-1659) on a report by Herman and Harris (“Models and regulatory considerations for transient temperature rise during diagnostic ultrasound pulses (*Ultrasound Med Biol* 2002;28:1217-1224). The commentary shows that the thermal doses Herman and Harris consider as ineffective (i.e., “safe”) for producing hyperthermia-induce teratologic effects can be highly effective ones. In making this commentary, heavy reliance was made upon an earlier published critical review (*Int. J. Hyperthermia* 2002;18:361-384) by Miller, with collaboration from Drs. W. L. Nyborg (U. Vermont), Jacques Abramowicz (U. Chicago), Andrew Brayman (U. Washington), W. C. Dewey (University of California at San Francisco) and M. J. Edwards (University of Sydney), as reported in last year's RCBU annual report.



## A generalized Kelvin-Voigt viscoelastic constitutive model for soft tissue

by Lawrence S. Taylor, Deborah J. Rubens  
and Kevin J. Parker



Sonoelastography researchers: (left to right) Lawrence S. Taylor, Man Zhang (Maggie), Brian Porter, and Zhe Wu (Clark) in the laboratory .

Ultrasonic attenuation in the very soft tissues is known to follow an empirical equation with power law frequency dependence not explained by spring and dashpot viscoelastic models. In a recent paper by Szabo and Wu, (JASA 2000) a generalized Kelvin-Voigt three parameter viscoelastic model was derived which explains this power law when frequency is raised to a non-integer power,  $1 < \gamma < 2$ . A modified constitutive equation of their model is presented and the stress relaxation, creep compliance, impulse response and complex modulus functions are derived. These time-domain and frequency-domain relations are found to follow power laws with non-integer exponents equal to  $\gamma - 1$ . In order to validate the applicability of this model, viscoelastic testing was performed on bovine liver specimens. The derived theoretical responses for creep, stress relaxation and complex modulus are compared to experimental data. Model parameters are

extracted from the tests and the linear correlation coefficient is calculated to derive the goodness-of-fit. For the complex modulus the best fits were  $R^2 = 0.992$  and  $0.995$  for thermally ablated and normal samples respectively. Model parameters for the power law exponent,  $(\gamma - 1)$ , were in the range 0.17 to 0.29, which corresponds to the reported range of  $\gamma$  for liver tissue in the ultrasonic literature.

It is believed that this model will be useful in various dynamic elasticity techniques when viscoelastic parameters need to be extracted and when estimates of material properties need to be extended to a range outside that which can be easily tested. Tests run on the same tissue will be needed to determine if the correspondence between the value of  $\gamma$  for MHz range attenuation, low frequency (0.1 - 25 Hz) cyclic testing, and stress relaxation (time domain) tests are merely coincidental.



## Effects of low frequency ultrasound on lung and intestine

by Diane Dalecki, Sally Z. Child, Carol H. Raeman, and Adam Brod

Low frequency ultrasound has potential applications in both therapy and sonar imaging. However, much needs to be understood on the interaction of low frequency ultrasound with biological tissues. The objective of several recent studies in our lab has been to determine the thresholds for ultrasound-induced damage to murine lung and intestine for frequencies ranging from ~20–500 kHz. In these studies, adult mice were anesthetized and exposed to ultrasound in a tank of degassed, deionized water. All animal protocols were approved by the University Committee on Animal Resources. Ultrasound pulse durations were 1 ms with a pulse repetition frequency of 10 Hz and frequencies investigated ranged from ~20–500 kHz.

Thresholds for lung hemorrhage were determined for five frequencies (27, 50, 120, 200, 500 Hz). For exposures above threshold, lung damage appeared as red hemorrhagic areas. Thresholds increased with increasing frequency and ranged from 0.08 MPa at 27 kHz to 0.6 MPa at 500 kHz. Thresholds for intestinal damage were determined for frequencies of 27, 120, and 200 kHz. Damage appeared as both petechia and bleeding into the intestinal lumen. Again, pressure thresholds increased with increasing frequency and ranged from 0.2 MPa at 27 kHz to 0.4 MPa at 200 kHz. When microbubbles (Optison™) were present in the vasculature, the extent of intestinal damage increased significantly.

Low frequency pulsed ultrasound can produce damage to mammalian lung and intestine. For each frequency investigated, thresholds for lung damage were lower than thresholds for intestinal damage. In studies of both lung and intestine, the threshold for ultrasound-induced damage increases with increasing frequency.



Adam Brod prepares for low frequency ultrasound experiment.



### A study of ultrasound pulse duration and contrast agents on the threshold for cardiac stimulation

by Claudio Rota, Carol H. Raeman, Sally Z. Child and Diane Dalecki

Early evidence that the mechanical energy of a sound wave can be used to generate cardiac electrical activity was reported in the early 1990's. At that time, initial animal experiments demonstrated that exposing the heart to acoustic pulses from either a lithotripter or an ultrasound source produced premature ventricular contractions (PVCs). Recently, our lab has demonstrated that cardiac tissues are far more sensitive to ultrasound stimulation when gas microbubbles (e.g., contrast agents) are present in the vasculature of the animals.

The use of ultrasound contrast agents in diagnostic ultrasound is a well-established method for obtaining images of enhanced clinical quality. Yet, while a great deal is understood about the physical and rheological properties of these agents, there continue to be concerns of potential cardiovascular side effects when these microbubbles are subjected to ultrasound. Several years ago, the American Institute of Ultrasound in Medicine summarized the current status of knowledge regarding the bioeffects of diagnostic ultrasound, both with and without contrast agents (*J. Ultrasound Med.* 19; 2000). Since then, reports have indicated that the heart is inherently more sensitive to mechanical stimulation when bubbles are present in the

vasculature. Figure 1 shows the generation of two PVCs in a mouse that was injected with a contrast agent and subsequently exposed to 1 MHz ultrasound pulses of 10  $\mu$ s duration and peak negative pressure amplitudes of 1.5 and 2.0 MPa (upward arrows).

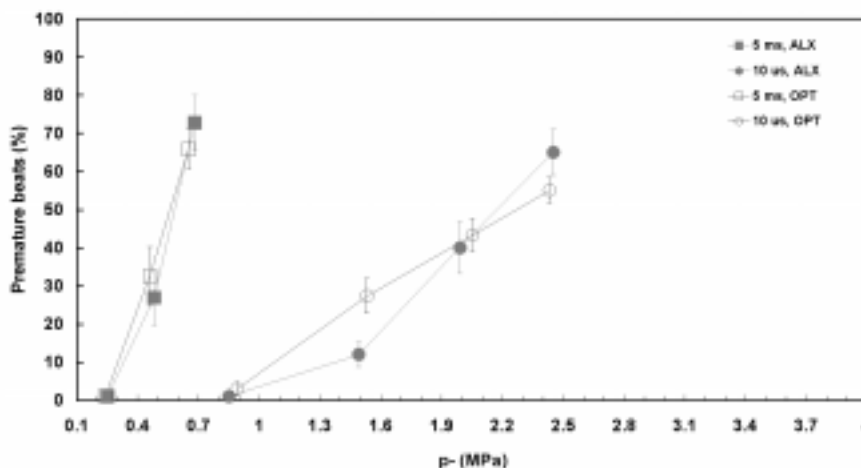
In order to better understand this phenomenon, we conducted experiments to investigate the effects of pulse duration and type of ultrasound contrast agent on the threshold for ultrasound-induced arrhythmias. All animal protocols were approved by the University Committee on Animal Resources. In these experiments, mice were given two injections of either one of two types of contrast agents (Albunex® and Optison®) at a dose of 0.1 mL/bolus. Acoustic exposures were performed with a focused 1.2 MHz ultrasound source and pulse durations of either 5 ms or 10 ms. Each exposure consisted of a single pulse of ultrasound.

The results of these studies are shown in Figure 2. PVCs were produced with both air-filled and perfluoropropane-filled contrast agents (Albunex® and Optison®, respectively), and the threshold for the effect was the same for each contrast agent. This suggests that the different chemical composition of the two suspensions does not produce a significant difference in the sensitivity of the heart to the ultrasound stimulus. In addition, the data demonstrate that the threshold for premature beats is dependent upon pulse duration. For each contrast agent investigated, the threshold was lower for longer pulse durations.

Figure 1



Figure 2





### **Prognostic value of contrast stress echocardiography in patients with image quality too limited for traditional noncontrast harmonic echocardiography**

by Naoyuki Yokoyama, M.D., Karl Q. Schwarz, M.D., FACC, Sherry D. Steinmetz RDMS, Xiang Li, and Xucai Chen, Ph.D.

Exercise with pharmacologic stress echocardiography has become one of the most widely used tests for the diagnosis of coronary artery disease and for assessment of prognosis in patients with known coronary artery disease. The sensitivity of stress echocardiography for detecting coronary artery disease has been reported to be in the 75% to 97% range with test specificities in the 64% to 91% range. However, stress echocardiography is quite operator- and patient population-dependent. Regarding the echocardiographic imaging phase, previous studies demonstrated that the images at rest or after stress were inadequate for analysis in 5% to 33% of patients referred for stress echocardiography.

Left ventricular (LV) opacification with a transpulmonary contrast agent can improve echocardiography imaging in many patients. There have been a number of studies addressing the safety, feasibility, and diagnostic usefulness of these agents. Thus, use of contrast agents for image enhancement improves endocardial definition during stress echocardiography and allows the testing of patients with poor noncontrast echocardiographic image quality. However, the technique has not been validated using clinical outcome measures.

The aim of the study was to determine the prognostic significance of contrast stress echocardiography (CSE) for predicting cardiac events for patients with image quality too limited for traditional noncontrast harmonic echocardiography. The study focused on patients with limited echocardiographic image quality within a group of patients referred for stress echocardiography. Thus, the population of this study has not been investigated fully.

From June 1998 through October 2000, clinically indicated stress echocardiography was performed on 3,142 patients (exercise stress for 2,244 and dobutamine stress for 898) at the echocardiography laboratory in Strong Memorial Hospital (Rochester, NY). Of the 3,142 patients, 415 (13.2%) had CSE because of nondiagnostic or limited diagnostic noncontrasted resting harmonic two-dimensional images. Of the 415 patients, 2 were excluded from analysis because an investigational contrast agent was used. The criterion for limited diagnostic images was the nonvisualization of at least 2 adjacent myocardial segments not correctable by using alternative acoustic windows (including nonstandard windows).

Nondiagnostic resting images were those with at least 3 pairs of nonvisualized segments. This definition agrees with the definitions used by recent published studies. Patient demographics, clinical history, and cardiovascular risk factors were collected at the time of CSE for the 413

patients. These were stored in a database system (Pronto, Clinical Insight, Canandaigua, NY) at the University of Rochester.

The clinical outcome variables were collected using mailed or telephone questionnaires under the auspices of the institutional cardiovascular outcomes monitoring program after a minimal interval of six months. The research subjects review board at the University of Rochester approved the study protocol and informed consent was possible for 332 (80.4%) of the 413 eligible patients. Of those who were contacted, 49 declined to participate in the follow-up study. Thus, the study group consisted of 283 patients. Excluding the patients who declined to participate, follow-up rate was 77.7%

The results of this study demonstrated that CSE contributes significantly to the stratification of cardiac risk for patients with image quality too limited for traditional noncontrast harmonic echocardiography. To our knowledge, the prognostic significance of CSE has not been shown previously in a similar patient population.

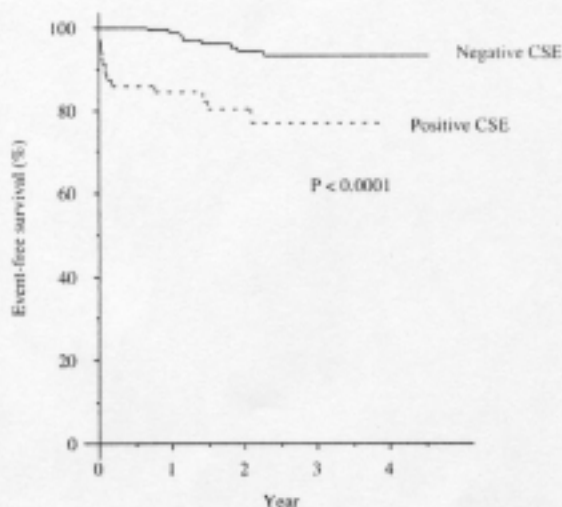
**Image Quality.** A significant number of patients referred from stress echocardiography have suboptimal images. However, intravenous echocardiographic contrast agents capable of producing LV opacification can be useful in delineating endocardial borders for these patients. Rainbird *et al.* have shown that the use of the intravenous contrast echocardiographic contrast agent dring dobutamine stress echocardiography improved wall segment visualization and image quality at rest and at peak stress, resulting in significantly improved confidence of interpretation. In the current study, contrast enhancement resulted in improved endocardial visualization for almost all cases. Only 7 of the 283 study patients (2.5%) with limited non-contrast images were nondiagnostic because of sub-optimal images. Therefore, diagnostic CSE information was obtained in more than 95% of patients even though they had noncontrast harmonic images too limited for traditional harmonic stress echocardiography.

**Prognostic Significance of CSE for Ischemia.** Previous studies have demonstrated that stress echocardiography is a strong independent predictor of future cardiac events. In this study, the negative predictive value of CSE for cardiac events was 95.5%.

The results of this study by Pingitore *et al.* showing a similar prognostic value of pharmacologic stress echocardiography without contrast agent for patients with optimal image quality. This study revealed that a negative CSE conferred an excellent outcome for patients with image quality too limited. Indeed, several studies without contrast agent for patients with optimal image quality found that a negative stress echocardiographic evaluation may also be prognostically helpful because it predicts a low cardiovascular event rate of 0.9% per person-year.

This study revealed that negative stress echocardiographic examination with contrast agent is also highly predictive of a good outcome, even in patients with poor noncontrast harmonic image quality.





**Figure 1** Kaplan-Meier curves for survival free of cardiac events for patients with negative contrast stress echocardiographic (CSE) result and in patients with positive CSE result for ischemia.

**Table 2** Univariate predictor of cardiac events

Variable	RR (95% CI)	P Value
Wall-motion abnormality at rest	5.2 (2.3-12)	.0001
Positive CSE	4.7 (2.1-11)	.0002
History of previous cardiac revascularization	4.1 (1.8-9.2)	.0011
Previous MI	3.2 (1.2-7.4)	.0186
Sex (male)	3 (1.3-8.4)	.0110
Rest LVEF	0.94 (0.92-0.97)	.0005

CI, Confidence intervals; CSE, contrast stress echocardiography; LVEF, left ventricular ejection fraction; MI, myocardial infarction; RR, risk ratio.

**Table 3** Multivariate predictor of cardiac events

Variable	RR (95% CI)	P value
Positive CSE	3.7 (1.6-8.7)	.0019
Rest LVEF	0.95 (0.92-0.98)	.0053

CI, Confidence interval; CSE, contrast stress echocardiography; LVEF, left ventricular ejection fraction; RR, risk ratio.

**Predictors of clinical outcome.** This study revealed that independent predictors of cardiac events were positive CSE, rest ejection fraction, wall-motion abnormality at rest, history of cardiac revascularization, previous myocardial infarction, and sex. As shown in previous studies for patients with optimal image quality and without contrast agent use, these parameters are related to cardiac death, myocardial infarction, and cardiac revascularization. In this study, contrast echocardiographic parameters were better predictors than clinical variables for advance cardiac events. This was the first study using CSE to confirm these results.

**Limitations.** The follow-up rate was relatively low (77.7%). However, the clinical characteristics of the patients who were lost to follow-up or declined to participate in the follow-up study were similar to those of the study population (Table 1). There were no significant differences in any of the parameters considered between the two groups. Therefore, it is highly unlikely that the omission of these patients would alter this study's primary conclusion that a negative CSE predicts the absence of cardiac events.

The cardiac events rate was relatively low (8.5%). The patient population in this study had a known high pretest incidence of coronary artery disease, with a 36.6% incidence of prior cardiac events (including myocardial infarction and previous cardiac revascularization) and a 26.4% incidence of wall-motion abnormalities at baseline. The overall low events rate in these patients with known coronary artery disease is consistent with the literature for patients treated medically.

**Conclusions.** Patients with limited and diagnostic harmonic two-dimensional echocardiographic imaging may be studied by CSE with a high expectation of diagnostic results (>95%). CSE can successfully predict cardiac events in these patients. The prognostic value of a negative CSE examination for predicting cardiac events is excellent.



**Investigations of the response of tissues to underwater sound**

by Diane Dalecki, Sally Z. Child, Carol H. Raeman, Claudio Rota, Yixen Ren, Sheryl M. Gracewski, Edwin L. Carstensen

Investigations are underway in our laboratory to study the effects of underwater sound on biological tissues. These projects are supported by the U. S. Navy and have relevance to the safety of divers and marine mammals exposed to sonar fields. Frequencies of interest span the large range from ~100 Hz to ~200 kHz. These investigations aim to develop a greater understanding of the response of biological tissues to underwater sound necessary for the development of guidelines for the safe use of sonar.

The biological effects of underwater sound are most pronounced in and near tissues that contain resonant gas bodies.

Through several different avenues, we have shown that murine lung and intestine respond to low frequency acoustic fields as resonant structures. Within our laboratory, two, specialized exposure systems are available for the generation of low frequency (100–3000 Hz) underwater sound fields. Measurements of acoustic scattering near murine lung demonstrated a pronounced resonance at ~335 Hz for adult mice. Measurements of the displacement amplitudes of lung, using a pulse-echo ranging technique, were consistent with observations made from acoustic scattering measurements. Similar measurements of acoustic scattering with young mice and adult rats indicated that the resonance frequency of lung scales approximately inversely with the cube root of body weight. Exposure to low frequency underwater sound at the resonance frequency of the lung can produce damage to the lung and surrounding tissues such as the liver. 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. For adult mice exposed at the resonance frequency, the threshold for

lung damage is ~187 dB re 1  $\mu$ Pa. The intestine also contains gas and can also respond as a resonant structure in an underwater sound field. Since the volume of a gas body in the murine intestine is less than the lung volume, the resonance frequencies of intestinal gas bodies investigated were within the frequency range of ~700-2500 Hz. Damage to the gas-filled intestine produced by exposure at the resonance frequency, however, was significantly less pronounced than that observed with the lung.

Work continues on several paths of investigation. Ongoing projects continue to focus on determining the mechanism of action for lung damage in response to exposure to low frequency underwater sound. Computa-



Bioeffects laboratory investigators: (left to right) Claudio Rota, Adam Brod, Yixen Ren, Carol Raeman, Sally Child, and Diane Dalecki.

tional efforts aim to model the response of resonant gas bodies exposed to underwater sound. Studies are also underway to characterize the response of intestine and heart to underwater sound fields when microbubbles are present in the vasculature. Additional studies are characterizing the response of tissues to underwater sound fields for frequencies ranging up to ~200 kHz.



### The influence of contrast agent dose on ultrasound-induced arrhythmias

by Claudio Rota, Carol H. Raeman, Sally Z. Child, and Diane Dalecki

Recent evidence from our laboratory has shown that the presence of an ultrasound contrast agent in the vasculature can enhance the production of ultrasound-induced premature cardiac beats. In this study we tested the effect of contrast agent dose on the effectiveness of the ultrasound pulse. Four doses of a perfluorocarbon-based ultrasound contrast agent (Optison®) were used (100, 10, 3, and 1  $\mu\text{L}$ ) and two boluses of the agent were given to each animal, prior to and during ultrasound exposure. For each contrast agent dose, a study was performed to determine the acoustic pressure threshold for the production of a premature beat. In each study, each exposure consisted of a single 10 ms pulse of ultrasound. Peak underated negative pressures ranged between 0.8 and 2.4 MPa.

For the range of contrast agent dose investigated, the threshold for the generation of premature beats was independent of contrast agent dose. That is, in spite of a 100-fold decrease in contrast agent dose, the total number of ultrasound-induced arrhythmias were comparable for similar pressure amplitudes. Thus, the lowest dose of Optison® was equally effective as the highest dose. At acoustic exposure levels below the current maximum outputs of clinical devices, we found evidence of cardiac hemorrhage in most of the animals that were injected with the contrast agent, but no damage among those animals that did not receive the contrast agent. However, decreasing the dose of Optison® produced a significant reduction in the size of the hemorrhagic area. The lowest dose produced no visible cardiac damage.

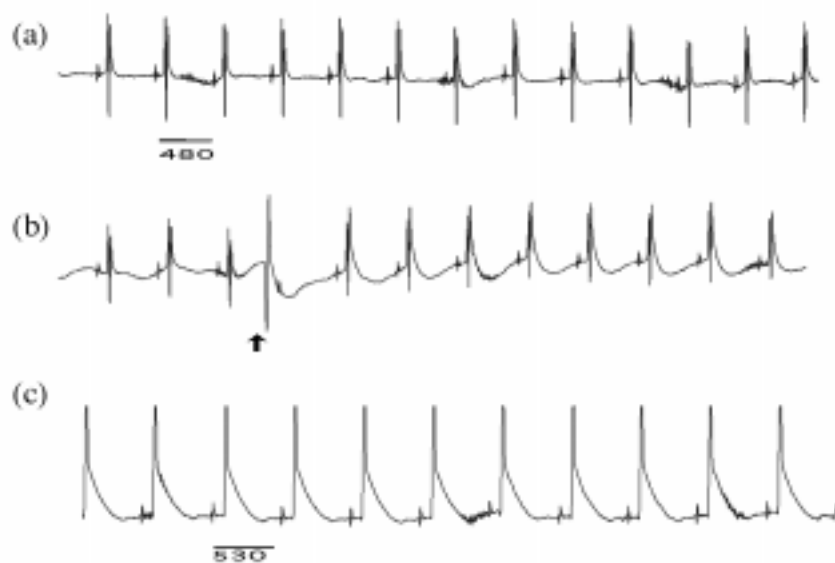
Finally, electrophysiological data collected from these experiments showed that the delivery of ultrasound pulses could progressively deteriorate the normal morphology of the mouse ECG. Typical changes included a broader and elevated QRS complex as well as baseline alterations. An example is shown in Figure 3, where the ECG trace prior to ultrasound exposure (a) is compared to the ECG trace following the delivery of the first pulse (b) and after 40 pulses of ultrasound (c). Numbers indicate the time interval between atrial depolarization (in milliseconds). The possibility that cardiac damage was responsible for these morphological changes in the surface ECG of the animal is currently under investigation.

### Simulation of ultrasonic focus aberration and correction through human tissue

by Makoto Tabei, T. Douglas Mast, Robert C. Waag.

Ultrasonic focusing in two dimensions has been investigated by calculating the propagation of ultrasonic pulses through cross-sectional models of human abdominal wall and breast. Propagation calculations used a full-wave k-space method that accounts for spatial variations in density, sound speed, and frequency-dependent absorption and includes perfectly matched layer absorbing boundary conditions. To obtain a distorted receive wavefront from a virtual array through the tissue path, as well as uncompensated focusing, focusing that employed time-shift compensation and time-shift compensation after backpropagation was investigated in both transmit and receive, and time reversal was investigated for transmit focusing in addition. The results indicate, consistent with measurements, that breast tissue causes great focus degradation than abdominal wall. The investigated compensation methods corrected the receive focus better than the transmit focus. Time-shift compensation after backpropagation improved the focus from that obtained using time-shift compensation alone, but the improvement was less in transmit focusing than in receive focusing. Transmit focusing by time reversal resulted in lower sidelobes but larger mainlobes than the other investigated transmit focus compensation methods.

Figure 3





### Three-dimensional sonoelastography imaging of HIFU-induced lesions in bovine livers: A preliminary study *in vitro*

by Man Zhang, Lawrence S. Taylor, Deborah J. Rubens, Kevin J. Parker

High intensity focused ultrasound (HIFU) is a non-invasive surgical tool which produces tissue coagulation necrosis for killing the malignant tumor within a well-defined volume in the tissue. As a real time lesion monitoring method, sonoelastography was investigated for the visualization of HIFU-induced lesions in the bovine liver *in vitro*. Tissue samples (4x4x4 cm<sup>3</sup>) were cut from fresh bovine liver and then degassed overnight. Lesions were created in tissue samples by a HIFU transducer. The compounding lesion size was determined by the number of individual lesions treated with identical HIFU exposure dose. Three-dimensional sonoelastography images were acquired from the liver-embedded agar phantom. Each lesion is displayed as a dark deficit area surrounded by a bright green background in the image. After imaging, lesions were examined by gross pathology to verify their size, shape and volume.

The gross pathology results showed that HIFU-induced compounding lesions were relatively uniform, palpably harder and brighter than the normal tissue and almost ellipsoidal in shape. The mean volumes of the three 2x2 compounding lesions and the two 3x3 lesions measured by fluid displacement were 2.3 cm<sup>3</sup> and 6.2 cm<sup>3</sup>, respectively. As the smallest lesion in the test, a 1x2 lesion with 1.5 cm<sup>3</sup> in volume was also successfully detected by 3D sonoelastography imaging. In the sonoelastography images, the edge of each lesion was a little ambiguous in a range of ~3 mm. When only the darkest region in the image was delineated as the lesion, the mean sonoelastography volume of the 6 lesions was 83% of the volume measured by fluid displacement. Good correlation between the lesion dimensions determined from sonoelastography images and gross pathology was also found. This study demonstrates that sonoelastography is a potential real-time method to accurately monitor the HIFU therapy of cancerous lesions.

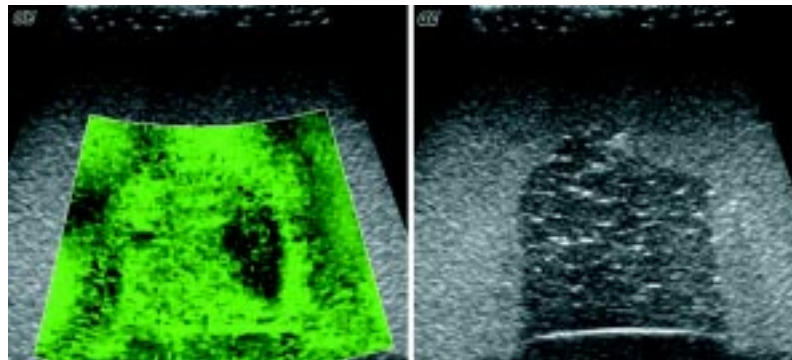


Figure 1. 2x2 HIFU-induced lesions



Figure 2. 3x3 HIFU-induced lesions



## Sonoelastic imaging of interference patterns for estimation of the shear velocity in homogenous biomaterials

by Zhe Wu, Lawrence S. Taylor, Deborah J. Rubens, Kevin J. Parker

Two novel approaches are proposed to quantitatively measure the shear wave velocities in homogeneous biomaterials. In one approach, two shear wave sources are placed on the opposing two sides of an elastic sample. The wave sources are driven by the same monochromatic signal. The two trains of shear waves from the sources interfere with each other to form standing wave patterns. The standing wave patterns are visualized by sonoelastography.

It is proven that the spacing between the standing wave patterns equals half of the shear wavelength. Therefore, the shear velocity can be obtained by taking the product of the wavelength and the frequency. This approach is referred to as the static pattern approach.

An alternate approach is to drive the two vibration sources at slightly different frequencies,  $f$  and  $f + \Delta f$ , respectively. In this case, the interference patterns no

longer remain stationary. If  $\Delta f$  is much smaller than  $f$ , it can be proven that the apparent velocity of the moving patterns is  $(\Delta f/2f)V_{\text{shear}}$ , where  $V_{\text{shear}}$  is the shear velocity in the medium. Since the apparent velocity of the moving patterns can be readily measured by analyzing the video sequence, the shear velocity can be obtained thereafter. This approach is referred to as the moving pattern approach.

These two approaches are validated against the conventional shear wave time-of-flight approach.

A 5% gelatin phantom, 6 x 8 x 12cm in size approximately, is used as the testing sample. Two bimorph piezo applicators [1cm x 2.5cm chips] are used as the vibration sources. Two "static pattern" experiments at 180Hz and 200Hz (Figure 1) yield shear wave speeds of 1.399m/s and 1.404m/s respectively. One "moving pattern" experiment at 200Hz yields the shear wave speed of 1.44m/s. The time-of-flight approach measures the shear wave speed to be 1.398m/s.

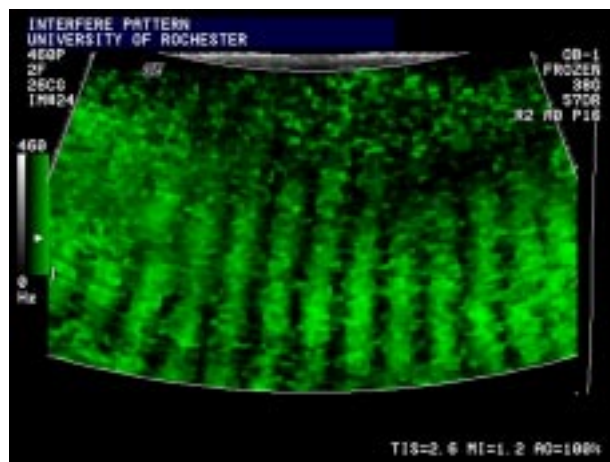


Figure 1. Sonoelastography image of shear wave interference pattern on GE Logiq 700. The sample is a 5% gelatin phantom. Both sources vibrate at 200 Hz. The peak vibration amplitude in the direction of the ultrasound wave is mapped to a green scale.



# People, Promotions, and Awards

**Diane Dalecki** and Denise Hocking (Department of Pharmacology and Physiology and Department of Biomedical Engineering) received a two-year grant from the NIH to investigate mechanisms of tissue remodeling with ultrasound.

**Deborah Rubens** and **John Strang** spoke at Confluence 2003 International Imaging Update in Mumbai, India. Dr. Rubens presented Renal Transplant Evaluation, Liver Doppler Evaluation, and Ultrasound Biopsy. Dr. Strang presented Multidetector CT-Angio, MRI of Thorax & Abdomen, Focus on Renal Angio-Techniques, and Advanced MRI Techniques and Applications.

**Susan Voci** was invited by Case Western Reserve University to present US Evaluation of the Thyroid, which she also presented at the 2003 Annual Roentgen Ray Conference in San Diego. Dr. Rubens presented Venous Doppler of the Extremities at ARRS as well.

At the 10th Congress of the World Federation for US in Medicine and Biology held in Montreal in June, Dr. Rubens gave a Meet-the-Professor session entitled Interventional Ultrasound Head to Toe and a lecture on Acute Hepatobiliary Problems.

In October, Drs. Rubens, Strang, and **Jean Cullinan** presented multiple lectures and “Hands-On” sessions at the 8th Annual US Imaging 2003 Conference held in Las Vegas. NIH honored the hard work of Dr. Rubens, **Kevin Parker, Larry Taylor**, and graduate students **Brian Porter, Maggie Zhang, and Zhe Wu (Clark)** with the award of a four year grant to further their research efforts with 3D Sonoelastography Imaging for Prostate Cancer. This grant also supports the work of GE collaborators Anne Hall from GE Medical Systems and Kai Thomenius at GE CR & D. Also in October, Dr. Rubens was elected a fellow in the Society of Radiologists in Ultrasound (SRU).

At this past December’s RSNA convention in Chicago, Dr. Voci, along with Drs. Strang & Rubens, and **Nancy Carson**, Chief Sonographer at URMU taught a hands-on Vascular course and Dr. Rubens and Vikram Dogra gave a refresher course entitled “Doppler US of the Acute Scrotum”.

Dr. Rubens, in collaboration with Dr. Dogra of Case Western Reserve University, recently released *Ultrasound Secrets* at RSNA in Chicago this past December. This book included chapters written by both doctors as well as Drs. Voci, **Jean Cullinan, Patrick Fultz, John Strang, David Dombroski, Amy Harrow, David Lee, Andrea Zynda-Weiss, Labib Syed, Ryan Lee, William Kuo, Christopher Bang, and Marat Bakman** as well as five of the URMU sonographers; Nancy Carson, **Mark Hall, David Schmanke, Jodie Crowley, and Hamad Ghazle**.

**Yan Yu** received a grant to continue ultrasound research: Amersham Health #02-ECH-001 “Ultrasound-based seed detection for prostate brachytherapy” (\$56,063), P.I. (Co-P.I. Dr. **Ralph Brasacchio**.)

Dr. Yu was also the recipient of: NCI R01 CA91763: “Robot-Assisted Platform for Intratumoral Delivery (RAPID)” (\$2,521,553), P.I. Major goal: To develop a Robot-Assisted Platform for Intratumoral Delivery (RAPID) for integrated treatment of prostate cancer, and to demonstrate the safety, efficacy and clinical effectiveness through a series of pre-clinical and clinical studies. (Other investigators include Drs. **Edward Messing, Okunieff, Deborah Rubens, John Strang**, Ng.)

**Feng Lin** and **Robert Waag** had a patent allowed: “Ultrasonic distortion compensation using blind system identification,” Serial No. 10/025,817 November 2003. Additionally, Robert Waag and Jeffrey P. Ashthimer have a patent in process, “Ultrasonic aberration compensation using statistical estimation of parameters in a linear filter propagation path model”.

## RUBI Program

Summer of 2003 marked another successful year of the University of Rochester RUBI Program. The RUBI Program—Research for Undergraduates in Biomechanics and



Imaging, is sponsored by the National Science Foundation REU Program. The Rochester RUBI Program is designed to provide summer research experiences in imaging and biomechanics for select undergraduates from across the nation. Center Members Amy Lerner and Diane Dalecki direct the RUBI Program. Students work directly with faculty members and participate in a variety of educational activities related to the integration of imaging and biomechanics. In 2003, Center Members Diane Dalecki, Amy Lerner, Kevin Parker and Larry Taylor participated as faculty mentors. Examples of student projects from these labs are given below. In 2004, the program aims to expand to RUBIN Program – Research for Undergraduates in Biomechanics, Imaging, and Neuroengineering.

Adam Brod (Dalecki mentor) “Thresholds for intestinal hemorrhage from exposure to 27 kHz ultrasound.” Ling Dong (Lerner mentor) “Modeling of a human cadaveric knee from magnetic resonance imaging (MRI).” Linsey Phillips (Parker/Taylor mentor) “Development of HIFU lesions and preliminary investigation into lesion imaging using sonoelastography.”





# Second International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity

Once again the RCBU was proud to co-sponsor the Second International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity. Dr. Jonathan Ophir from the Ultrasonics Laboratory at the University of Texas Medical School at Houston hosted the event in Corpus Christi, Texas. Researchers from all over the world attended the event. Drs. Ophir and Parker would like to thank the delegates, the reviewers, and session chairs; as well as Mannelle Price and Pam Clark for all of their hard work in helping to organize the conference and to Karen Ophir for preparing the posters, proceedings booklet, and other graphic design elements that helped make the conference a success.

## **Session A-1: Bench-Top Methods for Measuring the Elastic Properties of Tissues (In Vitro)**

**Chair: JM Rubin, USA; Co-Chair: T Krouskop, USA**

Bench Top Torsion Tests for Testing Tissue Viscoelastic Properties. E. Mazza. ETH Zurich, Swiss Federal Institute of Technology, Zurich, Switzerland.

Transient Elastography for Viscoelastic Measurements of Tissues. M. Fink. Laboratoire Ondes et Acoustique, E.S.P.C.I., Paris, France.

Indentation/Nano-Indentation and Vibration Tests in Soft Tissues. T. Krouskop. The University of Texas Medical School, Houston, TX. Baylor College of Medicine, Houston, TX, USA.

Frequency-Dependent Characterization of the Viscoelastic Properties of Soft Tissues. M.Z. Kiss. The University of Wisconsin-Madison, Madison, WI, USA.

## **Session A-2: Methods for Imaging Elastic Attributes of Tissue**

**Chair: J.M. Rubin**

Sonoelastography Imaging. L. Taylor. The University of Rochester, Rochester, NY, USA.

Elastography Imaging. T. Varghese. The University of Wisconsin-Madison, Madison, WI, USA.

Transient Elastography Imaging. M. Fink. Laboratoire Ondes et Acoustique E.S.P.C.I., Paris, France.

Radiation Pressure Vibro-Acoustography Imaging. P. Trompette, INSERM, Lyon, France.

## **Session B: Mechanical Measurement Techniques for Tissues.**

**Chair: M. Fink., France.**

Measurement of Viscoelastic properties of soft biological tissues with a dynamic torsion test. E. Mazza, D. Valtorta. ETH Zurich, Swiss Federal Institute of Technology, Zurich, Switzerland.

Nonlinear Interaction of shear waves in soft solids using transient elastography. J. L. Gennisson, X. Jacobs, S. Catheline, M. Tanter, C. Barriere, D. Royer, M.Fink. Laboratoire Ondes et Acoustique, E.S.P.C.I., Paris, France.

Viscoelastic properties of soft solids using transient elastography. S. Catheline, J. L. Gennisson, G. Delon, M. Fink. Laboratoire Ondes et Acoustique, E.S.P.C.I., Paris, France.

Vibrational Resonance Spectroscopy of Soft Tissues. G. S. Lin, L. M. Mobbs, B.S. Garra. Advanced Imaging Associates, Fremont California, U.S.; University of Vermont College of Medicine-Fletcher Allen Health Care, Burlington, VT, U.S.A.

Resonance Frequency of the Plantar Fascia. Y. J. Chiang, C. L. Wang, Y. W. Shau, H. M. Chai. National Taiwan University, Taipei, TAIWAN.

An optical validation for ultrasound elastomicroscopy. Y. Zheng, M. Lu, and Q. Huang. The Hong Kong Polytechnic University, Hong Kong.

Parameter Identification of Tissue Lumped Models Based on Sequences of Ultrasonic Strain Images. E. Turgay, S. MacIntosh, R. Rohling, S. Salcudean. University of British Columbia, Vancouver, British Columbia, Canada.

## **Mechanical Properties of Tissues**

**Chair: J. Bamber, UK.**

Viscoelastic characterization of in-vitro canine tissue. M.Z. Kiss, T. Varghese, U. Techavipoo, M. Hobson, T. J. Hall, E. L. Madsen, J. Jiang, J. A. Zagzebski, M. S. Klierer. The University of Wisconsin-Madison, Madison, WI, USA.

Nonlinear Shear Waves. M. F. Hamilton, Y. A. Ilinskii, G. D. Meegan, E. A. Zabolotskaya. The University of Texas at Austin, Austin, TX, USA.

Mechanical Property of the Achilles Tendon in vivo. M. C. Lee, Y. W. Shau, C. L. Wang, T. Y. Hsiao. National Taiwan University, Taipei, Taiwan; National Taiwan University Hospital, Taipei, Taiwan.

A Preliminary Comparison of Freehand Elastography and Reflex Transmission (Attenuation) imaging for visualizing thermally ablated tissue. L. Baker, A. Kolen, J. Bamber. Institute of Cancer Research and Royal Marsden NHS Trust, Sutton, Surrey, UK.

Freehand Elastography of thermal lesion arrays in excised liver. A. Kolen, J. Bamber. Institute of Cancer Research and Royal Marsden NHS Trust, Sutton, Surrey, UK.

## **Session D-1: Methods for Imaging Elastic Tissue Properties I.**

**Chair: T Varghese, USA.**

Estimation of strain tensor components from angular strain in elastography. U. Techavipoo, T. Varghese, Q. Chen, J. A. Zagzebski, E. L. Madsen. University of Wisconsin-Madison, Madison, WI, USA.

Brachytherapy seeds detection using vibro-acoustography: a pilot study. F. Mitri, P. Trompette, J. Y. Chapelon. INSERM U556, Lyon, France.

The feasibility of using elastography for imaging the local strain ratios in homogeneously porous media. R. Righetti, J. Ophir, S. Srinivasan, T. A. Krouskop. The University of Texas Medical School, Houston, TX, USA; University of Houston, Houston, TX, USA; Baylor College of Medicine, Houston, TX, USA.

Feasibility of Modulus imaging using nano-identification: comparison of modulus images with strain elastograms using phantoms, prostates, kidneys and cancers. S. Srinivasan, J. Ophir, T. A. Krouskop, R. E. Price. The University of Texas Medical School, Houston, TX, USA; University of Houston, Houston, TX, USA; Baylor College of Medicine, Houston, TX, USA; The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA.

Palpation imaging for biopsy guidance and haptic sensor-actuator applications in medicine. W. Khaled, S. Reichling, O.T. Bruhns, G. J. Monkman, S. Egersdrofer, M. Baumann, H. Boese, H. Freimuth, A. Tunayar, A. Lorenz, A. Pesavento, K. Kuehne, T. Senge, U. Scheipers, H. Emert. Ruhr-University, Bochum, Germany, Urology University Hospital, Ruhr-University Bochum, Herne, Germany, Fachhochschule Regensburg, special field engineering, Germany; Fraunhofer-Institut fuer Silicatforschung ISC, Wuerzburg, Germany, Insitut fuer Mikrotechnik, Mainz GmbH, Mainz, Germany; LP-IT Innovative Technologies GmbH, Bochum, Germany.

## **Session E: Clinical and Animal Applications and Results**

**Chair: B. Garra, USA.**



Sonoelastic detection of cancer in radical prostatectomy specimens. K. J. Parker, B.C. Porter, L. S. Taylor, G. Nadasy, Z. Wu, D. Pasternack, P.A. di-Santagnes, P. Nigwekar, R. B. Baggs, D. J. Rubens. University of Rochester, Rochester, NY, USA; Ohio State University Medical Center, Columbus, OH.

Shear Modulus imaging on interstitial electromagnetic wave coagulation treatment of human in vivo liver carcinoma. C. Sumi, M. Kubota, G. Wakabayashi, M. Tanabe. Sophia University, Tokyo, Japan; Yamachika Memorial Hospital, Kanagawa, Japan. Keio University Medical School, Tokyo, Japan.

Lesion Size Ratio for Differentiating among breast lesions. T. J. Hall, W. E. Svensson, P. Von Behren, Y. Zhu, J. Malin, C. Spalding, A. Connors, D. Chopra, C. Lowery. University of Wisconsin-Madison, Madison, WI; Charing Cross Hospital NHS Trust, London, UK; Siemens Medical Solutions, Ultrasound Group, Issaquah, WA, USA; University of Kansas Medical Center, Kansas City, KS, USA.

Optimization of precompression and compression for clinical breast elastography. B. S. Garra, E. Jannick, L. M. Mobbs, S. Felker, L. Weiss, S. Srinivasan, J. Ophir. University of Vermont College of Medicine-Fletcher Allen Health Care, Burlington, VT, USA; The University of Texas Medical School, Houston, TX, USA; University of Houston, TX, USA.

Initial demonstration of staging deep venous thrombosis using ultrasound elasticity imaging. J.M. Rubin, H. Xie, K. Kim, W. F. Weitzel, X. Chen, M. O'Donnell, S. R. Aglyamov, S. Y. Emelianov, S. K. Wroblewski, D. D. Meyers, T. W. Wakefield. University of Michigan, Ann Arbor, MI, USA; University of Texas at Austin, Austin, TX, USA.

Elastographic characteristics of benign breast lesions that sonographically may mimic cancer. B. S. Garra, L. M. Mobbs, G. S. Lin. University of Vermont College of Medicine-Fletcher Allen Health Care, Burlington, VT, USA; The University of Texas Medical School, Houston, TX, USA; University of Houston, Houston, TX.

Vibrational Doppler imaging in differentiation of benign versus malignant breast masses by VDI:B-scan lesion area ratio. B.S. Garra, L. M. Mobbs, G. S. Lin. University of Vermont College of Medicine-Fletcher Allen Health Care, Burlington, VT, USA; Advanced Imaging Associates, Fremont, CA, USA.

Intravascular Ultrasound strain imaging with rotating single element transducers: initial in vivo experiments. C. Perry, W. Bojara, S. Holt, M. Lindstaedt, H. Emert. Ruhr University Bochum, Germany.

Monitoring the effect of acupuncture needling on human connective tissue in vivo. H. M. Langevin, E. E. Konofagou, B. S. Garra. University of Vermont, Burlington, VT, USA; Brigham and Women's Hospital -- Harvard Medical School, Boston, MA, USA.

Noncontact ultrasound indentation using water beam. M. Lu, Y. Zheng. The Hong Kong Polytechnic University, Hong Kong.

Anisotropic properties of breast cancer -- in vivo results utilizing a cubic model. R. Sinkus, M. Tanter, T. Nisius, and C. Kuhl. Philips Research, Hamburg, Germany; Laboratoire Ondes et Acoustique, E.S.P.C.I., Paris, France; RheinAhrCampus, Remagen, Germany; University Hospital, Bonn, Germany.

Prostate elastography in vitro. R. Souchon, O. rouviere, A. gelet, J. Ophir, J. Y. Chapelon. INSERM U556, Lyon, France; Hopital Edouard Herriot, Lyon, France; The University of Texas Medical School, Houston, TX, USA.

HIFU lesion formation monitored by "passive" elastography in vitro. G. Bouchoux, R. Souchon, C. Lafon, D. Cathignol, J. Y. Chapelon. INSERM U556, Lyon, France.

Interference pattern approaches to measure the shear modulus of homogeneous bio-materials. Z. Wu, L. S. Taylor, D. J. Rubens, and K. J. Parker. University of Rochester, Rochester, NY USA.

A high frequency (20 MHz) ultrasound based elastography system for in vivo skin elasticity imaging. M. Vogt, S. Scharenberg, R. Scharenberg, K. Hoffman, P. Altmeyer, H. Ermert. Ruhr-University, Bochum,

Germany; Taberna Pro Medicum GmbH, Lueneburg, Germany.

A generalized kelvin-voigt viscoelastic constitutive model for soft tissue. L. S. Taylor, D. J. Rubens, and K. J. Parker. University of Rochester, Rochester, NY USA.

Forward and sensitivity studies related to transient elastography. E. Park, A. M. Maniatty. Rensselaer Polytechnic Institute, Troy, NY, USA.

Dynamic response of the plantar soft tissues under the metatarsal head in the young and elderly. T. C. Hsu, Y. W. Shau, C. L. Wang. Chang Gung Memorial Hospital, Taoyuan, Taiwan. National Taiwan University, Taipei, Taiwan, National Taiwan University Hospital, Taipei, Taiwan.

Breast and prostate cancer diagnosis by real-time tissue elasticity imaging system - a feasibility study. T. Shiina, M. Yamakawa, N. Nitta, E. Ueno, T. Matsumura, S. Tamano, R. Shinomura, T. Mitake, University of Tsukuba, Tsukuba, Japan; Hitachi Medical Corporation, Kashiwa, Japan.

Agar/gelatin low contrast spherical lesion phantoms for assessing MR and ultrasound elastography performance. E. Madsen, G. Frank, T. Krouskop, M. Hobson, H. Shi, M. M. Doyley, T. Varghese, J. Ophir, University of Wisconsin-Madison, Madison, WI, USA; The University of Texas Medical School, Houston, Texas, USA; Baylor College of Medicine, Houston, Texas, USA; Dartmouth College, Hanover, NH, USA.

Elasticity research platform. W. G. Scott, R. M. Schmitt, R. D. Irving. WinProbe Corporation, N. Palm Beach, FL, USA.

#### **Session H: Signal and Image Processing, and New Algorithms** **Chair: T. Hall, USA**

Ultrasonic temperature imaging for guiding focused ultrasound surgery: effect of angle between imaging beam and therapy beam. N. Miller, K. Bograchev, and J. Bamber. Royal Marsden NHS Trust/Institute of Cancer Research, Sutton, Surrey, UK.

The statistics of motion tracking with large deformations. T. J. Hall, L. T. Cool, Y. Zhu. University of Wisconsin-Madison, Madison, WI, USA. University of Kansas Medical Center, Kansas City, KS, USA.

Novel myocardial strain imaging based on 3D displacement vector measurement. N. Nitta, Y. Aoki, M. Yamakawa, T. Shiina. University of Tsukuba, Tsukuba, Japan.

Shear wave speed reconstruction in transient elastography. D. Renzi, J. McLaughlin. Rensselaer Polytechnic Institute, Troy, NY, USA.

#### **Session I: Forward Inverse Problems** **Chair: P. E. Barbone, USA.**

A variational formulation leading to direct elastic modulus reconstruction. P. E. Barbone. Boston University, Boston, MA, USA.

Interior elastodynamics inverse problems: shear wavespeed reconstruction in transient elastography. L. Ji, J. McLaughlin, D. Renzi, J. Yoon. Rensselaer Polytechnic Institute, Troy, NY, USA.

Direct reconstruction of elastic modulus images from ultrasound images. A. Oberai, N. Gokhale, and P. E. Barbone. Boston University, Boston, MA, USA.

#### **Session J: Cardiovascular Elasticity** **Chair: G. Cloutier, Canada**

Myocardial regional elastic properties mapping based on echocardiographic 3D reconstruction of the left ventricle. S. G. Kolchanova, S. S. Ustuzganin, S. Y. Sokolov, E. S. Saveljeva, E. V. Marchenko, V. v. Chestukhin, B. L. Mironkov, F. A. Blyakman. Ural State University, Ekaterinburg, Russia; Institute of Transplantology and Artificial Organs, Moscow, Russia.

Correction for simultaneous catheter eccentricity and tilt on strain estimation in intravascular elastography. H. Shi, T. Varghese, G. Gimelli, J. A. Zagzebski, M. Wolff, E. L. Madsen. Department of Medical





Physics, University of Wisconsin-Madison, Madison, WI, USA.

Non-invasive vascular elastography: theoretical investigation. R. L. Maurice, J. Ohayon, G. Finet, G. Soulez, G. Cloutier. University of Montreal Hospital - Research Center, Montreal, Canada; Institut A. Bonniot, La Tronche, France; Cardiovascular Hospital, Claude Bernard University, Lyon, France; University of Montreal Hospital, Montreal, Canada.

Imaging of vulnerable plaque in coronary artery by parametric ivus and acoustic microscopy. Y. Saijo, A. Tanaka, H. Sasaki, N. Owada, Y. Akino, M. Tanaka. Tohoku University, Sendai, Japan; Miyagi Social Insurance Hospital, Sendai, Japan.

Peripheral arterial strain imaging using external pressure equalization. W. F. Weitzel, K. Kim, J. M. Rubin, H. Xie, X. Chen, M. O'Donnell. University of Michigan, Ann Arbor, MI.

IVUS modulography of vulnerable plaques using a parametric finite element model: validation on a phantom and human coronary artery. R. A. Baldewsing, J. A. Schaaf, F. Mastik, C. W. J. Oomens, A. F. W. van der Steen, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands; Interuniversity Cardiology Institute of the Netherlands (ICIN), Utrecht, The Netherlands; Eindhoven University of Technology; Eindhoven, The Netherlands.

Non-invasive elasticity imaging in small vessels: experiments on tissue-mimicking phantoms. R. L. Maurice, M. Daronat, Z. Qin, F. S. Foster, G. Cloutier. University of Montreal Hospital -- Research Center, Montreal, Canada; Sunnybrook and Women's College Health Sciences Centre -- Univeristy of Toronto, Toronto, Canada.

#### **Session K: Complementary 3D and Multimodality Applications** **Chair: R. Sinkus, Germany**

Tissue region delimitation through statistically based parameter consolidation. E. E. W. Van Houten, K. P. Mecke, J. B. Weaver, K. D. Paulsen. University of Canterbury, Christchurch, New Zeland. Technische Universitat Darmstadt, Hessen, Germany; Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA; Dartmouth College, Hanover, NH, USA.

Shear modulus estimation using a parallelized partial volume reconstruction approach. M. M. Doyley, E. E. W. Van Houten, J. B. Weaver, S. Poplack, F. Kennedy, K. D. Paulsen. Dartmouth Medical School, Hanover, NH, USA; Dartmouth College, Hanover, NH, USA; Norris Cotton Cancer Center, Lebanon, NH, USA.

Numerical evaluation of a 1.5D 3x3 beamformer array for real time cross-correlation imaging (CCI). R. M. Schmitt, W. G. Scott, R. D. Irving. WinProbe Corporation, N. Palm Beach, FL, USA.

#### **Session D-3: Methods for Imaging Elastic Tissue Properties III** **Chair: J. L. Katz, USA**

Supersonic shear imaging: a new technique for tissue viscoelasticity mapping. In vitro and in vivo results. J. Bercoff, M. Muller, M. Tanter, M. Fink. Laboratoire Ondes et Acoustique, ESPCI, Paris, France.

An experimental characterization of spatial resolution in elastography: analysis of the tradeoffs between spatial resolution and contrast-to-noise ratio. S. Srinivasan, R. Righetti, J. Ophir. The University of Texas Medical School, Houston, TX, USA; University of Houston, Houston, TX, USA.

Intraoperative applications of elasticity imaging using vibrography. B. Brendel, S. Siebers, M. Scholz, C. Welp, J. Werner, A. Lorenz, A. Pesavento, H. Ermert. Ruhr-University, Bochum, Germany; LP-IT Innovative Technologies GmbH, Bochum, Germany.

Comparive evaluation of strain and reconstructive elastography. M. M. Doyley, S. Srinivasan, A. Mohns, J. Ophir. Dartmouth Medical School, Hanover, NH, USA; Dartmouth College, Hanover, NH, USA; The University of Texas Medical School, Houston, TX, USA; University of

Houston, Houston, TX, USA.

Continued scanning acoustic microscopy and ultrasonic wave propagation for imaging and measurements of connective tissue properties. J. L. Katz, Y. Wang, H. J. Hein, P. Spencer, D. Hazony. University of Missouri-Kansas City, Kansas City, MO, USA; Martin-Luther-University Halle-Saale Medical School, Halle-Saale, Germany; Case Western Reserve University, Cleveland, OH, USA.

#### **Session D-4: Methods for Imaging Elastic Tissue Properties IV** **Chair: Y. Zheng, Hong Kong**

Progress in the elastographic imaging of radiofrequency ablated thermal lesions. T. Varghese, U. Techavipoo, J. A. Zagzebski, Q. Chen, W. Liu, F. T. Lee, Jr. University of Wisconsin-Madison, Madison, WI, USA.

Information content in transient sonoelastography. J. McLaughlin, J. R. Yoon. Rensselaer Polytechnic Institute, Troy, NY, USA

Ultrasonic measurement of inhomogenous strains in articular cartilage induced by osmotic loading. Y. Zheng, J. Shi, L. Qin, S.G. Patil. The Hong Kong Polytechnic University, Hong Kong; The Chinese University of Hong Kong, Hong Kong.

Vibrational Doppler imaging of soft tissue mechanical properties. G. S. Lin, L. M. Mobbs, B. S. Garra. Advanced Imaging Associates, Fremont, California, USA; University of Vermont College of Medicine-Fletcher Allen Health Care, Burlington, VT, USA.

#### **Session P: Posters**

Development of real-time tissue elastography. T. Oosaka, T. Matsumura, N. Murayama, T. Mitake, E. Ueno, Y. Kim, T. Shiina. Hitachi Medical Corporation, Japan; University of Tskuba, Japan; University of Washington, USA.

X-ray tomosynthesis elastography: a feasibility study. M. S. Richards, P. E. Barbone, T. Wu, D. B. Kopans, R. H., Moore. Boston University, Boston, MA, USA; Massachusetts General Hospital, Boston, MA, USA.

Characterizaation of the mechanical behavior of the inclusion-matrix interface: theory and simulation of breast lesion models. E. Maciejko, M. Bertrand, T. A. Krouskop. Ecole Polytechnique de Montreal, Montreal, Quebec, Canada. Baylor College of Medicine, Houston, TX, USA.

Realization of realtime tissue stiffness estimation in medical ultrasound imaging system. M. Jeong, S. Kwon, J. Park, G. Cho. Daejin University, Pocheon, Kyeonggi, Korea.

Plantar tissues properties obtained using ultrasound indentation for rheumatoid arthritis and diabetes mellitus patients. Y. Zheng, A. P. C. Choi, J. M. W. Ho. The Hong Kong Polytechnic University, Hong Kong.

A proposal for an accurate data companding technique based on sequential detection of time delays. T. Sato, Y. Watanabe, S. Goka, H. Sekimoto. Tokyo Metropolitan University, Tokyo, Japan.

An ultrasound propagation model for characterizing biomechanical properties of ocular tissue. J. Liu, C. J. Roberts. The Ohio State University, Columbus, OH, USA.

Preliminary studies on nanoparticle elasticity contrast. J. Liu, T. J. Rosol. The Ohio State University, Columbus, OH, USA.

#### **Session X: Equipment Exhibit**

Hitachi Medical Corporation, Kashiwa, Japan.  
Medison Corporation, Seoul, Korea.



# Selected Publications

**Yokoyama N, Schwarz KQ, Chen X, Steinmetz S,** Becher H, Schimpky C, Schlieff R. The effect of echo contrast agent on Doppler velocity measurements. *Ultrasound Med Biol* 2003; 29(5): 765-770,2003.

**Yokoyama N, Schwarz KQ, Steinmetz S, Li X, Chen X.** Prognostic value of contrast stress echocardiography in patients with image quality too limited for traditional non-contrast harmonic echocardiography. *J Am Soc Echo* 2004; 17(1):15-20.

**Miller MW,** Luque AE, Battaglia LF, Mazza S, Everbach EC. Biological and environmental factors affecting ultrasound-induced hemolysis *in vitro*. 1. HIV macrocytosis (cell size). *Ultrasound Med Biol* 2003; 29:77-91.

**Miller MW,** Everbach EC, Miller WM, Battaglia LF. Biological and environmental factors affecting ultrasound-induced hemolysis *in vitro*. 2. medium dissolved gas (pO<sub>2</sub>) content. *Ultrasound Med Biol* 2003;29:93-103.

**Miller MW,** Miller WM, Battaglia LF. Biological and environmental factors affecting ultrasound-induced hemolysis *in vitro*. 3. Antioxidant (Trolox) inclusion. *Ultrasound Med Biol* 2003; 29: 103-112.

**Miller MW,** Battaglia LF. The relevance of cell size on ultrasound-induced hemolysis in mouse and human blood *in vitro*. *Ultrasound Med Biol* 2003; 29:1497-1485.

**Miller MW,** Dewey WC. An extended commentary on models and regulatory considerations for transient temperature rise during diagnostic ultrasound pulses by Herman and Harris (202). *Ultrasound Med Biol* 2003; 29:1653-1659.

**Fultz PJ,** Feins TH, **Strang JG,** Wandtke JC, Johnstone DW, Watson TJ, **Gottlieb RH, Voci SL, Rubens DJ:** Detection and diagnosis of nonpalpable supraclavicular lymph nodes in lung cancer at CT and US. *Radiology* 222(2) 245-51, 2003 January.

**Gottlieb RH, Voci SL,** Syed L, Shyu C, **Fultz PJ, Rubens DJ, Strang JG,** Carson N, DiGrazio WJ, **Francis CW.** Randomized prospective study comparing routine versus selective use of sonography of the complete calf in patients with suspected deep venous thrombosis. *American Journal of Roentgenology.* 180(1):241-5, 2003 January

Dogra VS, **Gottlieb RH,** Oka M, **Rubens DJ.** Sonography of the scrotum. *Radiology* 227(1):18-36, 2003 April.

**Fultz PJ,** Harrow AR, Elvey SP, Feins RH, **Strang JG, Wandtke JC,** Johstone DW, Watson TJ, **Gottlieb RH, Voci SL, Rubens DJ.** Sonographically guided biopsy of supraclavicular lymph nodes: A simple alternative to lung biopsy and other more invasive procedures. *American J Radiology.* 180(5):1403-9, 2003 May.

McAleavey SA, **Rubens DJ, Parker KJ.** Doppler ultrasound imaging of magnetically vibrated brachytherapy seeds. *IEEE Trans Biomed Engineering* 50(2):252-5, 2003 February.

Liu H, Cheng G, **Yu Y, Brasacchio R, Rubens D, Strang J,** Liao L, **Messing E.** Automatic localization of implanted seeds from post-implant CT images. *Physics Med Biol* 48(9): 1191-1203, 2003 May.

Jandzinski DL, **Carson N,** Davis D, **Rubens DJ, Voci SL,** et al. Treated needles: Do they facilitate sonographically guided biopsies? *J Ultrasound Med* (22)11:1233-7, 2003 November.

**Tabei M,** Mast TD, and **Waag RC.** Simulation of ultrasonic focus aberration and correlation through human tissue. *J Acoust Soc Am* 113(2):1166-1176 (2003).



Varslot TK and **Waag RC**. Spectral estimation for characterization of acoustic aberration. *J Acoust Soc Am*. Submitted 25 August 2003.

**Waag RC**. Imaging eigenfunctions of a scattering operator. *J Acoust Soc Am* 113(4): 2211 (2003)

**Pilkington WC**, Lacefield JC, and **Waag RC**. Image improvement with adaptive beam formation using aberration correction. *Ultrasound Med Biol* 29 (5S) 68 (2003).

**Tabei M**, Mast TD, and **Waag RC**. Comparison of aberration correction methods for transmit and receive focusing in ultrasonic imaging. *Ultrasound Med Biol* 29(5S) 69 (2003).

**Taylor LS**, **Lerner AL**, **Gracewski S**, Wang P, Gaborski TR, **Rubens DJ**, **Parker KJ**. Elastographic contrast and the frequency dependent Young's modulus of liver. Submitted to: *Ultrasound Medicine Biol*, 2003.

**Taylor LS**, **Lerner AL**, Lito M, **Rubens DJ**, and **Parker KJ**. "A Kelvin-Voigt fractional derivative model for viscoelastic characterization of soft biological tissue." Submitted to: *Annals of Biomed Engineering*, 2003.

**Taylor LS**, **Porter BC**, Nadasdy G, DiSantAgnes PA, Pasternack D, **Wu Z**, **Baggs RB**, **Rubens DJ**, and **Parker KJ**. Three-dimensional registration of prostate images from histology and ultrasound. *Ultrasound Med Biol* 30(2), 161-168, 2004.

Pakin SK, Gaborski RS, Barski LL, Foes DH, and **Parker KJ**. A clustering approach to bone and soft tissue segmentation of digital radiographic images of extremities. *Journal of Electronic Imaging* 12(1): 40-49, 2003.

Wang M, **Parker KJ**, Spaulding K, Yu Q, and Miller R. Optimal output level selection for multilevel halftoning based on visual experiments using spatially modulated gratings. *Journal of Imaging Science and Technology* 47(4): 309-326, 2003.

Alam SK and **Parker KJ**. Implementation Issues in Ultrasonic Flow Imaging. *Ultrasound Med Biol* 29(4): 517-528, 2003.

McAleavey SA, **Rubens DJ**, and Parker KJ. Doppler ultrasound imaging of magnetically vibrated brachytherapy seeds. *IEEE Trans Biomed Engineering* 50(2):252-254, 2003.

Susan Voci, M.D., (front), reviews images with Nancy Carson, R.D.M.S., R.V.T. (center, hidden), and Deborah Rubens, M.D.





## Selected Presentations

**Taylor LS, Rubens DJ, Parker KJ.** A generalized Kelvin-Voigt viscoelastic constitutive model for soft tissue. 2nd International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, Corpus Christi, TX 2003.

**Wu Z, Taylor LS, Rubens DJ, and Parker KJ.** Interference pattern approaches to measure the shear modulus of homogeneous biomaterials. 2nd International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, Corpus Christi, TX 2003.

**Parker KJ, Porter BC, Taylor LS, Nadasdy G, Wu Z, Pasternack D, diSantagnes, PA, Nigwekar P, Baggs RB, Rubens DJ.** Sonoelastic detection of cancer in radical prostatectomy specimens. 2nd International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, Corpus Christi, TX 2003.

**Taylor LS and Parker KJ.** Vibration amplitude sonoelastography lesion imaging using low-frequency audible vibration. 145th meeting Acoustical Society of America, Nashville, Tennessee 28 April-2 May 2003.

**Waag RC.** Ultrasonic imaging with aberration correction, Western New York Signal Processing Workshop. Rochester, NY, October 17, 2003.

**Waag RC.** Research in aberration correction at the University of Rochester. Phillips Ultrasound, Bothell, Washington, [simultaneously communicated to the Phillips Laboratory in Andover, MA], January 24, 2003.

**Waag RC.** Imaging with eigenfunctions of a scattering operator. 145th Meeting of the Acoustical Society of America. Nashville, TN, April 28-May 2, 2003.

**Pilkington WC, Lacefield JC, and Waag RC.** Image improvement with adaptive beam formation using aberration

correction. 10th Congress of the World Federation for Ultrasound in Medicine and Biology, Montreal, Canada, June 1-4, 2003.

**Tabei M, Mast TD, and Waag RC.** Comparison of aberration correction methods for transmit and receive focusing in ultrasonic imaging. 10th Congress of the World Federation for Ultrasound in Medicine and Biology, June 1-4, 2003, Montreal, Canada.

**Waag RC and Astheimer JP.** Statistical estimation of aberration parameters. [poster] 10th Congress of the World Federation for Ultrasound in Medicine and Biology, Montreal, Canada, June 1-4, 2003.

**Waag RC.** Research to improve ultrasonic image resolution. Ethicon Endo-Surgery, Cincinnati, OH, December 11, 2003.

**Dalecki D.** Measurements and bioeffects of resonant gas bodies *in vivo*. Presented at the 145th Meeting of the Acoustical Society of America, Nashville, TN, May 2003.

**Dalecki D.** Ultrasound contrast agent bioeffects *in vivo*. Presented at the British Medical Ultrasound Society (BMUS) 35th Annual Scientific Meeting, Harrogate, United Kingdom. December 2003.

**Dalecki D.** Bioeffects of ultrasound with contrast agents: *In vivo*. Presented at the 10th Congress of the World Federation of Ultrasound in Medicine and Biology (WFUMB), Montreal, Canada. July 2003. *Ultrasound Med. Biol.* 29:S79; 2003.

**Rota C, Raeman CH, Dalecki D.** Cardiac arrhythmias with ultrasound contrast agents in mice. Presented at the 10th Congress of the World Federation of Ultrasound in Medicine and Biology (WFUMB), Montreal, Canada. July 2003. *Ultrasound Med. Biol.* 29:S97; 2003.



## Selected Courses at the University of Rochester

**Biosolid Mechanics (BME483).** Application of engineering mechanics to biological tissues including bone, soft tissue, cell membranes, and muscle. Realistic modeling of biological structures, including the heart, cells, and musculoskeletal tissues. Experimental methods and material models. 4 credits

**Biomedical Ultrasound (BME451).** The course presents the physical basis for the use of high-frequency sound in medicine. Topics include acoustic properties of tissue, sound propagation (both linear and nonlinear) in tissues, interaction of ultrasound with gas bodies (acoustic cavitation and contrast agents), thermal and non-thermal biological effects of ultrasound, ultrasonography, dosimetry, hyperthermia and lithotripsy. This course is the graduate complement to BME251.

**Cell & Tissue Engineering (BME462).** This course teaches the principles of modern cell and tissue engineering with a focus on understanding and manipulating the interactions between cells and their environment. After a brief overview of Cell and Tissue Engineering, the course covers 5 areas of the field. These are: 1) Physiology for Tissue Engineering; 2) Bioreactors and biomolecule production; 3) Materials for Tissue Engineering; 4) Cell Cultures and bioreactors and 5) Drug Delivery and Drug Discovery. Within each of these topics the emphasis is on analytical skills and instructors will assume knowledge of chemistry, mass transfer, fluid mechanics, thermodynamics and physiology consistent with the Cell and Tissue Engineering Track in BME. In a term project, graduate students must identify a technological need and present, orally and in writing, a proposal to meet the need.

**Microhydrodynamics (BME 466).** In this course we develop insight into the motion of small particles in a viscous fluid. Such problems are encountered in biology, biotechnology, and composite materials processing. Specific topics include flow past spheres and arbitrary bodies, (thermally driven) motion of bubbles and drops, slender body theory, and leading-order inertial corrections.

**Reduction and Analysis of Noisy Data (ECE477).** Basic ideas of sampling, statistics, inference, and deduction from noisy data. Properties of various distributions, testing of hypotheses, statistical inference, analysis of variance, regression analysis, curve-fitting and non-parametric statistics, using problems and examples drawn from areas of interest. Emphasis on appropriate use of statistical measures in reporting and drawing conclusions from data.

**Continuum Mechanics (ME444).** 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. Applications to boundary value problems.

**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 in infinite, semi-infinite, and layered structures and waves in layers and cylinders.

**Acoustic Waves (ECE433).** Basic wave phenomena. Reflection, transmission, and excitation of plane waves. Radiation from vibration bodies. Scattering from simple objects and random media.

**Image Processing (ECE447).** Elements of image processing systems. Image model and imaging geometry. Image sampling and quantization. 2D Fourier transform and discrete Fourier and cosine transform. Image compression models and information theory basics. Error-free and lossy image compression. Image enhancement 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, videoconferencing, videophone and mobile image communications, advanced image compression techniques such as entropy coding, sub-band coding, and object-based coding.

**Bioelectric Phenomena (ECE 450).** Passive and active dielectric properties of biological materials including macromolecular solutions, membranes, cells, and tissues. Physical and biological effects of electric fields, including diagnostic and therapeutic uses and biological hazards of electrical fields and electromagnetic radiation. Effects of low frequency magnetic fields.

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 (585) 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.

## **Finite Amplitude Distortion-Based Inhomogeneous Pulse Echo Ultrasonic Imaging**

A method and system for imaging a sample. The method includes the steps of generating an ultrasonic signal, directing the signal into a sample, which signal is distorted and contains a first order and higher order component signals at first and higher frequencies respectively. The received distorted signal is processed, and an image is formed, and then displayed, from one of the higher order component signals of the received distorted signal. U.S. Patent No. 6,206,833 was issued to Ted Christopher on March 27, 2001. For further information contact Eugene Cochran, Research Corporation Technologies, at (520) 748-4461.

## **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 fastest 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: Seiko Epson, 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 sub-resolvable 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.



### **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.

### **System and Method for 4D Reconstruction and Visualization**

From raw image data obtained through magnetic resonance imaging or the like, an object is reconstructed and visualized in four dimensions (both space and time) by first dividing the first image in the sequence of images into regions through statistical estimation of the mean value and variance of the image data and joining of picture elements (voxels) that are sufficiently similar and then extrapolating the regions to the remainder of the images by using known motion characteristics of components of the image (e.g., spring constants of muscles and tendons) to estimate the rigid and deformational motion of each region from image to image. The object and its regions can be rendered and interacted within a four-dimensional virtual reality environment. U.S. Patent No. 6,169,817 was issued to co-inventors Kevin J. Parker, Saara S. M. Totterman, and Jose Tamez-Pena.

### **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.

### **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 with 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.

### **Apparatus for Bone Surface-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 No. 6,106,464 was issued on August 22, 2000, for this invention.



### **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.

### **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. U.S. patent allowed.

### **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 appropri-

ate 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 relatively few successive scan lines, and was found to outperform 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 an 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.