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Shear wave elastography with two-dimensional ultrasound transducer

Sao Paulo

2018

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Dissertation submitted to the School of Engineering
of the University of Sao Paulo to obtain the degree
of Master of Science.

Concentration area: Biomedical Engineering

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Sao Paulo

2018

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São Paulo, _____ de _____ de _____

Assinatura do autor:

Assinatura do orientador: _____

Catálogo-na-publicação

Santos, Djalma Simões dos

Shear wave elastography with two-dimensional ultrasound transducer /

D. S. Santos -- versão corr. -- São Paulo, 2018.

95 p.

Dissertação (Mestrado) - Escola Politécnica da Universidade de São Paulo. Departamento de Engenharia de Telecomunicações e Controle.

1.Elastografia 2.Diagnóstico por imagem 3.Ultrassonografia 4.Transdutor de ultrassom I.Universidade de São Paulo. Escola Politécnica. Departamento de Engenharia de Telecomunicações e Controle II.t.

Nome: Djalma Simões dos Santos

Título: Shear wave elastography with two-dimensional ultrasound transducer

Dissertação apresentada à Escola Politécnica da
Universidade de São Paulo para a obtenção do título
de mestre em ciências.

Aprovado em: 30/07/2018

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À Eszter e à minha família.

Agradecimentos

A Deus.

Ao Prof. Sérgio Furuie, pela confiança, ensinamentos e orientação.

Ao Fernando Cardoso, pelas contribuições para este trabalho e pela convivência.

Ao Diego Cárdenas, por todo o auxílio e pela convivência.

Ao Timóteo Oliveira, pela paciência e por todo conhecimento transmitido.

Ao Estevão Rodrigues, por suas contribuições.

Ao José Hilton, Tiago Ramos e demais colegas do laboratório de ultrassom por suas contribuições.

À Eszter Huszka, por sua compreensão e incansável apoio.

À minha família e amigos, pelo incentivo.

À CAPES, pelo apoio financeiro.

A todos que contribuíram de alguma forma para a realização deste trabalho.

“In science, it is not speed that is the most important. It is the dedication, the commitment, the interest and the will to know something and to understand it — these are the things that come first.”

Jenő Wigner

Abstract

Chronic liver diseases are the eighth leading cause of death in Brazil and a major public health problem in the world. Liver biopsy is the best available reference standard for evaluating and classifying stages of liver diseases, but it presents limitations and complications that are common in invasive methods. In recent years, elasticity imaging methods have been the focus of intense research activity with the ability to measure mechanical properties of soft tissues in a non-invasive way. Shear wave elastography is one of the most promising methods because it enables to quantitatively assess tissue elasticity. However, the current depth range of shear wave elastography impedes its application in obese patients, which have a great risk of developing liver disease. The aim of this study is to investigate the use of shear wave elastography in deeper tissues using a two-dimensional ultrasound transducer array. An efficient transducer array arrangement was simulated, fabricated and characterized. The results show that the proposed transducer configuration presents enhanced transmitting capabilities for generating tissue displacement in deeper tissues. In addition, numerical simulations were performed in order to track the tissue deformation and reconstruct its elastic properties.

Keywords: Shear wave elastography. Acoustic radiation force. Ultrasound transducer. Array transducer.

Resumo

Doenças crônicas do fígado são a oitava causa de morte no Brasil e um dos principais problemas de saúde pública do mundo. A biópsia do fígado é o melhor padrão de referência disponível para avaliação e classificação dos estágios das doenças hepáticas, mas apresenta limitações e complicações que são comuns nos métodos invasivos. Nos últimos anos, métodos de imagem por elasticidade têm sido o foco de intensa atividade de pesquisa, pois têm a capacidade de medir propriedades mecânicas dos tecidos moles de maneira não invasiva. A elastografia por ondas de cisalhamento é um dos métodos mais promissores, pois permite avaliar quantitativamente a elasticidade do tecido. No entanto, a atual faixa de profundidade da elastografia por ondas de cisalhamento impede sua aplicação em pacientes obesos, que apresentam grande risco de desenvolver doença hepática. O objetivo deste estudo é investigar o uso da elastografia por onda de cisalhamento em tecidos mais profundos usando um transdutor de ultrassom bidimensional. Uma configuração eficiente de transdutores matriciais foi simulada, fabricada e caracterizada. Os resultados mostram que o transdutor proposto possui capacidade de transmissão melhorada para gerar deslocamento em tecidos profundos. Além disso, simulações numéricas foram realizadas para monitorar a deformação do tecido e reconstruir suas propriedades elásticas.

Palavras-chave: Elastografia por onda de cisalhamento. Força de radiação acústica. Transdutor de ultrassom. Transdutor matricial.

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List of Acronyms and Abbreviations

2D	Two-dimensional
3D	Three-dimensional
ARF	Acoustic radiation force
ARFI	Acoustic radiation force impulse imaging
ASTM	American Society for Testing and Materials
BW	Bandwidth
CMR	Common-mode rejection
CNC	Computer numerical control
FDA	Food and Drug Administration
FFT	Fast Fourier Transform
FNM	Fast Nearfield Method
FOCUS	Fast Object-Oriented C++ Ultrasound Simulator
IL	Two-way insertion loss
In-amp	Instrumentation amplifier
IP	Internet protocol
MI	Mechanical index
NDT	Non-destructive testing
PVDF	Polyvinylidene fluoride
Pz37	Lead zirconate titanate
SCPI	Standard Commands for Programmable Instruments
SWEI	Shear wave elastography imaging
TCP	Transmission Control Protocol
TTP	Time-to-peak

List of Symbols

a	Particle acceleration
A	Wave amplitude; Area of the piezoelectric element
b	Body force; Absorption parameter
c	Wave propagation speed; Heat capacity
C	Capacitance
C_{ijkl}	Elasticity tensor
d	Distance; Thickness of the piezoelectric element
e	Euler's number
E	Young's modulus
F	Acoustic radiation force; Momentum
f	Force per unit of volume; Temporal frequency
h	Piezoelectric element height
I	Intensity
K	bulk modulus
k	Wave number; Kerf; Coupling factor
L	Inductance
n, N	Integer number
p	Pressure; Pitch
P	Electrical power
$Q_{m,t}$	Mechanical Quality Factor
q	Rate of heat production
r	Focal length
R	Electrical resistance
T	Temperature
t	Time
V	Voltage
W	Component in the transversal direction of wave propagation
w	Piezoelectric element width
Z	Acoustic impedance; Electrical impedance
u	Displacement field
v	Particle velocity
α	Attenuation coefficient
Γ	Elastic modulus
δ_{ij}	Kronecker's delta
δV	Infinitesimal volume of fluid
ε_{ij}	Strain tensor
ε^S	Clamped dielectric constant
η	Shear viscosity coefficient; Efficiency
η'	Bulk viscosity coefficient
μ	Lamé's constant; Shear modulus
θ	Focal angle
λ	Lamé's constant; Wavelength
ν	Poisson's ratio
ρ	Density
σ_{ij}	Cauchy's stress tensor
ϕ	Transformer's turns ratio
ψ	Component in the longitudinal direction of wave propagation
ω	Angular frequency

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1 Introduction

1.1 The importance of ultrasound in medicine

It is widely recognized that ultrasound has helped humankind in several areas since its first applications, and, perhaps, the most prominent one is medicine (Azhari, 2010). Originally a military modality used to detect objects underwater during the World War I, the development of high frequency sound equipment for general purposes began only after the World War II. The early ultrasound instruments applied the pulse-echo ranging principle (reflection technology), which is based on the emission of low frequency pulses of sound into the water and the subsequent reception of the sound that bounces off the object and returns as echo (Dempsey, 2004). When commercialized versions of these equipment were available, a few medical practitioners realized the possibility of using this instrument to probe the human body, which prompted investigations of the use of an analogous technique for medical purposes (Szabo, 2004).

Pioneering applications of ultrasound for medicine were reported in the early fifties by the remarkable studies of Wild and Reid (Wild & Reid, 1952). These early findings triggered enormous interest in medical diagnosis and many technical improvements began to be made. The lack of suitable devices started an intense period of experimentation and hopefulness, which inspired workers to do amazing things with surplus war equipment and to adapt other sonographic instruments for medicine (Szabo, 2004; Dempsey, 2004). Since then, the image quality of medical ultrasound has been advanced from low-resolution to images with much greater detail. From the clinical aspect, the ultrasound possesses priceless significance because of the following major advantages (Beutel, Kundel, & Metter, 2000; Azhari, 2010; Carovac, Smajlovic, & Junuzovic, 2011):

- a) Hazardless radiation: ultrasound is considered safe because it is noninvasive and has hazardless radiation characteristics. This allows repeated examinations of the same patient without risks using standard equipment;
- b) Compact and relatively easy use: most of the ultrasonic transducers are very compact, which enables to probe almost any region within the body;
- c) Wide variety of parameters can be measured to characterize tissues, *e.g.*: speed of sound, attenuation, acoustic impedance, dispersion, nonlinearity, and more;
- d) Cost effective: ultrasound systems are relatively inexpensive when compared to other medical modalities, which makes ultrasound an excellent choice from the economical point of view.

Continuous improvement in ultrasound technology has provided refined visualization of anatomy and physiology with high spatial and contrast resolution, particularly in superficial

structures such as breast, thyroid, musculoskeletal structures and the cardiovascular system, making ultrasound an important and often indispensable imaging modality (Benson & Fan, 2012).

1.2 Chronic liver diseases

Chronic liver disease is a major public health problem throughout the world. In Brazil, liver diseases are the eighth leading cause of death, having accounted for 308,290 deaths between the years 2001 and 2009. The prevalence of hospital admission due to liver disease in this period was 0.72% (853,571 hospitalizations), and the mortality rate was 3.34% (Nader, 2012).

The multiple causes of chronic liver disease (including hepatitis viral disease, nonalcoholic fatty liver disease, alcoholic liver disease and autoimmune liver disease) follow a common pathway towards liver fibrosis and finally cirrhosis, increasing the risk for the development of portal hypertension, hepatic insufficiency, and hepatocellular carcinoma (Pellicoro, Ramachandran, Iredale, & Fallowfield, 2014).

Currently, liver biopsy is the best available reference standard for evaluating and classifying stages of liver fibrosis/cirrhosis. However, liver biopsy has several limitations. It is invasive and can cause minor complications including temporary pain in approximately 20% of cases. Major complications, such as bleeding, haemobilia, bile peritonitis, bacteremia, sepsis, pneumothorax, hemothorax and even death, occur in 1.1% of liver biopsies. Moreover, liver biopsy is limited by under-sampling, with a typical biopsy core only representing roughly 1/50,000 of the entire liver volume (Sigrist, Liau, Kaffas, Chammas, & Willmann, 2017).

Since fibrosis associated with chronic liver diseases causes the liver to become stiffer than normal tissues due to collagen deposition and microstructural changes, assessing tissue elasticity (*i.e.*, the tendency of tissue to resist deformation with an applied force, or to resume its original shape after removal of the force) can hence be used to differentiate affected from normal tissue for diagnostic applications (Sigrist, Liau, Kaffas, Chammas, & Willmann, 2017).

Noninvasive modalities for chronic liver diseases evaluation have become more and more popular in the last 10 years, tending to replace at least a part of liver biopsies (Sporea, et al., 2012). Among these methods, the most prominent one is the acoustic radiation force based elastography, which will be the focus of this work.

1.3 Imaging the elastic properties of soft tissues with ultrasound

Since early medicine, doctors have used manual palpation to qualitatively assess tissue health and monitor disease progression because of the correlation that exists between tissue elasticity and pathological state – *i.e.*, necrotic regions are often stiffer than their surrounding healthy tissues (Palmeri & Nightingale, 2011; DeWall, 2013; Doherty, Trahey, Nightingale, & Palmeri, 2013). Although indispensable for medical diagnosis, manual palpation methods are

relatively subjective – it may vary from a doctor to another – and fail in many cases in which the lesion is small or located in regions of difficult access, making it impossible to be sensed manually (Chen, Fatemi, & Greenleaf, 2004). With the ability to measure the elasticity of tissues deep within the body, elasticity imaging techniques have been the focus of intense research activity and offer a great clinical promise (Doherty, Trahey, Nightingale, & Palmeri, 2013).

All elasticity imaging methods apply a mechanical excitation (stress) to tissues and measure the resulting tissue deformation (displacement) in response to that stress, using either ultrasound, magnetic resonance or optical imaging methods. When elastographic imaging methods were first proposed, tissue perturbation was accomplished by using either physiological tissue motion (such as pulsing blood vessels), dynamic external vibration (*i.e.*, sonoelasticity) or external static compression (*i.e.*, strain imaging). In 1990, Sugimoto et al. proposed the use of acoustic radiation force as a mechanical excitation source, revolutionizing the assessment of tissue elasticity (Sugimoto, Ueha, & Itoh, 1990).

Elasticity imaging methods that use radiation force as excitation source together with ultrasound tracking techniques to monitor tissue displacement are known as acoustic radiation force (ARF) based elastography (Palmeri & Nightingale, 2011; DeWall, 2013). A variety of ARF methods with different approaches have been investigated recently. These methods can be classified according to the temporal duration of the applied acoustic radiation force excitation, the relationship between pushing beam and tracking beam locations, and being qualitative or quantitative. Excellent reviews of these techniques have been provided by Doherty et al. (2013), Parker et al. (2011), and DeWall (2013).

The ability of conventional ultrasound imaging to differentiate various tissues within the body depends principally on variations in the acoustic impedance of the tissue under examination (Sarvazyan A. P., Rudenko, Swanson, Fowlkes, & Emelianov, 1998). On the other hand, ultrasound elastography derives a new subset of tissue properties and relies on differences in elasticity. An image based upon elasticity intrinsically answers a very natural question of the physician: “is the region of interest hard or soft?” and provides the physician with a virtual “finger” to probe internal regions of the body in a non-invasive way (Doherty, Trahey, Nightingale, & Palmeri, 2013; Benson & Fan, 2012; Sarvazyan A. P., Rudenko, Swanson, Fowlkes, & Emelianov, 1998; Palmeri, Dahl, Macleod, Grant, & Nightingale, 2009). Consider prostate or breast tumors as examples, these lesions can be much harder than the surrounding healthy tissue. However, these tumors might be invisible in standard ultrasound examinations, which have very poor image contrast when used to assess elastic features of soft tissues (Chen, Fatemi, & Greenleaf, 2004).

1.4 Acoustic radiation force based elastography

These methods use long-duration, focused ultrasound pulses (“pushing beams”) to generate acoustic radiation force to cause tissue displacements. Subsequently, “tracking beams” are used to monitor the resulting tissue motion, which can be related to qualitative and/or quantitative measures of stiffness (Palmeri & Nightingale, 2011).

Traditionally, ARF methods used to form a two-dimensional image providing a relative mapping of tissue elasticity. Although useful in detecting abnormal lesions, these methods are inadequate for assessing diffuse diseases such as liver fibrosis, where abnormality is not confined to a local region and there is no normal background tissue to provide contrast. Such circumstances require quantitative methods, where tissue elasticity is inversely solved in unit of Pascal (Chen, et al., 2009). Fig. 1.1 depicts the most common configurations to obtain qualitative and quantitative elastography images using acoustic radiation force.

1.4.1 Acoustic radiation force impulse imaging (ARFI)

This method uses acoustic radiation force to apply a normal stress to tissue. Subsequently, the normal strain (along the axis of the excitation beam) is monitored by tracking beams. A single ultrasound transducer is used to both induce and monitor the deformation response, with the tracking beam aligned with the pushing beam axis. On-axis methods only provide relative measurements of stiffness and are considered qualitative methods.

1.4.2 Shear wave elastography imaging (SWEI)

This method employs a pushing beam of acoustic radiation force to cause tissue displacement and generate shear waves that propagate in a perpendicular direction to the excitation beam. These shear waves are monitored at multiple off-axis locations by the same or a different transducer. Measurements of shear wave speed usually results in quantitative estimate of tissue stiffness (Sigrist, Liao, Kaffas, Chammas, & Willmann, 2017; Doherty, Trahey, Nightingale, & Palmeri, 2013; Nightingale, 2011).

Figure 1.1 - Main quantitative and qualitative ARF based methods. (a) Acoustic radiation force impulse imaging (ARFI). (b) Shear wave elastography imaging (SWEI).

Source: Adapted from Doherty et al. (2013).

1.5 Technical limitations of shear wave elastography

Measurement depth is a known barrier of ARF-based elastography due to several reasons. Sarvazyan et al. (2011) report that a major disadvantage of ARF methods is the difficulty to induce sufficient deformations beyond about 6 cm depth because of limits on the intensity used to avoid both mechanical and thermal bioeffects. Sigrist et al. (2017) mention factors associated with attenuation of compressional waves, which limit accurate assessment of deeper tissue or organs.

In addition, a number of studies have reported the unviability to apply shear wave elastography in overweight and obese patients¹ (Myers, et al., 2012; Sigrist, Liao, Kaffas, Chammas, & Willmann, 2017; Bota, et al., 2014). Obesity – defined as a body mass index (BMI) $\geq 30 \text{ kg/m}^2$ – is the strongest predictor of failed or unreliable liver stiffness measurements. Since subcutaneous fat attenuates the propagation of both shear waves into the liver and the tracking ultrasonic signals, failure (*i.e.*, no valid measurements) and unreliable results occur in $\approx 3\%$ -5% and 10%-15% of patients, respectively (Myers, et al., 2012).

Therefore, measurement depth is a potentially important limitation of current SWEI systems. Extending the depth range of this method to regions beyond 10 cm is crucial to enable the application of liver stiffness measurements in overweight/obese patients and ensure the effective translation of quantitative ultrasound elastography to clinical practice.

¹ According to the World Health Organization, worldwide obesity has nearly tripled since 1975. In 2016, more than 1.9 billion adults were overweight. Of these over 650 million adults were obese (World Health Organization, 2017). Moreover, since the 1980's, it has been reported that obesity increases the risk of developing several chronic diseases, including fatty liver disease (Clain & Lefkowitz, 1987).

1.6 Objectives

The main objective of the present dissertation is to develop a method to extend the depth range of quantitative ARF-based elastography to regions deeper than 10 cm. This work can be divided into the following specific objectives:

- a) Determine proper parameters for the design of a two-dimensional array transducer for acoustic radiation force generation in deeper tissues. This involves simulation, fabrication and characterization of the proposed transducer.
- b) Perform numerical simulations of the acoustic radiation force produced by the proposed ultrasound transducer together with the displacements induced by shear wave propagation in a tissue-like medium.
- c) Reconstruct tissue elastic properties based on the estimation of the speed of shear wave propagation.

2 Theoretical Background

In this section, theories, definitions and explanatory approaches in relation to this work are introduced. Firstly, mechanical properties of soft tissues and governing equations of the elasticity theory related to quantitative ultrasound elastography methods are presented. Then, the formula for acoustic radiation force generation is derived and the safety of ARF methods are discussed. Finally, the basics of ultrasound transducer is presented, which includes physical phenomena, construction aspects, equivalent circuits and efficiency.

2.1 Mechanical properties of soft tissues

The major differences in mechanical properties of materials allow them to be separated into two main groups: solid and liquid. Nevertheless, biological tissues exhibit properties of both viscous fluids and elastic solids (depending on the frequency of excitation) and are known as viscoelastic materials (Doherty, Trahey, Nightingale, & Palmeri, 2013; Sarvazyan, Fowlkes, Buxton, & Carson, 1995; Fung, 1993).

At frequencies above 100 kHz, soft tissues do not support shear stress and are more accurately modeled as viscous fluids (Palmeri, Sharma, Bouchard, Nightingale, & Nightingale, 2005). At lower frequencies (below 100 kHz), a linear elastic solid model is more suitable to describe their behavior. Herein, these two models (elastic solid and viscous fluid) shall be used to formulate a mathematical model for ultrasound based elastography.

When describing the phenomenon of acoustic radiation force generation, soft tissues will be considered to be fluids because the radiation force is induced by ultrasound waves at frequencies above 100 kHz. When describing the tissue response to this excitation, soft tissue will be treated as elastic solid because the frequency of the shear wave propagation (consequently, tissue deformation due to shear stress) is much lower than the frequency of the incident longitudinal ultrasonic wave.

2.1.1 Elastic moduli

Elastography assesses tissue elasticity, which is the tendency of tissue to resist deformation with an applied force, or to resume its original shape after the removal of the force. This can be expressed by the Hooke's law, *i.e.*, in terms of an elastic moduli Γ [Pa] or [N m⁻²], a given stress σ [Pa] or [N m⁻²], and the resulting strain ε [1], as:

$$\sigma = \Gamma \varepsilon \quad (2.1)$$

The higher the elastic modulus, the more a material tends to resist deformation. Assuming that a material is homogeneous, isotropic, and linear elastic, three types of elastic moduli can be defined as follow:

- Young's modulus (E) is defined when a normal stress produces a normal strain, *i.e.*, perpendicular to the surface.
- Shear modulus or modulus of rigidity (μ) is defined when a shear stress produces a shear strain, *i.e.*, tangential to the surface.
- Bulk modulus (K) is defined when a normal inward force or pressure produces a bulk strain or change in volume.

These relationships between stress and strain are illustrated in Fig. 2.1.

Figure 2.1 - Relationship between stress, strain and elastic moduli.

	Young's modulus (E)	Shear modulus (μ)	Bulk modulus (K)
Stress (σ)	$\sigma_N = \frac{F_n}{A}$	$\sigma_S = \frac{F_s}{A}$	$\sigma_B = \Delta P$
Strain (ϵ)	$\epsilon_N = \frac{\Delta l}{l}$	$\epsilon_S = \theta$	$\epsilon_B = -\frac{\Delta V}{V}$
Elastic moduli ($\mathcal{I}$)	$E = \frac{\sigma_N}{\epsilon_N}$	$\mu = \frac{\sigma_S}{\epsilon_S}$	$K = \frac{\sigma_B}{\epsilon_B}$

Source: Sigrist et al. (2017).

The following expressions make it possible to relate the three elastic moduli to each other (Sadd, 2005; Sarvazyan, Fowlkes, Buxton, & Carson, 1995; Sigrist, Liau, Kaffas, Chammas, & Willmann, 2017).

$$K = \frac{E}{3(1 - 2\nu)} \quad (2.2)$$

$$\mu = \frac{E}{2(1 + \nu)} \quad (2.3)$$

$$E = \frac{\mu(3\lambda + 2\mu)}{\lambda + \mu} \quad (2.4)$$

where λ is the Lamé's constant and ν is the Poisson's ratio.

Fig. 2.2 shows a scale of typical values of elastic moduli for various materials and body tissues. As can be seen, the bulk modulus (above arrow) for all soft tissues, liquids and solids are roughly in the same range. However, the range of the shear modulus (below arrow) differs widely from different types of tissues and materials in the body (Sarvazyan, Fowlkes, Buxton, & Carson, 1995).

Figure 2.2 - Variation of the shear and bulk moduli for various materials and body tissues.

Source: Sarvazyan et al. (1995).

Given the high-water content of soft tissues, they are nearly incompressible materials and have a Poisson's ratio (ν) close to 0.5. This means that an external stress only causes a change in the shape of the tissue, while its volume remains constant. If a soft tissue is subjected to a force, its resulting deformation is completely defined by the normal and shear stress-strain patterns, since its bulk pattern remains unchangeable (Doherty, Trahey, Nightingale, & Palmeri, 2013; Sarvazyan, Fowlkes, Buxton, & Carson, 1995; Sigrist, Liau, Kaffas, Chammas, & Willmann, 2017).

Therefore, in elastographic methods, the response of soft tissues to an applied excitation can be fully determined in terms of either shear or Young's moduli. This explains why conventional ultrasound methods – which are based on bulk compressional waves – are by no means related to tissue elasticity (*i.e.*, they do not provide any contrast directly related to the stiffness of the tissue). Nevertheless, only bulk modulus describes the impedance variation in tissues imaged by typical ultrasound imaging (Sarvazyan, Fowlkes, Buxton, & Carson, 1995).

2.1.2 Attenuation in soft tissues

In practice, an acoustic wave gradually loses energy during propagation. This phenomenon, called attenuation or loss, is caused by number of processes such as absorption, scattering, reflection, refraction and wave front divergence, being the first two processes the most common ones in soft tissues. Absorption occurs because the mechanical energy that is carried by the acoustic wave is converted into other forms of energy, mainly heat. Scattering occurs because of the reflection of the propagating wave in random directions by tiny particles inside the medium, as a result, the amplitudes of the acoustic field quantities are reduced in comparison with the lossless case. Mathematically, attenuation is defined in terms of the attenuation coefficient α [Np cm⁻¹] or [dB cm⁻¹] and the traveled distance of the wave x [cm], as:

$$A = A_0 e^{-\alpha x} \quad (2.5)$$

where A is the current wave amplitude and A_0 is the wave amplitude at $x = 0$.

Below 10 MHz, in most types of soft tissues, acoustic attenuation is dominated by the effects of absorption, with only a small contribution from scattering. Since it is very difficult to obtain accurate coefficients for absorption and scattering processes separately, both phenomena are usually combined and only the total attenuation is considered. The attenuation coefficient for most tissues satisfies an empirical frequency power law given by:

$$\alpha = \alpha_0 f^b \quad (2.6)$$

Here, α_0 [Np cm⁻¹ MHz^{-b}] or [dB cm⁻¹ MHz^{-b}] and b [1] are absorption parameters that depend on the medium under consideration, and f [MHz] is the frequency. Parameters for attenuation in water, blood, and some types of human tissue for frequencies below 10 MHz are listed in Table 2.1 (Verweij, Treeby, Dongen, & Demi, 2014; Amin, 1989).

Table 2.1 - Acoustic parameters for different medium of human tissue.

Medium	c_0 [m s ⁻¹]	ρ_0 [kg m ⁻³]	α_0 [Np cm ⁻¹ MHz ^{-b}]	b [1]
Water	1482	998	2.5×10^{-4}	2.0
Blood	1584	1060	1.6×10^{-2}	1.21
Brain	1562	1035	6.7×10^{-2}	1.3
Fat	1430	928	3.4×10^{-1}	1.0
Liver	1578	1050	5.2×10^{-2}	1.05
Muscle	1580	1041	6.3×10^{-2}	1.0

Source: Verweij et al. (2014); Duck (1990).

2.2 Elasticity theory applied to ARF-based elastography

The theory of acoustic radiation force methods rely on basic relations that govern displacement and motion. Observe Fig. 2.3, the focused ultrasound transducer applies a radiation force per unit of volume (f) that induces localized tissue displacement. This can be represented by a transformation of a body from a reference configuration (undeformed state) to a current configuration (deformed state). Since the force is applied directly to the region of interest and is associated with very small deformations, the hypothesis of geometric linearity can be assumed. Thus, the equations of equilibrium formulated in the reference configuration are not altered after the deformation (Doherty, Trahey, Nightingale, & Palmeri, 2013).

Figure 2.3 - Configuration of a body subjected to acoustic radiation force.

Source: Adapted from Doherty et al. (2013).

As an equation of equilibrium, the conservation of linear momentum can be expressed in terms of the Cauchy's stress tensor σ_{ij} [Pa] or [N m⁻²], with $i, j \in \{1, 2, 3\}$ as:

$$f_i = \frac{\partial \sigma_{ij}}{\partial x_j} + \rho b_i = \rho a_i \quad (2.7)$$

where f_i [Pa m⁻¹] or [N m⁻³] represents the externally applied force (*i.e.*, the radiation force), ρ [kg m⁻³] is the material density, b_i [Pa m⁻¹] or [N m⁻³] represents body forces (such as gravity), and $a_i = \partial^2 u_i / \partial t^2$ [m s⁻²] is the particle acceleration (Parker, Doyley, & Rubens, 2011; Doherty, Trahey, Nightingale, & Palmeri, 2013; Palmeri, Sharma, Bouchard, Nightingale, & Nightingale, 2005).

The strain tensor ε_{ij} can be expressed in terms of the particle displacement u_i [m] as follows:

$$\varepsilon_{ij} = \frac{1}{2} \left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right) \quad (2.8)$$

In order to construct a constitutive relation for the problem, it is assumed that each component of the stress tensor at a point is linearly related to each component of the strain tensor at that point (Saada, 1974; Sadd, 2005). Mathematically, this is expressed in standard tensor notation by writing:

$$\sigma_{ij} = C_{ijkl} \varepsilon_{kl} \quad (2.9)$$

where C_{ijkl} (with $i, j, k, l \in \{1, 2, 3\}$) is a fourth-order elasticity tensor whose components include all the parameters necessary to characterize the material. In general, the fourth-order tensor C_{ijkl} has 81 components. However, by assuming a homogeneous, isotropic, linear elastic material, the number of independent constants required to completely characterize the elastic properties of the material reduces to two (Sadd, 2005; Ophir, et al., 1996). These constants are the Lamé's constants λ and μ (shear modulus), which were previously introduced. The constitutive equations relating stresses to strains for an isotropic, homogeneous material can be written as:

$$\sigma_{ij} = 2\mu \varepsilon_{ij} + \lambda \delta_{ij} \varepsilon_{kk} \quad (2.10)$$

where δ_{ij} is the Kronecker's delta, which is unity when $i = j$ and zero otherwise (Sadd, 2005; Ophir, et al., 2002). Relations (2.10) are known as the generalized Hooke's law for linear isotropic elastic solids (expressed in terms of volumetric and deviatoric strain tensors).

It is possible to take the spatial derivative of the constitutive equations (Eq. 2.10) and substitute them into the balance of linear momentum (Eq. 2.7). Expressing the combined equations in terms of the particle displacement and neglecting body forces ($b_i = 0$) leads to:

$$(\lambda + \mu) \frac{\partial^2 u_j}{\partial x_j \partial x_i} + \mu \frac{\partial^2 u_i}{\partial x_j \partial x_j} = \rho \ddot{u}_i \quad (2.11)$$

This can be written in vector form as

$$(\lambda + \mu)\nabla(\nabla \cdot \vec{u}) + \mu\nabla^2\vec{u} = \rho\ddot{\vec{u}} \quad (2.12)$$

This equation governs the general dynamic response of a homogeneous, isotropic, linearly elastic material to a force or displacement excitation. If loads are applied slowly (quasi-statically) or if the displacement response to a constant load is measured after all the motion has stopped, then the right-hand side of this equation is negligible and set equal to zero. Therefore, this equation governs the static, quasi-static and dynamic responses that can occur in a tissue subjected to acoustic radiation force excitation (Parker, Doyley, & Rubens, 2011; Palmeri, Sharma, Bouchard, Nightingale, & Nightingale, 2005).

2.2.1 Speed of shear wave propagation and stiffness estimation

According to Achenbach (1976), the displacement field in a solid can be decomposed such that:

$$\vec{u} = \nabla\psi + \nabla \times \vec{W} \quad (2.13)$$

where ψ is a scalar that represents the components of the displacement that occur in the longitudinal direction (*i.e.*, compressional wave propagation) and $\vec{W}$ is a vector that represents the components of the displacement that occur in the transverse direction (*i.e.*, shear wave propagation). These scalar and vector displacement fields can be determined by using the Helmholtz decomposition (Palmeri, Sharma, Bouchard, Nightingale, & Nightingale, 2005). Substituting the displacement field (Eq. 2.13) into (Eq. 2.12) yields:

$$\nabla \left[(\lambda + 2\mu)\nabla^2\psi - \rho \frac{\partial^2\psi}{\partial t^2} \right] + \nabla \times \left[\mu\nabla^2\vec{W} - \rho \frac{\partial^2\vec{W}}{\partial t^2} \right] = 0 \quad (2.14)$$

The displacement components shown in Eq. 2.14 are separable. Each of them takes the form of a wave equation that describes the longitudinal and transverse (*i.e.*, shear) propagation, respectively expressed as:

$$\nabla^2\psi - \frac{1}{c_L^2} \frac{\partial^2\psi}{\partial t^2} = 0, \quad (2.15)$$

$$\nabla^2\vec{W} - \frac{1}{c_S^2} \frac{\partial^2\vec{W}}{\partial t^2} = 0, \quad (2.16)$$

where c_L [m s^{-1}] is the speed of the longitudinal wave propagation and c_S [m s^{-1}] is the speed of the shear wave propagation (Palmeri, Sharma, Bouchard, Nightingale, & Nightingale, 2005; Doherty, Trahey, Nightingale, & Palmeri, 2013). Assuming constant tissue density and incompressibility (*i.e.*, $\nu \approx 0.5$), these equations of wave speed can be written in terms of the elastic moduli as follows:

$$c_L = \sqrt{\frac{(\lambda + 2\mu)}{\rho}} \quad (2.17)$$

$$c_S = \sqrt{\frac{\mu}{\rho}} \quad (2.18)$$

These equations reveal c_L to be proportional to the material uniaxial modulus ($\sqrt{\lambda + 2\mu}$), which in fluids is commonly approximated by the bulk modulus K of the medium; and c_S to be proportional to $\sqrt{\mu}$, *i.e.*, the material shear modulus (Palmeri, Sharma, Bouchard, Nightingale, & Nightingale, 2005).

The propagation speed of longitudinal and shear waves are approximately 1540 m/s and 1-10 m/s in soft tissues, respectively. Relatively small variations in shear modulus (and hence in shear wave speed) allow suitable tissue contrast for shear wave elastography imaging (Sigrist, Liau, Kaffas, Chammas, & Willmann, 2017). Therefore, the goal of SWEI is to measure the shear wave propagation speed in order to obtain quantitative information about the stiffness (*i.e.*, shear or Young modulus) of soft tissues (Parker, Doyley, & Rubens, 2011; Doherty, Trahey, Nightingale, & Palmeri, 2013).

2.3 Acoustic radiation force formulation

Waves carry energy and momentum. Propagation through lossless homogeneous media implies the absence of interaction between the medium and the wave. However, in the case of a lossy medium, the energy and momentum can be transferred from the wave to the medium. The generation of acoustic radiation force occurs through a transfer of linear momentum from an acoustic wave to the soft tissue because of absorption, scattering or reflection. The derivation of acoustic radiation force cannot be directly obtained from the stress-strain relationships for a purely elastic material because no energy-loss mechanisms describe a change of linear momentum. In addition, at ultrasonic frequencies, soft tissues do not support shear stresses; thus, they are more accurately modeled as viscous fluids (Palmeri, Sharma, Bouchard, Nightingale, & Nightingale, 2005; Sarvazyan, Rudenko, & Nyborg, 2010; Jiménez, 2015).

Consider a homogeneous isotropic fluid in which the pressure, density and velocity at any point are given instantaneously by $p(x, y, z, t)$ [Pa] or $[\text{N m}^{-2}]$, $\rho(x, y, z, t)$ $[\text{kg m}^{-3}]$ and $v(x, y, z, t)$ $[\text{m s}^{-1}]$, respectively. Assuming that the only forces acting on a small volume δV of such fluid are the forces of elasticity and viscosity, the equation of motion of δV is given by the Navier-Stokes relation:

$$\begin{aligned} f &= -\nabla p + \left(\frac{4}{3}\eta + \eta'\right) \nabla \nabla \cdot v - \eta \nabla \times \nabla \times v \\ &= \rho \frac{dv}{dt} = \rho \left[\frac{\partial v}{\partial t} + (v \cdot \nabla) v \right] \end{aligned} \quad (2.19)$$

where f $[\text{Pa m}^{-1}]$ or $[\text{N m}^{-3}]$ is the force per unit volume due to stress; η and η' $[\text{Pa s}]$ or $[\text{N s m}^{-2}]$ are the shear viscosity coefficient and the bulk viscosity coefficient, respectively. Note that, for a fluid particle, the acceleration can be expressed as the sum of the local particle acceleration and the convective acceleration, *i.e.*, $a = \partial v / \partial t + v \cdot \nabla v$ (Doherty, Trahey, Nightingale, & Palmeri, 2013; Beyer, 1974).

The Navier-Stokes equation can be rewritten differently by making use of the equation of continuity

$$\frac{\partial \rho}{\partial t} + \nabla \cdot \rho v = 0 \quad (2.20)$$

to yield:

$$\frac{\partial(\rho v)}{\partial t} - F' = -\nabla p + \left(\frac{4}{3}\eta + \eta'\right) \nabla \nabla \cdot v - \eta \nabla \times \nabla \times v \quad (2.21)$$

where

$$-F' = \rho(v \cdot \nabla)v + v \nabla \cdot \rho v \quad (2.22)$$

The problem of modeling the acoustic radiation force reduces to obtain the time-average ($\langle \rangle$) of the change in momentum for a fluid as:

$$F' = -\langle \rho dv/dt \rangle \quad (2.23)$$

Nyborg (1965) proposed a method to approximate a solution to Eq. (2.21). This is based on series expansions of the pressure, density, and velocity in terms of successively higher order approximations (Beyer, 1974; Doherty, Trahey, Nightingale, & Palmeri, 2013):

$$\begin{aligned} p &= p_0 + p_1 + p_2 \cdots \\ \rho &= \rho_0 + \rho_1 + \rho_2 \cdots \\ v &= 0 + v_1 + v_2 \cdots \end{aligned} \quad (2.24)$$

The quantities p_0 and ρ_0 are the static or quiescent values of the pressure and density, respectively. The corresponding value of v is zero. Each term of a series is assumed to be much smaller than the preceding term (Sarvazyan, Rudenko, & Nyborg, 2010; Nyborg W. L., 1965). Substituting these series expansions in Eq. (2.21) and sorting out terms of corresponding order leads to:

zeroth order

$$-\nabla \rho_0 = 0 \quad (\rho_0 = \text{constant}) \quad (2.25)$$

first order

$$\rho_0 \frac{\partial v_1}{\partial t} = -\nabla p_1 + \left(\frac{4}{3} \eta + \eta' \right) \nabla \nabla \cdot v_1 - \eta \nabla \times \nabla \times v_1 \quad (2.26)$$

second order

$$\begin{aligned} \frac{\partial}{\partial t} (\rho_1 v_1 + \rho_0 v_2) + (\rho_0 v_1 \cdot \nabla) v_1 + \rho_0 v_1 \nabla \cdot v_1 \\ = -\nabla p_2 + \left(\frac{4}{3} \eta + \eta' \right) \nabla \nabla \cdot v_2 - \eta \nabla \times \nabla \times v_2 \end{aligned} \quad (2.27)$$

The expression for the acoustic radiation force is obtained by taking the time-average of Eq. (2.27) noting that the time-average of $\partial/\partial t \langle (\rho_1 v_1 + \rho_0 v_2) \rangle$ must be zero in the steady state. The last two terms in the left-hand side account for the nonlinearity of the material derivative and do not vanish (Beyer, 1974; Nyborg W. L., 1953). The remaining portion of the equation is therefore:

$$-F = -\nabla \langle p_2 \rangle + \left(\frac{4}{3} \eta + \eta' \right) \nabla \nabla \cdot \langle v_2 \rangle - \eta \nabla \times \nabla \times \langle v_2 \rangle \quad (2.28)$$

where the acoustic radiation force F is defined by

$$-F = \rho_0 \langle (v_1 \cdot \nabla) v_1 + v_1 (\nabla \cdot v_1) \rangle \quad (2.29)$$

This force is equivalent to an external force driving the second order system (Beyer, 1974). Thus, if considering a plane wave propagating in the x [m] direction in an absorbing-media with attenuation coefficient α , the first-order velocity is given by:

$$v_1 = A e^{-\alpha x} \sin(\omega t - kx) \quad (2.30)$$

where A is the wave amplitude, ω [Hz] is the angular frequency and k [m⁻¹] is the wave number. Then, the expression for the acoustic radiation force can be reduced to:

$$F_x = -2\rho_0 \langle v_1 \frac{\partial v_1}{\partial x} \rangle = \rho_0 \alpha A^2 e^{-2\alpha x} \quad (2.31)$$

If $\alpha x \ll 1$ over the region of interest, F_x is nearly constant and given by:

$$F_x = \rho_0 \alpha A^2 \quad (2.32)$$

For a sinusoidal wave, the time-average intensity I [W cm⁻²] is expressed as:

$$I = \frac{1}{2} \rho_0 c A^2 \quad (2.33)$$

where c is the wave speed propagation in the medium (Elert, 2017; Secomski & Nowicki, 2014). Thus, at any given spatial location, the time average acoustic radiation force F [kg s⁻² cm⁻²] is defined as:

$$F = \frac{2\alpha I}{c} \quad (2.34)$$

This is the most common approach to calculate the acoustic radiation force in absorbing media. It is seen that the resulting force is proportional to the wave intensity and the attenuation coefficient (Doherty, Trahey, Nightingale, & Palmeri, 2013; Jiménez, 2015).

2.4 Safety considerations of ARF-based elastography

The safety of ARF-based elasticity imaging methods should be investigated to minimize patient risk. With configurable parameters, including spatial location, excitation duration, pulse length, pulse repetition frequency, intensity, etc., there are many tradeoffs that balance frame rates and image quality versus patient safety (Doherty, Palmeri, Trahey, & Nightingale, 2015).

2.4.1 Tissue thermal response

Transient ARF-based methods typically employ excitation pulses with similar amplitudes and longer pulse durations – several hundred cycles – than those commonly used for diagnostic imaging (10–20 cycles for Doppler methods). Longer durations result in increased tissue heating, which makes necessary the monitoring of tissue thermal response. For a single impulsive radiation force excitation, heat loss owing to both perfusion and thermal conduction can reasonably be neglected, and the temperature rise ΔT [K] in the tissue can be estimated using:

$$\Delta T = \frac{q_v}{c_v} t = \frac{2\alpha I}{c_v} t \quad (2.35)$$

where q_v [W cm^{-3}] or [$\text{J s}^{-1} \text{cm}^{-3}$] is the rate of heat production per unit volume generated by the absorption of acoustic energy, c_v [$\text{W s K}^{-1} \text{cm}^{-3}$] or [$\text{J K}^{-1} \text{cm}^{-3}$] is the heat capacity per unit volume of the tissue and t [s] is the duration of the excitation. Both heating owing to acoustic absorption and transducer face heating must be considered when designing sequences for clinical use to maintain the temperature within diagnostic limits.

2.4.2 Cavitation

Cavitation bubbles is a phenomenon that occurs when sudden negative pressure is applied within fluidic mediums. The gases which are dissolved within the medium leave the solution mainly around small solid elements floating within the medium. When this happens, tiny gas bubbles are formed. Under ultrasonic excitation, the bubbles oscillate and – at sufficiently high ultrasonic pressure levels – they can collapse, as shown in Fig. 2.4. The collapse of these bubbles is a very aggressive process and the generated peak pressure and temperature may reach extremely high values (Azhari, 2010; O'Brien Jr., 2007). Cavitation generates a series of events that may be harmful to the patient: a) high amplitude shear waves, which may cause lysis of adjacent cells; b) acoustic shocks that can propagate stress waves outwards; c) harmful high pressures and temperatures; and d) enough energy to cause free radicals generation local to the collapsing bubble (Cardoso, Santos, & Furuie, 2016).

Figure 2.4 - Schematic depiction of an asymmetric collapse of a cavitation bubble. The formed jet may reach a velocity of several hundred meters per second.

Source: Azhari (2010).

2.4.3 Mechanical index

The mechanical index (MI) provides an indication of an ultrasound beam's ability to cause cavitation related bio-effects, and can be considered as a reasonable proxy for micro mechanical damage. A higher MI produces a larger bio-effect (cavitation). MI is expressed as:

$$MI = \frac{p_r}{\sqrt{f}} \quad (2.36)$$

where p_r [MPa] is the peak rarefactional pressure and f [MHz] is the ultrasonic frequency. Therefore, cavitation is less prominent at high frequencies whereas lower frequencies can be less safe. To reduce the likelihood of the generation of acoustic cavitation in diagnostic ultrasound, the Food and Drug Administration (FDA) states that $MI < 1.9$ is considered safe (Basaeri, Christensen, & Roundy, 2016; O'Brien Jr., 2007).

2.5 Ultrasound transducer basics

The transducer is the heart of any medical ultrasound imaging system. It performs the conversion of electrical energy into mechanical energy, and conversely, the conversion of mechanical energy into electrical energy (Hunt, Arditi, & Foster, 1983). The majority ultrasonic transducers used today is made of piezoelectric materials, which are based on the direct and inverse piezoelectric effect: if a voltage is applied on two opposite faces of a piezoelectric material, a mechanical deformation (shortening, elongation, shear, etc.) is produced. On the other hand, if opposite faces of a piezoelectric material are mechanically deformed, a voltage is generated between the two faces (Azhari, 2010).

Since piezoelectric materials are multidirectional, efforts have been made in order to achieve better conversion efficiency in the forward face of the element, *i.e.*, towards the tissue (Duck, Baker, & Starritt, 1998). Commonly, two additional layers are attached on both sides of the piezoelectric element, forming a sandwich structure such as the one shown in Fig. 2.5. At the front

side, facing the medium where acoustic waves are transmitted or received, an impedance matching layer is positioned. At the back side of the element, a backing layer is placed.

Figure 2.5 - The three layers that comprise an ultrasonic transducer.

Source: Azhari (2010).

2.5.1 The matching layer

The matching layer is used to avoid that ultrasonic waves transmitted from the piezoelectric element are reflected off due to the big difference in acoustic impedance between the piezoelectric element and the medium. The acoustic matching layer is designed to have an adequate acoustic impedance value using a combination of different resin materials. It can be easily shown that for a plane wave, 100% transmission occurs when: 1) the thickness d [m] of the matching layer equals $d = \lambda_M/4$, where λ_M [m] is the wavelength in the matching layer material; and 2) the characteristic impedance of the matching layer Z_M [MRayl] is the geometric mean of the loading medium Z_L and the piezoelectric material impedances Z_C , *i.e.*, $Z_M = \sqrt{Z_L Z_C}$ (Kinsler L. E., Frey, Coppins, & Sanders, 1999; Azhari, 2010; Szabo, 2004).

2.5.2 The backing layer

The backing material is located behind the piezoelectric element to prevent excessive vibration by absorbing energy transmitted to the back of the transducer. For this purpose, a suitable material with proper acoustic impedance and attenuation coefficient is used to damp mechanically the oscillations. However, it may slightly reduce the sensitivity of the transducer (Azhari, 2010). When a transducer is air-backed (*i.e.*, the backing layer is air), almost all acoustic energy at the backing interface is reflected into the forward direction due to the mismatch in acoustic impedance between air and the piezoelectric material. Thus, very little energy is lost. On the other hand, this mismatch, which produces the so-called ringing effect for pulse-echo applications, lengthens the pulse duration and lowers the bandwidth (Shung & Zipparo, 1996).

2.5.3 Ultrasound transducer arrays

Ultrasound transducer arrays are transducer assemblies with more than one piezoelectric element. The geometry of elements in a transducer array can be quite general, but rectangular elements are often used in practice because they are cost effective to manufacture (Goldberg & Smith, 2000). As shown in Fig. 2.6, linear and two-dimensional (2D) arrays are formed by rectangular elements with width w and height h . The space between two elements is called kerf (k), and the distance between the centers of two adjacent elements is called pitch (p). The kerfs may be filled with acoustic isolating material or simply air to minimize acoustic cross talk.

Source: Schmerr Jr. (2015).

2.5.4 Focusing and steering with ultrasound transducer arrays

If each piezoelectric element of a transducer array is driven simultaneously so that a voltage is applied to all elements at the same time (*i.e.*, no relative time delays among array elements), the resultant ultrasound beam of the array is similar to the beam generated by a single piezoelectric element of the same size as the entire array aperture. However, by varying the relative time delays of the electrical pulses that drive each array element, it is possible to electronically modify the resultant beam of the transducer array. With an appropriate combination of time delay laws, beam steering and/or focusing can be performed in different directions without requiring any motion of the transducer itself. As shown in Fig. 2.7(a), a linear array can focus and steer its ultrasound beam through a sector-shaped region only in one plane. A 2D array is able to steer and focus its beam throughout a three-dimensional (3D) volume, as shown in Fig. 2.7(b) (Schmerr Jr., 2015; Shung & Yen, 2015).

Figure 2.7 - Region scanned by the ultrasound beam. (a) Linear array. (b) 2D array.

Source: Goldberg & Smith (2000).

The essence of focusing an ultrasound beam is to align the pressure fields from all parts of the aperture to arrive at a desired point at the same time. This can be done by delaying or advancing the fields from individual array elements. The delay is determined using ray acoustics.

Figure 2.8 - Distance from the transducer array to the focal point.

Source: Author.

Consider the 4-elements array shown in Fig. 2.8. The distance from the transducer to the focal point (r) together with the speed of sound (c) in the medium provide the propagation time (t) of the acoustic wave, so that $t = r/c$. The propagating time of each array element is then adjusted (delayed) relatively according to a reference point. The propagation time t_i from the center of the element i to the focal point is:

$$t_i = \frac{1}{c} \sqrt{(x_i - x_f)^2 + (y_i - y_f)^2 + (z_i - z_f)^2} \quad (2.37)$$

where (x_f, y_f, z_f) is the position of the focal point and (x_i, y_i, z_i) is the center of the element i .

A point is selected on the whole aperture as a reference (normally the center of the array). The propagation time from the center of the array to the focal point is given by:

$$t_c = \frac{1}{c} \sqrt{(x_c - x_f)^2 + (y_c - y_f)^2 + (z_c - z_f)^2} \quad (2.38)$$

where (x_c, y_c, z_c) is the center of the aperture of the transducer. Thus, the delay to be applied on element i of the array is:

$$\Delta t_i = \frac{1}{c} \left(\sqrt{(x_c - x_f)^2 + (y_c - y_f)^2 + (z_c - z_f)^2} - \sqrt{(x_i - x_f)^2 + (y_i - y_f)^2 + (z_i - z_f)^2} \right) \quad (2.39)$$

The time delay has to be calculated to all array elements so that the propagating waves from all elements will arrive together at the focal point. The emitted pressure field is calculated by integrating the field over all elements of the aperture. A perception of the sound field for a fixed time instance can be obtained by employing Huygens' Principle in which every point on the radiating surface is the origin of an outgoing spherical wave. The spatial impulse response is found by observing the pressure waves at a fixed position in space over time by having all the spherical waves pass the point of observation and summing them (Kidav, Sujathakumari, & Laseena, 2015; Jensen, Fink, Kuperman, Montagner, & Tourin, 2002).

2.5.5 Transducer equivalent circuits

Numerous sophisticated equivalent circuits have been proposed to model the electrical and mechanical characteristics of ultrasound transducers. The usefulness of equivalent circuits approach is based on the ability to predict the frequency-dependent electrical impedance, and the transmitted and received ultrasound waveforms of a specific transducer (Hunt, Arditi, & Foster, 1983). The simplest construction of an ultrasonic transducer is a parallel-plate of piezoelectric material with electrodes for connection such as a capacitor structure. As the piezoelectric itself is a dielectric material, the corresponding transducer element has, therefore, a clamped capacitance, C_0 [F] (Zhou, Lam, Zheng, Qiu, & Shung, 2014; Szabo, 2004). At frequencies away from resonance, the clamped capacitance of a transducer is given by:

$$C_0 = \epsilon^s \frac{A}{d} \quad (2.40)$$

where ε^S [F m⁻¹] is the clamped dielectric constant, A [m²] is the area of the piezoelectric element, and d [m] is the thickness of the piezoelectric material (Goldberg & Smith, 2000).

A particularly useful equivalent circuit was proposed by Krimholtz, Leedom, & Matthaei (1970), which is referred to as the KLM model. In this model (illustrated in Fig. 2.9), the transducer is seen as a three-port network connected to the center of an acoustic transmission line, with two ports being mechanical ports representing the front and back surfaces of the piezoelectric crystal, and one being an electrical port representing the electrical connection of the piezoelectric material to the electrical generator (Shung & Zipparo, 1996). The roles of the electrical and mechanical ports are clearly distinguished, and the electrical input impedance for an arbitrary acoustic load can easily be calculated (or vice versa). The transmission line is driven by a perfect transformer with a frequency-dependent turns ratio $\phi:1$, where

$$\phi = k_T \left(\frac{\pi}{\omega_0 C_0 Z_C} \right)^{1/2} \text{sinc} \left(\frac{\omega}{2\omega_0} \right) \quad (2.41)$$

with $\text{sinc } x = \sin(\pi x)/\pi x$. The center frequency of the transducer is ω_0 [Hz], Z_C [MRayl] is the acoustic impedance, and k_T [1] is the coupling factor of the piezoelectric material (Szabo, 2004; Hunt, Arditi, & Foster, 1983). There is an additional reactance in series with the transformer which can be modeled as a variable capacitance of value:

$$C' = -C_0 / \left[k_T^2 \text{sinc} \left(\frac{\omega}{\omega_0} \right) \right] \quad (2.42)$$

As $|C'| \gg |C_0|$, it only has a minor influence on the operation of the transducer (Desilets, Fraser, & Kino, 1978).

Source: Krimholtz et al. (1970).

At resonance, the equivalent circuit for a transmitting transducer irradiating into a medium can be represented by two-port networks consisting of a capacitor and a resistor either in series or in parallel (Kino, 1987). Fig. 2.10 shows simplified series and parallel equivalent circuits for a transducer operating at resonance without losses and transmitting into low impedance acoustic loads.

Figure 2.10 - Simplified equivalent circuits for a single-element transducer at resonance. (a) Series. (b) Parallel.

Source: Shung et al. (1996).

Two important values of electrical impedance module are easily calculated by using this model: the resistance in series R_a [Ω], which is a local minimum point of the impedance; and the radiation resistance in parallel R_m [Ω], which is a local maximum of the impedance (Hunt, Arditi, & Foster, 1983). They are given by:

$$R_a = \frac{4k_T^2}{\pi\omega_0 C_0} \left(\frac{Z_C}{Z_R + Z_L} \right) \quad (2.43)$$

$$R_m = \frac{\pi}{4k_T^2\omega_1 C_0} \left(\frac{Z_R + Z_L}{Z_C} \right) \quad (2.44)$$

where ω_0 is the series or resonant frequency, ω_1 is the parallel or anti-resonant frequency, k_T is the electromechanical coupling coefficient of the piezoelectric material, Z_C is the acoustic impedance of the piezoelectric material, Z_R is the acoustic impedance of the transducer backing, and Z_L is the acoustic impedance of the load medium (body tissue). The power dissipated through R_m corresponds to the acoustic output power from the transducer (Goldberg & Smith, 1994; Kino, 1987).

The analysis of Eq. (2.40) and Eq. (2.43)-(2.44) enables to conclude that, as the size of the cross-sectional area A of the transducer decreases, the clamped capacitance C_0 decreases, and the resistances R_a and R_m increase. A large element electrical impedance brings a particular challenge that shall be considered when designing array transducer with small size elements: the transmit

efficiency, which is a very important factor for acoustic radiation force excitation transducers (Goldberg & Smith, 1994; Duck, Baker, & Starritt, 1998).

2.5.6 Power transfer efficiency

In fact, array transducers with small size elements have a very poor transmit efficiency because of the enormous impedance mismatch between a typical $50\ \Omega$ transmit circuitry and – about two orders of magnitude higher – impedance of the array element (Goldberg & Smith, 1994). To outline the effect of this large impedance mismatch in the power transfer, consider the block diagram in Fig. 2.11 that illustrates the electrical loads for a single array element connected to a typical ultrasound system.

Figure 2.11 - A single element of a transducer array connected to an ultrasound system.

Source: Goldberg & Smith. (1994).

The simplified circuit in Fig. 2.12 shows a transmit circuitry formed by a voltage source V_{in} with resistance R_0 connected to a transducer at series resonant frequency.

Figure 2.12 - Equivalent circuit of a piezoelectric transducer at its resonant frequency.

Source: Kino et al. (1987).

According to Kino (1987), the maximum power P_{in} [W] available from the voltage source is:

$$P_{in} = \frac{V_{in}^2}{8R_0} \quad (2.45)$$

The power delivered to the transducer is proportional to the power dissipated in R_a , which is:

$$P_{out} = \frac{V_{out}^2}{2R_a} = \frac{V_{in}^2 R_a}{2[(R_0 + R_a)^2 + (1/\omega_0 C_0)^2]} \quad (2.46)$$

where $V_{out} = V_{in} R_a / (R_0 + R_a + j1/\omega_0 C_0)$. Hence, the power efficiency η [%] is

$$\eta = \frac{P_{out}}{P_{in}} = \frac{4R_0 R_a}{(R_0 + R_a)^2 + (1/\omega_0 C_0)^2} \quad (2.47)$$

For a fixed-source impedance, the maximum power efficiency is obtained by taking the derivative of Eq. (2.47) with respect to R_a and setting it to zero, then, η is maximum when $R_0 = \sqrt{R_a^2 + (1/\omega_0 C_0)^2}$. Thus, the maximum power transfer occurs when the complex electrical impedance of the transducer is entirely real – the imaginary component of the electrical impedance must be tuned out – and the radiation resistance equals the electrical source resistance, *i.e.*, $R_0 = R_a$. (Desilets, Fraser, & Kino, 1978; Kino, 1987; Goldberg & Smith, 2000).

Researchers have investigated methods to improve the transmit efficiency of transducers by: 1) using transformers with adjustable turn ratio so that the element electrical impedance matches the voltage source impedance; 2) using electrical network of inductors to lower the imaginary component of the electrical impedance; 3) using multilayer piezoelectric material to increase the clamped capacitance of the array element and reduce its electrical impedance (Goldberg & Smith, 2000; Goldberg & Smith, 1994). The use of transformers is very difficult to implement in the large quantities required for an array transducer, mainly because of space limitations. Inductor networks have successfully been used in transducers for many years, however, an inductor network may significantly narrow the bandwidth of a very tiny element – generally, a more sophisticated tuning network is desirable for broader bandwidth operation (Desilets, Fraser, & Kino, 1978). Finally, the use of multilayer piezoelectric material can effectively improve the transducer transmit sensitivity by increasing the clamped capacitance of the layer structure. Nevertheless, the fabrication of multilayers involves thick film technologies that become very complex for a 2D array transducer (Goldberg & Smith, 1994).

3 Methods

In this section, the materials and methods utilized in this work are presented. The proposed method is divided into two stages. The first one consists of the design, fabrication and characterization of a two-dimensional transducer array for acoustic radiation force generation in deeper tissues. This part involved numerical simulations and experimental procedures to evaluate the transducer's performance. In the second stage, it is performed numerical simulations of shear wave ultrasound elastography in a tissue-like medium using the proposed transducer as the excitation source. Finally, the resulting tissue displacement is tracked to estimate the shear wave speed propagation and reconstruct the shear modulus of the region of interest.

3.1 Transducer Design

The decision to design a transducer for acoustic radiation force generation in a two-dimensional array configuration arose from the fact that, besides the ability to steer and focus in three-dimensions, a 2D array overcomes an inherent limitation of conventional linear arrays used in practice: the high energy concentration near the transducer surface when focused at deeper regions.

Palmeri et al. (2005) used linear array for ARF generation and demonstrated that, when the transducer is focused at deeper focal points, the radiation force magnitude close to the transducer is greater than at the focal depth. This great energy concentration may generate unwanted tissue displacement and shear wave generation. In addition, it maximizes the risk of heating, cavitation bubbles or other tissue damage.

Cardoso et al. (2016) compare the energy concentration of a linear and a 2D array with equivalent active aperture width and demonstrate that the 2D configuration performs beam focus at deeper regions without a great energy concentration near the transducer surface. Fig. 3.1 shows the typical pressure distribution (simulated) of a linear array focused at far depth. The simulation was performed using the program Fast Object-Oriented C++ Ultrasound Simulator (FOCUS).

As can be seen, the maximum pressure occurs near the transducer surface. This might be dangerous because, in order to induce sufficient energy at the focal point to create tissue displacement, an even greater energy is concentrated nearby the face of the transducer.

Thus, to mitigate this limitation, it was proposed a 2D array configuration designed specifically for ARF generation in deeper regions. Note that, the proposed transducer is used exclusively for ARF excitation (*i.e.*, transmission mode). In practice, another transducer (reception mode) is required to perform the shear wave tracking and image generation.

Figure 3.1 - Simulated pressure field of a linear array focused 120 mm deep. (a) Lateral-axial plane. (b) Axial profile. Main parameters of the simulation: 128-elements linear array; Element width=0.5 mm; Element height=5 mm; kerf=0; Center frequency=1 MHz; Lossless medium; Sound speed=1540 m/s;

Source: adapted from Cardoso et al. (2016)

3.1.1 Operational center frequency

Proper selection of transducer frequency is an important concept for providing optimal image resolution in ultrasound imaging. High-frequency ultrasound waves generate images with high axial resolution, but these waves are more attenuated than lower frequency ones. Conversely, low-frequency waves provide images with lower resolution, but can penetrate to deeper structures due to the low degree of attenuation.

Considering that the proposed transducer will operate only in transmission mode for ARF generation (*i.e.*, no images will be generated), a low center frequency is chosen to deepen the wave penetration. Good results were achieved (via simulation) using frequencies between 0.5 MHz and 1 MHz to focus the ultrasound beam beyond 100 mm depth (Cardoso, Santos, & Furuie, 2016). Thus, it was defined a center frequency of 800 kHz. In practice, another transducer (with higher center frequency) will be required to track the tissue displacement and generate elastographic images.

3.1.2 Array arrangement

The proposed 2D array transducer contains 130 elements arranged in a 10×13 matrix. In order to control all array elements, an individual connection from the ultrasound system to each element is necessary. However, addressing 130 elements individually is a great practical challenge due to the vast number of interconnections and the sampling and real-time processing this volume of data (Rasmussen & Jensen, 2013).

Again, considering that the proposed transducer is used only in transmission mode, its ultrasound beam can be constantly focused. Based on this, it was proposed an arrangement that takes advantage of the array symmetry to minimize the number of connections and channels necessary to drive the array elements. This arrangement is also beneficial to reduce the electrical impedance of the array elements, which shall be explained in a later section.

For the sake of simplicity, consider the linear transducer array connected to an ultrasound system shown in Fig. 3.2(a). The transducer consists of N elements driven by N channels programmed with N time delays that enable focus and steer the beam at a given focal point. Note that, when the ultrasound beam is focused at the center of the aperture, the delays applied on its symmetrical elements – in relation to the center of the aperture – are equivalent to each other, as depicted in Fig. 3.2(b). Therefore, if pairs of symmetrical elements are interconnected, the ultrasound beam will be constantly focused at the center of the aperture. In this case, the number of necessary channels to drive the array can be reduced by: 1) $N/2$ if N is an even number; or 2) $N/2 + 1$ if N is odd.

A consequence of the interconnection of symmetrical elements is that, a degree of freedom of the ultrasound beam is eliminated. In other words, the linear transducer will be capable of varying its focal length (r), but will be unable to vary its focal angle (θ).

In the case of 2D transducer, symmetrical element pairs can be formed in relation to the center of the aperture in the lateral or elevational directions, resulting in the cancellation of the azimuth or elevation degrees of freedom, respectively (in spherical coordinates). On this basis, it was applied the reduction of connections in one direction of the proposed transducer. The transducer geometry and coordinate system is shown in Fig. 3.3. Symmetrical elements in respect to the y -axis are interconnected and excited simultaneously. As seen, the resulting ultrasound beam can only be focused and steered throughout the yz -plane.

Figure 3.3 - Transducer array arrangement. (a) Element identification. (b) Coordinate system.

3.1.3 Element size and pitch

The proposed array has rectangular elements with 5.6 mm width and 4.9 mm height. The element size and aperture were chosen large to avoid a great energy concentration near the transducer surface when focusing at deeper distances. Due to construction aspects, the pitch of the proposed transducer was chosen to be 7.6 mm in the x direction and 5.0 mm in the y direction. Fig. 3.4 shows the element size and pitch of the proposed transducer.

Figure 3.4 - Element and pitch dimensions.

3.1.4 Grating lobes

It is well known that grating lobes will occur whenever the pitch of an array is equal to or greater than the wavelength λ , and there will be no grating lobes when the pitch is smaller than half a wavelength. For pitch between one-half and one wavelength, the generation of grating lobes will depend on the steering angle (Tumbull, Ken, & Foster, 1990; Lee & Choi, 2000).

Operating with the center frequency of 800 kHz in soft tissues, where the sound speed is approximately 1540 m/s, ultrasonic waves have a wavelength of around 1.9 mm. In order to avoid grating lobes, the pitch of the proposed transducer would have to be smaller than 0.95 mm in both

directions, which is impossible to be accomplished with an element size of 5.6×4.9 mm. Reducing the center frequency to values below 100 kHz could effectively eliminate grating lobes (since $\lambda \approx 15$ mm), but this frequency is out of the range of interest (*i.e.*, 0.5 – 1 MHz).

3.1.5 Pressure field simulations

Herein, the pressure field of the proposed transducer was simulated in order to evaluate the beam focusing and steering properties of the array. The simulations were carried out using the program FOCUS (Fast Object-Oriented C++ Ultrasound Simulator), which is a MATLAB (The Mathworks Inc.) toolbox based on the Fast Nearfield Method (FNM) with time-space decomposition. FOCUS is able to perform transient calculations very quickly and with low memory usage. However, the downside of this simulator is that it ignores attenuation (for transient simulations) and simulates acoustic waves (*i.e.*, longitudinal waves) in homogeneous medium only (Chen & McGough, 2008).

For all simulations, it was used a grid of $120 \times 120 \times 200$ mm in the x, y, z -directions, respectively, with a resolution of 1 mm in all directions. The medium parameters were defined as follows: sound speed of 1540 m/s, and density of 1000 kg/m^3 . The input excitation source was defined as a 5-cycles tone burst of 800 kHz. The sampling frequency of the simulations is 10 MHz.

Figure 3.5 shows the simulated pressure map (in the xz plane), the axial profile (along z -direction) and the lateral profile (along the x -direction) of the proposed transducer focused at $x=0; y=0; z=120$ mm.

Figure 3.5 - Simulated pressure field of the proposed transducer. (a) xz -plane. (b) Axial profile. (c) Lateral profile.

Source: Author.

The transducer is capable of focusing at 120 mm with a lower energy level near its surface, as desired to avoid heating and tissue damage. As can be seen, it presents grating lobes at around

$x=\pm 30$ mm, which is relatively far from the region of interest (*i.e.*, focal zone). In addition, the pressure level in the grating lobes is 10 dB less than the pressure level in the main lobe. Most likely, the intensity level of the grating lobes will be insufficient to generate undesired tissue displacement. The effect of these grating lobes to the acoustic radiation force generation and tissue displacement will be discussed in a later section.

Figure 3.6 - Simulated pressure field in the xy -plane ($z=100$ mm). (a) Focused at $x=0; y=0; z=100$ mm. (b) Focused at $x=10; y=0; z=100$ mm. (c) Focused at $x=0; y=10; z=100$ mm. (d) Focused at $x=15; y=15; z=100$ mm.

Source: Author.

Fig. 3.6 shows the simulated pressure field in the xy -plane ($z=100$ mm) of the transducer focused at different points on and off-axis. It is noticeable that the magnitude of the grating lobes along the aperture in the x - and y -directions are different from each other (grating lobes in the x -direction are much greater). This is due to the different pitches relative to the x and y -directions.

When the beam is steered (*i.e.*, focused at off-axis positions), as the focal point distances from the center of the aperture, the magnitude of the grating lobes increases, and the ultrasonic beam becomes more degraded. Acceptable levels of grating lobes were achieved within the range of ± 10 mm in the x and y -directions.

From now on, only simulations of the xz -plane will be shown herein because this is the most critical plane of pressure distribution of the proposed transducer due to the greater grating lobes.

3.2 Transducer fabrication

The piezoelectric ceramic chosen to fabricate the array transducer is Pz37 (lead zirconate titanate) of FERROPERM, whose characteristics are shown in Table 3.1. The main advantage of this piezoceramic is the very low acoustic impedance and broader bandwidth (Ferropem, 2016).

Table 3.1 - Main characteristics of Ferropem Pz37 (at 1MHz)

Property	Value
Center frequency f	1 MHz
Thickness	1.43 mm
Relative dielectric permittivity k_{33}^T	1150
Dielectric dissipation factor $\tan \delta$	0.015
Curie temperature T_C	350 °C
Coupling factor, lateral k_p	0.35
Coupling factor, thickness k_t	0.52
Mechanical Quality Factor $Q_{m,t}$	50
Acoustic impedance Z	18 MRayl
Density ρ	6600 kg/m ³

Source: Ferropem (2016).

The fabrication process starts with a plate of Pz37. The first step was to identify the direction of the piezoelectric polarization in order to optimize the construction. After properly cleaned, the piezoelectric ceramic was affixed on a phenolite board (used as a sacrificial layer) and glued together on a glass plate to eliminate any movement and enhance flatness during cut, as shown in Fig. 3.7(a). Then, the sandwich formed by the ceramic, phenolite and glass plate was placed on the vacuum chuck table of a dicing saw (Automatic Dicing Saw DAD322, DISCO Corporation) and two sets of perpendicular scribes – reference for cutting – were made with a 0.1 mm wide-blade.

Then, thirteen parallel sets of non-through cuts were made. The distance between cuts was 4.9 mm and the ground face of the ceramic remained intact. After that, the ceramic was cut through in ten parallel cuts – of 5.6 mm distance – in a perpendicular direction to the previous ones, resulting in ten separated piezoelectric ceramic strips with thirteen elements of dimensions of $5.6 \times 4.9 \times 1.43$ mm each and 0.1 mm kerf – blade thickness – between them. Due to the non-through cuts, all elements of each ceramic strip share a common ground to avoid soldering and to ease the alignment of the elements. The strips of ceramic are depicted in Fig. 3.7(b).

After properly arranging the strips to form the 2D array, electrode boards were placed between the strips to both give mechanical support and facilitate the electrical contact of the elements – Fig. 3.7(c). The thickness of the electrode boards is 2 mm, which is the kerf in the x -direction.

The electrical connections were carried out in three steps: firstly, wires were soldered to connect the elements to the electrode board, as shown in the Fig. 3.7(c); secondly, all symmetrical elements were electrically connected with wires – Fig. 3.7(d). Finally, a 1.5 m coaxial cable and a connector were added. The transducer was kept air-backed and its housing is made of phenolite board, which was posteriorly shielded with an electrically conductive adhesive tape.

The matching layer is a fabricated composite. Firstly, it was produced a loaded mixture consisted of resin (Araldite GY 279) and hardener (Aradur HY 951) with a mass ratio of 1:0.1, respectively. Secondly, a 0.25 volume fraction of alumina powder (average particle size of 6 μm) was added in the mixture to obtain a characteristic acoustic impedance of $Z_M=5.26$ MRayls (geometric mean of the Pz37 and soft tissues acoustic impedances). The composite was, then, placed on the front side of the transducer and polished to obtain the desired thickness of a quarter of wavelength (Zhou, et al., 2009; Kino, 1987; Kinsler & Frey, 1962; Oliveira, 2015; Hunt, Arditi, & Foster, 1983). A picture of the finished probe is shown in Fig. 3.7(e).

Figure 3.7 - Transducer fabrication. (a) Piezoelectric, phenolite and glass plate structure. (b) Piezoelectric strips. (c) Array arrangement with electrode boards. (d) Reflection procedure with wires. (e) Finished probe.

Source: Author.

3.3 Transducer characterization

The transducer characterization was performed by following a standard guide of practices and procedures for evaluating certain characteristics of ultrasonic transducers (ASTM E1065/E1065M - 14, 2016). The excitation source used to drive the fabricated transducer in all experimental procedures of this work is shown in Fig. 3.8. This is a negative square pulse of 100 V and 2 μ s pulse width generated by an ultrasonic pulser/receiver unit (5077PR, Panametrics-NDT).

Source: Author.

3.3.1 Electrical impedance analysis

3.3.1.1 Parallel connection of array elements

The parallel connection of symmetrical element pairs (described in the previous sections) reduces the quantity of driving ultrasound channels and also plays an important role in reducing the electrical impedance of each element of the fabricated transducer. As previously explained, an array transducer with small elements presents a very large electrical impedance, which results in poor transmitting efficiency.

To understand the performance of the proposed arrangement, consider the single piezoelectric element depicted in Fig. 3.9(a) and the two elements connected in parallel in Fig. 3.9(b). The equation of the theoretical clamped capacitance of a single element was already given previously. Nevertheless, when N piezoelectric elements are connected in parallel, the total cross-sectional area of the association will be the sum of the area A of all N elements, *i.e.*, A_N . Hence, the total clamped capacitance C_N of the configuration is increased by a factor N :

$$C_N = \frac{\varepsilon^S A_N}{d} = N \frac{\varepsilon^S A}{d} = NC_0 \quad (3.1)$$

Thus, when array elements are electrically connected in parallel, the resulting association has an increase of clamped capacitance and a decrease of electrical impedance, comparing to a single element. The theoretical clamped capacitance of a single array element of the fabricated transducer is 195.4 pF. For an element pair ($N = 2$), this value is 390.8 pF.

Source: Author.

3.3.1.2 Insertion of inductor's network

The parallel connection of symmetrical elements effectively reduces the magnitude of the electrical impedance of piezoelectric elements, however it does not alter its capacitive characteristic – *i.e.*, the electrical impedance is not purely real over the passband. In order to eliminate the imaginary component of the electrical impedance at resonance and enhance the power transferred to the transducer, an electrical impedance matching is required. This was done by adding an electrical network of inductors, which is responsible for tuning out the capacitive reactance X_C , keeping the element electrical impedance exclusively real. A series tuning inductive reactance X_L was chosen so that it equals the capacitive reactance

3.3.1.3 KLM model simulation

To provide a way of evaluating the electrical features of the fabricated transducer beforehand, a KLM model program was developed in MATLAB. The complex simulated electrical impedance of the transducer was compared with experimental impedance measurements. The main input parameters used in the KLM simulation are listed on the Table 3.2.

Table 3.2 - Main inputs for the KLM model simulator

Material	Sound speed c (m/s)	Acoustic impedance Z (MRayls)	Thickness
Load medium	1540	1.5	-
Matching layer	2823	5.26	$\lambda/4=0.7$ mm
Pz37	2727	18	1.43 mm
Backing layer	330	0.0004	-

Source: Author.

3.3.1.4 Electrical impedance measurements

The magnitude and phase of the electrical impedance of all array elements were measured using a precision impedance analyzer (4294A, Agilent Technologies). The experimental measurements were conducted underwater, reproducing the loading medium of the simulations.

3.3.2 Frequency response (pulse-echo measurements)

The frequency response is a measurement of the amplitude of the pulse-echo response of the transducer as a function of frequency. This response is used to calculate operating parameters of ultrasonic transducers, including center frequency, bandwidth, and insertion loss.

The bandwidth BW [%] of a transducer is a selected portion of the frequency response limited by a lower and upper frequency values. These lower and upper frequency values (f_l and f_u respectively) are defined as the values at which the amplitude of the pulse-echo response has fallen 6 dB below the peak of the frequency response curve. The bandwidth calculation is determined by the center frequency f_c as:

$$f_c = \frac{f_l + f_u}{2}$$

$$BW = \frac{f_u - f_l}{f_c} \times 100 \quad (3.2)$$

The two-way insertion loss IL [dB] measures the electromechanical efficiency of the transducer and is calculated as:

$$IL = 20 \times \log \frac{V_{out}}{V_{in}} \quad (3.3)$$

where V_{out} [V] is the amplitude of the signal and V_{in} [V] is the amplitude generated by the voltage source (ASTM E1065/E1065M - 14, 2016).

The setup for pulse-echo measurement is shown in Fig. 3.10. It consists of an ultrasonic pulser/receiver unit (5077PR, Panametrics-NDT), 10 dB amplifier, digital oscilloscope (MSO8064A Infiniium, Agilent Technologies) and a brass block target. The temperature of the water was 22 °C, which was measured using a thermocouple.

With the pulser/receiver unit operating in transmission/reception mode, an excitation pulse of -100 V is applied to the transducer and the echo reflected from the brass block target (placed at 50 mm distant from the transducer) is received by the pulser/receiver, amplified, and digitalized by the oscilloscope. Then, the digitalized signal is saved and transferred to a computer, where the Fast Fourier Transform (FFT) was performed to obtain the transducer's frequency response. This procedure was repeated for all array elements.

Figure 3.10 - Pulse-echo measurement.

Source: Author

3.3.3 Pressure field measurement with hydrophone scan

The setup used to measure the pressure field generated by the transducer is illustrated in Fig. 3.11. The arrangement includes an ultrasonic pulser/receiver unit (5077PR, Panametrics-NDT), a PVDF needle hydrophone of 1 mm diameter (built by the Ultrasound Laboratory of the University of Sao Paulo), a customized 40 dB gain instrumentation amplifier (see appendix A for discussion about the designed amplifier), water tank, xyz scanning, oscilloscope (MSO8064A Infiniium, Agilent Technologies) and two computers. The xyz scanning system consists of drive unit, stepper motors and positioning system controlled by the software LinuxCNC running in Computer 1. The data acquisition system was automated by implementing a MATLAB script (running in Computer 2) to control the oscilloscope and save data from it (see appendix B for information about the data acquisition system implementation).

Figure 3.11 - Experimental setup for pressure distribution measurements.

Source: Author.

Note that, the pulser/receiver unit used in the experiment is limited to a single transmitting channel. This makes it impossible to measure the pressure distribution of all array elements simultaneously and perform beam focusing/steering in real time. To overcome this limitation, it was proposed to record the pressure field of all elements separately and analyze the behavior of the entire array through post-processing. This process is summarized in Fig. 3.12.

Figure 3.12 - Pressure field measurement and post processing.

Source: Author.

3.3.3.1 Experimental stage

This stage involves the excitation of individual elements of the transducer, hydrophone scan, and the record of pressure field data. First, the pulser/receiver unit was switched to

independent transmission/reception mode and external trigger synchronization. Then, the transducer was connected to the transmitter connector and the hydrophone was connected to the receiver connector of the pulser/receiver. In the water tank (water at 22 °C), the transducer was held by a grip to be kept static, and the hydrophone was attached to a support that is movable and controlled by the xyz scanning system. Although the scanning system is able to sweep a 3D volume, it was programmed to scan only a single plane (perpendicular to the surface of the transducer) to reduce the scanning time.

The xz plane (*i.e.*, the scanning plane) is shown in Fig. 3.13. The size of the plane was defined as 80×140 mm and spatial resolution of 2 and 10 mm in the x and z directions, respectively. This results in 41 nodes along the lateral direction (x), 15 nodes along the axial direction (z), and 615 nodes in total. As seen in the picture, the scanning plane is translated 20 mm from the transducer in the z direction (due to interferences caused by the trigger pulse). Thus, the plane ranges from -40 to 40 mm in the x direction and from 20 to 160 mm in the z direction.

Figure 3.13 - The xz scanning plane and its spatial resolution. The red line represents the hydrophone scan path. The intersection between the red line and the dashed lines corresponds to the nodes of the scanning plane (*i.e.*, locations where data is acquired).

Source: Author.

At each of the 615 points of the plane, the scanning system sends a trigger pulse to the pulser/receiver unit (to perform a transmit/receive cycle) and to the oscilloscope (to acquire the waveform received from the hydrophone). The output of the pulser/unit is amplified and connected to the oscilloscope channel, where it is sampled at a rate of 50 MSa/s and averaged eight times at each spatial location. The averaged data is stored in 10,000 points record length and transferred to computer 2, where MATLAB saves the acquired data in a three-dimensional array structured according to the spatial location in the plane (positions x and z) and the temporal

record length. Therefore, the pressure distribution scan of each element is represented by a 3D array of size $41 \times 15 \times 10,000$.

A single scan of the xz plane requires a significant amount of time to be carried out – approximately 40 minutes. This long duration is due to the low rotational speed of the stepper motors to avoid abrupt disturbances in the water. Since performing the scan of all 65 pairs of elements individually would be a very time-consuming task, it was proposed to interconnect (*i.e.*, excite simultaneously) symmetrical element pairs also in relation to the x -axis to reduce the number of scans. As shown in figure 3.14, the configuration with interconnected elements contains 35 groups of elements that are symmetrical with respect to both x and y -axes, resulting in four symmetrical quadrants.

The downside of this configuration is that, by applying the same time delays to all symmetrical elements with respect to both x and y -axes, the resulting ultrasound beam can vary along the z direction, but it will be constantly focused at the center of the array aperture. This makes it impossible to perform beam steering (*i.e.*, focusing off-axis) with the obtained pressure data measurements.

Figure 3.14 - Array divided in 35 groups of symmetrical elements (with respect to both x and y axes). Identical numbers indicate that the elements are interconnected.

1	8	15	22	29	29	22	15	8	1
2	9	16	23	30	30	23	16	9	2
3	10	17	24	31	31	24	17	10	3
4	11	18	25	32	32	25	18	11	4
5	12	19	26	33	33	26	19	12	5
6	13	20	27	34	34	27	20	13	6
7	14	21	28	35	35	28	21	14	7
6	13	20	27	34	34	27	20	13	6
5	12	19	26	33	33	26	19	12	5
4	11	18	25	32	32	25	18	11	4
3	10	17	24	31	31	24	17	10	3
2	9	16	23	30	30	23	16	9	2
1	8	15	22	29	29	22	15	8	1

Source: Author.

3.3.3.2 Post-processing algorithm for delay-and-sum beamforming

The inputs for the post-processing algorithm are: the saved pressure field data of all array elements; transducer and medium parameters; and the desired focal point. Fig. 3.15 illustrates the process of delay-and-sum for two independent signals (top and bottom rows of Fig. 3.15(a)). A $10 \mu\text{s}$ delay is applied to signal on the top row in Fig. 3.15(b). The delay consists of zeros concatenated in front of the signal (red line). To make both signals have the same length and help

the program perform calculations, zeros are filled in the end of the signal on the bottom row (green line). In Fig. 315(c), both signals are then summed.

Figure 3.15 - Principle of delay and sum. (a) Two independent signals. (b) Application of delay to the top signal (red line) and addition of zeros in the end of the bottom signal (green line). (c) Sum of both signals.

3.4 Simulation of shear wave elastography imaging

In this section, numerical simulations of shear wave elastography are performed using the simulation package k-Wave. This is an open source toolbox for MATLAB that is designed for time domain acoustic and ultrasound simulations in complex and tissue-realistic media (Treeby, Jaros, Rohrbach, & Cox, 2014). The k-Wave simulator was chosen because it allows the use of heterogeneous/homogeneous and lossless/lossy medium for transient or continuous wave calculations. In addition, acoustic and elastic materials can be simulated with this toolbox.

Following the work developed by Prieur et al. (2016), simulating the propagation of shear wave elastography in k-Wave requires three stages. The first one involves the simulation of compressional waves emitted by the transducer to calculate its pressure, intensity field and spatial distribution of the acoustic radiation force. In the second stage, the radiation force is used as an input for computing the propagation of elastic waves in the medium. Finally, the third stage consists of estimating the shear wave speed in order to reconstruct the elastic moduli of the tissue (Prieur & Catheline, 2016; Prieur & Sapozhnikov, 2017). The block diagram in Fig. 3.16 summarizes the simulation stages. All simulations were performed on a computer equipped with an Intel Core i7, running at 3.6 GHz and 16 GB of memory.

Figure 3.16 - Stages for the shear wave elastography simulation.

Source: Author.

3.4.1 Compressional wave propagation

In the first stage of the simulation, it was used a three-dimensional computational grid of 232, 202 and 364 points in the x , y and z -directions, respectively. Choosing a spatial step size of 0.5 mm in all three directions, the total dimension of the grid is 232 mm in x , 101 mm in y , and 182 mm in z . To simulate free-field conditions, a perfectly matched layer (PML) was used to absorb the waves at the edge of computational domain. The size of the PML is 20 grid points (10 mm) in all directions. The medium density was set to 980 kg/m³, the longitudinal sound speed propagation was set to 1540 m/s and the attenuation coefficient to 0.7 dB/MHz/cm.

The designed transducer was simulated with a fixed focus in the z -direction at 120 mm in all simulations herein. The input signal of each array element was defined as a 5-cycle enveloped tone burst of frequency 800 kHz and pressure magnitude of 1.5 MPa. The pressure was then scaled and assigned to the simulation as a particle velocity source (using $v = p/\rho c$). The waves propagate for 130 μ s with a sampling frequency of 10 MHz and the simulation takes about 15 minutes to complete using C++/CUDA (an optimized capability of k-Wave).

This stage records the instantaneous pressure field and the components of the intensity field (*i.e.*, in x , y , and z directions) over the 3D computational grid. Then, the temporal average of the intensity is taken over a period of 5-cycles (approximately 6 μ s) in order to calculate the time averaged components of the acoustic radiation force on each point of the grid.

Due to symmetry, only the ARF components in xz -plane are used as inputs for the next stage of the simulation – the components out of this plane can be neglected. In order to represent a volume force in the xz -plane, the components x and z are multiplied by a delta function in the y direction (Prieur & Catheline, 2016; Prieur & Sapozhnikov, 2017).

3.4.2 Shear wave propagation

In this stage, the computational grid in the x, y and z directions was reduced to 153, 64 and 161 points (76.5, 32 and 80.5 mm) to speed up computing. The spatial step size is 0.5 mm in all three directions and the center of the grid was defined at the focal point ($z=120$ mm).

Both homogeneous and heterogeneous tissue-like medium were herein simulated. In the heterogeneous case, a stiff spherical lesion with 8 mm diameter was inserted in a homogeneous background. The main parameters of this stage of the simulation are shown in Table 3.3:

Table 3.3 - Medium parameters for shear wave simulation.

Young's modulus	Attenuation coefficient	Poisson's ratio	Shear modulus (background)	Shear modulus (lesion)
4 kPa	0.7 dB/MHz/cm	0.499	1.3342 kPa	8 kPa

Source: Author.

As previously mentioned, the ARF components F_x and F_y are inputs on this stage. However, since k-Wave does not provide a direct way to input volume force as a source, the force components are scaled to velocity by making $v_i = \frac{F_i \Delta x_i}{\rho \cdot 2c}$, where Δx_i is the spatial step in the chosen direction (Prieur & Sapozhnikov, 2017; Treeby, Cox, & Jaros, 2016). Finally, the velocity components are divided by the spatial step in the y direction (to ensure proper scaling of the delta function in the y direction) and applied as constant inputs for 200 μ s, which is the duration of the ARF pulse (starting at time=0). Since shear waves travel much slower, it was fixed a lower sampling frequency (133 kHz) with the waves propagating for a longer time (15 ms).

The output in this stage is the particle velocity of the elastic wave propagation. This velocity has to be integrated in time in order to obtain the final displacement of the shear wave propagation. This stage takes approximately 10 hours to complete and the output variables exceed 3 GB of memory.

3.4.3 Shear wave speed estimation using time-to-peak method

In this stage, the obtained displacement field is the input to characterize the shear wave propagation. Several methods have been proposed to quantify the speed of shear wave propagation and characterize mechanical properties of soft tissues. In practice, shear waves can be tracked using correlation-based algorithms (McLaughlin & Renzi, 2006); reconstruction algorithms based on wave equations (Sarvazyan A. P., Rudenko, Swanson, Fowlkes, & Emelianov, 1998); algorithms based on the Voigt model, which takes into account tissue elasticity and

viscosity (Chen, et al., 2009); and time-to-peak algorithms, which are time-of-flight methods (Palmeri, Wang, Dahl, Frinkley, & Nightingale, 2008).

Herein, the estimation of shear wave speed was performed based on the time-to-peak (TTP) method. Assuming that shear waves propagate exclusively in the plane perpendicular to the axial direction, and there is no dispersion in the analyzed region, this method quantifies the time-of-flight of the shear wave's peak over lateral positions (x direction) around the focal zone. Then, linear regressions are performed on the TTP measurements, with the slope (*i.e.*, the derivative) of the line representing the instantaneous rate of change (*i.e.*, the shear wave propagation speed). The TTP method is illustrated in Fig. 3.17.

Finally, the obtained shear wave speed is used to reconstruct the shear moduli of the medium by using $\mu = \rho c_s^2$ (Palmeri, Wang, Dahl, Frinkley, & Nightingale, 2008; Ahmed, Salem, Seddik, & Adawy, 2016).

Figure 3.17 - TTP method. The time of flight of the displacement's peak in consecutive positions is used to estimate the instantaneous speed of the shear wave propagation. The slope of the line (position vs. TTP) gives the instantaneous speed of shear wave propagation.

4 Results and Discussion

4.1 Transducer evaluation

4.1.1 Electrical impedance

Figure 4.1 shows that the measured and simulated electrical impedance magnitude of a single element of the proposed transducer. At series resonance (800 kHz), the magnitude of the electrical impedance is approximately 900 Ω , which is in relatively good agreement with the implemented KLM model at regions near the resonance frequency. Discrepancies found at some frequencies may be attributed to the accuracy of the model, which neglects external mechanical loads such as wires, solders and connectors.

After the parallel connection of element pairs, the electrical impedance was reduced by half, as can be seen in Fig. 4.2. However, the impedance characteristic is still essentially capacitive, *i.e.*, no changes occurred in the impedance phase spectrum.

Figure 4.1 - Electrical impedance magnitude and phase of a single element. (a) Experimental – element #54.

(b) Simulated.

Source: Author.

Figure 4.2 - Electrical impedance magnitude and phase of parallel connected elements. (a) Experimental – element pair #54 and #67. (b) Simulated.

Source: Author.

By separating the resistive and reactive components of the electrical impedance, it was observed that the element pairs displayed an average resistance of 130Ω and an average capacitance of 380 pF . Therefore, the averaged capacitive reactance X_C of the element pairs is:

$$X_C = \frac{1}{2\pi fC} = \frac{1}{2\pi \times 800 \times 10^3 \times 380 \times 10^{-12}} \approx 520\ \Omega \quad (4.1)$$

Hence, to eliminate the imaginary component of the electrical impedance at resonance, the series tuning inductive reactance X_L can be chosen so that:

$$X_L = 2\pi fL = 520\ \Omega$$

$$L = \frac{X_L}{2\pi f} = \frac{520}{2\pi \times 800 \times 10^3} \approx 100\ \mu\text{H} \quad (4.2)$$

Fig. 4.3 shows the measured electrical impedance of element pairs after the insertion of a series inductance. At this stage, the electrical impedance of the association is significantly changed – the complex impedance decreases and becomes entirely real near the resonance. The impedance magnitude is much closer to $50\ \Omega$ at resonance, thus the transducer operates with maximized efficiency. The inductive load reduces the resonance frequency of the element pair, which is slightly shifted to the left. This may not cause significant changes in the transducer operation.

Figure 4.3 - Electrical impedance after the insertion of inductor network. (a) Element pair #54 and #67. (b) Elements pairs #1-13 and #118-130.

Source: Author.

4.1.2 Frequency Response

Figure 4.4 shows the pulse-echo time-domain response (blue line) and its FFT (red line) of a single element, an element pair, and an element pair with inductor network. The time-domain responses are normalized with the maximum amplitude of the signal in Fig. 4.4(c). The pulse-echo results provided means to calculate the center frequency, bandwidth and two-way insertion loss of each element configuration.

The averaged overall performance of each element configuration is summarized in Table 4.1. Evidently, the proposed array arrangement provided a significant improvement in the power transfer efficiency of the fabricated transducer. It is plausible that the two-way insertion loss for an element pair with inductor network is 10 dB less when compared to the configuration with a single element. In other words, a gain of 10 dB was obtained with the designed array configuration together with electrical impedance matching. On the downside, the bandwidth was reduced by 11%.

Table 4.1 - Averaged results for a single element, element pair and inductor network

Configuration	Center frequency (kHz)	Clamped capacitance (pF)	Impedance magnitude (Ω) ⁽¹⁾	Impedance phase ($^\circ$) ⁽¹⁾	-6 dB bandwidth (%)	Insertion loss (dB)
Single element	961.15	254	803	-71	60.93	-35.86
Element pair	962	560	365	-69	60.97	-29.02
Element pair with inductor network	766	–	81	-1	49.31	-25.11

⁽¹⁾ measured at resonance

Figure 4.4 - Time and frequency-domain pulse-echo responses. (a) Element #18. (b) Element pair #18 and #109. (c) Element pair #18 and #109 with inductor network.

Source: Author

4.1.3 Pressure Field

The experimental and simulated (using k-Wave) pressure fields of groups of symmetrical elements are compared in Fig. 4.5. When performing pressure field measurements, the transducer must be precisely aligned in all three dimensions within the water tank to produce a radiation pattern that is symmetrical in relation to the center of its aperture (as happens in the simulated pressure field). Inaccuracies in the alignment may result in an asymmetrical shape field.

Figure 4.5 - Pressure field of element groups. (a) Experimental; (b) Simulation; (c) Elements in green are excited simultaneously.

Source: Author.

Fig. 4.6 shows experimental and simulated results for beam focusing at different depths.

Figure 4.6 - Experimental (left) and simulated (right) pressure field of the transducer. (a) Focused at $z=115$ mm. (b) Focused at $z=120$ mm. (c) Focused at $z=130$ mm.

Source: Author.

The comparisons between the theoretical and experimental pressure fields agrees well in radiation pattern, with the agreement decreasing for regions near the transducer surface. In the focal zone, the measured and simulated beams present a similar pressure distribution. The results in the focal depth are very satisfactory, with the experimental main lobe slightly longer than the simulated along the axial direction. Experimental measurements showed enlargement of the side lobes and produced considerable beam distortions in regions off-axis. Beam focusing in the desired depth was successfully performed with the delay-and-sum post-processing algorithm. The experimental measurements only involved relative values of peak-to-peak amplitude, since the hydrophone used in the experiment was not calibrated.

Figure 4.7 - Experimental and simulated pressure profile along the axial line. (a) Focused at $z=115$ mm. (b) Focused at $z=120$ mm. (c) Focused at $z=130$ mm.

Fig. 4.7 shows the experimental (top row) and simulated (bottom row) pressure profile along the axial line. The results show a good similarity in the focal zone, however, the measured

profile presents a secondary lobe with a considerable pressure level (-5 dB). The simulated profile does not present such secondary lobe, which might be an effect of the enlargement of the main lobe presented in the experimental measurements.

4.2 Simulation of shear wave elastography

4.2.1 Homogeneous tissue-like medium

Simulations in this section were performed using absolute values in order to obtain quantitative results for shear wave elastography.

The pressure and intensity fields obtained in the first stage of the simulation are shown in Fig. 4.8. In the focal region, the maximum pressure is around 3.5 MPa, which results in an intensity of approximately 1100 (W/cm²). This intensity is sufficient to generate tissue displacement and shear wave propagation.

Figure 4.8 - Pressure and intensity fields of transducer (focused at $z=120$ mm). (a) Maximum pressure. (b) Maximum intensity.

Source: Author.

The x and z components of the acoustic radiation force are depicted in Fig. 4.9. It is seen that the axial component F_z is positive and exceeds the values of the lateral component F_x almost all point of the grid (*i.e.*, the radiation force is mostly directed along the z direction). It is also seen that the component F_x presents forces that are equal in magnitude and opposite in direction, being zero along the beam axis. As expected, the resulting force acting on the focal zone is the force component F_z alone.

Figure 4.9 - Simulated acoustic radiation force. (a) Component F_z of the ARF. (b) Component F_x of the ARF.

Source: Author

The distribution of the shear displacement generated by acoustic radiation force at different times is shown in Fig. 4.10. The radiation force is applied in the tissue for 200 μ s, but the displacement field reflects the shape of the applied force field for a longer time – until around 2 ms, as seen in Fig. 4.10(a). Later in time, shear wave propagates away from the focal region and appears as two symmetric bands on both sides of the focal point, as shown in Fig. 4.10(b)-(f). The shear wave displacement peak amplitude decreases as it propagates to the surrounding region.

The temporal behavior of the lateral displacement at the focal point ($z=120$ mm) is presented in Fig. 4.11. The profile is normalized with the maximum displacement, which occurs at $t=0.5$ ms. The amplitude of the propagating shear wave is an order of magnitude smaller than the initial displacement.

Fig. 4.12 shows the simulated displacement through time profiles at different lateral (x) and axial (z) positions. Consider Fig. 4.12(b), which shows the displacement at the focal point ($z=120$ mm), the maximum displacement of the blue line occurs at 0.5 ms. Observing the pink line in the same figure, the maximum displacement occurs at 5 ms. These time values, *i.e.*, time-to-peak (TTP) measurements, together with position information, are used to estimate the speed of the propagating wave through the TTP method. Over time, the shear wave propagates away from the focal region, decreasing in amplitude along the traveled lateral distance. Note that, although the green line is located at $x=15$ mm, it does not decrease much in amplitude comparing to the red line (located at $x=10$ mm). This deviation is due to side lobes that appear near that region, increasing the amplitude of the green line. The presence of side lobes does not interfere in the monitoring of shear speed propagation at this location.

Figure 4.10 - Displacement field generated by ARF at different times (homogeneous medium). The fields are normalized with the maximum displacement, obtained at 0.5 ms. (a) $t=2\text{ms}$. (b) $t=4\text{ms}$. (c) $t=6\text{ms}$. (d) $t=8\text{ms}$. (e) $t=10\text{ms}$. (f) $t=12\text{ms}$.

Source: Author.

Figure 4.11 - Lateral displacements at the focal depth.

Source: Author.

Figure 4.12 - Displacements through time profiles. (a) $z=110\text{ mm}$. (b) $z=120\text{ mm}$. (c) $z=130\text{ mm}$.

Source: Author.

Fig. 4.13 shows the TTP displacement as a function of the lateral position (x) at three different axial positions (z). Note that, at $x \geq 5$ mm, the value of TTP is clearly linearly dependent of the lateral position (x). Therefore, the rate of change of the TTP displacement can be evaluated using linear regression within this interval. The inverse slope of the line represents the shear wave speed.

Fig. 4.14 shows the instantaneous speed of the shear wave propagation versus the corresponding x position, calculated from the rate of change of the TTP displacement. The shear wave speed presents a similar lateral profile at different axial depths, oscillating around 1.2 m/s, which is much slower than the propagation of compressional waves. The downside of this method is the derivative calculation, which is very sensitive to noise. With a better resolution in the lateral direction, the derivative could be performed using a moving window, which is more robust to noise because of averaged values.

The mean reconstructed shear modulus profile is shown in Fig. 4.15. The error bars associated with the Fig. 4.15(a) represent the variation in the reconstructed shear modulus over the three independent axial positions (*i.e.*, $z=110$, 120 and 130 mm). The error bars associated with the Fig. 4.17(b) represent variations over 20 independent lateral positions in the interval $5 \leq x \leq 15$ mm. The standard error is much smaller for trials with a fixed lateral position and a varying axial position.

Figure 4.14 - Instantaneous shear wave speed versus lateral position. (a) $z=110$ mm. (b) $z=120$ mm. (c) $z=130$ mm.

Figure 4.15 - Reconstructed shear modulus (bars represent standard error of the mean). (a) Variation over x position. (b) Variation over z position.

Fig. 4.16 shows the reconstructed shear modulus map of the homogeneous tissue. The resulting map agrees well with the theoretical value of the shear modulus (1.3342 kPa). It is seen that the map is divided in three distinct zones along the lateral axis, with the central zone presenting a shear modulus closer to the expected value. There is a slight over-estimation of the elastic modulus in the extremes.

Figure 4.16 - Reconstructed shear map (homogeneous medium).

Source: Author.

4.2.2 Heterogeneous tissue-like medium

The same procedure carried out for the shear wave elastography imaging in homogenous medium was repeated for a heterogeneous tissue-like medium. In this case, it was inserted an 8 mm diameter spherical inclusion (shear modulus of 8 kPa) in a uniform softer tissue (shear modulus of 2 kPa), as shown in Fig. 4.17.

Figure 4.17 - Stiffer lesion inserted in a softer tissue.

Source: Author.

Fig. 4.18 shows the shear wave displacement map at different instants. It is possible to notice the change in shape on the right side of the grid due to the inclusion. It is also seen that the shear wave traveling through the lesion has a faster wavefront due to the higher stiffness.

Figure 4.18 - Displacement field generated by ARF (heterogeneous medium). The fields are normalized with the maximum displacement, obtained at 0.5 ms. (a) $t=2$ ms. (b) $t=4$ ms. (c) $t=6$ ms. (d) $t=8$ ms. (e) $t=10$ ms. (f) $t=12$ ms.

Source: Author.

Fig. 4.19 shows the temporal behavior of the lateral displacement at the focal point. The profile is normalized with the maximum displacement (at $t=0.5$ ms). As can be seen, the shear waves are attenuated and degraded due to the stiffer lesion.

Figure 4.19 - Lateral displacements at the focal depth (heterogeneous medium).

Source: Author.

The reconstructed and theoretical tissue map are compared in Fig. 4.20. The reconstructed map clearly identifies the lesion and is able to quantify it relatively well in some regions. However, there are artifacts and degradation on the surface of the lesion, which are not present in the theoretical map. Additionally, over-estimation occurs in the background regions.

It was observed that the discontinuities present in the reconstructed shear modulus map are caused by the TTP tracking method. For better understanding, consider Fig. 4.21, which shows the lateral displacement in two different instants for the heterogeneous case. The TTP method takes into account only the movement of the peak of the displacement. It can be seen that, from 9.5 to 10.5 ms, the displacement's peak on the right side of the grid remains static at 12 mm (red arrow), thus, the rate of change in this interval is zero. However, the body of the waveform (green arrow) moves from 14 mm to 16 mm within the interval. In these cases – in which the peak of the waveform remains static, but its body moves – the TTP method fails to sense the tissue displacement. Therefore, the discontinuities seen on the surface of the lesions are produced by a

wrong estimation of the derivative. A more efficient motion tracking technique should be investigated to obtain reliable measurements in heterogeneous medium.

Figure 4.20 - Heterogeneous shear modulus map. (a) Reconstructed. (b) Theoretical.

Source: Author.

Figure 4.21 - Lateral displacements (heterogeneous medium). (a) $t=9.5$ ms. (b) $t=10.5$ ms. Although the peak of the displacement remains static within the interval, the body of the waveform does not. Ideally, the tracking method should be able to sense the movement of the entire waveform.

Source: Author.

5 Conclusion

This work has documented the principle and clinical importance of acoustic radiation force-based methods in the evaluation of tissue stiffness. In particular, shear wave elastography, which is a very promising modality for quantifying tissue elasticity, especially for diagnosis of liver fibrosis. The current measurement depth of shear wave elastography impedes its use in obese patients, which have a greater risk of developing fatty liver disease. Therefore, this study investigated a method to extend the use of shear wave elastography to deeper tissues by using a two-dimensional ultrasound transducer for acoustic radiation force generation.

It was proposed a transducer array configuration in which beamforming is conducted in groups of elements to reduce both the total number of ultrasound channels and the electrical impedance of the elements. The lower impedance of the array elements together with the insertion of an inductor network resulted in a gain of 10 dB when compared to a conventional transducer array without electrical impedance matching. Clearly, the proposed configuration may be of particular interest in the design of transducers for acoustic radiation force generation due to its enhanced transmitting capabilities.

Numerical simulations and experimental measurements were performed in this work. A KLM model was implemented in MATLAB and compared with impedance analyzer measurements to evaluate the electrical impedance of the transducer. The experimental measurements validated the model and the predictions that were made. The pressure field generated by the transducer was simulated using the MATLAB toolbox FOCUS, which is a very useful tool for visualizing ultrasound beamforming in lossless and homogeneous medium. Hydrophone measurements of pressure field agreed well with theoretical data, although only relative values were compared. Unfortunately, it was not possible to drive all array elements simultaneously due to the limitation of the ultrasound system available. For this reason, beam focusing was performed via post-processing algorithm.

The acoustic radiation force generated by the proposed transducer and the resulting tissue displacement were simulated in the k-Wave toolbox in homogenous and heterogenous media. The results are encouraging and showed that the transducer is capable of inducing shear wave propagation in regions beyond the depth limit of current ultrasound systems, which is a novel contribution.

The speed of the shear wave propagation was estimated by using the TTP method, which allowed the reconstruction of the elastic map of the tissue. The results were good for a homogenous medium and satisfactory in the case of a heterogeneous medium.

5.1 Future work

Future work should include absolute measurements of the pressure field generated by the proposed transducer using either a calibrated hydrophone or a radiation force balance. Additionally, all array elements should be excited simultaneously in order to evaluate beam focusing and steering faithfully, *i.e.*, without the need of a post-processing stage for delay-and-sum. Moreover, motion tracking techniques can be investigated more deeply to obtain reliable measurements of shear wave speed propagation. Finally, experimental measurements in tissue-mimicking phantoms should be performed and compared with simulated data.

5.2 Publications

Cardoso, F. M., Santos, D. S., & Furuie, S. S. (2016). Acoustic radiation force impulse in deep tissues using matricial array transducers. *XXV Brazilian Congress on Biomedical Engineering, CBEB 2016*, pp. 1075-1078. Foz do Iguaçu.

Santos, D. S., Cardoso, F. M., & Furuie, S. S. (2017). Development of a 2D array ultrasound transducer for acoustic radiation force impulse imaging in deep tissues. *23rd Congress of the European Society of Biomechanics, Abstracts of the 23rd ESB*. Seville.

Santos, D. S., Cardoso, F. M., & Furuie, S. S. (2017). Two-dimensional ultrasound transducer array for acoustic radiation force impulse imaging. *24th ABCM International Congress of Mechanical Engineering, COBEM 2017*. Curitiba.

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Appendix A – Instrumentation amplifier

A critical issue was faced when performing pressure field measurements with the needle hydrophone: the acoustic signals received from the hydrophone suffer severe disturbances due to ambient noise, which is a common problem in underwater applications, exhibiting different directional and spectral characteristics. Several ways were considered to reduce or eliminate the ambient noise and keep the received signal features as much as possible. This section presents the development of an instrumentation amplifier that successfully eliminates the inherent hydrophone noise.

An instrumentation amplifier (in-amp) is a device that amplifies the difference between two signals while rejecting any signals that are common to both inputs. The most important function that an instrumentation amplifier provides is the common-mode rejection (CMR), which is the property of canceling out any signals that are common (the same potential on both inputs), while amplifying any signals that are differential (a potential difference between the inputs).

Figure A.1 shows the electrical diagram of the designed in-amp. It was utilized a commercially available amplifier (INA103, Texas Instruments) for this purpose. The circuit consists of a second order high pass filter (cutoff frequency of 100 kHz), offset adjustment and gain stage.

Figure A. 1 - Electrical diagram of the designed instrumentation amplifier.

Source: Author.

External resistors were used to set the output gain, which is around 40 dB at 800 kHz (center frequency of the proposed transducer). Fig. A.2 shows the frequency response of the instrumentation amplifier. As can be seen, the curve is flat in the range from 100 kHz to 1 Mhz.

Figure A. 2 - Frequency response of the designed instrumentation amplifier.

Source: Author.

Fig. A.3(a) shows a real wave signal that was received by the hydrophone and completely degraded by the ambient noise. In several points, the amplitude of the noise is higher than the signal. In Fig. A.3(b), the same signal is amplified and its common mode noise is successfully rejected by the instrumentation amplifier. In addition to the noise rejection, a considerable gain is obtained.

Figure A. 3 - Hydrophone signals. (a) Noisy signal. (b) Amplified signal.

Source: Author

Appendix B – Data acquisition system

This section discusses a program that was implemented to automatically control both the motion of the xyz-scan and the data acquisition of the oscilloscope when performing pressure field measurements. The script, fully developed in MATLAB, integrates two other programming languages: G-code and Standard Commands for Programmable Instruments (SCPI). The main goal of this system is to allow averaging multiple hydrophone signals when scanning the pressure plane. Averaging the received data was crucial to reduce the noise level, especially in the signals with very small amplitude. Therefore, multiple signals were acquired and averaged at each position of the scanning plane, and only the averaged value was stored by the oscilloscope. The quality of the obtained signals was enhanced significantly with this artifice.

G-code generation

The xyz-scanning system used to measure pressure field is a CNC machine that is controlled by a software (LinuxCNC) using in G-code language. This programming language uses alpha numeric codes to instruct the machine where and how to move, besides other specific functions.

In the first stage of the designed system, a MATLAB script generates a G-code file according to the user parameters. Basically, the user defines the size of the scanning plane, the resolution in each direction and the number of averages to perform at each position (this means the number of external trigger signals that the scanning system will send in each position). Then, the generated G-code file is loaded in the LinuxCNC software to perform the machine control.

The MATLAB script of the first stage is listed below. In this example, the user defines a plane of 100 by 80 mm in the x and y directions, respectively; a spatial resolution of 10 mm in x and 2 mm in y ; and average number of 8. After running, the program generates a G-code file named "g_code.ngc" (which should be loaded in the LinuxCNC software) and two variables called "Longitudinal" and "Lateral", which will be inputs to the next stage of the system.

```

% =====
%
% This program generates a G-code file for a xyz scanning machine.
% Inputs: Size of the plane, spatial resolution, and number of
% averages
% Output: G-code file
%
% Author: Djalma Santos
% May, 2018
% =====

clc
clear all

%% User parameters

xySize = [100 80]; % Size of the plane [x y] (mm)
xyRes = [10 2]; % Spatial resolution [x y] (mm)
trigger = 8; % Number of averages

%% Creates a G-code file

fh = fopen('g_coge.ngc','w'); % File name
diary g_code.ngc

%% CNC initialization parameters

fprintf('G94\n')
fprintf('F 350.000000\n')
fprintf('S 0.000\n')
fprintf('T 0\n')
fprintf('M06\n')
fprintf('M05\n')
fprintf('M09\n')
fprintf('M49\n')
fprintf('G17\n')
fprintf('G21\n')
fprintf('G40\n')
fprintf('G49\n')
fprintf('G54\n')
fprintf('G64 P0.01\n')
fprintf('G91\n')
fprintf('G98\n')
fprintf('G92 X0.0 Y0.0 Z0.0 A0.0 C0.0\n')
fprintf('G92 B0.0\n\n')

%% Sweep parameters

xPos=0;
yPos=0;
minus=false;
for yy=0:xyRes(2):xySize(2)

    if yy==0
        fprintf(['\nG01 Y-',num2str(xySize(2)/2),'\n\n'])
        fprintf('G4 P0.8 \n')
        yPos=-xySize(2)/2;
    end

    for xx=0:xyRes(1):xySize(1)
        if ~minus
            xPos=xx;
            if xPos~=0
                fprintf(['\nG01 X',num2str(xyRes(1)),'\n'])
            end
            for t=1:1:trigger
                fprintf('G00 B0.01\n')
                fprintf('G4 P0.05\n')
            end
        else
            xPos=xySize(1)-xx;
            if xPos~=xySize(1)
                fprintf(['\nG01 X-',num2str(xyRes(1)),'\n'])
            end
            for t=1:1:trigger
                fprintf('G00 B0.01\n')
            end
        end
    end
end

```

```

        fprintf('G4 P0.05 \n')
    end
end
end

if yy~=xySize(2)
    fprintf(['\nG01 Y',num2str(xyRes(2)),'\n\n'])
    fprintf('G4 P0.8 \n')
    yPos=yPos+xyRes(2);
else
    fprintf(['\nG01 X',num2str(-xPos), ' Y',num2str(-yPos) ,'\n\n'])
end

    minus=~minus;
end

%% Finalization parameters

fprintf('G80\n')
fprintf('M2\n')
fprintf('\n')

diary off
fclose('all');

% Plot information input for acquisition
longitudinalPoints=length(0:xyRes(1):xySize(1));
lateralPoints=length(0:xyRes(2):xySize(2));
fprintf(['Longitudinal = ',num2str(longitudinalPoints),'\n']);
fprintf(['Lateral = ',num2str(lateralPoints),'\n']);
fprintf(['Total = ',num2str(longitudinalPoints*lateralPoints),'\n']);

% Clear variables that will not be used
clearvars fh minus t xPos xx xyRes xySize yPos yy

```

Data acquisition

In the second stage of the designed system, a MATLAB script connects to an Agilent oscilloscope to automatically control the data acquisition while scanning the plane. To perform this task, it is required to install the instrument I/O libraries in the computer running MATLAB (the I/O libraries can be download from Agilent/Keysight webpage). The communication between MATLAB and the instrument is realized via TCP-IP protocol, however, the instructions to the instrument are sent using SCPI commands (this is the programming language of the oscilloscope). In this script, the user input parameters are the variables that came from the previous stage: “Longitudinal”, “Lateral” and “trigger” (These variables will be automatically stored in the MATLAB workspace after creating a G-code file. However, if the workspace was cleared, the user may either enter the values of the variables manually or run the G-code generator again to retrieve them). In addition, the user must configure the IP address of the instrument and insert it in the code.

In the first part of the script, the code configures a TCP-IP connection (sets buffer size, timeout, IP address, port, etc.) and connects to the equipment. Then, it sets oscilloscope parameters (channel, trigger source, acquire mode, etc.) and starts the data acquisition. The acquisition is carried out until the total number of points of the plane is reached. A timeout error occurs if the oscilloscope does not receive an external trigger signal within 30 seconds after the acquisition has started.

Note that, this script was tested and validated performing data acquisitions with sampling frequency of 50 MSa/s and 10,000 points length. Thus, it is recommended to set the oscilloscope sampling frequency and number of points to these values manually before starting the automated acquisition (increasing sampling frequency and/or point length without properly updating the code may cause buffer overflow and communication errors). Care must be taken to not to press the “auto scale” or “default setup” oscilloscope keys, since they modify the current acquiring configurations.

The output of this script is the averaged hydrophone data acquired at each position of the scanning plane. The wave data is saved in a 3D matrix representing the longitudinal position, lateral position and time vector in the variable named “waveformDisplay”. In the end, the script plots the waveform vs. time for all points of the plane and plots the maximum pressure field.

```
% =====
%
% This program connects to an Agilent scope using TCPIP and
% sends SCPI commands to automate acquisition and download data
%
% It is required to have Agilent IO Libraries installed
% Inputs: number of longitudinal points, lateral points, and
% number of averages
%
% Output: 3D matrix with the pressure field at each point of the plane
%
% Author: Djalma Santos
% May, 2018
% =====

% User's parameters
longitudinalPoints=11;      % X direction of the scan
lateralPoints=41;          % Y direction of the scan
trigger=8;

%% =====
% INITIALIZATION
% =====

% Find a tcpip object.
obj1 = instrfind('Type', 'tcpip', 'RemoteHost', '192.168.1.124', ...
    'RemotePort', 5025, 'Tag', '');

% Create TCPIP object if it does not exist
if isempty(obj1)
    obj1 = tcpip('192.168.1.124', 5025);
else
    fclose(obj1);
    obj1 = obj1(1);
end

% Configure buffer size and timeout
set(obj1, 'InputBufferSize', 5000000);
set(obj1, 'OutputBufferSize', 5000000);
set(obj1, 'Timeout', 30.0);

% Open object
fopen(obj1);

% Print information about the device connected to
idn = query(obj1, '*IDN?');
if isempty(idn)
    fprintf(2, 'Connection fail');
    connected = 0;
    fclose(obj1);
else
```



```

        fprintf('Connected to: \n')
        fprintf(idn)
        fprintf('\n\n')
        connected = 1;
    end

%% =====
% CONFIGURATION
% =====

if connected == 1

    fprintf(obj1,':STOP'); % Stop scope to make changes

    % Channel commands
    fprintf(obj1, ':CHANnel1:DISPlay on');
    fprintf(obj1, ':CHANnel1:INPut ac');

    % Trigger commands
    fprintf(obj1, ':TRIGger:SWEep TRIGgered');
    fprintf(obj1, 'trigger:mode edge');
    fprintf(obj1, ':TRIGger:EDGE:SOURce AUX');
    fprintf(obj1, ':TRIGger:EDGE:COUPling DC');
    fprintf(obj1, ':TRIGger:EDGE:SLOPe pos');
    fprintf(obj1, ':TRIGger:LEVel AUX, 1');

    % Acquire commands
    fprintf(obj1, ':ACQuire:INterpolate off');
    fprintf(obj1, ':ACQuire:SRATe:AUTO off');
    fprintf(obj1, ':ACQuire:MODE HRESolution');
    fprintf(obj1, ':ACQuire:MODE RTIME');
    fprintf(obj1, ':ACQuire:AVERage ON');
    fprintf(obj1, [':ACQuire:COUNt ' ,num2str(trigger)]);

    % Read number of points and sampling frequency
    numberOfDataPoints = str2double(query(obj1,':ACQuire:POINts?'));
    fprintf('Number of acquisition points: \n')
    fprintf('%i',numberOfDataPoints)
    fprintf('\n')
    samplingFrequency = str2double(query(obj1,':ACQuire:SRATe?'));
    fprintf('Sampling frequency: \n')
    fprintf('%i', samplingFrequency)
    fprintf('\n')

    % Waveform commands
    fprintf(obj1, ':WAVEform:POINts:MODE normal');
    fprintf(obj1, ':WAVEform:SOURce CHAN1');
    fprintf(obj1, ':WAVEform:FORMat ASCii');
    fprintf(obj1, ':WAVEFORM:BYTEORDER LSBFirst');

    % Wait for operation to complete
    operationComplete = str2double(query(obj1,'*OPC?'));
    while ~operationComplete
        operationComplete = str2double(query(obj1,'*OPC?'));
    end

    fprintf('Ready to start acquisition! \n\n')

%% =====
% CAPTURE WAVEFORM
% =====

    % Allocate variable to store waveform
    cellWaveformChar{longitudinalPoints*lateralPoints}={};

    % Counter for maximum number of acquisition
    count=0;
    countMax=longitudinalPoints*lateralPoints;

    fprintf(obj1, ':OPEE 0'); % Disable interruptions
    fprintf(obj1, '*CLS');

    % Upon trigger, DIG acquires data and places it in the buffer
    fprintf(obj1, ':DIGitize CHANnel1');
    fprintf('Number of acquisitions: \n')
    timeLimit = 30; % Timeout in seconds

```

```

tic      % Start timer
while (toc<timeLimit) && (count < countMax)
    statusByte = str2double(query(obj1,'*STB?'));
    if ~isnan(statusByte)
        if bitand(statusByte,1)
            % Transfer waveform from oscilloscope to PC (char data)
            singleWaveformChar = query(obj1, ':WAVEform:DATA?');
            count=count+1;
            fprintf('%i \n', count)
            fprintf(obj1, '*CLS');

            % Save waveform in a cell
            cellWaveformChar{count} = singleWaveformChar;
            if count<countMax
                fprintf(obj1, ':DIGitize CHANnel1');
            end
            tic      % Update current time
        end
    end
end

% Query information about preamble
preambleBlock = query(obj1, ':WAVEform:PREamble?');
preambleBlock = strsplit(preambleBlock,',');
setup.points=preambleBlock{3};
setup.X_inc=preambleBlock{5};
setup.X_origin=preambleBlock{6};
setup.X_display_range=preambleBlock{12};
setup.X_display_origin=preambleBlock{13};
setup.Y_display_range=preambleBlock{14};

%% =====
% CHECK ACQUISITION STATUS
% =====

if (toc >= timeLimit)&&(count<countMax)
    fprintf(2,'TIMEOUT!!! \n \n');
    fprintf(2,'Fail to acquire all data. \n \n');
    status = 0;
    fprintf(obj1, ':RUN');
    fprintf(obj1, ':STOP');
    fprintf(obj1, ':RUN');
    fclose(obj1);
else
    fprintf('Acquisition complete!!! \n \n');
    status = 1;
    fprintf(obj1, ':RUN');
    fprintf(obj1, ':STOP');
    fprintf(obj1, ':RUN');
    fclose(obj1);
end

%% =====
% CREATE TIME VECTOR
% =====

fprintf('Formating data... \n \n')

% Configure total time vector
tStart=str2double(setup.X_origin);
tStep=str2double(setup.X_inc);
tEnd=tStart+(numberOfDataPoints-1)*tStep;
tTotal=tStart:tStep:tEnd;

% Configure time vector that is displayed in the screen
tRange=str2double(setup.X_display_range);
tDisp=str2double(setup.X_display_origin);
t=tDisp:tStep:tDisp+tRange-tStep;
dataStart=find(tTotal>=tDisp); % Index of start time

ampRange=str2double(setup.Y_display_range); % Amplitude range

%% =====
% FORMAT WAVEFORM
% =====
tic
    % Variables allocation

```

```

cellWaveformNum(countMax)=zeros;
waveformTotal(longitudinalPoints,lateralPoints,...
    numberOfDataPoints)=zeros;
waveformDisplay(longitudinalPoints,lateralPoints,length(t))=zeros;

% Convert waveform from char cell to numeric cell
for n=1:1:countMax
    cellWaveformNum{n} = str2num(cellWaveformChar{n});
end

cellWaveformNum = reshape(cellWaveformNum,longitudinalPoints,...
    lateralPoints);

% Invert waveform of odd numbers to correct the scan direction
cellWaveFlip{longitudinalPoints,lateralPoints}=zeros;

for la=1:1:lateralPoints
    for lo=1:1:longitudinalPoints
        if mod(la,2)
            cellWaveFlip{lo,la} = cellWaveformNum{lo,la};
            waveformTotal(lo,la,:)=cellWaveFlip{lo,la};
        end
        if ~mod(la,2)
            cellWaveFlip{lo,la} = ...
                cellWaveformNum{longitudinalPoints-lo+1,la};
            waveformTotal(lo,la,:)=cellWaveFlip{lo,la};
        end
    end
end

% Saves data with the number of points displayed in the screen
waveformDisplay=...
    waveformTotal(:, :, dataStart(1):dataStart(1)+length(t)-1);
toc
%% =====
% PLOT WAVEFORM
% =====
fprintf('Plotting... \n')

if status == 1
    for la=1:1:lateralPoints
        for lo=1:1:longitudinalPoints
            plot(t*1e6, squeeze(waveformDisplay(lo,la,:)));
            ylim([-ampRange/2 ampRange/2])
            pause(0.01)
        end
    end
end

%% =====
% PLOT ACOUSTIC FIELD
% =====
if status == 1
    pMax= max(abs(waveformDisplay), [], 3);

    % Normalize data
    pMaxNorm= (pMax - min(min(pMax)))/(max(max(pMax))-min(min(pMax)));
    x=linspace(20,160,longitudinalPoints);
    y=linspace(-40,40, lateralPoints);
    [X,Y]=meshgrid(y,x);
    figure
    subplot(1,3,1)
    surf(X,Y,pMaxNorm,'edgecolor','k');
    shading interp
    view(2)
    title('Maximum Pressure')
    colormap(jet);
end

fprintf('Done! \n')

save('waveform.mat','t','waveformDisplay');

else
    fclose(obj1);
end

```