ABSTRACTS

WEDNESDAY, JUNE 2

1. Tissue Parameters 1

1.1 **Ultrasound attenuation and backscatter (5-28 MHz) in carotid endarterectomy specimens: multiparametric discrimination,** S.L. Bridal,[1] B. Beyssen,[2] P. Fornès,[2] P. Julia[2] and G. Berger,[1] *[1]Laboratoire d'Imagerie Paramétrique UMR 7623 CNRS – Université Paris VI and [2]Hôpital Broussais, Paris, France 75006.*

Clinical ultrasound is routinely used to evaluate carotid stenosis but provides only qualitative description of plaque echogenicity and regularity. We have shown that backscattered radiofrequency signals can be used to construct high (30-50 MHz) and intermediate resolution (9-28 MHz) quantitative attenuation and backscatter images and that parameter values (30-50 MHz) are related to atherosclerotic plaque composition. We examined the question as to whether plaque identification is still possible with these parameters at frequencies necessary to image peripheral arteries. We used two lower frequency transducers to measure attenuation and backscatter as a function of frequency (4-28 MHz) in carotid plaque endarterectomy specimens. A total of 59 regions were studied from 15 independent plaques (stenosis 70%) from 12 patients (5 symptomatic). Parameter values (integrated backscatter, backscatter slope, integrated attenuation, slope of attenuation) were correlated with plaque types (calcified, intraplaque hemorrhage, thrombus, lipidic, mixed), and multiparametric plaque classification was tested by discriminate analysis.

Unopened, cylindrical plaques were pinned to a support and placed in 0.9 % saline (37°C) with the plaque's long axis perpendicular to the transducer's insonificiation direction. Radiofrequency signals were acquired across the entire 2-3 cm plaque length using 20 MHz and 10 MHz center frequency transducers, in turn. B-scans were constructed, providing circumferential cross-sections of the plaque with 500 μm between adjacent B-scans and 200 μm between the A-lines within B-scans. For the central zone of each B-scan, the average backscattered power was measured as a function of frequency from the FFT of the signal in a Hamming window (250 μm at 20 MHz, 500 μm at 10 MHz) beginning (400 μm at 20 MHz, 700 μm at 10 MHz) beneath the outer plaque surface. Starting at the same depths but including all signal (SNR > 10 dB), the attenuation was estimated using a multinarrow-band attenuation algorithm with diffraction correction. Following the measurement, the specimen was placed in 4% formalin, decalcified if necessary and histologic sections in the circumferential plane of the plaque were obtained at 2 mm intervals. Digitized images of histologic sections and B-scan images were visually correlated on computer to identify B-scans (n = 59) obtained at highly stenotic segments. The plaque composition of these segments was subsequently assessed by a pathologist and then correlated with ultrasound parameters.

X-ray angiograms, histology and ultrasound images correlated well. Discriminate analysis separated most calcified and lipidic plaques from others. Intraplaque hemorrhage and thrombus, however, were not well separated from mixed plaques. In conclusion, parametric images made by a multiparametric approach may discriminate certain types of carotid plaque but mixed plaques remain difficult to separate.

1.2 **Tissue characterization of intravascular ultrasound using polar coordinates, texture analysis and a neural network classifier,** Evelin Lieback, Isabelle Hadouin,

Jerome Armbruster, Michael Schartl, Jochen Boksch, Roland Hetzer, *German Heart Institute Berlin, Germany.*

Intravascular images show different tissues such as thrombi, soft or calcified plaques, as well as various wall layers arranged in concentric rings around the ultrasound catheter. Due to the circular geometry of blood vessels, regions of interest are better defined as circular portions than as rectangular windows as usually considered in image processing.

Methods: Intravascular images from patients undergoing P.T.C.A. were recorded on video tape and subsequently digitized into an image processing system. The gray level histogram, run length, co-occurrence matrices and power spectrum were computed for texture analysis. Co-occurrance matrices were calculated using radial and tangential displacements of value one, two and four for sectors and rings. Run lengths were similarly computed over rings and angels. Supervised learning classification methods (back propagation neural network) were used for segmenting the intravascular images.

Results: The accuracy of the classification result using the neural network classifier was 87% for calcified plaque, 88% for soft plaque, and 76% for thrombus. The neural classification process was therefore implemented as a visualization routine for on-line PC-supported classification. The next step was the on-line recognition of image contents. After choosing the region to be classified, the 51 texture parameters were computed and sent to the recall routine which delivered the neural classification results. The sector ROI was divided into evaluation windows which were classified separately. The windows were then color encoded with red, blue and green labels (calcified plaque, soft plaque, thrombus). This allowed visual evaluation of classification of different vascular pathology.

1.3 **Intima media layer thickness estimation from B-mode ultrasonic imaging,** Rainer M. Schmitt,[1,2] Jorge Millan,[1,4] and Holger H. Kiesewetter,[3] *[1]Fraunhofer Technology Center Hialeah, Hialeah, Fl 33010, [2]Cardiovascular Engineering Center, Florida International University, Miami, Fl 33172, [3]Institute for Transfusion Medicine, Universitaetsklinikum Charite, Schumannstr. 20/21 D-10117 Berlin and [4]Escuela de Ingenieria Electrica y Electronica, Universidad del Valle, Cali, Colombia.*

Intima media layer thickness in the wall of the carotid artery is a potential parameter for early diagnosis of arteriosclerotic plaque development.[1-3] During a large clinical study, the effect of pharmaceutical treatment of arteriosclerotic plaques was monitored over a five-year period. The study included 240 patients, from whom 80 were analyzed for intima media layer thickness, using ultrasound B-mode images. The images showing the carotid artery at its bifurcation in a longitudinal vessel plane were recorded digitally *in situ* from the video output of an ATL Mark 4 ultrasound unit operating at 7.5 MHz center frequency. Layer thickness was estimated from line profiles using an extrapolation algorithm for the identification of layer borders. Layer thickness was estimated as the average from measurements taken at least at three different locations. Based upon this approach of estimating intima media thickness, it has been demonstrated that layer thickness was reduced to about 30% in the treated group when it was compared to the untreated group. However, the variability of estimating layer thickness from video data is much higher when compared to the analysis of their corresponding rf data. A comparative *in vitro* study using a 7.5 MHz center-frequency transducer (fractional bandwidth 70%) demonstrated that rf data analysis estimates borders clearly with an accuracy of 0.1 mm compared to 0.3 mm using video signals.

Fraunhofer Technology Center Hialeah FTeCH is affiliated with the Fraunhofer Institute for Biomedical Engineering (IBMT), D-66386, St. Ingbert, Germany.

(1) Howard, G., et al, Carotid artery intimal-medial thickness distribution in general populations as evaluated by B mode ultrasound, *Stroke 24*, 1297-1304 (1993).

(2) Howard, G. et al, Relations of intima-medial thickness among sites within the carotid artery as evaluated by B mode ultrasound, *Stroke 25*, 1581-1587 (1994).

(3) Grobbee, D. F.and Bots, M.L., Carotid artery intima-media thickness as an indicator of generalized artherosclerosis. *J. Intern. Med. 236*, 567-573 (1994).

1.4 **The relationship of 1-D and 2-D ultrasonic spectrum-analysis features to scatterer morphology,** T. Liu,[1] F.L. Lizzi,[1] E.J. Feleppa,[1] P. Lee,[1] R.H. Silverman,[2] M. Rondeau[2] and D.J. Coleman,[2] *[1]Riverside Research Institute, 330 West 42nd Street, New York, NY 10036 and [2]Cornell University Medical College, 1300 York Avenue, New York, NY 10021.*

We have conducted a general analysis that relates calibrated 1-D and 2-D ultrasonic spectral parameters to the sizes, shapes, and concentrations of subresolution tissue scatterers. We have also confirmed salient results in ocular structures using examinations at 10- and 40-MHz center frequencies.

Calibrated 1-D power spectra are computed using digital analysis of radiofrequency (rf) echo signals as described in our previous reports. Our standard procedures summarize spectral features by applying linear regression analysis to spectra (in dB) as a function of frequency. We had previously derived closed-form solutions that explicitly relate spectral slope, intercept, and midband fit values to the effective sizes, concentrations, and relative acoustic impedances of internal tissue scatterers. The previous analysis treated isotropic scatterers as well as quasi-cylindrical and quasi-planar elements oriented perpendicular to the incident beam. We have now removed the restriction on angle-of-incidence and obtained general closed-form solutions for each spectral parameter as a function of tissue parameters, beam angulation, center-frequency and fractional bandwidth.

We have also investigated 2-D power spectra to elucidate the shape and orientations of constituent tissue elements. These spectra are computed from digital rf data obtained as the transducer is linearly scanned along the cross-range direction with increments smaller than a half beam width. Acquired data undergo 2-D Fourier transformation with respect to time (range) and cross-range coordinates. Our theoretical analysis has defined several features of 2-D spectra related to scatterer size, shape, orientation, concentration and relative acoustic impedance. Of most importance, 2-D spectra can differentiate shape factors that are not apparent in 1-D spectra.

We have confirmed important aspects of our analyses on rabbit and human eyes, using, e.g., corneal and retinal surfaces to represent quasi-planar elements. Our 1-D spectral results for quasi-cylindrical structures have now been applied to generate video-taped presentations of human ciliary-muscle changes during accommodation.

1.5 **Progress in prostate tissue-type imaging based on nonlinear classifiers,** Ernest J. Feleppa,[1] William R. Fair,[2] Harold Tsai,[2] Christopher Porter,[2] K.C. Balaji,[2] Tian Liu,[1] Andrew Kalisz,[1] Frederic L. Lizzi,[1] Angel Rosado,[1] Dimitris Manolakis,[1] William Gnadt,[1] Victor Reuter,[2] and Mary Jane Miltner[1], *[1]Riverside Research Institute, New York, NY and Boston, MA and [2]Memorial Sloan-Kettering Cancer Center, New York, NY.*

Objectives: Our general objective is to improve ultrasonic means of differentiating cancerous from noncancerous prostate tissue. Our specific objectives are: (1) to improve biopsy guidance; (2) to improve clinical staging and treatment planning; and (3) to improve lesion evaluation and treatment monitoring. *Methods*: We acquired ultrasonic, histologic, demographic and clinical data for over 300 patients, and our data base contains spectrum-analysis and histology results for over 2,000 biopsies. We distinguished between cancerous and noncancerous tissue by applying nonlinear classification tools to spectral parameters computed from radiofrequency echo signals and clinical variables (such as PSA level). We used these classifier tools on a pixel-by-pixel basis to generate images employ-

ing grey-scale or color to map levels of suspicion for cancer in 2-D. Look-up tables based on trained classifiers provided the basis for image encoding. We compared the classification performance of these tools with classification based on conventional ultrasound images, and have expressed performance using ROC curves. *Results*: ROC curves based on 644 biopsies produce areas of 0.64 0.04 for B-mode imaging, 0.77 0.03 for nearest-neighbor classification, and 0.87 0.04 for neural-network classification. At the specificity corresponding to an assumed sensitivity of 0.40 for B-mode, these ROC curves suggest that imaging based on neural-network classifier tools can provide a sensitivity of 0.70; at the specificity corresponding to a sensitivity of 0.50 for B-mode, these neural-network tools may provide a sensitivity of 0.80. Images based on neural-net classifiers effectively map the relative suspicion of cancer in the prostate and, therefore, may improve the distinction of suspicious from unsuspicious tissue for the purpose of biopsy guidance. *Conclusions:* Spectrum analysis of ultrasonic echo signals and nonlinear tissue-classification methods, particularly neural-network algorithms, show encouraging promise for better detection and management of prostate cancer. ROC curves comparing these new methods to current B-mode-based TRUS(TRansrectal UltraSound) imaging suggest a capability to improve the sensitivity of TRUS-guided biopsies by as much as 75%. When applied in real time, the apparent ability of these methods of generating grey-scale and color-encoded images to highlight suspicious regions of the prostate may markedly improve ultrasonic biopsy guidance. Further research currently is underway to asses the potential of 2-D and 3-D imaging based on these new methods for improving clinical staging of prostate cancer and noninvasive monitoring of treated or 'watched' cancers. This research is supported by NIH/NCI grant CA53561.

2. DOPPLER

2.1 **Velocity estimation of contrast agent flow using decorrelation,** T.A. Tuthill, J.B. Fowlkes, and J.M. Rubin, *Department of Radiology, University of Michigan, Ann Arbor, MI 48109.*

Current blood velocity measurements using Doppler are constrained by angle dependence and limited velocity ranges. Alternative velocity estimates using gray scale correlation are restricted by weak scattering blood cells. However, the addition of contrast agents increases the signal amplitude and provides true speckle statistics needed for accurate speed estimates from correlation curves. While directionality information is lost, the technique does provide high spatial resolution and can detect low flows. The decorrelation technique estimates the rate of change of the scattering intensity at given positions during the sampling period. After accounting for the transducer's point spread function, flow speed can be extracted from the normalized covariance curves. Using both *in vitro* and *in vivo* studies, we examined the feasibility of flow measurements using gray-scale correlation. For each study, the transducer beam profile was first calibrated for the specific image settings. The resolution cell size was computed as a function of depth by scanning a tissue-mimicking phantom at uniform increments in the elevational, lateral and axial directions. The frame-to-frame correlation for each pixel within a window was computed, and the average normalized correlation curve fitted to a Gaussian. The resulting standard deviation is the beam correlation width. For the *in vitro* experiments, a lipid-stabilized perfluorocarbon contrast agent was pumped through a 6.4 mm diameter dialysis tube in a water bath. Pump flow speeds ranged from 2.2 mm/s to 13 mm/s. An 8 MHz linear array probe was affixed for both longitudinal and cross-sectional scans, and B-scans were collected at 69 frames/s. Preliminary *in vivo* studies examined rabbit kidneys after injection of the contrast agent

MRX-115 (ImaRx Pharmaceutical Corp.). When the contrast level had reached a steady state, gray-scale images were stored on cine loop at 30 frames/s. For each pixel in the first frame, the temporal autocovariance was computed and normalized by the variance to produce a correlation coefficient. The tube flow results showed a parabolic velocity profile that scaled with velocity. Comparisons of longitudinal versus cross-sectional scans showed a small decorrelation residual due to Brownian motion and radiation force movement of the contrast agent out of the beam. Correlation images from the rabbit studies show a distinct difference between major vessels in the kidney and the renal cortex. These results show promise of the decorrelation technique in measuring blood flow. Design of a spherical resolution cell would ensure uniform decorrelation in all three dimensions and provide angle-independent flow estimates.

2.2 **Measurement of volumetric flow in a steady flow model using an ultrasonic error compensation method,** Ding-Yu Fei, Xunchang Chen and Subrahmanya S. Vedam, *Department of Biomedical Engineering, Virginia Commonwealth University, Richmond, VA 23298.*

A steady flow tube model has been used to evaluate the feasibility and accuracy of an error compensation method on volumetric flow measurements. The method, proposed by the author,[(1)] employs a multigate procedure to acquire flow velocity information along a line crossing the central axis of the vessel. Two intermediate flow rate results are calculated by the conventional velocity profile method ('first flow rate') and an average velocity profile method ('second flow rate') from the same experimental data. The second flow rate is the product of the area of vessel cross-section and the average velocity of the measured velocities across the vessel lumen. The estimated or corrected flow rate is calculated by adding a compensation term to the first flow rate. The compensation value here is the product of the difference between the second and first flow rates and a selected correction factor. The correction factor needs to be determined theoretically or experimentally.

In the experiments, a Doppler color imaging scanner was used to acquire the velocity information in a straight latex tube model with an internal diameter of 11.1 mm. The Reynolds numbers used in the study were from 400 to 1900. For each experiment, an optimal correction factor, which would reduce the error to zero, was determined from the calculated first and second flow rates as well as the true flow rate measured from a calibrated flow meter inserted in the return line of the flow stream. The average value of the optimal correction factors from all the experiments was used as the standard correction factor to calculate the corrected flow rate for each experiment. The preliminary results show that the average absolute error was 4.5 2.5% by the error compensation method. As a comparison, the average error was 10.2 3.3% for the velocity profile method and 7.2 3.5% for the average velocity profile method, respectively. Similar results were also obtained for flow conditions simulating the flow in common carotid arteries. It is shown that the error compensation method may be useful to significantly reduce the error encountered in conventional blood volumetric flow measurements.

(1) Fei, D.Y., *Ultrasound Med. Biol. 21*, 1047-1057 (1995).

2.3 **Efficient Doppler angle estimation using correlation,** Pai-Chi Li, Chong-Jing Cheng and Che-Chou Shen, *Department of Electrical Engineering, National Taiwan University Taipei, Taiwan, R.O.C.*

Doppler techniques have been widely used to determine blood flow velocity in medical ultrasound. Such techniques, however, can only detect the axial component of blood flow. To compute the true velocity, knowledge of the beam-to-flow angle is required. A number of techniques have been proposed to estimate the flow velocity in two or three dimensions. One of the techniques is based on the effects of the beam-to-flow angle on the Doppler band-

width. Since the Doppler bandwidth is inversely proportional to the transit time of sound scatterers crossing the sample volume, the beam-to-flow angle can be found by using the Doppler bandwidth and the sample volume geometry. A problem with this approach is that full Doppler spectrum is required in order to compute the Doppler bandwidth. Therefore, it is relatively computationally demanding and not suitable for real-time, two-dimensional Doppler imaging. To overcome this problem, an efficient correlation based method is proposed. Specifically, variance of the Doppler spectrum is calculated by the correlation function and is used to approximate the square of the Doppler bandwidth. Since variance is routinely computed in correlation-based color Doppler imaging systems, the implementation is very straightforward. On the other hand, since the true velocity is determined by the mean Doppler frequency shift and the variance, two-dimensional flow information can be calculated and mapped to different colors using existing two-dimensional color maps. Therefore, real-time, two-dimensional flow imaging with automatic angle correction only requires minimum modification to current commercial ultrasonic imaging systems. Both simulations and experiments were performed to test the efficacy of this approach. Simulation results show that the correlation-based variance estimator may produce significant errors if only a limited number of flow samples are available. Note that the number of flow samples is typically 4-10 in order to provide adequate frame rate for real-time two-dimensional imaging. By averaging the variance estimates, however, such estimation errors can be greatly reduced. The results were also confirmed by experiments. Flow data were acquired on a string phantom and the beam-to-flow angle was varied from 23^0 to 82^0. With averaging, results show that beam-to-flow angles estimated by the correlation based method can achieve good agreement with the true angles by using only four flow samples.

2.4 **Quantitative flow imaging with intravascular ultrasound,** J.R. Crowe,[1] and [1,2]M. O'Donnell, *[1]Department of Electrical Engineering & Computer Science and [2]Biomedical Engineering, University of Michigan, Ann Arbor, MI 48109-2125*.

Previously, we presented a method of real-time arterial color flow imaging using an intravascular ultrasound (IVUS) imaging system, where real-time rf A-scans were processed with an FIR filter bank to estimate relative blood speed. Although qualitative flow measurements are clinically valuable, realizing the full clinical potential of blood flow imaging requires quantitative flow speed and volume measurements in real-time. Unfortunately, the rate of rf echo-to-echo decorrelation is not directly related to scatterer speed in a side-looking IVUS system because the elevational extent of the imaging slice varies with range. Consequently, flow imaging methods using any type of decorrelation processing to estimate blood speed without accounting for spatial variation of the radiation pattern will have estimation errors prohibiting accurate comparison of speed estimates from different depths. The FIR filter bank approach measures the rate of change of the ultrasound signal by estimating the slow-time spectrum of rf echoes. A filter bank of N band pass filters is applied in parallel to estimate N components of the slow-time DFT. We present a derivation of the relationship between the slow-time spectrum, aperture diffraction pattern and scatterer speed for a simplified target. Since the ultimate goal of this work is to make quantitative speed measurements, we present a method to map slow time spectral characteristics to a quantitative estimate. Results of the velocity estimator are shown for a simulated circumferential catheter array insonifying blood moving uniformly past the array (i.e., plug flow) and blood moving with a parabolic profile (i.e., laminar flow).

3. ELASTICITY 1

3.1 **Fundamental limits on the estimation and imaging of transverse displacement, transverse strain and Poisson's ratio in elastography,** Elisa Konofagou,[1,3] Tomy Varghese[1] and Jonathan Ophir[1-3], *[1]Ultrasonics Laboratory, Department of Radiology, The University of Texas Medical School, Houston, TX 77030, [2]Department of Electrical Engineering and [3]Program in Biomedical Engineering, University of Houston, Houston, TX 77204.*

We have recently developed an elastographic method that measures the displacement and strain in a direction transverse to the beam with good signal-to-noise ratio.(1) This also allowed the measurement and imaging of the local Poisson's ratio in the scanned tissue. The method consists of tracking single axial rf segments transversely after correction for decorrelation noise (or, *recorrelation*) due to motion in an orthogonal direction, and using interpolation techniques to compute minute subpitch displacements. In this paper, we describe the theory that corroborates these previously reported results. We establish the fundamental limit associated with the estimation of transverse displacement and strain using this method and its dependence on parameters such as the beamwidth, pitch, interpolation scheme and decorrelation noise. Since the motion is coupled in all three directions, we demonstrate the effect of the recorrelation method using both theoretical and simulation results. We also show how recorrelation allows the use of higher bandwidths and finer beamwidths, thereby preserving higher resolution in both axial and transverse motion estimations, respectively. Furthermore, we compare the fundamental limit of this method to that of using the lateral envelope of the signal for motion estimation in the same direction. Finally, the fundamental limit associated with the estimation of the Poisson's ratio is described.

Supported in part by National Cancer Institute Program Project Grant P01-CA64597 to the University of Texas.

(1) Konofagou, E.E. and Ophir, J., A new elastographic method for estimation and imaging of lateral displacements, lateral strains, corrected axial strains and Poisson's ratios in tissues, *Ultrasound Med. Biol. 24*, 1183-1199 (1998).

3.2 **Spectral strain estimation in elastography,** T. Varghese , E. E. Konofagou, J. Ophir and S. K. Alam, *Department of Radiology, Ultrasonics Laboratory, The University of Texas Health Science Center at Houston, 6431 Fannin, Houston, TX 77030.*

Elastography is capable of producing quality images that depict new tissue information *in vitro* and *in vivo*. Strain estimation in standard elastography is performed using a coherent cross-correlation technique to estimate tissue displacements, with a subsequent gradient operation to estimate the strain. While coherent estimation methods generally have the advantage of being highly accurate and precise, even relatively small undesired motions may cause signal decorrelation, and thus significant degradation of the elastogram (due to the phase sensitivity of the coherent estimators). However, for elastography to become universally applicable for areas such as hand-held, intravascular and abdominal imaging, the limitations associated with coherent strain estimation methods that require tissue *and* system stability (instrumentation attached to a rigid frame) must be overcome. We propose the use of direct incoherent (phaseless) methods of estimating strain using the spectral upshift in the power spectrum due to the applied compression.(1,2) Spectral strain estimates are obtained using the spectral centroid shift(1) with strain or using spectral cross-correlation.(2) While the centroid shift estimator relies on the estimate of mean center frequency shift with strain, spectral cross-correlation estimates the shift over the entire spectrum. In addition, spectral strain estimation provide direct estimates of the strain and do not involve the use of the noise

amplifying gradient operation. We demonstrate that estimation of strain using the direct incoherent spectral techniques is moderately less precise but far more robust than that with the currently-used coherent cross-correlation method. In addition, we are able to produce quality elastograms in noisy environments where the traditional coherent estimators fail completely, as long as the statistics of the underlying power spectra remain stationary.

Supported in part by NIH Program Project Grant P01-CA64597.

(1) Konofagou, E.E., Varghese, T., Ophir, J., and Alam, S.K., Incoherent and direct spectral strain estimators in elastography, *Ultrasound Med. Biol.* (submitted, 1998).

(2) Varghese, T., Konofagou, E.E., and Ophir, J., Direct and incoherent strain estimators in elastography with spectral cross-correlation, *Ultrasonic Imaging* (submitted, 1999).

3.3 **Strain imaging using a joint local estimation of scaling factor and delay from rf ultrasound signals,** Elisabeth Brusseau, Philippe Delachartre, Didier Vray Creatis, *CNRS Research Unit (UMR 5515) affiliated with INSERM, Lyon, France.*

The determination of the elastic properties of soft biological tissues is of widespread interest in medical diagnosis since it has the potential to be a sensitive indicator of some pathological states. Elastography gives an estimation of local tissue strains, occuring in response to an externally-applied mechanical compression. T hese strains are estimated by tracking, in the ultrasonic signals, the changes produced by the compression of the target.

There are two main types of signal processing techniques for the computation of axial strain: the first consider that the postcompression signal is a delayed replica of the precompression signal. Thus, the local tissue displacement is assumed to be a simple shift, determined by crosscorrelating gated pre- and postcompression echo signals. The strain is then computed as the gradient of displacements. The second type of method takes into account the fact that the postcompression signal is a scaled replica of the precompression signal since there is a shape variation and, therefore, a scaling factor. The strain is then estimated by computing the local compression factor.

We propose a new method using jointly these two types of information. For the calculation of the local strain, this method takes into account that the externally-applied mechanical compression produced a local reduction of scale and a delay in the signal. Indeed, using both local scaling factors and delays permits one to better estimate the values of strain, and to improve the spatial localization of variations, and, in particular, discontinuities in strains. We first estimate the local time scaling by iteratively varying the compression factor until the correlation coefficient between the gated pre-and postcompression signals is maximised. Then the remaining delay is computed using the phase information from the complex correlation function. The strain is derived from these two parameters.

Simulations and experiments on tissue-mimicking phantoms are done to corroborate the theoretical developments. Results show an improvement of local strain images using the joint estimation of scaling factor and delay from pre- and postcompression rf signals.

3.4 **On the spatial resolution of strain images,** L.T. Cook, M.F. Insana, P. Chaturvedi and T.J. Hall, *Department of Radiology, University of Kansas Medical Center, Kansas City, KS 66160-7234.* 1cook1@kume.edu

The art of forming a diagnostic-quality strain image is still largely empirical. Spatial resolution is particularly complicated to define because there are many interdependent contributing factors. The pulse-echo imaging system, signal processing and applied deformation parameters all play a major role in determining spatial resolution. We are developing analytical tools that may eventually provide a rigorous definition of spatial resolution for strain imaging. A discrete model was developed that defines ultrasonic echo fields in deformed media. The waveform model is used to form a Fourier crosstalk matrix that measures how

well frequency components in the precompression signals map to those in the post-compression signals — a measure of coherence. Although the crosstalk matrix has many uses, its normalized trace defines the modulation transfer function (MTF) for displacement estimates used in strain images. We show how the crosstalk matrix can predict noise and spatial resolution properties of strain images using simulations and phantom images with a variety of transducer beams. The crosstalk matrix is an important criterion for guiding the design of elasticity imaging systems and is easily computed.

3.5 **Strain imaging algorithms with a deformable mesh,** Y. Zhu, P. Chaturvedi, M.F. Insana, L.T. Cook, T.J. Hall and J.G. Gauch, *Departments of Radiology and EECS, University of Kansas, Kansas City and Lawrence, KS.*

One realization of the maximum-likelihood (ML) displacement estimator is to filter, warp, and crosscorrelate ultrasonic echo waveforms. This approach reduces decorrelation errors and permits large applied compressions that maximize the contrast-to-noise ratio in strain images. The deformable mesh concept is an efficient means of implementing the ML estimator. With it, we can generate lower-noise strain images in less time and with less data than multicompression techniques. Simulations, phantoms, and tissue samples are used to demonstrate the relative merits of single- versus multicompression algorithms and two methods for computing strain from displacement: local mean versus linear regression. The deformable mesh algorithm is able to produce high-contrast strain images in simple, tissue-like media with 10% applied compression without significant decorrelation errors.

3.6 **Exploiting the nonlinear elastic properties of tissue in elasticity imaging,** R.Q. Erkamp,[1] S.Y. Emelianov,[1,2] M.A. Lubinski,[1] A.R. Skovoroda,[2] and M. O'Donnell[1], *[1]Biomedical Engineering Department, University of Michigan, Ann Arbor, MI 48109 and [2]Institute of Mathematical Problems in Biology, Russian Acadamy of Sciences, Pushchino, Russia 142292*.

Nearly all elasticity imaging procedures assume that the elastic modulus does not change with deformation. Most biological tissues, however, exhibit strain hardening. This nonlinear behavior makes contrast in elasticity images strain dependent, and, for soft tissue, generally results in suboptimal elastic contrast. To illustrate this, consider a block-shaped homogeneous phantom made of nonlinear material. As it is deformed between two plates (no slippage between phantom and plate), the strain will be much higher in the middle than near the plates. This strain distribution affects the elastic modulus, and, thus, the elasticity image of the homogeneous material does not appear uniform at all. Furthermore, when deformation is applied to a nonuniform phantom, softer regions generally tend to exhibit higher strain levels than stiffer regions. Thus, if a linear elastic model is assumed, then the elastic modulus of softer tissue is measured at higher strain values and contrasted against the elastic modulus of stiffer tissue at low strain. By collecting many data frames over a large deformation range, and processing multiple subsets, the nonlinear elastic behavior can be analyzed. Within a small deformation range (i.e., subset of frames), the elasticity can be considered strain independent. However, each subset has a different internal strain distribution. Thus, the elastic modulus of a material can be obtained as a function of its internal strain. This information can be used to control the contrast between materials with different nonlinear behavior, and therefore increase the detectability of pathological regions. In addition, strain hardening itself can differentiate tissue types — it is an independent tissue parameter. To illustrate some principles of nonlinear elasticity imaging, experiments were performed on agar-gel and tissue containing phantoms. Specifically, nonlinear elasticity images of a canine kidney demonstrate the independence of elastic modulus and strain hardening tissue parameters. The unaltered kidney is compared to a kidney where gluter-

aldehyde was injected into the parenchyma. This creates a localized lesion where the elastic modulus is increased, but strain hardening is reduced. Subsequent direct elasticity measurements confirmed the effects observed in the elasticity imaging experiment. Results of this study suggest that the nonlinear elastic properties of tissue, when taken into account properly, may both increase detectability in elasticity imaging and provide a new independent means of tissue differentiation. Thus, large deformations in elasticity imaging may have multiple benefits.

4. BONE

4.1 **Relationship between attenuation and backscatter in trabecular bone**, Keith A. Wear, *Food and Drug Administration, Center for Devices and Radiological Health, 12720 Twinbrook Parkway, Rockville MD, 20857.*

Ultrasound bone densitometry, based on measurements of attenuation and speed of sound in the calcaneus, is a rapidly emerging technology for diagnosis of osteoporosis and other diseases which affect bone density. Preliminary reports indicate that ultrasonic backscatter is a potentially useful measurement to assess bone density.[1-3] The objective of this work was to investigate the empirical relationship between backscatter and attenuation. Toward this end, eight defatted human calcanei were investigated *in vitro* at 500 kHz. Attenuation was measured using a through-transmission technique. Integrated backscatter was also measured. Samples with higher attenuation tended to exhibit higher integrated backscatter, suggesting that scattering may be an important determinant of attenuation.

(1) Wear, K.A. and Garra, B.S., Assessment of bone density using broadband ultrasonic backscatter, *Ultrasonic Imaging 19* (1997)(abstract).

(2) Giat, P., Chappard, C., Roux, C., Laugier, P. and Berger, G., Preliminary clinical assessment of the backscatter coefficient in osteoporosis, *Ultrasonic Imaging 19* (1997)(abstract).

(3) Wear, K.A. and Garra, B.S., Assessment of bone densit y using ultrasonic backscatter, *Ultrason. Med. Biol. 24*, 689-695 (1998).

4.2 ***In vivo*** **assessment of the impact of soft tissue on the evaluation of error bounds on calcaneal SOS caused by surrounding soft tissue,** C. Chappard, E. Camus, F. Lefebvre, J. Bittoun,[1] G. Berger and P. Laugier, *Laboratoire d'Imagerie Paramétrique CNRS – Université Paris 6. Paris and [1]CIERM, Hôpital du Kremlin-Bicêtre, France.*

Over the last decade, a considerable number of investigations have reported the use of ultrasonic parameters (slope of frequency attenuation, BUA, and speed of sound, SOS) for osteoporotic fracture risk prediction. Quantitative ultrasound (QUS) measurements at the heel are performed in the through-transmit mode, and, on the whole, the parameters are influenced by bone and soft tissue (mainly subcutaneous fat). Whether the impact of soft tissue on attenuation is probably limited due to the considerable difference of attenuation in soft tissue and cancellous bone, it is of particular concern for SOS, since the difference between velocities of cancellous bone and soft tissue is small. This work aimed at quantitatively assessing the error bounds caused by surrounding soft tissue (ST) on SOS at the heel in individuals. Toward this goal, site-matched measurements of ST thickness were performed using MRI of the heel. First, the SOS was measured at the right foot in 21 healthy subjects (30 7 years) with a UBIS 3000 (DMS, Montpellier, France), assuming a fixed bone thickness of 28 mm without correction for ST. Second, site-matched calcaneus width and ST thickness were measured from MR images (1.5 T, GE). Ultrasound and MR images

site-matching was achieved using a semi-automatic procedure. Third, bone velocity (V_b) was calculated by taking into account the bone width with correction for ST thickness. Upper and lower bounds of V_b were obtained assuming ST velocity to be a function of tissue composition and to vary from 1,450 to 1,490 m/s according to literature. The correction for bone width and ST thickness led to highly-significant differences ($p<10^{-4}$) between V_b and SOS (1,533 37 m/s) at both lower (1,542 34 m/s) and upper bounds (1,568 36 m/s) of V_b. Estimated measurement errors due to ST were about 2 to 8 times higher than technique reproducibility. These results indicate that SOS inaccuracies as high as 2% or more can be anticipated clinically. Therefore, individual SOS values without ST correction may not provide accurate follow-up of patients, particularly if variations in ST thickness and/or composition occur. The reliability of SOS estimation will be greatly enhanced, if adequate soft tissue corrections are implemented in future studies of longitudinal variations of bone under various clinical or experimental conditions.

4.3 **Quantitative ultrasound measurements reflect mainly bone density in human calcaneal cancellous bone, S.** Chaffaî, A. Elmoutaouakkil,[1] E. Cendre,[1] G. Peix,[1] A.M. Laval-Jeantet,[1] G. Berger and P. Laugier, *Laboratoire d'Imagerie Paramétrique CNRS – Université Paris 6. Paris and [1]INSA Lyon, France.*

The present study was designed to investigate the relationship between ultrasonic properties of human cancellous bone, mineral density and structural properties of bone. Ultrasonic measurements were made in transmission and reflection modes on 11 defatted, 10 mm-thick slices of trabecular bone specimens cut from cadaveric calcaneal bone specimens. A standard through-transmission insertion method was used to derive the slope of frequency-dependent attenuation coefficient (nBUA, dB/cm.MHz) and ultrasonic bone velocity (UBV, m/s) between 0.2-0.6 MHz. The frequency-averaged backscatter power (BUB, dB) was measured in the same frequency range. Bone mineral density (BMD) was determined using conventional X-ray quantitative computed tomography (QCT), and high resolution computed tomography (HRCT) was used to derive a range of microstructural parameters. Microstructural parameters were measured on HRCT images (300 µm-thick-slice; in-plane spatial resolution of 110 µm). Average values of all the parameters were obtained for identical site-matched ROIs on ultrasonic scans and CT images. There were significant correlations between all ultrasonic parameters and BMD (r^2=80-94%; $p<5\ 10^{-4}$), as well as between all ultrasonic parameters and bone trabecular volume (BTV, a parameter reflecting amount of bone derived from HRCT) (r^2=73-88%; $p<5\ 10^{-3}$). Several microstructural parameters were correlated with ultrasonic properties (r^2=40-60%; $p<5\ 10^{-2}$). In stepwise regression analysis including BMD and all of the microstructural parameters, BMD remained the primary determinant of UBV and BUB, BTV remained the primary determinant of nBUA. After adjusting for the amount of bone (e.g., BMD or BTV), few relationships between ultrasonic parameters and microstructural parameters remained and the additional variance explained by microstructural parameters was small (4% at best). These results indicate that combinations of structural parameters failed to contribute significantly to the variability of ultrasonic parameters.

THURSDAY, JUNE 3

5. IMAGING 1

5.1 **A normalized minimum variance pixel approach to autofocusing in medical ultrasound,** Seth D. Silverstein, *Department of Electrical Engineering, University of Virginia, Charlottesville, VA.*

This work introduces a novel autofocusing phase aberration correction algorithm for B-scan medical ultrasound imaging. The algorithm follows directly from a detailed theoretical analysis of the scattering of Gaussian wave packets from a fully-developed speckle phantom consisting of ~50 randomly-distributed scatterers in each range-azimuthal resolution cell. The scattering solutions are developed in the Born approximation. Phase in corrupt data signals is a combination of the necessary good phase that contains the geometrical and scattering phase information that would occur in a noncorrupted scattered signal, and the aberrant bad phase that serves to blur the image. In order to remove enough of the aberrant phases to improve the overall image quality, the method must provide some means of differentiating good from bad. The basic premise of our autofocusing methodology is to identify the pixel in a range-azimuth region for which the amplitudes of the channel signals varies minimally across the array. Two pixel selection metrics yield excellent simulation results.

The first metric selects the pixel with the smallest ratio of the variance of the focused channel amplitudes to the square of the mean of the focused channel amplitudes. This metric will be referred to as the Normalized Pixel Variance (NPV) metric. The second metric selects the pixel with the largest incoherent sum of channel signals across the array. This metric will be referred to as the Incoherent Pixel Amplitude (IPA) metric. For received elemental signals associated with the MVP, the leading order term in the array coordinates in the expansion of the phase will be approximately zero. The remaining phase of each of the elemental signals will be a combination of the first order good phase (the part that is independent of the array coordinates), and the aberrant phase that depends upon the array indices. The aberrant phase is then estimated using well known differential phase gradient techniques. The variance of the channel signals for the focused pixel depends strongly upon the azimuthal distribution of the scatterers in the focused pixel. If the pixel scatterers are narrowly distributed in azimuth around the focused angle, the variance of the channel signal amplitudes across the array will be small. This metric further normalizes the variance by dividing by the square of the mean of the channel amplitudes. This normalization scales out the effects of overall brightness from the measure, as possible errors in the MVP assignment could be made for a very dim speckle in the absence of the normalization. As the part of the good phase that is channel dependent will be very small for the MVP, we can effectively assume that the good phase has been stripped off the channel signals associated with the MVP. The estimate of the remaining bad, channel-dependent phase is made using well-known phase gradient techniques. Both the theoretical analysis and the simulation results will be presented.

5.2 **Linear and harmonic phase aberration profiles in the breast,** Gregg E. Trahey and Roderick C. Gauss, *Department of Biomedical Engineering, Duke University, Durham, NC.*

The design of adaptive ultrasound imaging requires pulse-echo phase aberration measurements. Transducer arrays for effective pulse-echo phase aberration measurements have additional requirements that conventional linear arrays cannot achieve. Array elements must be small to minimize the integration of the arriving wavefront across the face of the ele-

ment, and the array must be large enough provide effective beamforming. When constrained by the number of available channels, multi-row arrays with independently addressable rows of transducer elements provide a natural compromise between the number of elements and overall aperture size.

A Siemens Elegra scanner has been modified to image with a 3 by 80 element, 8.5 MHz transducer array. A custom data acquisition card provides 64 megabytes of high speed memory synchronized with real-time imaging functions of the scanner. The element data for 3 by 42 element subaperture was captured over an image segment at 36 MHz over 180 ms. Five data sets of this type were acquired from the left breast of a 30-year-old female volunteer at Duke University Medical Center. The speckle brightness algorithm was applied to each data set to perform receive only phase aberration correction. The element data was processed as a 3 by 42 element multi-row array and as a 42 element linear array. The mean integrated intensity was computed over an area four times as large as the region of interest used for the speckle brightness algorithm. For multi-row phase correction, the increase in mean integrated intensity ranged from 3% to 60% and the r.m.s. phase error ranged from 15 ns to 34 ns. Linear array phase correction produced changes in integrate intensity ranging from 8% to 14%, actually producing a dimmer image in one example, and the r.m.s. phase errors ranged from 7 ns to 17 ns.

We have recently modified the system to generate and record harmonic signals, allowing interleaved measurements of aberration profiles from linear and harmonic echoes.

Work supported by the National Institutes of Health, Grant R01-CA43334.]

5.3 **Tendon analysis using spectral components of echo texture from 3-D ultrasound data sets,** T.A. Tuthill, J.B. Fowlkes and J.M. Rubin, *Department of Radiology, University of Michigan, Ann Arbor, MI 48109.*

Elongated speckle patterns in anisotropic tissue structures are often disrupted through injury or disease. A technique was devised to quantitatively assess the echo texture in Achilles' tendon for diagnosing diffuse and focal abnormalities. Preliminary analysis of the spatial frequencies showed that the speckle asymmetry could be characterized by the tissue elliptical axis ratio (TEAR), which is based on the eccentricity of the 2-D spectrum. Previous studies[1] showed that the spectral features successfully discriminated healthy tissue (TEAR = 2.1 0.2 for the entire normal population) from acute tears and diffuse famial hypercholesterolemia (TEAR = 1.7 0.3). In this study, three-dimensional ultrasound data sets were collected from normal tendons using both cross-sectional and longitudinal scan sweeps of a 12 MHz, 1.5 D linear array probe attached to a position-encoding framework. A moving 2-D Hamming window was applied, and the spectrum fit to an ellipse based on the eigenvalues of the covariance matrix. A corresponding TEAR image was determined from the ratio of the major-to-minor axis lengths. For the cross-sectional sweeps, longitudinal images were reconstructed before processing. For normal tendons imaged longitudinally, a typical mean TEAR value was 2.15 0.36, with the surrounding tissue at 1.25 0.14. Using the 3-D set formed from longitudinal B-scans, the mean TEAR was 2.08 0.09, and the surrounding tissue was 1.26 0.02. The 3-D reconstructed longitudinal images provided a tendon TEAR value of 1.99 0.17, while the surrounding tissue was 1.52 0.06. The 3-D data sets acquired longitudinally improve the statistical significance of the TEAR technique. The variation in TEAR values from the cross-sectional scans is likely due to acquisition problems (i.e., nonuniformities in frame spacing) and rotation of the nonsymmetrical resolution cell.

(1) Tuthill, T.A, Rubin, J.M., Fowlkes, J.B., et al, in *Abstracts, RSNA 84th Scientific Assembly and Annual Meeting* (1998).

5.4 **Simulation of ultrasonic images of rough surfaces using a parametrized discrete-scatterer model,** Jason W. Trobaugh and R. Martin Arthur, *Department of Electrical Engineering, Washington University in St. Louis, St. Louis, MO 63130.*

Models for ultrasonic images of rough surfaces are of interest in Bayesian methods for image understanding,[1] with applications in such areas as image-guided surgery and radiosurgery.[2] The Bayesian approach ultimately requires a probabilistic image model based on the gross structure of the surface. Towards that goal, we have been investigating the suitability of a linear systems imaging model and various discrete-scatterer surface models for modeling images of rough surfaces. The models have been evaluated via comparisons of simulated and actual images of cadaveric vertebrae *in vitro*. The vertebral surface provides a good medium for evaluation because of its intricate curvature and subwavelength roughness. The models are sufficiently general, though, to describe images of any rough surface. Previous results from a simulation study demonstrated that much of the variability in ultrasonic images of vertebrae could be attributed to (1) the gross surface structure, (2) the subwavelength random roughness of the surface, and(3) the three-dimensional characteristics of the imaging system.[3] The imaging system has been characterized by a three-dimensional point-spread function, assumed separable and modeled with Gaussian envelopes and a 6 MHz carrier wave. The surface model has now been generalized to provide a more natural characterization of the surface, with discrete scatterers on the continuum instead of the previous uniform grid. This important feature permits various fundamental parametrizations of the surface. We have used scatterer concentration (scatterers / area) and roughness (Gaussian perturbation normal to the surface), with scatterer positions distributed randomly within the triangles that represent the surface. For comparison, images of a cadaveric vertebra were acquired with a Tetrad imaging system and a 6 MHz linear array transducer. The probe was tracked using an optical localization system to enable registration with CT images of the same vertebra. The vertebral surface was represented with a triangulated surface generated from a segmentation of the CT images using the Marching Cubes algorithm. In images simulated using the model, sites of coherent scattering and textures from incoherent scattering were accurately reproduced for several scanning angles and positions. Variation of the scatterer concentration and surface roughness parameters produced visible differences in the relative amplitudes of coherent and incoherent scattering sites, allowing adjustment for a close visual match between images. Quantitative evaluation is currently limited, however, by large errors (as much as 2 mm) in registration and tracking relative to a high sensitivity (less than one mm or one degree) of the images to surface position and orientation. Our parametrized surface model provides a fundamental basis for describing variations in the acoustic properties of the surface. Combined with the linear systems imaging model, it provides a suitable framework for the development of a probabilistic image model.

The authors wish to thank Surgical Navigation Technologies, the Tetrad Corporation, IntellX L.L.C, and the Department of Neurosurgery at the St. Louis University School of Medicine for their support in this work.

(1) Miller, M.I. and Grenander, U., Representation of knowledge in complex systems, *J. Royal Statistical Soc. 56*, 569-603 (1994).

(2) Trobaugh, J.W., Kessman, P.J., Dietz, D.R. and Bucholz, R.D. , Ultrasound in image fusion: a framework and applications, *in Proc. IEEE UFFC Conf.* (1997).

(3) Arthur, R.M., A simulation study of variability in ultrasonic images of vertebrae, *Ultrasonic Imaging 20*, (abstract) (1998).

5.5 **Higher order nonlinear ultrasonic imaging,** Bruno Haider and Richard Chiao, *General Electric, Corporate R&D, Schenectady, NY.*

Nonlinear imaging has become an important mode in medical ultrasonic imaging. In particular, the processing of second harmonic echoes from both tissue and contrast agents has generated significant interest. The question arises whether higher order nonlinearities can provide further information. The work presented here proposes a method of extracting the components of higher order nonlinearities. The underlying idea is to model the nonlinear wave propagation or reflection from a contrast bubble by a polynomial expansion of some basis waveform. When this model is excited by a number of transmit pulses that only differ in their amplitude and phase, then the coefficients of this model can be extracted through least squares inversion. The coefficients of the polynomial model correspond to the individual nonlinear components. The number of distinct transmit pulses depends on the model order. Using fewer transmit pulses than the model order creates an underdetermined system that cannot be uniquely inverted. With the number of pulses equal to or larger than the model orde,r a unique inversion is possible. Increasing the pulse count beyond the model order may improve the signal-to-noise ratio.

An important feature of the method is the evaluation of nonlinear components whose spectra are folded back into the transmission band. All odd order nonlinearities can create such echo components. The reception of these components eliminates the high bandwidth requirements encountered in second harmonic imaging. Higher-order even harmonics may also be detected by taking advantage of the harmonic fold-back process. Folded frequency components will be centered around DC and at two times the transmit frequency ($2f_0$). This still requires a bandwidth sufficient to detect signals at $2f_0$ but eliminates the reception at higher multiples of f_0.

The polynomial model makes assumptions about the wave propagation that are not met exactly. The conditions under which the approximation is valid are discussed. The method has been evaluated on a contrast phantom. Imaging results demonstrate the separation of the linear, second, third and fourth order nonlinearity. The results also indicate that a higher SNR than currently available is required to extract components past the forth order. The experimental data have been acquired with a commercial General Electric LOGIQ 700 system. Since the data acquisition chain by itself generates a small amount of nonlinear distortion, a processing scheme has been devised to compensate for the nonlinearity of the system.

6. ELASTICITY/TISSUE MOTION

6.1 **Tumor volume estimation using 3D sonoelastography,** L.S. Taylor, B. Porter, D.J. Rubens, and K.J. Parker, *Department of Electrical Engineering and Department of Radiology, Rochester Center for Biomedical Ultrasound, University of Rochester, Rochester, NY 14627.*

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

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

6.2 **Solution of the inverse problem in sonoelastography using an iterative forward approach**, Dongshan Fu,[1] Stephen Levinson,[1,3] Sheryl Gracewski[2] and Kevin Parker[1], *Departments of [1]Electrical & Computer Engineering, [2]Mechanical Engineering and [3]Physical Medicine and Rehabilitation, University of Rochester, Rochester, NY 14627.*

Finite-element methods have previously been presented for elastic reconstruction from displacement data in sonoelastography. Standard methods for solution of the inverse problem, however, rely on the use of first, second and even third-order spatial derivatives. Ultrasonic speckle tracking data contains noise from speckle decorrelation, quantization error and various other sources. Because even a small noise component will result in significant errors in the spatial derivative terms, we have found it necessary to apply regularization and filtering techniques that have the potential to introduce bias into the resulting elasticity formulation.

We have recently explored an alternative approach to vibration sonoelastography that does not rely on the estimation of spatial derivatives of measured displacements. In our experiments, three or more consecutive frames of image data are recorded. The 2-D displacements between each pair of consecutive frames are estimated using a mesh-based speckle tracking method previously presented. Motion estimates are obtained only from nodes that have high feature energies, minimizing the risk of speckle decorrelation. The amplitude, phase and direction of the motion vectors are calculated using a least-square estimator. Elastic reconstruction is then formulated as a forward problem based on finite element theory. The region of interest is subdivided into sample blocks in which the elasticity and viscosity are assumed to be constant. Given boundary conditions consisting of the measured amplitude and phase values on the boundary of each sample block, the motion vectors for the internal nodes can be estimated from finite element theory, given an assumed elasticity and viscosity. The predicted motions are then compared to the measured data and the sum-squared difference (SSD) is calculated. This procedure is repeated iteratively with different viscoelastic moduli until the minimum SSD is obtained.

Because both ultrasonic tissue motion estimation and elastic reconstruction are mesh-based, their integration provides a systems approach by which the mechanical properties can be measured directly from vibrating ultrasonic image sequences. The approach has been tested on both synthetic data and experimental data from a two layer tissue-mimicking phantom. The preliminary results are very encouraging and centimeter-level resolutions (1x1cm block size, 2 cm spatial resolution) have been realized.

6.3 **New trends in transient elastography,** Laurent Sandrin, Mickael Tanter, Stefan Catheline and Mathias Fink, *Laboratoire Ondes et Acoustique, E.S.P.C.I., Université Paris VII, U.R.A C.N.R.S 1503, Paris, France.*

Elastography is used in different ways to characterize soft tissues. J. Ophir uses static elastography to estimate strains in the tissue after a quasistatic compression. Strains can also

be measured by sonoelasticity using mechanically forced low frequency vibrations and the ultrasonic pulsed Doppler method (Parker and Sato). These techniques are subjected to bias due to unknown boundary conditions and to diffraction effects. In this article, we present a technique called transient elastography that is not sensitive to boundary conditions and to various diffraction limitations. It uses a low frequency pulsed vibration (~ 100 Hz) and a cross-correlation technique to measure displacements on the order of 1 m. This technique is now used with an array of 64 transducers to get time-dependent, two-dimensional displacements at a rate of 2,000 frames per second. Movies of the shear wave propagation through homogeneous, inhomogeneous phantoms and biological tissues have been obtained. We shall discuss how to inverse near-field data in order to recover the medium shear viscosity and elasticity fields.

6.4 **Kinetic acoustic vitreous examination: phantom studies,** W.F. Walker,[1,2] T.J. Mondzelewski,[1] M.J. McAllister,[1] F.J. Fernandez,[1] and C.A. Toth[3], *[1]Department of Biomedical Engineering, The University of Virginia, Charlottesville, VA 22903, [2]NovaSon Corporation, Charlottesville, VA 22901 and [3]Department of Ophthalmology, Duke University Medical Center, Durham, NC 27708.*

Traction and collapse of the vitreous body are known to contribute to the formation of both traction and rhegmatogenous retinal detachment. Although both slit lamp and ultrasonic observation can detect associated optical and ultrasonic changes, neither measures underlying mechanical changes of the vitreous. We are working to develop a new imaging method termed Kinetic Acoustic Vitreous Examination (KAVE) that utilizes acoustic radiation force to generate small displacements within the vitreous, while simultaneously utilizing ultrasound to track these displacements. Maps oflocal displacement are formed with the goal of depicting variations in tissue elasticity and local boundary conditions. A significant challenge to testing of KAVE has been the development of suitable tissue-mimicking phantoms. The vitreous body has an elastic modulus of approximately 0.1 Pa, making it roughly 5 orders of magnitude softer than other soft tissues, such as the breast. Thu,s existing phantoms are inappropriate. We have fabricated a series of phantoms based on low concentration acrylimide gels, with graphite particles added as scatterers. We present experimental results showing KAVE images for a seriesof phantoms with acrylimide concentrations varying between 4.3% and 4.8%. KAVE images clearly depict variations in acrylimide concentration of as little as 0.2%. Displacements of up to 100 m were generated in the softest gel. We also present theoretical predictions of displacement due to radiation force in a variety of tissues. This analysis predicts that KAVE will be able to generate detectable displacements in the vitreous at acoustic intensities that present little risk of thermal damage. Resultsin the breast and liver are less encouraging.

This work was supported by NIH grant R43-EY11456.

7. Tissue Parameters 2

7.1 **Ultrasonic spectrum analysis procedures for breast cancer classification,** S.K. Alam, F.L. Lizzi, E.J. Feleppa, T. Liu and A. Kalisz, *Riverside Research Institute, 330 West 42nd Street, New York, NY 10036.*

We have developed a series of spectrum analysis procedures designed to quantify ultrasonic breast cancer evaluations. The procedures have been planned to improve upon B-mode differentiation of benign and malignant lesions, which employs features such as ‘echogenicity,’ ‘heterogeneity’ and ‘shadowing.’ Our goal is to replace each of these subjective features with corresponding quantitative parameters based on spectrum analysis of

radiofrequency (rf) echo signals in order to remove operator dependence and to permit objective discrimination.

Our technique involves an image-based approach to calibrated spectrum analysis. This has been implemented using rf data digitally acquired from several clinical sites using an ATL Ultramark 9 system. The first step is the digital synthesis of spectral-parameter images derived with sliding-window Fourier transform techniques, as described in previous reports for other organs. Images of uncalibrated local values of spectral intercept and midband fit are generated using a new MATLAB® (The MathWorks, Inc., Natick, MA) implementation. These quantitative images are then calibrated using the spectrum of a planar target together with a range-dependent diffraction correction for each parameter. Diffraction correction employs power spectra measured from diffuse scatterers in a gel or rubber block; it depends upon the specific transducer array and transmit focal-length used in each examination.

Classification parameters are derived after tracing the boundary of breast lesions on midband fit images; each parameter replaces a specific B-mode descriptor. 'Echogenicity' is measured as the mean spectral intercept within the lesion, since this value is not significantly affected by frequency-dependent attenuation in intervening media. 'Heterogeneity' is measured as the statistical dispersion of midband fit values within the lesion. This definition is motivated by previous analysis that demonstrated how the histogram of midband fit, and its variance, can be related to tissue homogeneity. 'Shadowing' is quantified by measuring mean midband fit values in two comparable regions of posterior tissues that are shadowed and not shadowed, respectively, by the lesion. The lesion attenuation coefficient is estimated from the difference between these mean values and the lesion thickness.

Initial results on biopsy-proven cases are promising. We are now investigating additional descriptors for lesion surfaces to quantify the 'smoothness,' 'lobulation' and 'invasiveness' categories that have proven useful in B-mode evaluations.

7.2 **Progress in differentiating cancer-containing from cancer-free lymph nodes by spectrum analysis,** Ernest J. Feleppa,[1] Junji Machi,[2,3] Andrew Kalisz,[1] Frederic L. Lizzi,[1] Tomoaki Noritomi,[2] Tsutomo Tateishi,[2] Robert Oishi,[2,3] Eugene Yanagihara,[3] Laurence J. McCarthy,[3] Douglas Wong[4] and Paul Bernick[4], *[1]Riverside Research Institute, New York, NY, [2]University of Hawaii Medical College, Honolulu, HI, [3]Kuakini Medical Center, Honolulu, HI and [4]Memorial Sloan-Kettering Cancer Center, New York, NY.*

Lymph nodes are surgically excised for diagnostic and therapeutic purposes for many commonly-encountered types of cancer . For example, axillary nodes of patients with invasive breast cancer and prostate-cancer are dissected for diagnostic purposes; nodes of melanoma patients are dissected for therapeutic as well as diagnostic purposes. Excised nodes are evaluated histologically to establish a prognosis and to plan adjunctive therapy. However, many cancer-free nodes are unnecessarily dissected, and metastases in cancer-containing nodes go undetected. We performed preliminary *in vitro* studies of 40 axillary nodes of breast cancer patients and 40 abdominal nodes of colorectal cancer patients to compare the ability of B-mode criteria and radiofrequency (rf) echo-signal spectrum analysis to distinguish cancerous from cancer-free nodes. Scanning was performed immediately after surgery in a saline water bath and node status was then determined histologically. We found that node status was best determined from the slope and intercept parameters, and based on nearest-neighbor analyses of these parameters, spectrum analysis produced ROC-curve areas of >0.98 for axillary nodes and >0.95 for abdominal nodes. In comparison, B-mode criteria (i.e., size, diameter ratio, border definition and hilum echogenicity) produced ROC-curve areas of < 0.90 and < 0.84 for axillary and abdominal nodes respectively. Subsequent *in vivo* studies of axillary nodes produced comparable results that, like prior *in vitro* results, showed superior ability of spectrum analysis to distinguish cancerous from cancer-free

nodes compared to B-mode methods. Our recent preliminary studies are emphasizing sentinel-node approaches in breast-cancer applications and are investigating the use of these methods for transrectally accessed nodes in rectal-cancer applications. These preliminary studies continue to suggest that spectrum analysis may effectively distinguish cancerous from cancer-free nodes for a variety of types of cancer, and therefore may be useful for guiding dissections to improve the yield of metastatic nodes to minimize the excision of benign nodes.

7.3 **Use of cyclic variation measurements at rest to predict wall motion abnormalities during peak dobutamine stress echocardiography,** James G. Miller, Rupsa Ray Yee, Eduardo Segovia, Kirk D. Wallace, Chris Baumann, Mark R. Holland, Stephanie Loslo and Julio E. Perez *,Departments of Physics and Cardiology, Washington University, St. Louis, MO.*

The use of pharmacologic inotropic stimulation in conjunction with echocardiography has become a widely accepted tool for the detection of myocardial ischemia and for the elucidation of myocardial viability in the presence of coronary artery disease. The objective of this study was to determine whether measurements of the cyclic variation of integrated backscatter at rest can predict the development of new wall motion abnormalities at peak dobutamine stress. Our approach was to measure the magnitude and time delay of the cyclic variation in septal and posterior wall segments, visualized in the parasternal long axis view in 20 patients at rest, and to compare these measured values with the corresponding echocardiographic wall motion scores (normal or abnormal) obtained during peak dobutamine infusion. Results from this study show that the magnitude of resting cyclic variation was significantly depressed in those myocardial segments exhibiting normal wall motion at rest that subsequently developed wall motion abnormalities at peak dobutamine when compared with those segments that remained normal. Furthermore, there was a trend towards a lengthening of time delay in the resting cyclic variation for those segments that subsequently developed ischemia at peak dobutamine when compared with those segments that remained normal. Results of initial ROC analyses comparing the measurement of cyclic variation at rest with the segmental wall motion at peak dobutamine stress demonstrate an area under ROC curve of 0.81, with sensitivity = 0.80, specificity = 0.77, and accuracy = 0.78 at the optimal operating point. These preliminary results suggest that cyclic variation measurements at rest may provide a method for predicting the myocardial response at peak dobutamine stress.

[NIH Grants HL40302 and HL53461].

7.4 **Ultrasonic tissue characterization by means of wavelet coefficients,** David Lee and Joie Jones, *Department of Radiological Sciences, University of California Irvine, Irvine, CA 92697.*

In principle, any signal can be represented by a set of wavelets that form an orthogonal basis. This is similar to Fourier's idea that a signal can be thought of as comprised of a series of sinusoidal waves of different amplitudes and frequencies. Consequently, a signal can be viewed in either a time or a frequency domain. Wavelet transformation decomposes a time domain signal into smaller segmented time domain signals known as wavelets. Each wavelet has a different but finite duration while they all have the same shape. By adding or subtracting these wavelets via appropriate weighing factors, or wavelet coefficients, the original time domain signal can be reconstructed. For simplicity, a special basis known as the Harr wavelet is used in this study. Harr wavelets consist of finite pieces of 1's, 0's and -1's with various durations. A time domain signal decomposed by wavelet transformation is represented by a set of wavelet coefficients. These weighing factors can then be used to

reconstruct the time signal. Like the power spectrum in Fourier analysis, these wavelet coefficients provide an interesting insight as to the nature of the signal under investigation. In this paper, both computer simulated and physical data from a number of reticulated foam samples were studied via a method inspired by wavelet analysis. Using envelope-detected signals, we show that there is a definite relationship between the wavelet coefficients and the spatial dependence of the attenuation-slope of a medium. A histogram of these wavelet coefficients thus provides a novel and simple means for estimating attenuation and, perhaps, for also characterizing tissue and tissue state.

7.5 **Multivariate ROC analysis: new tools for assessment of image quality and computer-aided diagnosis,** Robert F. Wagner and Sergey V. Beiden (Research Associate, Oak Ridge Institute for Science and Education), *Center for Devices & Radiological Health (FDA), 12720 Twinbrook Parkway, Rockville, MD 20857.*

In recent years, a number of new approaches have been developed for incorporating several random effects into the analysis of the performance of diagnostic modalities using the ROC (receiver operating characteristic) paradigm. In the application to image quality assessment, these random effects include variations observed when sampling from a population of readers, a population of cases, and replications of image readings. In the application to the assessment of computer-aided diagnosis (including the general problem of quantitative tissue classification), there are additional random effects due to sampling from a population of training cases and a population of test cases. In this paper, we review recent advances in multivariate random-effects models for ROC analysis.[1-3] These approaches provide estimates of ROC performance parameters and their uncertainties that reflect, e.g., the effects of reader and case randomness, or the effects of randomness in training cases and testing cases. These tools will be necessary for rigorous assessment of the augmentation of human reader performance available from the incorporation of machine-assisted reading via quantitative tissue characterization. We shall provide examples from the literature on image assessment plus our own work on multivariate classifiers used in computer-aided diagnosis.[3]

(1) Dorfman, D., Berbaum, K.L. and Metz, C.E., Receiver operating characteristic rating analysis: generalization to the population of readers and patients with the jackknife method, *Invest. Radiol. 27*, 723-731 (1992).

(2) Gatsonis, C.A., Begg, C.B. and Wieand, S., Advances in statistical methods for diagnostic radiology: a symposium, *Academic Radiology 2, Suppl. 1* (1995).

(3) Wagner, R.F., Chan, H-P, Mossoba, J.T., Sahiner, B. and Petrick, N., Components of variance in roc analysis of classifier performance, in *Proc. SPIE 3338*, pp. 859-875 (1998).

7.6 **Statistical properties of estimates of lesion detectability for medical ultrasonic imaging systems,** Keith A. Wear, Robert M. Gagne, and Robert F. Wagner, *Food and Drug Administration, Center for Devices and Radiological Health, 12720 Twinbrook Parkway, Rockville MD, 20857.*

Uncertainties of estimates of focal lesion detectability for medical ultrasonic imaging systems are investigated. Two distinct theoretical approaches are used to derive expressions for bias and variance of estimates of detectability of a lesion consisting of fully-developed speckle embedded within a speckle background. The first method is based on an error propagation approach. The second method is based on approximations for the probability density functions for the numerator and denominator of the formula for lesion detectability. Good agreement is found for the two methods. The theory is validated using a computer simulation and experiments on tissue-mimicking phantoms. This work offers a systematic methodology for interpreting measurements on phantoms in order to assess lesion detectability. In addition, it provides useful results that may be used to improve design of phan-

toms and experiments for imaging system performance assessment. In many cases, such experiments may constitute an inexpensive and relatively objective alternative or supplement to clinical trials.

8. IMAGING 2

8.1 **Ultrasound 3D imaging techniques for frameless fusion,** B. Porter,[1] D. Rubens[2] and K.J. Parker[1,2], *[1]Department of Electrical and Computer Engineering, [2]Department of Radiology and Rochester Center for Biomedical Ultrasound, University of Rochester, Rochester, NY 14627*

We have derived 'frameless fusion' techniques to integrate MRI and ultrasound volumetric images, using internal vasculature as the fiducial markers. We now focus on the fusion of 3D ultrasound volumes to monitor lesions in patients receiving radiation, chemotherapy or ablation. In this talk, we focus on different ultrasound imaging strategies for rendering 3D vasculature.

In-vivo liver imaging (3-5 MHz) employed tissue harmonic imaging (THI), Color Doppler (CD) and Power Doppler (PD) modes. CINE sequences of 2D images were thresholded for vessels (hypoechoic or color regions), followed by 3D rendering. Baseline measurements for vessel diameter and branching order were determined by a trained radiologist. 3D reconstructions were assessed by comparisons of baseline measurements to segmented vessel size. We found the CD segmentation accuracy to range from +13% to +73%; the accuracy for PD ranged from 12% to +55%; and THI ranged from 14% to 19%. Detectability results were measured in terms of branching order of vessels (1st order indicates largest branches). THI and CD resolved 2-3 orders, PD 3-4 orders.

We conclude that THI provided the best 3D rendering of vessel diameter and shape, and is the preferred technique for segmentation of major hepatic vessels. However, it has limited ability to resolve smaller branches of vasculature. The PD technique better renders smaller vessels; however, its 3D reconstructions are contaminated by noise, blooming and flash artifacts.

8.2 **Estimation of 3-D motion field on ultrasonic images using regressive model and a respiratory signal,** Kazushi Ohta,[1] Norio Tagawa,[1] Akihiro Minagawa,[1] Tadashi Moriya[1] and Shinichi Minohara[2], *[1]Graduate School of Engineering, Tokyo Metropolitan University, Tokyo Japan and [2]National Institute of Radiological Science, Chiba, Japan.*

Estimating the motion of internal organs is essential in the effective treatment of cancer by radiation therapy. Such motion has been strongly correlated with respiration as demonstrated by ultrasonography.(1) By making use of this correlation, we have recently constructed an algorithm for 2-D motion estimation with ultrasonic images without using template matching.(2) In that algorithm, the 2-D motion was represented as an optical flow, which means an instantaneous 2-D velocity field, and was modeled as a regressive random variable with respect to the respiratory signal. The unknown regressive parameters as well as the 2-D motion were simultaneously estimated using the Expectation-Maximization (EM) algorithm as a maximum-likelihood estimator. This regressive model allows the appropriate temporal constraint for the motion to be introduced. However, the true motion of internal organs is generally three-dimensional. Then, if the motion is not parallel to the plane observed through sequential ultrasonic images, the image intensity of the organ will change before and after the motion. In that case, the gradient equation which is used in the proposed algorithm as a fundamental equation, does not completely hold. This may cause the estimated motion to be erroneous. Therefore, in this paper, we expand the 2-D algorithm

to the 3-D motion estimation problem using 3-D ultrasonic image sequences instead of 2-D sequences. Although this 3-D problem is further ill-posed than the 2-D problem, by applying the above regressive model, we observed that the estimation of the motion becomes stable. The validity and effectiveness of the model and algorithm were verified through simulations using numerical phantoms having definite 3-D motion fields. Although the algorithm does not arbitrarily use a spatial constraint for the motion, e.g., the smoothness constraint, the estimated motion field has an expectative smoothness automatically. This can be understood that the true motion is essentially smooth spatiotemporally and the temporal constraint used in the proposed algorithm enables us to detect the smooth motion without loss of spatial resolution.

Part of this work was supported by Research Project with Heavy Ions at NIRS-HIMAC from the Science and Technology Agency of Japan.

(1) Yonezawa, R. et al, in *World Cong. Med. Phys. Biol. Eng., Part I,* No.D89-OSI.02, 410 (1997) (abstract).

(2) Iida, M. et al, in *IEEE Ultrasonics Symp.*, 195 (1998).

8.3 **Very-high-resolution ultrasonic assays of 3-D ciliary body morphology,** F.L. Lizzi,[1] P. Lee,[1] A. Kalisz1, R.H. Silverman,[2] M. Rondeau,[2] and D. J. Coleman[2], *[1]Riverside Research Institute, 330 West 42nd Street, New York, NY 10036 and [2]Cornell University Medical College, 1300 York Avenue, New York, NY 10021.*

Our laboratories have been mapping the ciliary body with high-frequency ultrasound in order to determine quantitative morphologic indices that can be employed in glaucoma studies. Our overall objective is to provide a basis for describing normal anatomy, detecting anomalous deviations, and monitoring the effects of glaucoma and glaucoma medications.

Our examinations employ computer-controlled scanning of a transducer with a 40-MHz center frequency. Radiofrequency echo signals from the anterior ocular segment are acquired (8 bits) at a 250 MHz sampling frequency. Parallel-plane scanning, with planar separation as small as 80 μm, is used to obtain 3-D data. Postprocessing is employed to improve axial resolution (to 30 μm) or to generate cross-sectional images depicting spectral-backscatter parameters. Processed results from each scan plane are then combined using a Silicon Graphics Onyx workstation to synthesize interactive 3-D volume and surface renderings.

Our most extensive studies have treated the *in-vivo* rabbit eye, a widely-used model in glaucoma research. We have defined and implemented several quantitative morphologic descriptors of complex ciliary processes, which are responsible for aqueous-humor production. The descriptors measure the surface area, volume, spatial configuration and 3-D branching patterns of these processes. To complement standard 3-D renderings, we have developed interactive, PC-based algorithms that emulate dissection procedures to permit more cogent visualization of characteristic morphologic features.

These techniques are also being applied to 3-D data obtained from normal humans and glaucoma patients in order to follow the progression of disease, effects of aging and chronic effects of glaucoma medication.

8.4 **Low reflection coefficient materials for system characterization,** T.J. Hall, F. Dong, E.L. Madsen, I. Medina and G.R. Frank, *Department of Radiology, University of Kansas Medical Center, Kansas City, KS 66160-7234 and Medical Physics Department, University of Wisconsin-Madison; hall@research.kumc.edu.*

We have developed the use of liquid halogenated hydrocarbons in water as planar reflectors for system characterization. Use of these materials provides an accurately characterized reference reflector with an echo signal in the range of typical scattering samples, so that

the need for accurately calibrated attenuators is minimal. More specifically, acoustic reflection coefficients with magnitudes ranging from 0.005 to 0.1 were obtained with these materials. The acoustic reflection coefficient, and our uncertainty in its estimate, was measured for six pure samples of hydrocarbons in water and for three samples containing a mixture of hydrocarbons. Measurements were made at temperatures ranging from 18 to 24 C. In addition, similar measurements were made for three solid materials (stainless steel, fused silica, and polymethyl methacrylate) that are typically used as reference reflectors. Repeated measurements on a single sample show that our technique resulted in a precision of approximately 1%. Propagation of uncertainties in the reflection measurement suggest an uncertainty of approximately 2%. Sound speed and mass density of three fluid samples and the three solid materials were also measured at 22 C. The reflection coefficients (and the associated uncertainties) calculated from these values are in excellent agreement with the measured reflection coefficients. Comparison of the computed and measured reflection coefficients suggests that simple calculations for reflection from a perpendicular interface based on the acoustic impedances on either side of the boundary provide accurate reflection coefficients. Using these results, the acoustic reflection coefficients were fit to a function of hydrocarbon concentration and temperature. This function can be used to predict the reflection coefficient given the temperature and the mass density and acoustic propagation speed for the pure hydrocarbons. Thus, knowing the temperature at which the reflector will be used, the approximate concentrations of hydrocarbons can be selected to obtain a desired reflection coefficient from the functional fit. An accurate validation of the reflection coefficient can then be established with a single measurement of the mass density and sound speed for the chosen mixture. For example, the hydrocarbons used in this study allow us to obtain any desired reflection coefficients ranging from -0.0684 to 0.113 at 22.0 C.

This work was supported by grants NIH R42GM54377, NIH DK43007, and NSF/WF BES-9708221.

8.5 **Initial clinical trials using noncontact ultrasonic imaging for the evaluation of thermal injury,** Joie P. Jones,[1] Saeed Iraniha,[2] David Lee,[1] Marianne Cinat,[2] Victoria Vanderkam,[2] Mahesh Bhardwaj[3] and Bruce Achauer[2], *[1]Department of Radiological Sciences and [2]UCI Burn Center, University of California Irvine, Irvine, CA 92697 and [3]Ultran Laboratories, Boalsburg, PA 16827.*

At the 1997 Symposium, we presented, for the first time, some preliminary clinical results using noncontact (i.e., through air) ultrasonic imaging. At the 1998 Symposium, we presented additional clinical results using a greatly improved ultrasonic system. Here we present the results of an initial clinical trial of this technology applied to some 100 patients over a two year time period.

Although conventional wisdom suggests that ultrasonic imaging of the body cannot be accomplished without direct contact (or at least via water coupling), we have shown that noncontact imaging **is** possible, certainly for superficial body regions, provided judicious choices of piezoelectric materials and matching layers are made. In preliminary experiments reported here previously, noncontact imaging was demonstrated for the evaluation of thermal injury (including the quantitative measurement of burn depth), for the assessment of wound healing and for the examination of assorted skin lesions. Specifically, in the case of thermal injury, reflections from the dermal/fat interface in human skin were clearly seen using a noncontact 5 MHz transducer, with only somewhat poorer results obtained at 2 MHz. Such measurements proved sufficient to determine burn depth which, in turn, were sufficient to provide, for the first time, a quantitative and noninvasive method for burn evaluation and treatment specification.

Over the past two years we have collected data on some 100 burn patients enrolled in our study. For each patient, the burned areas as well as normal control skin sites were scanned by noncontact ultrasound on day one and on day three following the burn event. Selected patients were also scanned following a period of several weeks. Two experienced physicians, blind to the results of ultrasound, made independent clinical assessments of the burned areas on days one and three and on later days when feasible.

The noncontact ultrasound device used is a hand-held, battery-operated laboratory prototype that emits a pulse of ultrasonic waves with a center frequency of 5 MHz. The plane-piston transducer, acoustically matched to air, is held one to two inches from the skin surface under study. The reflected ultrasonic waves are recorded by the device as an individual A-line, a sequence of which are transformed into an image off-line by computer processing. Such processing requires calibration using an adjacent area of normal skin to insure the visualization of the dermal/fat interface. An investigator blind to the clinical findings interpreted the ultrasound results and predicted the type of burn visualized and whether or not the burn could heal without surgical intervention. Evaluating over 500 burn sites in some 100 patients, noncontact ultrasound showed an accuracy of 96% while standard clinical assessment showed an accuracy of 80%. The sensitivity for noncontact ultrasound was 100% compared to a sensitivity for standard clinical assessment of 65%. The specificity for ultrasound was 92% compared to a specificity for clinical assessment of 96%. The lower specificity for ultrasound may be a result of the fact that patient management was determined by clinical assessment alone. In any case, our study clearly demonstrates that noncontact ultrasonic imaging can be used for the rapid and accurate assessment of thermal injury, including the measurement of burn depth, with no patient discomfort. Our method is applicable to a conventional clinical environment as well as a battlefield situation and should prove particularly effective for large scale medical triage.

8.6 **Representation of solutions to wave equation with X waves**, Jian-yu Lu and Anjun Liu, *Ultrasound Laboratory, Department of Bioengineering, The University of Toledo, Toledo, OH 43606.*

Limited diffraction beams such as X waves are a new type of waves that can propagate to an infinite distance without spreading in both transverse and axial directions, provided they are produced with an infinite aperture and energy. In practice, when the aperture and energy are finite, these beams have a large depth of field. Because of this property, limited diffraction beams have applications in medical imaging, tissue property identification, blood flow velocity vector measurement, nondestructive evaluation (NDE) of materials, communications, and other areas such as optics and electromagnetics.

In this report, we study the intrinsic relationship between X waves and any solutions including limited diffraction solutions to the isotropic-homogeneous scalar wave equation. Results show that any well-behaved solutions to the wave equation can be expressed as a linear superposition of X waves (using X waves as basis functions). The coefficients of the expression can be obtained using the orthogonal property of X waves. These results produce a new transform, called X wave transform. The X wave transform is significant because it reveals the relationship between X waves and any waves including other limited diffraction beams. It can be used to design new limited diffraction beams that may also have practical applications.

FRIDAY, JUNE 4

9. ELASTICITY 2

9.1 **Elastographic imaging of the canine prostate *in-vitro,*** Faouzi Kallel,[1] Elisa Konofagou,[1] Roger E. Price,[2] R. Jason Stafford,[3] Raffaella Righetti,[1] and Jonathan Ophir[1] [1]*University of Texas Medical School, Department of Radiology, Ultrasonics Laboratory, 6431 Fannin St., Houston, TX 77030,* [2]*The University of Texas, M.D. Anderson Cancer Center of Veterinary Medicine and Surgery and* [3]*Section of Diagnostic Imaging Physics,1515 Holcombe Blvd., Houston, TX 77030.*

Ten freshly excised canine prostates were mounted inside of a homogeneous block of gel for support during elastographic imaging. Parallel equally-spaced cross-sectional elastograms were obtained at 5 MHz as well as matching sonograms. After data acquisition, the glands were carefully removed from the gel and fixed in formalin. The fixed prostate was sliced in 2.5 mm thick slices and the slices photographically documented. Selected slices were routinely processed and 6 mm sections cut and stained with hematoxyln and eosin or Masson's trichrome staining methods for histopathologic examination.

The normal prostate had a prominent radial arborizing network of fibrous connective tissue septae centered on the urethra. The network of branching fibrous connective tissue septae separated the lobules of glandular tissue. The central portion of the gland surrounding the urethra consisted of straighter glands with larger lumens and lined by smaller epithelial cells while the peripheral portion of the gland was composed of more tortuous glands with smaller lumens and lined by larger, more plump epithelial cells. The prostate was surrounded by a thin fibrous connective tissue capsule containing intermittent layers of smooth muscle.

The elastograms of the transverse cross-sections across the urethra demonstrated a consistent symmetry of the gland as well as clear anatomic structures. These include a central portion of the gland surrounding the urethra and a peripheral gland. The inner gland was consistently softer than the outer gland. At the level of the verumontanum, depicted as a hard circular area, the urethra was consistently demonstrated as a reversed soft 'V' shaped area. The network of branching fibrous connective tissue septae was depicted by the elastogram as linear features which converged on the urethra. In the anterior side of the gland the fibromuscular stroma is seen as a circumscribed hard tissue.

In conclusion, elastograms obtained from normal canine prostates demonstrated a well-defined symmetry of the gland with a clear depiction of its anatomical structure. In light of these results, elastography may become an important diagnostic imaging technique for the prostate, that overcomes the well known limitations of conventional diagnostic ultrasound techniques.

This work was supported in part by NIH grants R01-CA60520 and P01-CA64597 to the University of Texas Medical School. The canine prostates were obtained courtesy of Dr. B.D. Butler at UT Medical School.

9.2 **Real-time elastography: phantom studies and first *in-vivo* results,** Andreas Pesavento, Andreas Lorenz and Helmut Ermert, *Institute of Electrical Engineering, Ruhr-University Bochum, D-44780 Bochum, Germany. pes@hf.ruhr-uni-bochum.de*

Since the first elastograms have been presented by Ophir et al in 1991, elastography has become of high medical interest. In several studies, the medical significance of elastography has been shown. However, a major problem of elastography in the past was the lack of real-time capability. Due to the off-line calculation of elastograms a medical examination

using this technique was difficult. The quality of the acquired therefore data could not directly be evaluated; hence, decorrelation noise and motion artifacts were significant problems of *in vivo* applications. In this contribution a system is presented that continuously displays elastograms with up to 5 frames per second obtained by manually or semimanually compressing or releasing the tissue during an ultrasound examination. The rf echo data are acquired using a 7.5 MHz abdominal or a 7.5 MHz transrectal probe and are sampled by a conventional desktop PC (Pentium 200 MMX) and images of the axial strain are calculated using the fast phase-root-seeking technique. This technique has previously been proven to offer the same results as conventional cross-correlation techniques, but is computationally more efficient. Up to 5 elastograms per second of a tissue region of approximately 3.7 cm x 3.5 cm are displayed. Using our set-up, the data acquisition is an interactive process, since elastograms are continuously displayed. For an operator, it is now possible to adequately operate the probe in clinical *in vivo* studies. The acquired echo data is used for further off-line processing including lateral motion compensation and adaptive temporal stretching.

The limitations and advantages of the system will be discussed on phantom studies and our first *in vivo* results.

9.3 **Imaging skeletal muscle elasticity during force generation,** P. Chaturvedi, M.F. Insana, T.J. Hall and C. Luchies, *The University of Kansas Medical Center, Kansas City, KS 66160-7234.*

The relationship between stiffness and force generation in skeletal muscles determines the ability of muscles to perform normal function. To study this relationship, we recently developed algorithms to image strain in healthy anterior thigh muscles under an externally-applied compression. Simultaneously, muscle activity was monitored with electromyography (EMG) and the torque generated at the knee joint was measured with a dynamometer. Investigations were performed for muscles in the relaxed state, during isometric extension and during isometric flexion of the knee. We observed that different muscle groups could be visualized in strain images for all conditions of internal force generation studied. The quadriceps muscle appeared soft both in the relaxed state and during isometric flexion; the same muscles appeared stiff during isometric extension. Strain measurements at 5 MHz showed that muscle stiffness and EMG activity remained constant during isometric flexion of the knee joint. However, stiffness and EMG activity both increased linearly with torque during isometric extension up to 60% maximum voluntary contraction (MVC). EMG activity increased beyond the 0.6 MVC limit but the measured stiffness decreased as collateral muscles were recruited. Our results indicate that strain imaging using static external compression can noninvasively provide information about skeletal muscle elasticity during force generation.

9.4 **Elasticity imaging to monitor plaque rupture**, C.D. Choi,[1] B.M. Shapo,[1] M.A. Lubinski,[1] J.R. Crowe[1], A. Skovoroda,[2] S.Y. Emelianov[1] and M. O'Donnell[1], *[1]Biomedical Engineering Department, University of Michigan, Ann Arbor, MI 48109-2125 and [2]Institute of Mathematical Problems in Biology, Russian Academy of Sciences, Pushchino, Russia, 142292.*

Atherosclerotic plaque rupture is widely believed to be the leading cause of strokes and myocardial infarctions. Various *ex-vivo* studies have shown that some plaques are more vulnerable to rupture. Vulnerable plaques tend to be lipid-filled with a fibrous cap, where rupture usually occurs in the lipid-rich, and presumably softer, shoulder regions. Rekhter and Ryan have developed a vulnerable plaque model resembling human coronary lesions by embedding in the rabbit thoracic aorta a balloon catheter surrounded by a vein-derived

collagenous scaffold.(1) After a plaque develops around the balloon catheter, the aorta is excised and the balloon is inflated until the plaque ruptures. Preliminary *ex-vivo* results from rabbits fed either a low cholesterol or high cholesterol diet over three months suggest that the average aggregate elastic properties of the two groups are significantly different. We have estimated the average value of the Young's modulus from pressure-volume curves collected from these plaque rupture experiments. These curves were converted to a pressure-radial displacement relation assuming uniform radial inflation of the balloon. The estimated Young's moduli of the plaques from low and high cholesterol fed rabbits were 949.3 126 kPa and 549.4 148 kPa, respectively, with $p < 0.05$. In addition to Young's modulus estimates, rupturing pressure and collagen content for the low and high cholesterol groups were also different with $p < 0.05$. Combining intravascular ultrasound with the Rekhter-Ryan rabbit model, vulnerable plaques can be characterized with elasticity images. Using a 64-element Endosonics intravascular ultrasound array placed along the catheter center, displacement information was tracked in real-time as the plaque ruptured either *in-vivo* or *ex-vivo*. Strain and elasticity images derived from tracking images can provide spatial and mechanical insights into developing and ruptured plaques. Results from these experiments will be presented and compared to histologic and biochemical data to correlate mechanical and biochemical mechanisms of plaque rupture. Such comparisons should lead to a better understanding of plaque rupture and possible treatments for plaque stabilization.

(1) Rekhter, M.D. et al, Animal model that mimics atherosclerotic plaque rupture, *Circ. Res. 83,* 705-713 (1998).

9.5 **Statistical mechanics modeling and elastographic monitoring of soft tissues for heat therapies,** Alex Alaniz,[1,2], Faouzi Kallel,[2] Raffaella Righetti,[2] R. Jason Stafford,[3] Thomas Krouskop,[4] E. Hungerford[1] and Jonathan Ophir[2], *[1]University of Houston, Physics, Houston, TX 77204, [2]The University of Texas Medical School, Department of Radiology, Ultrasonics Laboratory, 6431 Fannin St., Houston, TX 77030, [3]M.D. Anderson Cancer Center, Section of Diagnostic Imaging, 1515 Holcombe Blvd., Houston, TX, [4]Baylor College of Medicine, Physical Medicine and Rehabilitation Department, 1333 Moursund Ave., Houston, TX 77030.*

The microscopic properties of soft tissue extracellular polymer protein networks (EPPNs) are dependent on tissue type and age, as well as tissue disease, thermal, mechanical and chemical histories. In turn, the macroscopic thermomechanical properties of soft tissues, including responses to heat therapies are significantly determined by their EPPNs. Therefore, responses to heat therapies may differ from samples of a specific type of tissue and from amongst various types of tissues. During heat based surgical procedures, the thermo- mechanical properties of soft tissues may be changed reversibly or irreversibly in response to energy deposited by lasers, microwaves and ultrasound. Molecular changes may also be caused by chemical reactions and mechanical actions such as from ultrasonic shock wave cavitation bubbles. These various modalities affect the EPPNs by making and/or breaking intra- and intermolecular bonds. In turn, these EPPNs contribute largely to the Young's and shear moduli of soft tissues as well as to their heat capacities and thermal expansion coefficients. Thus, there are several measurable thermomechanical properties of soft tissues which depend in large part on their EPPNs.

Statistical mechanics (SM) provides a theoretical framework for modeling the chemistry and thermomechanics of polymer networks. SM has been successfully applied to industrial polymers, simple protein gels and to one-dimensional connective tissue protein networks made of collagen, elastin, fibronectin, etc. As for *actual* heat treated soft tissues, there is an abundance of qualitative literature, but little quantitative data and little theory. In this paper, SM theory is used to model the thermomechanical properties of soft tissues. Data from a

one-dimensional quantitative study[1] of the mechanical changes of heat treated tissues corroborate the statistical polymer model. In addition, thermomechanical data were taken from *in vitro* tissue lesions induced by high intensity focused ultrasound (HIFU) while the temperature was monitored by MRI.[2] These data obtained by elastography at room temperature[2] further corroborate theoretical predictions connecting the measured thermal histories to the measured changes in moduli. As observed in reference 1, and as expected by theory, the HIFU lesion data indicate that thermal history is the key indicator to changes in tissue modulus. Elastography thus provides a method to monitor the effects of thermal, mechanical and chemical perturbations on soft tissue EPPNs and may serve as a tool for verifying theoretical soft tissue polymer models.

This work was supported in part by NIH grants R01-CA60520 and P01-CA64597 to the University of Texas Medical School.

(1) Chen, S.S., et al, Heat-induced changes in the mechanics of a collagenous tissue: pseudoelastic behavior at 37 C, *J. Biomech 31,* 211-216 (1997).

(2) Righetti, R., Kallel, F., Stafford, R.J., et al., Ophir, Elastographic characterization of HIFU-induced lesions in canine livers, *Ultrasound Med. Biol.* (submitted, 1998).

9.6 **Characterization of HIFU-induced lesions in canine livers using elastography,**
R. Righetti,[1] F. Kallel,[1] R.J. Stafford,[2] R.E. Price,[3] T. Krouskop,[4] J.D. Hazle[2] and J. Ophir[1],
[1]The University of Texas Medical School, Department of Radiology, Ultrasonics Laboratory, 6431 Fannin St., Houston, TX 77030, The University of Texas M.D. Anderson Cancer Center, [2]Section of Diagnostic Imaging Physics and [3]Department of Veterinary Medicine and Surgery, 1515 Holcombe Blvd., Houston, TX 77030 and [4]Baylor College of Medicine, Physical Medicine and Rehabilitation Department, 1333 Moursund Ave., Houston, TX 77030.

The elastographic visualization and evaluation of high intensity focused ultrasound (HIFU) induced lesions were investigated.[1] The lesions were induced *in vitro* in freshly-excised canine livers. The use of different treatment intensity levels and exposure times resulted in lesions of different sizes. Each lesion was clearly depicted by the corresponding elastograms. Generally, the lesions were not seen in the corresponding sonograms. Indeed, standard ultrasonic methods seem to be not sufficiently accurate for the detection of purely thermal lesions.[2]

The lesions appeared in the elastograms as hard areas embedded in a softer background. The strain contrast of the lesion/background was found to depend on the temperature increase inside the exposed tissue during the treatment. An accurate elastographic characterization of the appearance of the HIFU induced lesions revealed the presence of zones characterized by different strain contrast levels inside the damaged areas. The same lesions appeared histopathologically as nonuniform areas, suggesting the involvement of different types and/or degrees of damage during the creation of these lesions.

A lesion/background strain contrast between -2.5 dB and -3.5d B was found to enclose the entire zone of tissue damage. The areas of the lesions were automatically estimated from the gross pathology photographs and from the corresponding elastograms. A total of 16 lesions was considered. The estimated areas ranged between approximately 10 mm^2 and 110 mm^2.

A high correlation between the areas of damage as depicted by the elastogram, and the corresponding areas as measured from the gross pathology photograph was found (r^2=0.93, p-value<0.0004, n=16). This statistically-significant high correlation demonstrates that elastography has the potential to becomes a reliable and accurate modality for HIFU therapy monitoring.

This work was supported in part by NIH grant R01-CA60520 and Program Project Grant P01-CA64597 to the University of Texas Medical School. The canine livers were obtained courtesy of Dr. B.D. Butler at UT medical school.

(1) Righetti, R., Kallel, F., Stafford, R.J., et al., Ophir, Elastographic characterization of HIFU-induced lesions in canine livers, *Ultrasound Med. Biol.* (submitted, 1998).

(2) Hill, C.R and ter Haar, G.R. High intensity focused ultrasound- potential for cancer treatment, *Br. J. Radiol. 68*, 1296-1303 (1995).

9.7 **Development of a numerical thermoelastic model of soft tissues using a finite element method,** H. Jellab,[1], M. Bertrand,[1,2] and L. Soualmi [1,3], [1]*Institut de génie biomédical, École Polytechnique de Montréal,* [2]*Institut de Cardiologie de Montréal,* [3]*Montreal Neurological Institute.*

We report on the development of a model to investigate the soft tissue thermoelastic responses during hyperthermia treatments and study the potential application of thermoelastography for tissue characterization. For our study, we use a simple model for the material properties: the tissue is a linear isotropic thermoelastic body. The associated thermoelastic stress-strain relations, also known as the Duhamel-Neumann laws, are:(1)

$$_{ij} \quad 2 \; e_{ij} \qquad _{ij} e_{nn} \quad (3 \quad 2 \;) \; _{ij}$$

where $_{ij}$ and e_{ij} are respectively the stress and strain tensors, μ and are the Lamé's coefficients, $_{ij}$ is the Kronecker symbol, is the thermal expansion coefficient and is the temperature change. In the force equilibrium equations, the temperature related term is equivalent to an internal body force(2) which, if appropriately controlled, can be used to set a mechanical response. An interesting application of this would be to use HIFU to induce stresses in regions deep in a tissue in order to determine the local elasticity. The model we present is based on a finite element method (FEM) implemented in Matlab's PDE toolbox; the toolbox was extended to solve 2-D thermoelastic problems, the thermal problem being described through the bioheat equation. The thermoelastic equations are coupled through their time-dependent temperature and displacement field variables. To simplify, we consider a steady state problem. In practice, this means the temperature distribution can first be solved regardless of the displacement field, and then the displacement can be solved taking into account the changes in temperature profile. To verify the model, results from computer simulation are compared to theoretical prediction for simple geometry and temperature profile. We give simulation results using a simplified model predicting the thermoelastic tissue responses during transrectal HIFU hyperthermia treatments of prostates; we discuss the characteristics of the associated radial and angular strain maps (i.e., ideal elastograms) in relation with Young's modulus, thermal expansion coefficient and temperature distribution.

Supported by the National Research Council of Canada, FCAR Quebec Ministry of Education. A part of the project was performed pursuant to the University of Texas Grant CA64597-01 with the NIH, PHS.

(1) Saada, A.S., *Elasticity Theory and Applications*, 2nd ed. (Krieger Publishing Company, Malabar, FL, 1993).

(2) Nowinski, J.L., *Theory of Thermoelasticity with Applications* (1978).

1.6 **Tracking progressive renal disease with quantitative ultrasonic imaging**, T.J. Hall, H. Khant, M.F. Insana, P. Chaturvedi, J.G. Wood, D. Preston and B.D. Cowley, *Departments of Radiology, Physiology and Medicine, University of Kansas Medical Center, Kansas City, KS 66160-7234; hall@research.kumc.edu.*

We are combing techniques of quantitative ultrasonic imaging to study polycystic kidney disease (PKD) in a rat model as the disease progresses to renal failure. The goal of our work is to use ultrasound to noninvasively detect morphological changes early in the disease process when interventions are most successful and before there is a significant loss in renal function.

We are examining the kidneys of PKD and normal rats at various ages to determine when changes in microstructure (scatterer size and integrated backscatter) occur in the renal cortex. Results from histology show that renal parenchyma becomes distorted as early as three weeks age in rats that inherit one abnormal (PKD) gene, and there is a measurable increase in blood nitrogen as early as eight weeks age (indicating some loss of renal function). Measurements of renal function, i.e., glomerular filtration rate and effective renal plasma flow assessed using radionuclide imaging (99m-Tc-DTPA and 131-I-IOH), suggest that renal capacity is severely compromised in males after about 25-wks age. Ultrasonic measurements were correlated with microscopy measurements of glomerular and vascular sizes. Finally, gross alteration in parenchymal macrostructure were described using strain imaging. Preliminary results suggest that the cortex of PKD kidneys enlarge and soften as the disease progresses while increasing interstitial fibrosis reduces function. The combination of microscopy, functional imaging, elasticity imaging and scatterer size and integrated backscatter measurements will demonstrate the role for quantitative ultrasonography in the management of progressive renal failure.

This work was supported by grants NIH DK43007 and NSF/WF BES-9708221.