High-Frequency High Frame Rate Ultrasound Imaging System for Small Animal Imaging with Linear Arrays

Xiao-Chen Xu, Chang-Hong Hu, Lei Sun, Jesse Yen and K. Kirk Shung
NIH Ultrasonic Transducer Resource Center, Biomedical Engineering Dept,
University of Southern California, Los Angeles, CA 90089, USA.

Abstract—**Due to the fast heart rate of a mouse greater than 400 beats/min, cardiovascular research utilizing mice requires imaging modalities with high frame rate capability (>100 Frames/sec), which cannot be realized by Micro-CT and Micro-PET at present. High-frequency ultrasound imaging, on the other hand, is capable of achieving a better spatial resolution at an affordable price. In this paper, we report the development of a high-frequency high frame rate ultrasound imaging system using 30~35MHz linear arrays. The system includes 64 pulsers, 16 1:4 De-multiplexers, 16 4:1 multiplexers, 16-channel TGC amplifiers, an analog beamforming board, a microprocessor (89S8252), a 500MS/s 8-bit PCI A/D card and a PC supported by Labview based software. The system can display 30 images per second and acquire over 100 images per second for slow motion playback with 30MHz 48 element linear arrays. Tissue mimicking phantoms were used to assess image quality. Rabbit eye images and mouse heart images have been obtained *in vitro* and *in vivo* to demonstrate the potential of this system in biomedical applications.**

Index Terms—**High-frequency Ultrasound, High frame rate, Small Animal Imaging**

I. INTRODUCTION

SMALL animals like mice and rats are widely used in biology studies since they are the preferred animal model. Currently both Micro-CT, Micro-MRI and Micro-PET have been developed and used in small animal imaging. But their cost effectiveness and real-time capability are still of a great concern [1]. Due to the especially fast heart rate of a mouse (>400/min), cardiovascular research utilizing mice requires imaging modalities with high frame rate capability (>100 Frames/sec), which cannot be realized by Micro-CT and Micro-PET at present [2].

High-frequency ultrasound imaging (above 30MHz), on the other hand, is capable of achieving fine spatial resolution at an affordable price [3] [4]. High frequency ultrasound imaging for small animals is gaining both scientific and commercial interests at present. Single element transducer based commercial ultrasound backscatter microscopies (UBM) have been used in small animal studies. But the mechanical scanning structure and fixed focal point of UBM are still limiting the demands of high-frame rate and high resolution imaging in small animal cardiac studies [5].

Recently, high frequency ultrasonic arrays (>30MHz), which provide clinical convenience, reduce imaging time, and offer dynamic focusing, have been developed successfully [6]. Compared to current UBMs, a linear array based high-frequency ultrasound imaging system can alleviate the above mentioned limitations of UBMs. A sixteen-channel analog beamformer, which offers 4 dynamic focusing zones and acquires 10 frame images per second, had been designed and implemented to test high-frequency transducers at Penn. State University [7]. In this paper, a miniaturized analog beamformer has been designed and implemented to acquire more than 100 frame images per second with 48 element linear arrays. Rabbit eye images and mouse heart images have been obtained *in vitro* and *in vivo* to demonstrate the potential of this system in biomedical applications.

II. METHODS

A. System Description

Fig. 1 shows a block diagram of the high-frequency high-frame rate ultrasound imaging system with linear arrays. The whole system is shown in Fig. 2. The imaging system includes a PC with a Gage-8500 A/D card, a microprocessor (89S8252) based control board, 16 1:4 De-multiplexers, 64-channel high-voltage amplifiers, 64-channel transceivers, 146 4:1 multiplexers, 16-channel time gain compensation (TGC) amplifiers, a 16-channel cross point switch, a 16-channel receiving analog beamformer and a 30MHz linear array or a 35MHz linear array, which is described in [6] and [8]. The main chanllenge of the system design is to acquire and process the beamformed RF data for real-time or high frame rate imaging. The heart of the system is the microprocessor board supported by high-speed buffers (74AC573, ON Semiconductor). Upon each frame trigger signal given by the PC, the control board sends out large number of control signals for the 16 x 16 video crosspoint switch, multiplexers and De-multiplexers. After De-multiplexers, 16 -66V high voltage pulses are applied to appropriate elements of a transducer. The received 16 echoes are selected from 64 channel transceivers by multiplexers, band-pass filtered and amplified by TGC amplifiers, and manipulated by cross-point switches. Then the one-channel beamformed echo signals are

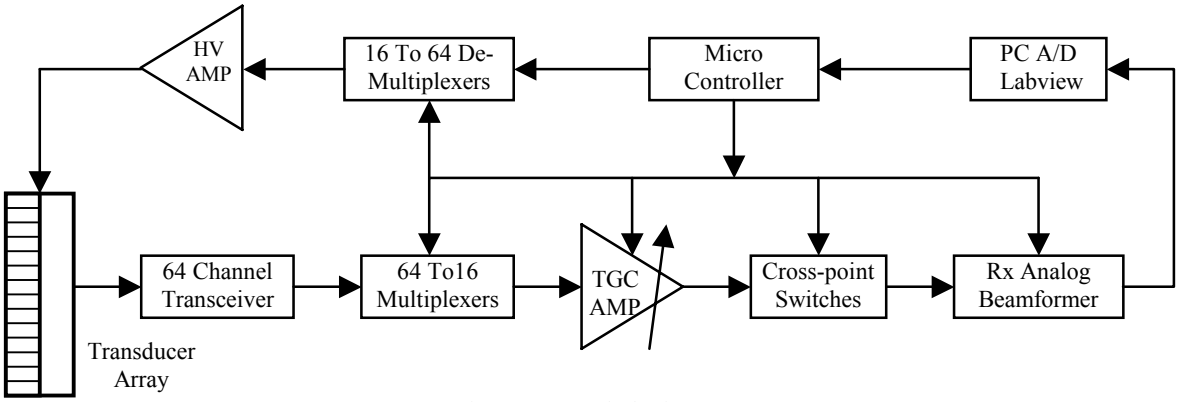

Fig. 1. System Block Diagram

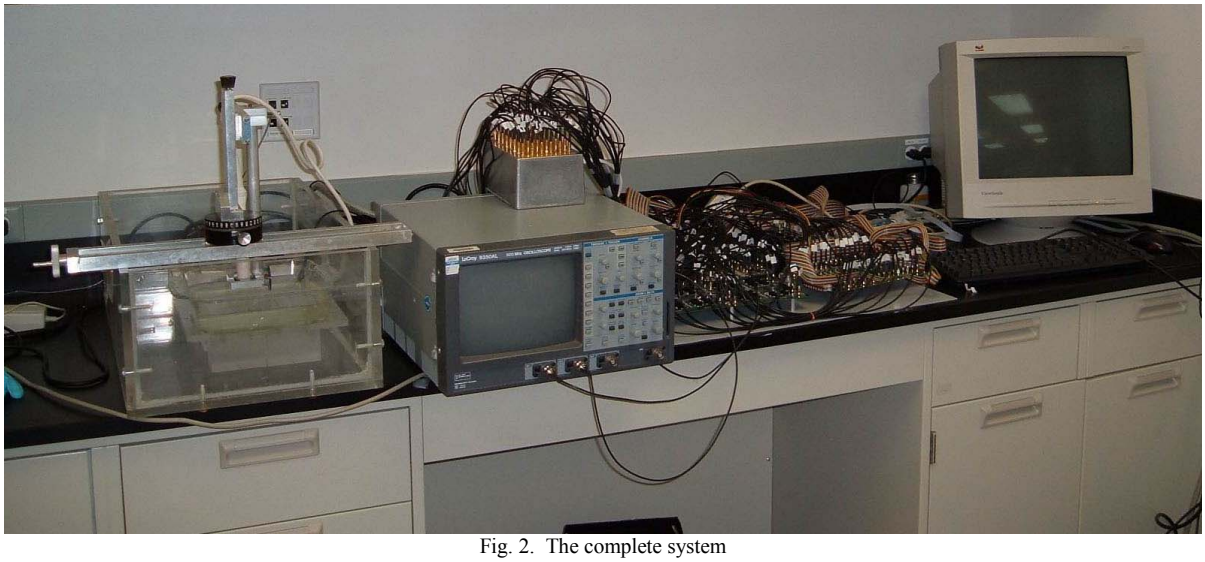

Fig. 2. The complete system

digitized by a PCI A/D card in the PC. Finally the acquired data are processed and B-mode images are displayed in real time by Labview-based software. The system can display 30 images per second and acquire over 100 images per second for slow motion playback with a 48 element linear array.

All circuit boards have been packed in a metal box for reducing noise and on-site *in vivo* experiments. Compared to the previous system developed at PSU, the new system is compact and more suitable for *in vivo* studies.

B. *Transducers*

The characteristics of three linear arrays used in the experiments are outlined in Table 1. All of them were fabricated in the NIH Resource Center for Medical Ultrasound Transducer Technology [6][8]. Different aperture sizes determine different lateral resolution as in (1) and grating lobe level as in (2):

$$R_L = \frac{F}{N_B \times d}\lambda \tag{1}$$

$$\theta = \arcsin(\pm\frac{\lambda}{d}) \tag{2}$$

where R_L is the lateral resolution, N_B is the channel number of a beamformer, d is the pitch size, λ is the wavelength in media, θ is the angel of the first grating lobe and F is the focal distance on elevation direction.

In order to achieve an image of better quality and wide field of view, an array with more elements is preferred as well as a beamformer with more channels.

TABLE 1
CHARACTERISTICS OF LINEAR ARRAYS

	Transducer 1	Transducer 2	Transducer 3
Element No.	48	64	64
Bandwidth	59%	55%	56 %
Element dimensions	1.5mm×82μm	3mm×36μm	2 mm×85μm
Kerf size	18 μm	14 μm	15 μm
Pitch size	100 μm	50 μm	100 μm
Focal distance	6.2mm	9.5mm	8 mm
Lateral Resolution	200μm	534μm	250μm
Field of View	3.3mm	2.4mm	4.8mm

Focal length is on elevation direction. Lateral resolutions were calculated based on 16-channel beamforming at the elevation focal point.

III. EXPERIMENTS AND RESULTS

Tissue mimicking phantom with a 1mm diameter bore inside was tested with Transducer 2 [11]. The image obtained in Fig.3 shows that the system can offer enough penetration depth and good signal to noise ratio for *in vivo* studies.

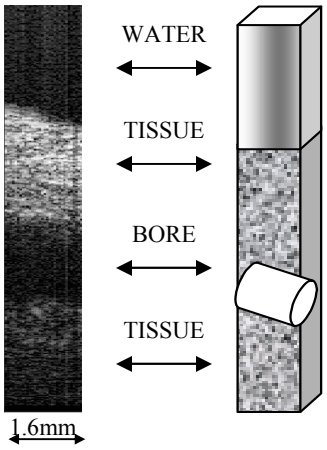

Fig. 3. Rabbit eye images obtained by Transducer 1. a) Cross section image at the center of the eye; b) cross section image at the

The *in vitro* rabbit eye images were acquired by placing the eye in 0.9% sodium chloride injection at room temperature. The array transducer was electronically scanned across the eye to obtain one frame image. With Transducer 1, the width of the field of view in azithumal direction is 3.3 mm. After one frame image was obtained, the linear array was mechanically moved 3.3 mm to acquire the next adjacent frame for covering a wider field of view. The composite eye images are shown in Fig. 4. The anterior region, consisting of structures such as cornea and lens, is resolved. Real time images of excised rabbit eye were obtained with Transducer 2. For each frame, the field of view in azithumal direction is 1.6mm (use only 48 elements concerning the real time capability 30 Frame/s). Two frame images were extracted from the movie file and listed in Fig. 5. Also resolved are the cornea, the lens and the iris.

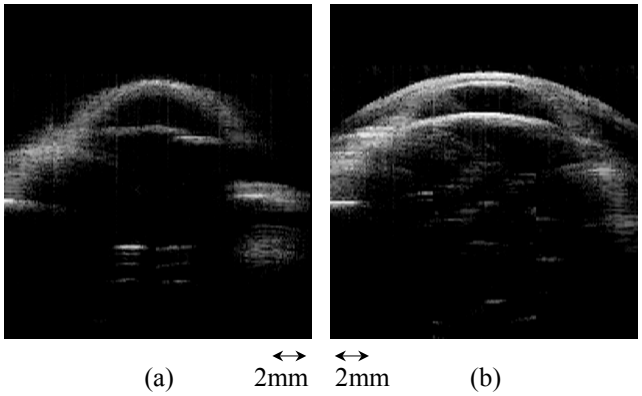

Fig. 4. Rabbit eye images obtained by Transducer 1. a) Cross section image at the center of the eye; b) Cross section image at the side of the eye

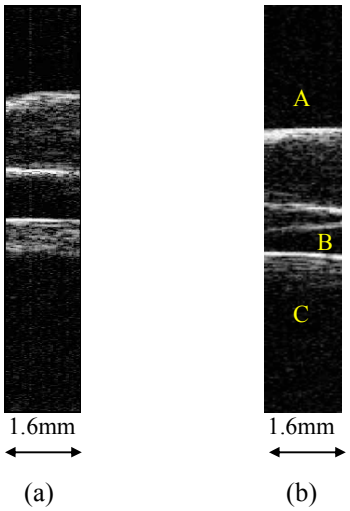

Fig. 5. Rabbit eye images obtained with Transducer 2, showing cornea (A), iris (B) and lens (C).

In vivo real-time imaging and high frame rate imaging were conducted on mice after anesthetizing and shaving. Ultrasound gel was used as a coupling fluid on skin. To gain images without shadows, the acoustic beam must be transmitted through the gap between two ribs. High frame rate images were acquired after positioning transducer at the area of interest.

Due to the field of view in azithumal direction, only a part of mouse heart was displayed. By mechanically scanning the whole heart with a transducer, structures such as atriums and ventricles were visible. In Fig. 6, heart images were extracted from the acquired movies. In the acquired movie, the heart rates in anesthetized mice are around 200-250 beats/min, which is approximately 45% of those of conscious mice [9][10]. In high frame rate acquisition mode, only half-second movie (50 frames) was saved and played back due to the limitation of on-board memory on Gage A/D Card.

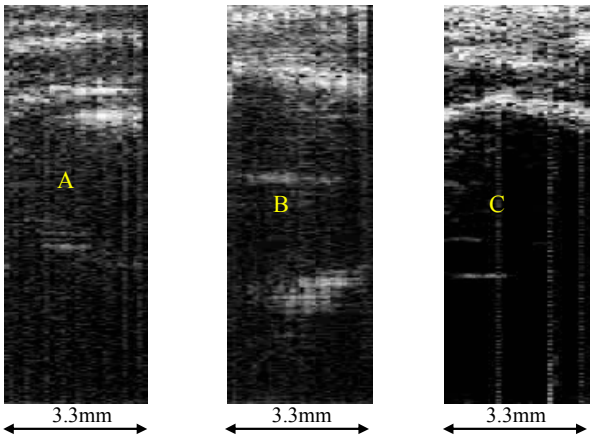

Fig. 6. Mouse heart images; (a) and (b) were obtained with Transducer 1at 30 frames/s; (c) was obtained with Transducer 3 at 100 frames/s, showing atrium (A) and ventricles (B) (C).

IV. Discussions and Future Work

High frequency ultrasound imaging is an affordable way to capture mouse heart images at high frame rate. We were able to acquire movements of cardiac structures in mouse heart and demonstrated the potential of this system in biomedical applications.

However, the field of view in the azithumal direction and the lateral resolution are still not satisfactory compared to the micro-CT and PET imaging modalities. In current commercial ultrasound system, linear arrays with 256 elements or more are required to obtain satisfactory resolution and field of view. Increasing the channel account of a beamformer with a large linear array could alleviate the above limitations. Meanwhile, decreasing the noise from analog front-end circuits is critical to the whole system's performance. New low noise amplifiers from Analog Devices will be employed in the future system.

The speed of microcontroller and the data transfer rate from A/D card to PC are bottlenecks for obtaining even higher frame rate. The current VLSI technology enables us to replace microcontroller with a FPGA or a CPLD to achieve the desired performance. Image compressing before data transferring is a solution to gain higher frame rate based on current PCI transfer rate.

Ultrasound Doppler flow meter is a basic function on all commercial ultrasound imaging systems. High-frequency Doppler enables us to measure and characterize the microcirculation as well as the hemodyanmics of the mouse circulatory system [5]. High-frequency pulsed-Doppler is being implemented on our high-frame rate ultrasound imaging system with high frequency linear arrays.

Acknowledgment

This work was supported by NIH grant number P41-EB2182. The authors thank Jonathan Cannata, Richard Tutwiler and Peijie Cao for providing valuable efforts to this project.

References

[1] AB Hwang, K Iwata, AE Sakdinawat, MC Wu, BH Hasegawa, "Gantry Specifications for a Dual Modality Imaging System for Small Animals", IEEE Nuclear Science Symposium Conference Record, vol.2, pp. 1303 – 1307, 2002.

[2] F. S. Foster, C. J. Pavlin, G. R. Lockwood, L. K. Ryan, K. A. Harasiewicz, L. Berube, and A. M. Rauth, "Principles and application of ultrasound backscatter microscopy," IEEE Trans. Ultras. Ferroelect. Freq. Cont., vol. 40, pp. 608-616, 1993.

[3] F. S. Foster, C. J. Pavlin, G. R. Lockwood, L. K. Ryan, K. A. Harasiewicz, L. Berube, and A. M. Rauth, "Principles and application of ultrasound backscatter microscopy," IEEE Trans. Ultras. Ferroelect. Freq. Cont., vol. 40, pp. 608-616, 1993.

[4] G. R. Lockwood, D. H. Turnbull, D. A. Christopher, and F. S. Foster, "Beyond 30 MHz: applications of high frequency ultrasound imaging," IEEE Eng. Med. Biol., vol. 15, pp. 60-71, 1996.

[5] F. S. Foster, M. Y. Zhang, Y. Q. Zhou, G. Liu, J. Mehi, C. E., K. A. Harasiewicz, B. G. Starkoski, L. Zan, D. A. Knapik, and S. L. Adamson,x "A new ultrasound instrument for in vivo microimaging of mice," Ultrasound Med. Biol., vol. 28, no. 9, pp. 1165-1172, 2002.

[6] T. A. Ritter, T. R. Shrout, R. Tutwiler, and K. K. Shung, "A 30-Mhz piezo-composite ultrasound array for medical imaging applications," IEEE Trans. Ultras. Ferroelect. Freq. Cont., vol. 49, pp. 217-230, 2002.

[7] J. P. Stitt, R. L. Tutwiler, and K. K. Shung, "An improved four-focal zone high-frequency ultrasound analog beamformer," IEEE Ultrason. Symp, Proc., vol. 1, pp 617-620, 2002.

[8] J. M. Cannata, "High frequency (>20 MHz) ultrasonic arrays for medical imaging applications," Ph.D. dissertation, University Park, PA: Penn State University, Aug. 2004.

[9] G Wang, Y Liu, Y Ye, S Zhao, J Hsieh, S Ge, "Top-level design and preliminary physical analysis for the first electron-beam micro-CT scanner", Journal of X-Ray Science and Technology, 2004.

[10] Yang XP, Liu YH, Rhaleb NE, Kurihara N, Kim HE, Carretero OA, "Echocardiographic assessment of cardiac function in conscious and anesthetized mice", Am J Physiol. Vol.277,pp.1967-74, 1999 .

[11] T. J. Hall, M. Bilgen, M. F. Insana and T. A. Krouskop, "Phantom Materials for Elastography", IEEE Trans. Ultras. Ferroelect. Freq. Cont., vol. 44 ,No.6, pp. 1355-1365, 1997.