tissue injuries including: the distribution of acoustic radiation force generated by transducers; the generalized tissue response to these acoustic radiation forces; and the use of ARFI imaging to distinguish both early and formative deep tissue injuries from surrounding healthy tissue. Although the principles of operation for ARFI imaging and quasi-static ultrasound elastography are the same—detecting the relative magnitude of deformation in regions of tissue in response to externally applied forces—ARFI imaging presents a key advantage over quasi-static ultrasound elastography in that it allows much greater inter-operator reliability and repeatability. ARFI imaging generates deformation within tissue automatically and without dependence on the operator which is key to developing a successful diagnostic modality.

A key parameter relating to the ability of acoustic radiation force impulses to generate adequate body loads in tissue is the depth at which the radiation force is focused at—increasing depth was found to induce the greatest reduction in the magnitude of the radiation forces and the subsequent magnitude of tissue deformation. This is of concern, as once the magnitude of tissue deformation becomes small enough these deformations will no longer be able to be tracked using conventional ultrasound beams. In order to counteract this, lower frequencies and greater transmit pressures may be used, however care must be taken to ensure the safety of patients undergoing such techniques as the energy resulting from acoustic radiation has the potential to result in tissue damage.

The results shown in Section 4.3.3 show that ARFI imaging is a suitable technique for differentiating both stiff and unstiff lesions from surrounding healthy tissue which may be indicative of deep tissue injury formation and progression. Overall, the detection sensitivity of ARFI imaging is less than

ideal with the stiffness of stiff lesions consistently underestimated and the stiffness of unstiff lesions consistently overestimated. ARFI imaging was found to not be dependent on lesion radius above radii of approximately 2.5 mm and aside from issues with deformation magnitude, the depth of the lesions has no appreciable effect on their detection ability. The amount of lesion blur also did not affect the detection sensitivity, which is advantageous for detecting lesions without clearly defined boundaries. Regions of clustered deep tissue injury lesions were detectable however decreasing the ratio of diseased to healthy tissue area in the lesion resulted in lower detection sensitivities. Lesions were still detectable in the complicated model of MRI-acquired geometry embedded within soft tissue layout extracted from the Visible Human project, although to a slightly lesser extent than uncomplicated hard-boundaried spherical lesions. The overall technique was experimentally validated, however it was found that the simulated lesions underestimated the lesion stiffness compared to their parametrically-identical experimental counterparts.

Future work involving ARFI imaging should investigate the disparity between the experimentally-acquired lesion stiffness ratios and the simulated lesion stiffness ratios in order to increase the validity of the models. In order to truly advance the technology toward its clinical adoption, experimental studies in animals and humans with known deep tissue injuries must be carried out to determine the applicability of ARFI imaging in a real-world setting.

Chapter 5

Numerical Characterization of Shear Wave Speed Quantification

5.1 Introduction

Shear wave speed quantification offers the most desirable method of detecting early deep tissues injuries as it takes the transducer-generated external deformation force that is the chief benefit of ARFI imaging and combines it with a quantitative measure of tissue elasticity rather than the qualitative measures used in both quasi-static elastography and ARFI imaging. Specifically, monitoring the speed of shear waves that are generated in the tissue as a response to a localized acoustic radiation force allows the calculation of tissue stiffness which may again be used as an analogue of tissue health. Further, since the technique is quantitative in nature, tissue stiffness may be accurately tracked over time, enabling physicians to appropriately monitor the progression and

treatment of a given deep tissue injury on a per-patient basis.

5.2 Method

In order to investigate the sensitivity and applicability of shear wave speed quantification for the early detection of deep tissue injuries, a combination of k-space pseudo-spectral models of acoustic wave propagation and time-domain finite-element models of tissue deformation were employed. The theory and procedure behind both the generalized acoustic simulations using k-space pseudo-spectral models and time-dependent solid mechanics finite-element models used here were presented in Chapter 4. As an alternative to monitoring the dynamic response of tissue at the focal point as in ARFI imaging, shear wave speed quantification tracks the velocity of shear waves which radiate laterally outward from the focal point of an ARFI load. If the focal point is positioned such that the generated shear waves propagate through a lesionous region and the speed of the generated shear wave is monitored, the stiffness of that region may be calculated.

5.2.1 Shear Wave Speed

The foundation of shear wave speed quantification with regards to detecting lesionous regions lies in the quantifiable relationship between shear wave speed and tissue stiffness. This relationship is derived here, assuming a linear elastic, isotropic material. Soft tissue is generally considered a viscoelastic material and as such modifications to the linear elastic wave speed are taken into account.

Equation 5.1 represents the constitutive equation of a linear elastic material

where the strain tensor is defined as per equation 5.2 such that equation 5.3 holds true.

$$\sigma_{ij} = \lambda_{tissue}\delta_{ij}\varepsilon_{kk} + 2\mu\varepsilon_{ij} \tag{5.1}$$

$$\varepsilon_{ij} = \frac{1}{2}\left(u_{i,j} + u_{j,i}\right) \tag{5.2}$$

$$\sigma_{ij} = \lambda_{tissue}\varepsilon_{ii}\delta_{ij} + \mu\left(u_{i,j} + u_{j,i}\right) \tag{5.3}$$

Neglecting time-invariant body loads, the balance of linear momentum is given for a linear elastic continuum is given in equation 5.4.

$$\sigma_{ij,j} = \rho\ddot{u}_i \tag{5.4}$$

Substituting equation 5.3 into equation 5.4 yields equation 5.5 which may be rearranged into equation 5.6 by noting that $\varepsilon_{ii,j} = u_{j,ij}$.

$$\lambda_{tissue}\varepsilon_{ii,j} + \mu\left(u_{i,jj} + u_{j,ij}\right) = \rho\ddot{u}_i \tag{5.5}$$

$$\rho\ddot{u}_i = \left(\lambda_{tissue} + \mu\right)u_{j,ji} + \mu u_{i,jj} \tag{5.6}$$

Utilizing the Helmholtz decomposition of the particle displacement given in equation 5.7, equation 5.6 becomes equation 5.8.

$$u_i = \partial_i\phi + \varepsilon_{ijk}\partial_j\psi_k \tag{5.7}$$

$$\nabla \left[\left(\lambda_{tissue} + 2\mu \right) \nabla^2 \phi - \rho \ddot{\phi} \right] + \nabla \times \left[\mu \nabla^2 \vec{\psi} - \rho \ddot{\vec{\psi}} \right] = 0 \tag{5.8}$$

Examining the transverse propagation component of equation 5.8 in one direction yields the familiar shear wave equation given in equation 5.9 such that the shear wave speed is given by equation 5.10.

$$0 = \frac{\partial^2 \vec{\psi}}{\partial x^2} - \frac{\rho}{\mu} \frac{\partial^2 \vec{\psi}}{dt^2} \tag{5.9}$$

$$c_T = \sqrt{\frac{\mu}{\rho}} \tag{5.10}$$

While the above equation holds for linear elastic materials, soft tissues in the human body are generally considered viscoelastic [138], [139]. In the case of viscoelastic tissues, complex Lamé parameters must be used, such that the shear wave speed is represented by equation 5.11 [123]. Note that viscoelastic shear wave speeds of viscoelastic tissues are generally acquired through empirical measurements rather than any sort of mathematical derivation [140], [141].

$$c_T = \sqrt{\frac{\mu^*}{\rho}} \tag{5.11}$$

5.2.2 Model Set Up

In order to study the feasibility of using shear wave speed quantification to detect and monitor deep tissue injuries, a collection of deep tissue injury models were investigated including: spherical lesions with hard and unstiff boundaries, clusters of small lesions that make up a larger lesionous region, and a

lesion with MRI-acquired geometry [67] embedded in geometry obtained from a Visible Human slice [126]. Each model investigated numerous parameters relating to the detection of lesions including ARFI focal depth, ARFI interrogation frequency, lesion size, distance of the focal point from the lesion (lesion offset), lesion blur radius, clustered lesion density, the size of individual lesions in the clustered lesion model, and the size and altitude of the lesion in the Visible Human model. The range of parameters investigated for each model are summarized in Table 5.1.

Figs. 5.1 portray the schematics of the lesion models investigated. Note that shear wave speed quantification typically applies the acoustic radiation force impulse to a location of tissue adjacent to the desired region such that the shear waves are fully developed by the time they reach the investigated region.

Table 5.1: Range of values of investigated parameters

Parameter	Symbol	Values	Units
Lesion depth	d	1, 2, 3, 4, 5, 6, 7, 8, 9	cm
Lesion diameter	$\varnothing S$	0.5, 1.0, 2.0, 2.5	cm
Lesion offset	d_{off}	0.00, 1.25, 2.50, 3.75	cm
Lesion stiffness ratio	E_{rel}	0.32, 0.56, 1.80, 3.20	
Blurred lesion blur radius	b_r	1.0, 2.5, 5.0, 7.5	mm
Clustered lesion density	b_ρ	10, 20, 30, 40	cm^{-2}
Clustered lesion radius	r_{bl}	0.5, 1.0, 1.5	mm
Visible human lesion width	$\varnothing L$	0.5, 1.0, 2.0, 2.5	cm

In all the shear wave speed quantification models, the acoustic radiation force and time-domain finite-element models of tissue deformation were the same as were used in the ARFI imaging simulations in Chapter 4 and described in Sections 4.2.1 – 4.2.3. The difference with the shear wave speed quantification presented here and the ARFI imaging presented in Chapter 4