Review on detection of tumor using Ultrasound Elastography

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Abstract— **Ultrasound elastography is an imaging technique used to image tissue elasticity and is often referred to as virtual palpation. This article reviews the principles of ultrasound elastography and its clinical applications. Originally, Elastography is a non-invasive method in which stiffness or strain images of soft tissue are used to detect or classify tumors by comparing pre- and post compression images. The tissue is compressed and relaxed using external force and pre- and post compression ultrasound images are acquired. This method is easy to use and also cheap as it does not require any additional hardware/circuits. While elastography can also be performed with MRI and CT, low cost and portability of ultrasound equipment makes it better choice for widespread application of elastography techniques in the medical imaging field. However, new techniques have been developed that use different excitation methods such as external vibration or acoustic radiation force to compress the tissues. Clinical use of elastography is increasing, with various applications including lesion detection and classification, treatment monitoring, fibrosis staging, vascular imaging and musculoskeletal applications. For successful clinical use in cancer diagnosis and monitoring the method should be robust to sources of decorrelation between ultrasound images.**

Index Terms—**Elastography, Ultrasound, tumor, strain images, elastogram, RF data.**

I. INTRODUCTION

Ultrasound

Ultrasound are acoustic waves with frequencies more than audible frequency range, from about 20 kHz to several hundred MHz. Medical ultrasound typically uses only the portion of the ultrasound spectrum between 1 MHz and 10 MHz due to the tradeoff between frequency and depth of penetration. Ultrasound waves are generated by small piezoelectric transducers, which that are electrically driven and typically placed on the skin. Piezoelectric transducers convert electrical pulses into mechanical vibrations and vice versa. The waves propagate into the tissue of the body where a portion is reflected from the large number of interfaces between tissues with different acoustic properties.

The most widely used applications of ultrasound in medical field involve the noninvasive imaging of internal organs of the body. Such imaging can provide valuable information regarding the shape and size, displacement, location or velocity of a given structure without the necessity of surgery or the use of potentially harmful imaging modalities which generates large amount of radiations, i.e. X-rays. Tumors and other regions of an organ that differ in density from surrounding tissue can be detected. In many instances, ultrasonic technique has replaced more risky or more traumatic procedures in clinical diagnosis. [1]

Display modes

To derive information about structures inside the body, the ultrasound device uses several different scanning modes: A-mode, B-mode, C-mode and M-mode.

A-mode:

A-scan mode is the oldest and simplest form of display. Each transmitted pulse triggers the sweep of an oscilloscope. That pulse (often attenuated) and the returning echoes are displayed as vertical deflections on the trace (Figure 1(a)). The sweep is calibrated in units of distance, and may provide several ranges in order to accurately determine the distance of the interfaces of interest. Often, the amplifier gain is varied with the sweep to compensate for the lower amplitude of more distance echoes. In most cases transducer is kept stationary so that any movement of echoes along the trace will be the result of moving targets. An example of A-scan display is that of the echoencephalogram.

M-mode:

As in the A-scan mode, each transmitted pulse triggers the oscilloscope sweep; however, the received pulses are used to brighten the tracer rather than control the vertical deflection, as shown in the figure 1 (b). The brightness level is set below the visibility threshold so that only the echoes, which appear as dots with brightness proportional to the intensity of each echo, can be seen. For the M-scan, the transducer is held stationary so that the movement of the dots along the sweep represents movement of received targets. If photographic paper is slowly moved past the face of the oscilloscope so that each trace lies immediately adjacent to the one preceding it, the dot representing each target will trace a line on the paper as shown in figure 2. A stationary target will trace a straight line,
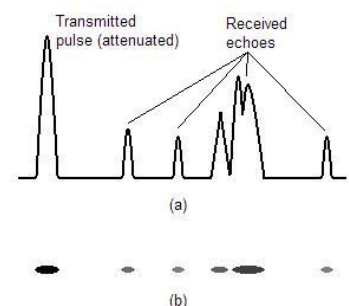

Figure 1: Ultrasound Display Principles. (a) Typical A-scan, Echoes cause vertical deflection of oscilloscope pattern. (b) Corresponding display in which echoes control brightness of oscilloscope beam. This principle is used in both B- and M-scan displays.

whereas a moving target will trace the pattern of its movement with respect to time. A light-pen recorder in which the intensity of the light source can be controlled may be used instead of an oscilloscope to produce a chart record of the movement of echoes with respect to time.

B-mode:

While the M-scan is used to display the movement of targets with respect to time, the B-scan presents a two-dimensional image of a stationary organ or body structure. As in the M-scan, the brightness of the oscilloscope or light-pen beam is controlled by returning echoes; however, in the B-scan the transducer is moved with respect to the body while the vertical deflection of the oscilloscope or movement of the chart paper is made to correspond to the movement of the transducer. The movement may be linear, circular, or a combination of the two, but where it is anything other than linear, the seep must be made to compensate for the variations in order to provide a true two-dimensional display of the segment being scanned. A real-time scan is provided by a B-scan system in which the scan rate of the transducer is fast enough to capture the movements of the organs being imaged. This type of system scan can capture the beating heart on the screen, allowing the physician to observe its motion. [2]

C-Mode:

C-mode image is one formed in a plane normal to a B-mode image; in this regard, it is similar to a classic x-ray image. To obtain a C-mode image, it is necessary to use a gate that selects data from a specific depth from an A-mode line and then to complete the image by a 2-D scanning movement of the transducer so that the entire region to be measured is sampled. One of the difficulties with the proposed method was the length of time required to complete a scan using a rectilinear scanning pattern that necessitated stopping and reversing the mechanism. Later, it was proved that by using a spiral scan, discontinuities in the transducer movement would be avoided, enabling the scan time to be reduced. By this means they estimated that an area of 100 cm2 could be scanned in around 10 seconds. [3]
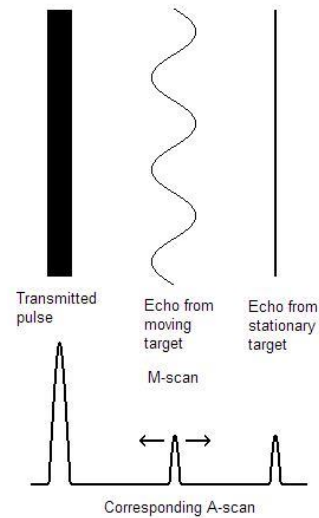

Figure 2: M-scan of moving and stationary target with corresponding A-scan.

The most commonly used display mode in medical ultrasound is B-mode imaging where an ultrasound transducer is placed against the skin directly over the region of interest (ROI). A typical ultrasound transducer employs an array of piezoelectric elements to generate short in duration, broadband pulses (with a center frequency of about 3-15MHz). The array size determines the imaging system's footprint. The same transducer also receives the reflected signals (echoes). The transmit signals passing to and the received signals passing from the array elements can be individually delayed by certain amount of time, defining a phased array. Delayed times in phased arrays are generally in microseconds. Phased arrays are used to electronically steer and focus the sequence of acoustic pulses through the target volume which is know as beam forming. Processing of these echo signals routinely begins at the individual channel (element) level to produce multiple A-lines (A-mode/ one dimensional wave equation of sound energy reflected from the target). Formation of B-mode sequences (Figure 4) commences with RF demodulation or envelope detection storing resulting A-modes in a 2D image matrix, followed by attenuation correction using time gain compensation (TGC) or swept and lateral gains to increase signal amplification from increasing depths. Next scan conversion (an 8 bit digitization) allows the B-mode to be displayed with a defined resolution (known as a B-scan), and finally logarithmic compression is used to adjust the large echo dynamic range (60-100 dB). The B-scan sequences captured and analyzed are those processed and displayed by the ultrasound machine, with a uniform dynamic range of intensities between 0 and 255. [4][5]

II. ELASTOGRAPHY

Introduction to Elastography

The term 'elastography' refers to methods of imaging the mechanical properties of tissue, specifically those related to the elastic (Young's) modulus. The idea of imaging the mechanical properties of tissue is not new; clinicians have employed manual palpation to feel for stiff lumps as long ago as 400 BC. However, recent improvements in imaging technology have allowed accurate, high resolution, in some cases quantitative visualization of the stiffness of relatively deep-lying structures. [6] The goal of elastic imaging is to map tissue properties such as Young's modulus or stiffness to provide useful clinical information. Changes in soft tissue stiffness may be related to an abnormal pathological process; for example, some tumors of the breast, liver and prostate are associated with increases in tissue elasticity caused by increased density. Physicians have relied on palpation of hard areas in tissue to aid in tumor detection. Present cross-sectional imaging methods display tissue parameters like attenuation (in X-ray), interferences (in ultrasound) or proton density (in MRI) not directly associated with the findings on palpation. Various elastography techniques developed using different modalities (ultrasound, MRI and optics), employ different tissue excitations and extracting different parameters of tissue motion. The most popular of these techniques is ultrasound, perhaps due to availability of Radio Frequency (RF) information/data of tissue, which represents propagation of sound waves through tissue. The ultrasound elastography method is based on external tissue compression with subsequent compression in strain profile along the transducer axis, which is developed from cross-correlation analysis of pre- and post compression A-line pairs. The strain profile can then be converted to an elastic modulus profile by measuring the applied force. [5]

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Palpation is the oldest method available for the detection of tumors. Before the advent of diagnostic imaging it was the only non-invasive way that tumors could be diagnosed. The variety of terms including rubbery, craggy or rock hard used to describe

tumors relate to the ease with which the mass may be distorted by pressure. Such terms are a very crude estimation of the elasticity (deformability) of the tissues. Deformability (ease of changing shape) is part of the algorithm to determine the likelihood of malignancy in routine ultrasound images but it only has moderate sensitivity in many lesions.

Measurement of tissue deformation, with applied force, by analysis of the returning ultrasound echoes, was described over 20 years ago. Ultrasound tissue elasticity has been an area of increasing research for the last two decades and has been applied to many different clinical situations including breast, prostate, skin, intra-operative brain imaging, cardiac and vascular imaging. Though most advanced in ultrasound, elasticity imaging is also being explored in other modalities including Magnetic Resonance Imaging (MRI) and Computerized Tomography (CT).

Tissue Elasticity

The physics of elasticity, according to Hooke's law, Young's modulus and Poisson's ratio, is based in mechanics and relates to the distortions which occur when matter is subjected to an external force or forces. Hooke's law states that strain is proportional to stress, and therefore the ratio of the two is a constant that is commonly used to indicate the elasticity of the substance. Young's modulus is the elastic modulus for small deformations and is the force per unit cross-sectional area of the material divided by the fractional increase/decrease in length resulting from the stretching/compressing of a material. Because compression along the line of the force results in distortions to the sides of that force line the ratio of the (lateral plus elevational) strain to the axial strain is defined as Poisson's ratio. The elasticity or stiffness of the tissues can be determined from changes in returning ultrasound echoes when the tissues are subjected to a load or force.

Principle of Elastography

To understand the principle of elastography and elastic property of tissue, consider a system with three springs of same length without any application of force. (Figure 3) Spring constant is defined as minimum force required to stretch (or compress) a spring by unit length. In the considered system, the springs have different spring constants; with the spring in middle having greater spring constant (more rigid) while other two springs having lesser spring constant (less rigid) than the one in middle. On application of equal forces on the springs, the less rigid spring will yield more displacement as compared to the rigid one. The rigid spring is mechanically less elastic; thereby producing less displacement compared to less rigid spring, which deforms more even due to the same force.
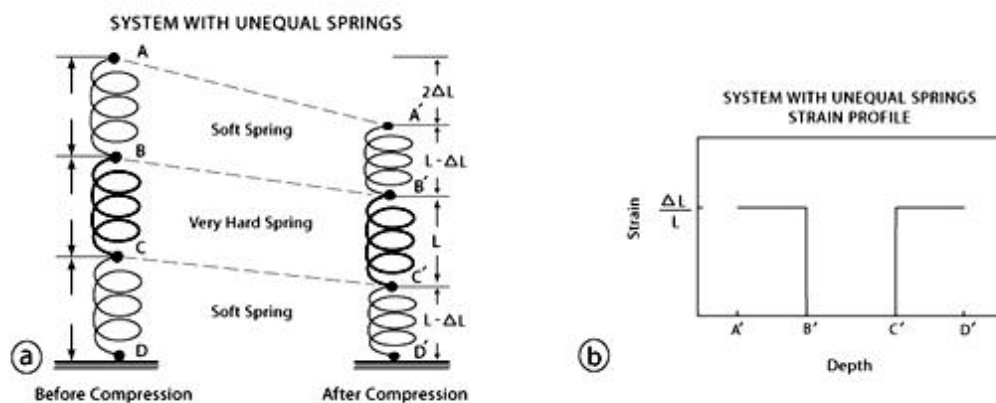

Figure 3: Measurement of strain in a one-dimensional cascaded system of unequal spring constants. (a) Pre-compressed state (b) post-compressed state.
Ultrasonic Imaging 13, pp. 111-134 (1991)

Elastography follows analogy of the spring example; tissues in general have varying mechanical properties. When subjected to similar forces, tissues with higher elastic modulus deform less, as compared to tissues with lower elastic modulus. Using cross-correlation function, one can measure such deformation (strain) and with information about the applied force (stress), one can deduce the elastic modulus of tissue. This noninvasive imaging procedure assesses the strain of soft tissues, providing structural information other than the morphologic features shown by conventional sonography. [8]

The essential components of quasi-static ultrasound elastography are summarized in figure 4. B-mode images are steadily acquired, with a slight varying pressure applied on the surface of the anatomy through the ultrasound probe. For scanning to 4 or 5 cm, physiological tremor is often enough to generate this pressure variation. It is from here that the term quasi-static derives, since the probe is in continuous motion, but with sufficiently low velocity and acceleration such that static mechanics can be assumed. The radio frequency (RF) ultrasound echo signals from each new image are compared with the previous image, and the tissue displacement is estimated at multiple locations along each signal (A-line). The axial strain is estimated by taking the gradient of this deformation data. An elastogram is displayed, which is a processed version of this strain data mapped to a color scale (grey in this case). Stiff regions compress less, and hence exhibit lower strain values.
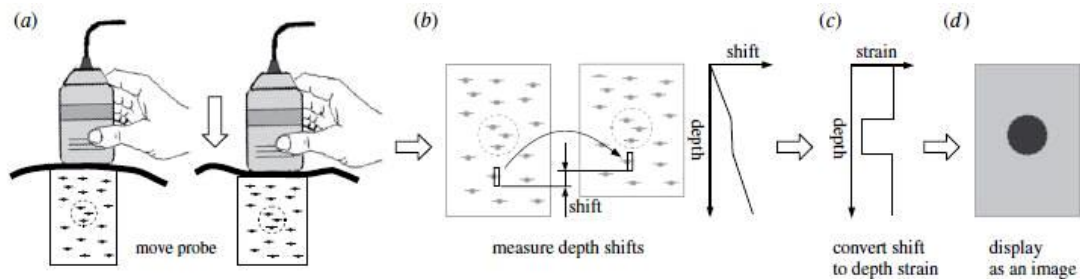
Figure 4: Overview of quasi-static elastography process. (a) The anatomy is scanned with conventional ultrasound probe, which is moved very slightly up and down (much less than is shown here). Here, the dashed circle is stiffer than the surrounding material. (b) Anatomical displacement is calculated everywhere in ultrasound image. (c) Gradient estimation in axial direction and filtering gives an estimate of axial strain. (d) A normalized version of axial strain is converted to grayscale and is displayed as an image, where black is stiff and white is soft.

III. VARIOUS METHODS IN ULTRASOUND ELASTOGRAPHY

A wide variety of approaches can be used determine the elasticity of different tissues based on comparing whole frame raw ultrasound data (radio frequency (RF) data) while changing the external force applied to tissues. Changes in this RF data can be recognized if there are distortions in some areas but not in others. The distortions are a reflection of the stiffness or elastic properties of the tissues under the investigation. Several different methods are being used to produce changes of pressure within tissues for elastography imaging. These have ranged from simple direct single compressive forces to well defined pressure waves with the use of external vibrating sources, which can be either pure mechanical or sound generated, to forces generated by cardiac and vessel pulsatile motion. A variety of techniques are used for analysis including Doppler effects, vibration propagation, tissue velocity measurement, tissue displacement and A-line analysis and cross correlation.

One of the earliest real time clinical descriptions of demonstration of stiffness which could not be perceived by simple compression was the utilization of the vibration of a patient's voice (vocal fremitus) and its effect on power Doppler images showing the Doppler signals within malignant lesions but not in benign lesions. The vibrational characteristics of tissues are also related to their elasticity. That vibration is demonstrated by power Doppler. If the patient makes a sound with a constant pitch such as that associated with the 'eeeeee!' though very crude, and both operator equipment and patient dependent, some idea of variation in tissue elasticity could be demonstrated (figure 3).
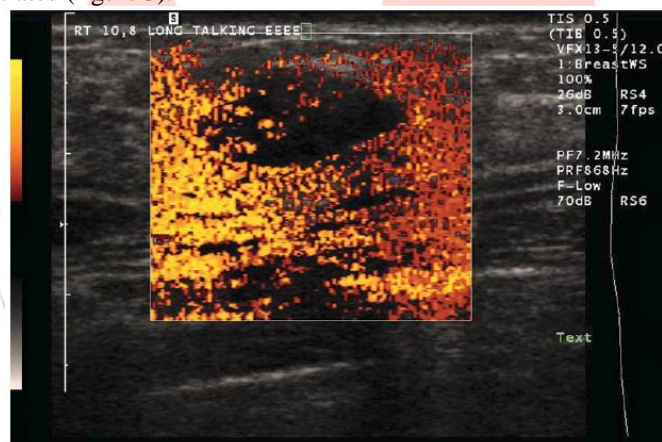

Figure 5: While using color Doppler the patient is asked to say 'Eeeeee'. The amount of vibration transmitted through tissues is related to the elasticity of the tissues. The tissue movement is detected by the power Doppler. The lesion which is demonstrated is a fibroadenoma which is stiffer (and vibrates less) than the surrounding tissues.

Pressure waves can be generated in tissues using external low frequency (10–1000 Hz) mechanical or acoustic vibration sources (dynamic vibrations). Using conventional linear array ultrasound probes, high energy focused ultrasound can be used to produce a single pressure wave (pulsed excitation). The mechanical and acoustical methods have the advantage of producing a uniform strain field but have proved to be more complex and difficult to standardize (surprisingly) than simple mechanical freehand (static) compression.

Freehand comparative compression elastography uses changes on digitized echo lines from the tissue region of interest before and after compression to determine differences in elasticity in adjacent tissues. The returning pulse from a single sound wave gives a line of high-frequency data, and much of the information in this ultrasound data is currently not utilized for producing the grey-scale image. If the RF data line is broken up into small segments, called kernels, it is possible to identify unique waveforms which are specific for a very small area or depths of tissue. As tissues are deformed these kernels will themselves not change as much in length as the distances between them (figure 4). Since the kernels have a unique waveform within them they can be identified along two pulses which are fired in quick succession down the same wave path or sound path. As tissues are deformed the change in distance can be used to determine the relative stiffness of the tissues (figure 5). If it is known how much force has been used to

compress those tissues an absolute measure of tissue elasticity could, in principle, be calculated. With free hand compression in vivo it is not possible to accurately estimate the forces involved so a comparative strain map of adjacent tissues is produced.

Freehand or compression elastography is the method of ultrasound elastography imaging which is currently becoming available for real time use with the present generation of new top end ultrasound machines. Two systems are well advanced making use of the RF signal of the returning ultrasound waves. One uses motion tracking while the other uses a combined auto correlation method which uses phase domain processing (similar to pulsed Doppler) and correlation of the phase component of the signal for displacement measurement. The tissue under investigation is compressed with the transducer while the scan line RF data is analyzed and compared with previous image frames. The same region of interest is kept within the frame from image to image, whist slowly deforming the tissues with the probe. Small amounts of displacement of between 0.5 and 2% are necessary between frames to allow estimation of stiffness. [9]
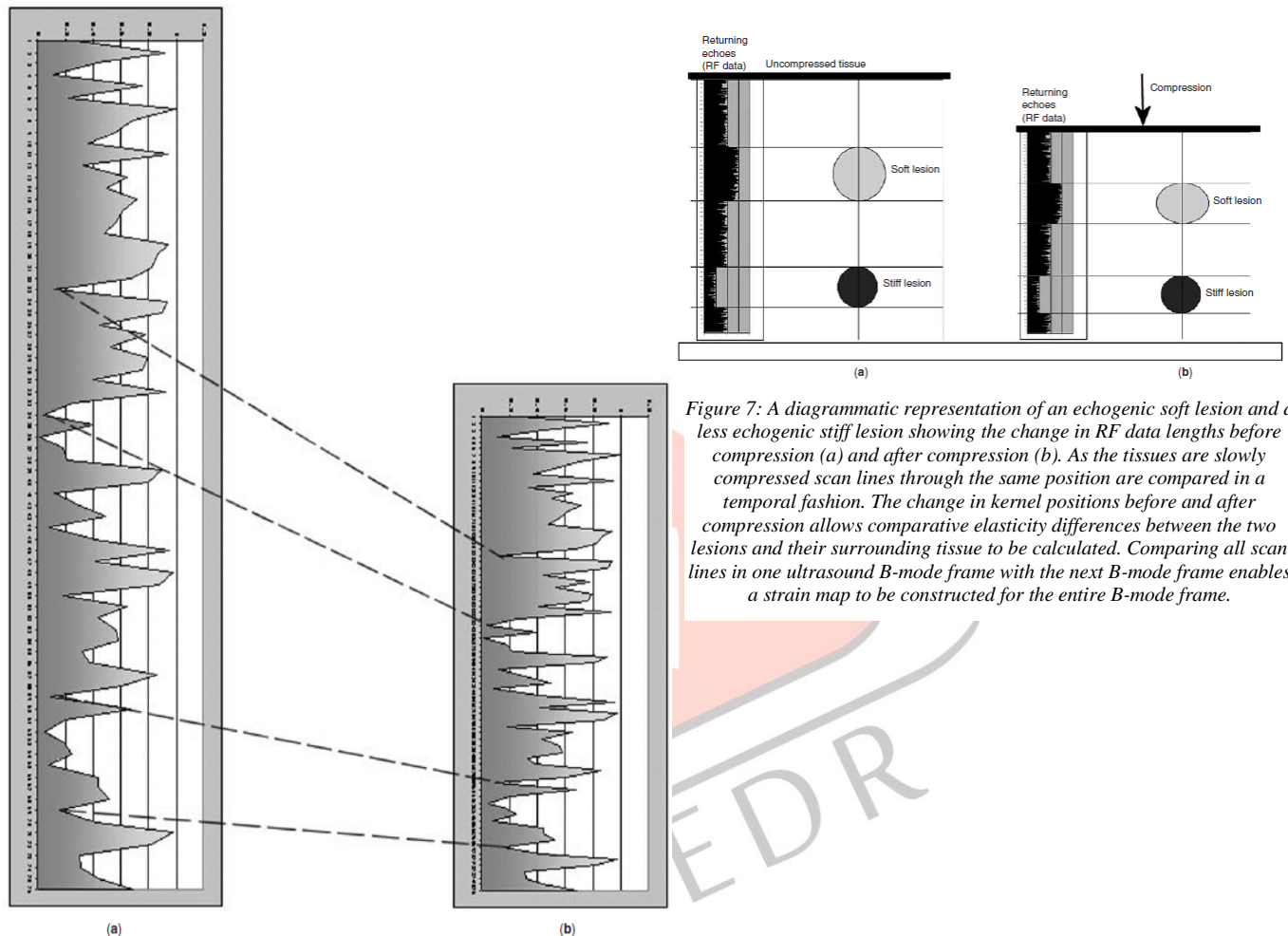

Figure 7: A diagrammatic representation of an echogenic soft lesion and a less echogenic stiff lesion showing the change in RF data lengths before compression (a) and after compression (b). As the tissues are slowly compressed scan lines through the same position are compared in a temporal fashion. The change in kernel positions before and after compression allows comparative elasticity differences between the two lesions and their surrounding tissue to be calculated. Comparing all scan lines in one ultrasound B-mode frame with the next B-mode frame enables a strain map to be constructed for the entire B-mode frame.

Figure 6: A diagrammatic representation of the effect on a short segment of returning echo RF data from the small same region of tissues before (A) and after (B) compression of the tissues. Kernels (short segments of RF data) do not compress as much (and are therefore more recognizable on each line) then the gaps between the kernels. The high-amplitude pulses can be recognized from both scan lines and the decrease in the gap between them indicates the distortion of that piece of tissue which occurs when compression is applied. These distances will be dependent on the elasticity of that part of the tissue being examined.

IV. METHODOLOGY

This section describe the workflow of ultrasound elastography technique which includes (1) the techniques of palpation utilized, (2) the means by which ultrasound data were transformed into ultrasound elastograms and (3) how the elastogram findings were compared with the benchmark of the surgical stiffness findings.

Technique of palpation

Two cycles of axial displacement by the ultrasound transducer were applied manually to the surface of the brain for each ultrasound echo data capture sequence. Each data-set lasted about two seconds providing 30 ultrasound echo frames. Axial displacements of no more than 5 mm were applied to the surface of the brain. Compression was only applied to the areas where resection would occur. Care was taken by visual observation of the real time B-mode ultrasound image during all acquisitions to minimize lateral and elevational displacements caused by undesired transducer motion, thus aiming to maximize correlation between pre-compression and post-compression radiofrequency (RF) images. The effect of altering the amplitude of axial compression on quality and information obtained on elastograms was evaluated.

Data and image processing

Ultrasound elastograms were produced by application of software programs developed at the Institute of Cancer Research on the ultrasound data. This data processing was performed retrospectively and is briefly described in this section. Analogue intermediate frequency (IF) data are the only output that could be exported from the Acuson 128 XP10 ultrasound scanner. These analogue IF data were digitized and converted to RF data offline. This process did not result in any degradation or loss of data. A two-dimensional cross-correlation-tracking algorithm was applied to pre-compression and post-compression RF data producing axial and lateral displacement images for that particular scan plane. A least squares strain estimator was applied to the displacement data producing strain images (elastograms).

Comparison of surgical findings with ultrasound elastogram findings

The next stage was to identify whether ultrasound elastography was an accurate method for identification of relatively stiff areas compared with softer areas intra-operatively during brain-tumor resection. This comparative assessment was between tumor and surrounding tissue, and also whether the tumor itself had intrinsic stiffness heterogeneity. There is no clinical method for measuring stiffness accurately intra-operatively hence there is no 'gold standard'. Attempts were made to mechanically test excised tissue; however, the results were not reliable (unpublished data). As the surgeon's assessment on stiffness is the main determinant of whether to resect an area and so represents current practice, ultrasound elastography was compared to this evaluation.

Information provided by the surgeon was not available when elastograms were produced to limit bias. Elastograms were processed and evaluated in conjunction with the B-mode ultrasound movie by the lead author only.

Relative strain of tumor compared with the brain was assessed as a means of comparing the stiffness of tumor to brain. The regions of interest chosen for this comparison were based on the presence of good echo data, good correlation imaging data (hence no out of plane motion) and the presence of a representative region of interest. [10]

V. PRACTICAL CHALLENGES & LIMITATIONS OF ULTRASOUND ELASTOGRAPHY

Despite having numerous potential clinical applications, several practical challenges have hindered wide application of static elastography. First, decorrelation between the pre-compression and post-compression images induces significant noise in the obtained displacement map and is one of the major limiting factors in elastography. Major sources of signal decorrelation are scattered motion in high axial compression, non-axial motions of the probe, and physiologic motion. Most elastography techniques estimate local displacements of tissue based on correlation analysis of radio-frequency (RF) echoes. Large windows are required to reduce the variance (i.e., noise) of the estimated displacement and to avoid ambiguity in time delay estimation, especially when tracking a motion that exceeds one wavelength. At the same time, signal decorrelation within large windows limits the tolerable level of compression. To reduce signal decorrelation, stretching methods have been proposed, which are computationally expensive and are not suitable for real-time elastography. Moreover, large errors due to false peaks and smaller errors, due to jitter limit the performance of correlation techniques.

Second, in many methods, the compression is applied by a mechanical actuator in order to generate an excitation that minimizes signal decorrelation or because accurate motion is otherwise required by the particular elastography technique. Freehand palpation elastography is a much more attractive alternative, as it requires no extra hardware and provides ease of use. It has attracted increasing interest in recent years, however it introduces additional sources of signal decorrelation caused by operator's hand unwanted motion.

Third, elastography is computationally expensive, making it challenging to display elastograms in real time. Real-time elastography provides the feedback to the operator to best capture the region of interest in the elastogram and is required for image guided surgical operations that can potentially use elastograms. Combined autocorrelation method and phase zero estimation are the first work that generate real-time elastograms. A real-time elastography system is introduced where tissue compression is performed by freehand palpation based on a 2-D block matching algorithm. Dynamic programming is used for one A-line of the image for guiding the block matching algorithm. While these methods use the displacement of each window to confine the search range for the neighboring windows, the displacement of each window is calculated independently and hence is sensitive to signal decorrelation.

Since data alone can be insufficient to solve ambiguities due to signal decorrelation, the physical prior of tissue motion continuity increases the robustness of the technique. The RF data is first upsampled by a factor of four in the axial direction. The image is then subdivided into four parts and a coarse displacement map is calculated for each part iteratively. Each part is subsequently divided into four parts and the displacement of each part is calculated by the same iterative technique using the displacement of the parent grid as an initial guess. The method is shown to generate accurate low noise displacement fields. However, the computation time is reported to be more than 1 min for a strain image that is less than half of the number of pixels in the strain images generated in this paper. Hence, the method is not immediately suitable for real time elastography. Compared to other optimization techniques, DP is an efficient non-iterative method of global optimization. [7]

Despite of the several researches in last to decades, field of ultrasound elastography still has many limitations. One limitation of this method is that a manual technique is used to generate the strain data. This might have resulted in inaccurate and inconsistent

sets of strain data. Considering the ultrasound elastography imaging technique, it is necessary obtain the B-mode images before the elastographic assessments can be done because the lesions were first detected and assessed with conventional sonography, and elastography was subsequently performed in real time using the same transducer. Moreover, the elastographic images are always superimposed on the B-mode image; consequently, the comparison of the diagnostic performance between both techniques was limited, introducing a bias. There are limitations directly related to the technique itself because it is so clearly operator dependant: it is crucial to keep light compression with the probe, avoiding lateral or angulated movements, to obtain acceptable images. [8]

VI. CONCLUSION

In conclusion, elastography is a simple, fast, and noninvasive technique, which can be performed immediately after conventional sonography technique. This technique can be used as a complementary technique in addition to B-mode sonography which increases the diagnostic specificity for breast lesions detection, thus reducing the false-positive rate.

Elasticity imaging adds useful diagnostic information which can help clinical management. Some areas where it is showing promise are in the accurate, unequivocal identification of lesions. The absence of any stiffness confirms the benign nature of the tumor. Initial work suggests that elasticity imaging may add to the accuracy of ultrasound determined tumor extent as it can demonstrate areas of tumor related stiffness in adjacent tissue to the grey-scale abnormality. Elasticity or strain imaging is a very different technique, method and image to learn, but increasing skill in interpretation appears to be providing greater accuracy in diagnosis. Like color Doppler, used as a stand alone method of differentiating benign from malignant, it is reasonably sensitive and specific, but taken with other observations within breast ultrasound imaging, it can help to improve diagnostic accuracy.

Recent work has confirmed that malignant tumors tend to appear larger in a strain (elasticity) image than in the typical ultrasound grey-scale (B-mode) image while the benign tumors tend to appear smaller in the strain image than in the grey-scale (B-mode) image. The extent of the strain image of cancers may be more accurate in demonstrating size of tumor than the grey-scale (B-mode) image.

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