In-Vivo Fetal Ultrasound Exposimetry

CHRISTOPHER M. W. DAFT, MEMBER, IEEE, T. A. SIDDIQI, D. W. FITTING, MEMBER, IEEE, R. A. MEYER, MEMBER, IEEE, AND W. D. O'BRIEN, JR., FELLOW, IEEE

Abstract—**An instrument has been developed to measure the acoustic pressure field *in vivo* during an obstetric ultrasound examination. This provides for improved intensity values for exposure calculations, to assist in assessment of bioeffects. Previous work has been based on intensities measured in water, and estimates of tissue attenuation. The ultrasonic field is sampled using a calibrated 7-element linear-array hydrophone of poly(vinylidene difluoride) transducers, which is placed as close as possible to the ovary, embryo, or fetus, using a vaginal approach. The RF signals from the hydrophone are digitized at 50 MHz, and the maximum amplitude waveform received in the examination is recorded. The output of the clinical *B*-scanner is calibrated by a measurement with the hydrophone in a water bath. From the hydrophone measurements, the *in vivo* I_{SPTA}, I_{SPTP}, and I_{SPPA} are computed. Further analysis allows the frequency-dependent tissue attenuation to be assessed.**

I. INTRODUCTION

Diagnostic ultrasound is widely used in all disciplines of medicine, and particularly in the reproductive sciences. Prior to conception, it is used to monitor follicular development and subsequent ovulation. Once pregnancy is confirmed, in a majority of obstetrical patients, the early human embryo is examined with ultrasound for confirmation of viability. Later in gestation, during the second and third trimesters, ultrasound studies are performed for a variety of indications [1].

It is assumed that ultrasound levels currently employed in diagnostic instruments are not associated with any biohazard to the embryo and growing human fetus. This assumption is maintained despite an almost complete lack of knowledge concerning the actual energy imparted to the ovary, early embryo, and fetus during diagnostic imaging. There is, therefore, concern about long-term fetal effects [2], [3]. The *in vivo* and *in vitro* investigations of bioeffects in the literature are difficult to apply to the human fetus for several reasons. Often high energy levels are used to produce bioeffects in nonclinical models; the effects of absorption and attenuation from the abdominal wall are not taken into account, and the effect of beam focusing is not considered.

There have been previous reports which have attempted to determine *in situ* ultrasonic intensity in both the gravid and nongravid uterus [4]–[8]. One of the earliest and best *in vivo* experiments [5] determined an average insertion loss between the skin and uterus to be around 2.5 dB at 2.25 MHz with an *in situ* hydrophone, while some of the later studies yielded higher insertion loss values, in the range from 9 to 20 dB [4], [6] or from 6 to 14 dB [7], frequency unknown, from the reflection from *in utero* metal structures.

A cooperative study between the University of Illinois and the University of Cincinnati has been developed to address *in situ* exposimetry. The purpose of this paper is to describe the system we have developed to quantify, *in vivo*, the amount of ultrasound delivered during routine obstetrical examinations.

II. INSTRUMENTATION

A block diagram of the experiment is shown in Fig. 1.

A. Hydrophone

Six side-looking hydrophone probes were constructed for the project. A seven element array of poly(vinylidene difluoride) (PVDF) transducers is positioned near one end of a curved stainless steel tube (see Fig. 2). A multielement array is needed because of the difficulty in aligning the ultrasonic field from the clinical transducer with the hydrophone *in vivo*. The continuous outer electrode on the 28-μm PVDF film provides a ground connection. Seven circular back electrodes (0.5-mm diameter, 1.5-mm spacing), fabricated on the other side of the polymer, define the elements of the hydrophone. The transducer array fits in a window in the tube, and is held in place with epoxy. A thin layer of epoxy over the array protects the transducers; this is machined flush with the tube walls before the whole assembly is polished. The device is sufficiently rugged to withstand gas sterilization with ethylene oxide.

In order to present a low input capacitance to the array elements and provide some current gain to drive the hydrophone cable, a surface mount JFET is connected in source follower configuration close to each transducer. The various signals and power supply lines are brought out to a connector on the handle of the hydrophone.

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C. M. W. Daft is with GE Corporate Research and Development Center, P.O. Box 8, Schenectady, NY 12301.

T. A. Siddiqi and R. A. Meyer are with the Departments of Obstetrics and Gynecology and Pediatrics, University of Cincinnati College of Medicine, 231 Bethesda Ave., Cincinnati, OH 45267.

D. W. Fitting is with NDE Systems, Inc., 2785 Heather Rd., Golden, CO, 80401.

W. D. O'Brien is with the Department of Electrical and Computer Engineering University of Illinois, 1406 West Green St., Urbana, IL 61801.

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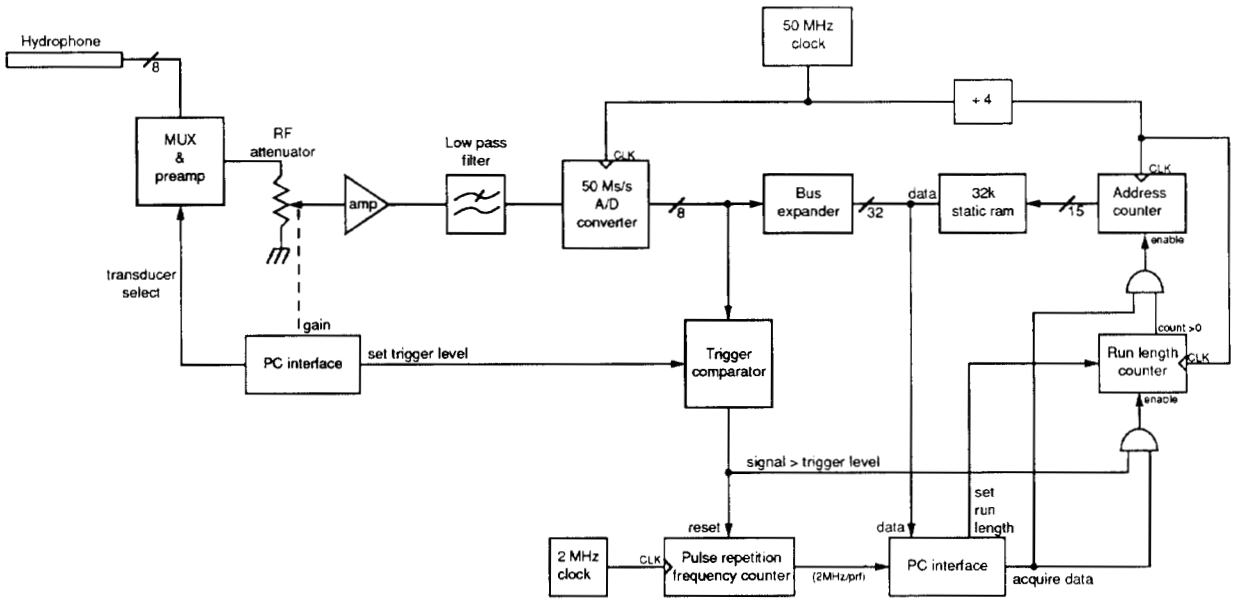

Fig. 1. Block diagram of experiment. Front end of the digital electronics (the trigger comparator and bus expander) is implemented in ECL due to the 50-MHz clock speed. System has no trigger connection to the B-scanner; it is triggered by the ultrasound pulse received by the hydrophone.

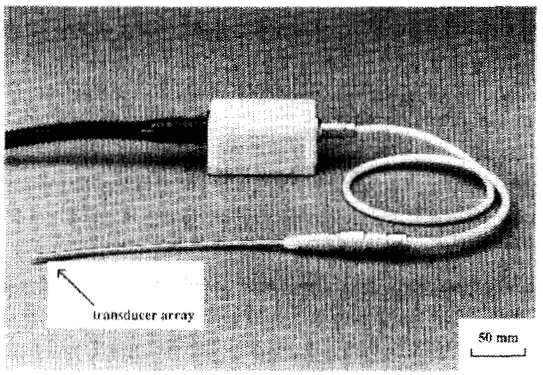

Fig. 2. *In vivo* hydrophone and multiplexer/preamplifier. Side-looking array is positioned at the end of the probe; seven JFET source followers are mounted in the handle.

The array was calibrated using a substitution technique. A 3-MHz Panametrics transducer was placed in a degassed, distilled water bath and impulse excited. The maximum pressure was found with a calibrated PVDF membrane hydrophone (Marconi, Chelmsford, England). Sensitivities for each of the elements were measured by positioning an element at the (known) pressure maximum and measuring the end-of-cable voltage.

B. Analog Electronics

The distance from the hydrophone to the A/D converter makes further buffering necessary. To accommodate this, a small enclosure containing a multiplexer for the RF signals, a preamplifier and a buffer amplifier is interposed in the signal path, four feet from the hydrophone. Selection of transducer element is achieved by three lines from the controlling PC.

The RF signal passes through an anti-aliasing filter and a "gain-riding" programmable attenuator before being digitized. The attenuator is changed before each data acquisition to compensate for variations in sensitivity between transducer elements. This ensures that the full dynamic range of the A/D converter (45 dB) is used at all times.

C. Digital Electronics

The digitizer used was a TDC1025 (TRW, La Jolla, CA), which provides 8 bits of resolution at 50 MHz. This chip is clocked continuously, and feeds a bus expander which produces 32 bit data at 12.5 MHz. The 32-kbyte data memory can then be conservatively designed with 55-ns components. Memory addresses are generated by the address counter in Fig. 1, which is enabled by an acquire data signal from the PC. The run length counter is loaded at the start of the cycle with the number of samples to acquire after the trigger. It begins counting down after the PC's "acquire data" line is asserted and an RF trigger is received. Notice that the data acquisition begins before the ultrasonic signal arrives. The equipment can, therefore, operate in a pretrigger mode, like a digital oscilloscope. This allows us to acquire data without modifying the clinical *B*-scanner.

The trigger circuit monitors the output of the A/D converter, which runs continuously. Two ECL comparators generate the trigger signal if the raw A/D signal exceeds a preset value for more than 40 ns. Once the data are stored in the digitizer memory, they are read out through a parallel I/O card to the PC. The trigger signal also feeds a counter that measures the time interval between ultra-

sound pulses. This is needed to convert temporal peak pressures to averages.

D. Software

Mouse driven control software was written for ease of use by clinical personnel. The user initially indicates which hydrophone is to be used, in order to recall the correct calibration data. Next, *in vivo* data are acquired. In this mode, the PC's screen behaves like an oscilloscope, so the clinician can view the incoming RF data. The largest waveform from each sweep through the seven transducers in the hydrophone array is displayed. The computer "beeps" each time a new maximum signal is received, providing an audible signal to the clinician, indicating that the study is progressing. Positioning of the *B*-scanner's transducer continues until no further maxima are indicated by the data acquisition system.

Immediately after the examination, and before any of the *B*-scanner's controls are altered, a reference ultrasonic signal is measured. The same *B*-scanner transducer and hydrophone are placed in a water tank. The signal with the peak RF pressure is recorded with the transducer and hydrophone the same distance apart as in the *in vivo* case. We can then compute *in vivo* and calibration values for I_{SPTP}, I_{SPTA}, and I_{SPPA} as defined in the AIUM/NEMA standard [9]:

$$I_{SPTP} = \frac{V_{max}^2}{K^2} \tag{1}$$

$$I_{SPTA} = \frac{1}{K^2(t_2 - t_1)} \int_{t_1}^{t_2} V^2(t)\, dt \tag{2}$$

$$I_{SPPA} = \frac{I_{SPTA}}{D} \tag{3}$$

where $V(t)$ is the hydrophone voltage, and K is its calibration constant; V_{max} is the peak of the waveform; t_1 and t_2 are the arrival times of two successive pulses; and D is the duty cycle of the ultrasound signal.

The *in vivo* and calibration pressure waveforms are stored for every study. Power spectra of the signals are computed for further characterization of the tissue.

III. Results and Discussion

To date, this system has been used to examine 35 nonpregnant women and seven pregnant women who were undergoing spontaneous abortion. This model has been approved by the University of Cincinnati Institutional Review Board. Informed consent was obtained from all patients. The data were obtained using a standard commercial 3.0-MHz ultrasound system. Fig. 3 is a sector *B*-scan of the abdomen with the hydrophone in position. The line to the right of the image indicates the TGC setting. The bladder is the dark area near the transducer, and the probe appears as a bright shadow beneath the bladder. The hyperechoic area furthest from the *B*-scan transducer shows the posterior structures, such as the surface of the backbone. The acoustic path was measured using on-screen

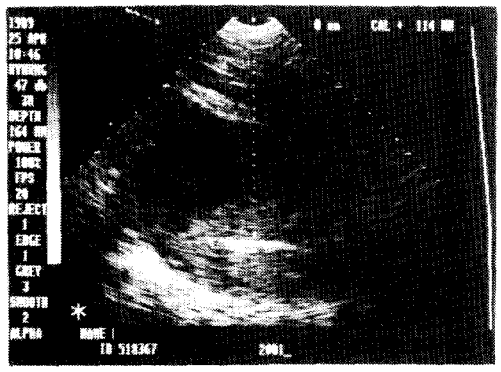

Fig. 3. *B*-scan of patient showing the bright linear shadow of the probe in the vagina (center of sector), hypoechoic bladder nearer the imaging transducer, and echogenic surface of the backbone at the bottom of the image. Calibration marks are spaced 1 cm apart.

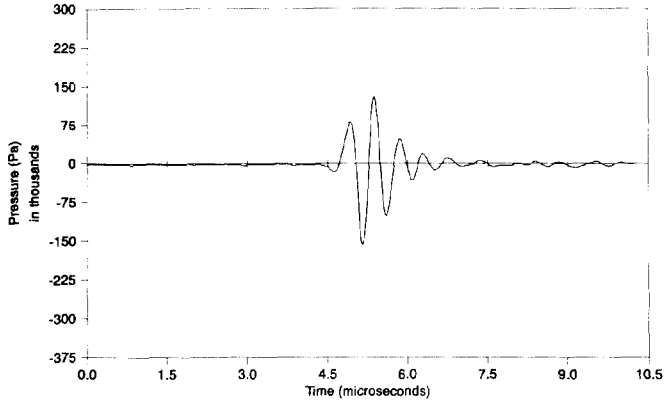

Fig. 4. *In-vivo* pressure waveform from a 3.0-MHz ultrasound system, recorded during a sector scan of the abdomen. The distance from the skin surface to the hydrophone is 9.5 cm in this case.

calipers; it is 11.4 cm in this case. The ability to view the hydrophone in this manner facilitates alignment of the transducers.

Figs. 4 and 5 show the *in vivo* and calibration pressure waveforms received by the probe. Due to tissue attenuation, the *in vivo* pressure is substantially smaller. Power spectra for these two signals are plotted in Fig. 6. It is interesting to note that the peak of the signal recorded in the water bath is 2.4 MHz, and the intensity is 7 dB less at its nominal frequency of 3 MHz. Since tissue attenuation increases with frequency, the centroid of the *in vivo* spectrum is shifted down in frequency. The ratio of the power spectra of the *in vivo* and calibration signals is plotted in Fig. 7. This deconvolved signal is an indication of the rate of increase of attenuation with increasing frequency in the tissue.

Table I lists values of three intensity quantities for each of the calibrated and *in vivo* experimental conditions. Based on these single observations, the tissue insertion loss values are 5.7, 7.3, and 7.1 dB, respectively, as determined from the I_{SPTA}, I_{SPPA}, and I_{SPTP} data. The patient data represented in Figs. 4–7 came from a 9.5 cm total tissue path length from transducer (at the skin surface) to hydrophone. Of this, 6.2 cm was bladder, which is as-

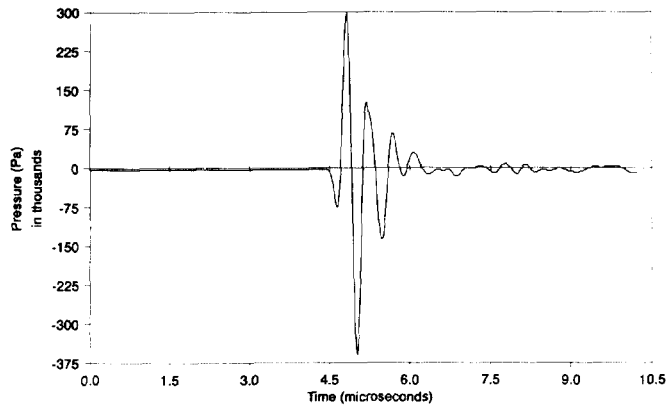

Fig. 5. Calibration pressure waveform, recorded with the same control settings on the *B*-scanner, with the hydrophone in a water tank.

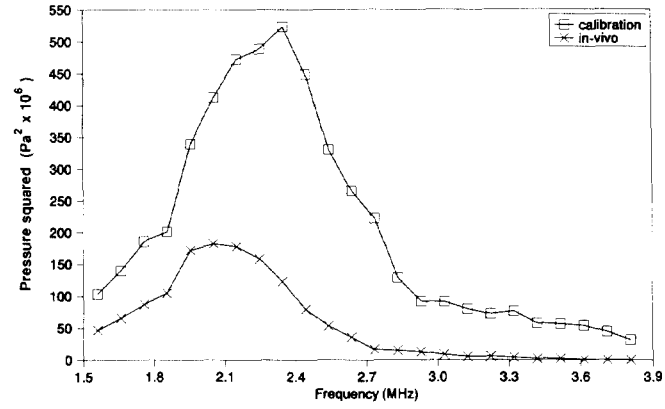

Fig. 6. Spectra of pressure (squared magnitude) for the *in vivo* and calibration waveforms.

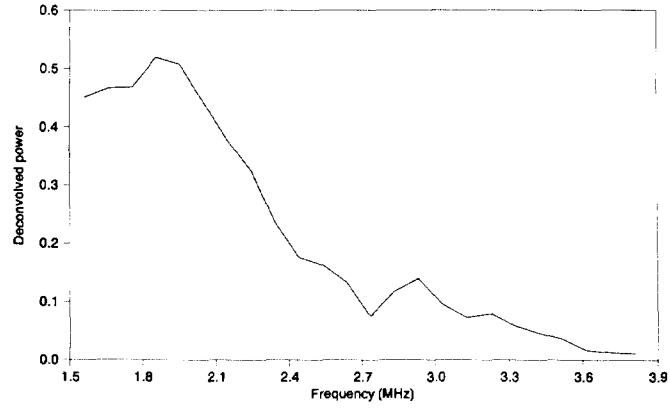

Fig. 7. Ratio of power spectra of *in vivo* and calibration waveforms, showing decreasing sound transmission with increasing frequency.

TABLE I[a]

	In Vivo	*Calibration*
I_{SPTA}	1.8×10^{-3}	6.7×10^{-3}
I_{SPPA}	0.24	1.3
I_{SPTP}	1.7	8.8

[a] The intensities in W cm^{-2} were computed from the data in Figs. 4 and 5.

sumed to negligibly attenuate the ultrasound. By considering the differences, that is, 3.3 cm through tissue, the insertion loss per unit distance (also called the attenuation coefficient) values are 1.7, 2.2, and 2.2 dB cm^{-1}. Normalized to 2.4 MHz, the attenuation coefficient values are 0.7, 0.9, and 0.9 dB cm^{-1} MHz^{-1}, respectively. The slight differences in these values may be because I_{SPTA} is less dependent upon waveform shape than the other two intensity values.

For comparison, the 510(k) process of the Food and Drug Administration's Center for Devices and Radiological Health (CDRH) uses a "derating factor" of 0.3 dB cm^{-1} MHz^{-1} to calculate the various estimated *in situ* intensity values [10]. This process assumes a homogeneous tissue model, that is, the attenuation coefficient is assumed to be the same along the entire path. Using CDRH's process with the previous three insertion loss values of 5.7, 7.3 and 7.1 dB, and a total 9.5-cm path length at 2.4 MHz, we obtain 0.25, 0.32 and 0.31 dB cm^{-1} MHz^{-1}, respectively. Thus, CDRH's derating factor appears to be a realistic estimate of the actual *in vivo* intensity estimate from this limited data set. However, their tissue model is not very realistic for this application. It has necessitated the use of an artificially low derating factor value, which is also used for non-obstetrical applications.

The nature of the experiments makes some sources of error difficult to quantify. The inability to maintain the transducer and receiving hydrophone in the same plane for more than a few seconds was anticipated. Recording the sound field at seven positions, and performing all data analysis on the strongest signal received during the study will minimize this problem. The calibration of the hydrophones has an uncertainty of $\pm 20\%$. Since the above measurement is of a ratio, this error cancels out.

In the ovarian studies, it is impossible to place the hydrophone within the ovarian substance, or even in immediate contact. Therefore, the actual energy received by the ovary will differ slightly from our data. In the embryo and fetal studies, the hydrophone is in physical contact with the products of conception at the mid-uterine cavity level.

IV. Conclusion

An exposimetry and tissue characterization technique has been presented that provides *in vivo* pressure measurements during obstetric ultrasound examinations. The instrument provides absolute pressure readings for the RF signal at or near the site of interest, and a comparable water-based reference RF signal. Seventy-five patients in the ovarian and embryonic studies, and 20 patients for the fetal study are planned.

The human *in vivo* data will provide the basis for developing quantitative tissue models. These tissue models are necessary to develop accurate mathematical models to estimate *in situ* exposure from diagnostic ultrasound systems that currently have their outputs characterized from water-based measurements. Further, such data and their

resultant models will provide a basis for designing and comparing *in situ* intensity exposures of laboratory animal experiments and their bioeffects with typical diagnostic examinations.

V. Acknowledgment

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Christopher M. W. Daft (M'87) was born in Dundee, Scotland, and received the B.A. and Ph.D. degrees from Oxford University, England, in 1984 and 1987, respectively.

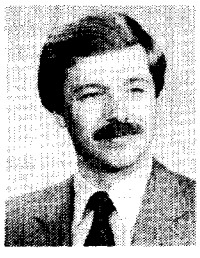
From 1987 to 1990 he was with the Bioacoustics Research Laboratory of the Department of Electrical and Computer Engineering at the University of Illinois at Urbana-Champaign, as an Assistant Professor. He is currently working for the Corporate Research and Development Center of General Electric, in Schenectady, NY, in the Ultrasound Program.

Dr. Daft's research interests include ultrasonic imaging, tissue characterization, tomography, neural networks and acoustic microscopy.

Tariq A. Siddiqi was born in Rawalpindi, Pakistan in 1952. He received his undergraduate degree from Government College, Lahore, Pakistan in 1969 and his M.B.B.S. degree from King Edward Medical College, University of the Punjab, in 1975.

After completing Residency training in Obstetrics and Gynecology in 1981 at St. Agnes Hospital, Baltimore, MD, he was accepted as a Fellow in Maternal-Fetal Medicine at the University of Cincinnati Medical Center. He was certified by the American Board of Obstetrics and Gynecology in 1984 and by the Maternal-Fetal Medicine section in 1985.

Dr. Siddiqi is currently Associate Professor in the Department of Obstetrics and Gynecology, University of Cincinnati, College of Medicine and is Director of the Division of Maternal-Fetal Medicine. His research interests include ultrasound dosimetry, the intrauterine growth retarded fetus and ultrasonic assessment of fetal cardiovascular function.



Dale W. Fitting (M'74-S'76-S'78-S'80-M'80) received the B.S. degree in engineering physics from the Colorado School of Mines, the M.S. degree in radiological physics from the University of Colorado, Boulder, and the Ph.D. degree in engineering science and mechanics from the University of Tennessee, Knoxville, in 1971, 1973, and 1982 respectively.

He has been involved in ultrasonics research and development as well as teaching at the University of Tennessee, Oak Ridge National Laboratory, Ohio State University and the Univeristy of Michigan. At the University of Michigan he was involved in development of phase-insensitive ultrasonic arrays for tissue characterization and imaging. He has coauthored a book reviewing spectral analysis techniques employed for ultrasonic nondestructive evaluation. He is now working for the National Institute of Standards and Technology (formerly National Bureau of Standards) - Boulder Laboratories, investigating the use of ultrasonic arrays for characterzing advanced materials such as composites.

Dr. Fitting is a member of ASA, AIUM, AAPM and ASNT.

Richard A. Meyer was born in Brooklyn, NY, in 1938. He received the B.A. degree in pre-medicine in 1960 from Washington and Jefferson College, Washington, PA, and an M.D. from the University of Cincinnati, College of Medicine, in 1964. He did a pediatric residency at Children's Hospital Medical Center, Cincinnati, OH, from 1965 through 1967.

He served as a pediatrician in the navy from 1967 through 1969 at Quantico, VA, and then obtained a pediatric cardiology fellowship from 1969 through 1971 at Children's Hospital Medical Center, Cincinnati, OH. In 1971 he joined the Department of Pediatrics, Division of Cardiology and has remained there since. He currently serves as Director of the Cardiac Ultrasound Laboratory and is a professor of pediatrics and attending cardiologist at Children's Hospital Medical Center.

Dr. Meyer is a member of numerous national professional socities and is a past president of the American Institute of Ultrasound in Medicine. In 1969 he developed applications of diagnostic ultrasound in congenital and acquired heart disease in infants, children and young adults. More recently, he has investigated the use of fetal echocardiography and transesophageal echocardiography. Currently, his research interests include the bioeffects of ultrasound and ultrasonic dosimetry.

William D. O'Brien (S'64-M'70-SM'79-F'89), for a photograph and biography, please see page 175 for the of the May issue of this TRANSACTIONS.