ultrasonic gel). This difficulty suggests that acoustic radiation force impulse (ARFI) elastography would be a more appropriate method to acquire DTI elastograms. ARFI elastography works on the same principles as quasi-static elastography with the exception that tissue deformation is caused by localized large-amplitude acoustic waves generated by the transducer such that human factors play a far less substantial role in image acquisition.

3.4 Conclusion

This work represents a numerical characterization of the use of quasi-static ultrasound elastography for the early detection of deep tissue injuries (DTI). There is a real clinical need for an objective tool that is capable of detecting the formation and progression of DTI in human subjects as these wounds are generally not visible from the surface of the skin until they have broken through and already caused substantial damage.

Through this numerical characterization, quasi-static ultrasound elastography was found to be an effective tool for detecting and monitoring DTI in theoretical simulations. Overall, detection sensitivity was less than expected. Small lesions (with diameters $\leq 1.0\,\mathrm{cm}$) were more difficult to differentiate due to the low lesion detection sensitivity. While lesion depth, altitude above the underlying bone, and probing frequency did not have significant effect on the lesion detection sensitivity, it was found that applying high levels of compressive strain ($10\,\%$) introduced severe error for both very unstiff and very stiff lesions, thus it is recommended that diagnosticians only apply moderate ($\leq 5\,\%$) compressive strain when interrogating potential lesions. Larger strains may alternately be induced by slowly palpating the tissue with very

minor strains frame-by-frame and cumulating the displacement fields across these smaller palpations. Care must be used when palpating the tissue, lest "vigorous" palpations cause harm to the already sensitive injury. In the more complicated model of co-located lesions, while the separation distance between adjacent lesions did not affect the detection sensitivity, the placing of adjacent lesions generated "phantom" lesion regions with altered strain that may appear to be diseased tissue when they are in fact healthy. In a model lesion with gradual blurred boundaries, the effect of blur radius only affected the detection sensitivity and ability to differentiate unstiff lesions. Specifically, unstiff lesions with large blur radii became nearly impossible to differentiate as these lesions all showed a measured lesion stiffness ratio of approximately 1 which would show up as regular, healthy tissue. In the case of numerous clustered small lesions, both decreased lesion density and decreased individual lesion size caused a decrease in lesion detection sensitivity, likely due to the averaging effect of healthy tissue and diseased tissue in near proximity. Finally, in the Visible Human-MRI acquired lesion model, lesions with widths $\leq 1.0\,\text{cm}$ are nearly impossible to differentiate as they are hidden by the strain field generated by the bony prominence. Lesion depth did not have an effect on the detection sensitivity, though deeper lesions (lesions which were closer to the bony prominence) had overestimated stiffnesses with respect to their more superficial counterparts.

Although the studies presented here resulted in less-than-ideal detection sensitivities, the technique was still able to pick out lesions from the surrounding unstiff (and hard) tissue. Work done by Solis et al. [67] has shown that untreated DTI are multiple centimetres in size, while work done by Gefen et al. [5] has shown that deep tissue injuries exhibit 1.8-fold to 3.3-fold mechanical

stiffening. The work presented here has shown that quasi-static ultrasound elastography is adequate at detecting deep tissue injury lesions in these ranges of parameters and will thus be adequate to detect and monitor progress DTI. However, without further real-world experimentation on the exact nature of newly-forming DTI, the detection sensitivity required to detect newly-forming DTI is indeterminate.

A subset of the results found through simulation were compared with similar experiments done using a tissue mimicking phantom model. The experimental results using the phantom model generally agreed with those found from simulation cases. It was also noted that the manual skin indentation technique involved with quasi-static ultrasound elastography proved to be difficult to produce reliable images. This difficulty suggests that an alternate method of performing ultrasound elastography may be preferable to quasi-static ultrasound elastography with manual indentation. Acoustic radiation force impulse (ARFI) elastography may be a more appropriate method to acquire DTI elastograms as although ARFI elastography works on the same principles as quasi-static elastography, the difference lays in the fact that tissue deformation is caused by localized large-amplitude acoustic waves generated by the transducer. This means that human factors play a far less substantial role in image acquisition and would likely improve repeatability and inter-operator reliability. Nevertheless, the work done here to characterize the use of quasi-static ultrasound elastography is an important step along the path of generating a useful clinical tool for detecting formative and monitoring progressive deep tissue injuries.

Chapter 4

Numerical Characterization of Acoustic Radiation Force Impulse Imaging

4.1 Introduction

Acoustic radiation force impulse imaging presents a chief benefit over quasi-static ultrasound elastography in that since the external deformation force is applied by the transducer itself rather than through manual indentation of the transducer by the diagnostician, the inter-operator reliability may be greatly increased. The net effect of this is an expected decrease in the required amount of training of diagnosticians as well as an expected increase in the sensitivity and specificity of early deep tissue injury detection.

4.2 Method

In order to numerically characterize acoustic radiation force impulse imaging for the early detection of deep tissue injuries, a combinatory model of acoustic radiation force simulations and time-domain finite-element models of tissue deformation were used. Acoustic radiation force distributions were calculated using a k-space pseudo-spectral model of ultrasonic acoustics which simulated the acoustic intensities and subsequent radiation force developed by an ultrasonic transducer applying deep body loads to soft tissue. These forces were then combined with a temporal finite-element model of tissue deformation to model the response of the tissue to the body force impulses generated by the transducer. The use of these models allowed extensive simulation and parameter sensitivity analysis in order to numerically characterize the use of acoustic radiation force impulse imaging for detecting deep tissue injuries.

4.2.1 K-Space Pseudo-spectral Model of Acoustic Fields

In order to simulate the body loads generated within deep tissue by a continuous ultrasound beam, a k-space pseudo-spectral model of acoustic field intensities was generated. The body load fields that were generated as a result of this model were fed into a temporal soft tissue deformation model to investigate the dynamic response of tissue to ARFI loads.

The governing equations used for the k-space pseudo-spectral model were the set of coupled first-order partial differential equations 4.1a – 4.1c. These equations are the first-order equivalents of the wave equation given in equation 4.2 taking into account acoustic absorption, tissue heterogeneities, and acoustic wave non-linearities [134]. Equations 4.1a, 4.1b, and 4.1c represent

the momentum conservation, mass conservation, and pressure-density relation terms respectively.

$$\frac{\partial \vec{v}}{\partial t} = -\frac{1}{\rho_0}\nabla p \tag{4.1a}$$

$$\frac{\partial p}{\partial t} = -\left(2\rho + \rho_0\right)\nabla \cdot \vec{v} - \vec{v} \cdot \nabla \rho_0 \tag{4.1b}$$

$$p = c_0^2\left(\rho + \vec{u} \cdot \nabla \rho_0 + \frac{B}{2A}\frac{\rho^2}{\rho_0} - \mathbf{L}\rho\right) \tag{4.1c}$$

In equations 4.1, $\vec{v}$ is the acoustic particle velocity, p is the acoustic pressure, ρ is the acoustic density, ρ_0 is the equilibrium density, c_0 is the acoustic sound speed, $\vec{u}$ is the acoustic particle displacement, and $^B/_A$ is a nonlinearity parameter which models alterations to the sound speed [135].

$$\nabla^2 p - \frac{1}{c_0^2}\frac{\partial^2 p}{\partial t^2} = 0 \tag{4.2}$$

The $\mathbf{L}$ operator used in equation 4.1c accounts for acoustic absorption and dispersion which follows a frequency power law and is defined as per equations 4.3a – 4.3c where α_0 is the power law prefactor and y is the power law exponent of the tissue. τ and η represent absorption and dispersion proportionality coefficients respectively.

$$\mathbf{L} = \tau\frac{\partial}{\partial t}\left(-\nabla^2\right)^{\frac{y}{2}-1} + \eta\left(-\nabla^2\right)^{\frac{y+1}{2}-1} \tag{4.3a}$$

$$\tau = -2\alpha_0 c_0^{y-1} \tag{4.3b}$$

$$\eta = 2\alpha_0 c_0^y \tan\left(\frac{\pi y}{2}\right) \tag{4.3c}$$

In order to integrate pressure sources in equations 4.1a – 4.1c, equation 4.1b is modified to include a mass source term, S_M which counts as a pressure source term through changing density to form equation 4.4.

$$\frac{\partial p}{\partial t} = -\left(2\rho + \rho_0\right) \nabla \cdot \vec{v} - \vec{v} \cdot \nabla \rho_0 + S_M \tag{4.4}$$

The k-Wave MATLAB® toolbox version 1.0 was used to solve for the time-variant intensities resulting from simulated acoustic radiation force impulses applied to heterogeneous soft tissue using equations 4.1a, 4.4, and 4.1c with the acoustic properties listed in Table 4.1. Sample source code for performing these simulations using the k-Wave toolbox is given in listing B.4 in Appendix B.

Table 4.1: K-Space pseudo-spectral model parameters

Property	Symbol	Value	Units
Nonlinearity parameter	B/A	8	–
Power law prefactor	α_0	0.7	$\mathrm{Np\,(rad/s)^{-y}\,m^{-1}}$
Power law exponent	y	0.95	–
Density	ρ_0	1,060	$\mathrm{kg\,m^{-3}}$

4.2.2 Derivation of Acoustic Radiation Force

Acoustic radiation force arises as the result of absorption of linear momentum within tissue as acoustic waves travel though it with the requirement that the tissue is a viscoelastic medium—no energy would be absorbed in a purely linear elastic model. Further, at the super-MHz frequencies involved in ultrasound interrogation, tissue may be considered a viscous fluid [113].

Using a perturbative expansion of the general equation of linear momentum given in equation 4.5, acoustic radiation force can be expressed as per equations

4.6 [136]. In equations 4.6, $\langle\rangle$ represents the time-average operator, $\vec{v_1}$ and $\vec{v_2}$ are the first and second order terms in the perturbative expansion of particle velocity, p_2 is the second order pressure term in the perturbative expansion, while $\vec{F}$ represents the acoustic radiation force developed in the tissue.

$$\sigma_{ij,j} + \rho b_i = \rho f_i \tag{4.5}$$

$$\vec{F} = \nabla p_2 - \mu_{tissue} \nabla^2 \vec{v_2} \tag{4.6a}$$

$$\vec{F} = \rho \langle \vec{v_1} \nabla \cdot \vec{v_1} + \vec{v_1} \nabla \vec{v_1} \rangle \tag{4.6b}$$

For a plane wave, equation 4.6b can be reduced to equation 4.7. Further, substituting the generalized wave particle velocity solution given in equation 4.8 in equation 4.7, the magnitude of acoustic radiation force may be calculated as per equation 4.9.

$$\vec{F} = 2\rho \langle \vec{v} \vec{v}_{,x} \rangle \tag{4.7}$$

$$\vec{v} = i\omega A e^{-\alpha x + i(\omega t - kx)} \hat{x} \tag{4.8}$$

$$\left| \vec{F} \right| = A^2 e^{-2\alpha x} \rho \alpha \tag{4.9}$$

Further using the acoustic field intensity, the acoustic radiation force may be calculated as per equation 4.10 where α is the absorption coefficient of the tissue in $\mathrm{Np\,m^{-1}}$, I is the temporal average acoustic intensity in $\mathrm{W\,m^{-2}}$, and

c is the longitudinal speed of sound in the tissue in $\mathrm{m\,s^{-1}}$ [113].

$$\left|\vec{F}\right| = \frac{2\alpha I}{c} \tag{4.10}$$

Once acoustic radiation force body loads were calculated as per equation 4.10, they were used as initial conditions to the temporal finite-element model of soft tissue deformation described in Section 4.2.3.

4.2.3 Temporal Finite-Element Model of Soft Tissue Deformation

In response to the relatively short duration ("impulse") acoustic radiation force body load applied to tissue in ARFI imaging, the interrogated tissue will exhibit a dynamic response—namely that tissue deformation will propagate outwards as the absorbed acoustic energy diffuses through the soft tissue.

In order to simulate the dynamic tissue deformation generated by the acoustic impulse force, a generalized Maxwell viscoelastic model of tissue deformation was used [137]. The simulated tissue properties are summarized in Tables 4.2 and 4.3.

Table 4.2: ARFI model tissue properties

Property	Symbol	Value	Units
Bulk Modulus	K	515.7	kPa
Shear Modulus	μ_{tissue}	1.0	kPa
Density	ρ	1,060	$\mathrm{kg\,m^{-3}}$

The time-dependent displacement fields were calculated according to equation 4.11 where σ is the Cauchy stress tensor, $\vec{F}$ are the applied body forces, and $\vec{u}$ is the particle displacement, and ρ is the density.

Table 4.3: ARFI Maxwell model tissue properties

Branch	Shear Modulus (Pa)	Relaxation Time (s)
1	791.0	2
2	66.5	40
3	0.6	80

$$\rho \frac{\partial^2 \vec{u}}{\partial t^2} - \nabla \cdot \sigma = \vec{F} \tag{4.11}$$

In order to include viscoelastic effects through a generalized Maxwell model of soft tissue, equation 4.12 was used where σ_0 is the initial stress distribution in the tissue, C is the 4^{th} order elasticity tensor, ε is the strain, G_m and τ_m are the shear modulus and relaxation time of the m^{th} branch of the Maxwell model respectively, and γ_m is an additional auxiliary degree of freedom used to represent the extension of the abstract springs in the Maxwell model.

$$\sigma - \sigma_0 = C : \varepsilon + \sum_m 2 G_m \tau_m \dot{\gamma}_m \tag{4.12}$$

In the simulations, the boundary equations 4.13 were used to apply a fixed boundary condition to the both the bottom (deep) and top (superficial) boundaries of the model in the axial direction at both boundaries and in the lateral direction at the deep boundary. All other boundaries of the model were free to translate in all dimensions. A visual representation of these boundary conditions is given in Fig. 4.1. The acoustic radiation force was applied as a body load to the tissue in the model with the distribution calculated by the k-space pseudo-spectral model and resultant body forces described in Sections 4.2.1 and 4.2.2. In order to prevent reflections from the model boundaries that