Elastography: ultrasonic estimation and imaging of the elastic properties of tissues

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Abstract: The basic principles of using sonographic techniques for imaging the elastic properties of tissues are described, with particular emphasis on elastography. After some preliminaries that describe some basic tissue stiffness measurements and some contrast transfer limitations of strain images are presented, four types of elastograms are described, which include axial strain, lateral strain, modulus and Poisson’s ratio elastograms. The strain filter formalism and its utility in understanding the noise performance of the elastographic process is then given, as well as its use for various image improvements. After discussing some main classes of elastographic artefacts, the paper concludes with recent results of tissue elastography in vitro and in vivo.

Keywords: elastography, elastogram, elasticity, Young’s modulus, stress, strain, ultrasound, imaging, elastic modulus, Poisson’s ratio, breast, prostate, kidney

1 INTRODUCTION

Predicting and understanding the behaviour of materials when they are subject to mechanical forces is the basis for many aspects of modern engineering practice, from the design of structures to the design of solid propellant rockets [1]. In the early development of the field of mechanics, studying the behaviour of materials often involved applying loads to the system until the system failed, and then the failure mechanism was studied and used to infer the behaviour of the material prior to failure. Then, as technology advanced, it became possible to study the behaviour of complex material systems using non-destructive testing procedures, e.g. X-ray analysis, acoustic behaviour and photoelastic behaviour. The results of the experimental studies have contributed to the development of understanding how materials behave and to the development of mathematical models that help predict the behaviour of more complex material systems that are fashioned in very complex patterns [2].

In contrast to engineering materials, biological tissues are not very well behaved, in the sense of being easily described in closed-form mathematical expressions, because they are time and moisture dependent. When living, they are metabolically active and exhibit certain mechanical properties, which change soon after death. Moreover, these mechanical properties may be age, strain rate and strain range dependent [3–6]. To simplify the characterization of a tissue when the loading is of short enough duration that the viscous nature of the material can be ignored, the tissue can be assumed to behave elastically. This means that the state of the tissue only depends on the current loading; there is no effect from previous loading. By idealizing the tissue as an elastic material, the task of describing its behaviour is reduced to a matrix of 81 stiffness constants that must be specified [1]. Since obtaining these constants is a very challenging process, additional assumptions are often made to reduce the complexity of describing the tissue behaviour [7].

It is important to recognize the assumptions that are often employed to create a simple mathematical model of a tissue system. Tissue has a hierarchical structure and by choosing the scale or size of the tissue samples that are being studied, it is often possible to assume that the tissue is orthotropic, so the number of constants is reduced to 27. Then, by further restricting the scale of the sample so that the small structures in the system are randomly and uniformly distributed in the sample, the assumption of homogeneity is usefully employed so that only 12 constants are needed to describe the tissue.
Again, if the scale of the tissue is picked with care, it may be appropriate to approximate the tissue as an isotropic material so that only two constants are needed to describe the tissue’s response to mechanical loads. These two constants are the Lamé constants, or their technical derivatives, Young’s modulus and Poisson’s ratio.

The elastic properties of soft tissues depend on their molecular building blocks, and on the microscopic and macroscopic structural organization of these blocks [8]. The standard medical practice of the soft tissue palpation is based on qualitative assessment of the low-frequency stiffness of tissue. Pathological changes are generally known to be correlated with changes in tissue stiffness as well. Many cancers, such as scirrhus carcinoma of the breast, appear as extremely hard nodules [9]. In many cases, despite the difference in stiffness, the small size of a pathological lesion and/or its location deep in the body preclude its detection and evaluation by palpation. In general, the lesion may or may not possess echogenic properties which would make it ultrasonically detectable. For example, tumours of the prostate or the breast could be invisible or barely visible in standard ultrasound examinations, yet be much harder than the embedding tissue [10]. Diffuse diseases such as cirrhosis of the liver are known to significantly increase the stiffness of the liver tissue as a whole [9], yet they may appear normal in conventional ultrasound examination. Since the echogenicity and the stiffness of tissue are generally uncorrelated, it is expected that imaging tissue stiffness or strain will provide new information that is related to pathological tissue structure. This expectation has now been confirmed [10]. In addition to pathology, there is additional evidence that various normal tissue components possess consistent differences in their stiffness parameters as well. For example, in the ovine kidney, the stiffness contrast between the cortex and the medullary pyramids has recently been measured to be only about 6 dB, and strain images showing easily discernible contrast have been made [11]. This observation provides the basis for imaging the normal anatomy as well.

Over the past 20 years there have been numerous investigations conducted to characterize the mechanical properties of biological tissue systems [3–6, 12–21] which have been idealized often as homogeneous, isotropic elastic materials. Much of the work has focused on bone, dental materials and vascular tissue. There are articles that discuss methods used to characterize these tissues and there is a large volume of experimental data about the mechanical response of these tissues to various types of loadings [17, 22–27]; however, there is a void in the retrievable literature regarding the mechanical properties of tissue systems tested in vitro. In fact, there is very limited information about the mechanical properties of most of the soft tissue systems that make up the body’s organs. Yamada’s book [21] presents a relatively broad range of data, but much of the data are derived from experiments using animal tissues and all of the information relates to uniaxial tensile tests of the tissue.

The stiffness parameter cannot be measured directly. A mechanical stimulus of some kind must be propagated into the tissue, and precision means for detecting the resulting internal tissue motions must be provided. Such means may include ultrasound, magnetic resonance imaging (MRI) or other diagnostic imaging modalities. In the last 15 years, interest has been mounting in the ultrasonic imaging of tissue elasticity parameters. A comprehensive literature review of this field can be found in Ophir et al. [25] and in Gao et al. [17], and will not be repeated here. Tissue elasticity imaging methods based on ultrasonics fall into two main groups: (a) methods where a quasi-static compression is applied to the tissue and the resulting components of the strain tensor are estimated [24, 28, 29] and (b) methods where a low-frequency vibration is applied to the tissue and the resulting tissue behaviour is inspected [23, 30–33]. Among the techniques based on the quasi-static estimation of tissue strain, elastography [24] is based on estimating the tissue strain using a correlation algorithm, whereas another elasticity imaging technique [28] is based on estimating such strain using signal phase information. Most importantly, however, in both methods, local tissue displacements are estimated from the time delays between gated pre- and post-compression echo signals, whose axial gradient is then computed to estimate and display the local strain. Recently, intravascular application of elastographic techniques have also been reported [34–36]. In this paper, emphasis is placed on describing the recent progress in elastography, which is being developed in the authors’ laboratory. Among the second group of techniques, in sonoelastography imaging [30, 31], the vibration amplitude pattern of the shear waves in the tissue under investigation is detected using Doppler methods, and a corresponding colour image (similar to a colour Doppler display) is superimposed on the conventional grey-scale image. An absence of vibration may signify the presence of tumours. A theory of sonoelasticity imaging was developed [37] and an in vitro study on excised human prostate showed better sensitivity and specificity than conventional transrectal ultrasound [38]. Yamakoshi et al. [32] developed a method to map both the amplitude and the phase of low-frequency wave propagation in the tissue. These can be used to derive the velocity and dispersion properties of the wave propagation. Krouskop et al. [23] used a single-element pulsed Doppler instrument to measure the tissue flow at points of interest under external vibration.

Somewhat later, a parallel development has occurred in MRI. Plewes et al. [39] have developed a method that is based on the compression of the tissue and estimation of the resultant strains using MRI. Fowlkes et al. [40] have discussed an MRI-based method to measure tissue displacements. They have also shown mathematical reconstruction of the distribution of the moduli for select
examples. Muthupillai et al. [41] developed an MRI method similar to the ultrasonic Doppler method described by Yamakoshi et al. [32].

First some basic tissue stiffness results are presented which demonstrate the existence of stiffness contrast among normal tissues and between normal and pathological tissues in the breast and prostate. These data provide the continued motivation for further development of this field. Then the elastographic process is described, starting from the tissue elastic modulus distribution, progressing through various algorithms for precision time delay estimation of echoes from strained tissues and culminating in the production of the elastogram. Several kinds of elastograms are then described, each displaying a different quantity, which is related to the elastic properties of the tissue, and each having been derived using different methodologies. These include axial strain, lateral strain, modulus, Poisson’s ratio and elastograms [42]. The use of ultrasound to acquire tissue motion information results in certain basic limitations on the attainable elastographic image parameters, which may be described by the theoretical framework known as the strain filter [43]. The strain filter may be used to predict and design important improvements to various elastographic image attributes, such as dynamic range expansion and improvement in the signal-to-noise ratio in elastography (SNRe) through multiresolution processing [44]. In combination with certain contrast transfer efficiencies (CTEs) inherent in the conversion of the modulus to strain contrast [45, 46], the strain filter formalism may be used to predict the upper bound as well as the practically attainable performance of the contrast-to-noise ratio in elastography (CNRe). After a brief description of the mechanical, acoustic and processing artefacts that may be encountered in the practice of elastography, recent results that demonstrate that quality elastograms may be produced and interpreted under low and high elastic contrast conditions are produced for both in vitro and in vivo studies.

2 BASIC DATA ON TISSUE STIFFNESS

Very little basic data are available in the literature on the stiffness of soft tissues. Perhaps this is due to the fact that, until recently, such data were of no practical consequence. However, the paucity of data does not change the well-known fact that tissue elasticity is intimately related to the higher levels of tissue organization. In view of the present ability to visualize the elastic attributes of tissues, it is inevitable that more data will become available in the ensuing years. Some data have been collected by Sarvazyan et al. [47], Parker et al. [48] and Walz et al. [49]. Some of the authors’ recent results on breast and prostate tissues in vitro are given in Table 1 [50]. These results indicate that in the normal breast fibrous tissues are stiffer than glandular tissues, which are in turn stiffer than adipose tissues. The two kinds of tumours studied show different behaviours, with the infiltrating ductal carcinomas being significantly stiffer than the ductal tumours. Some of the tissues exhibit marked non-linear changes in their stiffness behaviour with applied precompressive strain, while others remain unchanged. There appear to be opportunities in differentiating breast tissues based on their stiffness values as well as their non-linear stiffness behaviour. Significant differences are also evident among normal, BPH and cancerous tissues of the prostate (Table 2).

Table 1 Results of actual stiffness measurements (in kPa) of normal and abnormal breast tissues in vitro

<table>
<thead>
<tr>
<th>Strain rate</th>
<th>5% pre-compression</th>
<th>20% pre-compression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1%</td>
<td>10%</td>
</tr>
<tr>
<td>Normal fat</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Normal glandular</td>
<td>28</td>
<td>33</td>
</tr>
<tr>
<td>Fibrous</td>
<td>97</td>
<td>107</td>
</tr>
<tr>
<td>Ductal CA</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>Infiltrating ductal CA</td>
<td>106</td>
<td>93</td>
</tr>
</tbody>
</table>

Table 2 Results of actual stiffness measurements (in kPa) of normal and abnormal prostate tissues in vitro (BPH = benign prostatic hypertrophy, CA = prostatic carcinoma)

<table>
<thead>
<tr>
<th>Strain rate</th>
<th>2% pre-compression</th>
<th>4% pre-compression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.4%</td>
<td>4%</td>
</tr>
<tr>
<td>Normal anterior</td>
<td>55</td>
<td>62</td>
</tr>
<tr>
<td>Normal posterior</td>
<td>62</td>
<td>69</td>
</tr>
<tr>
<td>BPH</td>
<td>38</td>
<td>36</td>
</tr>
<tr>
<td>CA</td>
<td>96</td>
<td>100</td>
</tr>
</tbody>
</table>
3 THE ELASTOGRAPHIC PROCESS

Several years ago the authors introduced a new method termed elastography for direct imaging of the strain and Young's modulus of tissues [24, 51, 52]. Elastography differs from some of the vibrational methods that were described above in several important aspects:

1. The stress applied to the tissue is not vibratory, but rather quasi-static. This tends to avoid problems due to reflections, standing waves and mode patterns which may be set up in the tissue and which may interfere with quality image formation.

2. The applied quasi-static uniaxial stress reduces the complexity of the generalized one-dimensional discrete viscoelastic equation of forced motion of the form

$$\frac{d^2x}{dt^2} + R \frac{dx}{dt} + Kx = F_0 \cos \omega t$$

which contains inertial (M), viscous (R) and stiffness (K) controlled terms, and where x is the displacement, $F_0$ is the force amplitude and $\omega$ is the angular vibrational frequency. The reduced form is the much simpler Hookean equation $Kx = F_0$, since $\omega = 0$ and x is a constant, the velocity and acceleration terms vanish. In principle, this allows the isolation and direct extraction of the local tissue stiffness parameter (K) from measurement of the differential applied force (or stress) $F_0$ and the resulting local changes in displacement x. For the continuous case, the equivalent equation becomes $\varepsilon E = \sigma$, where $\varepsilon$ is the elastic modulus, $E$ is the strain and $\sigma$ is the applied stress.

3. The average levels of strain produced in the tissue are usually very small (on the order of 0.01). These strain levels are considered small enough to keep the Hookean equation well within the linear range, based on the linear stress-strain relationships for gels and human muscle in vivo reported by Mridha and Ødmann [53] which were valid up to a strain level of 0.25. They are kept small also in order to keep the distortion in the time-shifted echo signals (before corrections) to a minimum, hence maintaining a low level of decorrelation noise in the elastogram. If proper corrections can be made, however, it is possible to increase the applied strain and gain in image contrast, to within the limits of the correction methods, and perhaps most importantly.

4. Elastography is capable of producing high-resolution images (elastograms) [24, 27]. The term 'elastogram' is used in this article as a generic descriptor of all the different kinds of images that display some parameters that are related to the elastic behaviour or nature of the tissue. In this sense, elastograms will be described that display axial or lateral strains, the elastic moduli or Poisson's ratio distributions in tissues.

When an elastic medium, such as tissue, is compressed by a constant uniaxial stress, all points in the medium experience a resulting level of longitudinal strain whose principal components are along the axis of compression. If one or more of the tissue elements has a different stiffness parameter than the others, the level of strain in that element will generally be higher or lower; a harder tissue element will generally experience less strain than a softer one. The longitudinal axial strain is estimated in one dimension from the analysis of ultrasonic signals obtained from standard medical ultrasound diagnostic equipment. This is accomplished by acquiring a set of digitized radio-frequency (RF) echo lines from the tissue region of interest by compressing the tissue with the ultrasonic transducer (or with a transducer/compressor combination) along the ultrasonic radiation axis by a small amount (about 1 per cent or less of the tissue depth) and by acquiring a second, post-compression set of echo lines from the same region of interest. Congruent echo lines are then subdivided into small temporal windows which are compared pairwise by using cross-correlation techniques [54], from which the change in arrival time of the echoes before and after compression can be estimated. Due to the small magnitude of the applied compression, there are only small distortions of the echo lines, and the changes in arrival times are also small. The local longitudinal strain is estimated as [24]

$$\varepsilon_{11,\text{local}} = \frac{(t_{1b} - t_{1a}) - (t_{2b} - t_{2a})}{t_{1b} - t_{1a}}$$

where $t_{1a}$ is the arrival time of the pre-compression echo from the proximal window, $t_{1b}$ is the arrival time of the pre-compression echo from the distal window, $t_{2a}$ is the arrival time of the post-compression echo from the proximal window and $t_{2b}$ is the arrival time of the post-compression echo from the distal window.
estimated axial tissue displacements are used for the reconstruction. It has also become possible to generate lateral strain elastograms based on incompressibility processing [59] or from direct lateral strain estimations [42]. Poisson’s ratio elastograms have also been reported [42].

It is important to emphasise that elastography is a method that ultimately can generate several new kinds of images. As such, all the properties of elastograms are different from the familiar properties of sonograms. While sonograms convey information related to the local acoustic backscatter energy from tissue components, elastograms relate to its local strains, Young’s moduli or Poisson’s ratio. In general, these elasticity parameters are not directly correlated with sonographic parameters, i.e. elastography conveys new information about internal tissue structure and behaviour under load that is not otherwise obtainable.

The general process of creating strain and modulus elastograms, beginning with the modulus distribution in tissue and ending with a corresponding modulus elastogram, is shown in Fig. 1, showing a block diagram of the process. The input to the process is the intrinsic tissue modulus distribution. The outputs can be either the strain (axial and/or lateral) elastograms, the Poisson elastogram or the modulus elastogram. The tissue strain obtained by a quasi-static tissue compression, restricted by the mechanical boundary conditions, is measured using the ultrasound system. The block describing the strain filter [43] embodies the selective filtering of the tissue strains by the ultrasound system and signal processing parameters. The strain filter predicts a finite dynamic range and respective elastographic signal-to-noise ratio (SNRE) at a given resolution in the elastogram, limited by noise and/or decorrelation. The contributions of the signal processing and ultrasound system parameters and other algorithms are indicated as inputs into the strain filter. The optimized strain elastogram is used as an input to the (optional) inverse problem solution block, where the contrast transfer efficiency (CTE) is improved, with subsequent reduction of artefacts in the modulus elastogram. All these blocks are described later in this article. A complete description may be found in Ophir et al. [26].

4 CONTRAST-TRANSFER EFFICIENCY

Using ultrasonic techniques, it is only possible to measure some of the components of the local tissue strain tensor. The local components of the stress tensor remain unknown. If the optional inverse problem solution is not used (e.g. because of incomplete knowledge of the boundary conditions, complexity of the assumptions or computational load), the strain elastogram is all that is available to represent the distribution of tissue elastic moduli. This representation may result in mechanical artefacts and in a limitation of the contrast-transfer efficiency (CTE) [45, 46] under certain conditions. The CTE was defined by Ponnkanti et al. [45] as the ratio of the observed (axial) strain contrast measured from the strain elastogram and the underlying true modulus contrast, using a plane strain state model. Expressed in
decibels, it is given by

$$\text{CTE(dB)} = |C_{0}(\text{dB})| - |C_{t}(\text{dB})|$$

where the magnitude is used in order to have the CTE normalized to the zero dB level; i.e. the maximum efficiency is reached at 0 dB for both hard and soft inclusions. This property of elastography represents a fundamental limitation that has been verified by finite element (FE) simulations [45] and was also corroborated theoretically by Kallel et al. [46]. Figure 8 in a later section shows the behaviour of the CTE parameter over an 80 dB dynamic range of true modulus contrast as measured from simulated data and as predicted using an analytical model. It is clear from the figure that for low modulus contrast levels (a high level of target modulus homogeneity), the elastographic strain contrast is nearly equal to the modulus contrast (CTE $\approx$ 1 or 0 dB). This is a very important observation, since it suggests that for low modulus contrast tissues, the simply computed axial strain elastogram itself is nearly proportional to the true modulus elastogram. This expected result has been verified experimentally using ex vivo ovine kidneys [11]. Stiff inclusions have a relatively high level of contrast-transfer efficiency. However, soft inclusions that are completely surrounded by harder background material have a low contrast-transfer efficiency, and thus may not be well visualized by elastography. The reason for this limitation lies in the fact that due to the incompressible nature of many soft tissues (Poisson’s ratio $\sim$0.5), the soft inclusion will be so constrained that it will not be able to deform under pressure as it might otherwise do without constraints, thus assuming instead elastic properties that are closer to those of the surrounding stiffer material. Later it will be shown that after considering elastography within the framework of the inverse problem solution, the CTE may be significantly improved.

5 AXIAL STRAIN ELASTOGRAPHY

Elastography is inherently a three-dimensional problem. However, the early elastograms estimated and displayed strains in the axial direction only [24]. Until recently, all the tissue motion in the lateral and elevational directions were ignored. However, recent work by Lubinski et al. [59], Chaturvedi et al. [60, 61] and Konofagou and Ophir [42] have taken into account the non-axial tissue movement, and even used the lateral displacement to compute lateral strain elastograms [42]. In this section, however, it will be assumed that there is no non-axial tissue movement, thus concentrating only on the axial displacement and strain estimation.

5.1 Time delay estimation (TDE) of signals from strained tissues

Time delay is a very important parameter in elastography. The tissue strain is typically estimated from the gradient of tissue displacements. The local tissue displacements are estimated from the time delays of gated pre- and post-compression echo signals [24]. Time delays are generally estimated from the location of the peak of the cross-correlation function between the gated pre- and post-compression echo signals.

The quality of elastograms is highly dependent on the quality of the TDE. TDE in elastography is mainly corrupted by two factors: firstly, the random noise (electronic and quantization) introduces errors in the TDE and, secondly, tissue needs to be compressed to produce elastograms. The very same compression of the tissue distorts the post-compression signal such that it is not an exact delayed version of the pre-compression signal. This decorrelation increases with increasing strain and is independent of the signal-to-noise ratio in the echo signals (SNRs). Any phenomenon (such as lateral and elevational motions) that degrades the precision of the time delay estimates will also degrade the strain estimates, thus introducing additional noise into the elastogram.

5.2 Decorrelation and stretching

Echo signal decorrelation is one of the major limiting factors in strain estimation and imaging. Alam and Ophir [62] have demonstrated that for small strains, temporal stretching [52, 63, 64] of the post-compression signal by the appropriate factor can almost entirely compensate for the axial decorrelation. When the post-compression echo signal is stretched, it in effect realigns all the scatterers within the correlation window. In other words, appropriate temporal stretching removes the mean intra-window strain. Global stretching (of all windows equally) was found to significantly improve the SNRe and expand the strain dynamic range in elastograms. Moreover, this step is computationally not very intensive. Thus, a uniform global stretching of the post-compression A-line prior to the displacement estimation is highly advisable. In low-contrast targets and/or low strains, this is a very efficient displacement estimator. In these situations, it produces quality elastograms without significantly adding to the computational load. However, if the applied strain is large in high-contrast targets, there will be significant overstretching in the areas of low strains, which by itself can significantly degrade elastograms in these areas. However, stretching is mandatory in the presence of large strains; otherwise the elastograms are so noisy that they are practically useless. It also enhances the dynamic range of elastography. It must be remembered that axial stretching can only recover most of the decorrelation suffered due to scatterer motion in the axial direction; decorrelation due to lateral and elevational motions, as well as other sources of decorrelation, cannot be compensated for in this way, and require other methods. Alam et al. [65]
have shown that a deconvolution filtering approach may be useful in reducing the remaining decorrelation that results due to stretching of the point spread function (PSF) when the post-compression echo is stretched.

5.3 Other estimators

5.3.1 Adaptive stretching

Temporal stretching significantly improves TDE in elastography. However, the proper temporal stretching factor is dependent on the local strain, an unknown parameter one is trying to estimate. In an elastically inhomogeneous tissue, the strains will vary and thus, ideally, the stretching factor will have to be varied at different window locations. Since temporal stretching by the factor that compensates for the strain maximizes the correlation, an iterative algorithm is indicated. In this algorithm, the local temporal stretching factor is adaptively varied until a maximum in the correlation is reached. The local strain is then computed directly from this temporal stretching factor. Since the axial correlation is maximized at each data window between the pre- and post-compression A-lines, this estimator is an ‘optimal’ (one-dimensional) estimator of strain. It is also well known that the gradient operation amplifies noise in the displacement estimates. Since adaptive stretching involves only intra-window operations and no inter-window operation, it does not suffer from this type of degradation. Overall, adaptive stretching may help in improving the elastographic performance by a large factor. Like the uniform global stretching, it also increases the dynamic range of elastography [66].

Figure 2 shows elastograms for various methods discussed in this section for an inhomogeneous tissue-mimicking phantom. The applied strain was 2 per cent. Figure 2a shows the elastogram produced with no stretching. At this strain, the gradient method without stretching fails to produce a useful elastogram due to severe decorrelation. Figures 2b and c show elastograms produced with uniform stretching and adaptive stretching respectively. Both elastograms have low noise, but the elastogram produced using adaptive stretching appears less noisy. Figure 3 shows the elastograms produced on an in vitro ovine kidney that has a thermal lesion in the upper pole. The applied strain was 0.5 per cent. Figure 3a was produced with no stretching and Fig. 3b was produced using adaptive stretching. This last image shows better details and has less visible noise.

5.3.2 Correlation coefficient

It has been discussed how the correlation between the pre- and post-compression echoes can decrease with applied strain. However, decorrelation itself has been used to estimate delay and/or strain. Various researchers used the correlation coefficient to estimate tissue motion.

![Fig. 3 Elastograms of an ovine kidney in vitro with an approximately 3 mm diameter induced thermal lesion (black circle) in the upper pole. The applied strain is 0.5 per cent. Window size = 2 mm, window overlap = 50 per cent. Elastograms: (a) conventional gradient method, (b) adaptive stretching. The actual lateral width of each elastogram is 40 mm](image)

![Fig. 2 Inhomogeneous phantom experiment with 2 per cent applied strain. Window size = 3 mm, window overlap = 50 per cent, no median filtering. Elastograms: (a) gradient, (b) gradient with stretching and (c) adaptive stretching](image)
Bamber and Bush [72] proposed using the decorrelation coefficient (1 minus the correlation coefficient) for the envelope signals for freehand elasticity imaging. Varghese and Ophir [73] have demonstrated that the decorrelation coefficient has poor precision as a strain estimator. Alam and Ophir [74] have demonstrated using simulated data that changes in the centre frequency and SNRs (both the PSF and the SNR vary due to frequency-dependent attenuation, changes in the beam, etc., as the ultrasonic pulse propagates through the tissue) introduce unknown variable bias. Because of its simplicity, this estimator may be a valuable tool for freehand elasticity imaging. However, the disadvantages need to be recognized and care should be taken when using this estimator.

5.3.3 Phase-based methods

It is also possible to use phase to measure small tissue displacements [55], and commercial ultrasound scanners use phase change to estimate motion for Doppler processing. At least one group working on elasticity imaging uses a phase-based displacement estimator [28]. Since the phase is only well defined for narrowband systems, some bandpass filtering is done prior to the computation of the phase, which may introduce a loss in spatial resolution.

5.3.4 Least-squares strain estimator

A least-squares strain estimator (LSQSE) for elastography has been proposed [75]. It was shown that with such an estimator the signal-to-noise ratio in an elastogram (SNRe) was significantly improved due to the reduction of the displacement noise amplification due to the gradient operation. The LSQSE results in an increase of the elastographic sensitivity (the smallest strain that could be detected), thereby increasing the strain dynamic range that is depicted on the elastogram. Using simulated data, it was shown that a trade-off exists between the improvement in SNRe and the reduction of strain contrast and spatial resolution.

5.3.5 Butterfly search

Alam and Parker [76–78] developed the ‘butterfly search’ technique for complex envelope signals from a deterministic analysis, derived using Schwartz’s inequality. Since this method can simultaneously analyse more than two successive A-lines, it is a natural candidate in multiparameter elastography. Preliminary results have shown that it may improve the SNR and the dynamic range in elastography.

5.3.6 Direct, incoherent, spectral strain estimators

Elastography has been shown to be capable of producing quality strain images in vitro and in vivo. Standard elastography uses a coherent cross-correlation technique to estimate tissue displacement and tissue strain using a subsequent gradient operator. While coherent estimation methods [24, 28, 29, 63] generally have the advantage of being highly accurate and precise, even relatively small undesired motions are likely to cause signal decorrelation, and thus significant degradation of the elastogram. For elastography to become more universally practical in applications such as intravascular and abdominal imaging, limitations associated with coherent strain estimation methods that require tissue and system stability must be overcome. On the other hand, incoherent estimators [79–83] are moderately less precise but far more robust.

The principal idea behind the spectral approach is based on the Fourier scaling property. The previously used spectral method proposed by Talhami et al. [79] relates the relative change in the mean coherent scatterer spacing [79, 84–90] to the strain, and uses it for intravascular applications. This method assumes the presence of coherent tissue scatterers as well as underlying tissue periodicities in the tissue structure, which may not hold in most cases. In contrast, the spectral methods presented in this section [82, 83] make no assumptions regarding the composition or distribution of the tissue scatterers.

An important advantage associated with the spectral estimators [82, 83], as with adaptive stretching [66], is that they may be used to estimate strain directly (i.e. without using noise-amplifying gradient operators) within a single estimation window. Tissue strain using the spectral shift can be measured via the spectral centroid shift [82] or spectral cross-correlation [83]. The spectral centroid [91–94] has been widely used in estimating the Doppler shift, attenuation [91] and backscattering [94]. While the downshift in the spectrum with frequency-dependent attenuation complicates the estimation process for the Doppler shift, in elastography this problem is not encountered since differential estimates are used, which suffer common frequency-dependent attenuation effects. The upshift in the centre frequency estimate with strain is illustrated with a simulation in Fig. 4.

For the spectral strain estimator using the centroid shift [82], it is found that if the bandwidth of the scattering noise process is much larger than the bandwidth of the system PSF, then

\[ \frac{f_{c2} - f_{c1}}{f_{c1}} \geq A_s \]

where the strain estimate is equal to the fractional shift in the centre frequency of the power spectra, \( f_{c1} \) and \( f_{c2} \), of the pre- and post-compression signals respectively within a scaling constant \( A \). In the case of spectral cross-correlation [83], the ratio of the spectral shift, which was measured using cross-correlation of the spectra, to the centre frequency of the PSF is proportional to the tissue strain. Interestingly, this equation is of the same form.
as the defining equation for the strain itself, which is given as
\[
\frac{L_1 - L_0}{L_0} = s
\]
where \(L_0\) is the original length of the segment and \(L_1\) the new length after compression. Comparison of the estimation performance using coherent cross-correlation and the direct spectral strain estimators are illustrated qualitatively in Fig. 5 using elastograms obtained from an inhomogeneous experimental phantom containing an inclusion three times stiffer than the background at both low (0.5 per cent) and high (3 per cent) applied strains [82, 83]. Note that coherent strain estimation provides the least noisy elastogram for the low compression of 0.5 per cent [Fig. 5(i)], when compared to the spectral methods. However, for the large applied compression of 3 per cent [Fig. 5(ii)], the coherent strain estimator fails when compared to the spectral methods that produce reasonable elastograms. No stretching techniques were used. Finally, the method of spectral cross-correlation provides the least noisy elastogram in this case [83].

5.4 Options in the treatment of non-axial motions

When tissue is compressed, in addition to the axial motions it also undergoes non-axial motions that introduce additional decorrelations [95]. There are various ways to handle this problem:

1. Use small compression steps (typically <1 per cent applied strain). This reduces the motion of the scatterers in the lateral and elevational directions, and thus scatterers do not move substantially in and out of the beam. It is also possible to perform strain imaging by averaging the elastograms over a number of small applied strain increments [28, 96]. Varghese and Ophir [97] have shown that in multicompression elastography there exists an optimal incremental applied strain that maximizes the achievable SNRe.

2. The tissue can be mechanically confined to reduce lateral motion. This increases the elevational motion, but since the beam is broader in that direction, its effect can be neglected for the most part [95].

3. Use incompressibility processing, originally proposed for modulus reconstruction purposes [59], where the lateral strains are computed from the axial strains under certain assumptions. However, this method assumes Poisson’s ratio to be 0.5, which may not always be true [53], and the contour of the zero lateral displacement must be accurately estimated.

4. Use a method to correct for non-axial motion. Chaturvedi et al. [60, 61] have proposed a companding method that reconstructs the pre-compression sonogram by compensating for lateral motion. Konofagou and Ophir [42] have proposed a method that can estimate the lateral displacement with high precision and produce excellent corrected axial and lateral strain elastograms. This approach will be briefly discussed in the next section.

6 LATERAL STRAIN ELASTOGRAPHY

A major disadvantage of the current practice of elastography is that only the axial component of the strain
tensor is used to produce the elastogram, while the lateral and elevational components are basically disregarded. However, all three components are needed to fully characterize the motion of a three-dimensional target [98]. Furthermore, the lateral and elevational components can severely corrupt the axial strain estimates by inducing decorrelation noise [98, 99]. A new method has therefore been developed that produces high precision lateral displacements [42]. In reference [42] it is shown that the higher the interpolation scheme, the higher the number of independent displacement estimates and thereby the higher the precision of the estimation. Due to this high precision lateral tracking, quality lateral elastograms can be generated that display the lateral component of the strain tensor. The main requirements on the transducer specifications are: (a) a minimum of 50 per cent overlap between adjacent beams and (b) a well-focused beam (on the order of 1 mm). Preliminary studies [42] have shown that the precision increases with a beamwidth decrease (possibly due to the subsequent improvement in the ultrasonic lateral resolution) and this constitutes a topic of current investigations. Briefly, the new method works as follows. Interpolated post-compression A-lines are generated via a method of weighted interpolation [42] between neighbouring A-lines. Then, pre-compression segments are cross-correlated with original and interpolated post-compression segments [42] and the location of maximum correlation indicates the amount of lateral displacement that resulted from the compression. A least-squares algorithm [75] is used to derive the lateral strain from the lateral displacement information.

A correction for lateral motion has been described by Chaturvedi et al. [61] using a block-matching technique described by Bohs and Trahey [100]. The correction results in a significant increase of both the signal-to-noise ratio and dynamic range of the axial elastogram at large applied strains. This is similar in principle to the one-dimensional axial motion compensation and stretching described by Césedes and Ophir [63] as a means for reducing the noise in elastograms. Taking into account the coupling between axial and lateral motion, an iterative method has been developed of successive corrections for and estimations of axial as well as lateral motion [42]. This led to a consistent increase of the signal-to-noise ratio of both axial and lateral elastograms. Results of the iterative method are shown in Figs 6 and 7 from finite element simulations and in vitro prostate data respectively [42]. Figure 6 shows that the technique is able to remove large (curtain noise) near the edges of the image) as well as smaller (close to the centre of the image) decorrelation effects due to lateral motion, which are responsible for poor contrast-to-noise ratios for the hard lesion. This kind of improvement was predicted by Kallel et al. [99] via the calculation of the corresponding theoretical strain filters. In a similar fashion, the axial and lateral elastograms of the prostate in vitro (Fig. 7) show consistent improvement following the corrections. The part of the axial elastogram in Fig. 7c most corrupted by correlation noise coincides with the part of the maximum lateral displacement in Fig. 5d. This, along with the corrected axial elastogram of Fig. 7f, verifies the assumption that the decorrelation noise unaccounted for in Fig. 7c is due to lateral motion. From Figs 7e and f it may be concluded that axial and lateral elastograms are different due to existing compressibility and/or anisotropy in the prostate tissue. In a later section (Section 8) a method is proposed to measure compressibility through calculation of the local Poisson ratio. The iterative method has also been proven to be useful in breast data in vivo [42].

7 MODULUS ELASTOGRAPHY

Elastography based on quantitative strain imaging suffers from mechanical artefacts (shadowing and target hardening artefact [24]) and from limitations to the contrast-transfer efficiency (CTE). To go beyond such presumed limitations, a few groups independently considered elastography as a new, challenging inverse problem [56–58, 101]. The inverse problem (IP) approach is used extensively in electromagnetics, optics and geophysics research [102]. In the biomedical field it has been extensively studied in bioelectricity to determine the distribution of potentials on the surface of the heart or the brain from a limited number of peripheral potential measurements. However, it is relatively new in the field of continuum mechanics [103–105] and until recently it was not applied in the field of biomechanics, to which elastography belongs.

For many reasons (non-linearity, noise in the data, lack of complete data set, etc.), most of the IPs are ill-posed in the sense of Hadamard [106]. Therefore, finding a unique and stable solution of an IP is very difficult. To this end, during the second half of this century, many techniques have been proposed [107]. Since these techniques usually require several big matrix inversions, they remain complex, consuming computer time and memory. In elastography it is fortunate that the solution of the IP is an option rather than a necessity (Fig. 1) unlike in many other fields. Conceivably, the exercise of this option will be restricted to cases where the simple strain images alone are not sufficient to adequately complete a given task (detection, characterization, etc.). Below is a short summary of the different techniques proposed to solve the IP in elastography, followed by typical results obtained using the technique of Kallel and Bertrand [101]. The simulation results of the elastic modulus reconstruction were obtained after a total of 10 iterations of the linear perturbation technique proposed in reference [101].

The approach proposed by Skovoroda et al. [57] and