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Quo vadis medical ultrasound?

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Abstract

The last three decades of development in diagnostic ultrasound imaging and technology are briefly reviewed and the impact of the crucial link between the two apparently independent research efforts, which eventually facilitated implementation of harmonic imaging modality is explored. These two efforts included the experiments with piezoelectric PVDF polymer material and studies of the interaction between ultrasound energy and biological tissue. Harmonic imaging and its subsequent improvements revolutionized the diagnostic power of clinical ultrasound and brought along images of unparalleled resolution, close to that of magnetic resonance imaging (MRI) quality. The nonlinear propagation effects and their implications for both diagnostic and therapeutic applications of ultrasound are also briefly addressed. In diagnostic applications, the impact of these effects on image resolution and tissue characterization is reviewed; in therapeutic applications, the influence of nonlinear propagation effects on highly localized tissue ablation and cauterization is examined. Next, the most likely developments and future trends in clinical ultrasound technology, including 3D and 4D imaging, distant palpation, image enhancement using contrast agents, monitoring, and merger of diagnostic and therapeutic applications by e.g. introducing ultrasonically controlled targeted drug delivery are reviewed. Finally, a possible competition from other imaging modalities is discussed.

Keywords: Ultrasound imaging; Diagnostic and therapeutic ultrasound; Biomedical ultrasonics; Ultrasound imaging transducers

1. Introduction

Diagnostic ultrasound is used in almost all medical fields and has already become the preferred imaging modality in a variety of clinical situations. For example, in many cardiovascular diseases diagnostic ultrasound has already replaced invasive methods as the primary means of evaluation. Also, as the equipment for ultrasound imaging is in general less expensive than that used in radiographic, ionizing radiation techniques, it is becoming more widely available.

The specific technologies that have recently made their mark in clinical practice are not of primary interest in this review. Although such recent advances as B-mode flow imaging, coded ultrasound imaging, real time spatial compounding, tissue harmonic imaging, extended field of view and last but not least 4D, or true real time 3D imaging, are discussed, the attempted goal of this review is to demonstrate the links and developments that made the high resolution current ultrasound technology possible and to focus on the upcoming advances in the ultrasound imaging devices and their clinical impact. Accordingly, after a brief survey of the very recent progress in diagnostic ultrasound imaging, the attention is focused on the most likely developments and future trends in ultrasound imaging technology.

2. Near past and present

Ultrasound image quality upon which the final diagnosis critically depends has improved significantly in the past decade; this would not have been possible without several engineering and technological innovations and breakthroughs. These major innovations included the introduction of a new generation of enhanced bandwidths transducers or scanheads, almost total elimination of analog electronics, and the advent of contrast agents. The superwideband, sensitive, multi-element imaging transducers provided highly improved image resolution which was further enhanced by the introduction of digital technology platform including

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digital beamformers which assured high dynamic range (exceeding 100 dB) and electronically controlled multifocal zones. As indicated in the following, the concurrent introduction of contrast agents resulted, somewhat accidentally, in the discovery of harmonic imaging, which truly revolutionized the quality of images and brought along images of unparalleled resolution, close to those achievable using magnetic resonance imaging (MRI). It is not immediately obvious what caused that rapid improvement and it would be instructional to point out two apparently independent research efforts that significantly contributed to the recent progress in medical ultrasound and, in particular, accelerated advances aiming at the high resolution imaging with the underlying goal of improving clinical diagnosis. These two efforts, described in more detail in the following, included the experiments with piezoelectric PVDF polymer material and studies of the interaction between ultrasound energy and biological tissue.

It is well known that optimization of the trade-off between high image resolution and penetration depth (that also determines field of view) requires significant compromises in the performance of the imaging scanners. Higher frequencies that could provide the desirable improvement in both spatial and temporal resolution are more quickly attenuated in the interrogated tissue than the lower ones and as a result the penetration depth decreases with increasing frequencies. Consequently, advances in image quality including high image resolution that increases the confidence in diagnosis are of primary interest in clinical ultrasound applications. It is interesting to note that the advent of piezoelectric PVDF polymer has indeed had a significant impact on advances in medical ultrasound. Ultrasound probes made of this material provided evidence that the acoustic wave propagating through tissue undergoes nonlinear distortion and associated generation of harmonics. Prior to availability of PVDF material the solid piezoelectric ceramic probes used occasionally to probe the field featured too narrow bandwidth and dynamic range to faithfully reproduce the nonlinear waveforms. Another major technological breakthrough was aided by the arrival of piezoelectric composite transducers and the growing interest in improving image quality by using spherical gas voids or microbubbles as contrast agents. The subsequent research in contrast agents spurred interest in improvements of the fundamental model describing dynamics of the bubble and led to the experimentally verified conclusion that the harmonic of bubble's resonance frequency provided optimum image enhancement. That finding prompted the need for imaging transducers capable of operating at both fundamental and harmonic frequencies. It should be noted that then-used imaging transducers were made of solid piezoelectric ceramic, exhibited rather narrow fractional bandwidth (on the order of 30–35%) and were not capable of reproducing frequency higher than fundamental. The solution to this problem was offered by invention of piezocomposite materials that significantly broadened the fractional bandwidth. Very briefly, the piezocomposites used solid ceramic material that was diced in appropriate manner and the removed solid material was replaced by epoxy filler. In a nutshell, this technology improved the pulse–echo sensitivity of the imaging transducers, allowed acoustic impedance of the transducer to be controlled by the volume ratio of soft filler and solid PZT ceramic and also lowered mechanical quality factor. As a result, the transducer's efficiency was significantly improved and its bandwidth was almost doubled. Closer testing of piezocomposite transducers led to serendipitous discovery that echoes returning from the interrogated tissue volume contained both fundamental and harmonic frequencies. These echoes were filtered and processed to be displayed as harmonic images; it turned out that the harmonic imaging proved to be capable of providing a degree of detail, which clearly surpassed that available with conventional, fundamental frequency gray scale imaging. In this context it should be mentioned that one of the reviewer's offered an alternative account, namely that some physicians misunderstood a manufacturer's request for them to test an experimental scanner designed to detect second harmonics from a contrast agent and, instead, used it without contrast agent. Everyone was amazed by the better picture "quality". It is also worthwhile to note that the piezocomposite materials facilitated development of 1.5 D arrays. These arrays in connection with digital beam formers and when provided with digital beam formers delivered dynamic focusing and uniform beam cross-section that significantly augmented image resolution.

In present clinical applications, two harmonic imaging modes can be identified: in contrast agent harmonic imaging the higher frequencies are generated upon reflection and scattering from the microbubbles, whereas in tissue or gray-scale harmonic imaging the harmonic frequency energy is generated gradually as the ultrasonic wave propagates through the tissue.

3. Near future

3.1. Harmonic imaging

As noted above harmonic imaging is capable of providing more detailed, enhanced contrast images. It has also proven to be particularly helpful, especially during examining of heavy, technically challenging patients. This is because, as indicated above, harmonic imaging offers better resolution both in cardiologic and deep tissue imaging applications and thus, it will contribute to make the images less operator dependent.

Hence, within the next half decade it may be expected that harmonic imaging capability will become a standard available in a new generation of ultrasound imaging equipment and will be widely used in all clinical ultrasound applications. For instance, one of the most challenging tasks in cardiology applications is myocardial perfusion imaging; contrast agents are of great help here. However, as a totally noninvasive procedure to assess the presence or absence of coronary disease and quantify its seriousness is preferable, gray scale harmonic imaging may provide a better solution. Harmonic imaging will also become routinely used in the diagnosis in the pancreas, biliary system, and retroperitoneum. In general, wherever the low megahertz frequency ultrasound exam is needed, harmonic imaging may prove advantageous. Among the benefits of the harmonic imaging technology in abdominal applications are reduced image artifacts, absence of body wall distortion, controlled spectrum, higher contrast images, and enhanced diagnostic confidence. The harmonic technology is also applicable in totally new diagnostic applications. For example, common duct stones that are virtually invisible when using conventional (fundamental frequency) imaging can be better identified with harmonic imaging.

3.2. Contrast agents

The rapidly advancing field of ultrasound contrast agents will continue to challenge the performance of the imaging devices. So far the new applications of contrast agents have been achieved by modifying the existing equipment to match the characteristics of the contrast medium. However, it can be expected that in the future these agents will be optimized for desirable harmonic characteristics. For instance, it is conceivable that contrast agents that are specifically developed for a given application such as tissue perfusion will become available. Further advancements in contrast agents will promote synergy between therapeutic and diagnostic applications of ultrasound by allowing the agents to act initially as image enhancement bodies and subsequently as targeted drug delivery devices. The drug delivery itself will take place by increasing the diagnostic pulse amplitude to the level sufficient to cause the rupture of the microbubble.

3.3. 3D and 4D imaging

A variety of new contrast agents will also promote three-dimensional (3D) and 4D, or real time, ultrasound imaging. Preliminary results indicate that the 3D reconstruction of harmonic data obtained with a contrast agent can provide a vascular anatomy details not available using conventional gray scale, color, and power Doppler. In addition, as 3D data provide digitally encoded images they will allow manipulation of images by removing image of the obscuring anatomy that may inhibit diagnosis and provide the view of the underlying tissue structure. This feature of 3D imaging is already proving to be of invaluable assistance to clinicians in advanced planning of difficult surgeries. Echocardiography and vascular imaging, particularly of the carotids and veins in the legs, appear to be some of major future applications for 3D, however a real time implementation of this technology, as described in the following, will require another technological breakthrough in transducer array design. At present, 3D imaging is primarily implemented with arrays, which generate 2D slices while the third dimension is obtained by mechanical movement, which, in general, is too slow for moving structures like the heart. Real-time heart imaging needs a frame rate of 30 or more per second to be of true diagnostic interest, which, in turn, calls for a 2D transducer array. In general, currently used "one-dimensional" arrays typically contain between 48 and 192 elements and an equivalent 2D array would need tens of thousands of channels making it economically unaffordable. In this context, it is interesting to note that that very recently several tens by several tens elements 2D arrays have become commercially available. It would appear that the future development of 3D imaging would require the design of substantially less expensive "sparse" arrays, which will use number of elements of the same order of magnitude as the existing arrays or introduction of new imaging transducer technology discussed in the following. In addition to application in echocardiography, the availability of real time 3D imaging will prompt applications in obstetrics, as in general, 3D data can improve operator's comprehension. In particular, 3D ultrasound shows great promise in improving the ability to detect and differentiate between many types of functional abnormalities such as those present within the fetus (including improved congenital abnormality detection) as well as in tumors to study vascular distribution.

3.4. Sonoelasticity imaging and elastography

The future research in diagnostic ultrasound will also entail sonoelastic images constructed from the recorded differences in viscoelastic properties of the tissue. Strictly speaking sonoelasticity employs the mechanical vibrations, whereas elastography uses a small (approximately 1%) quasi-static tissue compression to induce strain within the interrogated tissue volume. Elastograms can be presently obtained at the rate of about eight frames per second and sonoelasticity may become a major pathology correlation tool in such applications as sonomammography, where sonographic pathology correlation and evaluation of cystic and solid lesions of the breast are of importance. It can also be expected that sonoelasticity will come to play a major role in assessment and evaluation of prostate malignancies.

3.5. Second order phenomena

It can be expected that second order phenomenon such as acoustic streaming will gain increased attention in the efforts to improve diagnostic confidence. It has already been demonstrated that acoustic streaming can be used to differentiate between solid lesions and liquid cysts. Such differentiation is important as in many cases it allows distinction between the malignant and cystic benign lesions, and hence it may aid to decrease the need for biopsies and lower patient discomfort. It is likely that future generations of ultrasound scanners will be capable to induce the low velocity acoustic streaming pattern within the cyst and will exhibit Doppler sensitivity adequate to detect extremely low velocity (less than 10 mm/s). Measurement of streaming parameters will also provide information on viscosity of the liquid within the cyst and thus will allow evaluation of the solidity of lesions.

Acoustic streaming is caused by radiation force and it can be expected that radiation force produced by the acoustic wave will gain attention because it has several potential applications. These applications include remote palpation and muscle or nerve stimulation. Accurate remote palpation is of interest in screening for malignant breast and prostate tissues. The possibility of muscle and nerve stimulation induced by radiation force may introduce another major application field in clinical practice.

3.6. Very high frequency imaging and new generation of imaging transducers

Further advancement in diagnostic ultrasound will also include very high frequency imaging and it can be expected that the current imaging frequency range (1–15 MHz) will be enhanced by the microsonography devices that will offer sub-millimeter resolution imaging at the frequencies ranging from 20 to 100 MHz. Those frequencies will be widely employed in the design of catheter based ultrasound transducers. These miniature (less than 2 mm in diameter) devices operating at frequencies above 20 MHz are already available and can be placed within the blood vessels, urethras, etc., to study abnormalities from within. For instance, they offer the ability to observe the function of esophagus with detection of abnormalities and functional disorders, as they are capable to produce images showing more details than the images made from the information obtained from the external body scanning.

Small animal scanners that operate at frequencies beyond 40 MHz allow practical implementation of ultrasound biomicroscopy (UBM) have recently become available and proven useful in biomedical ultrasound research. These scanners have also been used together with optical coherence tomography (OCT) that measures low-coherence optical interferometry to obtain micron-scale resolution tomographic images of subsurface tissue. Comparisons between the 40–55 MHz UBM scanner and OCT system operating at 1300 nm used for structural and Doppler flow imaging indicated that the techniques are complementary in applications in embryo imaging in tadpoles. Briefly, UBM offered deeper (up to 3–5 mm) penetration depth with spatial resolutions of 30 and 60 μm for axial and lateral resolution, respectively. OCT provided better spatial (both axial and lateral) resolution of approximately 10 μm at the expense of lower, approximately 2 mm, penetration depth.

At the technological end, the research into new piezoelectric transducer materials will result in improvement of the scanheads' sensitivity and hence in the overall image quality. Nonpiezoelectric transduction imaging transducers will also become widely available. Prototypes of nonresonant transducers operating in the frequency span wider then the one achievable using current piezocomposite technology have already been described. The transduction principle of these new devices is similar to that of a condenser microphone (that can also be used as an acoustic source) with a DC voltage prebiased moving membrane. The devices are manufactured using integrated circuit technology. Because physical dimensions of an individual "condenser microphone cell" are on the order of 100 μm, the adjacent cells can be readily connected to form virtually any shape. This feature is of interest as it allows realization of an electronically swept annular array. Annular arrays offer desirable zoom along the acoustic axis and also provide uniform image resolution independent on deflection angle. Introduced in the early eighties they were mechanically deflected and capable of providing uniform high resolution image within the field of view. This is in contrast with presently used multi-element transducers, where image quality decreases with increasing deflection angle. However, with a growing industrial preference for enhanced reliability, annular arrays were phased out and replaced by presently ubiquitous electronically steered scanheads, including linear, phased and curvilinear arrays. It is very likely that the "condenser microphone" cells, also termed capacitive micromachined ultrasound transducers or CMUTs, will result in significant improvement in image quality, similar to that obtained in the late eighties when solid piezoelectric ceramic material was replaced by two-phase piezocomposite that exhibited higher coupling efficiency and wider bandwidth. It is also conceivable that the pricing of CMUT arrays will be advantageous as they can be manufactured using proven solid-state technology. As already noted this technology can potentially implement steerable annular arrays that can provide advantageous uniform high resolution imaging independent on angle of deflection.

3.7. Truly portable or wearable high resolution scanners

The new generation of silicon technology imaging transducers combined with ongoing electronic miniaturization and availability of extremely fast and powerful portable laptop computers will result in the availability of truly portable or even wearable high resolution, clinically acceptable scanners and provide instantaneous optimization of spatial and contrast resolution and penetration. If successfully developed, such portable devices can also take advantage of wireless data transfer. Such development and availability of wireless hand held high resolution ultrasound scanners will enhance applications of ultrasound technology and will also help to make this technology affordable in remote locations. Moreover, it will provide a useful portable tool in physicians' offices and will be useful as a less expensive and complementary application with other imaging modalities such as CT or MRI.

3.8. Advanced signal processing

Increasing computational power of laptop computers will additionally facilitate diagnosis of technically difficult patients. Also, automatic optimization of the images will improve image quality, minimize the possible, operator dependent inconsistency in the images and, therefore, it will also contribute to the increase of diagnostic confidence. Moreover, the availability of image data in a digital form will enhance the possibility of providing clinical expertise globally, via remote, wireless consultation. The ongoing miniaturization of ultrasound scanners will make them available as truly portable, high image quality devices and it is likely that such miniature, laptop based scanners will become a part of emergency equipment. It can be expected that pricing of the portable and perhaps even wearable ultrasound scanners will make them affordable to general practitioners. Such development would ensure that the application of ultrasound technology as the preferred imaging modality in a variety of clinical situations will continue to grow.

3.9. Diagnostic and therapeutic applications

It is conceivable that in the near future the synergy between diagnostic and therapeutic applications of ultrasound will increase markedly. In comparison with other treatment modalities, ultrasound offers easily implemented focusing of high energy in tissue. It is likely that in the near future diagnostic scanners will be supplied with both diagnostic and therapeutic transducers. Identification of the malignant tissue using diagnostic ultrasound and then immediate localized treatment or thermal tissue ablation under constant monitoring will become clinical reality. Another advantage associated with focusing of ultrasound energy is that it can be used for externally induced, minimally invasive cauterization.

Also, the application of ultrasound in assisted drug delivery and drug efficacy monitoring will gain attention. Monitoring of drugs' effect and acoustic energy-controlled extracorporeal release of a given drug (introduced with acoustic contrast agent as a carrier) in the vicinity of the malignant tissue seems to support the notion of an upcoming merger of diagnostic and therapeutic uses of ultrasound energy in clinical practice. Ultrasonically induced gene delivery should also be mentioned as a major future research activity.

3.10. Doppler ultrasound

Increasing recognition of Doppler ultrasound will also solidify ultrasound applicability in clinical practice. Doppler ultrasound exhibits superb performance in hemodynamic studies and is well suited for constant monitoring needed in tissue transplants. It can also be used as an early warning device for imminent rejection of the transplant, so immuno-suppressing drugs could be delivered or administered in time. Tissue Doppler imaging is capable of providing information about rejection and hence it would reduce the number of biopsies and other invasive studies. As already noted, it is likely that future generation of ultrasound scanners will exhibit Doppler sensitivity adequate to detect extremely low velocity (less than 10 mm/s). New generation of high frequency Doppler machines will make this technique directly applicable in intra- and post microsurgery, including implants to evaluate the flow in the narrow vessels or capillaries affected by the procedure. In emergency units the possibility of noninvasive hematocrit measurements using Power Doppler approach would be of major interest.

3.11. Ultrasound versus other imaging modalities

Clinical ultrasound is at times criticized for its well-known shortcomings such as its inability to penetrate and image bones and tissue containing gas. In such applications other modalities may be preferable. However, in light of the many advantages mentioned above, the competition with other imaging modalities will most likely transfer into synergy and complementary use. The most recent generation of diagnostic ultrasound scanners is capable of delivering images strikingly similar to those obtained using magnetic resonance or computerized tomography. Although very fast imaging is possible with X-ray fluoroscopy, ultrasound is second-to-none as a nonionizing radiation modality with providing real time images (e.g. in cardiology). In addition, the most sophisticated scanners cost less then a half in comparison with other modalities, and last but not least, the portability of ultrasound scanners is unmatched making them the tools of choice in emergency units and on-site diagnosis. Ultrasound imaging also appears to be particularly well suited to offer noninvasive and economic solution to mass screening; mass screening leads to earlier detection and effective treatment of presymptomatic disease. There is no doubt that further advances in the technology and the gradual introduction of 4D imaging will make clinical examination less operator dependent. The availability of 3D data will improve reproducibility and reduce the need to rescan the patient. To stay ahead ultrasound scanners will constantly improve image quality; spatial compounding for improved enhancement of tissue contrast and boundary outlining, and multi-frequency harmonic imaging that would increase the contrast of solid masses will be introduced into portable machines.

4. Conclusions

A brief assessment of the current ultrasound technology and the most likely future developments were reviewed. It was pointed out that the new silicon technology generation of ultrasound imaging transducers would make true 2D arrays economically affordable. Contrast agents and ultrasound assisted drug delivery will continue to evolve and images based on viscoelastic properties of tissue will provide additional diagnostic information. Possible applications of radiation force in remote palpation and local nerve stimulations were also described along with an indication of a likely fusion between diagnostic and therapeutic applications of medical ultrasound. In closing, it is appropriate to note that the above review hardly covers all possible future developments, however, it brings into the focus the most likely avenues of biomedical ultrasound advances in the next half decade.

The author has reviewed almost 200 references to compile the information provided above. Due to space limitation, rather than list all of the references, only those that are particularly relevant to the specific sections of this article are listed below.

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