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High Frequency Ultrasound: a New Frontier for Ultrasound

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Abstract— **High frequency ultrasonic imaging is considered by many to be the next frontier in ultrasonic imaging because higher frequencies yield much improved spatial resolution by sacrificing the depth of penetration. It has many clinical applications including visualizing blood vessel wall, anterior segments of the eye and skin. Another application is small animal imaging. Ultrasound is especially attractive in imaging the heart of a small animal like mouse which has a size in the mm range and a heart beat rate faster than 600 BPM. A majority of current commercial high frequency scanners often termed "ultrasonic backscatter microscope or UBM" acquire images by scanning single element transducers at frequencies between 50 to 80 MHz with a frame rate lower than 40 frames/s, making them less suitable for this application. High frequency linear arrays and linear array based ultrasonic imaging systems at frequencies higher than 30 MHz are being developed. The engineering of such arrays and development of high frequency imaging systems has been proven to be highly challenging. High frequency ultrasound may find other significant biomedical applications. The development of acoustic tweezers for manipulating microparticles is such an example.**

I INTRODUCTION

Ultrasonic imaging is one of the most important clinical diagnostic tools today. Modern ultrasonic scanners are capable of producing real-time gray scale images delineating anatomy and color image describing Doppler blood flow information [1,2]. High frequency (HF) imaging (higher than 30 MHz) yields improved spatial resolution at the expense of a reduced depth of penetration [2,3]. The axial resolution is determined by the pulse duration or bandwidth of the pulse. The lateral resolution at the focal point is determined by the product of f-number, defined as the ratio of the focal distance to the spatial dimension of the transducer, and wavelength. For a fixed number of cycles per pulse, an increase in frequency would result in a reduction in wavelength and thus pulse duration. As ultrasound frequency is increased to 50 MHz, an axial resolution and lateral resolution of better than 20 and 100 μm for a f# of 2.9 can be achieved respectively. The price to be paid is an increase in attenuation in tissues which is linearly proportional to frequency [1,2]. At 50 MHz, the depth of penetration for most tissues would be approximately to 8-9 mm. A number of clinical problems has benefited from high frequency ultrasonic imaging [2,3]. Ultrasound probes mounted on catheter tips with a frequency as high as 60 MHz has been used for intravascular imaging [1,2]. Medical efficacy of HF ultrasonic imaging of anterior segments of the eye in diagnosing glaucoma and ocular tumors and in assisting refractive surgery has been demonstrated [2,3]. The availability of a non-invasive imaging tool may reduce the number of biopsies that are associated with patient discomfort and could better demarcate tumor involvement in skin imaging. Small animal imaging is of intense interest recently because of such small animals as mouse and zebrafish are good animal models in assessing drug and gene therapy. MicroMR, microCT, optical coherent tomography (OCT) and microPET have all been developed to meet this need. Ultrasound thus far has only played a limited role.

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II. HIGH FREQUENCY IMAGING DEVICES

In a majority of HF ultrasound imaging devices, dubbed "ultrasound biomicroscopes" or "UBMs" [2,3] an image is formed by mechanically scanning a single element transducers which is either piezoelectric polymer PVDF or the copolymer P(VDF-TrFE) based or lithium niobate based [3,4]. The construction of a UBM is very similar to a static B-mode scanner, a block diagram of which is shown in Fig. 1. The positional control of the transducer must have an accuracy of a few μm. The analog to digital converter (ADC) typically has a sampling frequency higher than 200 MHz to more than 8 bits. UBMs have been used to image anterior segment of the eye, skin and small animals like mice and zebrafish. Fig. 2 shows an UBM image of an excised eye obtained at 80 MHz. The exquisite improvement in spatial resolution and image quality compared to clinical ultrasound images is apparent. Improved image quality may be achieved by better utilizing the focus of the transducer in B-D scan (D stands for depth) in which the transducer is incrementally moved in the axial direction. A composite image is formed by combing the focused segments of

multiple images acquired as the transducer is moved in the axial direction. A drawback of this mode of scanning is a reduction in the frame rate. Commercial UBMs can achieve a frame rate of 40/sec because the excursion range is relatively small. This is still inadequate for imaging the hearts of small animals like rats or mice which beat at a rate

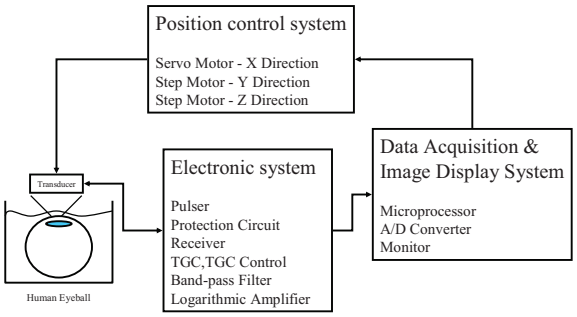

Fig. 1: Block diagram of a UBM system

of 4-6 beats/s, much faster than the typical 1-2 beats/s human heart rate. Mechanical scanning of a single element transducer has other drawbacks: poorer resolution and motion of the probe. Single element transducers can only produce beams with a fixed focus which means the spatial resolution of the device is best only within the depth of focus, i.e., in a very tight zone and degrades rapidly beyond the focal point. Mechanical motion of the transducer limits the frame rate, is unreliable, and may cause patient discomfort and, at worst, may be hazardous to the patient. These problems can be overcome by adopting linear arrays.

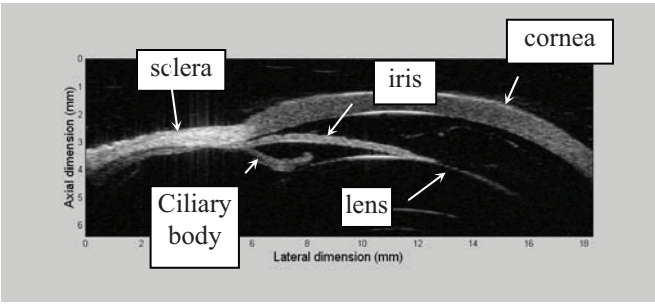

Fig. 2: UBM image of anterior segment of an excised eye at 80 MHz

III. HF ARRAY IMAGING

The problems facing mechanical scanners may be overcome by adopting linear array technology [2,5,6] in which an image is formed by electronically sweeping a beam [1,2,]. Array systems use electronic scanning to form an image slice and therefore can achieve much higher image frame rates. Also, the emitted sound beam can be steered and dynamically focused in the image plane yielding improved spatial resolution and image quality. Finally, the lack movable parts make these arrays less likely to be hazardous to patients. There are three major challenges in HF linear array fabrication: small kerf (the gap between two elements) width, large electrical impedance mismatch and increased crosstalk. In order to minimize grating lobes, typically in linear array and linear phased array design, the pitch that is the distance between the centers of two elements must be less than 1λ and $(1/2)\lambda$ respectively [2]. This means that the pitch must be less than 50 μm at 30 MHz. To insure good sensitivity in linear arrays, the element size should be made as large as possible. Therefore the kerf width should be made as small as possible, making it very difficult if not impossible to dice with current dicing machines. A confounding factor is that unless a suitable kerf filler is found, the crosstalk level will increase as a result of the smaller kerf width. It should be noted here that in phased arrays the element size should also be judiciously chosen to assure a broad steering angle.

Efforts are now underway to develop 20 – 50 MHz linear arrays [5,6,7]. Piezoelectric composites have been used in these designs to increase sensitivity and bandwidth. Fig. 3 shows a recently developed 256 element 30 MHz linear array with an aperture size of 8mm x 22mm. The elements are prepared from 1-3 PZT composites with a 50 μm pitch. It has one matching layer and a custom designed flex circuit interconnect. It is self-focused with a f# of 4, has a bandwith of 55% and an insertion loss of -29 dB. A new technology that utilizes MEMS technology called cMUT (capacitive micromachined ultrasonic transducer) appears to hold great promise [8]. Developing linear arrays at 50 MHz or even higher frequencies and phased arrays at 30 MHz remains quite a challenge technically. Thin film and thick film piezoelectric materials may offer a better alternative in this case [9].

Analog and digital HF imaging systems are also being developed [10]. The frame rate for these systems may approach as high as 400 frames/s. A commercial linear array based small animal imaging system has been recently launched. The system which is more expansive than most clinical scanners offers linear arrays with center frequencies ranging from 15 to 50 MHz.

IV. HIGH FREQUENCY ULTRASOUND APPLICATIONS

HF ultrasound because of its smaller wavelength has been used to characterize cellular processes like apoptosis [11] and lens hardness in the eye [12]. Both the attenuation and sound velocity have been shown to be related to eye hardness. A potential clinical application in the latter is to assist the surgery in determining ultrasonic energy level during phaco-surgery.

For the past few years the feasibility of a device using a highly focused ultrasound beam to manipulate or trap

microparticles similar in many ways to optical tweezer termed acoustic tweezer have been studied [13]. Theoretically it has been shown that it is possible to produce

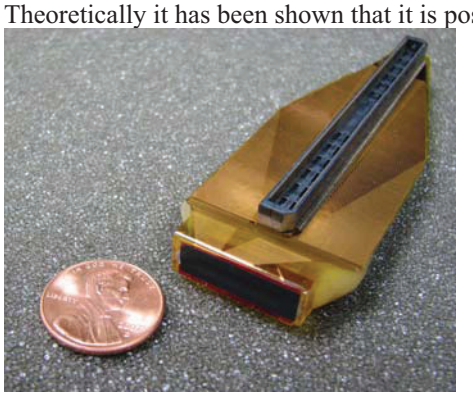

Fig. 3: Photograph of a 30 MHz linear array with flex circuit.

forces perpendicular to or opposite to the beam direction under the conditions that (1) the bean intensity gradient is sharp compared to the particle size, (2) the particle size must be greater than the wavelength, and (3) the acoustic impedance of the particle is slightly smaller than the surrounding fluid. This has been demonstrated experimentally recently with an experimental arrangement shown in Fig. 4. A mylar film which is acoustically transparent prevents the lipid spheres of 100-150 μm diameter from rising to the top of the water tank and is placed at the focal point of a sharply focused transducer (f# = 0.75). When the 37 MHz ultrasound beam is turned on, a movement of the sphere lateral to the beam can be observed by the video camera mounted on an optical microscope and captured by a computer. A maximal range of movement of the microspheres of 300-400 μm can be produced depending upon the ultrasonic beam intensity before they burst. It is worth noting here that this type of action can be produced on smaller spheres if the frequency is increased. It is conceivable that acoustic tweezer one day may be used to trap or manipulate cells.

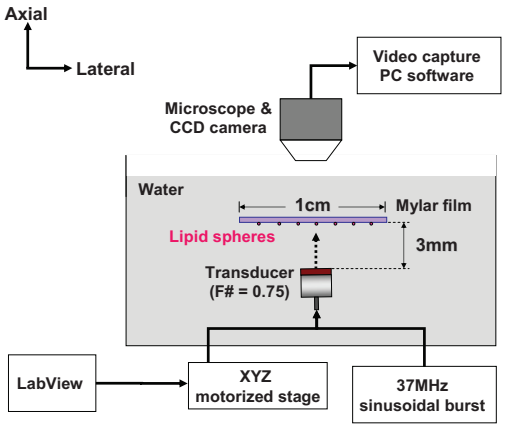

Fig. 4: Block diagram of acoustic tweezer experiment.

V. CONCLUSION

This paper reviews recent developments in HF ultrasonic imaging including transducers and systems at frequencies higher than 30 MHz. Potential preclinical, clinical, and biomedical applications are addressed. There is no reason not to believe that in the near future HF imaging systems with a capability similar to current clinical scanners will become more widely available and their applications expanded into other biomedical disciplines.

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