Ultrasonic Methods to Measure Shear Wave Velocity and Absorption for Tissue Viscoelasticity Characterization

by

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Abstract

Characterization of the viscoelasticity for soft tissues is useful for medical diagnosis. Various ultrasound and magnetic resonance-based techniques have been developed over the past few decades. With ultrasound methods, generating and tracing a shear wave (SW) propagating within the soft tissue was one of the promising approaches to measure the SW velocity and absorption, which were the key parameters to derive the tissue viscoelasticity. When the SW method was employed, several problems, such as undesired SW reflection, motion artifact and SW diffraction could occur in practical experimental configuration, which caused on SW measurements. Advanced ultrasound imaging system with high frame rate may be able to overcome these problems, yet the configuration of such system was complex and thus expensive. In this thesis, methods to solve the above-mentioned problems were proposed by using conventional ultrasound imaging system with a relatively less complex design and low frame rate. In the proposed methods, the undesired SW reflections were able to be distinguished and removed from the observed SW in the spatial domain using the scanning time delay in the B-mode measurement of conventional ultrasound system. The causes of the motion artifact were examined through the temporal domain analysis, and temporal frequency filter was used to reduce the undesired motions. In addition, the measurement configuration to minimize the diffraction effect on the SW measurement was investigated. Furthermore, a numerical method to compensate the diffraction effect was developed for the absorption measurement. The effectiveness of these proposed methods was verified by numerical

simulations as well as by experiments using soft-tissue mimicking phantom specimens. The proposed methods were finally applied for *in-vivo* measurements and successfully demonstrate the stiffness difference of an upper arm muscle with and without muscle contraction.

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List of Acronyms

Acronyms (Sort by Alphabet)	Definition
ARF	Acoustic radiation force
ARFI	Acoustic radiation force imaging
BPF	Bandpass filter
$BPF_{spatial}$	Spatial bandpass filter
$BPF_{temporal}$	Temporal bandpass filter
CUSE	Comb-push ultrasound shear elastography
DAQ	Data acquisition
DC	Direct current
FOV	Field of view
FOV _x	Field of view in depth
FOV _z	Field of view in length
LPF	Low pass filter
LW	Longitudinal wave
MRI	Magnetic resonance imaging
PRF	Pulse repetition frequency
rf	Radio frequency
ROI	Region of interest
SDUV	Shear wave dispersion ultrasound vibrometry
SMURF	Spatially modulated ultrasound radiation force

SNR	Signal-to-noise ratio
SSI	Supersonic shear imaging
STD	Standard deviation
SW	Shear wave
SWEI	Shear wave elasticity imaging
<i>WINDOW</i>	Window function
WGN	White Gaussian noise
2D	Two dimensional

List of Symbols

Symbols (Sort by Alphabet)	Definition
a	Characteristic size of rectangular SW source in x -direction (depth)
A_B	Amplitude of backward SW
A_F	Amplitude of forward SW
A_I	Amplitude of induced SW
A_{rf}	Amplitude of the received rf signal
A_S	Initial SW amplitude at the SW source
ATT	Attenuation due to the diffraction effect
b	Characteristic size of rectangular SW source in y -direction (width)
c_0	Ultrasound speed
E	Young's modulus
f_{FR}	Frame rate of imaging system
f_{MA}	Frequency of motion artifact
$f_{measured}$	Aliased SW frequency
f_S	SW frequency
G	Shear elasticity (shear modulus)
$\mathcal{H}_z\{\}$	Hilbert transform
I	In-phase signal
$\mathbf{Im}\{\}$	Imaginary component of a complex signal

j	Imaginary unit
K	Bulk modulus
k_{Sa}	k_{Sa} value, a product of SW wavelength and the characteristic size of SW source
k_S	SW wavenumber
k_B	Wavenumber of backward SW
k_F	Wavenumber of forward SW
n	Integer multiple of f_{FR}
N_F	Fresnel distance
Q	Quadrature signal
r_I	Distance from an arbitrary point on SW source to an arbitrary point on SW reflector
$Re\{\}$	Real component of a complex signal
S	Normalized distance in length
S_{ref}	Complex reference signal
S_{rf}	Received rf signal
S_T	Transmitted ultrasound signal
t	Time
Δt	Temporal sampling interval
u_i	Scatterer displacement along direction i (x , y , or z)
v	Velocity of scatterer displacement
v_L	LW velocity
v_{scan}	B-mode scanning speed
v_S	SW velocity
Δv_{S_High}	v_S change at higher v_S value

Δv_{S_Low}	v_S change at lower v_S value
V	SW displacement
V_B	Backward SW displacement
V_F	Forward SW displacement
V_I	Induced SW
V_{MA}	Displacement of undesired motion
V%	Volume percent
W%	Weight percent
x	Depth
y	Width/thickness
Y	In-phase quadrature signal
z	Length
Δz	Spatial sampling interval
α_S	SW absorption
β	Conversion index from displacement to phase
Γ_{SS}	Amplitude of reflected SW from incident SW in mode conversion
ε	Strain
η	Shear Viscosity
θ	Angle between the direction of ultrasound transmission and scatterer displacement
θ_L	Reflection angle of LW
θ_S	Incident angle of SW
λ_S	SW wavelength
μ	Shear viscoelasticity

ξ_B	Normalized spatial frequency of backward SW
ξ_F	Normalized spatial frequency of forward SW
$\Delta\xi_F$	Spatial frequency change
ρ	Density
σ	Stress
φ	Angle between r_l and z
φ_B	Initial phase of the backward SW
φ_F	Initial phase of the forward SW
φ_I	Initial phase of the induced SW
φ_{rf}	Phase component of the rf signal
φ_V	Change of the phase of the rf signal
φ_S	Phase of velocity of the scatterer displacement
φ_0	Initial phase of the rf signal
ω_d	Doppler shift frequency
ω_i	Instantaneous angular frequency of received rf signal
ω_S	SW angular frequency
ω_0	Ultrasound angular frequency
∇^2	Laplace operator

Chapter 1

Introduction

This chapter is the introduction of this thesis. Motivation and the overview of the research are presented, followed by potential problems and the proposed solutions.

1.1. Overview

Characterization of the viscoelasticity for soft tissues is useful for medical diagnosis but considered a challenging topic which has been widely studied for decades. Two shear properties: shear elasticity and viscosity, are often referred to represent the tissue viscoelastic properties. Shear elasticity represents the stiffness of the material. In medical diagnosis, the determination of elasticity is a popular topic since it can be used to evaluate the soft tissue health according to the stiffness difference between normal and abnormal tissues [1]. Viscosity represents the resistance to the deformation of the material by shear stress. Although in most tissues, shear elasticity may be a primary parameter to characterise the tissue mechanical property and viscosity was neglected, many studies still suggested that not only the elasticity but also the viscosity was useful and could be an interesting index of tissue health as well [2], [3].

One way to determine the tissue viscoelastic properties was based on the analysis of stress-strain behavior of a soft tissue specimen, which was commonly called a quasistatic measurement [1], [4]. Under compressive forces, soft tissue with different

elasticity will exhibit different deformation, *i.e.* the greater strain indicates the smaller stiffness and vice versa, and the viscosity can be estimated by measuring the relaxation time of the specimen from the compressive force [5]. Another way to determine the viscoelasticity was based on tracing and analyzing a shear wave (SW) propagation inside a specimen, which was commonly called a dynamic measurement or SW measurement [4]. With such type of measurement, the shear elasticity can be estimated by measuring the velocity of SW (v_s) and the density of the specimen. In addition, the viscosity can be determined by measuring both the v_s and SW absorption coefficient (α_s) at a known SW frequency (f_s), or from analyzing the v_s dispersion [6]. Greater α_s or stronger v_s dispersion indicates a greater amount of viscosity, and vice versa.

In practice, it may be difficult to precisely measure an external stress during *in-vivo* experiments, thus the quasistatic measurement usually only provides a relative contrast between the stiffer and softer materials based on their strain difference under the same amount of external stress. Besides, it could also be difficult to make the tissues or organs located at deeper area be appropriately compressed with the quasistatic measurement. As a contrast, SW measurement can measure the absolute value of the tissue viscoelasticity at any depth in the tissue of interest. Therefore, the SW measurement may be more competent and outperforms the quasistatic measurement.

Ultrasound and magnetic resonance imaging-based SW measurement methods have been developing rapidly through the past three decades [1], [4], [7]–[25]. Many clinical applications using either method have also been demonstrated [26]–[33].

In the ultrasonic method, the v_s can be determined either through a time-of-flight technique by measuring the time spent on a certain distance which an impulse SW

traveled through [10], or by analyzing the wavelength of a continuous SW waveform at a known f_s [4]. The measurement of impulse SW required high frame rate ultrasound scanning system, while such requirement was not necessary for the measurement of continuous SW. The accurate measurement of α_s , however, was usually more challenging than v_s . This was because in order to determine α_s , the attenuation of the SW amplitude caused by the mode conversion, scattering effect and diffraction effect should be firstly compensated, and such compensation requires mathematical model and intense computation.

Currently, the most promising implementation of the SW measurement could be tracing an impulse SW by using a high frame rate plane wave ultrasound system. However, the design of such system could be rather complex with intense signal processing involved. For instance, an advanced SW measurement systems, such as supersonic shear imaging [16], may be expensive, and thus not be available for some research organizations. Although the SW measurement systems using continuous SW traced by the conventional B-mode scan of focused ultrasound were relatively less expensive, they experienced several practical experimental problems, such as the undesired SW reflections, motion artifacts, and diffraction effect on the measurement of SW.

Motivated by these problems and inspired by the innovations from the developed technologies, methods were proposed through this thesis research to address the experimental problems mentioned above. In this thesis, the SW measurement used a conventional B-mode scan of a focused ultrasound and a single external continuous SW source. Consequently, the ultrasound system was not only less expensive, but also more

popular than the plane-wave-based ultrasound system. In addition, the use of a single external SW source can simplify the overall experimental configuration compared with the use of multiple SW sources, such as the crawling wave method [34], and/or reduce the complexity of the SW generation compared with the use of a radiation force technique [10]. With the proposed experimental configuration, both v_S and α_S can be measured in the same experiment.

Detailed problem statements will be given in **Section 1.2**, and the thesis objectives will be presented in **Section 1.3**.

1.2. Problem Statements

Although the SW measurement using conventional B-mode scan and external SW source could be low in cost and simple in configuration, several practical problems exist. Errors may be added onto the measurement results of v_S and/or α_S , if these problems were not appropriately addressed. Three major problems addressed in this thesis are listed as follows:

1) Undesired SW reflection from tissue boundary

In some experiments, especially when the specimen of interest was relatively small, an induced SW may be reflected at the tissue boundaries, and thus both the induced and reflected SWs existed at the same time. As a result, the observed SW would be an interfered waveform if the continuous SW was employed. However, the conditions of the reflection, such as the location where the reflection occurred and the reflection coefficient, may be unknown. Therefore, the amplitude and

phase of the reflected SWs were unpredictable. Unless the undesired reflected SW was removed from the observed SW waveform, the errors on the estimation of v_S and α_S could occur.

Currently, an effective solution to remove the undesired SW reflection was a directional filtering technique with a plane wave ultrasound imaging system [35]–[37]. However, this technique was not applicable to the SW measurement with the conventional B-mode scanning system of the focused ultrasound used in this thesis research.

2) **Motion artifact on the measurement of shear wave displacement**

In an ideal SW measurement, any tissue displacement observed inside the specimen should be solely triggered by the SW propagation. However for a practical case, tissue displacement could also be generated by undesired motions. Motions from the equipment and/or environment in practical measurements, as well as involuntary *in-vivo* activities, such as heartbeat/pulse, breathing, and/or body movement [38], [39], may be unavoidable. All these undesired motions were considered as motion artifacts and would contribute offsets to the observed SW displacements. Consequently, this would result in errors on the estimation of v_S and α_S .

When the external SW source such as a vibrator or shaker was used, the measurement error due to the motion artifacts may become negligible with great magnitude of the induced SW by increasing the SW source power. However this could bring discomfort to the patient. Therefore, it was crucial to develop a

method to reduce motion artifacts from the observed SW wave form with lower SW source power for practical clinical applications.

3) **Diffraction effect on the measurement of shear wave absorption**

The purpose of the α_S measurement was to determine the tissue viscosity. In principle, α_S can be estimated from the attenuation measurement of SW amplitude. However, the SW amplitude attenuated not only by the absorption, but also by the mode conversion, scattering and diffraction during the SW propagation in a specimen. Therefore, in order to estimate α_S from the measured SW attenuation, the mode conversion, scattering and diffraction should be taken into account. The diffraction was a nonlinear phenomenon [40], and the attenuation compensation was required based on the diffraction theory. In addition, the motion artifact could deform the SW waveforms, resulting in significant errors on the attenuation measurement. Because of such difficulties and challenges, measuring and analyzing the v_S dispersion instead of directly measuring the SW attenuation to estimate the α_S was a common way, in order to determine the tissue viscosity. The v_S dispersion could be obtained from the one measurement if the impulse SW having a broad frequency bandwidth was used. However, when the continuous SW was used, the dispersion method would require multiple measurements at different f_S , which may prolong the time of the measurement. Considering the discomfort of the patient, a quick measurement was desired by the one measurement of the SW attenuation to estimate the α_S . Among the attenuation factors mentioned above, the mode conversion and scattering effects could be negligible with the proposed measurement configuration in this thesis. Thus, the

compensation of the diffraction effect on the estimation of the α_S needed to be discussed.

1.3. Objectives of the Thesis

Estimating the v_S and α_S parameters of soft tissues by using conventional B-mode scan of a focused ultrasound system is a meaningful approach. Its advantage is reflected not only through the reduced cost and configuration complexity, but also through the high popularity of the focused ultrasound system around the world. Therefore, a SW measurement using such ultrasound system with a relatively simple experimental configuration could both help reduce expenses, and show good potential in clinical applications. In order to realize the proposed measurement configuration as well as to address the problems stated in **Section 1.2**, the following objectives were expected to be achieved by the accomplishment of this thesis study.

- 1) **Develop a measurement model of SW displacement by using B-mode scan of focused ultrasound and external shear wave source.**

The measurement of both v_S and α_S depended on a successful measurement of the SW displacement. A measurement model of the SW displacement was developed by using a conventional B-mode scan of a focused ultrasound system. An external SW source was used in this model to generate continuous SWs in a specimen at a chosen monotonic frequency. The **Objectives 2 and 3** would be based upon this measurement model.

2) **Remove undesired SW reflections.**

A method to remove the undesired reflected SW was proposed by using the B-mode scanning time delay of the conventional focused ultrasound system. The accomplishment of this objective would address **Problem 1** in **Section 1.2**.

3) **Reduce motion artifacts.**

A method to reduce the motion artifacts from the observed SW waveform was proposed by using a temporal frequency filtering technique. The accomplishment of this objective would address **Problem 2** in **Section 1.2**.

4) **Minimize diffraction error on the estimation of SW absorption.**

A measurement of α_S required a compensation of diffraction effect, while the diffraction effect was location-dependent. In order to minimize the error that occurs during the compensation of diffraction effect, the optimized measurement location was investigated. The accomplishment of this objective would address **Problem 3** in **Section 1.2**.

1.4. Contributions of the Thesis

Throughout this thesis research, several academic contributions were achieved upon the accomplishment of the thesis objectives. They were summarized and listed as follows.

- 1) A method to remove the undesired SW reflection was developed based on the use of B-mode scanning time delay of focused ultrasound. Removing undesired SW reflection made the estimation of v_S and α_S more accurate.

- 2) A method to reduce the motion artifacts was developed in the proposed ultrasound system which used low frame rate B-mode scanning and external SW source. Such method reduced the error on the measurement of SW displacement due to undesired tissue motions and made an *in-vivo* experiment feasible and reliable.
- 3) A method to obtain the α_S was developed based on the compensation of the diffraction effect on the SW attenuation measurement. Such method minimized error due to positioning error/misreading of the measurement location and made the measurement of α_S more accurate.
- 4) Several academic papers were published and submitted during the thesis research as listed below. These publications could be inspirations and/or references for future research.

Publications:

- Z. Qu and Y. Ono, “Measurement of shear wave velocity with a method to reduce motion artifact using conventional B-mode ultrasound scanning,” to be submitted as journal paper. (**Chapters 5-6**)
- Z. Qu and Y. Ono, “Measurement of shear wave absorption with correction of the diffraction effect,” to be submitted as journal paper. (**Chapter 7**)
- Z. Qu and Y. Ono, “Measurement of shear wave velocity for elastography using conventional B-mode scan of focused ultrasound,” accepted by *IEEE International Symposium on Medical Measurements and Application (MeMeA)*, May 7-10, 2017, Rochester, MN. (**Chapter 4**)

- Z. Qu and Y. Ono, “A method to reduce the influence of reflected waves on shear velocity measurements using B-mode scanning time delay,” *Japanese Journal of Applied Physics*, Vol. 54, pp. 07HF01_1-6, 2015. (**Chapter 3**)
- Z. Qu and Y. Ono, “A method to reduce the influence of reflected shear waves on shear velocity measurement,” *35th Symposium on Ultrasonic Electronics*, pp. 547-548, December 3-5, 2014, Tokyo, Japan. (**Chapter 3**)
- Z. Qu and Y. Ono, “Ultrasonic measurements of shear wave propagation in soft tissue phantom for tissue characterization,” *IEEE International Symposium on Medical Measurements and Application (MeMeA)*, pp. 40-43, May 4-5, 2013, Gatineau, QC. (**Chapter 7**)

1.5. Organization of the Thesis

This thesis was constructed into eight chapters, briefly described as follows:

Chapter 1. Introduction

This chapter was the introduction of this thesis. Motivation and the overview of the research were presented, followed by potential problems and the proposed solutions.

Chapter 2. Background and Technical Review

This chapter was the literature and technical review. The mathematical basis of tissue characterization was firstly presented, and then the state-of-the-art measurement techniques were introduced.

Chapter 3. Development of Shear Wave Velocity Measurement Method Using Focused Ultrasound and External Shear Wave Source

This chapter presented the basic concept of the SW velocity measurement method with a method proposed to remove the undesired SW reflections. Phantom experiments were demonstrated to verify the method.

Chapter 4. Modification of Shear Wave Velocity Measurement Method

This chapter improved the SW velocity measurement method to overcome a limitation of the method proposed in **Chapter 3**. The modified measurement method was verified by the experiments using a phantom with an inclusion structure. Performance of the measurement accuracy was also investigated through numerical calculation.

Chapter 5. A Method to Reduce Motion Artifacts

This chapter proposed a method to reduce the motion artifact based on the modified measurement method of SW velocity. The proposed method was verified by the phantom experiment and numerical calculation.

Chapter 6. *In-vivo* Measurement of Shear Wave Velocity

This chapter demonstrated the shear wave velocity measurements for *in-vivo* tissues with using the methods proposed in **Chapters 4-5**.

Chapter 7. Measurement of Shear Wave Absorption with Correction of the Diffraction Effect

This chapter discussed a measurement method of SW absorption. The measurement location was arranged at a certain place where the diffraction effect

was relatively less sensitive to the change of the SW amplitude. Thus the calculation error due to diffraction would be minimized. The measurement method was verified by phantom experiment.

Chapter 8. Conclusions

The last chapter summarized and reviewed the thesis research and pointed out potential topics for future study.

Chapter 2

Background and Technical Review

The purposes of this chapter are to introduce the mathematical basis of tissue characterization and to review the state-of-the-art ultrasound elastography and viscoelasticity measurement techniques along with their clinical applications.

2.1. Mathematical Basis of Tissue Characterization

It was well known that most of the soft tissues contain more than 70-w% of water, thus they can be considered as fluid-like solids, which means these kinds of materials have characteristics of both solids and fluids [41]. Therefore, a way to characterize such material was to analyze their viscoelastic properties, such as the elasticity and viscosity.

Elasticity is a physical property which describes the ability of a material to return to its original shape after stress is removed [42], and it mainly reflects the solid properties of material. There are three major moduli to represent the elasticity of a material: Young's modulus (E), shear modulus (G), and bulk modulus (K). E defines the ratio between tensile stress (σ) and tensile strain (ε) of a material as $E = \sigma / \varepsilon$ [43], while G defines the ratio of shear stress and shear strain of a material. K is defined as the ratio of the pressure and volume change. It should be noted that for a incompressible material (which applies to human soft tissues, which are nearly incompressible), it can be assumed that $E = 3G$ [14], [44], [45], besides, E and G have broader dynamic range among

different types of human tissues than K [41], The comparison between K and E (or G) is shown in **Fig. 2.1**. Thus E and G could be of more interest/significance for characterization of human tissues. On the other hand, viscosity (η) describes the ability of material to resist deformation due to tensile stress or shear stress [42], and it mainly reflects the liquid properties of material. A Voigt material model, as shown in **Fig. 2.2** [46], was used in this thesis to describe the viscoelastic materials. It is represented by a purely elastic spring connected in parallel to a purely viscous damper. Such model can be used to describe either a tensile viscoelastic material or a shear viscoelastic material. A material with only elasticity is called a purely elastic material, and a material with only viscosity is called a Newtonian fluid [47]. A soft tissue or soft tissue-like material is between these two extreme conditions and is called a viscoelastic material [48].

Figure 2.1. Moduli variance with different types of human tissues (reproduced from [41]).

Figure 2.2. Voigt material model.

Basically, methods of determining the elasticity and/or viscosity were all based on the same objective, which was to find a way to detect the response of a tissue to a mechanical excitation. Then the mathematical relation between the response and excitation was used to derive the viscoelastic parameters [49]. The methods could be divided into two groups according to the temporal difference of the excitation [4], [14]: quasistatic measurement and dynamic measurement (also termed SW measurement). The quasistatic measurement method can determine E by measuring the strain ϵ caused by a known compressive force σ and the area of such force, while the η can be determined by measuring the relaxation time of the specimen from the compressive force with knowing of the E [5]. The SW measurement method can determine both G and η by tracing and analyzing a propagated SW in the specimen. In addition, although the quasistatic measurement provided contrast in terms of relative stiffness to detect abnormal lesions from healthy tissue, limitation also existed and restricted such technique [20]. For instance, it could be difficult to make compress organs located at deeper areas with the quasistatic measurement. Therefore, the SW measurement could be a more benefited method in such case.

SW, also called transverse wave, is a moving mechanical wave that consists of particle oscillations occurring perpendicular to the direction of the energy transfer [44], as depicted in **Fig. 2.3**. In a viscoelastic material, the SW equation is given by [50]:

$$\rho \frac{\partial^2 u_i}{\partial t^2} - \mu \nabla^2 u_i = 0, \quad (2.1)$$

$$\mu = G + j\omega_s \eta, \quad (2.2)$$

where ρ is the density of the specimen, u_i is the particle displacement occurred in the i direction, and t is time. μ denotes the shear viscoelasticity and represents G and η . $\nabla^2 u_i$ is the spatial Laplacian of the particle displacement. $\omega_s (= 2\pi f_s)$ is the angular frequency of the SW, and j denotes the imaginary unit, where $j^2 = -1$.

Figure 2.3. Particle oscillation of shear wave.

When the specimen is homogeneous and isotropic, one of the solutions of the wave equation **Eq. (2.1)** is the plane SW. As shown in **Fig. 2.3**, assuming that particle displacement occurs only at x direction ($u_y = u_z = 0$), thus the displacement, u_x , of the plane SW propagating along z -direction can be expressed as:

$$u_x = A_s \sin(k_s z - \omega_s t), \quad (2.3)$$

where A_s is the amplitude, and $k_s (= \omega_s / v_s)$ is the wavenumber of the SW.

Based on the Voigt model, the velocity and the absorption of the SW, v_S and α_S , respectively, have the following relationships with G and η [51]:

$$v_S = \sqrt{\frac{2(G^2 + \omega_S^2 \eta^2)}{\rho(G + \sqrt{G^2 + \omega_S^2 \eta^2})}}, \quad (2.4)$$

$$\alpha_S = -\sqrt{\frac{\rho \omega_S^2 (\sqrt{G^2 + \omega_S^2 \eta^2} - G)}{2(G^2 + \omega_S^2 \eta^2)}}. \quad (2.5)$$

Therefore, G and η can be determined by solving the **Eqs. (2.4) and (2.5)**, as expressed by the following equations:

$$G = \frac{\rho \omega_S^2 v_S^2 (\omega_S^2 - \alpha_S^2 v_S^2)}{(\omega_S^2 + \alpha_S^2 v_S^2)^2}, \quad (2.6)$$

$$\eta = \frac{\rho \omega_S^2 v_S^2 \cdot 2 \alpha_S v_S}{(\omega_S^2 + \alpha_S^2 v_S^2)^2}. \quad (2.7)$$

It is worth noting that for a soft tissue, its elastic property dominates the tissue mechanical property and the viscous property was often negligible. In such case, it was considered as a pure elastic material and α_S could be negligible. Then, **Eq. (2.6)** can be simplified to:

$$G = \rho v_S^2. \quad (2.8)$$

When the η was taken into account for tissue characterization, according to **Eq. (2.7)**, η can be determined either using both v_S and α_S , or alternatively by evaluating the dispersion of v_S with respect to ω_S without the value of α_S , which means, solving the **Eq. (2.7)** by knowing multiple pairs of v_S and ω_S [6].

2.2. Notable Techniques of Viscoelasticity Measurement

It was known that human has been using the sense of touch to attempt at diagnosis and/or treatment of some of the illnesses for thousands of years. For example, palpation has been used to detect breast tumors since 2,000 years ago [52]. Throughout the past century, modern medicine found that most of the tumors could be harder/stiffer than the surrounding normal tissues, and many research findings revealed that the viscoelastic properties could reflect the pathological information of tissues [10]. In addition to the pathology, as mentioned earlier in the previous section and shown in **Fig. 2.1**, the shear modulus of various normal tissue spans over orders of magnitude [41], potentially providing high contrast among different tissues/organs regarding their mechanical properties, which is something different from what most of the conventional medical anatomic imaging techniques could provide. Therefore, during the last three decades, medical research on human tissue viscoelasticity became more popular, as noninvasive and quantitative measurements of the viscoelastic properties of tissue can be very useful in medical diagnosis [1], [4], [52].

Through tens of years, many notable methods and techniques have been proposed and developed to quantify and visualize the tissue viscoelasticity. Most of the developed methods were based on either ultrasound technique or magnetic resonance imaging (MRI) [8]–[25], [33]. Ultrasound technique typically used ultrasound transducers to collect the information of the compressive force or SW excitation response by means of the tissue displacement. In such technique, the field of view (FOV) was limited by the penetration depth of the ultrasound, thus the region of interest (ROI) at deeper area or for obese subjects may possibly not be reached [20]. As a contrast, MRI technique was not

subjected to those limitations. Measurement of elasticity with MRI has shown promise in the detection and diagnosis of liver [27], [53]–[55], breast [45], [56], [57], prostate [8], [14], [58], [59], and brain [60], [61]. However, MRI required a relatively long acquisition time (more than 10 min), and it was also expensive and weak in portability.

Ultrasound-based techniques were also very actively studied and developed over the years [26]–[33], [62]–[67]. With ultrasound-based techniques, methods of tissue characterization could be divided into two groups according to the temporal difference of the excitation: quasistatic measurement method and SW measurement method.

Temporally, a quasistatic measurement was implemented at two relatively static steps: one without the employment of compressive force, and another with it. The schematic and concept of this measurement method can be seen in **Fig. 2.4**. Assuming the subject specimen was an elastic spring with an original length of l , when compressive force was applied onto the top of the spring, a displacement Δl occurred along the axial direction due to the stress-strain behaviour, and the strain ε was then defined by $\Delta l/l$. Both Δl and l can be obtained by an ultrasound probe posited at the top of the specimen. Since the stress σ may not be measured in practice, the absolute value of E may not be determined. Instead, a relative stiffness could be determined, *i.e.* higher ε represented a softer tissue whereas lower ε represented a stiffer tissue, as indicated in **Fig. 2.4**. J. Ophir and his colleagues in 1991 firstly proposed and described this quasistatic measurement method [1]. Considering that such method found the elastic property of the tissue, it was named as “elastography” at that time. It was worth noting that, after a widely referred review paper by Gao *et al.* in 1996, the term “elastography” was widely expanded to describe all types of elasticity imaging [4]. It should be also noted that with a quasistatic

measurement, tissue viscosity can also be determined by knowing the elasticity and measuring the relaxation time of the tissue from the compressive force [5], [68], [69].

Figure 2.4. Schematic to explain the principle of compressional elastography (adopted from [45]).

The SW measurement method obtains the viscoelastic parameters according to **Eqs. (2.1)-(2.8)**, by tracing and analyzing a SW propagation in a specimen of interest. In 1988, R. Lerner and K. Parker proposed a method to map the propagation of low frequency SW with a *Doppler* ultrasound displacement detection technique [70], and such image of SW displacement would reflect the tissue stiffness. Later in 1990, Y. Yamakoshi *et al.* proposed a dynamic measurement method to measure the v_s using an external mechanical vibration source [7]. A configuration of this method can be seen in

Fig. 2.5. In this method, v_S could be determined by analyzing the wavelength of a continuously propagated SW through the ultrasound *Doppler* technique.

Figure 2.5. Experimental configuration of Yamakoshi's method (reproduced from [7]).

Instead of measuring continuous SW, Catheline and M. Fink developed an impulse SW measurement method in 1999, which used a fast frame rate plane wave ultrasound imaging, to trace the wave front of an impulse SW [71]. In this method, an ultrasonic probe was located at one side of the specimen to capture the propagation of the impulse SW that was generated by mechanical vibrator located at the other side of the specimen, using a plane wave ultrasound system. A conventional focused ultrasound system triggered ultrasound transducers sequentially from one edge of the linear array transducers to another for B-mode scan in which a frame rate was typically less than 100 frame/sec. On the other hand, a plane wave ultrasound system triggered all the ultrasound transducers at the same time to emit a plane ultrasound wave, enabling it to have a high frame rate (more than 1,000 frame/sec) of B-mode measurement. The v_S was determined through a time-of-flight technique by measuring the time elapse of the impulse SW

traveling through two locations with a known distance. Since such a method used impulse SW, it was also called transient SW imaging, or transient elastography. The transient SW measurement using a plane wave ultrasound system required intensive signal processing, making the overall cost of such system more expensive than that of a conventional focused ultrasound system.

Another notable SW measurement method was developed in 2004 by the group of K. Parker [34]. In this method, two SW sources located at two opposite sides of the specimen generated continuous SWs toward each other with slightly different SW frequencies, as shown in **Fig. 2.6**. Due to the frequency difference, the interfered SW patterns moved with a much slower speed than its actual v_S . Thus such a moving pattern was termed as a “crawling wave”. Since the movement of the crawling wave was significantly slower than v_S , it was able to be observed with a conventional low frame rate B-mode scanning system. Once the speed of the crawling wave was obtained, the v_S can be calculated.

Figure 2.6. Experimental configuration for measurement of crawling wave, ① and ② are vibrators (reproduced from [34]).

The SW measurement methods mentioned above use the external vibration source(s) to generate a SW propagating in the specimen. The SW excitation can be also conducted at the inside of the specimen by means of an ultrasound radiation force (or acoustic radiation force, ARF) technique [10]. Many creative methods of elastography have been developed based on the use of the ARF technique.

In 1998, Sarvazyan *et al.* developed a SW measurement method, termed shear wave elasticity imaging (SWEI), by using a SW remotely generated by the ARF of a focused ultrasound beam [10], as can be seen in **Fig. 2.7**. In this method, a transient SW pulse was firstly produced at the focus of the ultrasound beam and propagated along sideways (perpendicularly to the axis of the focused ultrasound beam). Then, imaging transducers were used to trace the moving of the SW wavefront and viscoelastic parameters can be derived thereafter. In 1998, Fatemi and Greenleaf developed a method to produce an oscillatory ARF by mixing two ultrasound beams with different frequencies [11]. A harmonic (continuous) or tone-burst SW was generated and propagates along sideways in this method, which made the SW narrow-band (while the SW generated by Sarvazyan's method was broadband) and then v_s can be determined by finding the phase difference between the SWs at two apart locations [17]. By repeating the measurement with continuous SWs at different frequencies, or retrieving different frequency components of a tone-burst SW, both G and η can be derived according to **Eqs. (2.6)-(2.7)**. Greenleaf later termed this method as SW dispersion ultrasound vibrometry (SDUV) [20], and its measurement configuration was illustrated in **Fig. 2.8**.

Figure 2.7. Schematic concept of acoustic radiation force to excite a transient SW (adopted from [45]).

Figure 2.8. Measurement configuration of SDUV (reproduced from [20]).

In 2001, Nightingale *et al.* introduced a different measurement modality termed as acoustic radiation force imaging (ARFI) [72]. Unlike other SW measurement methods which generated and analyzed SW, the ARF has been used to push and displace local tissues in ARFI technique. Depending on the stiffness of the tissue, the maximum displacement, and/or the relaxation time of the pushed tissue may be varying, and those parameters reflected the tissue elasticity. Because the principle of such technique was similar to a quasistatic measurement strategy, it was also called a remote palpation.

Later in 2004, based on the combination of Catherine's impulse SW method [71] and the ARF technique [10], Bercoff *et al.* developed an advanced SW measurement method which was termed as supersonic shear imaging (SSI) [16]. In this method, an ultra high speed scanner was used (could reach a frame rate at 10,000 frames/second), then multiple APF impulses excited very quickly at different depths, and each excitation produced a SW that propagates along sideways. All resulting SWs interfered constructively and created two plane SWs propagating in opposite directions, as can be seen in **Fig. 2.9**. By using the ultra high speed scanner to trace these SWs, a two dimensional (2D) v_S image can be obtained. Moreover, since this technique created broadband SWs, tissue viscosity can be estimated through the v_S dispersion method (using the same principle as SDUV).

Another ARF-based method was proposed in 2007 by McAleavey *et al.*, named as spatially modulated ultrasound radiation force (SMURF) [50]. This method excited multiple ARFs together along a lateral direction (called comb-push excitation) to generate a SW at a desired wavelength (λ_S). So the v_S can be calculated through $v_S = \lambda_S / f_S$, by measuring f_S in temporal domain.

Figure 2.9. Generation of the supersonic plane shear wave (adopted from[16]).

More recently (in 2012), Greenleaf and his team developed a SW method which also used the comb-push excitation. This measurement method was termed as comb-push ultrasound shear elastography (CUSE) [24], [73], [74]. A schematic of the measurement configuration and observed SW patterns were illustrated in **Fig. 2.10**. It firstly generated

multiple unfocused ARF excitations at different spatial locations to generate multiple SWs by using push mode of the ultrasound probe, and then quickly switched to the scanning mode of the probe to detect the SW propagation. Therefore the v_s would be measured through the time-of-flight technique by tracing the movement of SW wavefront (as indicated by the arrows at different moments in **Fig. 2.10**) from each SW source. The use of comb-push excitation provided multiple SW sources in the specimen so that such method effectively compensated the worse signal-to-noise ratio (SNR) due to SW attenuation at the location far away from the single SW source.

Figure 2.10. A schematic of the measurement configuration and observed SW patterns of CUSE (reproduced from [24]).

By far, many studies have proved that the SSI technique may provide the most promising result among all the methods. Such technique was less affected by the problems stated in **Section 1.2**, and it has been generally acknowledged as the most advanced technique at present, in the field of ultrasound tissue characterization. The drawback of this technique could lie in the complexity of the system design and its expensive cost.

2.3. Clinical Applications with Ultrasound Technique

Over the past several years, many characterization methods have been applied into clinical applications. The techniques have already been adopted by the clinicians on diagnosis of several organs [45], [75]. Liver elastography was mainly used for the evaluation of liver stiffness to diagnose the patients with hepatitis (e.g. liver fibrosis and steatosis) [76]. A limitation lay in the depth of penetration, which could result in unsuccessful measurement with large patients or patients with ascites [45]. As a contrast, measurement at superficial regions could be more effective, such as the diagnosis of breast lesions and tumors. Both quasistatic [77] and dynamic [78] measurements were applied to detect the lesions in breast.

Diagnosis on prostate using elastography was a good complementary method to detect the potential cancer area [58]. When the lesion was identified, elastography may help the clinicians to make decision on whether to carry out a biopsy in the lesion area. Besides, elastography in thyroid was also employed to differentiate the cancers by evaluating the tissue stiffness [63]. Other applications, such as the characterization with

musculoskeletal [65], Achilles tendon [79], cardiovascular [80], and lymph nodes [81] also showed good results that reflected the difference between normal and abnormal tissues. Moreover, some studies also pointed out that the measurement of elastic property could also be adopted to monitor the thermal therapy [82]–[84].

Many of the SW measurement methods have already been implemented in the commercial devices. Some of the typical devices are introduced here:

Echosens’ FibroScan (France) – It is a machine based on transient elastography technique, which has been used in the detection of liver stiffness and used in Canada since 2009 [26], [76], [85].

SuperSonic Imagine’s Aixplorer (France) – It is a machine based on the SSI technique, which has been widely used in many applications as introduced in the previous paragraph [30], [73], [79], [82], [86].

Siemens’ Virtual Touch Quantification products (Germany) – Many modes are available, such as ACUSON NX3, ACUSON S2000, and ACUSON S3000. Those machines are based on the ARFI technique, which can be applied to liver, breast, thyroid, and abdominal [78], [87], [88].

General Electric (GE)’s LOGIQ E9 (US) – It is a machine that generates comb-push ARFs and estimates v_s from each ARF through the time-of-flight technique, which can be used to detect liver disease and breast lesions [73], [89].

At present, the improvement of measurement precision and accuracy of existing techniques was always an interesting and active topic. In addition, the most discussed parameter in the clinical applications was the tissue elasticity, while the measurement of

viscosity was relatively less discussed. Therefore, the development of the comprehensive measurement of human soft tissue characteristics, such as viscosity, anisotropy, nonlinearity, and etc., could be the interesting research direction for the field of tissue characterization in the future.

Chapter 3

Development of Shear Wave Velocity Measurement

Method Using Focused Ultrasound and External Shear Wave Source

3.1. Introduction

When an induced SW was reflected from the tissue boundary, the observed SW could be an interference waveform. This may affect the measurement accuracy of the SW velocity, since the amplitude and the phase of the reflected SW may be unknown. Influence due to the reflection can be reduced by applying a directional filter at a spatio-temporal domain of the observed SW by using a plane wave ultrasound imaging system [35]–[37]. However, the use of a plane wave ultrasound did not meet the objective of this research (described in **Section 1.3**). Therefore, in this chapter a measurement method of SW velocity was proposed using a conventional B-mode scan of a focused ultrasound system with a single external SW source. First, the SW measurement model and ultrasound rf signal analysis procedure were presented. Then, the proposed method was verified experimentally by using a soft tissue mimicking phantom specimen.

3.2. Methodology

An ultrasound brightness mode (B-mode) scan was composed of multiple sequential amplitude mode (A-mode) signals. A procedure was shown in **Fig. 3.1**. For most of the conventional ultrasound systems using a focused ultrasound, multiple ultrasound transducers were assembled as a linear array in an ultrasound probe. A focused ultrasound beam was formed by several consecutive activated transducers. Such beam would be transmitted into a specimen that the probe surface contacts, and ultrasound signals reflected from the inside of the specimen were received by those transducers. This procedure was defined as one A-mode scan. A-mode scan would be repeated sequentially from the one edge of the array transducer to another. The multiple consecutive A-mode scans formed a 2D image, defined as a B-mode image. Therefore, when the ultrasound signals were acquired by a focused ultrasound scanning system in B-mode scan, there was a time delay among the sequential A-mode measurements [73].

Figure 3.1. The procedure of B-mode scan using focused ultrasound.

This scanning time delay caused an artificial spatial frequency shift in the observed SW propagating along the normal direction of focused ultrasound beam. The amount of the frequency shift depended on the propagation direction of SW with respect to the B-mode scanning direction. Therefore, forward and backward SWs could be separated from the observed SW using a spatial domain filter.

A measurement model of SW propagation using B-mode scan of focused ultrasound was depicted in **Fig. 3.2**. The origin of the coordinate system was selected at the center of the ultrasonic linear array probe and the SW source. The ultrasound probe was placed on top of the soft tissue specimen. In each A-mode measurement ultrasound rf signals were acquired along the depth (x -direction) of the specimen.

Figure 3.2. Measurement model of SW velocity.

A continuous SW vibration source contacted one side of the specimen. Thus, the SW propagated along the specimen length (z -direction) which was parallel to the scanning direction of the B-mode measurement. The induced SW was assumed to be a

plane wave. The induced forward SW may be reflected from the opposite end or the boundaries in the specimen, resulting in a reflected backward SW. The backward SW could interfere with the forward SW. It was assumed that no SWs were converted into a longitudinal wave (LW) due to the mode conversion under the measurement model employed. For detailed explanation on mode conversion was given in **Appendix A**.

The tissue displacements in the specimen due to the SW propagation were obtained from the acquired ultrasound radio-frequency (rf) signals using a phase tracking method, and the SW displacement pattern in z -direction was observed. Then, the propagation velocity of SW was estimated from the phase variation of the observed SW. A flowchart of the ultrasound rf signal processing procedure to obtain the SW velocity, v_S , was depicted in **Fig. 3.3**.

Figure 3.3. Flow chart of signal processing procedure for acquired ultrasound rf signals.

The tissue displacements along the depth x caused by the shear vibration were obtained by analyzing the phase of acquired ultrasound rf signals in each A-mode measurement [90], using an in-phase/quadrature detection technique (Step 1) [91]. Then, the waveform of SW displacement was obtained along the z -direction at a chosen depth x (Step 2). For detailed signal processing procedures to obtain the SW displacement from rf signals was given in **Appendix B**.

The displacement of the observed SW, $V(t, z)$, was expressed by a summation of forward, $V_F(t, z)$, and backward, $V_B(t, z)$, SWs by **Eq. (3.1)**, where t was the time. By considering the B-mode scanning time delay, the $V_F(t, z)$ and $V_B(t, z)$ observed in B-mode measurement can be represented by **Eqs. (3.2) and (3.3)**, respectively.

$$V(t, z) = V_F(t, z) + V_B(t, z), \quad (3.1)$$

$$\begin{aligned} V_F(t, z) &= A_F \cos \left[\omega_S \left(t + \Delta t \frac{z}{\Delta z} \right) - k_S z + \varphi_F \right] \\ &= A_F \cos \left[\omega_S t - \left(k_S - \frac{\omega_S \Delta t}{\Delta z} \right) z + \varphi_F \right], \end{aligned} \quad (3.2)$$

$$\begin{aligned} V_B(t, z) &= A_B \cos \left[\omega_S \left(t + \Delta t \frac{z}{\Delta z} \right) + k_S z + \varphi_B \right] \\ &= A_B \cos \left[\omega_S t + \left(k_S + \frac{\omega_S \Delta t}{\Delta z} \right) z + \varphi_B \right], \end{aligned} \quad (3.3)$$

where A_F and A_B are the SW amplitude, and φ_F and φ_B are the initial phase, of the forward and backward SWs, respectively. Δt and Δz are the temporal and spatial interval, respectively, between two consecutive A-mode measurements.

Due to the scanning time delay in the B-mode measurement, the time of each A-mode measurement at the location z had a delay, given by $\Delta t(z/\Delta z)$, from the first A-mode measurement. It resulted in the negative and positive artificial spatial frequency shift of

$\omega_S \Delta t / \Delta z$ from k_S for observed V_F and V_B , respectively, as represented in **Eqs. (3.2) and (3.3)**. Therefore, $V_F(t, z)$ can be retrieved from the measured $V(t, z)$, by using a low pass filter (LPF) in spatial domain (Step 3).

We defined the scan speed, v_{scan} , of the B-mode measurement by **Eq. (3.4)**. Then, **Eq. (3.2)** may be rearranged to **Eq. (3.5)**.

$$v_{scan} = \frac{\Delta z}{\Delta t}, \quad (3.4)$$

$$V_F(t, z) = A_F \cos \left[\omega_S t - \omega_S \left(\frac{1}{v_S} - \frac{1}{v_{scan}} \right) z + \varphi_F \right]. \quad (3.5)$$

Therefore, it can be seen from **Eq. (3.5)** that the observed V_F artificially moved backwards due to the scanning time delay when $v_{scan} < v_S$. Furthermore, the V_F was observed with the same magnitude value at all positions of z at a selected time t when $v_{scan} = v_S$.

An out-of-phase signal with 90° phase shift for the V_F at an arbitrary time t with respect to z was calculated by a Hilbert transform ($\mathcal{H}_z$) to create an analytic complex signal V_F^* as follows (Step 4):

$$V_F^*(z) = V_F(z) + j \cdot \mathcal{H}_z\{V_F(z)\}, \quad (3.6)$$

where j is the imaginary unit, which equals to $\sqrt{-1}$.

In the Hilbert transform of **Eq. (3.6)**, we did not consider mathematically whether the observed V_F moves forwards, or backwards artificially due to the scanning time delay. Therefore, the phase value of V_F in **Eq. (3.5)** was obtained with the absolute value of the spatial phase component of V_F^* using **Eq. (3.7)** (Step 5). By taking the spatial derivative of **Eq. (3.7)** with respect to z , v_S at each z was finally calculated using **Eq. (3.8a)** or

(3.8b) (Step 6).

$$\begin{aligned}\angle V_F^*(z) &= \tan^{-1} \left[\frac{\text{Im}[V_F^*(z)]}{\text{Re}[V_F^*(z)]} \right] \\ &= \omega_S \left| \frac{1}{v_{scan}} - \frac{1}{v_S} \right| z + \varphi_F,\end{aligned}\tag{3.7}$$

$$v_S(z) = \frac{1}{\frac{1}{v_{scan}} - \frac{1}{\omega_S} \cdot \frac{\partial[\angle V_F^*(z)]}{\partial z}}, \quad \text{for } v_{scan} < v_S \tag{3.8a}$$

$$v_S(z) = \frac{1}{\frac{1}{v_{scan}} + \frac{1}{\omega_S} \cdot \frac{\partial[\angle V_F^*(z)]}{\partial z}}, \quad \text{for } v_{scan} > v_S \tag{3.8b}$$

In order to measure the waveform of the V_F along the B-mode scan direction (z -direction) without aliasing, the spatial sampling interval given by Δz needed to satisfy the Nyquist sampling theorem expressed by **Eq. (3.9)**. Therefore, the highest applicable f_S was limited, as expressed by **Eq. (3.10)**.

$$\Delta z < \frac{1}{2} \cdot \frac{1}{f_S \left| \frac{1}{v_{scan}} - \frac{1}{v_S} \right|}, \tag{3.9}$$

$$f_S < \frac{1}{2 \cdot \Delta z \left| \frac{1}{v_{scan}} - \frac{1}{v_S} \right|}. \tag{3.10}$$

Figure 3.4 represented the highest f_S with respect to v_S under our measurement condition of $v_{scan} = 2.26$ m/s (would be introduced in detail later). It was shown that the highest f_S of 2847 Hz at $v_S = 1$ m/s was the smallest in the v_S range from 1 to 10 m/s. It was noted that most of SW measurements for tissue characterization were conducted at SW frequencies below 1000 Hz because of large attenuation of SW in biological soft tissues [7], [17], [21], [71]. In this chapter, f_S of 500 Hz was chosen to demonstrate the feasibility of the proposed method.

Figure 3.4. Highest SW frequency with respect to SW velocity to satisfy the Nyquist sampling theorem with ultrasound scanning system used in this chapter.

3.3. Experimental Setup

3.3.1. Hardware Equipments and DAQ Program

The hardware equipments used in the experiments shown in **Fig. 3.5**.

Ultrasound imaging system: the system model was a conventional B-mode scanning system (model: **Picus**) with a linear array ultrasound probe (model: **L10-5**, 5-MHz nominal operating frequency). This equipment was from **Esaote Europe**, Maastricht, Netherlands.

Mechanical stage: The mechanical stage was built by a positioning device (Model: **BiSlide**, from **VELMEX Inc.**, USA). It was moveable in three directions (x , y ,

and z directions), and it was used to position the ultrasound probe onto a chosen location of a specimen.

External SW source: The SW source was assembled based on an acoustic speaker. An L-shape rigid plastic rod was permanently glued onto the diaphragm of the speaker, and a thin Plexiglas plate was mounted onto the other end of the rod. The Plexiglas plate was changeable, and it would contact onto the specimen and induce the SW into the specimen during the experiment.

Digital signal generator: Model: **SFG-1003**, from **GW INSTEK**, Taiwan. The digital signal generator was used to drive the acoustic speaker at a desired frequency.

Besides, an **ART.LAB** program was preinstalled in the ultrasound **Picus** system as a data acquisition (DAQ) program. It was used to monitor the B-mode or motion-mode (M-mode) image during the measurement and acquire the ultrasound rf signals as digital data.

There were 127 A-mode scan lines to form into a B-mode scan for our ultrasound probe. The spatial interval (Δz) between two consecutive A-mode scan lines was $315\ \mu\text{m}$ and the ultrasound pulse repetition frequency (PRF) of A-mode scan was 7187 Hz, from the manufacture report. The frame rate (f_{FR}) of the B-mode scanning was also indicated at 30 Hz. The exact values of the PRF and f_{FR} were essential for the accurate SW measurement by the method proposed in this thesis. Therefore, in order to verify the value of PRF, the scanning time delay ($\Delta t = 1/\text{PRF}$) between two consecutive A-mode scan lines was inspected as shown in **Fig. 3.6**.

Figure 3.5. Equipments used in the experiment.

Figure 3.6. Verification of pulse repetition frequency and B-mode scan frame rate.

After the inspection, it was found each B-mode scan composed of 127 A-mode scans requires total 33.3 ms to be completed as seen in **Fig. 3.6(b)**, thus f_{FR} was verified 30 Hz (1/33.3 ms). The duration between every two groups of excitations was considered to be the waiting time for signal processing and/or data archiving. The time interval between two consecutive single excitations was around 139 μ s as seen in **Fig. 3.6(d)**, thus the PRF value was 7187 Hz as indicated in the manufacture since Δt was calculated at 139.1 μ s (1/7187 Hz), which was very close to our result. Therefore, v_{scan} of this ultrasound system in **Eq. (3.4)** was calculated 2.26 m/s.

3.3.2. Fabrication of Tissue-mimicking Phantom

Phantom specimens were used in the experiments to verify the proposed SW measurement method. The phantom was hydrogel-based using either agar or gelatin to mimic soft tissues.

It took more than one day to accomplish the fabrication process of a hydrogel phantom. A general process was given as follows [92]:

- 1) Decided the concentration of the agar/gelatin in the phantom (which would determine the stiffness of the phantom fabricated), and weight the ingredients, such as agar/gelatin, graphite powder, alcohol and water, accordingly.
- 2) Prepared plenty of ice water for later use.
- 3) Boiled the water for around 30 minutes to degas it.
- 4) Kept on warming the boiled water to maintain the temperature above 90 °C.
- 5) Stirred the water constantly (it is suggested to use a magnetic stirrer). Adjusted the stirring speed to avoid introducing air bubbles into the degassed water.
- 6) Mixed agar or gelatin powders into the water slowly to prevent them from forming into lumps.
- 7) Kept on stirring the solution until the powders were totally dissolved (powders were totally dissolved when the solution becomes transparent). Time consumption in this step would be subject to the amount and temperature of the solution. It may take tens of minutes to few hours.

- 8) Mixed graphite particles into the solution slowly to prevent them from forming into lumps. The graphite particles were used as the ultrasound scatterers.
- 9) Kept on stirring the mixture for another hour to ensure the graphite particles being distributed uniformly.
- 10) Mixed more degassed heated water to compensate the loss due to evaporation. Controlled the water amount to maintain the solution at the desired agar/gelatin concentration.
- 11) Stopped heating the solution but kept on stirring it to avoid the sediment.
- 12) (Optional) Mixed certain amount of alcohol into the mixture to prevent the growth of bacteria to extend the lifetime of the phantom.
- 13) Kept on stirring the mixture until its temperature drops below 60 °C.
- 14) Got the phantom mould ready and let it be surrounded by the ice water (the ice water is prepared earlier as indicated in step 2). This step should be carried out a little earlier before the temperature of the mixture is below 60 °C.
- 15) Stopped stirring the mixture when its temperature is below 60 °C. Poured the mixture into the mould slowly to avoid introducing air bubbles.
- 16) Left the liquid phantom in the mould for at least an hour (ice water bath accelerates the solidification of the mixture).
- 17) Transferred the mould into the fridge from the ice water and waited for 24 hours to let it become totally solidified.

- 18) Removed the solid phantom from the mould, and wrapped it with preservative film to minimize the evaporation of water component. Preserved the phantom in the fridge.

Every time before using the phantom for experiment, phantom would be taken out of the fridge for a few hours to let it reach the room temperature. This procedure was very important since the tissue viscoelastic properties may vary with the temperature.

Based on our experience, when alcohol was added, a hydrogel phantom which was made of agar could last for one to two months without changing its stiffness, and then it may start shrinking and hardening due to the water loss, while for a gelatin-based phantom, it may last for about two weeks. Yet when alcohol was not added, both phantoms may start molding and decaying within one to two weeks. Physically, an agar phantom seemed more durable than a gelatin phantom.

Note that it was relatively difficult to precisely adjust the acoustic properties, such as density, speed of sound, and attenuation, of the agar and gelatin phantoms. Therefore, the fabricated phantoms used in this thesis research were not adjusted to meet the recommended ultrasound properties for biological soft tissues (LW velocity around 1540 m/s, and attenuation around $0.5 \text{ dB}\cdot\text{cm}^{-1}\cdot\text{MHz}^{-1}$) [93]. The objective of the phantom experiments was to verify the proposed SW measurement method, but not the fabrication of bio-tissue phantom. Furthermore, the proposed method measured the shear properties but not the longitudinal properties of a specimen.

3.4. Experiments

Two soft tissue mimicking phantoms were fabricated through the process described in **Section 3.3.2** for the experiments to verify the proposed method. One was constructed using 2-W% agar, and the other was using 9-W% gelatin. They were hydrogel phantoms with 2-V% isopropanol (99% purity) and 2-W% fine graphite particles. The graphite particles applied had a nominal diameter of 50 μm . Both phantoms had a cubic shape with a side length of 50 mm. Based on a tactile comparison, the gelatin phantom was softer than the agar phantom.

In order to characterize elastic properties of the fabricated phantoms, their mechanical parameters, such as Young's modulus, density, and LW velocity, were measured. First, stress-strain measurements (quasistatic method) were conducted to measure the Young's modulus. A weight of 200 g was applied uniformly on the entire top surface of the phantom, and the resulting thickness change of the phantom was measured by using a digital caliper with a resolution of 0.1 mm. From the stress-strain analysis, the Young's modulus of the agar and gelatin phantom were obtained to be 78 ± 16 kPa and 49 ± 6 kPa, respectively. The densities of both phantoms were 1.1 g/mL calculated from the dimensions and weight of each phantom. Finally, the LW velocity was measured by using an ultrasonic pulse echo technique. A single element 4 MHz ultrasonic probe was attached on the top surface of the phantom, and the first and second round-trip ultrasonic signals reflected from the bottom surface were acquired. The LW velocity of the agar phantom was 1467 ± 1.4 m/s, and 1490 ± 1.5 m/s for the gelatin phantom.

The v_s of each phantom can be estimated from the Young's modulus, LW velocity,

and the density of a homogeneous isotropic material [94]. The v_s was calculated 4.9 m/s for agar phantom, and 3.9 m/s for the gelatin phantom by using the measured elastic parameters presented above. The estimated v_s of each phantom was greater than v_{scan} (2.26 m/s) of our ultrasound system. Thus, **Eq. (3.8a)** was used to obtain v_s from the SW measurements with the phantoms.

After the measurement of elastic properties of each phantom, the two phantoms were jointed to mimic a heterogeneous material as shown in **Fig. 3.7(a)**. One surface of each phantom was slightly melted with a heat source, then the melted surfaces were attached together. The combined phantom was cooled to solidify the joint boundary. **Figure 3.7(b)** presented a B-mode ultrasound image of the combined phantom. The vertical line at the center presented the interface of the agar and gelatin phantoms, and the horizontal line was the bottom echo.

The **ART.LAB** program was used to visualize the B-mode image and save the ultrasound rf signals. FOV of a B-mode scan was 40 mm in length (z -direction) and 34 mm in depth (x -direction). In each measurement, a total of 180 frames of B-mode measurement were acquired in 6 seconds.

Two SW experiments were described in this chapter. In the first experiment, v_s of each phantom (agar or gelatin) was measured with the proposed method. A 50 mm $\times$ 50 mm square Plexiglas plate with a thickness of 5 mm was contacted onto the side surface of the agar (or gelatin) phantom as the SW vibration source, and the ultrasonic probe was attached on the top surface of the selected phantom, as depicted in **Fig. 3.8(a)**. The acoustic speaker was driven continuously by sinusoidal signals at 500 Hz during the experiments. Therefore a monochromatic SW was transmitted into the phantom, which

induced vertical displacement of particles in the phantom.

In the second experiment, the SW source contacted the side surface of the agar phantom, as shown in **Fig. 3.8(b)**, so that the SW could propagate in the entire specimen through the interface of the agar and gelatin phantoms. The ultrasonic probe was attached on the top surface of the interface so that the FOV could cover both regions of the agar and gelatin phantoms.

Figure 3.7. (a) Photo and (b) ultrasound B-mode image of a soft tissue mimicking phantom with combination of agar and gelatin phantoms used in the experiments.

Figure 3.8. Experimental configuration of SW velocity measurement for (a) the individual phantom, and (b) the combined phantom.

3.5. Results and Discussions

For the first experiment, the observed SW displacements, V , of the agar phantom were shown in **Fig. 3.9(a)**. The displacement along z -direction at $x = 0$ was also presented in **Fig. 3.9(b)**, in which the interference of the forward (V_F) and backward (V_B) SWs was clearly observed as a fluctuation of the displacement from a sinusoidal-shape pattern. **Figure 3.9(c)** presented the spatial frequency spectrum of the measured SW displacement in **Fig. 3.9(b)**. In **Fig. 3.9(c)**, the two frequency components corresponding to the V_F and V_B were seen. The V_F was retrieved from V by the spatial LPF with a cutoff frequency of 1.4 rad/mm, and the filtered results corresponding to the measured results in **Figs. 3.9(a)-(c)** were shown in **Figs. 3.9(d)-(f)**, respectively. It was noted that, in principle, v_S can also be obtained through V_B instead of V_F . However, V_F was used because of its greater energy and better signal-to-noise ratio than V_B . The same measurement procedure and data analysis were performed for the gelatin phantom.

The result was averaged with 180 frames and was shown in **Fig. 3.10(a)**. The v_S result for the gelatin phantom was also shown in **Fig. 3.10(b)**. The mean value of the v_S in the FOV of the agar phantom was 5.9 m/s with a standard deviation of 1.1 m/s, and that of gelatin phantom was 3.3 m/s with a standard deviation of 0.52 m/s. The measured v_S of the agar phantom was 2.6 m/s (78.8%) greater than that of gelatin phantom.

Figure 3.9. Observed SW displacements (a) in the entire FOV and (b) along z -direction at $x = 0$, and (c) spatial frequency spectrum of the displacement shown in (b). Those of filtered SW displacements were presented in (d)-(f) respectively.

Figure 3.10. Measured SW velocity obtained from the filtered SW displacements of (a) the agar phantom and (b) the gelatin phantom.

In order to verify the reliability of the measurement results, the v_s of both phantoms were also measured with an impulse technique [71]. An M-mode measurement with 935 Hz frame rate was conducted with the same ultrasound system to trace the propagation of an impulse SW induced by the SW source, and the configuration of such measurement can be seen from **Fig. 3.11**. Then, v_s obtained from the impulse technique and calculated from the measured Young's modulus, LW velocity and density of the

phantom were compared with v_s obtained from the continuous SW measurement method proposed in this chapter. The results were summarized in **Table 3.1**.

Figure 3.11. Configuration of the measurement on SW impulse using M-mode.

Table 3.1. A comparison of SW velocity obtained from different methods.

Method	SW velocity, v_s (m/s)		Difference from proposed method	
	Agar	Gelatin	Agar	Gelatin
Proposed method	5.9	3.3	---	---
Impulse technique	6.0	2.9	1.7%	-12.1%
Calculation with Young's modulus, LW velocity, and density	4.9	3.9	-16.9%	18.2%

Measurement results with the impulse technique had better agreement with the proposed method than the results obtained from the Young's modulus, especially for the agar phantom. This may be due to the fact that both the impulse technique and our proposed method were dynamic measurements of SW propagation. On the other hand,

the estimation from the measured Young's modulus was based on static measurements.

The result of the v_S measurement in the second experiment with the combined phantom was shown in **Fig. 3.12**. The interface of the phantoms was seen at $z = 0$ where a sharp change of the v_S due to the stiffness difference between the agar and gelatin phantoms was clearly observed. The mean velocity of the left half (agar) was 5.9 m/s and that of the right half (gelatin) was 3.7 m/s, which had good agreement with the measured v_S of each phantom in the first experiment.

Figure 3.12. Measured SW velocity of the combined phantom.

It was noted that the variations of the measured v_S from the average velocities could be resulted from the inhomogeneity of the fabricated phantoms and the estimation error of the phase slope of the analytic V_F^* signal calculated by the Hilbert transform. The accuracy of Hilbert transform was highly dependent on the shape or frequency of processed signals [95].

3.6. Summary

The research in this chapter was aiming to develop a measurement method of SW velocity, and to address the **Problem 1** described in **Section 1.2** related to the undesired SW reflections. It was found that the scanning time delay resulted in an artificial spatial frequency shift between the induced and reflected SWs observed. Therefore the scanning time delay can be considered as an advantage factor and the forward SW can be retrieved from an interfered SW by using a spatial frequency low pass filter. With the proposed method, SW velocity was measured from the phase slope of the retrieved forward SW. Thesis **Objective 1** in **Section 1.3** was partially accomplished and **Objective 2** was accomplished by the research of this chapter. However, a shortcoming of the proposed measurement method should also be noticed: the calculation of SW velocity required a prior knowledge of the relationship between the B-mode scanning speed and SW velocity, which in practice may be unknown without experiments, making the appropriate calculation of SW velocity uncertain. An improved measurement method of SW velocity would be proposed in the following **Chapter 4**.

Chapter 4

Modification of the Shear Wave Velocity Measurement

Method

4.1. Introduction

In **Chapter 3**, a measurement method of SW velocity was developed by using B-mode scan of a focused ultrasound and a single external SW source. The developed method took the B-mode scanning time delay into account and also removed the undesired SW reflections. Although the method allowed higher values of SW frequency, it also required a prior knowledge of the relationship between the SW velocity and the B-mode scanning speed, *i.e.* which one was greater. However, such a relationship for an arbitrary specimen may not be available prior to the experiments. In this chapter, a modified SW velocity measurement method was proposed in order to address the above-mentioned shortcoming.

4.2. Methodology

4.2.1. Modification of Measurement Model

According to the measurement model in **Fig. 3.2**, the induced SW was the V_F upon that configuration and it was used to calculate the v_S due to its better signal-to-noise ratio

(SNR). From **Eq. (3.2)** it can be seen that the sign of the spatial frequency of the V_F , k_F ($= \omega_S \left(\frac{1}{v_S} - \frac{1}{v_{scan}} \right)$), could be reversed if $v_S > v_{scan}$. Furthermore, no SW propagation would be observed if $v_S = v_{scan}$ since it resulted in the same magnitude values at all positions on z . However, the relationship between v_S and v_{scan} may be unknown for an arbitrary specimen. As a contrast, V_B never changed the sign of its spatial frequency, k_B ($= \omega_S \left(\frac{1}{v_S} + \frac{1}{v_{scan}} \right)$), according to **Eq. (3.3)**, regardless of the relationship between v_S and v_{scan} . Therefore, the measurement model in this chapter was modified to make the induced SW become V_B so that the prior knowledge of the relationship between v_S and v_{scan} would no longer be required.

In order to realize such desire, the modified measurement model was shown in **Fig. 4.1**. The origin of the coordinate system was at the center of the ultrasound probe and SW source. The ultrasound probe was placed on the top of the specimen. The SW source was now contacting the other side of the specimen from the location it used to be in **Fig. 3.2** so that it induced the SW against the direction of B-mode scanning (toward the negative z -direction). The induced SW may be reflected at the other side or the boundaries in the specimen. Tissue displacements along the x -direction caused by the SWs were detected by the ultrasound probe. The SW that had the same propagation direction (positive z -direction) as the B-mode scanning direction was termed as forward SW (V_F) and that with opposite direction (negative z -direction) was termed as backward SW (V_B). Therefore, the mathematical expressions of V_F and V_B remained the same as **Eqs. (3.2)** and **(3.3)**, respectively. Only the induced SW became the V_B in this chapter.

Figure 4.1. Modified measurement model of SW velocity.

At a certain time t , the temporal term ω_{st} in **Eqs. (3.1), (3.2) and (3.3)** became constant, so these equations were simplified to:

$$V(z) = V_F(z) + V_B(z), \quad (4.1)$$

$$V_F(z) = A_F \cos \left[-\omega_S \left(\frac{1}{v_S} - \frac{1}{v_{scan}} \right) z + \varphi_F \right], \quad (4.2)$$

$$V_B(z) = A_B \cos \left[\omega_S \left(\frac{1}{v_S} + \frac{1}{v_{scan}} \right) z + \varphi_B \right]. \quad (4.3)$$

In order to estimate v_S , V_B must be isolated from the V . Since the k_F and k_B were different, V_B can be retrieved from the obtained V by using a spatial frequency filter. A spatial bandpass filter (**$BPF_{spatial}$**), which only passed V_B , was designed and applied on the interfered SW V . A window function **$WINDOW(z)$** was then multiplied on the filtered V_B in order to reduce the spectral leakage effect due to the waveform discontinuity. Together, these two steps can be expressed by **Eq. (4.4)**:

$$V_B(z) = \mathbf{BPF}_{spatial}\{V(z)\} \cdot \mathbf{WINDOW}(z). \quad (4.4)$$

Then after the Hilbert transform ($\mathcal{H}_z$) on the filtered $V_B(z)$, the v_S at each z would finally be calculated through the following equations:

$$V_B^*(z) = V_B(z) + j \cdot \mathcal{H}_z\{V_B(z)\}, \quad (4.5)$$

$$\begin{aligned} \angle V_B^*(z) &= \tan^{-1} \left[\frac{\text{Im}[V_B^*(z)]}{\text{Re}[V_B^*(z)]} \right] \\ &= \omega_S \left(\frac{1}{v_S} + \frac{1}{v_{scan}} \right) z + \varphi_B, \end{aligned} \quad (4.6)$$

$$v_S(z) = \frac{1}{\frac{1}{\omega_S} \frac{\partial [\angle V_B^*(z)]}{\partial z} - \frac{1}{v_{scan}}}. \quad (4.7)$$

4.2.2. Removal of Shear Wave Reflection

In order to remove the V_B from V using a **BPF**_{spatial}, the spatial frequencies of V_F and V_B , k_F and k_B , respectively, must be separable within the passband of the **BPF**_{spatial}. Therefore, no overlap should be existed between k_F and k_B within the passband. The k_F and k_B were normalized by ω_S as ξ_F , and ξ_B , respectively, by **Eqs. (4.8) and (4.9)**:

$$\xi_F = \frac{k_F}{\omega_S} = \left| \frac{1}{v_S} - \frac{1}{v_{scan}} \right|, \quad (4.8)$$

$$\xi_B = \frac{k_B}{\omega_S} = \frac{1}{v_S} + \frac{1}{v_{scan}}. \quad (4.9)$$

Note the ξ_F in **Eq. (4.8)** was an absolute value since we did not consider the artificial movement direction of V_F in the spectrum analysis. Then, the variations of ξ_F and ξ_B , respectively, with respect to the v_S under our B-mode scanning condition of $v_{scan} = 2.26$ m/s, were calculated and plotted in **Fig.4.2**.

Figure 4.2. Normalized spatial frequencies of forward and backward SWs with respect to the SW velocity when $v_{scan} = 2.26$ m/s.

It can be seen that both ξ_F and ξ_B decreased from an infinite large with respect to the v_S when $v_S < v_{scan}$. Then ξ_F reached its minimum value zero at $v_S = v_{scan}$. When $v_S > v_{scan}$, the ξ_B continued the downtrend while the ξ_F started increasing with respect to the v_S . In addition, ξ_F and ξ_B were symmetric to $1/v_{scan}$ (0.44 s/m) when $v_S > v_{scan}$. According to **Fig. 4.2**, in order to separate ξ_F and ξ_B , **Eq. (4.10)** should be satisfied:

$$\min\{\xi_B\} \geq \max\{\xi_F\}, \quad (4.10)$$

When $v_{scan} = 2.26$ m/s, this condition was satisfied in the v_S range of $1.02 \text{ m/s} \leq v_S \leq 10 \text{ m/s}$, as illustrated in **Fig. 4.3(a)**. Thus the **BPF_{spatial}** could be designed to retrieve ξ_B accordingly, as illustrated in **Fig. 4.3(b)**. The lower and higher spatial cut-off frequencies were calculated 0.54 s/m for $v_S = 10$ m/s, and 1.42 s/m for $v_S = 1.02$ m/s, respectively, by using **Eq. (4.9)**.

Figure 4.3. (a) The dispersion of normalized spatial frequencies of forward and backward SWs. (b) The coverages of normalized spatial frequencies of forward and backward SWs when $1.02 \text{ m/s} \leq v_s \leq 10 \text{ m/s}$. $v_{scan} = 2.26 \text{ m/s}$.

It should be noted that for most of the soft tissues, their v_S was in the range from 1 m/s to 10 m/s [86]. Since our ultrasound system of which v_{scan} is 2.26 m/s was capable of measuring v_S from 1.02 m/s to 10 m/s, the proposed measurement method of SW velocity was applicable to characterize most of soft tissue materials.

4.2.3. Selection of Shear Wave Frequency

In order to observe the waveform of V_B along z -direction without aliasing, the spatial sampling interval given by Δz needs to satisfy the Nyquist sampling theorem expressed by **Eq. (4.11)**. Therefore the highest applicable f_S was limited and expressed by **Eq. (4.12)**.

$$\Delta z < \frac{1}{2} \cdot \frac{2\pi}{k_B}, \quad (4.11)$$

$$f_S < \frac{1}{2 \cdot \Delta z \left(\frac{1}{v_S} + \frac{1}{v_{scan}} \right)}. \quad (4.12)$$

In addition, in order to accurately determine the spatial frequency of V_B , it was desirable that the FOV in z -direction (FOV_z) contained at least one full period/wavelength (λ_B) of the measured waveform of V_B . This restriction was expressed in **Eq. (4.13)**. Therefore the lowest applicable f_S was limited as expressed by **Eq. (4.14)**.

$$\lambda_F \leq FOV_z, \quad \text{where } \lambda_B = \frac{2\pi}{k_B}, \quad (4.13)$$

$$f_S \geq \frac{1}{FOV_z \cdot \left(\frac{1}{v_S} + \frac{1}{v_{scan}} \right)}. \quad (4.14)$$

For v_S ranging from 1.02 m/s to 10 m/s, according to our measurement conditions of $\Delta z = 315 \mu\text{m}$, $FOV_z = 40 \text{ mm}$, and $v_{scan} = 2.26 \text{ m/s}$, the restriction of the f_S with respect

to the v_S was calculated and plotted in **Fig. 4.4**. The upper limits of f_S calculated by **Eq. (4.12)** were indicated by dash-line and the lower limits calculated by **Eq. (4.14)** were indicated by solid-line for each v_S . Therefore, the highest f_S should be less than 1115.6 Hz when $v_S = 1.02$ m/s in **Eq. (4.12)**, and the lowest applicable f_S was 46.1 Hz (inclusive) when $v_S = 10$ m/s in **Eq. (4.14)**. As discussed in **Chapter 3**, the highest f_S that was obtained by using V_F is 2847 Hz (refer to **Fig. 3.4**). Although the highest f_S obtained for V_F was about 2.6 times greater than that obtained for V_B , the preferred f_S range for a SW measurement for soft tissue characterization was typically from 100 Hz to 1000 Hz due to the significant attenuation of SW at higher frequencies. Thus the applicable range of f_S with V_B in this modified measurement model was still wide enough for v_S measurements for the soft tissue characterization.

Figure 4.4. The highest and lowest applicable SW frequency with respect to shear wave velocity.

4.3. Experiment

4.3.1. Experimental Configuration

A soft tissue mimicking phantom was fabricated for the experiments to verify the modified v_s measurement model and method. **Fig. 4.5** presents a structure of the phantom, its photograph of top surface at the x - z plane, and its B-mode ultrasound image at $y = 0$. The phantom was composed with a relatively soft surrounding body (as a background area) and a relatively stiffer inclusion. The background was made by 5-W% gelatin in water and shaped to a cube with a side length of 50 mm. The stiffer inclusion was made by 2-W% agar in water and shaped to a cylinder with a diameter of 20 mm and the length of 50 mm. 2-V% isopropanol (70% purity) was added to both parts to prevent bacteria growth. The graphite particles with a nominal diameter of 50 μm were dispersed in each part as ultrasound scatterers. The tactile feeling of the inclusion part was stiffer than that of the background part. The inclusion part was first made and shaped. It stood on the center of a cubic mould along the y -direction. Then, the dissolved gelatin solution for the surrounding part was poured into the cubic mould around the cylindrical inclusion part. The phantom was kept in a fridge for more than 24 hours to solidify.

The experimental configuration was depicted in **Fig. 4.6**. A thin Plexiglas plate with a size of 10-mm square was contacted onto the side surface of the phantom as a SW vibration source. The square plate was connected to an acoustic speaker through an L-shaped rigid plastic rod, and the speaker was driven continuously at 230 Hz during the experiment. The ultrasonic probe was attached on the top surface of the phantom. The

SW was induced toward the negative z -direction and the B-mode scanning direction was toward the positive z -direction as shown in **Fig. 4.1**.

Figure 4.5. A structure (top left), photograph (top right), and B-mode ultrasound image (bottom) of the phantom fabricated.

Figure 4.6. Experimental configuration.

4.3.2. Experimental Result

The filtered V_B obtained at a specific B-mode frame was shown in **Fig. 4.7(a)**. The waveform profile of the V_B at the centerline along the z -direction (indicated by the dash-line in **Fig. 4.7 (a)**) was also shown in **Fig. 4.7(b)**. It can be seen that the SW wavelengths of the inclusion area (from $z = -10$ mm to $z = 10$ mm at $x = 0$) were greater than those of the background area. **Figure 4.7(c)** represents the spatial frequency spectrum of the filtered V_B in **Fig. 4.7(b)**. The $BPF_{spatial}$ in **Eq. (4.4)** was designed accordingly as described in **Section 4.2.2**, which covered a v_S range from 1.02 m/s to 10 m/s.

Figure 4.7. Measurement results of (a) filtered backward SW (V_B) in the phantom, (b) profile of SW waveform on the centerline as indicated in (a), and (c) the normalized spatial frequency spectrum of filtered backward SW (V_B) at centerline.

The v_S of the phantom was calculated by using **Eq. (4.7)**. The result of v_S image was averaged with 180 frames. The v_S map was shown in **Fig. 4.8(a)**. Any v_S value calculated outside the range of 1.02 m/s to 10 m/s would be considered invalid and blackened out with N/A notation in **Fig. 4.8(a)**. A median filter was applied on the v_S image to remove outlier results. The mean value of v_S of the inclusion area was calculated inside the ROI as indicated by the 10-mm radius dash circle in **Fig. 4.8(a)**. The N/A values were excluded from the calculations. The mean value of the v_S in the inclusion area was 4.4 m/s and the STD was 1.7 m/s, and the values of the background (the area outside the dash circle) were 1.9 m/s and 0.36 m/s, respectively. The v_S image was superimposed onto the B-mode image in **Fig. 4.8(b)**. The v_S image contrast between two areas had a good agreement with its physical structure as seen in the B-mode image. The v_S of the relatively stiffer inclusion was 2.3 times greater than that of the relatively softer background.

Figure 4.8. (a) Measurement result of SW velocity, dash circle indicated the area of the inclusion used to determine the mean value of the SW velocity. (b) A superposition of B-mode image and SW velocity.

4.4. Discussions

4.4.1. Numerical Validation of Phantom Experiment

It was seen that the values of v_S were greater around $z = 0$ and ± 5 mm than the v_S mean value of the inclusion. This could result probably from a calculation error in the Hilbert transform. Validation was conducted by using numerical simulation. The simulation mimicked the phantom experiment as presented in **Section 4.3.1**, and constructed numerically a stiffer 10 mm-radius circular inclusion with softer background, with SW induced toward negative z -direction. The v_S of inclusion was assumed 5.2 m/s and that of the background was 1.8 m/s. These v_S values were used to simulate V_F and V_B waveforms using **Eqs. (4.2)** and **(4.3)**, respectively. These v_S values were used in the simulation since they would yield similar calculation results as obtained from the experiment (see below). The f_S , v_{scan} , FOV, and $BPF_{spatial}$ were the same as those used in the experiment. The simulation results corresponding to the experimental results in **Fig. 4.7** were presented in **Fig. 4.9**. Then the v_S image calculated from the simulated V_B in **Fig. 4.9(a)** was given in **Fig. 4.10**.

Figure 4.9. Simulation results of (a) filtered backward SW (V_B), (b) profile of SW waveform on the centerline as indicated in (a), and (c) the normalized spatial frequency spectrum of filtered backward SW (V_B) at centerline.

Figure 4.10. (a) SW velocity that calculated from the simulation, and (b) the difference between the calculation result and actual value of the SW velocity. Dash-circle indicated the area of the inclusion used to determine the mean value of the SW velocity.

The v_S calculated in this simulation was presented in **Fig. 4.10(a)**. The dash-circle was the ROI that indicated the inclusion area. It was $4.4 \text{ m/s} \pm 0.72 \text{ m/s}$ (mean value $\pm$ STD) in the inclusion area and $2.0 \pm 0.28 \text{ m/s}$ in the background. The difference between the calculated v_S and its assumed value (calculated $v_S - \text{assumed } v_S$) was presented in **Fig. 4.10(b)**. It can be seen that the pattern of the calculated v_S in the inclusion area had a remarkable variation/fluctuation along z -direction, and great deviations were also found at the boundaries and edges in **Fig. 4.10(b)**. This was possibly due to the calculation error from the Hilbert transform. Consequently, the mean value of the calculated v_S (4.4 m/s) was 0.8 m/s less than its assumed value (5.2 m/s) in the inclusion area. A comparison between the experimental and simulation results were listed in **Table 4.1**.

Table 4.1. Comparison between experimental and simulation results.

	Experimental Results of v_S (m/s)			Simulation Results of v_S (m/s)		
Phantom Part	Actual Value	Calculation Results		Actual Value	Calculation Results	
		Mean Value	STD		Mean Value	STD
Inclusion	N/A	4.4	1.7	5.2	4.4	0.72
Background	N/A	1.9	0.36	1.7	2.0	0.28

The tendency of the variation/fluctuation in the v_S calculated from the inclusion area in **Fig. 4.10(b)** generally matched with that of the experimental result in **Fig. 4.8(a)**, yet the STD of the experimental result (1.7 m/s) was about 2.5 times greater than that of the simulation (0.72 m/s). This could be a result from the combination of SW absorption, diffraction effect, and refraction [19], [35], [96]. Since those factors were rather complex, they were not implemented into the simulation. In addition, the spatial resolution of the v_S

measurement in z -direction was limited by the SW wavelength. Nevertheless, the modified measurement method of v_S could still distinguish materials with the size at centimeter-level and provide reasonable v_S values. Comprehensive study on SW propagation with a complex geometric condition could be an interest topic for future research.

4.4.2. Influence of Shear Wave Reflection on Shear Wave Velocity Measurement

The influence of SW reflection on the measurement of v_S was investigated by a numerical simulation in this section. A waveform of interfered SW signals V was simulated by using **Eqs. (4.1), (4.2) and (4.3)** with $v_{scan} = 2.26$ m/s, $v_S = 2, 4, 6, 8$ m/s, and $f_S = 227$ Hz. The FOV_z was 40 mm (from $z = -20$ mm to $+20$ mm). An amplitude ratio between the reflected SW (V_F) and induced SW (V_B), as defined by A_F / A_B , was changed from 0 (no reflection) to 1 (V_F has the same amplitude as V_B). Then v_S was calculated from **Eqs. (4.4)-(4.7)**.

In the first simulation, the ***BPF_{spatial}*** was substituted by an all-pass filter, which means the removal of the reflection had not been implemented. The mean value and STD of the estimated v_S were calculated within a ROI from -10 mm to +10 mm. The results with respect to the amplitude ratio were shown in **Fig. 4.11**. In this figure, the errors were plotted as percentage, defined by: $[(\text{estimated } v_S - \text{actual } v_S) / \text{actual } v_S \times 100\%]$. The error bar indicated the $\pm$ STD. Note that the ROI was determined to avoid the relatively greater v_S estimation error at the edge regions due to the calculation error of the Hilbert

transform. From the results in **Fig. 4.11**, the error and STD of the calculated v_s were increased with respect to the amplitude ratio for all assigned v_s values. In addition, the calculated v_s went beyond twice of its actual value (more than 100% error) when the amplitude ratios were greater than 0.6 for all the simulations. Therefore, such investigation indicated that measuring the v_s without the removal of the undesired reflection would possibly lead to great errors.

Figure 4.11. Estimation error of SW velocity without using the spatial frequency filtering. Error bar indicated the +/- standard deviation.

Now in the second simulation, $BPF_{spatial}$ was applied to investigate the effectiveness of the $BPF_{spatial}$ to remove the influence of SW on v_s estimation. The $BPF_{spatial}$ was designed as described in **Section 4.2.2**. The results of estimated v_s with $BPF_{spatial}$ were shown in **Fig. 4.12**. It can be seen that the errors were much smaller than the results without $BPF_{spatial}$ in **Fig. 4.11**. The mean errors were within $\pm 2\%$ for all the

amplitude ratio range from 0 to 1, and the STD values were within $\pm 5\%$. Therefore, the effectiveness of $BPF_{spatial}$ was verified by this investigation.

Figure 4.12. Estimation error of SW velocity with using the spatial frequency filtering. Star-dash-line represented the simulation with actual $v_s = 2$ m/s, while square-dash-line represented 4 m/s, triangle-dash-line represented 6 m/s, and circle-dash-line represented 8 m/s.

4.5. Summary

In this chapter, the shortcoming (prior knowledge of the relationship between the SW velocity and B-mode scanning speed) of the SW velocity measurement method proposed in **Chapter 3** had been addressed. In the modified measurement method, SW was induced into a specimen opposite to the B-mode scanning direction. Phantom experiment and numerical simulations were conducted to verify the modified method. Thesis **Objectives 1** in **Section 1.3** had been accomplished by the research presented in this chapter.

Chapter 5

A Method to Reduce Motion Artifacts

5.1. Introduction

In practical *in-vivo* experiments of SW measurements studied in this thesis, an ultrasound scatterer in tissues and tissue boundaries could experience motions from multiple sources, in addition to the SW propagation, such as the motions caused by the experimental environment, handheld probe movement, voluntary or involuntary muscle contraction, as well as the passive motions caused by the heart beat and respiration. Since some of the undesired motions may be unavoidable, they could influence the accurate measurement of the SW displacement.

For measurement with external SW vibration source, increasing the SW source power to induce the greater SW amplitude may be one solution since it would help to get better SNR of the SW amplitude. However, this may bring discomfort to the patient. Therefore, the smaller SW vibration would be desirable. For measurement with radiation force, amplitude of the SW was much smaller than that generated from the external source. With the radiation force technique, a motion filtering method was commonly applied to reduce the motion artifacts [97], [98]. The tissue displacement caused by the cardiac and respiratory motions could be filtered out, since their frequencies were consistent and measureable. On the other hand, the displacement due to the experimental

random noises could be reduced by averaging the measured displacements among multiple scans [22], since those motions were considered to be non-coherent over scans. However, unexpected movement of the patient and/or probe may still exist. It was also found that if the measurement time could be shortened, the chance to have body and/or probe movements would be reduced. Therefore, the supersonic shear imaging technique [16], [22], [99] could effectively prevent the influence of any type of motion artifacts because of its ultra-short acquisition time. Nevertheless, those solutions were not applicable to our ultrasound system and proposed SW measurement method. Therefore, a method to reduce the motion artifacts was developed based on our ultrasound system and method in this chapter. Phantom experiment and numerical simulation were presented to verify the proposed method.

5.2. Methodology

In this study, displacement caused by the undesired motion (V_{MA}) from all the sources other than SW displacement (V) was termed as motion artifact. The tissue displacement along x -direction defined in **Fig. 2.3**, u_x in the temporal domain was described by **Eq. (5.1)**. It was assumed that each undesired motion had its own temporal frequency denoted by f_{MA} .

$$u_x(t) = V(t) + V_{MA}(t). \quad (5.1)$$

On one hand, motion artifacts arose from experimental environment. Excitations such as an air flow from the venting system, and/or a passing-by vehicle near the building, would possibly result in resonance vibrations to the laboratory where the experiment was

taken place. These undesired motions would be conveyed into the specimen through the measurement platform and lead to undesired tissue displacements. Practically, the f_{MA} of such motion artifact can be obtained through a phantom experiment without applying SW. Since phantom did not move by itself and all the motion frequencies obtained in the phantom experiment were considered as the motion artifacts from experimental environment. The value f_{MA} was considered a constant among different experiments as long as the experiment was always taken place at the same experimental setup. This was because f_{MA} represents the frequency of the resonance vibration and/or its harmonics, which was subject to the nature of the architectural structure and material of the building.

On the other hand, motion artifacts also can be generated by a patient and an operator of ultrasound system, such as the unavoidable body/organ movements of the patient and the probe movement if it was handheld by the operator. Although the occurrence and duration of those movements were unpredictable, the frequencies of common physiological activities, such as the muscle and organ motions, were relatively low and assumed to be measureable by our ultrasound system without aliasing.

As a result, the f_{MA} could either be measured or be predicted, thus the SW displacement can be ideally isolated from those motion artifacts by using a temporal frequency filter on the measured tissue displacement, as long as the f_S was separable from the f_{MA} of those motions. However, the temporal frame rate (f_{FR}) of the B-mode scanning was 30 Hz in our experiment, while the employed f_S was typically above 30 Hz. The temporal sampling of the SW displacement with such f_{FR} belonged to an undersampling, which means, from the frequency spectrum analysis, the measured f_S (termed $f_{measured}$) was aliased. Mathematically, the relationship between $f_{measured}$ and f_S with respect to f_{FR}

was expressed by **Eq. (5.2)** [100]. More descriptions on undersampling were given in the **Appendix C**.

$$f_{measured} = |n \cdot f_{FR} - f_S|, \quad (5.2)$$

where n is the closest integer multiple to make $f_{measured}$ less than the Nyquist frequency ($1/2f_{FR}$).

Therefore, the method to reduce the motion artifact was designed based on a temporal frequency filtering technique. The flowchart of the processing procedure for such task was depicted in **Fig. 5.1**.

Figure 5.1. Flowchart of signal processing procedure to reduce the motion artifact.

First, the f_{MA} was estimated, and then f_S was intentionally assigned to a specific value to avoid the $f_{measured}$ being overlapped with any of the applicable f_{MA} . Next, a temporal bandpass filter ($BPF_{temporal}$) was designed to retrieve the signals at $f_{measured}$. Finally, by applying such filter on the observed displacement u_x with respect to the t over all the locations in FOV, the displacement caused by the motion artifact would be reduced and the SW displacement V will remain. Such process was expressed by **Eq. (5.3)**, and after this process, v_S would be calculated through **Eqs. (4.4)-(4.7)** as presented in **Chapter 4**.

$$V(t) = BPF_{temporal}\{u_x(t)\}. \quad (5.3)$$

It should be noted that the ultrasound probe only acquired signal along x -direction according to the experimental setup, thus theoretically the $BPF_{temporal}$ was effective to those displacements that occurred on x -direction.

5.3. Experiments

In order to verify the proposed method of motion artifact reduction, a phantom experiment was conducted. A soft tissue mimicking phantom was fabricated according to **Section 3.3.2** by using 2-W% agar, 2-V% isopropanol (70% purity), and 2-W% fine graphite particles. Ultrasound system and SW source used for the experiment were the same as those presented in **Chapter 4**.

Three measurement procedures were included in this experiment in order to conduct the motion artifact reduction. The first procedure was to detect the motion artifact caused by the measurement environment. The experimental configuration was

seen in **Fig. 5.2(a)**. The phantom was placed on a stable stage on an experimental table, while the ultrasound probe was held by a positioning device stably placed on the same table. No SW was introduced in this measurement, thus it was assumed that there was no relative movement between the probe and the phantom. Therefore, all the detected displacements, if applicable, would be considered as the motion artifact of the experimental environment, so the f_{MA} from the environment could be found through this experiment.

The second procedure was to introduce the motion artifact intentionally caused by the human body movement. The experimental configuration was seen in **Fig. 5.2(b)**. The ultrasound probe was held by a hand with no SW introduced. The handholding could cause unpredictable motions during the 6-second-long measurement, so such design was used in experiment to simulate an *in-vivo* condition where undesired patient/probe movement existed. Although the movement due to the hand-holding would not be identical among different measurements, it was assumed that the frequency range of the movement due to the hand-holding could be similar. Therefore, the f_{MA} of the hand-holding could be roughly estimated through this measurement.

The third procedure was to measure the v_S . Ultrasound probe was held by hand in this measurement, and SW source was placed on the experimental table stably and the Plexiglas plate was contacted with the phantom and driven continuously by sinusoidal signal. The experimental configuration was seen in **Fig. 5.2(c)**. Motion artifact was reduced according to the procedures presented in **Fig. 5.1**, and v_S was estimated by using the modified v_S measurement method presented in **Chapter 4**. It should be noted that the experiment was conducted under the room temperature (around 20 °C), and it was

assumed that there were no v_s changes due to temperature variation caused by the hand-holding.

Figure 5.2. Experimental configuration for motion artifact reduction: (a) test without SW in a stage-holding probe design, (b) test without SW in a hand-holding probe design, and (c) SW velocity measurement in a hand-holding probe design.

5.4. Experimental Results

5.4.1. Motion Artifact Due to Experimental Environment

Temporal frequency response of the tissue displacement in the first measurement procedure was obtained and averaged in the entire FOV. The result of the frequency spectrum was plotted in **Fig. 5.3**.

Figure 5.3. Temporal frequency spectrum of the first measurement procedure in which SW was not applied, and ultrasound probe was held by the positioning device.

Two noticeable frequencies of 6 Hz and 12 Hz, and a zero frequency offset, were observed in **Fig. 5.3**. These frequencies were considered to be the f_{MA} arising from the experimental environment of our laboratory. It should be noticed that these frequencies could be actual frequencies or aliased frequencies if the actual frequencies of the motions were greater than 15 Hz (as the Nyquist frequency of our system).

5.4.2. Motion Artifact Due to Handheld Probe

Temporal frequency response of the tissue displacement in the second measurement procedure was obtained and averaged in the entire FOV. The result of the frequency spectrum was plotted in **Fig. 5.4**. The scale of the magnitude in this figure was the same as that of **Fig. 5.3**.

Figure 5.4. Temporal frequency spectrum of the second measurement (SW was not applied, ultrasound probe was hand held).

The overall spectrum magnitude observed in **Fig. 5.4** was stronger than that observed in **Fig. 5.3**, and the f_{MA} in **Fig. 5.4** covered the entire measurement range from 0 to 15 Hz. Lower frequency components showed relatively stronger magnitudes than those in higher frequencies.

Based on the result in **Fig. 5.3**, f_S and the passband of the $BPF_{temporal}$ can be decided. The f_S was set to 227 Hz, which would result in an $f_{measured}$ of 13 Hz with $n = 8$.

Then the $BPF_{temporal}$ with a passband of 12.5 Hz to 14 Hz was designed, since no remarkable f_{MA} in **Fig. 5.3** was found and a relatively weaker magnitude in **Fig. 5.4** was observed above 12 Hz. It should be also noted that 227 Hz was selected because the amplitude of SW at such frequency was found stronger in our SW source, while the amplitudes of most other qualified frequencies may be too weak to be detected in practice.

5.4.3. Shear Wave Velocity Measurement

Temporal frequency response of the scatterer displacement in the third measurement procedure was obtained and averaged in the entire FOV. The result of the frequency spectrum was plotted in **Fig. 5.5**. The scale of the magnitude in this figure was the same as that of **Fig. 5.3** and **Fig. 5.4**.

Figure 5.5. Temporal frequency spectrum of the second measurement (SW was applied, ultrasound probe was hand held).

The $f_{measured}$ was observed at 13.7 Hz, which was slightly different from the setting value of 13 Hz ($f_{FR} = 30$ Hz and $n = 8$ in **Eq. (5.2)**). This was probably because small deviations existed between the set and actual value of f_s in the practical experiment. Nevertheless, such value was still within the passband of $BPF_{temporal}$ (12.5 Hz to 14 Hz), so it would not affect the following calculations.

The motion artifact was reduced by using **Eq. (5.3)** with the $BPF_{temporal}$ and the SW displacement V would be obtained. An example of the observed SW displacement V was shown in **Fig. 5.6(a)**. The displacement along z -direction at the centerline ($x = 0$), indicated by the white dash-line in **Fig. 5.6(a)**, was plotted in **Fig. 5.6(b)**, and its spatial magnitude spectrum was shown in **Fig. 5.6(c)**. In **Fig. 5.6(c)**, two frequency components corresponding to V_F and V_B were noticed. The $BPF_{spatial}$ was designed by following **Section 4.2.2**, and then the V_B was retrieved from V by the spatial frequency filtering. The filtered results were shown in **Figs. 5.6(d)-(f)**.

If the process of motion artifact reduction was not applied, both V and V_B would contain more noise/error information, as presented in **Figs. 5.7(a)-(f)** with regard to **Figs. 5.6(a)-(f)**, respectively.

The v_s estimated with and without the reduction of motion artifact were presented in **Figs. 5.8(a)** and **(b)**, respectively. Both results were averaged with 180 frames. The mean value of the v_s in the ROI (as indicated by the dash-box) of **Fig. 5.8(a)** was calculated at 5.91 m/s with a STD of 0.63 m/s, and those of **Fig. 5.8(b)** were 2.55 m/s and 0.37 m/s, respectively.

Figure 5.6. Observed SW displacements (a) in the entire FOV and (b) along z -direction at centerline ($x = 0$), and (c) magnitude spectrum of (b). And filtered SW displacements (d) in the entire FOV and (e) along z -direction at centerline, and (f) magnitude spectrum of (e). Results above were obtained with the reduction of motion artifact.

Figure 5.7. Observed SW displacements (a) in the entire FOV and (b) along z -direction at centerline, and (c) magnitude spectrum of (b). And filtered SW displacements (d) in the entire FOV and (e) along z -direction at centerline, and (f) magnitude spectrum of (e). Results above were obtained without the reduction of motion artifact.

Figure 5.8. Results of SW velocity (a) with motion artifact reduction process, and (b) without motion artifact reduction process.

The v_S estimated with the motion artifact reduction was consistent (5.9 m/s) with that estimated from the phantom of the same composition and structure presented in **Chapter 3**, whereas the v_S calculated without the reduction of motion artifact showed a great difference (3.36 m/s or 56.9%). In addition, the strongest SW amplitude measured in this experiment was less than 6 μm , while the amplitudes of the SW vibration in most

of the published works which used external SW source were more than 100 μm [7], [101], [102]. The smaller SW amplitude would be more desirable since it reduces the discomfort of the patient.

5.5. Discussion

The influence of the motion artifacts on the v_S measurement was investigated by numerical simulations in this section. V was simulated by using **Eqs. (4.1), (4.2) and (4.3)** with $v_{scan} = 2.26$ m/s, $v_S = 1.02$ m/s to 10 m/s, $f_S = 227$ Hz. The amplitude ratio $A_F / A_B = 1$ was used to represent a total reflection and no SW attenuation was assumed. The FOV had the same size (40 mm in length and 34 mm in depth) as that in the phantom experiments. By considering that the V_{MA} in **Eq. (5.1)** could be caused from multiple sources with different amplitudes and phases in practical experiments, it may be difficult to simulate V_{MA} objectively. Therefore, a white Gaussian noise (WGN) was used to simulate V_{MA} at any frequencies in the **Eq. (5.1)**. WGN with a SNR at 10 dB, 20 dB, and 30 dB were added into the simulations, respectively. It is noted that the values of the SNR chosen in this study may not be the actual ones in experiments. However, the purpose of the simulations was to investigate the effectiveness of the proposed motion artifact reduction method.

Two groups of simulations were conducted. In the first group, **$BPF_{temporal}$** in **Eq. (5.3)** was defined to an all-pass filter, which means the process of motion artifact reduction was not conducted. Then in the second group, the process of motion artifact reduction was conducted. The same **$BPF_{temporal}$** as used earlier in **Section 5.3** (12.5 Hz to

14 Hz) was created and applied in **Eq. (5.3)**. Then in each group, the v_s over the FOV was calculated and smoothed by median filter. The mean values from the ROI (the same as those in **Fig. 5.8**) and STD of the v_s calculated were shown in **Fig. 5.9**.

Figure 5.9. Calculated shear velocities versus to their actual values at different SNRs (a) without, and (b) with the process of motion artifact reduction, while black-dot-line represented the simulation with 10 dB WGN, Blue-dot-line represented 20 dB, and red-dot-line represented 30 dB.

Most of the mean values of estimated v_S agreed with their set value (errors were less than $\pm 5\%$ with the exception of $v_S = 1.02$ m/s and 10 m/s, whose errors were less than $\pm 30\%$) except for the simulation that used 10 dB WGN without applying the motion artifact reduction. In that simulation result the estimated v_S started to deviate from its set value when v_S was approximately greater than 6 m/s. It can be seen that at a certain v_S value and SNR, the estimated v_S had less STD when the motion artifact reduction was applied, which means there were smaller errors in the estimation. For all the simulations, the STDs became smaller as SNR gets bigger. However, it was also found that the STDs would become greater with respect to the v_S . This was because the ξ_B did not linearly change with v_S according to **Eq. (4.9)**. The change of ξ_B with respect to the v_S was calculated and shown in **Fig. 5.10**. It can be seen that the absolute gradient ($|d\xi_F / dv_S|$, as indicated by green-solid-line) of the curve was greater when v_S was lower, and *vice versa*. Therefore, with a same amount of spatial frequency change $\Delta\xi_B$, the velocity changes (Δv_S) calculated at the lower v_S value (Δv_{S_Low} , as indicated by blue-dot) were different from that calculated at the higher v_S value (Δv_{S_High} , as indicated by red-dot). The Δv_{S_Low} was less than Δv_{S_High} , which means the measurement resolution of v_S on specimens with relatively lower v_S values would be better than those of specimens with relatively higher v_S values.

Figure 5.10. The change of the normalized spatial frequency of backward wave (V_B) with respect to the SW velocity.

5.6. Summary

The research of this chapter addressed the motion artifact of the **Problem 2** in **Section 1.2**. The method of the motion artifact reduction was proposed and applied based on the modified SW velocity measurement method presented in **Chapter 4**. The SW frequency was assigned to a specific value which was different from the frequencies of the predictable motion artifact so that the motion artifacts were reduced by applying a temporal bandpass filter on the measured tissue displacements. Phantom experiment was conducted to verify the proposed method and procedure. The performance of the method was verified by the numerical simulations. Therefore, the thesis **Objectives 3** in **Section 1.3** had been accomplished by the research of this chapter.

The strongest SW amplitude measured in this experiment was less than 6 μm , while the amplitudes of the external SW vibration in most of the published works were more than 100 μm . The smaller SW amplitude would be desirable since it reduced the discomfort of the patient. The proposed method of motion artifact reduction in this chapter could be useful to lower the external SW vibration source power.

Chapter 6

***In-vivo* Measurement of Shear Wave Velocity**

6.1. Introduction

The measurement method of SW velocity was developed in the **Chapters 3-4**. A method of motion artifact reduction was proposed in **Chapter 5**, and the reduction of the motion artifacts would also enhance the accuracy of the estimated SW velocity. More importantly, such method was able to lower the external SW amplitude so that cause less discomfort to the patient. In this chapter, *in-vivo* experiments on human ankle and upper arm were conducted to demonstrate the proposed measurement methods for 2D SW velocity image.

6.2. Experimental Setups

Two *in-vivo* experiments were conducted. The first experiment was targeting at the v_s measurement on the left ankle, and the second experiment was targeting at the upper limb of the author of this thesis, respectively. Experiments were conducted with a healthy male subject (age 32, weight 75 kg).

The first experiment at ankle demonstrated the v_s measurements of different types of *in-vivo* tissues. The reason to choose the ankle was because both heel tendon and

skeleton muscle could be observed within the FOV (40 mm in length and 34 mm in depth) of the ultrasound system employed, and they would have noticeable difference in the v_S values [33], [79]. In this experiment, the leg and foot were kept relaxed. A configuration of this experiment was shown in **Fig. 6.1**. The linear ultrasound probe was held by a stage and attached to the skin above the heel tendon. The head of the plastic rod of the external SW source was in contact with the leg and about 2 cm away from the near edge of the ultrasound probe. The SW source was held by hand during the experiment and driven continuously by sinusoidal signals at 227 Hz from a signal generator. The B-mode scanning direction was from the heel to the popliteal fossa, which allowed the ultrasound probe to detect the SW propagating along the tendon and the muscle. No other intentional movements were involved during the experiment to minimize the noise.

The second experiment at upper arm demonstrated the v_S changes of *in-vivo* muscle tissues due to the muscle contraction. The muscle activity could result in stiffness change and lead to a v_S change in the target muscle. Therefore, a dynamic v_S change could be observed due to muscle contraction. To achieve this, muscles in the upper arm were contracted and relaxed during the SW measurement. In this experiment, the arm was kept flexed and placed on a flat panel of a portable stage. A configuration of this experiment can be seen in **Fig. 6.2**. The ultrasound probe was fixed on the portable stage and attached to the upper arm above the biceps. The head of the plastic rod of the external SW source was in contact with the upper arm, close to the elbow and about 5 cm away from the near edge of the ultrasound probe. The external SW source was held by a hand and driven continuously at 227 Hz. During the experiment, the upper arm was fixed (moderately clamped) by the probe and panel to minimize involuntary motions from the

body. Soft foam was placed between the panel and arm to make the arm comfortable. The B-mode scanning direction was from the shoulder to the elbow, which allowed the ultrasound probe to detect the SW propagating along the muscle fibers. At the beginning of the experiment, the bicep muscle was kept voluntarily contracted for a few seconds and then relaxed for the rest of the experiment.

Figure 6.1. A schematic (top) and photograph (bottom) of the experimental configuration of shear wave velocity measurement at ankle.

Figure 6.2. Experimental configuration of shear wave velocity measurements at upper arm.

It should be noted that the experimental configuration of both *in-vivo* experiments were not strictly the same as that of the phantom experiment presented in **Fig. 4.1**. SW source in the *in-vivo* experiments were located beside the ultrasound probe due to the limitation of the practical condition. Nevertheless, the round surface of the SW source generated SWs into a fan-shaped area (as indicated by the red ripples in **Figs. 6.1** and **6.2**), thus partial SWs would propagate through z-direction and they were observed by the ultrasound probe. The optimized location of probe and/or SW source for *in-vivo* experiment could be investigated in the future research.

6.3. Results and Discussions

6.3.1. Ankle Experiment

Temporal tissue displacements due to SW propagation were analyzed. Their temporal frequency spectrum averaged in the entire FOV was plotted in **Fig. 6.3**. The $f_{measured}$ was found at 13.7 Hz and had a 0.7 Hz shift to its expected 13 Hz estimated from the under sampling ($f_{FR} = 30$ Hz and $n = 8$ in **Eq. (5.2)**) of the SW at f_S of 227 Hz. This frequency shift was consistent with the result in **Fig. 5.5**. In order to reduce the motion artifacts and noises within the passband of $BPF_{temporal}$, the passband of $BPF_{temporal}$ was set from 13.5 Hz to 14 Hz in this chapter.

Figure 6.3. Temporal frequency spectrum averaged in the entire field-of-view. The dash-line represented the spectrum before the motion artifact reduction and the solid-line represented the spectrum after the motion artifact reduction.

The B-mode image, v_S image with an average of 180 frames, and a superposition of B-mode image and v_S image, obtained from the ankle experiment were presented in **Figs. 6.4(a)-(c)**, respectively. The Achilles tendon was observed in the region indicated by the arrows in the B-mode image in **Fig. 6.4(a)**. A clear v_S image contrast was observed in **Fig. 6.4(b)** so that the v_S were different between tendon tissue and muscle tissue. Two ROIs indicated by upper and lower white dash-boxes in **Fig. 6.4(b)** included the tendon tissue and muscle tissue, respectively. The estimated v_S values below 1.02 m/s or above 10 m/s were considered as calculation error, and thus they were blackened and noted as N/A in **Fig. 6.4(b)**. The averaged v_S at the ROI of the tendon tissue was calculated 4.6 m/s with a STD of 1.7 m/s, and those of muscle tissue were 2.5 m/s and 0.75 m/s, respectively. The v_S of tendon tissue was 2.1 m/s (46%) greater than that of muscle tissue. From **Fig. 6.4(c)** it can be seen that the v_S image contrast had a good correlation with the anatomical structure observed in the B-mode image. It is noted that the value of the v_S dropped at the edges of the tendon area. This could be due to the calculation errors from the Hilbert transform.

Figure 6.4. Results of ankle experiment: (a) B-mode image, (b) SW velocity image, and (c) a superposition of B-mode image and SW velocity image. Arrows indicated the Achilles tendon.

In order to investigate the stability of the v_S measurements during the measurement time of 6 seconds, the mean values of the v_S in the both tendon and muscle tissues, as indicated by the ROIs in **Fig. 6.4(b)**, were calculated and averaged with every 10 consecutive frames. For instance, v_S at frame #90 was an average result of frames from #86 to #95. The results were plotted in **Fig. 6.5** with respect to the frames. The results in tendon area were plotted in **Fig. 6.5(a)** and those in muscle area were plotted in **Fig. 6.5(b)**.

Figure 6.5. The change of the mean value of the SW velocity with respect to the temporal frames within the ROIs as indicated by the dash-box in **Fig. 6.4(b)**. The result in the ROI of tendon was plotted in (a) and that of muscle was plotted in (b).

From **Fig. 6.5** it can be seen that the v_s variation (twice of the STD) in **Fig. 6.5(a)** was 0.17 m/s and that in **Fig. 6.5(b)** was 0.24 m/s based on the 10-frame averaging. Averaging the v_s result with more temporal frames could be a selection to further improve the measurement accuracy. The v_s difference between tendon and muscle tissues was consistent throughout the SW measurement.

Although the v_s contrast between different tissues was observed in the v_s results, it should be noticed that these estimated values of v_s were relatively less than some published results [33][79]. This was possibly because a practical $BPF_{spatial}$ applied on the spatial signal was not an ideal rectangular filter, so transition zones existed around the cut-off frequencies in its spatial frequency domain. If the spatial frequency corresponding to the v_s was located in the transition zone of the filter, it may be removed or attenuated by the $BPF_{spatial}$ unexpectedly. Thus the estimated v_s from the filtered V_B may experience

bias to its actual value. A frequency-domain filtering technique could potentially help to avoid such concern, and a brief analysis with such technique was discussed in **Appendix D**.

It was also noted that according to the discussion in **Section 5.5**, the absolute accuracy of the estimated v_S could be varying among different tissues depending on the SNR within the $BPF_{spatial}$. Further study on the absolute accuracy of the estimated v_S with the SNR could be a future research topic.

6.3.2. Upper Arm Experiment

In the upper arm experiment to monitor v_S change of muscle due to muscle contraction, an alternative $BPF_{spatial}$ was assigned based on the frequency-domain filtering technique (see **Appendix D**). The passband of the alternative $BPF_{spatial}$ was set from 0.54 m^{-1} to 0.94 mm^{-1} in order to measure v_S between 2 m/s and 10 m/s since the v_S values of muscles were typically in this range [21], [99], [101], [103]. Making the passband narrower helped to remove more noises, and thus improve the SNR of desired SW signals. B-mode image, observed SW displacement, filtered SW displacement, and v_S image, respectively, at the selected frames #10 (0.3 seconds), #50 (1.7 seconds), #90 (3.0 seconds), #130 (4.3 seconds), and #170 (5.7 seconds), were shown in **Figs. 6.6(a)-(d)**, respectively. The v_S image presented at each frame was averaged over every 10 consecutive frames.

The mean value of the v_S in ROI, indicated by the dashed-rectangular in **Fig. 6.6(d)**, were calculated at each frame, and plotted in **Fig. 6.7**.

Figure 6.6. Results of arm measurement: (a) B-mode image, (b) observed SW displacement, (c) filtered SW displacement, and (d) SW velocity image. Dash-boxes in (d) were the ROIs to indicate the bicep muscle. Those results at frame #10 (0.3 seconds after the start of the measurement), #50 (1.7 seconds), #90 (3.0 seconds), #130 (4.3 seconds), and #170 (5.7 seconds) were illustrated from top to bottom.

Figure 6.7. The change of the mean value of the SW velocity within the ROI in **Fig. 6.6(d)** with respect to the temporal frames.

It can be seen that the mean value of v_s at bicep muscle was estimated above 5 m/s between frame #50 and #90 (as highlighted in **Fig. 6.7**), which was within the duration that the muscle was voluntarily contracted (approximately before frame #100). This value became 4 m/s to 4.5 m/s when the muscle was totally relaxed (approximately after frame #110). These results were close to the published results of contraction-relax measurement with bicep muscle [99], [101]. However, it was also noticed that the v_s estimated before frame #50 (when the muscle should be still contracted) had the similar value as those estimated when the muscle was relaxed. This may be because of the inconsistency of the muscle area voluntarily contracted during the experiment. Nevertheless, the v_s change due to muscle contraction was dynamically observed with the

proposed SW measurement method in **Fig. 6.7**, according to the results of the v_S measurement stability at the relaxed muscle in **Fig. 6.5**.

6.4. Summary

In this chapter, the *in-vivo* experiments of SW velocity image were conducted using the SW velocity measurement method proposed in this thesis. The SW velocity difference between the muscle and tendon tissues at ankle was clearly observed. In addition, the change of the SW velocity of bicep muscle at upper arm due to muscle contraction was dynamically observed by using the proposed method. Since the SW velocity was related to the tissue stiffness which may reflect the tissue health, the proposed measurement method could be used to diagnose the muscle injury, and/or to evaluate the muscle strength/health level [12], [65], [67], [99], [104]. The measurement reproducibility could be improved with a stronger SW source which produces SWs with the better SNR. However, the patient discomfort may increase.

Chapter 7

Measurement of Shear Wave Absorption with Correction of the Diffraction Effect

7.1. Introduction

Shear elasticity and viscosity are two important parameters to characterize the mechanical properties of soft tissues. The methods to estimate the shear elasticity had been already implemented in some of commercial ultrasound imaging devices, while the viscosity measurements were still in research stage.

As described in **Chapter 2**, viscosity can be estimated either by an analysis on the dispersion of SW velocity with multiple SW frequencies, or through measuring both the SW velocity and absorption at a chosen frequency. There were various demonstrations to estimate the soft tissue viscosity by SW velocity dispersion analysis [17], [20], [76], [99], [105]. The advantage of such method was that it avoided the direct measurement of SW absorption, which was rather challenging to measure precisely. However, the dispersion method requires multiple measurements at different frequencies to determine the SW velocity dispersion unless using an impulse SW having a broad frequency bandwidth with a high frame-rate system [99]. The proposed SW measurement method in this thesis used a continuous SW at a chosen frequency. Thus the dispersion method required multiple measurements with our system used in this thesis. However, the prolonged

measurement time may not be desired since it could increase the patient discomfort and the difficulty of the measurement reproducibility. Therefore, it was preferable to measure SW velocity and absorption simultaneously with a single same experiment.

In this chapter, a measurement method of SW absorption was proposed based on the SW attenuation measurement with a compensation of diffraction effect using the same measurement configuration of the SW velocity presented in **Chapters 3, 4, 5** and **6**. Since precise measurement of SW absorption for a 2D absorption image was rather challenging, the objective of this chapter was to develop a measurement method to estimate an averaged SW absorption of the entire specimen. Therefore, it was assumed that a specimen was homogenous and isotropic. Although the proposed method in this chapter remained in a preliminary stage, it could provide a reference value of SW absorption of soft tissue. Such information could be useful for some clinical applications, such as a biopsies.

7.2. Methodology

7.2.1. Measurement Model of Shear Wave Absorption

SW attenuation was represented by the amplitude loss of a SW propagating a certain distance. When a SW propagation medium was homogenous and had an infinite size, the absorption, scattering and diffraction effect were the main factors of the SW attenuation. If the propagation medium had a finite size or had boundaries, additional factors such as reflection and mode conversion also changed the SW amplitude. In order to

experimentally estimate the absorption from the measured SW attenuation, these factors needed to be taken into account.

In this chapter, it was assumed that a tissue specimen was homogenous and isotropic, and had a finite size. With these assumptions, scattering effects and conversion were negligible in our measurement configuration (to be discussed later). In addition, the SW reflected at the edge of the specimen can be removed by the method using a B-mode scanning time delay proposed in **Chapters 3 and 4**. Therefore, the absorption and diffraction were the main factors of the SW attenuation. The absorption converted the SW mechanical energy to heat [106]. The diffraction effect made an induced SW a divergent wave rather than a plane wave. It was also known that the diffraction nonlinearly affected the amplitude change in the spatial domain.

Figure 7.1 showed the SW absorption measurement configuration which was the same as the one used in SW velocity measurement in **Fig. 4.1**, except two modifications made in the measurement coordinate system. The origin of the coordinate system was moved to the center of the interface between the SW source and the specimen, and the direction of z -axis was the same as that of the backward SW. As discussed in **Chapter 4**, the induced SW displacement $V_i(z)$ can be retrieved from the observed SW displacement $V(z)$ using the B-mode scanning time delay.

Figure 7.1. Measurement model of SW absorption.

According to the theory of Rayleigh scattering [107], [108], the amplitude of the scattered wave was proportional to the inverse fourth power of the wavelength and the sixth power of the scatterer's radius (assuming that the scatterer can be considered as spherule). Under a practical condition, the SW wavelength $\lambda_s (= v_s / f_s)$ was usually in a few centimeters, while the size of the scatterer in soft materials was usually as small as a few to a few tens of micrometers (e.g. the nominal diameter of graphite particle used in the phantom was 50 μm). So the size of scatterer was much less than the wavelength. Therefore, the scattering effect was considered to be negligible.

The energy of a propagated SW would be reduced due to a mode conversion when such wave experienced a reflection. However, even though a reflection may happened at the top and/or bottom edge of the specimen if the induced SW was diverged due to diffraction, it would only lead to a negligible energy loss to the V_I from mode conversion (see **Appendix A**). Therefore, such factor was also neglected.

According to the measurement configuration in **Fig. 7.1**, the induced SW $V_I(z)$ was expressed by **Eq. (7.1)**. Noted that the **Eq. (7.1)** was equivalent to the backward SW $V_B(z)$ as presented by **Eq. (4.3)** in **Chapter 4**. The variation of amplitude $A_I(z)$ with respect to the z -direction was used to determine the SW absorption α_S of a viscoelastic tissue at a chosen frequency. $A_I(z)$ was expressed by **Eq. (7.2)**.

$$V_I(z) = A_I(z) \cos \left[-\omega_S \left(\frac{1}{v_S} + \frac{1}{v_{scan}} \right) z + \varphi_I \right]. \quad (7.1)$$

$$\begin{aligned} A_I(z) &= |V_I^*(z)| \\ &= A_S \cdot ATT(z) \cdot e^{-\alpha_S z}, \end{aligned} \quad (7.2)$$

where φ_I is the phase of the $V_I(z)$. $V_I^*(z)$ is the complex induced SW signal calculated using Hilbert transform as presented by **Eq. (4.5)**. $ATT(z)$ is the attenuation due to the diffraction effect and α_S is the SW absorption coefficient. A_S is an initial SW amplitude at the SW source ($z = 0$).

Figure 7.2 presented an example of the SW amplitude variations measured with a hydrogel phantom [109]. SW amplitude over the entire FOV, amplitude profile of the centerline (along x -direction at $x = 0$), and along x -direction at $z = 12$ mm, were shown in **Figs. 7.2(a), (b), and (c)**, respectively. A rectangular Plexiglas plate was used as the SW source which had dimensions of 30 mm in height, 15 mm in width, and 1 mm in thickness. The f_S of the experiment was 322 Hz. The v_S was measured at 4 m/s. In this experiment, M-mode measurements were conducted repeatedly at different z locations to map the SW displacement, instead of the B-mode measurement.

From **Fig 7.2** it can be seen that the SW amplitude was the greatest at the area close to the SW source with the presented experimental configuration employed. The SW

amplitude and beam width then gradually decreased along the z -direction due to the diffraction and absorption of the SW. The slight asymmetric amplitude with respect to the centerline was probably due to the inhomogeneity of the phantom material fabricated and/or alignment error of the SW source employed in the experiment. In addition, the observed amplitude along x -direction at $z = 12$ mm had an “M” shape profile but not the plane wave, due to the nonlinear diffraction effect.

Figure 7.2. An example of measured SW amplitude variations: (a) SW amplitude map over entire FOV, (b) amplitude profile along the centerline, and (c) amplitude profile at $z = 12$ mm.

$ATT(z)$ in **Eq. (7.2)** can be numerically calculated by a diffraction theory [40] with known parameters of the measurement configuration as described in **Section 7.2.2**. Thus,

the measured $A_I(z)$ in a chosen range of z was compared to the $A_I(z)$ calculated by **Eq. (7.2)** with an assumed α_S value to find the best estimated α_S which gave the minimum mean square error between the measured and calculated $A_I(z)$.

7.2.2. Numerical Simulation of Diffraction Effect

The SW amplitude change with respect to the distance z due to the diffraction can be calculated using a Huygens-Fresnel diffraction theory [40] with the known values of v_S and f_S , and the characteristic size of the SW source a and b which were the half length and width of the square SW source, respectively.

According to the Huygens-Fresnel principle of a rectangular source, when a and b were comparable to the wavelength of the SW applied, the SW was experiencing diffraction. Then the equations of SW V can be expressed as the followings.

$$V(x, y, z) = \frac{-1}{4\pi} \cdot \int_{-a}^{+a} \int_{-b}^{+b} 2A_S \cdot \cos \varphi \cdot \left(ik_S - \frac{1}{r_I} \right) \cdot \frac{e^{ik_S r_I}}{r_I} dx' dy', \quad (7.3)$$

$$r_I = \sqrt{(x - x')^2 + (y - y')^2 + z^2}, \quad (7.4)$$

$$\cos \varphi = \frac{z}{r_I}, \quad (7.5)$$

where r_I is the traveling distance of the SW from an arbitrary point $(x', y', 0)$ on the SW vibration source to an arbitrary point (x, y, z) inside the specimen. φ is the angle between r_I and z -direction. The geometry of such diffraction is demonstrated in **Fig. 7.3**.

Figure 7.3. The geometry of Fresnel diffraction of a rectangular source with considering the interference between induced and reflected waves.

V_I on the xz -plane was calculated by **Eq. (7.3)** using MATLAB. The vibration direction of the SW source is along x -direction. The spatial intervals in the vibration source dx' and dy' were assigned to 100 μm . Note that simulation with even smaller dx' and dy' values were also conducted, but it did not show noticeable difference. Therefore in order to reduce the time consumption of computation, dx' and dy' at 100 μm were used in the following calculation results.

2D maps of the SW displacement and amplitude at $y = 0$ were calculated on semi-finite mediums with $\lambda_S = 10 \text{ mm}$ ($f_S = 500 \text{ Hz}$ and $v_S = 5 \text{ m/s}$) and with $a = b = 0.5 \text{ mm}$, 2.5 mm, 5 mm, 10 mm, 20 mm, and 40 mm. The calculated results in xz -plane were shown in **Fig. 7.4**. It can be seen that the SW displacements were more close to plane waves as the characteristic size a increases, while the SW displacements were more diverged when a was comparable to and smaller than the λ_S . The SW amplitude changed with z due to the diffraction.

$\lambda_S = 10 \text{ mm}$
 $a = 0.5 \text{ mm}$

$\lambda_S = 10 \text{ mm}$
 $a = 2.5 \text{ mm}$

$\lambda_S = 10 \text{ mm}$
 $a = 5 \text{ mm}$

$\lambda_S = 10 \text{ mm}$
 $a = 10 \text{ mm}$

$\lambda_S = 10 \text{ mm}$
 $a = 20 \text{ mm}$

$\lambda_S = 10 \text{ mm}$
 $a = 40 \text{ mm}$

Figure 7.4. The appearance of the SW displacements (left) and amplitudes (right) calculated from different size of the SW sources. The SW wavelength (λ_S) was 10 mm, and the characteristic sizes (a) of the SW source were 0.5 mm, 2.5 mm, 5 mm, 10 mm, 20 mm, and 40 mm, from top to bottom.

7.2.3. Selection of Absorption Measurement Location

The SW amplitude change due to diffraction effect depended on z locations where the SW propagated. According to the Fresnel diffraction theory, the SW amplitude change with respect to z caused by the diffraction effect ($ATT(z)$) was associated with the $k_S a$ value (a product of k_S and a) and normalized distance S ($= z / N_F$), where S is the normalized distance and N_F is the Fresnel distance expressed by **Eq. (7.6)** [40]. A simulation of the SW amplitude change along the z centerline ($x = 0$) due to the diffraction was conducted with the $k_S a$ value of 10. The result of the amplitude profile was plotted in **Fig. 7.5** with respect to a normalized distance S .

Figure 7.5. A simulation of amplitude change due to diffraction effect on centerline with respect to a normalized distance. The $k_S a$ value was 10.

$$N_F = a^2 \cdot \frac{f_S}{v_S}. \quad (7.6)$$

It can be seen that the amplitude fluctuates and changed quickly when the normalized distance $S < 1$ (near field). It had a peak value at $S = 1$ and started to decrease monochromatically after $S = 1$. Therefore, the slope of the amplitude change due to diffraction was depending on the S .

Figure 7.6 presented $ATT(z)$ calculated with different $k_S a$ values with respect to the normalized distance S . $k_S a$ values were 2, 5, 10, and 20, and α_S was 0 Np/m for each calculation.

Figure 7.6. Simulations of amplitude change due to diffraction effect on centerline with respect to a normalized distance. Black-line represented $k_S a = 2$, blue-line represented $k_S a = 5$, green-line represented $k_S a = 10$, and red-line represented $k_S a = 20$.

Since α_S was determined by the measured SW amplitude change with the compensation of the diffraction effect, the accurate estimation of $ATT(z)$ by numerical calculation was crucial. The measurement accuracy of the z -range where the SW

amplitude was measured was depending on the precision of the positioning device employed. Therefore, inaccurate measurement of the z -range due to the limitation of the positioning device could cause an error in the $ATT(z)$ calculation, and thus resulted in α_S estimation error. In order to minimize the $ATT(z)$ calculation error due to the positioning error of z -range of the SW amplitude measurement, z -range where the $ATT(z)$ change was less sensitive to z was investigated through numerical simulations as follows.

The factor of positioning error of z -range was added into the simulations as follows. Assuming that the coverage of S -range was 5, the ATT was calculated in five different S -ranges for each $k_S a$ value as follows: $S = [0, 5]$, $S = [1, 6]$, $S = [2, 7]$, $S = [3, 8]$, and $S = [4, 9]$. It was assumed that the positioning error of the S -range was $S + 0.5$ or $S - 0.5$ as listed in **Table 7.1**. For instance, in region #2 of the simulation with $k_S a = 10$, an $A_B(S)$ that calculated in $S = [1, 6]$ was mistakenly recorded at $S = [0.5, 5.5]$ or $S = [1.5, 6.5]$, and it was termed $A_{B_mr}(S \pm 0.5)$. Such example was shown in **Fig. 7.7**. It was noted that the positioning error of $S - 0.5$ was not applicable in #1 ($S = [0, 5]$).

Table 7.1. Five regions in simulations to investigate the error due to positioning error.

Region #	S -range	Positioning Error on S location
#1	0 – 5	+ 0.5
#2	1 – 6	± 0.5
#3	2 – 7	
#4	3 – 8	
#5	4 – 9	

Figure 7.7 showed the calculation results of SW amplitude change due to diffraction with $k_{sa} = 10$. True S -range was $[1, 6]$ (top), positioning error of S values with -0.5 was $[0.5, 5.5]$ (middle), and that with $+0.5$ was $[1.5, 6.5]$ (bottom).

Figure 7.7. Simulation of SW amplitude change due to diffraction with $k_{sa} = 10$, the actual S -range was $[1, 6]$ (top), and was mistakenly recorded to $S = [0.5, 5.5]$ (middle), and $S = [1.5, 6.5]$ (bottom).

Estimation error of α_s due to the positioning error of S -range was investigated using the calculation results in **Fig. 7.7** as follows. A least square curve fitting technique

was used to find of the best α_S value that yielded an $A_B'(S \pm 0.5)$ which best fitted the profile of $A_{B_mr}(S \pm 0.5)$. Since the true α_S value was zero for the calculated SW amplitude changes in **Fig. 7.7**, estimated value of α_S was considered as the calculation error due to the positioning error. The curve fitting resulted $A_B'(S \pm 0.5)$ for $A_{B_mr}(S \pm 0.5)$ in **Fig. 7.7** were demonstrated by the dot-lines in **Fig. 7.8**.

Figure 7.8. Curve fitting results (indicated by dot-lines) of the SW amplitude with positioning error (indicated by solid-lines) in **Fig. 7.7**.

Figure 7.9 showed the estimation errors of α_S caused by the positioning error for different $k_S a$ values. All the $k_S a$ values examined had the greatest error at #1 S -range (where only had a positioning error of + 0.5). The smallest α_S estimation error was expected at the S -range [2, 7] for $k_S a = 2$, and after [2, 7] for other $k_S a$ values. It can be seen that the α_S estimation error was greater in the Fresnel field ($S < 1$), thus the effect of the positioning error was relatively great if the location of the measurement started from $S = 0$. It can be also seen that the error could be even smaller with the S -range far away from the SW source. However, the strength and SNR of the SW signals decreased when the S -range in the SW amplitude measurement was away from the SW source in practice.

Figure 7.9. Calculation error on the amplitude change of diffraction effect due to positioning error. Red-circle dash line represented the positioning error for $S + 0.5$, and blue-circle dash-line represented the positioning error for $S - 0.5$.

7.3. Experiment

7.3.1. Experimental Setup

A homogeneous hydrogel phantom was fabricated for the experiment to verify the proposed method. The phantom had a cubic shape with a side length of 50 mm. It was made of 9-W% gelatin and 2-W% graphite. The averaged v_s of the phantom was measured 2.15 m/s by the proposed v_s measurement method developed in **Chapter 4**. The v_s image of the phantom was shown in **Fig. 7.10**.

Figure 7.10. SW velocity image of the gelatin phantom.

In this experiment, the f_s was 227 Hz, and the a of the square SW source was 5 mm, so the $k_s a$ value was calculated 3.32. The amplitude change due to diffraction with this $k_s a$ value was calculated and plotted in **Fig. 7.11**. The error on a_s measurement due to positioning error was investigated according to the method described in **Section 7.2.3**. Twenty one (21) ranges in z -direction (z -range) were defined and listed in **Table 7.2**. The

coverage of each z -range was 30 mm. ± 1 mm positioning error (except the first z -range, which only had + 1 mm positioning error) was assumed for each z -range. **Fig. 7.12** showed the estimation error of α_s for each z -range.

Figure 7.11. A simulation of amplitude change due to diffraction effect on centerline with respect to the length z . The k_{sa} value was 3.32.

Figure 7.12. Estimation error of SW absorption due to the positioning error of z -location for $k_{sa} = 3.32$. Red-circle dash-line represented the positioning error of $z + 1$ mm, and blue-circle dash-line represented the positioning error of $z - 1$ mm.

Table 7.2. Twenty one regions in phantom experiment to investigate the error due to positioning error.

Region #	z-range (mm)	Positioning Error on z location (mm)
#1	0 – 30	+ 1
#2	1 – 31	± 1
#3	2 – 32	
#4	3 – 33	
#5	4 – 34	
#6	5 – 35	
#7	6 – 36	
#8	7 – 37	
#9	8 – 38	
#10	9 – 39	
#11	10 – 40	
#12	11 – 41	
#13	12 – 42	
#14	13 – 43	
#15	14 – 44	
#16	15 – 45	
#17	16 – 46	
#18	17 – 47	
#19	18 – 48	
#20	19 – 49	
#21	20 – 50	

From **Fig. 7.12** it can be seen that the error on the α_S measurement due to the positioning error reached the minimum values at $z = 1$ to 31 mm ($S = 0.38$ to 11.7), for $z + 1$ mm (red-circle dash-line). The minimum error for $z - 1$ mm (blue-circle dash-line) was found at $z = 2$ to 32 mm ($S = 0.76$ to 12.1), where such z -range also resulted in the second minimal error values for $z + 1$ mm. Therefore, z -range of 2 to 32 mm was used in the measurement of the α_S presented in the next section.

7.3.2. Measurement of Shear Wave Absorption

The experimental configuration of the α_S measurement was depicted in **Fig. 7.13**. The SW source (square Plexiglas plate) had a 10 mm side length ($a = b = 5$ mm). The SW source was continuously driven by 227 Hz during the measurement. The setup of the ultrasound system was the same as that used for the v_S measurements. According to the above discussion, the field-of-view (FOV) in z -direction (FOV _{z}) in this measurement was 30-mm and the z -range was selected at $z = 2$ to 32 mm.

Figure 7.13. Experimental configuration of SW absorption measurement.

7.4. Results and Discussion

A chosen frame of the induced SW over the FOV was presented in **Fig. 7.14(a)**. SW amplitude A_I at each frame was calculated by **Eq. (7.2)** and then averaged with 180 frames. The result of A_I was shown in **Fig. 7.14(b)** to be used to find the centerline ($x = 0$), as indicated by the dash-line. The A_I on the centerline was shown in **Fig. 7.14(c)** as the blue-dot.

Figure 7.14. The experimental result of (a) induced SW displacement (V_I), (b) SW amplitude (A_I), and (c) the SW amplitude on the centerline ($x = 0$) in (b).

By using the least square curve fitting technique, the calculated best fit curve (red-solid line) to the experimental result (blue-dot line) was obtained with $\alpha_S = 11.6$ Np/m in **Eq. (7.2)**.

A simulation of the A_I was calculated by using $v_S = 2.15$ m/s, $\alpha_S = 11.6$ Np/m, and $f_S = 227$ Hz in **Eq. (7.2)**. **Fig. 7.15(a)** showed the simulation result over the entire FOV

comparing with the experimental result in **Fig. 7.15(b)** under the same amplitude scale. The simulation result showed a good correlation to the experimental result.

Figure 7.15. Comparison between the simulation result (a) and experimental result (b) of the SW amplitude.

Finally, the shear elasticity G and viscosity η of the phantom were calculated by using **Eqs. (2.6)** and **(2.7)**. The G was calculated 5.06 kPa, and the η was calculated 0.12 Pa·s.

Standard tissue-mimicking phantoms were available commercially for the calibration of ultrasound system (*i.e.* the actual longitudinal parameters, such as LW velocity and attenuation were known in those phantoms) [110]. However, after a careful literature research, as far as the author was concerned, no commercial phantom was available specifically for the measurement of viscoelasticity. In most cases the researchers would have to fabricate soft tissue-mimicking phantoms by themselves for individual experiment to reach their experimental desires. As a result, the actual shear

parameters, such as ν_S and α_I would be unknown for those phantoms [93], [105], [110]–[112]. Currently, the most promising method to verify the viscoelastic properties of a sample tissue could be the supersonic shear imaging (SSI) [16], yet such method was not available in our measurement system. Therefore, the calculated G and η in this study were only compared with the published results using similar phantom specimens, as listed in the **Table 7.3**.

Table 7.3. A comparison between our result and published results using similar phantom specimens.

Measurement Method	Phantom	Shear Modulus G (kPa)	Shear Viscosity η (Pa·s)	Reference
SSI	Gelatin + agar, percentage was not specified	4	0.3	[15]
SDUV	10-W% Pigskin powder + 20-W% Castor oil	4.49	2.41	[105]
SDUV	12-V% “Bloom 75” gelatin	2.22	0.24	[17]
	12-V% “Bloom 300” gelatin	5.36	0.38	
SWEI	3-W% gelatin	2.01	0.6	[112]
	6-W% gelatin	8.05	1.14	
Crawling Wave	Gelatin phantom, percentage was not specified	8.61	2.98	[101]
Our Method	9-W% gelatin	5.06	0.12	N/A

The published results had a relatively great variance of the η (about 10 times difference between the minimum 0.24 Pa·s and the maximum 2.98 Pa·s in the **Table 7.3**), yet the variance of the G was relatively less (about 4 times difference between the minimum 2.01 kPa and the maximum 8.61 kPa). Although the viscosity result in our method was less than the published results, it was still in the same order of magnitude of the listed references and it was a reasonable value by considering that the water-based phantom could be a less viscous material [105]. Fabrication and study on the viscous phantom could be good topic for future research.

7.5. Summary

This chapter aimed to address the problem due to diffraction effect during the direct measurement of the SW absorption. The SW amplitude was measured by using the same experimental configuration as that for the measurement of SW velocity. The diffraction effect was mathematically calculated by knowing the characteristic size of SW source, SW velocity, and SW frequency, and then it was compensated from the measured SW attenuation. The calculation error during the compensation of the diffraction effect could arise from the positioning error, and such error can be reduced by arranging the measurement onto a spatial region that was less sensitive to the positioning error. Finally the shear elasticity and the viscosity of a specimen were estimated together from the same SW measurement result. **Objective 4** in **Section 1.3** was achieved by the accomplishment of the research in this chapter. It should be noted that such research was preliminary

compared with the research on the measurement of SW velocity as presented through **Chapters 3-6**.

It should be also noted that as the SW absorption measured by the method in this chapter was only an averaged value of the entire specimen. Therefore, the estimated shear elasticity and viscosity values also represented the overall viscoelastic properties of the specimen. Nevertheless, the proposed measurement method of SW absorption could still be useful as it can be used to provide reference parameters of viscoelasticity for phantom study and/or *in-vitro* tissue study such as biopsies.

Chapter 8

Conclusions

8.1. Summary of Thesis Research

SW measurement methods for soft tissue characterization were developed with the use of conventional B-mode scan of focused ultrasound and the use of a single external SW source. The proposed methods could reduce the cost and the complexity of overall experimental configuration. A successful measurement of ν_s and α_s would make a proper determination of the tissue shear elasticity and viscosity. Three practical challenges in SW measurement configuration used in this research: 1) Undesired SW reflection, 2) motion artifact, and 3) diffraction effect were studied and addressed as summarized below.

1) Undesired SW reflection from tissue boundary

When measuring the spatial SW displacement in some experiments, the continuously-induced SW were reflected at the tissue boundary, and interfered with itself. This could cause the deformation of observed SW waveform pattern, and result in errors in the measurement of SW. It was found that the B-mode scanning time delay of a focused ultrasound made the spatial frequencies of the induced and reflected SWs different. Therefore, the undesired SW reflection was

able to be removed by using a spatial frequency filter on the observed interfered SW displacement. This problem had been addressed in **Chapter 3** and **Chapter 4**.

2) **Motion artifact on the measurement of shear wave displacement**

The tissue displacement in a practical SW measurement could include both desired SW displacement and motion artifacts. The undesired motions from the experimental environment and involuntary *in-vivo* activities may be unavoidable, and resulted in errors in the measurement of SW. In order to overcome this problem, the SW frequency was assigned to a specific frequency which was different from the frequencies of the predictable motion artifacts. This allowed the application of a temporal bandpass filter to reduce the motion artifacts from the measured tissue displacement. This problem had been discussed and addressed in **Chapter 5**.

3) **Diffraction effect on the measurement of shear wave absorption**

When the wavelength of a SW was comparable to or larger than the size of the SW source, the diffraction effect must be considered. In order to estimate α_s from the measured SW attenuation, the attenuation due to diffraction should be compensated mathematically. The diffraction effect was nonlinear and location-dependent. Therefore, the calculation error during the compensation of the diffraction effect could arise from the inaccuracy of the measurement location. Such error can be reduced by arranging the measurement onto a spatial region that was less sensitive to the positioning error. This problem had been discussed and addressed in **Chapter 7**.

8.2. Scope and Limitation

The measurement methods of v_S and motion artifact reduction were conducted with the phantom specimen and *in-vivo* tissues. The experimental results positively verified the reliability and usefulness of the proposed measurement methods. The v_S is related to the tissue stiffness which may reflect the tissue health. The proposed method of motion artifact reduction was capable of addressing the practical problem of undesired tissue motions during the measurements. Therefore, the proposed measurement method of v_S has good potential to be applied for clinical applications such as the diagnosis of the organic lesions, and/or the evaluation of the muscle strength in sports medicine.

The research on the measurement of α_S in this thesis was still preliminary. Nevertheless, the shear elasticity and the viscosity of a specimen were estimated together from the same SW measurement result. At current stage, the proposed α_S measurement method could be used to provide reference parameters of viscoelasticity for phantom study and/or *in-vitro* tissue study such as biopsies.

8.3. Future Research

The following subjects were not the focus of this thesis, yet they could also be useful for the research on tissue characterization. Therefore, they were listed here and could be good potential research topics in the future.

1) **Measureable range of shear wave velocity and B-mode scanning speed**

From the study in **Chapter 4** it was found that the estimation of v_S was depending on the v_{scan} value of the ultrasound system. Therefore, a change of the v_{scan} value

could result in variations of the measureable range and possibly the measurement accuracy of the v_S . A study on the relationship between the measureable range of v_S and the v_{scan} could be interest and useful if the system allows user to change the v_{scan} .

2) **Discrimination of unreliable SW signals**

In practical experiments, the SNR of induced SW may not be known, while weak SW signals (poor SNR) could result in more error. Therefore, method to discriminate the estimated v_S from the unreliable SW signals would be helpful to make the v_S result more trustworthy. The relevant study is recommended in the future research.

3) **Improvement of filtering technique**

In this thesis, a spatial frequency filter was designed and used to remove the unwanted reflected SW. The transition zones in the frequency domain of the filter could undesirably attenuate/remove the wanted induced SW and result in error on the v_S measurement result (as discussed in **Section 6.3** for the *in-vivo* experiment). A frequency-domain filtering technique may help to avoid such concern [113]–[116]. With this filtering technique, a rectangular mask was directly applied on the spatial frequency domain to retain the wanted frequency component and made unwanted ones zero. Thus, the transition zones would not exist. Preliminary study on such filtering technique had been conducted and demonstrated in **Appendix D**. Further study is recommended in the future research.

4) **Phantom Fabrication**

Most of the phantoms prepared for this thesis research were dominated by their elastic properties. It was challenging to fabricate a phantom that had both remarkable shear elasticity and viscosity [68], [69], [93], [102], [105], [112], [117], [118]. In addition, the reproducibility of the phantom fabrication was limited. Phantoms with the same compositions but were fabricated at different times could occasionally have remarkable difference in their elasticities. Moreover, phantoms with viscoelasticity covering full range of bio-tissues could also be good references for the research with the interest of tissue characterization. Therefore, specific study on phantom fabrication and characterization could be helpful, and it is recommended as a future research topic.

5) **More *In-vivo* Experiments and Clinical Trials**

At last, in-vivo experiments in more subjects and at different body areas are recommended to be carried out in future. Clinical trials could also be considered in even further stages.

Appendix A. Mode Conversion from Shear Wave to Longitudinal Wave

According to a wave mode conversion theory, an induced SW would not be totally reflected as SW during a reflection and partial energy of the induced SW would convert into a LW [119], [120]. Relevant equations were shown as follows.

$$\Gamma_{SS} = -\frac{\sin 2\theta_S \sin 2\theta_L - (v_L/v_S)^2 \cos^2 2\theta_S}{\sin 2\theta_S \sin 2\theta_L + (v_L/v_S)^2 \cos^2 2\theta_S} \quad (\text{A.1})$$

$$\frac{\sin \theta_L}{\sin \theta_S} = \frac{v_S}{v_L}, \quad (\text{A.2})$$

where Γ_{SS} is the amplitude of a reflected SW from an incident SW. v_L is the LW velocity of the specimen. **Equation (A.2)** follows the Snell's law which is described in **Fig. A.1**. θ_S is the incident angle of SW, and θ_L is the reflection angle of LW.

Using **Eqs. (A.1) and (A.2)**, a numerical calculation was conducted to estimate the energy loss of the induced SW due to the mode conversion during the reflection. The value of v_S was set from 1 m/s to 10 m/s with 0.1 m/s step, and the v_L was assumed at 1500 m/s. The reflection was assumed to be a total reflection. All the possible θ_S and θ_L were considered, then the energy conversion rate $|\Gamma_{SS}|^2$ from the incident SW to the reflected SW was calculated. The result was illustrated in **Fig. A.2**. Due to the great difference between v_S and v_L , the critical incident angle (which is the maximum θ_S that would lead the θ_L to 90°) was less than 0.4° , and at most, there would be only $1.8 \times 10^{-4}\%$

of the induced SW energy being converted into LW, which can be ignored. Therefore, it was assumed that in this thesis research, mode conversion was not involved.

Figure A.1. Induced and reflected SWs with mode conversion.

Figure A.2. Energy reflection coefficient of SW.

Appendix B. Measurement of Tissue Displacement

Using Ultrasound RF Signal

Ultrasound was generated from the probe then reflected at the scatterers and acquired by the probe. Assume the transmitted ultrasound signal S_T with a center frequency of ω_0 was described as:

$$S_T(t) = \cos(\omega_0 t). \quad (\text{B.1})$$

According to the principle of Doppler Effect, when an incident wave reached a moving target, the frequency of its reflection wave would experience a Doppler shift. Therefore, the received ultrasound rf signal S_{rf} , can be written as [121]:

$$S_{rf}(t) = A_{rf} \cos \left[\int_{-\infty}^t \omega_i(t) dt \right], \quad (\text{B.2})$$

where A_{rf} is the amplitude of the received rf signal, $\omega_i(t) = \omega_0 + \omega_d(t)$, is the instantaneous angular frequency that is composed of the ultrasound frequency ω_0 and the Doppler shift frequency $\omega_d(t)$ due to the displacement of the target (ultrasound scatterer). The Doppler shift frequency was defined by:

$$\omega_d(t) = \frac{2\omega_0}{c_0} \cos \theta \cdot v(t), \quad (\text{B.3})$$

$$\begin{aligned} v(t) &= \frac{\partial u_x}{\partial t} \\ &= \omega_s A_s \cos(\omega_s t + \varphi_s), \end{aligned} \quad (\text{B.4})$$

where c_0 is the ultrasound speed, θ is the angle between the direction of ultrasound transmission and the direction of the scatterer displacement. It should be noted that $\theta = 0$ in this thesis. u_x is the scatterer displacement as defined by **Eq. (2.3)**. φ_s is the phase of the velocity ($v(t)$) of the scatterer displacement. Then substituting **Eqs. (B.3)** and **(B.4)** into **Eq. (B.2)**, the received rf signal can be rewritten as a frequency modulation (FM) equation [122]:

$$S_{rf}(t) = A_{rf} \cos[\omega_0 t + \varphi_0 + \beta \cdot u_x(t)], \quad (\text{B.5})$$

where φ_0 is the initial phase of the received rf signal at $t = 0$ when there is no motions. β , as expressed in **Eq. (B.6)**, is the index of the FM and directly convert the amplitude of scatterer displacement (with a unit of meter) into phase component (with a unit of radian).

$$\beta = \frac{2\omega_0}{c_0}, \quad (\text{B.6})$$

Now let us consider a three-dimensional displacement, where the scatterer displacement occurred at a (x, z) spatial plane with respect to the time t , so **Eq. (B.5)** can be rewritten as:

$$S_{rf}(t, x, z) = A_{rf}(x, z) \cos \left[\omega_0 \frac{2x}{c_0} + \varphi_{rf}(t, x, z) \right], \quad (\text{B.7})$$

$$\varphi_{rf}(t, x, z) = \varphi_0(x, z) + \varphi_V(t, x, z), \quad (\text{B.8})$$

$$\varphi_V(t, x, z) = \beta \cdot u_x(t, x, z), \quad (\text{B.9})$$

where $A_{rf}(x, z)$ is the amplitude of the rf signal at location (x, z) . $2x/c_0$ is the time consumption of the pulse-echo round trip for an ultrasound pulse that travels from the probe to the target scatterer and back to the probe. The phase component $\varphi_{rf}(t, x, z)$ represents the position of the scatterer located at (x, z) at time t , which was composed of

the initial phase ($\varphi_0(x, z)$) of rf signal located at (x, z) and $t = 0$ when there was no scatterer motions. $\varphi_I(t, x, z)$ is the change of the phase, which was caused by the scatterer displacement $u_x(t, x, z)$.

Technically, $\varphi_{rf}(t, x, z)$ can be retrieved from the received rf signal using an in-phase/quadrature detection technique at a known ultrasound transmission frequency ω_0 [91], as follows:

$$S_{ref}(x) = e^{-\omega_0 \frac{2x}{c_0}}, \quad (\text{B.10})$$

$$\begin{aligned} I(t, x, z) &= LPF\{S_{rf}(t, x, z) \cdot Re[S_{ref}(x)]\} \\ &= \frac{A_{rf}(x, z)}{2} \cdot LPF\left\{\cos[\varphi_{rf}(t, x, z)] + \cos\left[2\omega_0 \frac{2x}{c_0} + \varphi_{rf}(t, x, z)\right]\right\} \\ &= \frac{A_{rf}(x, z)}{2} \cos[\varphi_{rf}(t, x, z)], \end{aligned} \quad (\text{B.11})$$

$$\begin{aligned} Q(t, x, z) &= LPF\{S_{rf}(t, x, z) \cdot Im[S_{ref}(x)]\} \\ &= \frac{A_{rf}(x, z)}{2} \cdot LPF\left\{\sin[\varphi_{rf}(t, x, z)] - \sin\left[2\omega_0 \frac{2x}{c_0} + \varphi_{rf}(t, x, z)\right]\right\} \\ &= \frac{A_{rf}(x, z)}{2} \sin[\varphi_{rf}(t, x, z)], \end{aligned} \quad (\text{B.12})$$

$$Y(t, x, z) = I(t, x, z) + j \cdot Q(t, x, z)$$

$$Y(t, x, z) = \frac{A_{rf}(x, z)}{2} e^{j\varphi_{rf}(t, x, z)}, \quad (\text{B.13})$$

$$\varphi_{rf}(t, x, z) = \angle Y(t, x, z), \quad (\text{B.14})$$

where S_{ref} is a complex reference signal with the same angular frequency as that of S_{rf} . The reference signal was multiplied to the rf signal to create an in-phase, denoted by $I(t, x,$

z), and a quadrature signal, denoted by $Q(t, x, z)$. Low pass filtering (*LPF*) was then applied on the in-phase and quadrature components, respectively.

Once the $\varphi_{rf}(t, x, z)$ was retrieved, the initial phase $\varphi_0(x, z)$ was considered as a phase offset and it can be removed by subtracting the mean value of the obtained $\varphi_{rf}(t, x, z)$ over time t . Then $u_x(t, x, z)$ would be calculated by removing the FM index β . If the displacement due to motion artifact was taken into account, it can be reduced by applying a temporal frequency filter on the $u_x(t, x, z)$ with respect to t , as long as the f_s employed in the experiment was separable from the frequencies of undesired motions. The details of such process were described in **Chapter 5**.

Appendix C. Undersampling of Tissue Displacement in Temporal Domain

The ultrasound system used in this thesis had a B-mode scanning rate (or frame rate, f_{FR}) of 30 Hz. However, the f_S could be from around 100 Hz to 1000 Hz in practical experiment. This resulted in undersampling of the scatterer displacement in the temporal domain. Nevertheless, the undersampling in temporal domain did not affect the measurement of SW displacement, as long as the actual f_S assigned did not make $f_{measured}$ become 0 (see **Eq. (5.2)** in **section 5.2**). If $f_{measured}$ became 0, there would be no phase differences among the different moments of an arbitrary scatterer, *i.e.* the $\varphi_r(t, x, z)$ obtained from **Eq. (B.14)** became a constant.

Figure C.1 demonstrated an example of SW propagation along z -direction at a certain depth x with respect to different time t . Assuming such SW propagated towards the positive z -direction in spatial domain, and the sampling in its temporal domain was undersampled, while that in its spatial domain was normal sampled.

At a certain z , the displacement was caused by the term ω_{st} in **Eq. (2.3)** and presented in **Fig. C.1(b)**. At a certain t , the displacement was caused by the phase variation $k_S z$ in **Eq. (2.3)** and presented in **Fig. C.1(c)**. As long as the sampled SW waveform in z -direction, indicated by the dash-dot in **Fig. C.1(c)**, was not aliased, the wavenumber k_S can be estimated correctly, so that v_S would be estimated accordingly.

Figure C.1. A demonstration of SW displacement in (a) both temporal and spatial domain, (b) only temporal domain at a certain (x, z) , and (c) only spatial domain at a certain (x, t) .

Appendix D. Frequency-Domain Filtering

The $BPF_{spatial}$ used in **Chapters 4 and 5** was a rectangular FIR with a filter order number of 42. With using such filter, V , V_B at a certain frame of the ankle experiment demonstrated in **Section 6.3.1**, and their spatial frequency spectra at centerline ($x = 0$) were illustrated in **Figs. D.1(a), (b), and (c)**, respectively. A strong frequency component was found at 0.55 s/m in the spectrum of V (indicated by dash-arrow in **Fig. D.1(c)**), which represented the dominant spatial frequency of the backward SW V_B . It can be seen that such frequency component was close to the lower spatial cut off frequency and probably located within the transition zone of the $BPF_{spatial}$. As a result, it was attenuated after the filtering process, and shifted to 0.77 s/m, as can be seen in the spectrum of V_B (indicated by solid-arrow in **Fig. D.1(c)**). According to **Eq. (4.9)**, a greater value of spatial frequency meant lower value of v_s , hence the v_s estimated from the V_B by using such $BPF_{spatial}$ should be lower than its actual value. Practically, this issue may have remarkable influence on the material that had a relatively greater v_s . In addition, the attenuation of the SW amplitude after the filtering process due to the transition zone also led to a weakening of the SNR, which would consequently reduce the accuracy of the v_s estimation as presented in **Fig. 5.9** of **Section 5.5**.

Figure D.1. The spatial SW displacement (a) before the spatial filtering, and (b) after the spatial filtering. The frequency spectrum at centerline ($x = 0$) of each displacement was averaged over 180 frames and plotted in (c).

An alternative $BPF_{spatial}$ that applying on the frequency domain using the frequency domain filtering technique [113]–[116] may address such issue. The design of such $BPF_{spatial}$ followed the next steps:

1) Fourier Transform:

At every temporal frame, conducted Fourier transform of the obtained $V(x, z)$ in its spatial domain (with respect to z) at each depth x . Then calculated the frequency spectrum of the Fourier transform.

2) Spatial Frequency Filtering:

Applied a rectangular mask on the frequency spectrum, and made the magnitude zero for the spatial frequencies outside of the desired passband of the $BPF_{spatial}$. For the spatial frequencies within the passband, remained their original magnitudes.

3) Inverse Fourier Transform:

At last, conducted the inverse Fourier transform of the masked frequency spectrum at each depth x . Then the filtered backward SW displacement $V_B(x, z)$ would be obtained.

Theoretically this alternative $BPF_{spatial}$ did not have transition zone in the spatial frequency domain. As long as the spatial frequency of SW was within the desired passband, it should be fully retained. However, it should be also noted that in practice, the sudden change of magnitudes at the cut-offs (assigning the magnitude to zero) in step 2 may lead to discontinuity in spatial frequency domain, and it may introduce errors such as ringing effects in the spatial domain. Improvement of the filtering process could be an interest topic in the future research.

Now the data of ankle experiment in **Section 6.3.1** was reanalyzed by using the alternative $BPF_{spatial}$. In addition, considering the fact that the v_S of Achilles tendon may be close to or greater than 10 m/s [79], the passband of the alternative $BPF_{spatial}$ were set to let a SW with v_S between 2 m/s and 15 m/s pass,. Those presented in **Fig. D.1** were reanalyzed and presented in **Figs. D.2**, accordingly. The dominant spatial frequency of the V_B was now the same as that of V within the passband.

Figure D.2. The spatial SW displacement (a) before the spatial filtering, and (b) after the alternative spatial bandpass filtering. The frequency spectrum at centerline ($x = 0$) of each displacement was averaged over 180 frames and plotted in (c).

The v_s was reestimated by using the alternative $BPF_{spatial}$ then averaged with 180 frames, and shown in **Fig. D.3**, the v_s estimated beyond 2 m/s to 15 m/s was considered as calculation error so blackened and noted as N/A in the image. The mean value and STD of the v_s of tendon tissue in the ROI were calculated 8.9 m/s and 2.0 m/s, respectively. Those of muscle tissue were 5.1 m/s and 1.8 m/s, respectively. Results of v_s with two spatial filtering approaches were compared and listed in **Table D.1**. The “Difference” in the table was determined by: $(\text{Alternative } BPF_{spatial} - \text{Original } BPF_{spatial}) / \text{Alternative } BPF_{spatial} \times 100\%$.

Figure D.3. SW velocity calculated with the alternative spatial filtering.

Table D.1. Shear velocities calculated using original $BPF_{spatial}$ and alternative $BPF_{spatial}$.

	Original $BPF_{spatial}$		Alternative $BPF_{spatial}$		Difference	
	<i>Tendon</i>	<i>Muscle</i>	<i>Tendon</i>	<i>Muscle</i>	<i>Tendon</i>	<i>Muscle</i>
Mean value of v_S (m/s)	4.6	2.5	8.9	5.1	+48%	+51%
Standard deviation (m/s)	1.7	0.75	2.0	1.8	+15%	+58%

The v_S of both tendon and muscle tissues were calculated at greater values when using the alternative $BPF_{spatial}$. The v_S of tendon tissue showed good agreement with the published results [33], [79]. As mentioned earlier, the alternative $BPF_{spatial}$ caused sudden change of magnitudes at the cut-offs and resulted in discontinuity in spatial frequency domain. Therefore, variation of the v_S image can be noticed in **Fig. D.3**, so that the calculation errors (blackened areas) appeared at $z = 0$ mm, ± 10 mm, and ± 15 mm could be

due to this issue. In **Fig. D.4**, the v_S image was superimposed on the B-mode image. It can be seen that the v_S difference between tendon and other tissues followed their anatomical structures.

Figure D.4. A superposition of B-mode image and SW velocity image. Arrows indicated the Achilles tendon.

The results of v_S in tendon and muscle areas averaged with 10 consecutive frames as those demonstrated in **Fig. 6.5** were recalculated with using the alternative $BPF_{spatial}$, and shown in **Fig. D.5**. Both v_S results were apart (as shown in **Table D.1**) with a certain amount value and they were consistent throughout the SW measurement. The v_S variation (twice of the STD) in **Fig. D.5(a)** was 0.15 m/s and that in **Fig. D.5(b)** was 0.29 m/s.

(a)

(b)

Figure D.5. The change of the mean value of the SW velocity with respect to the temporal frames within the ROIs as indicated by the dash-box in **Fig. D.3**. The result in the ROI of tendon was plotted in (a) and that of muscle was plotted in (b). Both results were calculated by using the alternative $BPF_{spatial}$.

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