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Recommendations on the requirements of measurement infrastructure for elastography metrology

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EXECUTIVE SUMMARY

Elastography is a rapidly evolving diagnostic technique applicable to imaging modalities such as Ultrasound, Magnetic Resonance Imaging and Optical Coherence Tomography. The technique is sensitive to tissue stiffness and is capable of differentiating various pathological states known to cause changes to the mechanical properties of tissue which may not be very apparent with existing imaging techniques. Due to this ability the technique is increasingly being investigated by researchers across the world and commercial implementations have proliferated amongst almost all manufacturers. However, the metrological aspect relevant to this relatively new technique has not seen much progress. This is due to the fact that mechanical properties of tissue can be estimated using multiple techniques. These techniques could be relative or quantitative which provide different perspective of pathological/diseased state of tissue being investigated and hence coinciding clinical uncertainty. Therefore the objective of this paper-based scoping study was to identify key metrological areas within this emerging field in order to support/develop a measurement infrastructure for enabling standardisation of reporting methods of dynamic mechanical properties.
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1 INTRODUCTION

It is common for healthcare practitioners to use palpation as a diagnostic aid during physical examinations. Palpation is a method of feeling, with the fingers or hands, the patient's body to examine the size, consistency, texture, location, and tenderness of an organ or body part. The efficacy of this method relies on the premise that pathological tissues are often harder or stiffer than the surrounding normal tissue i.e. the strain in the tumour is less than the surrounding tissue. Technological advancements in medical diagnosis have enabled healthcare practitioners to obtain diagnostic information where traditional methods of palpation are not possible, for example heart, arteries and deep organs. Elastography or elasticity imaging is a remotely applicable non-invasive technique where the mechanical property of tissue such as its stiffness is assessed in response to an applied deformation. The resulting tissue displacement to a known applied mechanical deformation can then be represented as a strain image (Fig.1).

![Strain image of breast using SuperSonic Imagine Axiplorer ShearWave™ Elastography system.](http://www.supersonicimagine.com/Aixplorer-R/General-Imaging)

Since the production of the first images using ultrasound roughly 20 years ago the technique has proliferated across various imaging modalities including magnetic resonance imaging (MRI) and emerging technologies such as optical coherence tomography (OCT). Almost every ultrasound imaging equipment manufacturer has introduced elasticity imaging as a feature in their high end products. The imaging equipment is capable of providing radiologists and clinicians with either quantitative or qualitative information about tissue stiffness according to the technique applied by the
individual manufacturer. The clinical applications include breast imaging, liver, prostate, small parts imaging for endocrinology and cardiology, for detection of cancer and/or abnormal tissue.

1.1 GENERAL GOVERNING PRINCIPLES OF ELASTOGRAPHY

The soft tissue material properties such as stiffness can be described by their Young's modulus \((E)\), which is a measure of a material's resistance to compressive deformation (Lai W M et al 1999, Palmeri M L et al 2011). Tissues with higher Young's moduli, such as muscle and fibrous tissue, are more resistant to deformation than more compliant tissues, such as fat (Duck F 1990, Sarvazyan A et al 1995, 2001). Tissue deformations occur in response to a stress \((\sigma)\) being applied to the tissues and this deformation in response to this applied stress is known as the strain \((\varepsilon)\). Many assumptions are made in the field of elasticity imaging to simplify the analysis and interpretation of elasticity image. Common material assumptions include that the tissue is: linear (i.e., the amount of strain resulting from an applied incremental stress is not a function of the absolute stress applied), elastic (i.e., the tissue returns back to its non-deformed state when an applied stress is removed and the deformation state is not dependent on the rate of the applied stress), isotropic (i.e., the tissue's material properties are not orientation dependent) and incompressible (i.e., the volume of the tissue remains the same when strained due to its high water content) (Palmeri M L et al 2011). Under these assumptions, stress and strain can be related to each other by the Young's modulus, \(E\) (Lai W M et al 1999):

\[
\sigma = E\varepsilon
\]  

(1)

The elastic properties of a material can also be determined by monitoring the propagation of shear waves. Unlike compressive waves that propagate in the same direction as the tissue displacement, shear waves propagate in a direction orthogonal to the direction of the induced tissue displacement. Under the simplifying material assumptions discussed above, shear wave propagation is governed by the Helmholtz equation (Palmeri M L et al 2011):

\[
\mu \nabla^2 u - \rho \frac{\partial^2 u}{\partial t^2} = 0,
\]  

(2)

where \(u\) is the displacement, \(\rho\) is the material density, \(\nabla^2\) is the Laplacian operator and \(t\) is time. The speed of propagating shear (or transverse) waves \((c_T)\) can be related to the shear modulus \((\mu)\) by:

\[
c_T = \sqrt{\frac{\mu}{\rho}}
\]  

(3)

and, the shear modulus is related to Young's modulus by Lai et al. (Lai W M et al 1999):

\[
\mu = \frac{E}{2(1+\nu)}
\]  

(4)

Soft tissues are commonly considered to be incompressible, with a Poisson’s ratio (fraction of expansion divided by the fraction of compression) \((\nu)\) of 0.5 in materials with the assumptions stated above, leading to the relation \(\mu = E/3\). Some elasticity imaging modalities do not make as many assumptions about tissue material properties; two common deviations from these assumptions include modelling the tissue as being viscoelastic and being nonlinear. The introduction of viscosity to the tissue description allows the tissue stiffness to be a function of the excitation frequency (i.e., \(E(f)\)), where higher frequency excitations or vibrations yield a stiffer tissue response compared with lower frequency excitations. These viscous mechanisms also result in energy loss in the tissue. Tissue nonlinearities imply that the strain in response to an applied stress is dependent on the absolute stress that is applied to the tissue (i.e., Young's modulus is a function of strain, \(E(\varepsilon)\)).
1.2 DYNAMIC MECHANICAL PROPERTIES OF TISSUE

Most commercial elastography equipment diagnoses tissue pathology as a relative stiffness map (grey scale or colour) in assisting clinicians to distinguish healthy tissue from diseased tissue. Newer equipment such as those based on transient ultrasound elastography are capable of reporting quantitative information such as Young’s modulus for applications in diagnosing liver fibrosis and breast cancer. The compendium of Young’s modulus (Wells PNT et al 2011) suggest that there is wide variation in the reported values by different authors—even for tissue of the same type and are therefore of limited quantitative use. The uncertainty in the measurements is partly owing to different measurement methods and conditions under which the excised tissue was subjected. In a recent evidence-based review (Cole JA et al 2009) it is suggested that only transient ultrasound elastography can be used alone or in conjunction with other tests in assessing liver fibrosis. A reasonable body of evidence was found for breast imaging but advises that is can be used as an adjunct to conventional ultrasound rather than a replacement. Due to limited evidence in other applications such as prostate, endoscopic and vascular imaging the review reports that it is not possible to draw firm conclusions and further clinical trials are needed to evaluate its potential. Wells PNT et al 2011 suggest that uncertainty on the biomechanical properties of tissue in health and disease requires major efforts to collect, classify and disseminate the information which is available and to fill the gaps by making the necessary measurements.

1.3 MEASUREMENT OF EXPOSURE PARAMETERS

In any new imaging technique the benefits should not outweigh the risks and therefore careful measurements are necessary to evaluate any potential risks to patient due to exposure of low frequency vibrations used in elastography. Some elastography methods use external vibrators to couple low frequency shear waves in the frequency range 20 Hz to 50 Hz. Whilst in other methods low frequency shear waves are induced within the human body using radiation force using focused ultrasonic beam. The propagation of the shear waves are tracked using diagnostic imaging using very high frame rates lengthening the exposure time thereby increasing the potential risks involved.

International Electrotechnical Commission (IEC) Technical Committee (TC) 87 Ultrasonics, American Institute of Ultrasound in Medicine (AIUM) and the National Electrical Manufacturers Association (NEMA) in the US are responsible for standardisation activities related to medical ultrasound. These organisations are responsible for preparing standards related to the characteristics, methods of measurement, safety, and specifications of ultrasonic fields, equipment and systems in the domain of ultrasonics. Marketing of medical ultrasound devices in the US require for example compliance to Food and Drug Administration (FDA) 510 (k) regulation which in turn refers to IEC and AIUM/NEMA standards, and in Europe it is regulated by the European Commission (EC) Medical Devices Directive (MDD). IEC standard IEC 61157 specifies a standard means and format for the reporting of the acoustic output and IEC 62359 aids in assessing the thermal (Thermal Index, TI) and non-thermal hazard (Mechanical Index, MI) caused by exposure to a particular ultrasonic field used for medical diagnosis or monitoring. However the standards in its current form are not sufficient to address the latest developments in elastography such as use of focused ultrasonic fields to generate shear waves or low frequency vibrations induced using external applicators and tracking of the same with very high frame rate imaging technology. Skurczynski MJ et al 2009 undertook an experimental study to evaluate methods for assessing safety for ultrasound radiation force elastography. They used readily available test methods i.e. Thermal Test Object (TT) (Shaw A et al 1999) and Cavitation Detector (Zeqiri B et al 2003) to evaluate TI and MI from a focused transducer developed for radiation force based shear wave imaging research. They concluded that both test methods were adequate for estimating the relevant hazard and were within the safety limits imposed by the standard. However, commercial systems operate under more complicated signal transmission and receive regimes and therefore are not usually straightforward to work through all possible operating conditions to assess the safety levels. There is therefore a need to assess the hazard levels from a range of commercial elastography systems and identify any potential risks to human exposure of ultrasound and in particular to consider the hazards posed by stimulus modalities.
1.4 ELASTOGRAPHY PHANTOMS

Ultrasound phantoms are an important aspect of QA/QC in hospitals and industry. They aid in assessing the performance of equipment over time, phantoms mimicking certain anatomical parts of human body are used in training by medical practitioners for example in ultrasound guided biopsy procedure and to test equipment in a manufacturing line. The development of elastography phantoms and phantom materials has been an on-going effort since the early development of elastography imaging technique itself (Hall 1997). Unlike phantoms developed for use in ultrasound diagnostic pulse-echo imaging where properties such as speed of sound and attenuation matched closely to soft tissue have proved sufficient but not in the case of phantoms required for elastography. This is complicated by a wide range of values that exists for Young’s modulus within healthy soft tissue (tendons, ligaments, skin, fibrous tissues, fat, muscles, nerves and blood vessels) i.e. 0.5 – 70 kPa and for cancerous soft tissues it is 20 – 560 kPa (Hoskins 2012). Therefore an anthropomorphic elastography phantom depicting a range of Young’s modulus values within a particular anatomical region and also various regions of the human body under healthy and diseased conditions is desirable. This enables medical practitioners and medical physicists to understand the differences originating from applying different elastography techniques and help them improve the diagnosis for any particular condition. To this end there are two commercial elastography phantoms available from Computerized Imaging Reference Systems, Incorporated (CIRS) and Blue Phantom™. The breast elastography Blue Phantom™ is a training phantom and CIRS also produces training phantoms for breast, prostate and in addition a specific multi-target phantom for sonoelastography which comprises of a background material of Young’s modulus of 25 kPa and four lesions in the range 8 kPa – 80 kPa but there is no mention of uncertainty of the stiffness values.

2 IMAGING TECHNIQUES FOR ELASTOGRAPHY

Generally elasticity imaging methods involves two common elements: the application of a force or stress and the measurement of a mechanical response. The most common types of stress have been external sources such as compressive devices, external vibrators, or acoustic radiation force. The primary (physiological sources motion), particularly cardiac motion, secondary, and fluid flow have been used but to lesser degrees. Review papers from Parker KJ et al 2010, Wells PNT et al 2011, and Sarvazyan A et al 2011 were valuable in compiling various techniques for elastography tabulated in Table 1.
### Table 1 Imaging techniques for elastography

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Technique</th>
<th>Measured Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ultrasound:</strong></td>
<td><strong>Vibration amplitude sonoelastography</strong></td>
<td>Relative image contrast related to local hardness.</td>
</tr>
<tr>
<td>A low-frequency (20–1000 Hz)</td>
<td>vibration is externally applied to excite internal shear waves within tissue of interest. A disruption in the normal vibration patterns will result in a stiff inhomogeneity is present in soft tissue surroundings. Measurement of shear wave speed is estimated using Doppler detection algorithms or ultrasound imaging techniques (Lerner and Parker 1987, 1988). More recently the method has been modified to incorporate two mechanical actuators on the opposite sides of the object and driven at slightly different frequencies. It is estimated that local velocity of the slowly moving interference pattern termed ‘crawling waves’ is proportional to the underlying shear velocity which in turn can be used to estimate the elasticity modulus of the tissue (Wu et al 2004, 2006).</td>
<td></td>
</tr>
<tr>
<td><strong>Ultrasound:</strong></td>
<td><strong>Compression elastography (Static)</strong></td>
<td>Relative strain and modulus images. Estimate elastic nonlinearity.</td>
</tr>
<tr>
<td>Compression elastography utilises a comparison of ultrasound B-scan rf information from tissue before and after a modest compression. Displacements are estimated by comparing the echoes before and after compression by correlation methods or by other techniques. Compression elastography thus produces image of relative strain which are simple to interpret so long as the applied stress is relatively uniform (Ophir et al 1991). Efforts have been made to solve the inverse problem and create quantitative estimates of tissue elasticity from models (Barbone and Gokhale 2004, Fehrenbach 2007) applied to the raw data. The straightforward implementation has helped to disseminate the approach on a number of commercial platforms.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ultrasound:</strong></td>
<td><strong>Acoustic Radiation Force Impulse (ARFI) imaging</strong></td>
<td>Viscoelastic characterisation.</td>
</tr>
<tr>
<td>The impulsive acoustic radiation force generates a localized displacement of the tissue. When the force ceases, the tissue relaxes to its original position. A number of parameters can be used to characterize the response of the tissue, including the peak displacement, the time that it takes to reach peak displacement, and the recovery time. Typically, the peak displacement is displayed in an image (Nightingale et al 2001).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Ultrasound: Transient shear wave imaging**

In this method the focus is on the propagating shear wave that results from a transient excitation of tissue. In radiation force generated shear wave the local propagation from a focus is analysed to estimate the local shear properties (Sarvazyan et al 1998). Another method uses an external actuator to provide a single cycle of low frequency (typically around 50 Hz) vibration and ultrasound methods are used to track the resulting motion. An extension to ARFI imaging is to focus the radiation force in one location and then change the depth of the focal location so that the shear waves created from multiple focal locations constructively interfere to make a conical shear wave (Bercoff et al 2004). This method is called supersonic shear imaging (SSI) because the radiation force focal point moves at a rate that is faster than the speed of the shear wave in the medium. The shear wave created forms a kind of Mach cone and the Mach number of the excitation can be adjusted to make the shear wave directionally oriented. A critical element to the performance of this method is the ability to image the shear wave propagation which requires the use of an ultrafast scanner that is capable of 5000 frames/second or more. The shear wave propagation is measured over a large field of view and the wave equation inversion is used to assess the shear wave speeds and therefore the viscoelastic moduli. More recently a method has been devised which uses spatially modulated ultrasound radiation force (SMURF) (McAleavey and Menon 2007).

**Ultrasound: Vibro-acoustography**

Vibro-acoustography (VA) is a variant of the use of focused ultrasonic radiation force method that uses the acoustic response (acoustic emission) of an object to the harmonic radiation force of ultrasound for imaging and material characterisation (Fatemi and Greenleaf 1998, 1999, 2000 and Greenleaf and Fatemi 2003). The acoustic emission is generated by focusing two ultrasound beams of slightly different frequencies at the same spatial location and vibrating the tissue as a result of ultrasound radiation force exerted on the object at a frequency equal to the difference between the frequencies of the primary ultrasound beams. The two co-focused ultrasound beams of slightly different frequencies intersect at their joint focal point. The radiation force from these two beams has a component at difference frequency or beat frequency (called dynamic ultrasound radiation force), which vibrates the object. The acoustic response of the object to this force is detected by a hydrophone. The co-focus of the ultrasound beams is raster scanned across the object, and the resulting acoustic signal is recorded. An image of the object is formed by modulating the brightness of each image pixel proportional to the amplitude of the acoustic signal from the excitation point of the object.

| Relative strain images with high spatial resolution. |
| MRI: Magnetic Resonance Elastography (MRE) | MRE was developed to measure the propagation of shear waves in tissue by employing a phase-contrast technique in a conventional Magnetic Resonance Imaging (MRI) to measure the displacement patterns of the induces waves (Muthupillai R et al 1995, Kruse S A et al 2000, Manduca A et al 2001). An external actuator induces a harmonic shear wave in the tissue with frequencies in the 50–1000 Hz range. A motion-sensitizing gradient is used to measure the motion in a specified direction at a specific frequency. The use of different motion-sensitizing gradients, polarized in different directions, allows for the acquisition of the full three-dimensional (3D) displacement field. The induced shear wave motion can be tracked for displacement amplitudes as small as 100 nm (Muthupillai R et al 1995). | 3D displacement maps of large organs. |
| OCT: Optical Coherence Elastography (OCE) | Optical Coherence Elastography (OCE) measures tissue displacement using Optical Coherence Tomography (OCT) and benefits from the high resolution of this imaging technology. The increased resolution comes at the expense of limited imaging penetration depth, which is on the order of a few millimetres. OCE is a relatively new elastography technology used to measure biomechanical properties of soft tissue in which a free-space Michelson interferometer and utilising speckle tracking to determine displacements and then calculate strain (Schmitt J et al 1998). Others include Doppler and correlation techniques to track the tissue responses (Wang et al 2006, Kirkpatrick et al 2006, Liang et al 2008, 2010, and Kennedy et al 2009). | Relative strain images. |
| Mechanical Imaging | Mechanical Imaging also Stress Imaging or Tactile Imaging is a branch of Elasticity Imaging which visualizes internal structures of tissue by measuring stress patterns on the surface of tissue compressed by a probe with a pressure sensor array mounted on its contact surface (Sarvazyan A 1998). Temporal and spatial changes in the stress pattern provide information on the tissue internal structures with different elastic properties. Surface stress data recorded by mechanical imaging provide information on the elastic structure of the tissue and allow two-dimensional and three-dimensional reconstruction of tissue structure in terms of elasticity modulus. The data acquired allow the calculation of internal lesions such as size, shape, nodularity, consistency/hardness, and mobility. Mechanical imaging, like nonlinear quasi-static elastography and manual palpation, provides high local deformations of tissue. | Quantitative tissue nonlinear elasticity. |
## 3 COMMERCIAL SYSTEMS

### Table 2 Commercial elastography systems

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Model</th>
<th>Technique / Manufacturer Advertised Clinical Application</th>
<th>FDA Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philips</td>
<td>iU22 xMATRIX</td>
<td>Compression elastography; Relative stiffness map (colour gradient or grey scale) for Breast imaging.</td>
<td>FDA 510(k) approved.</td>
</tr>
<tr>
<td>Siemens</td>
<td>ACUSON Antares and ACUSON S2000 with eSie Touch™</td>
<td>Compression elastography; Breast and small parts imaging</td>
<td>Awaiting FDA 510(k) approval.</td>
</tr>
<tr>
<td>Siemens</td>
<td>ACUSON S2000 with Virtual Touch tissue imaging and Virtual Touch tissue quantification</td>
<td>ARFI (Propriety feature “Tissue Imaging” uses push pulse to compress tissue and detection pulses to track amount of compression and “Tissue Quantification” uses push pulse and tracking beams to estimate shear wave velocity); Abdominal, Breast and small parts imaging</td>
<td>FDA status unavailable. Virtual Touch applications are not commercially available in the USA.</td>
</tr>
<tr>
<td>Esaote</td>
<td>MyLab™ClassC (XStrain™, ElaXto-Elastosonography)</td>
<td>Compressive elastography; Strain-Strain Rate top analysis technique for myocardial function evaluation Elastosonography - non-invasive method to assess tissue elasticity</td>
<td>FDA status unavailable. ElaXto quantification is not for sale in the USA.</td>
</tr>
<tr>
<td>Samsung Medison</td>
<td>Accuvix A30</td>
<td>Compression elastography; ElastoScan™ for breast imaging Thyroid ElastoScan™ for small parts imaging or endocrinology</td>
<td>Accuvix A30 is FDA 510(k) approved.</td>
</tr>
<tr>
<td>Ultrasonix</td>
<td>SonixTouch, SonixSP</td>
<td>Compression elastography; Breast imaging and endocrinology</td>
<td>SonixTouch is FDA 510(k) approved.</td>
</tr>
<tr>
<td>Hitachi Medical Systems</td>
<td>HI VISION Preirus</td>
<td>Compression elastography; Breast imaging</td>
<td>FDA status unavailable.</td>
</tr>
<tr>
<td></td>
<td>HI VISION Avius</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HI VISION 900</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EUB-7500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SuperSonic Imagine</td>
<td>Aixplorer with ShearWave™ Elastography</td>
<td>Supersonic Shear Wave Imaging; Quantitative elasticity map (in kPa) of tissues, used in various organs including the liver, prostate, thyroid and breast</td>
<td>FDA 510(k) approved.</td>
</tr>
<tr>
<td>echosens</td>
<td>FibroScan® 502</td>
<td>Vibration-Controlled Transient Elastography (VCTE™); Liver stiffness</td>
<td>FDA 510(k) approved.</td>
</tr>
<tr>
<td></td>
<td>FibroScan® 502 Touch</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fibroscan® 402</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toshiba</td>
<td>Aplio Series with Real-time elastography</td>
<td>Compression elastography; Abdominal, Breast and small parts imaging</td>
<td>FDA status unavailable.</td>
</tr>
<tr>
<td>GE</td>
<td>LOGIQ E9</td>
<td>Compression elastography; Breast imaging</td>
<td>FDA status unavailable.</td>
</tr>
</tbody>
</table>
4 MEASUREMENT METHODS

Independent measurement methods to validate the output conditions generated by commercial elastography systems for example on a phantom material will help in identifying the performance differences across various elastography systems, assessment of biological hazard and enable clinicians to arrive at better diagnosis of the tissue pathology. From the literature review two methods which are independent to each other (and not based on ultrasound motion tracking) have been identified i.e. rheological and optical techniques to characterise the viscoelastic properties of tissue like phantoms.

4.1 RHEOLOGICAL TECHNIQUE

Rheology by definition is the science of deformation and flow. It is used to understand how the stress in a material or force applied to a material is related to deformation (change of shape) of the material. The dynamic mechanical properties of phantom materials can be characterised by what is known as rotational/shear rheometer. The apparatus consists of two concentric, rigid, circular parallel plates between which the specimen is placed. One of these plates oscillates at a constant angular frequency while the other remains at rest. An angular displacement and a torque measuring device record the strain and the stress during the test. Test procedures involve subjecting the specimen to either a sinusoidal torque (controlled-stress mode) or sinusoidal angular displacement (controlled strain-mode). In the controlled-stress mode the resultant displacement and the phase shift between torque and displacement are registered. In the controlled-strain mode the resultant torque and the phase shift between torque and displacement are registered. Physical quantitates such as complex shear modulus as a function of frequency, temperature, strain and time can be measured. Since Poisson’s ratio is approximately 0.5 for incompressible materials Young’s modulus ($E$) is equal to $3\mu$.

An IEC agar Tissue Mimicking Material (TMM) (IEC 2001) was tested for its viscoelastic properties using an AR-G2 rotational rheometer. The IEC TMM is widely used as a phantom material for research in ultrasound pulse-echo imaging but its viscoelastic properties haven’t been investigated. Therefore it was identified as a suitable candidate to get some first pass measurements using rheological technique. Test specimens required in the form of thin cylindrical discs (2 mm to 3 mm) were prepared and employed in the AR-G2 rotational rheometer. The specimen was subjected to strain and frequency sweep and the results are graphically depicted in Figure 2 through to Figure 4. These characteristic results are in-line with those reported by other authors (Hall 1997, Pavan 2010) who employed agar and gelatine based TMM as an elastography phantom using rheological technique. The stress-strain curve (Fig.2) exhibits similar non-linear behaviour seen in soft tissue, the TMM behaves as an elastic material (Fig.3) for applied strains of up to 1% and is plastic thereafter and finally the frequency sweep (Fig.4) suggest that the material is non-dispersive for at least within a narrow range of frequencies investigated.

![Fig.2. Stress-strain curve for IEC agar TMM.](image)
OPTICAL TECHNIQUES

There exist a number of optical techniques to quantify tissue stiffness for imaging underlying tissue pathology which is already covered in Section 2. The optical techniques mentioned in this section are mostly laboratory based techniques and fall into two main categories i.e. displacement sensing utilising laser Doppler vibrometry (Chen 2004) and those based on image analysis (Cheng 2012, Bouchard 2009, Li 2011).

In the method utilising laser Doppler vibrometry (Chen 2004) vibrations were introduced in a gelatine phantom loaded with micro mirror using a 3 MHz focused ultrasound transducer. The amplitude of the drive signal was modulated to introduce harmonic radiation force within the medium. The frequency of the harmonic radiation was swept from 100 Hz to 2 kHz. The vibration of the micro mirror was detected by the laser vibrometer. The phase of the shear waves was measured with a lock-in amplifier, whose reference is provided by the sinusoidal signal that modulates the amplitude of ultrasound. The measurements were performed at several distances away from the transducer focus. From any two measurement locations the phase difference and the distance between measurements locations was used to calculate the shear wave speed for each modulating frequency. The shear wave dispersion curve is then used to derive the complex shear wave modulus.

The image analysis methods are either based on tracking microspheres (Bouchard 2009) or speckle contrast analysis (Li 2011, Cheng 2012) from the images acquired using a high speed CCD camera. Time-to-peak (TTP) algorithms are employed for time-of-flight estimates by tracking image kernels for various distances away from the transducer focus which yielded the shear wave speed. Although
optical techniques are able to provide very high spatial resolution they suffer from penetration depth for other than clear homogenous phantoms.

5 CONCLUSIONS

The literature review has enabled us to identify key areas for further development such as elastography phantoms, measurement of exposure parameters and independent measurement methods for viscoelastic characterisation of phantoms. In order to objectively assess different elastography methods, standardised tissue mimicking materials with well characterised viscoelastic properties of those observed clinically need to be developed. Rheological techniques have the potential to be adopted as a standardised method for viscoelastic characterisation of elastography phantoms but a critical analysis of the systematic effects still remains to be investigated. Some newer techniques based on laser Doppler and optical image analysis also has the potential to be advanced as a measurement standard but it is restricted to clear homogenous medium. Transient elastography employing ARFI requires very high frame rate to track the propagating shear waves and this significantly increases the potential for thermal damage. International standards currently do not address methods to quantify the exposure parameters from transient elastography systems which perhaps are reflected by many commercial systems currently awaiting approval-seeking approval from FDA for marketing in the United States and elsewhere. There is a greater emphasis for quantitative imaging among clinicians and therefore quantitative methods based on transient elastography will gain significant popularity in the future. This emphasis the need to standardise the phantom materials and develop validated dynamic measurement methods to ensure the performance of these new diagnostic devices are fully characterised so that ultimately clinicians are able to make improved diagnosis of the underlying disease or pathology.

6 RECOMMENDATIONS

Following recommendations are made in regards with establishing a measurement infrastructure to advance metrology and traceability in the field of elastography, based on the work conducted in this report:


- Develop independent measurement methods (for e.g. Opto-acoustics) based on shear wave propagation and detection for further validation of the rheological technique.

- Identify, develop and characterise materials suitable for elastography phantoms possessing stiffness values (Young’s modulus) typical of those found in biological media under healthy and diseased states and compile a comprehensive NPL reference database.

- Develop universal anthropomorphic elastography phantoms applicable for a range of available commercial elastography systems to assist in understanding performance differences across various systems.

- Conduct a national/international intercomparison exercise using a well characterised elastography phantom to assess the performance of commercial elastography systems.

- Publish good practice guides for clinicians in collaboration with Institute of Physics and Engineering in Medicine and British Medical Ultrasound Society.

- Encourage other NMI’s to participate in collaborative projects such as IEC to standardise reporting methods of dynamic mechanical properties.
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