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Stable, intelligible ultrasonic strain imaging

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Abstract

Background—Freehand quasistatic strain imaging can reveal qualitative information about tissue stiffness with good spatial accuracy. Clinical trials, however, repeatedly cite instability and variable signal-to-noise ratio as significant drawbacks.

Methods—This study investigates three post-processing strategies for quasistatic strain imaging. *Normalisation* divides the strain by an estimate of the stress field, the intention being to reduce sensitivity to variable applied stress. *Persistence* aims to improve the signal-to-noise ratio by time-averaging multiple frames. The persistence scheme presented in this article operates at the pixel level, weighting each frame's contribution by an estimate of the strain precision. *Precision-based display* presents the clinician with an image in which regions of indeterminate strain are obscured behind a colour wash. This is achieved using estimates of strain precision that are faithfully propagated through the various stages of signal processing.

Results and discussion—The post-processing strategy is evaluated qualitatively on scans of a breast biopsy phantom and *in vivo* head and neck examinations. Strain images processed in this manner are observed to benefit from improved stability and signal-to-noise ratio. There are, however, limitations. In unusual though conceivable circumstances, the normalisation procedure might suppress genuine stiffness variations evident in the unprocessed strain images. In different circumstances, the raw strain images might fail to capture significant stiffness variations, a situation that no amount of post-processing can improve.

Conclusion—The clinical utility of freehand quasistatic strain imaging can be improved by normalisation, precision-weighted pixel-level persistence and precision-based display. The resulting images are stable and generally exhibit a better signal-to-noise ratio than any of the original, unprocessed strain images.

Keywords

Elastography; Strain Imaging; Normalisation; Persistence

Introduction

The mechanical properties of tissue have long been recognised as a useful indicator of disease. While manual palpation was described as early as 400 BC by Hippocrates,¹ more recent advances in technology have opened the way to quantitative assessment of relatively deep-lying structures. The general principle is to image the tissue deformation induced by some sort of applied mechanical stress. The measured deformation, taken alongside any knowledge of the stress, allows estimation of the tissue's mechanical properties. Ophir et. al.

coined the term “elastography”² to describe this general paradigm which embraces a wide range of different techniques, the principal distinguishing factors being how the stress is applied and how the deformation is measured. The former ranges from external palpation² to internal ultrasonic radiation force,³ while the latter might involve imaging modalities as diverse as MRI⁴ and ultrasound.⁵

Before proceeding further, it is important to clarify what is meant by “mechanical properties”, how they might be useful for medical diagnosis and whether they can be readily measured. A material exhibits mechanical properties at a range of scales, from the quantum to the macroscopic, including many phenomena that are not yet fully understood. Nevertheless, several models have been proposed and validated in the physical sciences, and it is to these that we turn when considering biological tissue. The linear elastic model^{6,7} relates stress to strain via a 21-degree-of-freedom elastic modulus tensor. It models anisotropic material properties but not any time-dependent effects. At the next level of complexity, the linear viscoelastic model^{6–8} accounts additionally for the time dependence of the stress-strain response. Alternatively, the simpler poroelastic model accommodates time-dependent effects by considering the material to comprise a solid, isotropic, linear-elastic matrix suffused by an incompressible, near-inviscid fluid.⁹

It has been suggested that viscoelastic time constants are related to biochemical changes,¹⁰ while poroelastic measurements might be useful for assessing oedematous tissue.^{11,12} Nevertheless, the simplest and most practical approach to elasticity imaging is to ignore viscous and porous effects, focusing instead on those material properties that might loosely be referred to as “stiffness”. These are embodied in the 21 parameters of the linear elastic model: such a large number of parameters is required to describe the anisotropic relationships between the various longitudinal and shear stresses and strains. However, estimating all 21 parameters from ultrasonic measurements is far beyond the capabilities of current technology, prompting the common assumption of isotropy. For isotropic materials, the stiffness relationship between stress and strain can be reduced to a two-parameter model, for instance the Young’s modulus E and the Poisson ratio ν . Moreover, the further assumption of incompressibility (a reasonable assumption for many biological tissues) fixes $\nu = 0.5$. The remaining parameter E fully characterises an incompressible, isotropic material’s stiffness. It has been suggested that this parameter accounts almost entirely for the useful information accessible by manual palpation.^{13,14}

An appealing way to estimate E is by freehand quasistatic ultrasonic elasticity imaging.² This technique uses a standard, clinical ultrasound scanner without hardware modification, the only difference being in the signal processing software. The clinician holds the transducer over the area of interest while gently varying the contact pressure, thus inducing mechanical stress in the targeted tissue, predominantly in the axial direction. Consecutive frames in the B-scan sequence are compared to estimate the resulting axial displacement which, in turn, is differentiated to arrive at the axial strain field. Assuming an isotropic, incompressible, linear elastic model, the Young’s modulus is then the ratio of the stress to the strain.

A clear difficulty with this approach is that the stress field is not known. The finite element simulation in Figure 1 (Abaqus 6.7, Simulia, Rhode Island, USA) illustrates the problem. In (a), we see a probe in contact with a relatively thick layer of background material, in which are embedded two circular lesions of hard and soft material. Following a slight compression, (b) shows the axial stress field and (c) the associated strain. In the context of quasistatic elasticity imaging, (c) is what is measured, (a) is what is required, but this involves dividing (b) by (c), where (b) is unknown.

One way forward is to attempt to solve the so-called inverse problem, by which both (a) and (b) are estimated from (c). This is theoretically possible, as long as either the stress or the Young's modulus is known everywhere on the scan boundary.¹⁵ Since measuring the stress on the internal sides of the boundary is implausible, the usual approach is to make gross assumptions—for instance, assumptions of uniformity¹⁶—regarding the Young's modulus at the boundary. Unfortunately, the solution to the inverse problem is highly sensitive to these boundary conditions, so inaccurate assumptions lead to totally incorrect Young's modulus images.¹⁵ Moreover, inverse problems are generally tackled using expensive, iterative algorithms, and are therefore not amenable to real-time implementation on a clinical scanner.

Nevertheless, returning to Figure 1(c), it is clear that the strain image itself contains much in the way of clinically useful information. Even though the background is misleadingly nonuniform, the hard and soft inclusions are visible with high contrast and good spatial accuracy. Freehand quasistatic strain images of this nature can be generated in real time and have been the subject of several clinical trials. The results indicate that tumours are sometimes easier to detect in strain images than in B-scans.¹⁷ Indices derived from strain images may differentiate between benign and malignant lesions, and distinguish between different types of malignancy.^{18,21} Presumably encouraged by this evidence, several manufacturers now offer strain imaging on their flagship ultrasound systems. However, despite the early promise, there is still no convincing case for the adoption of strain imaging in routine clinical practice. The problem is not with the difference between strain and Young's modulus images, but rather the difficulty of achieving an acceptable signal-to-noise ratio in the strain images themselves: the quality of strain images continues to be unreliable.^{18,19,21}

The nature of this unreliability is evident in Figure 2, which shows several strain images from a freehand scan of a breast biopsy phantom (Computerised Imaging Reference Systems, Virginia, USA). Typical, inexperienced scanning induces not only axial probe motion, but also elevational and lateral slip and some side-to-side rocking. In (c), the probe was pressing harder on its left side, producing more strain (and thus the illusion of less apparent stiffness) towards the left. Rocking to the right reverses this pattern in (d). In both (c) and (d), the background strain appears to decrease with depth, suggesting higher stiffness, though this is again an artefact of the stress variation and not indicative of true stiffness. At many points in the sequence, estimation of the axial displacement is unreliable due to excessive signal decorrelation between the two frames being compared. When this happens, the strain image exhibits high levels of noise, as in (b). How is a clinician supposed to interpret this stream of noisy, inconsistent images?

This article presents improvements that go some way towards addressing this question. The aim is to produce a stream of stable, consistent strain images, irrespective of the sonographer's expertise in freehand elasticity scanning. This is achieved through post-processing the strain images in three ways. Firstly, a per-pixel estimate of strain precision is calculated and displayed alongside the strain estimates, making it clear where there is signal and where there is noise. Secondly, the strain images are normalised by an estimate of the stress field, reducing stress-induced variations in the background stiffness without incurring the computational expense and instability of the full inverse problem. Finally, the stream of normalised strain images are time-averaged (persisted) to improve the stability of the real-time display. The persistence calculations use per-pixel precision estimates to ensure that signal is favoured over noise. The result is a real-time system that offers the sonographer stable, intelligible strain images after the shortest of learning curves. Although technical details of current commercial systems are not available, the images they produce do not appear to benefit from the sort of normalisation and persistence schemes described here.

Methods and Results

Strain precision

All the strain images presented in this paper were obtained using previously documented, real-time, phase-based displacement tracking techniques.^{22,23} The underlying principle is to split the post-compression RF frame into small data windows, and then match each window to a corresponding window in the pre-compression frame. The precision (defined as the reciprocal of the variance or the mean squared error) of each displacement estimate is then approximately²⁴

$$\frac{XY\rho}{1-\rho} \quad (1)$$

where ρ is the normalised correlation coefficient between the RF data in the matched windows, X is the window width in A-lines, and Y is the window length in samples. Strain is then estimated at each display pixel (x, y) using a least-squares regression kernel, centred on the pixel, to differentiate the displacement estimates in the axial direction. The precision of the strain estimates is then²⁴

$$W_A(x, y) = \frac{\left(\sum_i \tilde{y}_i^2\right)^2}{\sum_j \tilde{y}_j^2 (1 - \rho_j) / (X_j Y_j \rho_j)} \quad (2)$$

where the summations are over displacement windows in the regression kernel, and $\tilde{y}$ denotes axial distance from the kernel centre.

The strain estimation precision $W_A(x, y)$ can be displayed alongside the strain estimates themselves, allowing the clinician to appreciate where there is good data and where there is noise. Figure 3 shows one way to do this, with a user-defined threshold on $W_A(x, y)$. Strain estimates with precision exceeding the threshold are displayed in greyscale, while those below the threshold are progressively obscured behind a red wash, with the least reliable estimates completely masked out. These are the same three strain images as in Figure 2(b–d), except it is now evident where the strain estimates are to be believed and where they are to be ignored. Importantly, this information is available at the pixel level: it is not necessary to accept or reject entire frames.

Strain normalisation

Raw strain estimates can be normalised to produce images that exhibit less of the stress-induced variation evident in Figures 2(c) and (d). We refer to the normalised quantity as “pseudo-strain”. While pseudo-strain images are often better approximations to true Young’s modulus images, the primary motivation is to arrive at a quantity that is reasonably stable throughout an image sequence. Without this, the subsequent time-average (persistence) stage is far less effective.

We assume that the unknown stress field takes the form

$$\widehat{s}(x, y) = \beta_1 (1 + 2\beta_2 y) (1 + \beta_3 x) \quad (3)$$

where β_1 , β_2 and β_3 are constants. This is a linear formulation that allows for stress variation in both the axial and lateral directions, modelling depth-dependent stress decay and side-to-side probe rocking respectively. Under the strong assumption that the imaged material has uniform stiffness, Equation (3) also describes the expected form of the strain field. This

assumption allows us to estimate $\hat{s}(x, y)$ by finding the β parameters that make $\hat{s}(x, y)$ best match the measured strain in a least-squares sense.

In practice, it is more accurate to estimate $\hat{s}(x, y)$ directly from the displacement field, before it is differentiated to obtain strain. Integrating Equation (3) with respect to y , the corresponding displacement field is

$$\widehat{d}(x, y) = \alpha_0 + \alpha_1 x + \beta_1 y (1 + \beta_2 y) (1 + \beta_3 x) \quad (4)$$

The α and β parameters are found by least-squares regression on the displacement field, with each displacement estimate weighted by its precision (Equation (1)) in the regression calculation, thus reducing the influence of unreliable displacement estimates. Then, denoting pseudo-strain by $s_B(x, y)$ and raw strain by $s_A(x, y)$, pseudo-strain is calculated according to

$$s_B(x, y) = s_A(x, y) / \widehat{s}(x, y) \quad (5)$$

Normalisation also affects the precision of the pseudo-strain estimates, which is given by

$$W_B(x, y) = W_A(x, y) \times \widehat{s}(x, y)^2 \quad (6)$$

Figure 4 shows the results of normalising the raw strain images in Figure 3. The results are interesting on two counts. Firstly, it is evident that pseudo-strain is less sensitive to stress variation than raw strain. One can imagine time-averaging the three frames in Figure 4 to further improve the image stability and the signal-to-noise ratio: the same cannot be said of the images in Figure 3.

More surprising, though, is the effect of the updated precision estimate $W_B(x, y)$. In Figure 4(a), the normalisation procedure has inferred large positive and negative stresses at the lateral extremities of the B-scan, and low stress around a central pivot axis: the probe would appear to have rocked between the pre- and post-deformation frames, inducing severe compression on one side and expansion on the other. At high strain there is significant intra-window signal decorrelation, which is why the raw strain estimates in Figure 2(b) were deemed to be low precision and masked out in Figure 3(a). When normalised by a large value of $\hat{s}(x, y)$, however, Equations (5) and (6) reinterpret the measurements as indicative of lower pseudo-strain with higher precision. Conversely, around the central pivot axis and towards the bottom of the frame, $\hat{s}(x, y)$ is small and precision remains low. From unpromising beginnings in Figure 2(b), useful pseudo-strain estimates have emerged in parts of the frame, despite the severity of the side-to-side rocking motion. Figures 4(b) and (c) show less dramatic though equally plausible improvements. The stress-induced variations have been reduced, with less confidence in the strain estimates where the assumed stress is low towards the right of Figure 4(b), the left of Figure 4(c), and the bottom of both frames.

Precision-weighted persistence

Having arrived at a reasonably consistent sequence of pseudo-strain images, the final step is to further improve the stability and the signal-to-noise ratio, by time averaging in a similar fashion to conventional B-scan persistence. An important difference, however, is that the averaging is weighted by precision on a per-pixel basis.

As each new frame f arrives, pixel-level persistence requires the accumulation of two buffers, a precision-weighted sum $S(x, y, f)$ of the pseudo-strains, and the sum $\Omega(x, y, f)$ of the precisions. Both are initially cleared to zero. The update rules are then

$$S(x, y, f) = \gamma S(x, y, f - 1) + W_B(x, y, f) s_B(x, y, f) \quad (7)$$

$$\Omega(x, y, f) = \gamma \Omega(x, y, f - 1) + W_B(x, y, f) \quad (8)$$

where γ is a user-defined parameter in the range 0 (no persistence) to just less than 1 (high persistence). The displayed quantity is $S(x, y, f)/\Omega(x, y, f)$, the precision-weighted average of the pseudo-strains. Moreover, $\Omega(x, y, f)$ provides a valid quality measure for the display, since the precision of a precision-weighted average of data with uncorrelated errors is equal to the sum of the precisions.²⁴ As long as γ is less than 1, and assuming the statistics of $W_B(x, y, f)$ to be stationary, $\Omega(x, y, f)$ will eventually stabilise around a finite value, allowing a constant threshold to be set for the precision-based display.

Compared with frame-level persistence, pixel-level persistence not only produces superior images,²⁴ but also allows the retention of per-pixel precision estimates, without which it would not be possible to produce a precision-based display. Figure 5 shows how persistence affects the pseudo-strain images in Figure 4. Despite the challenging probe motion, the display rapidly settles on a stable pseudo-strain image, with good background uniformity, accurate geometrical delineation of the stiff inclusion, and plausible masking of the less reliable strain estimates. Comparing Figure 5(a) with Figure 4(a) raises the important issue of time lag, an inevitable consequence of all persistence schemes. Figure 5(a) exhibits more masking than Figure 4(a), since $\Omega(x, y, f)$ is initially cleared to zero and these low precision values persist for some time, even after the arrival of good quality pseudo-strain estimates. However, the precision weighting in Equations (7) and (8) ensures that incoming high quality data affects the display rapidly, while incoming low quality data takes much longer to have any visible effect.

By way of further illustration, Figure 6 shows a frame sequence spanning the first second of the examination of a large follicular adenoma in the thyroid of a 53 year old female. A good pseudo-strain image is achieved within half a second of the transducer contacting the skin. The pseudo-strain image is subsequently stable, despite the non-axial strain induced by pulsation of the carotid artery. Note how the artery itself is correctly masked in all four frames, since elevational lumen flow causes severe signal decorrelation between the pre- and post-deformation frames. Figure 7 shows a similar sequence revealing a stiff, 5 mm pleomorphic adenoma (top centre of frame) in the parotid gland of a 22 year old female.

Discussion

While persisted pseudo-strain is arguably state of the art in the context of real-time, clinical elasticity imaging, it is certainly not infallible. One important source of error is the assumption of uniform stiffness underlying the normalisation process. Extreme deviations from this assumption can result in pseudo-strain images discarding valid information accurately captured in raw strain images. For example, a stiffness distribution that increases linearly with depth would be misinterpreted as depth-dependent stress decay and normalised away. That said, our clinical experience is that normalisation invariably improves image quality, especially in combination with persistence, though there is probably scope for application-specific alternatives to Equation (3) that account for prior knowledge of the anatomical site under examination.

A more fundamental limitation concerns the effectiveness of strain imaging as a proxy for true Young's modulus imaging. While we observed in Figure 1 that the strain image conveys much information regarding the underlying stiffness distribution, the finite element simulations in Figure 8 tell an altogether different story. In this case, the hard and soft

inclusions are sandwiched between the transducer face and an immovable lower plate. Mechanical modelling shows how the stress concentrates around the hard inclusion, with the consequence that it deforms about as much as the soft inclusion, making it hard to distinguish the two in the strain image. We have observed similar phenomena in clinical practice when imaging superficial lesions above shallow bony structures. Interestingly, such lesions are easily palpated, since palpation amounts to the clinician's fingers "feeling" surface stress, not strain. It is convenient that the strengths of manual palpation (Figure 8) and strain imaging (Figure 1) are to some extent mutually complementary.

With the reliability offered by pseudo-strain persistence, we anticipate that clinical trials of quasistatic strain imaging will soon demonstrate specific protocols of undoubted clinical utility. The simplicity and affordability of quasistatic strain imaging — it requires only software updates to many existing scanners—suggest that it has a long term future as a toggle on/off imaging option, in much the same way as colour Doppler is used now. Nevertheless, this sort of strain imaging will always be a qualitative tool, unable to measure absolute material properties to any degree of accuracy. The most promising quantitative technique is perhaps supersonic shear wave imaging,²⁵ which involves ultrafast imaging of Mach cone propagation to measure the Young's modulus. Although supersonic shear wave imaging cannot be implemented on current generation scanners, commercial development is already underway (SuperSonic Imagine, Aix-en-Provence, France). There is every chance that this technology will evolve to offer a practical, quantitative (albeit expensive) imaging modality, though a question mark remains over the achievable spatial resolution, which could well turn out to be lower than that of quasistatic strain imaging.

Conclusions

Under certain conditions, freehand quasistatic strain images can reveal qualitative information regarding tissue stiffness with good spatial accuracy. However, clinical trials have identified poor stability and variable signal-to-noise ratio as major drawbacks. This article has presented techniques that go some way towards addressing these issues, namely normalisation, precision-weighted pixel-level persistence and precision-based display. The resulting images are stable and relatively insensitive to the nuances of the scanning technique. In general, they also exhibit superior signal-to-noise ratio than any of the original, unprocessed strain images.

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Figure 1. Finite element simulations

(a) Geometry and mechanical properties: the deformation is induced by translating the probe 1% of the way towards the rigid base plate. (b) Axial stress, where black–white represents 0–2% of the Young’s modulus of the background material. (c) Axial strain, where black–white represents 0–2% compressive strain.

Figure 2. Why strain imaging is unreliable

A B-scan (a) and strain images (b–d) of a phantom containing a spherical, stiff inclusion embedded in uniform background material. Some strain images exhibit high levels of noise (b), while others suggest a strong signal but nevertheless display inconsistent background strain (c,d). The strain images employ black and white for high and low strain respectively. The raw RF echo data was acquired on a Diasus (Dynamic Imaging, Livingston, UK) ultrasound scanner.

Figure 3. Strain images with precision-based display

Areas of the image where the estimated strain precision falls below a user-defined threshold are progressively washed out in red. These are the same three frames as in Figure 2(b–d).

Figure 4. Pseudo-strain images with precision-based display
These are the same three frames as in Figure 3.

Figure 5. Pseudo-strain images with pixel-level persistence and precision-based display
These correspond to the same three frames as in Figure 4.

Figure 6. Sequence of persisted pseudo-strain images at the start of a clinical examination
The frames are approximately 250 ms apart. The subject is a large follicular adenoma in the thyroid of a 53 year old female. The raw RF echo data was acquired on a T3000 (Terason Ultrasound, Massachusetts, USA) ultrasound scanner.

Figure 7. Sequence of persisted pseudo-strain images at the start of a clinical examination
The frames are approximately 250 ms apart. The subject is a 5 mm pleomorphic adenoma (top centre of frame) in the parotid gland of a 22 year old female. The raw RF echo data was acquired on a T3000 (Terason Ultrasound, Massachusetts, USA) ultrasound scanner.

Figure 8. Finite element simulations

Axial stress (a) and strain (b) for a hard and soft inclusion embedded in a thin layer of background material, sandwiched between the transducer and an immovable lower surface. The deformation (1% axial probe displacement) and grey scales are the same as in Figure 1.