ULTRASONIC GUIDED WAVE MEASUREMENTS IN BONE

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Abstract

Osteoporosis is a widespread and growing clinical problem, and provides the primary motivation for developing improved methods for the in vivo assessment of bone. Such methods should ideally be easy to use, safe, inexpensive, reliable, and, above all, should provide clinically-useful information. They should be sensitive to the early signs of bone deterioration, so that problems can be detected early and the benefits of treatment can be maximised. As the existing diagnostic methods, based mainly on X-ray absorption, can only provide information on bone density and geometry, there is growing interest in ultrasonic methods which have the potential to assess aspects of the material properties of bone.

The aim of the present study was to evaluate the feasibility of using ultrasonic guided waves for the quantitative assessment of bone. A prototype device was developed for low frequency ultrasonic transmission measurements along human long bones. Analytical plate and tube models were used for identification of the measured wave modes. The phase velocities of two guided wave modes were thereby determined. In addition, an inversion scheme was developed for determining the cortical bone thickness from guided wave ultrasound data.

Experimental work confirmed that guided waves could be excited and detected in human bones as well as in bone phantoms. Data from a small scale clinical pilot study indicated increased sensitivity to osteoporosis for guided wave measurements. A large scale in vivo study in a group of 106 pubertal girls was completed, and this demonstrated that guided wave measurements were sensitive to both bone material properties and bone thickness. A comparative in vitro study for human radius specimens indicated that the velocity of the fundamental antisymmetric guided wave correlated significantly with cortical bone mineral density, as did the lateral wave velocities measured with other devices. However, this guided wave velocity had an advantage over any lateral wave measurement in that it was significantly correlated with cortical bone thickness as well as mineral density. In addition, it was demonstrated that the use of an inversion scheme, based on plate or tube theory, enables respectively the assessment of plate or tube wall thickness. It was shown also, that the use of tube model is preferred when analysing guided wave measurements for thick-walled bones.

Despite the successes listed above, problems have been identified that must be addressed before guided wave measurements can progress as a reliable and useful clinical technique. In the work to date the effects of the soft tissue overlying the bone have been found to be a major factor. It is proposed that the key issue in understanding this problem is to consider wave propagation in a bilayer system, composed of solid bone and liquid-like soft tissue. The initial results in immersed bone phantoms suggest that the use of an adequate bilayer theory can potentially eliminate the influence of soft tissue on the in vivo guided wave measurements. The results for human bones in vivo are under way of being analysed.

Based on these results, it is concluded that the measurement of ultrasonic guided waves in human long bones is indeed feasible and offers advantages over existing techniques. However, further modelling of guided waves is of crucial importance for a precise and reliable interpretation of clinical guided wave measurements in bone.
Preface

The work reviewed in this thesis has been carried out in the Departments of Health Sciences and Physics at the University of Jyväskylä from January 2001 to December 2004.

I would like to thank my supervisors, Prof. Jussi Timonen and Prof. Sulin Cheng for the opportunity to chase my skills in this challenging interdisciplinary project, in an international collaboration with leading scientists. You have encouraged me during the process and taught me to face problems with open mind. I would like to address my great gratitude to my instructor, Dr. Patrick Nicholson for inspiring ideas, encouragement and patience in teaching scientific work. Especially, I would like to thank Mr. Vantte Kilappa for conscientiously and carefully performing a great deal of experimental hard work. I would also like to thank Dr. Pascal Laugier for sharing bone samples, Dr. Maryline Talmant for invaluable help with guided wave modelling, Ms. Marie Muller for collaborating with a publication, Prof. Tommi Kärkkäinen for invaluable help with signal analysis routines, Dr. Erkki Heikkola for writing the programs for numerical modelling of wave propagation, and everyone in the CALEX group for invaluable help with the in vivo measurements. It has been great for working with all of you.

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Säynätsalo, December 2004

Petro Moilanen
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List of publications

This thesis consists of an overview and the following publications:


V P. Moilanen, P.H.F. Nicholson, V. Kilappa, J. Timonen and S. Cheng, Measuring the phase velocity of guided waves in free and immersed plates as bone phantoms, Submitted for publication.

The author has had an active role in all stages of the research. He has been involved in planning and conducting the research. He has assembled the ultrasound device and performed all the experimental measurements used in Publications I and II. He has designed and developed the methods of analysis for the ultrasonic guided wave measurements used in all five Publications. He has developed a numerical routine for determining the dispersion curves based on the analytical theory of guided waves, which have been used as the basis for Publications I, II, IV and V. He has actively contributed to the ideas reported in Publications I and IV, and written parts of them. He has written publication V and the first drafts of publications II and III.
Chapter 1

Introduction

Osteoporosis is a widespread and growing clinical problem which most often manifests itself clinically as fractures of the wrist, spine or hip. Therefore understanding the determinants of fracture risk is of crucial importance. The changes seen in osteoporotic bone include density changes (e.g. reduced trabecular and cortical bone mineral density), geometrical changes (e.g. reduced bone thickness and cross-sectional area) and mechanical changes (e.g. reduced strength and stiffness).

Diagnostic methods based on x-ray absorption are the current “gold standard” for quantitative assessment of bone but they provide incomplete information. Whilst they can provide reasonably good data for bone mineral density (BMD) and geometry, they are not intrinsically sensitive to the mechanical properties or microarchitecture of bone. The clinical value of such additional information has yet to be conclusively demonstrated, but there is growing interest in the potential for assessing aspects of bone “quality” in addition to “quantity”. In addition, X-ray technologies are expensive, non-portable and use ionizing radiation with a consequent health risk. Ultrasound offers an alternative approach to bone assessment that has a unique potential to characterise the material and structural properties of bone. Furthermore, ultrasound is safe, relatively cheap, and portable.

The ultrasonic methods and devices can be divided into two main categories according to the type of bone (trabecular or cortical, see Chapter 2) to be measured. More attention has been paid to measuring the trabecular bone, at sites such as the heel [35, 28, 23] or finger phalanges [75, 91]. These methods are generally seen as being more directly relevant to the sites (hip and spine) where osteoporotic fractures most often occur. It must be noted, that direct ultrasonic measurement of the hip and spine is difficult as these sites are located deep under soft tissue. It has been shown, however, that ultrasound attenuation (referred to as Broadband Ultrasound Attenuation, BUA) or speed of sound (SOS), as measured for the heel, predict fractures at hip [35, 9, 82, 28, 45] and spine [38, 23]. In addition, the interest in measuring cortical bone, at sites such as the tibia or radius, has increased during recent years. In osteoporosis the deterioration of bone affects adversely the properties and the effective thickness of the cortical bone wall, and it has been suggested that a multi-site assessment could improve the diagnostic power of ultrasound [48, 36]. However, there are devices from only one manufacturer on the market today for the clinical assessment of long bones. It has become evident that these devices, based on measuring the so-called lateral waves which propagate along the interface of periosteal
(outer) bone and soft tissue [16, 11], are relatively insensitive to the changes seen in osteoporosis that occur largely in the endosteal (inner) bone region [31, 89].

The so-called guided waves have been a topic of considerable interest in the field of non-destructive testing, dating back to the 1960’s [110, 109, 106]. Guided waves propagate in bounded media such as plates or layered structures, and carry information of the material properties (e.g. elasticity and density) as well as the geometry (e.g. thickness) of this waveguide [32, 87, 106]. The various applications of guided waves include, e.g., the defect detection or health monitoring of water pipe lines, aircraft wings and different composite laminates [96, 58, 33, 22, 21, 20, 17]. Cortical bone is a plate- or tube-like composite material which might also be expected to support the propagation of guided waves. This could thereby yield an improved ultrasonic assessment of cortical bones, reflecting aspects of the average bone properties throughout the cortical layer. Though only a little attention has been paid to ultrasonic guided wave measurements of human bones [41, 78, 99], recent studies in bone phantoms and animal bones in vitro reflect growing interest in this approach [54, 52].

The purpose of this work was to develop an axial transmission device and methods for measuring guided waves (GW) as well as the first arriving signal (FAS) at approximately 200 kHz central frequency in human bones. This frequency was considerably lower than that used in the currently available commercial axial transmission devices, and thus provided new means for assessing the effects of thickness on the ultrasound velocities. The effect of thickness was verified by comparing phantom measurements with analytical plate theory. The method was tested for the first time on human bones in vitro and in vivo, verifying the relationships between ultrasound velocities and cortical thickness and bone mineral density. Simple plate theory was used here for developing an inversion scheme for estimating the cortical thickness. We also incorporated the tubular shape of bones in the theory, and found thereby a better correspondence between guided wave results and the actual bone properties. In addition, a water-solid bilayer model was used qualitatively to explain the contribution of an overlying soft tissue to in vivo guided wave measurements.
Chapter 2

Bone

2.1 Structure and function

Bone as a material can be classified into organic and inorganic components. The organic material mainly consists of type I collagen and amorphous substance which contains glycoproteins and proteoglycans [8]. The inorganic part of bone is composed of minerals, mostly hydroxyapatite (Ca_{10}(PO_{4})_{6}(OH)_{2}) crystals, and represents about 65% of the wet weight of bone [61, 73]. Together the organic and inorganic components form so-called extracellular bone matrix. Collagen gives bone flexibility, toughness and tensile strength, and also provides loci for nucleation of the mineral crystals which give bone its rigidity and compressive strength [61, 90].

Bone as a tissue consists of cortical and trabecular bone. Cortical (compact) bone forms the majority (approximately 85%) of the bone in the body, and is relatively most abundant is the shafts of the long bones such as the radius, tibia and femur [68]. Cortical bone is relatively dense, with an apparent density of approximately 1.7-2.0 g/cm³ [85], and this is due to its low porosity (typically 5 - 10%) [14, 61]. The shaft (diaphysis) of the long bones consists of a thick tubular cortex of compact bone surrounding the medullary canal that is filled with bone marrow. The cortical bone wall is composed of osteons (see below) that are aligned parallel to the long axis of bone (Fig. 2.1). This alignment is due to bone’s natural ability to organise its structure in order to optimise strength according to different levels of loading applied in different directions. Consequently, cortical bone is anisotropic having the greatest strength and stiffness in the main load-bearing direction, and has a structure designed to resist torsional and bending forces where these occur [14, 61, 101]. Trabecular (cancellous) bone is composed of an interconnected network of bone plates, struts and rods (trabeculae) surrounded by bone marrow. Trabecular bone has essentially the same matrix composition and ultrastructure as compact bone [61], but it has a much higher porosity (50-95%) and consequently a lower apparent density. Trabecular bone absorbs the impact loads and allows bones to broaden near the articular surfaces without the need for excessive increase of bone mass. Trabecular bone can be found at the ends of long bones and in the cores of flat bones. In both cases, the trabecular bone is covered by a thin layer of cortical bone [14].
Bone has a hierarchical architecture with several levels of structure (Figs. 2.1 and 2.2). Mineralised collagen forms long fibrils, which pack together as fibres. In so-called lamellar, or osteonal, bone, collagen fibres organise themselves into planar arrangements called lamellae. The sheets of lamellae wrap as concentric layers around a central canal forming osteons (Haversian systems) with typical diameters ranging from 100 to 300 µm and length 10 mm. The central canal (Haversian canal) of an osteon has a diameter of around 50 µm and contains blood vessels and nerves [61]. The fibres can also form so-called woven bone where fibre orientation is less well distinguished. Woven bone occurs mainly at the early stages of growth and fracture repair. In addition, some of the lamellae do not wrap but remain as planar layers, and together with woven bone form layers of so-called lamellar bone with thickness ranging typically from 150 to 300 µm [86, 14, 61].

The function of bone is to provide mechanical support for the body, as well as to serve as a dynamic mineral reserve and to produce red blood cells. The type of function determines the specific structure of each bone in different parts of the skeleton [14]. Bone at the organ level can be classified into two types: flat bones (skull bones, scapula, mandible, and lileum) and long bones (tibia, femur, humerus, radius, etc.).

![Hierarchical structural organisation of bone](image)

**Fig 2.1.** Hierarchical structural organisation of bone: (a) cortical and cancellous bone; (b) osteons with Haversian systems; (c) lamellae; (d) collagen fiber assemblies of collagen fibrils; (e) bone mineral crystals, collagen molecules, and non-collagenous proteins (After Rho et al 1998 [86]).
Fig 2.2. Structure of cortical bone (After Buckwalter et al [14]).

2.2 Growth, aging and disease

2.2.1 Bone growth

The growth of bone occurs by two different mechanisms, the so-called endochondral and intramembranous ossification. The former conducts the longitudinal growth, whereas the latter is responsible of the growth in diameter as well as of the remodelling process of the bone tissue [77].

Longitudinal growth takes place in the regions called the growth plate or physis that are located near each end of long bones. In the growth plate new cartilage is constantly formed by chondrocytes. On the side of bone shaft (methaphyseal side) the growth plate mineralises and becomes part of the methaphyseal bone. Consequently, the length of bone
shaft is increased while the thickness of the growth plate remains constant. As bones reach their adult length the growth plates are no longer needed and the physes close by ossification [77].

The growth in diameter is another type of mechanism of bone formation, which in addition to growth is also responsible of reshaping the bones. Bone must be removed in some places while it is added to others. This continuous process of bone resorption and formation is known as modelling and it is responsible of the changes both in size and shape. In addition, the architecture of bone must adapt to varying loading conditions and fatigue damage must be repaired throughout the life. These changes are accomplished by a similar removal-replacement process, known as remodelling. The modelling and remodelling refer to actions of osteoblasts and osteoclasts, the former being responsible of formation and the latter of resorption. In modelling these bone cells act independently from each other, whereas remodelling involves coupled actions of these two types of bone cells [68, 61, 15].

2.2.2 Aging

Bone mass is gained through puberty and rises to a peak during the second to third decade [79]. Thereafter, a gradual loss of bone takes place. Women loose about 35-40% of the cortical bone and 55-60% of the trabecular bone whereas in men the bone loss is somewhat smaller by a factor of about a third. As the bone growth stops in the adulthood, this is the point where the peak bone mass is reached. After that, remodelling continues and the rate of loss of bone depends on the balance between bone resorption and formation. The good coupling between these parallel processes is crucially important in order to retain bone mass. Mechanical stimulation of the bone as well as the hormonal effects play important roles in the quality of the coupling. During the normal aging process the coupling weakens and bone balance tends always towards the negative side. This means that the bone mass begins to slowly decrease from that of the peak level reached during the period of growth [79, 73].

2.2.3 Disease

The most common metabolic bone diseases are osteoporosis and osteomalacia. The currently-accepted definition of osteoporosis, as set out by the National Institute of Health Consensus Conference of 1993, is that osteoporosis is “a disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk” [2]. Osteoporosis typically develops over a long period of time without necessarily causing any symptoms. The first symptoms are fractures caused by minor trauma. The insidious nature of osteoporosis, coupled with the absence of effective therapies capable of replacing bone once it has been lost, makes it a severe and problematic disease.

It has been estimated that 54% of postmenopausal white females in the United States have osteopenia (pre-stage of osteoporosis), and another 30% have osteoporosis [103]. In Finland, the impact of osteoporosis can be seen in the age-adjusted incidence of low-trauma ankle fractures which rose in both women (from 66 in 1970 to 174 in 2000, a 164% increase) and men (from 38 in 1970 to 114 in 2000, a 200% increase) [43]. The most serious complication resulting from osteoporosis is fracture of the hip. The number of hip fractures in Finnish people aged 50 or more has risen from 1857 in 1970 to 7122 in
The average 1-year total costs of a patient with a hip fracture were Euro 14,410, with about one quarter of these costs being expended on acute care [76]. This gives some idea of the significance of osteoporosis as a public health challenge.

Several subtypes of osteoporosis can be distinguished. Involutional osteoporosis, meaning gradual and progressive bone loss, can be one of two types: postmenopausal osteoporosis and senile osteoporosis [88]. Postmenopausal osteoporosis affects women and occurs mainly between the ages of 50 and 65 years. With this condition, resorption of trabecular bone is accelerated due to oestrogen deficiency associated with the menopause, and this often manifests in wrist and/or spine fracture. Senile osteoporosis occurs both in men and women aged 70 years and older, with a loss of both trabecular and cortical bone, manifesting in fractures of the hip, proximal humerus, tibia and pelvis [88]. So-called secondary osteoporosis is osteoporosis that is caused by factors such as chronic diseases, malabsorption, endocrine disorders, or use of drugs such as corticosteroids. The progress of osteoporosis can be slowed down by proper nutrition and physiological exercise as well as by appropriate medication, such as hormone replacement therapy or bisphosphonate treatment [55].

In osteoporosis, the porosity of bone increases and consequently its apparent density decreases [25]. In trabecular bone, architectural changes occur such as the loss of trabecular struts and perforation of plates. In cortical bone, bone loss occurs mainly in the endosteal region so that the marrow cavity expands and consequently the effective thickness of the compact bone decreases [88].

Osteomalacia is also a metabolic bone disease that occurs as defects in the amount or quality of the mineralization of bone matrix. Thus, osteomalacia can be characterised by relative deficiency of mineral in relation to collagen, which distinguishes it from osteoporosis in which a normal mineral to collagen ratio is observed [103]. Deficiencies of vitamin D, calcium, or phosphorus due to inadequate nutritional intake are the usual causes of osteomalacia [46].

In addition, there are several skeletal disorders which related to genetic, developmental, and dysplastic problems, such as osteogenesis imperfecta, ostosclerosis, and fibrous dysplasia. Osteogenesis imperfecta is a heritable disorder of connective tissue that is caused by abnormalities in type I collagen [84]. Consequently the elastic abilities of the extracellular matrix weaken and bone becomes brittle [105].
2.3 Mechanical properties of bone

The primary function of skeleton is to provide mechanical support for the body in locomotion and static loading. To this end, bone is an adaptive tissue and has optimal mechanical properties, specific to each part of the skeleton. The mechanical properties of bone can be distinguished as the mechanical behaviour of the bone tissue as a material and as the mechanical behaviour of the whole bone as a structure. The material behaviour reflects the intrinsic properties of the bone material itself, being independent of the shape and size of the actual bone. The material properties can be determined by performing mechanical tests on standardised specimens. In addition to material properties, the structure of bone has an important role in terms of the strength. The structural properties include the effect of bone geometry as well as the material properties. The structural properties can be determined by mechanical testing of the whole bone specimens [37, 13, 61].

In vivo the bone is affected by loading of different origins, including external (ground reaction and impact forces) and internal forces (ligament tension, muscle contraction and bone-on-bone contact forces) [13].

The purpose of mechanical testing is to determine the relationship between loading (force applied to bone) and the magnitude of consequent deformation. When the bone is deformed, its response is to the applied stress $\sigma = F / A$, where $A$ is the cross-sectional area of the bone. The definition of compressive and tensile stresses is thereby identical to that of pressure. However, the loading of solid material can also be tension, shear or torsion, yielding the stresses and deformations in the corresponding directions. The magnitude of a local deformation is given by strain $\varepsilon$ (compression, tension) or $\gamma$ (shear) as deformation $\Delta l$ per unit length $l$ (Fig 2.3). The stress is generally linearly dependent on the strain (Fig 2.3b), and the slope gives the elastic (or Young’s) modulus $E$. This region is called the elastic region. When the loading is increased, at a certain point the material begins to undergo permanent deformations, and the stress response ceases to be linear. This point is known as the yield point followed by the yield (or plastic) region. The stress corresponding to the yield point is called the yield strength $\sigma_y$ of the material. The load that causes complete breakage of the material is known as the ultimate (or failure) load, and the corresponding stress as the ultimate strength $\sigma_u$ [13, 61].

When performing structural testing of the whole bone, it is typical to measure the deformation against the applied force directly. This measurement yields a corresponding figure to Fig 2.3, but the stress is replaced by the force and strain by the actual deformation. The corresponding slope is then called the stiffness [13].
Mechanical testing is said to be non-destructive when exploring only the linear elastic region, and the yield point is not reached. The benefit of this approach is that the same specimen remains available for further testing. However, the elastic modulus can be determined more precisely when measuring near the yield point. Also, determination of yield and ultimate strength provides a more complete picture of the mechanical properties of the specimen [13].

If the elastic modulus of the material is independent of the direction of examination, the material is said to be isotropic. In cortical bone, however, the elastic modulus in the direction of the long axis of bone (i.e. the direction of osteons) is approximately two times higher than those in the transverse directions. Thus, cortical bone is anisotropic material. Particularly, it can be modelled using transverse or orthotropic isotropy [5, 39, 81]. The typical longitudinal and transverse elastic moduli of human cortical bone are 17 and 10 GPa, respectively, and the shear modulus is 3.5 GPa [13, 61]. The strength properties of cortical bone depend on the direction also. However, unlike the elastic moduli, the strength is greater in compression than in tension or shear. This alone suggests that the cortical bone has adapted to the conditions where compression loading is greater than tension, and together with the anisotropy, that longitudinally directed loading is greater than transversely directed loading [13].

Unlike those of cortical bone, the mechanical properties of trabecular bone vary a lot depending on the site. For instance, at vertebral bodies the trabecular bone is fairly anisotropic whereas in the femoral head it is nearly isotropic. The elastic modulus of trabecular bone is generally significantly lower than that of cortical bone, ranging roughly within 0.01-10 GPa. These differences in the properties of trabecular bone can indeed be understood due to its adaptation to different loading conditions at different skeletal sites, and the wide range in porosity and microarchitecture adopted to meet these different conditions [13].
Chapter 3

Quantitative ultrasound applied to cortical bone

3.1 The basic physics of ultrasound

Ultrasound is propagation of a mechanical disturbance in a solid or fluid medium at frequencies higher than the upper limit of the audible sound range for humans (∼20 kHz). The field of ultrasonics dates back to the end of the 19th and the beginning of the 20th century, when piezoelectricity was discovered and its first applications were developed during the World War I. An in vivo application of bone ultrasound measurement was reported for the first time by Siegel et al in 1958 [94], who used it for monitoring fracture healing in tibia. Today ultrasound has a wide range of medical uses, including diagnostic, therapeutic and surgical applications. Diagnostic ultrasound has several applications, such as non-invasive imaging of different parts of the body and measurement of tissue motion or blood flow. Ultrasound imaging techniques are attractive due to the absence of ionising radiation and the availability of compact devices that provide real time images at lower cost compared to other imaging modalities.

An ultrasound wave emerges as a tiny disturbance of the medium particles around their equilibrium positions, as the matter is excited by a mechanical impulse or vibration. The medium can be considered as a model in which mass points (particles) are connected to each other by strings. Due to the string interactions, the disturbance is transmitted step-by-step to other parts of the medium. The intrinsic elastic properties of the medium, modelled by the strings and particles, define the propagation velocity of the acoustic wave \( c \). In the real life, the string constant corresponds to an elastic modulus and particle mass the mass density of the material, which correspondingly define the velocity of the acoustic wave.

The ultrasonic waves can be divided into longitudinal (compression) and shear (transverse) waves. The longitudinal wave denotes a wave in which the particles oscillate along the longitudinal axis of wave propagation, whereas the shear wave refers to the motion that takes place perpendicularly to the direction of propagation. In perfect fluids (gases or liquids) only longitudinal waves can propagate. Shear waves are not possible because these materials do not support shear forces and the particles are free to slide parallel to each other without any interaction. Elastic solids support both compression and shear motions, thus both of the longitudinal and shear waves can propagate. In a viscous
fluid, longitudinal and shear waves can both propagate, but the shear waves are strongly attenuated. Biological soft tissues have similar mechanical properties as viscous fluids, thus in practice only longitudinal waves can propagate in them. Bone is a hard solid tissue in which both longitudinal and shear waves can propagate [51].

In an isotropic solid the speed of the longitudinal wave $c_L$ is given by

$$c_L = \sqrt{\frac{E(1-\nu)}{\rho(1+\nu)(1-2\nu)}},$$  (3.1)

where $E$ is Young’s modulus, $\nu$ Poisson’s ratio and $\rho$ the density. Correspondingly, the propagation speed of the shear wave $c_T$ is given by

$$c_T = \sqrt{\frac{\mu}{\rho}},$$  (3.2)

where $\mu = E / 2(1+\nu)$ is the shear modulus. $c_T$ is typically less than 0.5 $c_L$. The velocity of the so-called Rayleigh wave is $c_R = 0.9 c_T$. The Rayleigh wave propagates along the surface of a semi-infinite medium.

The characteristic acoustic impedance of the medium, $Z$, is determined as

$$Z = \rho c.$$  (3.3)

Reflection and refraction will occur at the boundary between two media with different acoustic impedances. The refraction is governed by Snell’s law,

$$\frac{\sin \theta_1}{c_1} = \frac{\sin \theta_2}{c_2},$$  (3.4)

where $c_1$ is the velocity of the incident wave, $c_2$ that of the transmitted wave and $\theta_1$ and $\theta_2$ the angles of incidence and transmission, respectively.

For longitudinal waves on a planar surface of two ideal fluids, the (intensity) reflection and transmission coefficients $R$ and $T$ are given by [104, 51]

$$R = \frac{I_r}{I_i} = \left( \frac{Z_2 \cos \theta_1 - Z_1 \cos \theta_2}{Z_2 \cos \theta_1 + Z_1 \cos \theta_2} \right)^2,$$  (3.5)

$$T = \frac{I_t}{I_i} = \frac{4Z_1 Z_2 \cos \theta_1 \cos \theta_2}{(Z_2 \cos \theta_1 + Z_1 \cos \theta_2)^2},$$  (3.6)

where $I_i$, $I_r$, $I_t$ are the incident, reflected and refracted intensities, and $Z_1$ and $Z_2$ are the acoustic impedances of the first and second media. Obviously $T + R = 1$. The amount of energy in the reflected wave depends upon the mismatch in acoustic impedance of the two media. The greater the mismatch, the greater the reflected energy.

When either or both of the media are solids, then the energy of the incident wave, longitudinal or shear, will be converted as reflected and refracted longitudinal and shear waves. The number of possible waves depends on the type and order of the two media. If a fluid-solid interface (e.g. soft tissue and bone) is considered, then the incident longitudinal wave can be reflected only as a longitudinal wave and refracted both as longitudinal and
shear waves. For the fluid-solid case, Eqs. (3.5-3.6) are only valid at normal incidence. For other angles of incidence the equations become much more complex [51].

If the medium is inhomogeneous, the primary ultrasonic wave interacts with the boundaries of the particles that have different physical properties than the surrounding medium. This process is called scattering, yielding an emission of secondary (scattered) waves. There are three different mechanisms of scattering. a) If the dimensions of the scattering object are significantly larger than the ultrasonic wavelength, specular reflection takes place and Eqs. (3.4-3.6) can be utilised. b) If object dimensions are significantly smaller than the ultrasonic wavelength, then ultrasound is scattered uniformly in all directions, and the incident wave suffers minor perturbations due to diffraction at the edges. c) If the dimensions of the object are of the same magnitude with the wavelength, the scattered radiation exhibits a complex pattern which depends on the acoustic impedance, shape and dimensions of the object. Only two useful cases are relatively easy to calculate: scattering from a sphere and from a cylinder [65, 100].

The attenuation of an ultrasonic wave is a material property and represents the signal loss due to absorption and scattering by objects with scales too small to be captured by the wave. Ultrasound attenuation is characterised by an exponential decrease of the intensity with propagation distance $x$,

$$I = I_0 e^{-2\alpha(f)x},$$

(3.8)

where $I_0$ is the intensity at $x = 0$ and $\alpha(f)$ is the pressure attenuation coefficient expressed as a function of frequency $f$. The factor 2 in the exponent results from transforming pressure into intensity, since intensity is proportional to the square of pressure for a plane progressive wave [65, 100, 51]. Other factors such as reflection (interface) losses, beam spreading (diffraction) and mode conversion may contribute to a reduction in the intensity of the signal, but in experimental measurements the effects of these extrinsic factors should be removed where possible.
### 3.2 Axial transmission

The so-called axial transmission technique has been used to assess long bones for over four decades [94, 30, 102, 16]. With this method an ultrasonic signal is mediated to bone at one point, allowed to propagate along the long axis of bone, and recorded from the same side of the bone at a given distance \( r \) apart from the emitter (Fig. 3.1). Figure (3.2) illustrates a typical recorded signal as a response to excitation of bone in vitro. The transit time \( t \) of the first arriving signal is determined, e.g., according to a certain threshold value, or the location of the first maximum, and the velocity \( v_1 \) (also called as the apparent speed of sound) of the first arriving signal (FAS) is obtained as the ratio between \( r \) and \( t \).

![Fig. 3.1. Principle of a typical axial transmission measurement: a transmitter is excited by a pulse or toneburst, a longitudinal wave propagates near the dense periosteal surface of long bone, and this is received as the first arriving signal (FAS) at the receiver.](image)

![Fig. 3.2. Typical recorded axial ultrasound signal. a) The first arriving signal (FAS) and an additional “guided wave”. b) FAS in the close-up. The time-of-flight can be determined according to the first maximum, threshold or zero-crossing point. (Low-frequency axial transmission scanner, human radius in vitro).](image)
Generally, the FAS corresponds to an axial longitudinal wave, provided that the wall thickness \( h \) of bone is greater than the acoustic wavelength \( \lambda \). In bone, the speed of the axial longitudinal wave is approximately 4000 m/s [53, 81].

As the bone is surrounded by soft tissue, the FAS corresponds to the so-called lateral longitudinal (or P-head) wave, which propagates along the interface between these two media [16]. In this case, the excitation is mediated to bone through an overlying soft tissue and the lateral wave is born as a linear wave front which connects the refracted longitudinal wave to the reflected wave. This provided that the incident angle \( \theta_1 \) is equal to or greater than the critical angle \( \theta_c = \sin^{-1}(v_{st}/v_1) \), where \( v_{st} \) is ultrasound velocity in the soft tissue (approximately 1500 m/s). The velocity of the lateral wave has been shown to be consistent with that of the longitudinal wave in bone [16], and this essentially enables the clinical measurement of the SOS in bone.

Commercial devices using the axial ultrasound transmission are currently available only from one manufacturer (Sunlight Medical Ltd., Tel Aviv, Israel). These devices operate at a central frequency of 1.25 MHz, which corresponds approximately to a 3 mm acoustic wavelength for the longitudinal waves in bone. It has been demonstrated that the FAS measured under these conditions indeed corresponds to a longitudinal lateral wave that propagates along the dense periosteal (outer) cortical bone [16, 11]. This fact is confirmed by the close agreement between clinically-measured velocities in the human tibia [27, 92, 102, 53, 83, 95] and in vitro measurements of the axial longitudinal wave velocity in human cortical bone specimens [5, 49, 3, 81].

There is, however, evidence indicating that the apparent speed of sound (SOS) is lower than that of the longitudinal wave when the acoustic wavelength \( \lambda \) is greater than the thickness \( h \) [74]. Recent numerical simulations and measurements in bone phantoms suggest that the apparent SOS under this condition tends towards that of the fundamental symmetric guided wave (S0 mode) [72, 11, 12]. In vivo studies indeed support this idea that the apparent SOS measured at low ultrasonic frequencies is sensitive to bone thickness. When using a device operating at \( f = 250 \text{ kHz} \) (\( \lambda \approx 15 \text{ mm} \)), a significant correlation between the apparent SOS and bone wall thickness was obtained, whereas in another study using a high-frequency device at \( f = 1.25 \text{ MHz} \) (\( \lambda \approx 3 \text{ mm} \)), no correlation in the tibia and only a modest correlation in the radius was found.

As in the in vivo bone measurements the excitation must be mediated to bone through the overlying soft tissue, and recorded via soft tissue at a given distance \( r \) away from the emitter, the consequent delays due to signal passing through the soft tissue must be eliminated (Fig 3.3). This is achieved simply by considering the difference between time delays \( t_1 \) and \( t_2 \) obtained from consecutive measurements made at two different distances \( r_1 \) and \( r_2 \), respectively. Now the inverse of \( v_1 \) is given by [60]

\[
\frac{1}{v_1} = \frac{dt}{dr}, \tag{3.9}
\]

where \( dt = t_1 - t_2 \) and \( dr = r_1 - r_2 \). The use of multiple transmitter-receiver distances \( r \) improves the precision of the velocity \( v_1 \) that is determined as an inverse slope through Eq. (3.9) [60].

As discussed above, the soft tissue on top of the bone contributes to the reliability of measuring FAS by affecting the timing of the signal. The delay caused by soft tissue of
constant thickness $a$ in the range of consideration can be eliminated using Eq. (3.9) or linear regression. A linearly changing $a$ can easily yield a remarkable bias in the obtained velocities, and this can be reduced using so-called bi-directional approach. The measurement must be performed in both directions yielding $v_1^+$ and $v_1^-$, and the actual $v_1$ is given by

$$\frac{1}{v_1} = \frac{1}{2} \left( \frac{1}{v_1^+} + \frac{1}{v_1^-} \right) \cos \alpha,$$

(3.10)

where $\alpha = \cos^{-1}\left((a_1-a_2)/dr\right)$ [10]. In addition, soft tissue must be thin enough compared to the emitter-receiver distance $r$ in order to obtain the fastest signal path via bone, i.e. for the given soft tissue thickness $a$, distance $r$ must be greater than $r_{\min}$ defined by [16]

$$r_{\min} = \frac{2\alpha \left(1 + \frac{v_{st}}{v_1}\right)}{\left(1 - \left(\frac{v_{st}}{v_1}\right)^2\right)},$$

(3.11)

where $v_{st}$ is ultrasound velocity in the soft tissue.

Fig. 3.3. Diagram of an in vivo axial transmission measurement when the thickness $a$ of the soft tissue changes linearly.
3.3 Guided waves and bone

In addition to FAS, completely different types of wave modes can also propagate in the long bone (Fig. 3.4). These so-called guided wave modes (GW) propagate, not only in the dense endosteal layer, but throughout the entire cross-section of cortical bone wall in the form of bending waves. As it is known that bone resorption starts in the endosteal bone, and that the consequent decrease of the solid cortical wall thickness yields increased fracture risk (Chapter 2), GW techniques may yield an improved diagnostic bone assessment. However, very little consideration has been given to measuring the GW in bone. A few studies have reported low frequency ultrasonic measurements ($f = 100$ kHz) of a slow antisymmetric flexural wave in the tibia, mapping the spatial variation in the velocity and quantifying changes during weightlessness [41, 78, 99, 62]. In addition, two recent in vitro studies demonstrated that velocities of guided waves measured in animal bones ($f = 100$ kHz and $f = 50$-500 kHz, respectively) correspond with close agreement to guided waves in a plate [54, 52].

![Fig. 3.4. Principle of an axial guided wave measurement. A guided wave arises from multiple reflections at the periosteal and endosteal boundaries, and propagates as a bending vibration of the whole cortical layer.](image)

In general, there is a whole family of different guided wave modes (GW). They arise from reflections, mode conversions and interference of longitudinal and shear waves, and propagate within the boundaries of plate and tube like layered media (Fig 3.4). The velocities of guided waves are functions of wavelength, frequency and layer thickness, and they are in addition determined by the elastic properties and density of the material [106]. These relationships will be treated in more detail in Chapter 4. In terms of the bone application, the endosteal surface of a long bone must be considered as the inner layer and periosteal as the outer layer of a tubular or plate like structure. If either of these assumptions can be made, then ultrasonic waves propagate guided by the bone cortex, and their characteristics are determined by the cortical thickness as well as the elasticity and density of the bone. Potentially, the most interesting guided wave mode regarding the bone applications is the fundamental antisymmetric flexural mode (A0). The velocity of A0 saturates to that of Rayleigh wave in thick layers, but decreases towards zero with decreasing cortical wall thickness.

In addition to the guided wave modes, FAS can also show dispersive behaviour as mentioned in Section 3.2. However, FAS cannot be classified as a pure guided wave
mode, but rather as a complicated transition mode between the lateral and fundamental symmetric guided wave (S0), when its wavelength is of the order of or greater than the bone thickness.

The effects of overlying soft tissues are considerably more complicated for guided waves than for FAS, as guided waves cannot usually be considered as bulk waves but preferably as bending motion of the whole solid layer. The energy propagating in bone can easily leak to surrounding soft tissues causing attenuation and coupling. Coupling between bone and soft tissue means that they form a joint bilayer system in which a guided wave can propagate. Hence, any model of a single bone layer alone cannot very accurately explain the dispersion that takes place in the in vivo measurement of human bone. Thus the bilayer model, which takes the soft tissue coupling into account, will be discussed in Section 4.2.
Chapter 4

Theory of Guided Waves

Though the concept of guided ultrasonic waves is novel in the field of bone quality assessment, guided waves have been widely used for many years in different applications of non-destructive testing for the assessment of plates, tubes and more complex structures [21, 20, 19, 17, 44]. This chapter reviews approaches to the theoretical description of guided waves with particular emphasis on those aspects of the theory relevant to the applications of guided waves for bone assessment.

The propagation of guided waves in solids is governed by partial differential wave equations that arise from theory of elasticity. These governing equations are identical for guided as well as for bulk longitudinal and shear waves. The fundamental difference that distinguishes the guided waves from the bulk waves is that the latter propagate in the bulk of a material, independent of the boundaries, whereas the guided waves are born due to boundary interactions. Guided waves arise due to reflection, refraction, and mode conversion of longitudinal and shear waves at the boundaries of the media resulting in resonant modes whose frequency and propagation speed correspond to standing waves in the thickness direction of the structure. Mathematically, the solution of a guided wave must satisfy a number of boundary conditions, and the introduction of the boundary conditions makes the problem of guided waves difficult to solve. In most cases no analytical solution can be found, and often the use of numerical methods is needed [87].

Classically, the problem of guided waves is associated with waves in a traction-free isotropic plate (Lamb waves) [50, 106]. Due to the complexity of guided wave problems, a solution for the free plate case may be a convenient starting point for understanding the actual application. Sometimes it may be possible to consider the actual structure, e.g. a tubular bone, as a plate within a sufficient precision [54]. It is possible also to generalise the problem to deal e.g. with tubular shape, anisotropy and multilayer structures [32, 87].
4.1 Waves in plates

Lamb waves are two-dimensional elastic waves that propagate in a traction-free solid elastic plate of finite thickness \( h \). They can be modelled using four partial waves, downward and upward propagating longitudinal and shear waves (Fig 4.1).

Fig 4.1. Geometry of the free plate problem. Plate thickness is \( h \). Lower-case \( k_{L,T} \) are respectively the wave numbers of the longitudinal and shear partial waves, capital \( K_{L,T} \) are the corresponding vertical wave numbers, and \( k \) is the wave number of the propagating guided wave.

The motion of a homogeneous, linear elastic solid can be modelled by Navier’s displacement equations of motion,

\[
(\lambda + \mu)u_{j,ij} + \mu u_{i,jj} = \rho \ddot{u}_i, \quad (4.1)
\]

where \( u_i \) is the displacement vector,

\[
u_{k,ij} = \frac{\partial^2}{\partial x_i \partial x_j} u_k,
\]

\( \rho \) is the mass density and \( \lambda \) and \( \mu \) are the Lamé constants. Summation over a repeated index is assumed. The displacement vector can be expressed via Helmholtz decomposition,

\[
u_i = \frac{\partial \phi}{\partial x_i} + e_{ijk} \frac{\partial \psi_k}{\partial x_j}, \quad (4.2)
\]

where \( \phi \) and \( \psi \) are scalar and vector potentials, respectively, and \( e_{ijk} \) is the permutation symbol. Substitution of Eq. (4.2) into Eq. (4.1) yields two uncoupled wave equations

\[
\left( \nabla^2 - \frac{1}{(c_L)^2} \frac{\partial^2}{\partial t^2} \right) \phi = 0, \quad \left( \nabla^2 - \frac{1}{(c_T)^2} \frac{\partial^2}{\partial t^2} \right) \psi = 0, \quad (4.3)
\]

where \( \nabla^2 = \partial^2/\partial y^2 + \partial^2/\partial z^2 \), \( c_L \) is the bulk longitudinal velocity and \( c_T \) the bulk shear velocity. According to the partial wave formalism [87], the solutions of Eqs. (4.3) can be written as

\[
\phi = C_1 e^{ik_L(z \sin(\theta_L) + y \cos(\theta_L))} + C_2 e^{ik_L(z \sin(\theta_L) - y \cos(\theta_L))}, \quad (4.4a)
\]

\[
\psi = C_3 e^{ik_T(z \sin(\theta_T) + y \cos(\theta_T))} + C_4 e^{ik_T(z \sin(\theta_T) - y \cos(\theta_T))}, \quad (4.4b)
\]

where
\[ \theta_L = \arcsin \left( \frac{k}{k_L} \right), \quad \theta_T = \arcsin \left( \frac{k}{k_T} \right), \]

\( k_L \) is the wavenumber of a longitudinal wave component, \( k_T \) the wavenumber of a shear wave component and \( k \) the wavenumber of a guided wave (in the direction of propagation) (Fig 4.1). The constants \( C_1, C_2, C_3 \) and \( C_4 \) are arbitrary unknowns and will be determined by the boundary conditions.

Both of the potentials in Eqs. (4.4) now consist of two terms, one representing a downward propagating plane wave (positive \( y \) in the exponential term) and one representing an upward propagating plane wave (negative \( y \) in the exponential term). Technically we have thus assumed that there are four plane bulk waves in the solid, two longitudinal and two shear (Fig 4.1).

Displacements \( u_i \) can now be obtained from Eq. (4.2), and stresses \( \sigma_{ij} \) are given by
\[ \sigma_{ij} = \lambda \delta_{ij} \epsilon_0 + 2 \mu \epsilon_{ij}, \quad (4.5) \]

where \( \delta_{ij} \) is the Kronecker delta, the dilation is \( \epsilon_0 = \epsilon_{11} + \epsilon_{22} + \epsilon_{33} \), and the strains are
\[ \epsilon_{ij} = \frac{1}{2} \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right). \quad (4.6) \]

By requiring traction-free boundary conditions, \( \sigma_{yy} = \sigma_{yz} \equiv 0 \) at the free plate surfaces \( y = 0 \) and \( y = h \), where \( h \) is the plate thickness, and ignoring the shear horizontal displacements \((u_x \equiv 0)\), four equations will be obtained,
\[ \{ \lambda k_L^2 + 2 \mu K_L \} \{ C_1 + C_2 \} + 2 \mu K_T \{ C_3 - C_4 \} = 0, \quad (4.7a) \]
\[ -2 \mu K_L \{ C_1 - C_2 \} + \mu \{ k_T^2 - 2 k_T^2 \} \{ C_3 + C_4 \} = 0, \quad (4.7b) \]
\[ \{ \lambda k_L^2 + 2 \mu K_L \} \{ C_1 e^{ik_L h} + C_2 e^{-ik_L h} \} + 2 \mu K_T \{ C_3 e^{ik_T h} - C_4 e^{-ik_T h} \} = 0, \quad (4.7c) \]
\[ -2 \mu K_L \{ C_1 e^{ik_L h} - C_2 e^{-ik_L h} \} + \mu \{ k_T^2 - 2 k_T^2 \} \{ C_3 e^{ik_T h} + C_4 e^{-ik_T h} \} = 0, \quad (4.7d) \]

where
\[ K_{LT} \equiv k_{LT} \cos(\theta_{LT}) = \sqrt{k_{LT}^2 - k^2} = \sqrt{\left( \frac{\omega}{c_{LT}} \right)^2 - k^2}, \]

and \( \omega \) is the angular frequency.

This system of equations, Eqs. (7a-7d), can be expressed in a matrix form
\[ [G] \{ C \} = 0, \quad (4.8) \]

where \([G]\) is the global matrix,
\[ [G] = \begin{bmatrix} \lambda k_L^2 + 2 \mu K_L & \lambda k_L^2 + 2 \mu K_T & 2 \mu K_T & -2 \mu K_T \\ -2 \mu K_L & 2 \mu K_T & \mu(K_T^2 - 2 k_T^2) & \mu(K_T^2 - 2 k_T^2) \\ (\lambda k_L^2 + 2 \mu K_L) e^{ik_L h} & (\lambda k_L^2 + 2 \mu K_T) e^{-ik_L h} & 2 \mu K_T e^{ik_T h} & -2 \mu K_T e^{-ik_T h} \\ -2 \mu K_L e^{ik_L h} & 2 \mu K_T e^{-ik_L h} & \mu(K_T^2 - 2 k_T^2) e^{ik_T h} & \mu(K_T^2 - 2 k_T^2) e^{-ik_T h} \end{bmatrix}, \]
and vector \( \{ C \} \) contains the four unknown constants \( C_i, i = 1, \ldots, 4 \). The matrix equation Eq. (4.8) is satisfied when the determinant of matrix \([G]\) vanishes. The characteristic equation for a plate in vacuum (with given wavenumber \( k \), angular frequency \( \omega \), bulk velocities \( c_L \) and \( c_T \), and plate thickness \( h \)) can thus be written as

\[
\det(G(\omega, k, c_L, c_T, h)) = 0.
\] (4.9)

The roots of this characteristic (or dispersion) equation provide the dispersion relations for the given structure, and can be solved numerically [87, 59, 80].

The technique described above is known as the global matrix method. Though not as elegant as the classical solution for Lamb waves [50, 106, 32], it is powerful as the global matrix \([G]\) can easily be extended to different multilayer plate and tube structures. This is a useful property, for instance, if attempting to model the coupling effects of a soft (e.g. liquid) overlayer on top of bone or bone phantoms (see section 4.2).

Classically, the solutions of Eq. (4.3) are sought in forms [32]

\[
\phi = f(y)e^{i(kx-\omega t)},
\]

\[
\psi = ih(y)e^{i(kx-\omega t)},
\] (4.10)

where \( f(y) = C_i \sin(K_L y) + C_4 \cos(K_L y) \) and \( h(y) = C_3 \sin(K_T y) + C_4 \cos(K_T y) \). Here the exponential term represents the propagating wave in the axial (horizontal) direction, and \( f(y) \) and \( h(y) \) standing waves in the vertical direction. The displacements, strains and stresses are obtained from Eqs. (4.2), (4.6) and (4.5), and requiring the traction-free boundary conditions \( \sigma_{yy} = \sigma_{yz} = 0 \) at the free plate surfaces \( y = \pm h/2 \), for convenience) consequently yields the classical Rayleigh-Lamb frequency equation

\[
\tan(2K_L h) + \frac{4K_L K_T k^2}{(k^2 - K_T^2)^2} \left[ \frac{\tan(2K_T h)}{4K_L K_T k^2} \right] \pm 1 = 0.
\] (4.11)

This equation divides in two parts that correspond to axially symmetric modes (+1) and antisymmetric modes (-1). The dispersion relations of Eq. (4.11) are identical with those of Eq. (4.8), and must also be solved numerically.

### 4.2 Fluid-solid bilayer

The purpose of developing a model for Lamb waves in a fluid-solid bilayer was to explain the effect of soft tissue on top of the bone. In this model the liquid on top of a solid plate played the role of soft tissue.

The problem of a fluid-solid bilayer has been discussed comprehensively e.g. by Yapura and Kinra [111]. At an interface between solid and fluid the energy of guided waves leaks from solid to fluid in the form of leaky waves. The leaky waves, however, are reflected back at the top boundary of the thin fluid overlayer and propagate back to the solid substrate. As a consequence the guided waves propagate, not in the fluid or solid layer alone, but in the whole bilayer structure. This coupling affects strongly the dispersion characteristics of the guided wave modes. As this kind of coupling is expected
when there is a layer of soft tissue on top of bone (in vivo measurements), a bilayer model is needed in the analysis of measurement results.

Yapura and Kinra [111] developed a bilayer counterpart to Eq. (4.11) using the classical approach. In the following, however, the partial wave formalism will be used to extend the global matrix of the solid plate (Eq. 4.8) into the fluid-solid bilayer case [87].

Fig. 4.2. Geometry of the fluid-solid bilayer plate problem. Lower-case \( k_{L,T,F} \) are respectively the wave numbers of the longitudinal, shear and fluid partial waves, capital \( K_{L,T,F} \) are the corresponding vertical wave numbers, and \( k \) is the wave number of the guided wave.

The ideal fluid can be treated similarly than the elastic solid, except that fluid only sustains longitudinal waves. As in the solid we had four partial waves, the fluid overlayer increases the number of partial waves by two (Fig 4.2).

The wave equation for the fluid is given by

$$
\left( \nabla^2 - \frac{1}{(c_F)^2} \frac{\partial^2}{\partial t^2} \right) \phi_F = 0,
$$

where \( \phi_F \) is the scalar potential, \( c_F = \lambda_F/\rho_F \) is the bulk velocity, and \( \lambda_F \) and \( \rho_F \) are respectively the bulk modulus and density of the fluid. The scalar potential \( \phi_F \) can be expressed analogously to Eq. (4.4a), when replacing the sub-index \( L \) with \( F \). The vector potential \( \psi_F = 0 \). The corresponding displacements \( u_{iF} \), strains \( \varepsilon_{ijF} \) and stresses \( \sigma_{ijF} \) can be obtained from Eqs. (4.2), (4.6) and (4.5).
The six boundary conditions that must be satisfied are

\[\begin{align*}
\sigma_{yF} &\Big|_{y=0} = 0 \\
u_y &\Big|_{y=a} = u_y \Big|_{y=a} \\
\sigma_{yF} &\Big|_{y=a} = \sigma_{yF} \Big|_{y=a} \\
\sigma_x &\Big|_{y=a} = 0 \\
\sigma_y &\Big|_{y=a+h} = 0 \\
\sigma_y &\Big|_{y=a+h} = 0.
\end{align*}\] (4.13)

These boundary conditions yield six boundary condition equations that can be expressed in the matrix form

\[ [G] \{C\} = 0, \] (4.14)

where \([G]\) is the global matrix and \(\{C\}\) the vector of six unknowns \(C_i, i = 1, \ldots, 6\). The elements of the matrix \([G]\) are given by

\[
\begin{align*}
G_{11} &= -\lambda_F k_F^2 & G_{41} &= 0 \\
G_{12} &= -\lambda_F k_F^2 & G_{42} &= 0 \\
G_{13} &= 0 & G_{43} &= -2\mu k_F e^{iK_x a} \\
G_{14} &= 0 & G_{44} &= 2\mu k_F e^{-iK_x a} \\
G_{15} &= 0 & G_{45} &= \mu(K_T^2 - k^2) e^{iK_T a} \\
G_{16} &= 0 & G_{46} &= \mu(K_T^2 - k^2) e^{-iK_T a} \\
G_{21} &= K_F e^{iK_x a} & G_{51} &= 0 \\
G_{22} &= -K_F e^{-iK_x a} & G_{52} &= 0 \\
G_{23} &= -K_L e^{iK_x a} & G_{53} &= (\lambda k_F^2 + 2\mu k_L^2) e^{iK_x (a+h)} \\
G_{24} &= K_L e^{-iK_x a} & G_{54} &= (\lambda k_F^2 + 2\mu k_L^2) e^{-iK_x (a+h)} \\
G_{25} &= -ke^{iK_T a} & G_{55} &= 2\mu k_F e^{iK_T (a+h)} \\
G_{26} &= -ke^{-iK_T a} & G_{56} &= -2\mu k_F e^{-iK_T (a+h)} \\
G_{31} &= \lambda_F k_F^2 e^{iK_x a} & G_{61} &= 0 \\
G_{32} &= \lambda_F k_F^2 e^{-iK_x a} & G_{62} &= 0 \\
G_{33} &= -(\lambda k_F^2 + 2\mu k_L^2) e^{iK_x a} & G_{63} &= 2\mu k_L e^{iK_x (a+h)} \\
G_{34} &= -(\lambda k_F^2 + 2\mu k_L^2) e^{-iK_x a} & G_{64} &= -2\mu k_L e^{-iK_x (a+h)} \\
G_{35} &= -2\mu k_F e^{iK_T a} & G_{65} &= -\mu(K_T^2 - k^2) e^{iK_T (a+h)} \\
G_{36} &= 2\mu k_F e^{-iK_T a} & G_{66} &= -\mu(K_T^2 - k^2) e^{-iK_T (a+h)}.
\end{align*}\] (4.15)

Equation (4.14) is satisfied when the determinant of the global matrix \([G]\) vanishes. The dispersion equation for the fluid-solid bilayer can thus be written as
\[
\text{det}(G(\omega,k,c_F,c_L,c_T,a,h,\rho_F,\rho)) = 0.
\]  
(4.16)

where \(c_L\) and \(c_T\) are respectively the bulk longitudinal and shear velocities, \(\rho\) the density, \(h\) the thickness of the solid substrate, \(c_F\) the bulk velocity, \(\rho_F\) the density and \(a\) the thickness of the fluid overlayer. The roots of Eq. (4.16) must be solved numerically.

### 4.3 Effect of anisotropy

The anisotropy of cortical bone has been studied by several researchers and experimental results for the anisotropy of the elastic constants have been reported [5, 39, 81]. Long bones can be considered transversely isotropic or orthotropic. In addition, the effect of anisotropy on the propagation of guided waves is well known e.g. in non-destructive testing of composite laminates [87, 80, 69, 70, 34]. However, the incorporation of anisotropy in the guided wave model of bone is as yet unexplored.

This study did not include an extensive consideration of bone anisotropy. We, however, briefly comment here, how to incorporate anisotropy in the Lamb wave theory.

The fundamental difference between the treatment of wave propagation in an isotropic and an anisotropic medium is that in the anisotropic case the governing equations of motion cannot be expressed as two simple equations, as Eqs. (4.3), by substituting the displacements \(u_i\) to the equations of motion using the Helmholtz decomposition, Eq. (4.2). As it is not convenient to use this so-called method of potentials (Helmholtz decomposition is a function of the scalar and vector potential) for the anisotropic materials, a more general solution is often considered [87].

For zero body forces, the propagation of elastic waves in anisotropic media is governed by the equation [87]

\[
C_{ijkl} \frac{\partial^2 u_k}{\partial x_j \partial x_l} = \rho \frac{\partial^2 u_i}{\partial t^2},
\]  
(4.17)

where \(C_{ijkl}\) is the elastic tensor, which defines the elastic constants and the anisotropy for the medium. A single guided wave mode in an anisotropic plate is composed of six partial waves (instead of four for an isotropic plate), whose displacements \(u_i\) can be expressed as

\[
u_i = \alpha_i \exp[i(k(z + l_y y)\exp[-i\alpha]],
\]  
(4.18)

where the \(\alpha_i\) are the amplitudes and \(l_y = k_y/k_z\) is the ratio of vertical to axial wave number. Each of these partial waves satisfies the homogeneous Eq. (4.17), and the substitution of Eq. (4.18) into Eq. (4.17) allows to determine the \(l_y^{(n)}\) for each partial wave modes \(n = 1, 2, ..., 6\). Requiring traction-free boundary conditions \(\sigma_{xy} = \sigma_{xz} = \sigma_{yx} \equiv 0\) at the upper and lower boundaries of the plate, then finally yields the characteristic dispersion equation for an anisotropic plate [87].
4.4 Effect of tubular shape

The problem of guided waves in tubes has been a topic of considerable interest in non-destructive testing [112, 64, 96, 107, 108, 80, 18, 47, 4, 67, 34], but no extensive studies have been made considering the bone application.

Fig. 4.3. Geometry of the free tube problem, \( a \) is the inner and \( b \) the outer radius.

The exact solutions to the axially propagating guided waves in hollow traction-free tubes were first published by Gazis [29], and followed e.g. by Graff [32], Pavlakovic [80] and Rose [87]. In tubes the guided waves must be modelled in three dimensions, whereas two-dimensional modelling was sufficient for an isotropic plate. It is convenient to consider the tube problem in cylindrical coordinates \( r, \theta \) and \( z \) (Fig 4.3).

The traction-free boundary conditions are

\[
\sigma_{rr} = \sigma_{r\theta} = \sigma_{rz} = 0 \quad \text{at} \quad r = a, \quad \text{and} \quad r = b.
\] (4.19)

The assumed radial, circumferential and axial displacement components can respectively be given by

\[
u_r = U_r(r) \cos n \theta \cos(\alpha z + k z),
\]

\[
u_\theta = U_\theta(r) \sin n \theta \cos(\alpha z + k z),
\]

\[
u_z = U_z(r) \cos n \theta \sin(\alpha z + k z),
\]

where \( n = 0, 1, 2, 3, \ldots \) is the circumferential order, and \( U_r, U_\theta \) and \( U_z \) are the corresponding displacement amplitudes composed of Bessel and modified Bessel functions.

When considering the axial transmission, i.e. wave propagation along the long axis of the tube, the guided waves modes can be divided into three classes [112, 96]:

- longitudinal modes \( L(0, m) \) (axisymmetric modes),
- torsional modes \( T(0, m) \) (axisymmetric modes),
- flexural modes \( F(n, m) \) (non-axisymmetric modes).

Here \( n = 1, 2, 3, \ldots \) is the circumferential order and \( m = 1, 2, 3, \ldots \) is the number of mode [87]. The counterpart of the fundamental antisymmetric plate mode (A0), which we have
mostly been interested in regarding the bone application, is the fundamental flexural tube mode \( F(1,1) \) (hereafter referred to as \( F_{11} \)).

The dispersion equation for the hollow traction-free tube can be expressed as

\[
\det([G]) = 0,
\]

where \([G]\) is a six-by-six global matrix. The first three rows of the matrix elements are [87]:

\[
\begin{align*}
G_{11} &= [2n(n-1) - (\beta^2 - k^2)a^2]Z_n(\alpha a) + 2\gamma_1 \alpha a Z_{n+1}(\alpha a), \\
G_{12} &= 2k\beta a^2 Z_n(\beta a) - 2k a(n+1) Z_{n+1}(\beta a), \\
G_{13} &= -2n(n-1)Z_n(\beta a) + 2\gamma_2 n \beta a Z_{n+1}(\beta a), \\
G_{14} &= [2n(n-1) - (\beta^2 - k^2)a^2]W_n(\alpha a) + 2\alpha a W_{n+1}(\alpha a), \\
G_{15} &= 2\gamma_1 k \beta a^2 W_n(\beta a) - 2k a(n+1)W_{n+1}(\beta a), \\
G_{16} &= -2n(n-1)W_n(\beta a) + 2n \beta a W_{n+1}(\beta a), \\
G_{21} &= 2n(n-1)Z_n(\alpha a) - 2\gamma_1 n \alpha a Z_{n+1}(\alpha a), \\
G_{22} &= -k\beta a^2 Z_n(\beta a) + 2k a(n+1) Z_{n+1}(\beta a), \\
G_{23} &= -[2n(n-1) - \beta^2 a^2]Z_n(\beta a) - 2\gamma_2 \beta a Z_{n+1}(\beta a), \\
G_{24} &= 2n(n-1)W_n(\alpha a) - 2n \alpha a W_{n+1}(\alpha a), \\
G_{25} &= -\gamma_1 k \beta a^2 W_n(\beta a) + 2k a(n+1)W_{n+1}(\beta a), \\
G_{26} &= -[2n(n-1) - \beta^2 a^2]W_n(\beta a) - 2\beta a W_{n+1}(\beta a), \\
G_{31} &= -2n k a Z_n(\alpha a) + 2\gamma_1 k a a^2 Z_{n+1}(\alpha a), \\
G_{32} &= -n \beta a Z_n(\beta a) + (\beta^2 - k^2)a^2 Z_{n+1}(\beta a), \\
G_{33} &= n k a Z_n(\beta a), \\
G_{34} &= -2n k a W_n(\alpha a) + 2k a a^2 W_{n+1}(\alpha a), \\
G_{35} &= -\gamma_1 n \beta a W_n(\beta a) + (\beta^2 - k^2)a^2 W_{n+1}(\beta a), \\
G_{36} &= n k a W_n(\beta a),
\end{align*}
\]

where \( Z_n \) and \( W_n \) represent incoming and outgoing Bessel functions, \( k \) is the axial wavenumber, \( \mu \) one of the Lamé constants, \( \alpha^2 = \omega^2/c_L^2 - k^2 \), \( \beta^2 = \omega^2/c_T^2 - k^2 \), \( \alpha = (|\alpha^2|)^{\frac{1}{2}} \), and \( \beta = (|\beta^2|)^{\frac{1}{2}} \). The remaining matrix elements, \( G_{41} \) to \( G_{66} \), are obtained from elements \( G_{11} \) to \( G_{36} \) by replacing \( a \) with \( b \) in Eq. (4.22). The proper criteria for choosing the Bessel functions can be found in Table 4.1. The incoming wave \( Z_0 \) can be substituted by the Bessel function \( J_n \) or modified Bessel function \( I_n \), and the outgoing wave \( W_n \) by the Bessel function \( Y_n \) or modified Bessel function \( K_n \). Parameters \( \gamma_1 \) and \( \gamma_2 \) account for differences in the recurrence relationships of different Bessel functions (Table 4.1).

The roots of Eq. (4.21) yield the dispersion relations of a free tube and they must be solved numerically. The principle of a numerical solution routine is described in Section 4.5.
4.5 Implementation of numerical solution

The dispersion equations of guided waves, such as (Eq. 4.9), cannot be solved analytically but a numerical solution must be used. In order to find a point on a dispersion curve, a root of the characteristic equation (Eq. 4.9) must be found. A root corresponds to a point where the determinant of the complex-valued global matrix $[G]$ is zero. The coefficients of matrix $[G]$ depend on the geometry of the system (e.g. plate thickness $h$), material properties (e.g. $c_L$ and $c_T$), frequency $f$, real wave number $k$ and attenuation coefficient $\alpha$.

The latter three, $f$, $k$ and $\alpha$, must be varied in order to find valid roots. If the materials are elastic and the waveguide is considered as free in the vacuum, as it was the case in this study, then there is no way for energy to leave the system and the attenuation will be zero. This simplifies the root search as the roots will be real. In the case when attenuation is involved, the roots will be complex and a more complicated two-dimensional root search routine is required. The imaginary part of the complex wave number corresponds to the attenuation coefficient $\alpha$.

Figure 4.4 illustrates one example of a surface corresponding to the magnitude of $\text{det}([G])$ drawn in logarithmic absolute scale. The minima observed in this surface correspond to the roots $(c_p, f)$ of the dispersion equation, and they determine the trajectories of the dispersion curves. The phase velocities $c_p$ can be obtained from the wave numbers by $c_p = 2\pi f / k$, and it is a matter of choice whether to consider the problem in terms of $c_p$ or $k$.

An efficient method used for tracing the trajectories of the dispersion curves was adopted from Lowe [59] and Pavlakovic [80]. The procedure was started with a frequency sweep, followed by curve tracing routines. The frequency sweep sought for the minima $f$ of $\text{abs}([G])$ (Fig. 4.1) for given $c_p$ or $k$, and then the exact $f$ were determined using the Newton-Raphson algorithm. The points obtained from the frequency sweep were used as the starting points in tracing the individual curves. In the curve tracing routine, the starting point was used as the first initial guess, and as the number of obtained roots increased, linear or quadratic extrapolation was used for predicting the next points that fall on the
trajectory of the sought dispersion curve. The use of extrapolation made this process efficient and robust, increasing the precision of the initial guess.

The curve trace yielded the dispersion curves in terms of $f$, $k$, and $c_p$. The corresponding group velocities were obtained by $c_g = 2\pi df / dk$.

Some examples of the dispersion curves for plate, fluid-solid bilayer and tube structures are shown in Figure 4.5. The curves were computed using parameters similar to those of cortical bone.

![Fig. 4.4. The magnitude of the determinant of the global matrix $[G]$ illustrated in logarithmic absolute scale. The minima of the surface correspond to the roots of the dispersion equation and determine the dispersion curves.](image)
Fig. 4.5. Phase and group velocity dispersion curves respectively for a), b) a free isotropic plate, c), d) a fluid-solid bilayer and e), f) a free hollow tube. Material properties were $c_L = 4000$ m/s, $c_T = 1800$ m/s, $c_F = 1500$ m/s, $\rho = 2.0$ g/cm$^3$, $\rho_f = 1.0$ g/cm$^3$. The fluid to solid thickness ratio was 0.5 (c,d) and the wall thickness to outer radius ratio was 0.4 (e,f).
Chapter 5

Experimental and numerical methods

5.1 Device

Experimental measurements were performed using an axial pulse transmission scanner with a pair of unfocussed low-frequency contact transducers. The transducer diameter was approximately 5 mm. The transducers were orientated perpendicularly to the surface of the object to be measured and ultrasonic gel was applied as a coupling agent. The vertical and lateral position of each transducer could be adjusted manually and the axial position (scanning direction) using computer controlled stepper motors. The contact pressures between the transducers and the specimen were monitored using two precision load cells (Sensotec Model 31). During the scan, the transmitter was kept fixed and the receiver was moved away from the transmitter in steps (Fig 5.1). Typically the measurement was made at 40 transmitter to receiver distances $r$ ranging from 20 to 50 mm corresponding to step size of 0.75 mm. The receiving transducer was, in effect, dragged along the surface of the object to be measured with acoustic coupling maintained by the presence of ultrasonic gel and a near constant contact pressure. Lateral position was not adjusted during scans. The transmitter was excited by a square wave pulser (Panametrics 5077PR) yielding a signal bandwidth of 50 to 350 kHz (-20dB). The received signal was amplified and then digitised with a PC-based digital oscilloscope (National Instruments 5102) sampling at 10 MHz and averaging over, typically, 100 acquisitions. The received distance ($r$) - time ($t$) signal matrix was then visualised as a so-called $(r,t)$ diagram (Fig 5.2), in which the intensity was represented conveniently using an absolute-valued grey scale.
Fig. 5.1. a) Schematic diagram of the axial scanner device, and photographs of b) an in vitro and c) in vivo measurement.

Fig. 5.2. A typical \((r,t)\) diagram (human radius in vitro).
5.2 Methods of analysis

In the \((r,t)\) diagrams two distinct wave modes were consistently observed (Fig. 5.2). The first of these (Wave 1) was a fast first arriving signal (FAS) and the second (Wave 2) was slower and corresponded to the fundamental antisymmetric Lamb mode (A0). The velocities of Wave 1 \(v_1\) and Wave 2 \(v_2\) were determined in the distance-time plane. In addition, two-dimensional spectral analysis was used for a more precise determination of \(v_2\).

5.2.1 Distance-time analysis

Determination of the velocity in the distance-time plane consisted of two phases, a) detection of the time-of-arrival \(t_i\) at the given distances \(r_i\) and b) linear regression in the detected points \((r_i,t_i)\). This approach eliminated the delay due to overlaying soft tissue as discussed in Chapter 3.

The time-of-arrival corresponding to Wave 1 were determined using a 25% threshold of the amplitude of the first detectable peak (Fig 3.1). A robust linear regression based on the least median of squares was then used for determining the velocity. The reason for using the robust regression was that often some failure points were involved among the determined time-of-arrivals, and this robust regression, giving lower weights for these failure points, determined the velocity more reliably than the ordinary least-mean-of-squares algorithm.

Determining the time-of-arrival for Wave 2 was considerably more difficult than for Wave 1, as Wave 2 was dispersive and interfered by other wave modes. Therefore, different approaches for analysing Wave 2 were developed. The time-of-arrival were always determined according to the maxima of the corresponding wavefront. Sometimes Wave 2 was strong enough and the time-of-arrivals could be read from the recorded raw \((r,t)\) diagram. The \((r,t)\) matrix could also be processed using strong band-pass filtering, which enabled the measurement of dispersion, i.e. to determine the velocity at specific frequencies. When Wave 2 was weak compared to interfering waves, then specific group-velocity filtering and spectrum analysis methods were needed for a proper determination of \(v_2\).

Where \(v_1\) or \(v_2\) are given without indication of the corresponding frequency, the frequency range from \(f = 250\) to 300 kHz was used for \(v_1\) and that from \(f = 100\) to 150 kHz for \(v_2\).

5.2.2 Spectral analysis

Two-dimensional fast Fourier transform (2D-FFT) has been used by several researchers for analysing distance-time matrices similar to the ones measured with the described low-frequency axial ultrasound scanner [1, 93, 54]. The 2D-FFT method was developed specifically for analysing signals which consist of overlapping wave modes that cannot be separated in the time history of the signal. The FFT separates such wave modes in terms of frequency and wavenumber. In the wavenumber-frequency plane the intensity maxima correspond to propagating wave modes, and if guided waves propagate, the locations of these intensity maxima are supposed to correspond to trajectories of guided waves (Fig. 5.3). Thus, the two-dimensional spectral analysis allows direct comparison between
experimental results and theory. Moreover, determination of the velocities and dispersion of the identified wave modes is as well possible.

The 2D-FFT was based on the two-dimensional Fourier transform, as given by [1]

\[
V(k, f) = \int_{-\infty}^{+\infty} \int_{-\infty}^{+\infty} u(r, t) e^{-i(kr+\omega t)} dr dt ,
\]

(5.1)

where

\[
u(r, t) = A(\omega) e^{i(\alpha r - \theta)}
\]

(5.2)
is the displacement on the surface of the structure (assuming that a harmonic wave is propagating), \(A(\omega)\) is a frequency-dependent amplitude constant, \(\omega = 2\pi f\) is the angular frequency, \(k\) is the wave number and \(\theta\) the phase. The measured \((r, t)\) matrix represented the displacement \(u(r, t)\).

The 2D-FFT made for the \((r, t)\) matrix was often expressed as functions of phase velocity and frequency. The transformation from wavenumber \(k\) to phase velocity \(c_p\) was made point-by-point as \(c_p = 2\pi f / k\) (Ref. V) (Fig. 5.3).

Fig. 5.3. 2D-FFT shows a ridge of intensity maxima that corresponds to a propagating wave mode. This result is for a free aluminium plate.

### 5.2.3 Inversion scheme

Inversion schemes have been used successfully for analysing guided wave data in different applications of non-destructive testing (e.g. Karim et al [44]) and also in one bone measurement study by Lefebvre et al [54]. The purpose of an inversion scheme is to determine one or more properties of the medium based on the measured guided wave ultrasound data. Karim et al introduced a method in which the dispersion equation of the given structure was minimised in terms of the elastic modulus in a large number of experimentally measured phase-velocity-frequency points. Lefebvre utilised this method using plate theory for axial transmission measurements of bovine bones, and determined
estimations for the Young’s modulus. These approaches, however, require a broad-band multi-mode guided wave measurement.

We developed a fairly different approach because we, so far, only measured one genuine guided wave mode (A0) and a reliable identification of this mode required the use of selective time domain filtering. In addition, our essential interest here was to clarify how well the measured A0 Lamb mode could reflect the thickness of a plate or a cortical wall. Therefore we did not attempt to determine the Young’s modulus, as yet, but made the inversion in terms of thickness $h$ with given material properties (e.g. $c_L$ and $c_T$).

While the time-domain (or group-velocity) filtering included adjustable input parameters, the inversion scheme was actually considered as a theory based signal processing feedback loop (Fig. 5.4). The preliminary input parameters were material properties (e.g. $c_L$ and $c_T$), thickness $h$ and time delay $t_d$. The output parameters were $(v_e^i, f_i)$, $h$ and $t_d$, where $v_e^i$ were the experimental phase velocities at corresponding frequencies $f_i$; and $h$ and $t_d$ the fitting parameters. The fitting was made by means of the minimisation

$$\min \left( \sum_{i=1}^{N} (v_e^i(f_i, t_d) - c_p(f_i, h))^2 \right),$$

where $c_p(f_i, h)$ were the computed theoretical phase velocities. The approach can be applied either using an assumed constant $c_g$ value or allowing to $c_g$ to vary as a function of frequency. In general, a constant $c_g$ value was used. The constant $c_g$ was typically determined according to the average or maximum level of the corresponding group velocity curve.

Our inversion scheme was thus tightly connected with the identification of an experimental wave mode, yielding more reliable phase-velocity trajectory $(v_e^i, f_i)$ than the 2D-FFT alone. Therefore we called this process also as the selective 2D-FFT (Ref. V).

![Fig. 5.4. Principle of the inversion scheme and signal processing feedback loop.](image-url)
5.3 Finite-element simulation

Analytical modelling of guided waves is possible only in simple uniform sample geometries, such as plates and tubes. Thus the effect of some relevant bone properties, such as a non-symmetrical shape, porosity and defects, must be modelled using numerical simulation of wave propagation. The methods of numerical modelling date back to the 1940’s, though the more active interest in the utilisation of these methods has arisen together with the rapid development of computers after the 1960’s [113]. There are two principal approaches of numerical modelling, finite-difference and finite-element method (FEM) [1, 24]. Since then, it has been shown that FEM is more effective and accurate in terms of modelling guided waves, as the free boundaries are better accommodated with this method [1, 66, 93]. Also, the axial propagation of the lateral wave in cortical bone has been modelled using a two-dimensional [11, 72] (Ref. I) and three-dimensional finite-difference method [12]. In contrast with some previous results, the finite-difference method (more specifically the so-called Virieux difference method) was found as to be the most accurate approach for simulating the fluid-solid interaction in immersed bone samples [12]. However, it must be noted that comparison of these two approaches is not as simple, as plenty of different modifications of the finite-difference and finite-element method have been developed for the needs of various applications [24].

Several commercial general-purpose programs are available for numerical modelling, such as ABAQUS/Explicit (ABAQUS Inc., Warwick, Rhode Island, USA) [93], and Wave2000 Pro (CyberLogic Inc., New York, USA). Sometimes these programs may, however, lack features that are required for specific wave propagation problems. It may thus be more flexible to use a custom made, specialised wave propagation code.

Our purpose was to simulate the low-frequency ultrasonic guided wave measurements in simple two- and three-dimensional structures in order to validate the measurement principle against analytical theory, and to model the properties of bone that affect the measurement but are not possible to model analytically. We started the simulations using Wave2000 Pro (Ref. I), based on the finite difference method, but encountered some difficulties in observing guided waves. Therefore, we began to seek custom-made software to handle the two-dimensional simulation of guided waves in a traction-free isotropic plate. This software was developed in collaboration with our group by Erkki Heikkola in a related AKTINUM-project at VTT Processes (Jyväskylä, Finland) and Numerola Oy (Jyväskylä, Finland).

The finite-element method was used to simulate the vibration of an isotropic plate. The plate, denoted by $\Omega$, is assumed to be homogeneous and to have uniform thickness $h$ (see Fig. 5.5). Simulations were based on the two-dimensional linear elasticity equation with the plane strain assumption. In this case, the displacement $\vec{u} = (u_1, u_2)^T$ is governed by the system of equations

$$\rho \frac{\partial^2 \vec{u}}{\partial t^2} - \mu \Delta \vec{u} - (\lambda + \mu) \nabla (\nabla \cdot \vec{u}) = 0,$$

(5.4)

where $\lambda$ and $\mu$ are the Lamé constants and $\rho$ the density of the material. These parameters are connected to the pressure and shear (longitudinal and transverse) wave velocities such that
The stress tensor $\tau(\mathbf{u})$ of the elastic medium is given by

$$\tau_{ij} = \lambda \delta_{ij} (e_{11} + e_{22}) + 2\mu e_{ij}, \quad i, j = 1, 2,$$

where $\delta_{ij}$ is the Kronecker symbol and $e_{ij}$ is the linear strain tensor,

$$\delta_{ij} = \begin{cases} 1, & i = j, \\ 0, & i \neq j, \end{cases} \quad e_{ij} = \frac{1}{2} \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right).$$

The condition on the boundaries of the plate is of the form $\tau(\mathbf{u})\mathbf{n} = \mathbf{g}$, where $\mathbf{n}$ is the outward unit normal to the boundary. The right-hand side of the boundary condition is zero on all other boundaries except the transducer interface $\Gamma_t$. This case corresponds to the interface of a solid with air. On the transducer interface the second component of vector $\mathbf{g}$ is a time-dependent signal corresponding to vibration of the transducer in the direction perpendicular to the plate. This signal initiates the vibration of the plate, and the frequency band of the signal is bounded to the interval 100-300 kHz.

The signal in the receiver at time $t$ is measured by computing the following integral over the receiver interface $\Gamma_r$:

$$\int_{\Gamma_r} [\mathbf{u}(t) \cdot \mathbf{n}]^2 \, ds.$$  \hfill (5.8)

Attenuation of the vibration is modelled by adding mass proportional damping to Eq. (5.4). This assumption leads to the system of equations

$$\rho \frac{\partial^2 \mathbf{u}}{\partial t^2} + 2\alpha \rho \frac{\partial \mathbf{u}}{\partial t} - \mu \Delta \mathbf{u} - (\lambda + \mu) \nabla (\nabla \cdot \mathbf{u}) = 0,$$

where the attenuation parameter $\alpha > 0$ determines the rate of decay with respect to mass and velocity deformation.

The finite-element method requires the following formulation of the elasticity equation. Find the displacement field $\mathbf{u}$ such that

$$\int_{\Omega} \rho \frac{\partial^2 \mathbf{u}}{\partial t^2} \cdot \mathbf{v} \, dx + 2\alpha \int_{\Omega} \rho \frac{\partial \mathbf{u}}{\partial t} \cdot \mathbf{v} \, dx + \int_{\Omega} \varepsilon(\mathbf{u}) : \varepsilon(\mathbf{v}) \, dx = \int_{\Gamma_r} \mathbf{g} \cdot \mathbf{v} \, ds.$$  \hfill (5.10)
for all displacement fields $\vec{v}$. This equation holds at all times $t$, and time-dependent
simulation is started from the initial conditions $\vec{u}(0) = 0$ and $\frac{\partial \vec{u}(0)}{\partial t} = 0$.

Spatial discretisation with the finite-element method requires a triangular mesh for
the plate. The number of nodes in the mesh is denoted by $N$. Discretisation leads to the
semi-discrete equations of motion
\[ M \frac{\partial^2 U}{\partial t^2} + 2\alpha M \frac{\partial U}{\partial t} + K U = G, \]  
where the $2N \times 2N$ -matrices $M$ and $K$ are the finite-element mass and stiffness matrices.
The vector $G$ corresponds to the source signal $\vec{g}$ and vector $U$ contains the nodal values of
the displacement components.

The standard central-difference method is used to discretise the equation with
respect to time. If we denote the discretisation time step by $\Delta t$, and the solution $U$ at time
$t_i = i\Delta t$ by $U_i$, then the equation for computing the solution $U_{i+1}$ from the two previous
time steps is given by
\[ (1 + \Delta t \alpha)MU_{i+1} = M(2U_i - U_{i-1}) + \Delta t \alpha MU_{i-1} - \Delta t^2 KU_i + \Delta t^2 G_i. \]  
Each time step involves the solution of this linear system, which is obtained by Cholesky
factorisation of the mass matrix $M$. The central-difference method is second-order
accurate with respect to time, but it is only conditionally stable. In other words, the time
step $\Delta t$ needs to be smaller than a given threshold depending on the finite-element mesh
density and the wave velocity. If the mesh is refined, also the time step needs to be
reduced to keep the time iteration stable.
Chapter 6

Results

6.1 Validation of the measurement principle
(2D simulations for plates)

A two-dimensional finite element approach was used to simulate wave propagation in a free plate. Source and receiver geometry corresponded to that of the experimental axial transmission system, and the frequency range of the short transmitted pulse was 50-350 kHz (-20 dB). The objective of these simulations was to investigate the nature of the propagating signals in the proposed low-frequency axial scanning method. More specifically, the aims were to measure the velocities of the wave modes present, assess their dispersion and relation to plate thickness, and to compare the simulated results to those expected for Lamb waves in plates.

Material properties corresponding approximately to those of an isotropic bone (Young’s modulus $E = 23.8$ GPa, Poisson ratio $\nu = 0.3$ and density $\rho = 2.0$ g/cm$^3$) were chosen as the simulation parameters. According to Eqs. (3.1) and (3.2), the corresponding bulk velocities were $c_L \cong 4000$ m/s and $c_T \cong 2140$ m/s.

Figure 6.1 shows $(r,t)$ diagrams for simulations in plates with thickness ranging from 1.0 to 4.0 mm. The fast Wave 1 (First Arriving Signal or FAS) and a slower Wave 2 can be identified in all diagrams. Wave 1 had a lower intensity than that of Wave 2. The velocity $v_1$ of Wave 1 ranged from 3616 to 4006 m/s for thicknesses $h = 1 - 10$ mm, respectively (Fig 6.2). The mean frequency of Wave 1 was estimated roughly as 300 kHz by looking at the pulse lengths of the first arriving signal. Wave 2 was strongly dispersive in a thin plate, the higher frequency components arriving first and the lower frequency ones arriving later, considerably delayed. In a thick plate dispersion was much weaker, as expected. The velocity $v_2$ (100 kHz) ranged from 790 to 1800 m/s for $h = 1 - 10$ mm, respectively (Fig 6.2).
Fig. 6.1. Effect of plate thickness $h$ on the wave modes seen in the (r,t) diagrams. FEM simulation results for plates with isotropic material distribution.
Fig. 6.2. FEM simulation results for the phase velocities of Wave 1, Wave 2 and fundamental Lamb modes as functions of the thickness to wavelength ratio.

Velocity $v_1$ was consistent with that of the lateral wave propagating at the bulk velocity when thickness to wavelength ratio $(h/\lambda)$ was greater than 0.5. For $h/\lambda < 0.5$, $v_1$ decreased towards the phase velocity of an S0 Lamb mode. For a 1 mm plate $v_1 = 3616$ m/s, corresponding exactly to the saturation level $(f \rightarrow 0) c_{S0} = (E/(\rho(1-\nu^2)))^{1/2} \cong 3616$ m/s of the S0 mode in the thin plate and low frequency limits [32]. Velocity $v_2$ was fairly consistent with the phase velocity of an A0 Lamb mode throughout the simulated thickness range.

Using 2D-FFT within the frequency range $f = 50 - 350$ kHz, clear intensity maxima curves were obtained (Fig 6.3). The intensity maxima $(v_2^i, f_i)$ (diamond markers) were in excellent agreement with the computed phase velocities of the A0 Lamb mode (solid lines, computed for the same material parameters and plate thickness as used in the simulation).

Fig. 6.3. The locus of the intensity maximum in the $(v_i, f)$ plane for FEM simulations of isotropic bone plates with thicknesses of a) $h = 1.5$ mm and b) $h = 4.0$ mm.
6.2 Validation of the measurement system (results for plates)

The low frequency axial transmission device was used to measure a range of acrylic plates in order to confirm the presence of two propagating waves, and to assess the velocity of these waves as a function of frequency and plate thickness.

Perspex acrylic \((c_L = 2730 \text{ m/s}, c_T = 1325 \text{ m/s} \text{ and } \rho = 1.186 \text{ g/cm}^3\), corresponding to Young’s modulus \(E = 5.60 \text{ GPa}\) and Poisson ratio \(\nu = 0.347\)) was chosen as the phantom material. Twelve plates with thicknesses ranging from 2 to 24 mm were measured. The plate thickness \(h\) was measured using a caliper. For each plate the ultrasound scan was repeated three times.

The \((r,t)\) diagrams for the acrylic plates were similar to those for the numerical simulations. Two wave modes, Wave 1 and Wave 2, were observed consistently (Ref. I). Wave 1 (estimated \(f = 250 \text{ kHz}\)) was consistent with the lateral wave in thick plates and it tended towards an S0 Lamb mode for \(h/\lambda < 0.5\) (Fig 6.4, cross markers). Wave 2 \((f = 100 \text{ kHz}\)) was consistent with an A0 Lamb mode for \(h/\lambda < 0.5\). However, in thick plates the observed \(v_2\) was affected by the S0 as well as the A0 mode, and the results were not clear for \(h/\lambda > 0.5\) if no selective filtering was used (Fig 6.4, dot markers). When using selective time domain filtering (or group-velocity filtering), \(v_2\) as a function of frequency followed more precisely the dispersion curve of the A0 mode also for thick plates (Fig 6.4, circle markers).

When using the selective 2D-FFT and inversion scheme within the frequency range \(f = 30 - 350 \text{ kHz}\), clear intensity maxima \((v_1^i,f_i)\) (diamond markers) were obtained for thin as well as for thicker plates (Fig 6.5). These experimental results were in a good agreement with the computed dispersion curves of A0 mode (solid lines).

![Fig. 6.4. Experimental results for acrylic plates. Velocities \(v_1, v_2\), and phase velocity of fundamental Lamb modes are shown as functions of the thickness to wavelength ratio.](image-url)
Fig. 6.5. The locus of the intensity maximum in the \((v, f)\) plane as measured for acrylic plates with thicknesses of a) \(h = 2.2\) mm, and b) \(h = 12\) mm. Diamond markers denote the measured velocity of Wave 2 as determined from the intensity maxima (white) and the solid lines show the respective phase velocities of the plate A0 mode. Selective 2D-FFT was used.

The inversion scheme used yielded an estimate \(h_e\) for plate thickness, which was in excellent agreement with the true plate thickness \(h\) in the thickness range 2 to 8 mm (Ref. V). For thicker plates there is less dispersion in the phase velocity in the investigated frequency range, and therefore thickness estimation was not as accurate as for thin plates.

### 6.3 Effect of sample geometry (results for tubes)

The objectives of this study were to clarify how a tubular shape of the sample affects the measured velocities \(v_1\) and \(v_2\), and also how reliably the wall thickness of the tube can be estimated when using plate theory in the inversion scheme.

Acrylic was again used as the phantom material. Four hollow tubes with an outer radius of \(b = 10.0\) mm and a wall thickness \(e\) ranging from 2.2 to 8.0 mm, were measured such that each ultrasound scan was repeated three times.

Fig. 6.6. The velocity of Wave 1 as measured for acrylic tubes and plates of varying thickness.
The velocity $v_1$ measured for tubes showed a similar dependence on wall thickness as that measured for plates (Fig 6.6). However, $v_1$ was about 4% higher for tubes than for plates when the thickness was less than 6 mm. When the thickness was 6 mm or greater, then the difference was not clear between the velocities for plates and tubes.

Dispersion curves for velocities $v_2$ were determined using a selective 2D-FFT assuming plate theory in the inversion scheme. When the tube-wall thickness $e$ was small compared to the outer radius of the tube $b$, then the fundamental flexural tube mode (F11) was fairly consistent with the trajectory of the A0 plate mode in the investigated frequency range (Fig 6.7). Indeed, the experimental velocities (square markers) corresponded fairly well to those of F11 (or A0) when the tube wall was thin ($e = 2.2$mm). When thickness $e$ increased with respect to $b$, then $v_2$ was higher than that of the A0 mode. Correspondingly, the phase velocity of F11 increased as well, being in satisfactory agreement with the experimental results.

![Fig. 6.7. Experimental velocities for Wave 2 as measured for hollow acrylic tubes, and the theoretical curves computed with the corresponding tube dimensions. Experimental velocities were determined using a selective 2D-FFT together with an inversion scheme based on plate theory.](image-url)
Fig. 6.8. Ultrasound thickness $h_e$ versus the actual tube-wall thickness $e$. Ultrasound thicknesses were obtained by an inversion scheme using a) a plate A0 mode (diamond markers) and b) a tube F11 mode (circle markers) when fitting the results measured for acrylic tubes.

The inversion scheme used also provided wall-thickness estimates $h_e$ (Fig 6.8). When using the plate model (A0 mode), the obtained thickness $h_e$ was in good agreement with the actual wall thickness $e$ only when $e/b$ was small ($e = 2.2 \text{ mm}$). For $e > 2.2 \text{ mm}$, $h_e > e$, and the error between $h_e$ and $e$ increased with increasing ratio $e/b$, being 60% at $e = 8 \text{ mm}$. When using the tube model (F11 mode) and constant $c_g$, the wall-thickness estimate $h_e$ agreed, with a difference of at most 10%, with the true thickness in the thickness range $e = 2.2 - 6.0 \text{ mm}$, and with a 15% difference for $e = 8.0 \text{ mm}$. Using variable $c_g$ improved the precisions of $h_e$ slightly. At this stage of method development the use of variable $c_g$ in the inversion scheme has not been optimised, however.

6.4 Effect of irregular cross-section
(results for anatomically shaped bone phantoms)

Measurements were made with the axial transmission device in phantoms with an anatomically realistic (non-spherical) cross-sectional shape in order to clarify how cross-sectional geometry affects the measured velocities $v_1$ and $v_2$, and the thickness estimate $h_e$ (using plate theory).

Polyvinyl chloride (PVC, $c_L = 2400 \text{ m/s}$, $c_T = 1060 \text{ m/s}$ and $\rho = 1.4 \text{ g/cm}^3$) was chosen as the phantom material as it was easy to manufacture in an anatomical shape. One drawback of using PVC is that its longitudinal and shear velocities are substantially lower than those in bone, and this must be remembered when interpreting results from such phantoms. Two tubular bone phantoms had a circular central hole and an outer cross-sectional profile mimicking that of the human tibia. A "thick" and "thin" phantom were manufactured, having medullary canal diameters of 15 mm and 19 mm, respectively. The cross-sectional profiles of the two phantoms are shown in Fig. 1 of Ref. III. Ten
measurement sites were marked around each phantom. At each measurement site, the thickness of the phantoms along a line normal to the surface of the inner circle was measured using a caliper (the mean value of three measurements). In the ”thick” phantom local thickness determined in this way varied from 5.2 to 13.3 mm, and in the ”thin” phantom it varied from 2.6 to 10.2 mm.

For PVC plates results corresponding to those obtained for acrylic plates were first measured for calibration purposes.

For anatomically shaped bone phantoms the dependence of $v_1$ on the local radial wall thickness was confirmed. As expected, $v_1$ decreased with the decreasing wall thickness (Figs. 2 and 3 of Ref. III). The measured $v_1$ was found to vary by 17.1% and 21.4% depending on the location of the measuring site around the ”thick” and “thin” phantom, respectively. Measured $v_1$ was strongly linearly correlated with the local thickness ($r^2 = 0.81, p<0.001$) (Fig. 3 of Ref. III).

Correspondingly, $v_2$ (at $f=100$kHz), as determined using the selective 2D-FFT and the inversion scheme (plate theory), correlated linearly with the local thickness ($r^2 = 0.76, p<0.001$). The value of $v_2$ (at $f=100$kHz) varied by 18.8% and 33.0% depending on the location of the measuring site around the ”thick” and “thin” phantom, respectively. The local wall thickness estimate $h_e$, obtained from the inversion scheme, correlated linearly with the actual local wall thickness $h$ ($r^2 = 0.78, p<0.001$), though $h_e$ was 30% lower than $h$ (p<0.001) (Fig. 6.9). The trend of this difference is contradictory with the expected difference between the plate and tube models (Figs. 6.7, 6.8), and the explanation remains, as yet, inconclusive.

![Fig. 6.9. a) Wall thickness estimates $h_e$ for the “thick” (diamond markers) and “thin” (square markers) anatomically shaped bone phantom as a function of measurement site. Corresponding local thicknesses $h$ are shown by dashed lines. b) Correlation between the ultrasound thickness $h_e$ and local wall thickness $h$ (results for two phantoms).](image-url)
6.5 Effect of overlying soft tissue (results for immersed plates)

Immersed plate was measured using the axial transmission device in order to test if immersion affects the reliability of measuring Wave 1, to test if plate model yields a satisfactory interpretation of Wave 2 in this case, and to evaluate the usefulness of the fluid-solid bilayer model so as to provide an improved interpretation of Wave 2.

Aluminium plate \( (h = 4.0\, \text{mm}, \; c_L = 5950\, \text{m/s}, \; c_T = 3120\, \text{m/s} \text{ and } \rho = 2.7\, \text{g/cm}^3 \), corresponding to Young’s modulus \( E = 68.9\, \text{GPa} \) and Poisson ratio \( \nu = 0.31 \) was chosen as the bone phantom and water \( (c_T = 1500\, \text{m/s}) \) on top of the plate played the role of soft tissue. All measurements were made underwater, in varying immersion depths of 0 to 12 mm. The thickness of the thin overlying water layer was carefully adjusted according to the area of the water tank and the volume of the new water added. Transducers were hold on top of the water, and their vertical position was controlled within 0.1 mm.

The velocity of Wave 1 was \( v_1 = 5383\, (cV = 2.5\%) \) for immersion depths \( a \leq 8 \text{ mm} \) (Fig. 6.10). For \( a > 8 \text{ mm} \), a reliable determination of \( v_1 \) was not possible. For a dry aluminium plate \( v_1 = 5533\, (cV = 1.2\%) \). The mean error when measuring \( v_1 \) for an immersed plate was thus -2.7\%. The thickness to wavelength ratio was \( h/\lambda = 4.0\, \text{mm} \cdot 300 \text{ kHz} / 5500\, \text{m/s} = 0.22 \), thus \( v_1 \) can be assumed to be lower than \( c_L = 5950\, \text{m/s} \) and slightly greater than \( c_{S0} (h,f \to 0) = (E/(\rho(1-\nu^2)))^{1/2} \approx 5313\, \text{m/s} [32] \).

Fig. 6.10. Velocities \( v_1 \) (triangle) and \( v_2 \) (diamond) as functions of overlayer thickness. The velocities of the S0 and A0 Lamb modes, computed for similar plates, are shown for comparison.
From Eq. (3.12) we recall that the overlayer must be thinner than \( a_{\text{max}} = r_{\text{min}} \left[ 1 - \left( \frac{c_F}{v_1} \right)^2 \right]^{\frac{1}{2}} \left[ 2 \left( 1 + \left( \frac{c_F}{v_1} \right) \right) \right]^{\frac{1}{2}}, \) where \( c_F \) is the sound velocity in the fluid overlayer and \( v_1 \) the signal velocity in solid. When \( r_{\text{min}} = 20 \text{ mm}, v_1 = 5500 \text{ m/s} \) and \( c_F = 1500 \text{ m/s} \), then \( a_{\text{max}} = 7.6 \text{ mm}. \) In practice, however, \( v_1 \) should be determined correctly if it is identified as the first arriving signal at least within 2/3 of the scanning range \( (r_{2/3} = 30-50 \text{ mm}) \). Thus \( r_{\text{min}} = 30 \text{ mm} \) yields \( a_{\text{max}} = 11 \text{ mm}. \)

It was not possible to measure \( v_2 \) reliably through a thin overlayer using the distance-time analysis or ordinary 2D-FFT. Only the use of the selective 2D-FFT approach yielded a satisfactory identification for Wave 2 (Ref. V). Using plate theory and constant \( c_g \) in the inversion scheme, the 2D-FFT yielded the mean velocity \( v_2 = 1600 \text{ m/s} \) \( (c_v = 14 \%) \), at \( f = 100 \text{ kHz} \) for \( a = 0 - 12 \text{ mm} \). For \( a = 0 - 4 \text{ mm}, v_2 = 1663 \text{ m/s} \) \( (c_v = 1.5 \%) \). For a dry plate \( v_2 = 1705 \text{ m/s} \) \( (c_v = 1.0 \%) \) and the computed phase velocity \( (f=100\text{kHz}) \) is \( c_{A0} = 1719 \text{ m/s}. \)

The inversion scheme (plate theory) yielded a satisfactory estimate \( h_0 \) of the plate thickness for up to \( a = 6\text{mm}. \) For larger immersion depths \( a, \) the plate thickness could not be determined using plate theory in the inversion scheme (Ref. V).

The selective 2D-FFT approach was also tested using the first wave mode (BL1) of the water-solid bilayer model. BL1 required the use of a variable \( c_g(f) \) as the group velocity changed considerably at the investigated frequencies and thicknesses. The plate \( (h = 4\text{mm}) \) was measured for immersion depths of \( a = 1, 3, \) and \( 5 \text{ mm} \), and for parameters \( a \) and \( h \) their known values were used in the selective 2D-FFT. Doing so, the experimental dispersion curves for \( v_2 \) were qualitatively consistent with those of BL1 calculated using the corresponding values of \( a \) and \( h \) (Fig 6.11). Use of bilayer theory in the inversion scheme (i.e. in the determination of \( h_0 \)) is not possible yet, but will soon become possible.


6.6 Application to real bone (in vitro)

Human radius specimens were measured using three different ultrasonic devices. The objectives were to show that Wave 1 (FAS) and Wave 2 (A0 guided wave) can be measured also in an actual bone, that the theory for plates can satisfactorily be used in the interpretation of the guided wave results, and that the theory for tubes can improve the interpretation. Another purpose was to verify that the two ultrasound velocities measured reflect bone quantities, such as bone mineral density (BMD) and cortical thickness (cTh).

In vitro measurements were made in collaboration with the Laboratoire d’Imagerie Paramétrique, Université Paris 6. Forty one (n=41) fresh human radius specimens were measured at the lateral mid-shaft (45% from the distal end). Three repeated measurements per specimen were made. The radius specimens were, in addition, measured with two other axial ultrasonometers, Omnisense (Sunlight Medical Ltd., Tel Aviv, Israel), and a bidirectional axial ultrasonometer prototype (Laboratoire d’Imagerie Paramétrique, Université Paris 6, Paris, France). Both of these devices operated at around 1 MHz frequency, being considerably higher than those used in our low-frequency axial scanner. The actual values of bone mineral density (BMD) and cortical thickness (cTh) were assessed using peripheral quantitative computed tomography (pQCT) (Norland/Stratec XCT 2000, Stratec Medizintechnik, Pforzheim, Germany).

The low-frequency Wave 1 ($v_1 = 3799 \text{ m/s} \pm 179 \text{ m/s}$) and Wave 2 ($v_2 = 1280 \text{ m/s} \pm 142 \text{ m/s}$) were both significantly slower than the FAS measured with the 1 MHz axial ultrasonometers ($p < 0.001$). Velocities $v_1$ and $v_2$ correlated significantly with cortical BMD ($r=0.40$, $p<0.01$; $r=0.67$, $p<0.001$, respectively) and cTh ($r=0.33$, $p<0.05$; $r=0.72$, $p<0.001$, respectively) (Table 3 of Ref. IV). The speed of sound (SOS) measured with the French prototype device yielded a relatively high correlation with cortical BMD ($r=0.72$, $p<0.001$) and also a weak correlation with cTh ($r=0.36$, $p<0.05$), whereas that of the Omnisense only correlated with the cortical BMD ($r=0.50$, $p<0.001$). In multivariate regression models (step-wise) $v_2$ was determined best by the combination of cTh and cortical BMD ($r^2 = 0.62$, $p<0.001$), or trabecular BMD and cortical BMD ($r^2 = 0.62$, $p<0.001$). However, all of the FAS velocities (including the low-frequency and both of the 1 MHz devices) were best determined by the cortical BMD alone. These results are described in detail in Ref. IV (note the difference in the notations of velocities).

The low-frequency measurements were also analysed using the inversion scheme and spectral analysis approach. The theoretical tube and plate models were used with $c_L = 4000 \text{ m/s}$, $c_T = 1800 \text{ m/s}$ and $\rho = 2.0 \text{ g/cm}^3$. In the tube model the outer radius $b$ was approximated using the mean radius based on the total cross-sectional area measured by pQCT, yielding $b = 6.28 \text{ mm} \pm 0.71 \text{ mm}$. The corresponding wall thickness was $e = c_{Th} = 2.53 \text{ mm} \pm 0.50 \text{ mm}$, and the thickness-to-radius ratio was $e/b = 0.40 \pm 0.07$. From the latter it can be seen that the radius bones are quite strongly tubular, justifying the need for using the tube model (see Fig 6.7).
The thickness estimate obtained from the inversion scheme, when using the tube model, was $h_e = 2.53 \text{ mm} \pm 0.67 \text{ mm}$, and it yielded a relatively high correlation with $cTh$ ($r=0.71, p<0.001$) (Fig 6.12). In comparison, when using the plate model in the inversion scheme, the thickness estimate ($h_e = 4.2 \text{ mm} \pm 1.8 \text{ mm}$) did not correspond well to the actual $cTh$, but correlation with $cTh$ ($r=0.67, p<0.001$) remained as significant.

![Graph showing thickness estimate versus actual cortical thickness](image)

**Fig. 6.12.** The thickness estimate $h_e$ (using tube model) versus actual cortical thickness $cTh$.

### 6.7 The clinical application (in vivo)

Human tibia was measured using the low-frequency axial scanner and one commercially available axial ultrasonometer (Omnisense, Sunlight Medical Ltd., Tel Aviv, Israel). The objective was to demonstrate that Wave 1 and Wave 2 can also be measured in vivo, reflecting the aspects of bone properties. Bone mineral density (BMD) and cortical bone thickness ($cTh$) were assessed using peripheral quantitative computed tomography (pQCT) (Norland/Stratec XCT 2000, Stratec Medizintechnik, Pforzheim, Germany) in the same site where the ultrasound measurements were made.

Two in vivo studies were made. In a small pilot study eight healthy normal and eight osteoporotic female volunteers were measured (Ref. I). The osteoporotic group had axial bone mineral density values, as measured using dual-energy x-ray absorptiometry, more than two standard deviations below the normal group. A more extensive study was made in a hundred and six 12-14-year-old girls (Ref. II).

The velocities of Wave 1 and Wave 2 were lower in the osteoporotic group (OP) than in healthy normal group (N) (Fig 6.13). However, a significant difference between these two groups was only obtained for Wave 2. In comparison, neither the speed of sound (SOS) nor cortical BMD discriminated significantly between the two groups.
In the pubertal girls the velocities of Wave 1 and Wave 2 were \( v_1 = 3713 \) (182) m/s and \( v_2 = 1720 \) (92) m/s. Velocity \( v_1 \) correlated significantly with \( v_2 \) (\( r=0.57, p<0.001 \)), and both of these velocities correlated weakly but significantly with SOS. Velocities \( v_1 \) and \( v_2 \) correlated significantly with cortical BMD (\( r = 0.47, p < 0.001 \) and \( r = 0.46, p < 0.001 \), respectively) and weakly but significantly with cTh (\( r = 0.24, p < 0.05 \) and \( r = 0.28, p < 0.01 \), respectively) (Table 6.1) (Ref. II).
Two further in vivo studies were performed in Caucasian females, one for the tibia (age 32-90 years, n=65) and one for the radius (age 22-83 years, n=107). However, we encountered difficulties in measuring Wave 2 reliably at least in 1/3 of the subjects measured for the tibia and in 2/5 in those for the radius. The difficulties were identified as a consequence of too thick soft tissue on top of the bone (Fig 6.14). In the tibia the local soft tissue thickness (as measured using the pQCT at the site where the ultrasound measurements were made) ranged from 4 to 14 mm (±1 s.d.) between the subjects, and in the radius from 7 mm to 15 mm (±1 s.d.). As the soft tissue was thicker on top of the radius, this partly explains why the measurements were also more difficult for the radius than for the tibia.

Due to these difficulties in measuring through the soft tissue, we began an extensive program for explaining the effect of soft tissue theoretically and to develop more efficient analysis methods in order to eliminate the adverse effect of soft tissue. As yet, we have tested the plate model (A0 mode) with the inversion scheme and selective spectral analysis method for the improved determination of \( v_2 \) for the radius in vivo. This method enabled an automatic determination of the reliability of guided wave measurement based on the quality of the curve fit according to Eq. (10) of Ref. V. As a result, the in vivo radius data was divided, again, as a good fit (small fitting error between plate A0 mode and \( v_2 \), n=45) and poor fit group (large fitting error between plate A0 mode and \( v_2 \), n=62). Indeed, the soft tissue was thinner for the good fit (9.9 mm ± 3.1 mm) than for the poor fit (11.7mm ± 3.1 mm) sub-set of the radius data (p<0.01).

In the good fit group (n=45), velocity \( v_2 \) (as defined using the selective 2D-FFT and plate model) correlated significantly with the cortical BMD as well as cTh (Fig 6.15). No
correlations between $v_2$ and the bone quantities were found for the poor fit group (n=62), but instead, $v_2$ yielded a strong correlation with the local soft tissue thickness (Fig 6.16).

![Figure 6.15](image1.png)

**Fig. 6.15.** Guided wave velocity $v_2$ (as determined using the selective spectral analysis and plate theory for the good plate theory fit group) versus bone quantities for the radius in vivo.

![Figure 6.16](image2.png)

**Fig. 6.16.** Guided wave velocity $v_2$ (as determined using the selective spectral analysis and plate theory for the poor plate theory fit group) versus local soft tissue thickness for the radius in vivo.

The cortical thickness estimate $h_e$, as determined using the inversion scheme (plate model), was significantly higher than the actual $cTh$, and the correlation between $h_e$ and $cTh$ (good plate theory fit group) was slightly lower (but significant) than that of $v_2$. These observations were obviously caused by the compatibility issues between the simple plate model and the in vivo problem (as the bone has tubular shape and it is overlyed by a layer of soft tissue). However, the tube or bilayer models have not yet been tested with the inversion analysis of the in vivo data. Further work is needed to optimise the inversion scheme for in vivo measurements exploring the use of tube and bilayer models, but this was outside the scope of the current work. It may also be necessary to combine the two into a tubular bilayer model.
Chapter 7

Discussion

In this study we introduced an axial scanner device, operating at low ultrasonic frequencies \( f = 50-350 \) kHz, and a method for measuring two ultrasonic wave modes (Wave 1 and Wave 2) simultaneously in cortical bone using this device. The measurement principle was verified with two-dimensional finite element simulations as well as with experimental measurements for bone phantoms. Wave 1 was shown to be the fast first arriving signal (FAS) and Wave 2 was consistent with the fundamental antisymmetric (or flexural) guided wave \( (A0) \). The effects of tubularity and overlying soft tissue were investigated theoretically and experimentally, and measurements were made on specific bone phantoms to illustrate the effect of anatomical bone shape. In addition, we reported guided wave results for human bone in vitro and in vivo - to our best knowledge, as the first group after Jansons et al [41] and Tatarinov et al [99].

The finite element simulations and the experimental results for plates were in excellent agreement with the theory of Lamb waves as well as with the previous finite difference simulation results by Bossy et al [11, 12] regarding the thickness effects of FAS. Wave 1, corresponding to FAS, was consistent with the lateral longitudinal wave if thickness-to-wavelength ratio was \( e/\lambda >> 0.5 \). When \( e/\lambda \) was close to 0.5, then a clear decrease in the velocity of Wave 1 was observed, and when \( e/\lambda << 0.5 \) Wave 1 was close to or consistent with the fundamental symmetric guided wave \( (S0) \). In addition, a slight increase in \( v_1 \) compared to its high-frequency saturation value \( (c_L) \) was observed at around \( e/\lambda = 0.7-1.0 \), which was as well in agreement with Bossy’s results. According to our measurements for human bone, the cortical thickness varied in the range 2.5-6.5 mm in the tibia and 1.0-4.0 mm in the radius. When measuring Wave 1 \( (f = 250-300 \) kHz), these ranges correspond roughly to \( e/\lambda = 0.2-0.5 \) and \( e/\lambda = 0.1-0.3 \), respectively, indicating that Wave 1 is expected to be sensitive to cortical thickness in the tibia, and that in the radius the thickness sensitivity may be impaired due to plateau of S0. In comparison, the French prototype device \( (f = 1.0 \) MHz) corresponds respectively to \( e/\lambda = 0.6-1.6 \) and \( e/\lambda = 0.25-1.0 \), and Omnisense \( (f = 1.25 \) MHz) to \( e/\lambda > 0.8-2.0 \) and \( e/\lambda = 0.3-1.3 \). Thus, neither of these devices is expected to be sensitive to the cortical thickness of the tibia, but especially the French device may be sensitive to that of the radius.

Velocity \( v_2 \) of Wave 2 \( (f = 100 \) kHz), being consistent with A0, saturated to Rayleigh velocity \( c_R \) for \( e/\lambda > 2 \) (Figs 6.2, 6.4). For \( e/\lambda < 2 \), \( v_2 \) began to decrease slightly, and for \( e/\lambda < 0.5 \) strongly with decreasing \( e/\lambda \). The cortical thicknesses measured in the tibia and radius correspond respectively to \( e/\lambda = 0.1-0.3 \) and \( e/\lambda = 0.2-0.5 \) when measuring...
Wave 2 at $f = 100$ kHz (by chance similarly as with Wave 1). Thus, $v_2$ is expected to be highly sensitive to cortical thickness in the radius as well as in the tibia.

Measurements in vitro confirmed the thickness sensitivity of Wave 1 and Wave 2. The correlation between $v_2$ and cTh was strong and significant, partly confirming the consistency between Wave 2 and A0 guided wave. However, $v_1$ only yielded a modest correlation with cTh, which could partly be explained due to the S0 plateau effect at low $e/\lambda$. The inferiority of $v_1$ results could also be explained due to impaired coupling of Wave 1, as the low-frequency device is not optimised for measuring the Wave 1 alone. Transducers were orientated perpendicularly to the specimen, whereas properly tilted transducers would have concentrated more of the energy into the longitudinal wave. Also, the resolution of the data acquisition device (8 bits, 10 MHz) was limited and it was not possible to completely filter the digitising noise of the poorly coupled, low-intensity signals.

The main interest was in the investigation of the sensitivity of ultrasonic velocities to the cortical thickness. Therefore, the thickness was chosen (as an only material property) as the fitting parameter in the inversion scheme. In plates the plate theory inversion yielded exact thickness estimates $h_e$ (10% precision) for plates thinner than 8 mm, which is considered as sufficient regarding the cortical thicknesses of human bones. However, when using the plate theory inversion in tubes, the estimate was exact only when the wall thickness $e$ was low compared to the outer radius $b$ of the tube ($eb < 0.3$), but for $eb$ larger than that the error increased with increasing $eb$. It was proposed that the difference between plate and tube models could explain this phenomenon, and successfully it was shown that using the tube model inversion, the thickness estimate $h_e$ corresponded nicely (10% precision) to the actual tube wall thickness $e$, provided that $eb < 0.8$ and $e < 8$ mm. This is indeed considered sufficient within the range of human bone cortical thicknesses.

The inversion for the human radius in vitro (mean $eb = 0.4$) yielded the thickness estimate range $h_e$ matching exactly to that of the actual cTh. However, the correlation between $h_e$ and cTh was not higher than $r=0.71$ ($p<0.001$), and there was clear scattering in the points seen in Fig 6.11. This can obviously be explained due to the choice of constant tube radius $b$ in the inversion model. This $b$ was defined according to the mean radius of the radius bones, thus the variation of the actual radius clearly explains the scattering of the observed result. In addition to $b$, the elastic properties of the bone were assumed as constants, and this assumption affects scattering as well.

In addition, it was shown that $v_1$ and $v_2$ are dominated by the local rather than average thickness of anatomically shaped bone phantoms. This denotes that the placement and alignment of an ultrasonic probe on top of bone is critical in order to obtain reliable and reproducible results. However, when comparing the acoustic wavelengths between bone and PVC, the effective size of the anatomically shaped phantoms (made of PVC) matches to that of approximately 1.6 times greater bone. Therefore, as the diameter-to-wavelength ratio of actual human bones is smaller than in these experiments, the ultrasound velocities may more strongly be affected by the mean cortical thickness. This consideration can justify the use of the mean cortical thickness in the pQCT measurements of bone in vitro and in vivo. The mean thickness was much more precise than the local cortical thickness, which had to be determined using a slow manual analysis of the pQCT images.
The effect of the material properties (elastic modulus and density) on $v_1$ and $v_2$ was not considered in detail in the simulations or experimental measurements in phantoms. In theory, the material bulk velocities $c_L$ and $c_T$ are affected by Young’s modulus $E$ and density $\rho$, and Poisson’s ratio $\nu$ according to Eqs. (3.1) and (3.2), where $\nu$ is defined by $c_L$ and $c_T$ as

$$\nu = \frac{1 - 2\left(\frac{c_T}{c_L}\right)^2}{2 - 2\left(\frac{c_T}{c_L}\right)^2}.$$ 

Biomechanical studies indicate that $E$ is approximately proportional to $\rho^n$ where estimates of $n$ range in the literature from 2 to 3 in cortical bone. From Eq. 3.1 this implies that velocity should then be function of $\rho^m$ where $m$ should vary from 0.5 to 1. This explains the positive correlations obtained between ultrasound velocities and the bone mineral density (BMD). As velocity $v_1$ saturates to $c_L$, and $v_2$ to $c_R \approx 0.9 c_T$, this defines the relationships between $v_1$, $v_2$ and the elasticity and density via the bulk velocities of the material.

In general, the bulk velocities alone define the dispersion curves for a plate, and thus the inversion from the experimentally measured guided wave velocities is possible to the bulk velocities and further to elastic constants properties of the plate. This inversion approach has been successfully utilised, e.g., by Karim and Mal, Lefebvre et al and Gsell et al [44, 54, 34]. It is provided, however, that the thickness and density of the plate (or tube wall) are known. Considering the bone guided wave application, the thickness could, for instance, be measured using a simple pulse-echo measurement, in the contrary to the complicated guided wave inversion approach discussed in this study. As mentioned in Section 5.2.3, velocities of several genuine guided waves should be measured within a broad frequency range in order to successfully use the elastic modulus inversion. The thickness inversion approach was the most suitable for this application, as it also helped in solving the wave identification problems (due to low spatial resolution) together with the selective 2D-FFT method.

Remaining relevant questions that arise in the applicability of guided waves in the assessment of long bones are the effects of endosteal porosity, bone heterogeneity and anisotropy. It is known that anisotropy of cortical bone can be considered according to transversely isotropic or orthotropic symmetry [81]. In addition, the analytical guided wave models (plate and tube) can be expanded to anisotropic case, though a more general solution method must be used [87, 80, 34]. This must obviously be made next in the progress of bone guided waves research.

Endosteal porosity is also a critical issue, as it affects roughness of the inner cortical layer, and the theory of guided waves provides an ideal layer with smooth top and bottom surfaces. Clearly, the roughness scatters the partial ultrasonic waves, and consequently affects attenuation of the propagating guided wave. If the size of the scatterers is significantly smaller than the acoustic wavelength, then only the attenuation (without more complex effects) takes place and the guided wave is expected to propagate. As the size of the pores in endosteal bone is of the order or less than 1 mm, and the acoustic wavelength of the A0 guided wave is of the order of one or two centimetres ($f = 100\text{kHz}$), the
condition between the pore size and wavelength is satisfied. However, as the frequency increases, the wavelength decreases. So, consequently the propagation of higher order guided waves may not be possible in the bone, especially in osteoporotic bone. The effect of surface roughness on guided waves has also been studied theoretically and experimentally by Lobkis and Chimenti [56, 57]. 3D simulations in bone [12] indicate that the increasing endosteal porosity decreases the velocity of the FAS. In addition, the experimental phantom measurements, made by Tatarinov et al [98], suggest that the velocity of flexural guided wave (i.e. A0) is decreased by the increased amount of endosteal porosity ($f = 100$ kHz). Thus, both Wave 1 and Wave 2 are expected to be affected by the porosity, in a manner that these low frequency ultrasonic waves in a way sense the effective thickness of the compact bone. As a conclusion, the low-frequency guided waves are therefore expected to be good indicators of the cortical thickness.

The in vivo results in a hundred-and-six pubertal girls were in an agreement with the in vitro results, suggesting correlations between the guided wave velocities ($v_1$, $v_2$) and bone properties (BMD, cTh). The correlations between the guided wave velocities and cortical BMD were, in general, as high as expected from the in vitro study. Velocity $v_1$ yielded slightly better correlation in vivo than in vitro, which may indicate that the overlying soft tissue improves the coupling of the longitudinal first arriving wave (Wave 1). Velocity $v_2$, in turn, was slightly lower than its in vitro counterpart. This clearly is the first sign to indicate the problems in the reliable identification of the fundamental flexural (or antisymmetric) guided wave (Wave 2) through the overlying soft tissue. However, the preliminary results comparing the small group of osteoporotic females with a normal healthy control group, in spite of the soft tissue effects, only the Wave 2 can significantly discriminate between osteoporotic and healthy bone. These data suggest that the guided waves may yield a clinically relevant bone assessment and thus justifies the need for more extensive in vivo measurements and further investigation and development of the method.

Further in vivo measurements were made for the tibia of sixty five and for the radius of a hundred and seven subjects. In the analysis of these measurements we, however, encountered serious difficulties in obtaining a good fit between Wave 2 and A0 plate mode. As a result, we found out that the difficulty in observing a clear A0 like Wave 2 increased with increasing on-site soft-tissue thickness. The classification based on the quality of plate theory fitting yielded the rejection of $1/3$ to $2/3$ of the subjects when choosing the sub-set of good fit data. This classification helped in obtaining the expected correlations between $v_2$ and bone quantities in the small good plate theory fit sub-sets. However, the only strong and clear (negative) correlation was obtained between $v_2$ and the soft tissue thickness in the sub-set classified as poor plate theory fit group. These findings, unfortunately, raise also the preliminary positive results into a doubtful light. In the preliminary phase Wave 2 was analysed using semi-automatic line fitting in $(r,t)$ diagrams, and thus the human judgement of the proper fitting may have had a strong influence on the obtained $v_2$. Though being blind on the bone properties, the automatically determined $v_1$ was known when determining $v_2$. Later, different automatic analyses, based on filtering and line fitting in the distance-time plane or the spectral analysis, were developed to achieve more reliable determination of $v_2$. However, no expected correlations have, as yet, been obtained. The results do suggest that visual analysis of the $(r,t)$ diagrams by a human observer may actually work better than the current automatic processing algorithms. This gives further confidence that there is valuable, though complicated, information present in the signals, and that further refinement of the signal analysis procedures is likely to bring
improved results. The data also indicate that, for a human observer, knowledge of \( v_1 \) may improve the determination of \( v_2 \) and this suggests that automatic analysis based on the information from both waves is worth investigating.

These difficulties yielded the motivation for developing the fluid-solid bilayer model for explaining the effects of the overlying soft tissue layer. It is obvious to expect that the guided waves propagate, not in the bone or soft tissue alone, but in the whole bilayer system composed of bone and soft tissue. Therefore, it is highly possible that this bilayer model could explain the problem of in vivo guided wave measurement. In this model, the contribution of soft tissue is mostly related to the thickness of the soft overlayer (assuming that the sound speed in soft tissue can be approximated e.g. with that in water). This prediction is in close agreement with the experimentally obtained negative correlation between \( v_2 \) and soft tissue thickness. Therefore, the purpose is to use the soft tissue thickness \( a \) as the known input parameter in the inversion scheme and selective spectral analysis method, and this way to eliminate its effect by seeking for the contribution of bone thickness \( h \) alone (or any bone material parameter) to the experimentally measured bilayer velocities.

The limitations of the suggested solution approach to the soft tissue problem are tightly connected to those of the inversion scheme and selective two-dimensional spectral analysis method. The inversion was shown to work with plates, tubes and bones in vitro. As the thickness \( h_e \) was allowed to range over the whole spectrum of the results, it was shown that the inversion scheme works provided that a proper theory and input parameters are chosen. Therefore, the accuracy of this method relies on the choice of theoretical model and input parameters. Also, this means that satisfactory in vivo results cannot be obtained until the theory behind the guided wave propagation problem in vivo can be modelled and is known well enough. To this end the modelling of the effects of bone as tube, anisotropy, inhomogeneity and endosteal roughness are warranted. But more importantly, the effects of the overlying soft tissue and interior bone marrow should be addressed. Modelling the soft tissue or bone marrow as ideal elastic fluid may not, however, be sufficient, as the soft tissue and marrow are viscous (or visco-elastic) materials and may strongly affect the dispersion behaviour of guided waves. Previous studies, made regarding the effects of viscous tube core, viscous loading and visco-elastic bilayer [107, 108, 26, 71, 97], could be used as the starting point in these problems.

A strong limitation of the two-dimensional spectral analysis was the short spatial scanning length (typically 30 mm). The short scanning length was necessary as to be able to approximate that there is no significant variability in the bone properties within the scanning range. This, however, yielded flat spectral peaks and thus low resolution in discriminating different wave modes in the phase-velocity (or wavenumber) domain. As a result, joint peaks were formed if two wave modes were too close to each other (in many cases already, e.g., the phase velocity difference of 1000 m/s was too close). We tested the adverse effect of the short scanning length (results not shown here) by finite-element simulations, and a 200 mm scanning length, for instance, yielded an excellent peak resolution. The selective 2D-FFT method was developed in order to eliminate the effect of other wave modes and thus to improve the reliability of mode identification. The fast Fourier transform could, however, be replaced with some more efficient spectral analysis approach, such as the Prony method [108, 47] or matrix pencil method [40, 34]. Also, it could be worth of trying to try to extend the scanning length in order to improve the resolution. This, however, must be made by the cost of increasing variability of bone
properties, which obviously may be adverse on the propagation of guided waves. But being able to measure guided waves over a longer range, then this could yield an average result reflecting more completely the properties (strength) of bone.

The ultimate question, which arises, is the clinical relevance of the bone assessment using the guided ultrasonic waves, a) in general and b) using the proposed measurement approach. Clinically it would be relevant to have methods which can discriminate between osteoporotic or fractured and a healthy bone. Also, it would be warranted to assess the early signs of bone deterioration and to predict the risk for bone fracture at an early phase, thus maximising the benefit of medication. It may be difficult to displace the dual energy x-ray absorptiometry, the “golden standard” of bone assessment, completely. However, in general ultrasound provides three advantages over the X-ray based methods. Ultrasound is believed to be tissue safe, as long as intensity levels are kept below well recognised maximum permissible levels, and the equipment can be built as small and easy-to-use devices with an economy price. But more importantly, ultrasonic velocity reflects the material elasticity as well as its density, whereas the X-ray absorption is only affected by the density. Therefore, the comparison between ultrasonic and X-ray methods should be made bearing in mind that these methods are expected to reflect quite different properties of bone. The density takes no account of the underlying hierarchical microstructure that defines the mechanical properties of bone. The density thus yields only a fraction of the information that is needed to define the strength of bone. For instance, disorganised bone, such as that found in Paget’s disease, may have normal density but dramatically reduced elastic modulus and is expected to be weak and fracture easily. However, X-ray absorption cannot predict this, provided that the density is close to the normal level. But the ultrasonic velocity gives a direct insight into the ratio between elasticity and density. Therefore, the ultrasonic velocity may reflect the bone strength more completely than X-ray attenuation, lacking, however, information of the absolute magnitude of the density.

The question of guided waves builds up on top of understanding of the behaviour of the ultrasonic waves in general, as the guided wave is composed of the conventional ultrasonic longitudinal and shear waves between two boundaries of a medium. As discussed in this Thesis, the velocities of the measured guided waves were strongly related to the thickness of the waveguide due to dispersion. It was also described that the guided wave is a bending vibration of the whole structure. The guided wave velocity can therefore reflect aspects of the average elasticity and density throughout the bone thickness, as well as the effective thickness itself. A broad-band guided wave measurement can yield a multivariable inversion problem, i.e. a set of guided wave velocities \( (v_{ei}f_i) \), which can with certain approximations be quite accurately inversed as different material properties of the medium in which they were measured from. Therefore, a single guided wave velocity, e.g. that we have referred to as \( v_2 \), can reflect only a fraction of the potential of guided waves. On the other hand it must be acknowledged that the possibility of measuring additional guided modes in bone has not yet been confirmed and hence the prospects for developing a successful inversion scheme for both geometric and material properties are not clear. Furthermore, even if a successful inversion scheme were possible allowing determination of elasticity, this would still only be a surrogate for bone strength rather than a direct measurement. It may be that optimal prediction of bone strength is to be obtained by combining a range of measurements including bone density, cortical thickness and elasticity.
Finally, however, theoretical considerations cannot, on their own, confirm the clinical applicability and value of a proposed new bone measurement method. This can only be made with in vivo measurements in large sample populations in comparison with the standard bone densitometry methods. A strength of this present study was its aim to collect such clinical evidence in the in vivo measurements. Measurements in girls confirmed the ability of guided waves to capture information on bone thickness in addition to bone density, in contrast to existing ultrasonic measurements of bone. Pilot data from a small number of older women suggested that guided waves may have an enhanced ability to detect osteoporosis. However, some difficulties were encountered in vivo due to the overlying soft tissue. In any future work, these difficulties should be addressed by extending the modelling work to include the modelling of bone as an anisotropic tube, and the soft tissue and bone marrow respectively as a viscous liquid layer and core. The large amounts of in vivo data that have been gathered already will be useful in any future work.

As, noted above, future work could thus include the development of an appropriate wave propagation model for a multilayer structure in order to better interpret the in vivo guided wave measurements in bone. In this model the bone should preferably be considered as an anisotropic tube, and the soft tissue and bone marrow respectively as a viscous liquid layer and core. In addition, further technical development of the measurement system is warranted. The speed of data acquisition should be increased, thereby enabling a better precision through increased signal averaging. Also, it would be warranted to move the recording position slightly sideways on top of the bone between the scans in order to seek for an optimal contact and signal response. All of these requirements could be achieved by an array probe in which the necessary transducer elements were built inside a single casing, and scanning could be performed electronically. Finally, the ultrasonic guided wave assessment of bone does not necessarily need to be limited in the transmission principle, but also the measurement of a specular reflection spectrum may be worth investigating. This approach has been successfully used for measuring the guided wave dispersion curves for composite laminates [6, 7], and it also provided an efficient implementation of an inversion scheme [44]. A similar approach, known as the Ultrasonic Critical angle Reflectometry (UCR), has been used for determining the pressure and shear wave speeds for bone [3, 63]. However, the reflection-based measurement of guided waves has not yet been reported for bone. This approach would be attractive as it provides a localised point measurement, and allows the simultaneous measurement of several guided wave modes.

As a conclusion, it was shown that the methods introduced in this Thesis provide useful information of bone phantoms and bone in vitro, and despite of the effects due to overlying soft tissues, also of bone in vivo. These results thereby indicate that the use of ultrasonic guided waves is a feasible and clinically useful assessment of cortical bone, providing advantages over the existing axial transmission techniques. In addition, this Thesis forms a firm basis for any future endeavours to improve the clinical performance of the guided wave bone assessment by further modelling work and technical development of the device and methods of analysis.
References


Publication I
Guided ultrasonic waves in long bones: modelling, experiment and in vivo application

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Abstract

Existing ultrasound devices for assessing the human tibia are based on detecting the first arriving signal, corresponding to a wave propagating at, or close to, the bulk longitudinal velocity in bone. However, human long bones are effectively irregular hollow tubes and should theoretically support the propagation of more complex guided modes similar to Lamb waves in plates. Guided waves are attractive because they propagate throughout the bone thickness and can potentially yield more information on bone material properties and architecture. In this study, Lamb wave theory and numerical simulations of wave propagation were used to gain insights into the expected behaviour of guided waves in bone. Experimental measurements in acrylic plates, using a prototype low-frequency axial pulse transmission device, confirmed the presence of two distinct propagating waves: the first arriving wave propagating at, or close to, the longitudinal velocity, and a slower second wave whose behaviour was consistent with the lowest order Lamb antisymmetrical (A\textsubscript{0}) mode. In a pilot study of healthy and osteoporotic subjects, the velocity of the second wave differed significantly between the two groups, whereas the first arriving wave velocity did not, suggesting the former to be a more sensitive indicator of osteoporosis. We conclude that guided wave measurements may offer an enhanced approach to the ultrasonic characterization of long bones.

Keywords: bone, ultrasound, guided waves, osteoporosis, tibia

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1. Introduction

The so-called *axial transmission technique* has been used to assess long bones for over four decades (Siegel *et al* 1958, Gerlanc *et al* 1975, Van der Perre and Lowet 1996, Camus *et al* 2000). With this method, an ultrasonic pulse is transmitted along the long axis of a bone (typically the tibia) from a transmitter to a receiver and the velocity is estimated from the transit time of the first arriving signal and the propagation distance. To account for the effects of overlying soft tissue, either a multiple transmitter/receiver configuration can be used (Saulgozis *et al* 1996), or transit time can be determined as a function of distance as one transducer is moved relative to the other (Van der Perre and Lowet 1996, Lowet and Van der Perre 1996). At least two commercial clinical devices for bone assessment using axial ultrasound transmission have been produced (Hans *et al* 1999): the Soundscan 2000/Compact (Myriad Ultrasound Systems Ltd., Rehovot, Israel) operating at 250 kHz, and the Omnisense (Sunlight Medical Corp., Rehovot, Israel) operating at 1.25 MHz. A recent investigation by Camus *et al* (2000) into the axial transmission technique indicated that, under certain conditions, the first arriving signal can correspond to a lateral wave (or head wave) propagating along the surface of the solid at the bulk longitudinal velocity. The conditions under which lateral waves were observed included an appropriate measurement geometry (in terms of the separation of the transducers and their distance from the surface), an approximately point-like transmitter and receiver (spherical wavefronts), and the use of wavelengths less than the thickness of the solid layer. Tibial ultrasound velocity values measured *in vivo* (Foldes *et al* 1995, Saulgozis *et al* 1996, Van der Perre and Lowet 1996, Lee *et al* 1997, Prevhral *et al* 2001, Sievanen *et al* 2001) are comparable to, or slightly lower than, *in vitro* measurements of the axial longitudinal wave velocity in excised human cortical bone specimens (Ashman 1982, Lakes *et al* 1986, Antich *et al* 1991). However, there is experimental evidence indicating that the velocity of the first arriving signal is lower than the longitudinal velocity when the wavelength is greater than the bone thickness (Njeh *et al* 1999). A simulation study by Bossy *et al* (2002) showed similar trends, and indicated that the waves contributing to the first arriving signal change as the sample becomes thinner. Clinical evidence for such thickness effects is, as yet, inconclusive (Prevhral *et al* 2001, Sievanen *et al* 2001), but this may be due to differences in the ultrasonic frequencies used by the different commercial systems, or other methodological factors.

Tibial ultrasound velocity measured using current commercial devices correlates with tibial bone mineral density (BMD), and, to a lesser extent with BMD at other skeletal sites (Foldes *et al* 1995), and also reflects cortical bone elastic modulus (Lee *et al* 1997). However, tibial ultrasound is a poor discriminant of osteoporotic fracture (Stegman *et al* 1995), and is only weakly correlated with femoral strength and BMD (Bouxsein *et al* 1999). There are a number of reasons why current tibial ultrasound measurements may be sub-optimal in terms of their sensitivity to relevant bone properties. Waves propagating at the bone surface may preferentially reflect the material properties of bone in the periosteal region. In osteoporosis, cortical bone changes occur primarily in the endosteal region. The porosity of endosteal bone increases leading eventually to endosteal resorption, ‘trabecularization’, and thinning of the cortex (Parfitt 1984, Kanis 1994). In addition, recent nanoindentation studies suggest there may be differential changes with ageing in the elastic properties of periosteal and endosteal bone purely at the material level (Rho *et al* 2002). Ultrasonic methods that target these known pathological changes are likely to prove more valuable clinically. A further concern is that if density and elasticity both change in the same direction, for example, as a result of a change in porosity, ultrasound velocity may not be altered because the two effects tend to cancel out, since longitudinal velocity varies as the square root of elasticity divided by density.
These considerations suggest that any improved ultrasonic method for cortical bone assessment should be sensitive to one of more of the following factors: (a) reduced cortical thickness, (b) structural changes in the endosteal region, such as increased porosity, and (c) changes in bone density and elasticity at the material level, ideally independently of each other.

In general, little consideration has been given to the possibility of using different types of ultrasonic waves in long bones. One exception has been a series of studies reporting low-frequency ultrasonic measurements of ‘surface wave’ velocity in the tibia, mapping the spatial variation in velocity and quantifying changes during weightlessness (Jansons et al 1984, Oranov et al 1988, Tatarinov et al 1990, McCarthy et al 2000). However, since pure surface waves only exist in structures that are much thicker than the wavelength, it is likely that these researchers were actually measuring a guided wave mode reflecting both bone thickness and material properties. Guided waves propagate within bounded or layered media, and their characteristics are determined by the geometrical and material properties of the structure and of the surrounding media. They arise from the reflection, mode conversion and interference of longitudinal and shear waves within the structure (Victorov 1969). The theory of guided waves in plates (Lamb waves) is summarized below. Ultrasonic guided waves are used in non-destructive testing for the assessment of plates, tubes and more complex structures (Chimenti and Martin 1991, Chimenti 1997, Cheeke et al 1999, Castaing and Hosten 2001). In some instances inversion schemes have been developed for estimating material and/or geometrical properties of the structure under test (Karim et al 1990, Chimenti 1997).

Our aim in this study was to investigate whether guided waves might offer an improved approach to characterizing human long bones. We aimed to use Lamb wave theory and numerical simulations of wave propagation to predict the expected behaviour, to test these predictions by experimental measurements in acrylic plates, and finally, to attempt measurements in the tibia with a small group of healthy and osteoporotic human volunteers.

2. Lamb wave theory

Lamb waves are two-dimensional elastic waves that propagate in a free solid elastic plate of finite thickness in a vacuum. They arise from the multiple reflection and mode conversion of longitudinal and shear waves from the upper and lower surfaces of the plate (Victorov 1969). They exist in the form of resonant modes where the combination of frequency and phase velocity corresponds to standing waves in the thickness direction. It can be shown that Lamb waves are described by the following characteristic equation (Lamb 1917, Victorov 1969, Graff 1991):

$$\frac{\tan \beta d/2}{\tan \alpha d/2} = \left(\frac{4\alpha \beta k^2}{(k^2 - \beta^2)^2}\right)^{1/4}$$

(1)

where $d$ is plate thickness, $k$ is the component of the wavenumber parallel to the interface ($k = \omega/c$, where $c$ is the phase velocity of the Lamb wave and $\omega$ is angular frequency in radians/second), and $\alpha$ and $\beta$ are given by

$$\alpha^2 = \frac{\omega^2}{c_l^2} - k^2$$

(2a)

$$\beta^2 = \frac{\omega^2}{c_t^2} - k^2$$

(2b)

where $c_l$ is the longitudinal velocity and $c_t$ is the shear velocity. The velocities of longitudinal and shear waves in the solid are $c_l$ and $c_t$ respectively. In equation (1), the exponent for the
right-hand term is +1 for symmetric modes and −1 for anti-symmetric modes (see below). In symmetric modes, identified as S0, S1, S2, etc, the motion is symmetric about the mid-plane of the plate, whereas in anti-symmetric modes (A0, A1, A2, etc) the motion is anti-symmetric. Numerical evaluation of equation (1) yields Lamb wave dispersion curves which define the variation in phase velocity $c_p$ as a function of the thickness–frequency product $F \times d$ (figure 1(a)). Group velocity ($c_g$) dispersion curves (figure 1(b)) can be calculated using the following equation:

$$c_g = \frac{\partial \omega}{\partial k}.$$ (3)
Each continuous curve in figure 1 represents a guided wave mode. From these dispersion curves it can be seen that all but the two fundamental modes, S0 and A0, have a cut-off frequency–thickness product. Thus, for very low frequencies, or for very thin plates, only the fundamental (S0 and A0) modes can be excited. In these conditions, the phase velocity of the S0 wave approaches that predicted by the 'thin plate' theory, given by an equation analogous to the bar wave equation (Graff 1991):

\[ c_p = \sqrt{\frac{E}{(1 - v^2)}\rho} \]

where \( E \) is Young's modulus, \( v \) is the Poisson ratio, and \( \rho \) is density.

With increasing \( F \times d \), the velocities of all of the Lamb modes asymptotically approach the Rayleigh velocity (figure 1). The Rayleigh velocity is that of a pure non-dispersive surface wave, given by Graff (1991) as

\[ c_R \approx c_t(0.87 + 1.12v) \]

\[ (1 + v) \]

where \( c_t \) is the shear wave velocity in the solid, as before.

Lamb wave terminology is often used to describe wave propagation in plates loaded with an external medium such as a fluid. The boundary conditions are modified by the presence of a surrounding medium and the characteristics of Lamb waves in a fluid-immersed plate are different from those of Lamb waves in a free plate. For example, if the phase velocity of the fluid is close to the phase velocity of a Lamb mode, the mode continuously radiates into the fluid and therefore its attenuation is high.

3. Numerical simulation of wave propagation

To simulate wave propagation in solid half-layers and plates, we used a two-dimensional finite-difference time-domain approach implemented with commercial software (WavePro2000, Cyberlogic Inc., New York) based on a published algorithm (Schechter et al 1994). In the work reported here, the acoustic transmitter and receiver were modelled as 1 mm diameter longitudinal wave transducers in contact with the solid at right angles to the surface, 25 mm apart. The transmitted signal was a single-cycle Gaussian-windowed sine function with a frequency of 250 kHz and a duration of 4 \( \mu \)s. The solid was acrylic surrounded by a vacuum.

We studied two different types of geometry: (a) a semi-infinite solid half-space with the transducers on the free surface, and (b) infinite solid plates, with thickness of 10, 5, 2, 1, 0.5 and 0.25 mm, with the transducers on the upper free surface (figure 2). Typical snapshots of acoustic wave propagation in these two cases show the longitudinal and shear wavefronts, and the Rayleigh wave localized close to the surface (figure 2), although the shear and Rayleigh waves are superimposed and cannot be easily distinguished from each other. The lateral or head wave is shown as the component of the longitudinal wave propagating at, and parallel to, the surface. It should be noted here that Camus et al (2000) use the term lateral wave in a different sense as referring to the wavefront in a fluid connecting the refracted longitudinal wave in the solid and the reflected wave in the fluid.

The simulated time-domain signals from the receiver for the half-space show the arrival of the relatively small-amplitude lateral wave ahead of the slower, but higher amplitude, Rayleigh surface wave (figure 3). In the plates, the situation becomes much more complex due to the presence of the additional guided wave modes. However, in the thinnest plates, two distinct arrivals are again visible: the first arriving signal clearly arrives later than in the case of the half-space, and the second, slower wave exhibits pronounced dispersion as would be expected.
Figure 2. Numerical simulations of wave propagation in a solid half-space and in plates. The distance between the transmitter ($t$) and receiver ($r$) is 25 mm. In these images the grey level is inversely proportional to the particle displacement allowing the different propagating waves to be visualized. The images show the situation at $t = 9.77 \mu s$ as the first arriving wave approaches the receiver. In the plates reflection and mode conversion at the lower and upper surfaces give rise to the guided (Lamb) modes.

for a Lamb A0 wave. The apparent velocity of the first arriving signal was determined as a function of plate thickness by dividing the transducer separation by the time taken for the first detectable signal to arrive at the receiver (figure 4). This velocity was constant at the longitudinal velocity in thick plates (>3 mm), but decreased with decreasing plate thickness for thicknesses below 3 mm (figure 4).

### 4. Experimental measurements

#### 4.1. Ultrasonic measurement system

Experimental measurements were performed using a prototype axial pulse transmission system with a pair of custom-made unfocused low-frequency contact transducers. The transducers had a centre frequency of approximately 200 kHz and a diameter of 5 mm. They were orientated perpendicularly to the surface of the object to be measured and an ultrasonic gel was applied as a coupling agent. The vertical and lateral position of each transducer could be...
Figure 3. Simulated time-domain signals for wave propagation in an acrylic half-space and in plates of varying thickness. In the half-space, two arrivals (arrows) are visible: the lateral wave (L) and the slower travelling Rayleigh wave (R). In the plates it is difficult to distinguish the presence of specific guided modes due to their temporal superimposition.

Figure 4. Dependence of the apparent velocity of the first arriving wave on plate thickness for acrylic predicted by the numerical wave propagation simulations. Velocity was calculated from the arrival time of the first detectable signal divided by the distance between the transducer centres. The dotted line is the longitudinal velocity in acrylic.
Figure 5. Typical \((r, t)\) diagrams for (a) 3 mm thick acrylic plate, (b) 15 mm thick acrylic plate, (c) healthy female tibia \textit{in vivo}, and (d) osteoporotic female human tibia \textit{in vivo}. These diagrams represent the absolute amplitude of the received signal as a function of time (horizontal axis, 0–92 µs) and transducer separation (vertical axis, 20–50 mm). Greyscale equalization has been used to enhance the visibility of the first arriving wave, hence amplitude information is not accurately portrayed in these images. Two propagating waves were observed consistently: the first arriving wave (white arrow) and the second, slower, wave (black arrow). The second wave behaved as expected for the Lamb A0 wave (see figure 6 and text). Note that dispersion of the second wave in the 3 mm acrylic plate explains the ‘corkscrew-like’ appearance of the wave packet due to the difference in phase and group velocities.
Figure 6. Experimentally measured velocities as a function of thickness for acrylic plates. Experimental measurements of the first arriving wave velocity are shown as solid circles, whilst the second wave velocity values are shown by open circles. The velocities of the two fundamental Lamb waves are also shown. The dotted line is the longitudinal velocity in acrylic. The first arriving wave propagated at the longitudinal velocity in thick plates, as expected for a lateral wave, but velocity decreased with decreasing thickness towards that of the Lamb S0 wave. The slower wave behaved closely as expected for the Lamb A0 wave. The velocities assumed for acrylic in calculating the theoretical Lamb wave velocities are the same as in figure 1.

the chance of jumping to another, incorrect, peak. This process continued through all of the RF lines, and then a straight line was fitted to the points. Errors could be corrected manually by the user and a new fit made. The phase velocities of the first and second waves were then calculated as the slopes of the linear fits to the points in the first and second wave packets respectively.

4.2. Acrylic phantom measurements

A series of acrylic plates was used as bone-mimicking phantoms. Acrylic was selected since it is easily obtained, has well-documented material properties, and has been used as a bone mimic in earlier studies (e.g. Njeh et al 1999). A selection of plates was prepared with thicknesses ranging from 2 mm to 24 mm. To minimize material differences between plate samples, only moulded ISO 9002 rated Perspex from a single supplier was used. Each acrylic phantom was measured five times. As already described, two distinct propagating waves were seen and measured in the \((r, t)\) plots (figure 5). The measurement precision for the two wave velocities in acrylic, calculated as root mean square coefficients of variation (RMS CV), were 0.6% and 1.5% for the first and second waves respectively. Comparing the velocities of these two waves as a function of thickness with predictions for the two fundamental Lamb waves (S0 and A0), it can be seen that the slower wave behaved as expected for the Lamb A0 wave (figure 6). The first arriving wave propagated at the longitudinal velocity in thick plates, but its velocity decreased in thinner plates (<4 mm), mirroring the behaviour observed in the numerical simulations (figure 4). However, in the thinnest plates the numerical simulations predicted velocities of approximately 2200 m s\(^{-1}\) (figure 4) but the experimentally derived velocities tended towards a higher value of approximately 2400 m s\(^{-1}\) (figure 6).
Table 1. Tibial ultrasound and bone density measurements in normal and osteoporotic subjects.

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<th></th>
<th>Normal</th>
<th>Osteoporotic</th>
<th>Difference</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_1$ (m s$^{-1}$)</td>
<td>3946 (190)</td>
<td>3867 (165)</td>
<td>−2%</td>
<td>n.s.</td>
</tr>
<tr>
<td>$V_2$ (m s$^{-1}$)</td>
<td>1615 (60)</td>
<td>1399 (117)</td>
<td>−15%</td>
<td>0.004</td>
</tr>
<tr>
<td>Tibial SOS (m s$^{-1}$)</td>
<td>3800 (179)</td>
<td>3771 (186)</td>
<td>−1%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Cortical BMD (mg ml$^{-1}$)</td>
<td>1018 (39)</td>
<td>920 (111)</td>
<td>−11%</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Mean values are shown with standard deviation in parentheses. The $p$-value is the level of significance for the comparison between normal and osteoporotic, assessed using a two-sample $t$-test (n.s. not significant).

$V_1$ is the velocity of the first arriving signal measured with the prototype ultrasound device.

$V_2$ is the velocity of the second wave measured with the prototype device, believed to be a Lamb $A_0$ guided wave (see text).

Tibial SOS is the ‘speed of sound’ value recorded by a Sunlight Omnisense commercial bone ultrasonometer.

Cortical BMD is the bone mineral density of the tibial cortex as measured using peripheral quantitative computed tomography.

4.3. In vivo measurements

Measurements were attempted in the tibia of eight healthy normal and eight osteoporotic volunteers. The osteoporotic group all had axial bone mineral density values, as measured using dual-energy x-ray absorptiometry, more than two standard deviations below the mean of normal young adults. All the subjects gave informed consent to participate in the study, and local ethical committee approval was sought and attained. Measurements were made at the mid-tibial level, with the transducers aligned along an axis positioned approximately 1 cm medially from the anterior tibial crest. Coupling of the transducers was achieved using gel. Each in vivo measurement was repeated twice, and the average of the two values was calculated. The measurements were made by a single operator who was not blinded as to the status of the subjects. As for the acrylic measurements, two waves were consistently observed in the $(r, t)$ plots (figure 5). In vivo precision for measurements of the two wave velocities, expressed as RMS CV, was 1.5% for the first wave and 1.7% for the second. In addition to measurement with our prototype ultrasonic system, the tibial ‘speed of sound’ was measured using a commercial tibial ultrasonometer (Sunlight Omnisense), and tibial cortical bone mineral density was determined using peripheral quantitative computed tomography (Stratec XCT2000). These measurements were made at the same anatomical site as described above.

Comparing the velocity of the two waves measured with our device in the normal and osteoporotic groups, only the velocity of the second wave was significantly different ($p = 0.004$, two-sample $t$-test) between the two groups (table 1). In osteoporotics the velocity of the first wave was, on average, 2% lower than in normals but the second wave was 15% lower. Neither tibial speed of sound, measured with the Sunlight Omnisense, nor tibial cortical BMD discriminated significantly between the two groups (table 1).

5. Discussion

This study represents the first systematic investigation into the possibility of using ultrasonic guided waves to assess human bones. Lamb wave theory provides a useful starting point in seeking to understand wave propagation in a bone layer, and predicts the existence of two or more guided modes, depending on the frequency–thickness $(F \times d)$ product. These
modes are generally very dispersive. We demonstrated the use of a numerical simulation of wave propagation in a solid layer or half-space excited by a small-diameter low-frequency transducer. In these simulations a lateral wave could be observed, together with slower travelling contributions from guided modes. These simulations allow the complexity of the underlying phenomena to be appreciated, and also permit quantitative prediction of, for example, the effects of plate thickness on velocity.

Our experimental measurements with a prototype low-frequency axial pulse transmission device demonstrated the presence of two propagating waves in acrylic plates. In thick plates the first arriving signal was consistent with a lateral wave, propagating at the bulk velocity in thick plates. However, in thin plates (<4 mm thickness), the velocity was seen experimentally to decrease with decreasing thickness. The numerical simulations predicted similar behaviour for the first arriving signal, except that the velocity predicted for thin plates (2200 m s\(^{-1}\)) was lower than seen experimentally (2400 m s\(^{-1}\)). We cannot at present account for this discrepancy. However, there were differences between the simulations and the experimental measurements, notably in transducer size, and such differences could be one factor contributing to the discrepancy. We note that data from previous experimental studies (Njeh et al 1999) and simulation studies (Bossy et al 2002) suggest that the higher figure is correct, with the velocity in thin plates tending towards that of the Lamb S0 wave (about 2400 m s\(^{-1}\) in acrylic). These earlier studies also indicate that a decrease in the velocity of the first arriving signal begins at thickness/wavelength ratios of approximately 1.0, whereas our data show the decrease starting at a thickness/wavelength ratio of approximately 0.4. One possible explanation may lie in the differences between our measurement approach, using small-diameter, low-frequency transducers in direct contact, and the approaches adopted in other studies. Transducer, coupling and test geometry differences may affect the distribution of acoustic energy into different modes and wave paths, and, together with differences in the methods used to define the apparent velocity, these could account for discrepancies between the studies.

The first arriving signal velocities measured in the tibia with our device were very similar to the values obtained using the commercial ultrasonometer, strongly suggesting that the same type of wave is being measured. Our pilot data, admittedly from a small number of subjects, indicate that the velocity of the first arriving wave, measured either with our device or with a commercial device, is not a good discriminator between normal and osteoporotic women.

We measured a second, slower, wave in acrylic plates which behaved as predicted for the lowest order Lamb anti-symmetric (A0) guided mode. This wave travelled close to the Rayleigh velocity in thick plates, with velocity decreasing strongly with decreasing thickness in excellent agreement with the predictions for the Lamb A0 wave. The A0 wave is essentially a flexural wave (Graff 1991), and is likely to have been the type of wave measured previously by others in the tibia (Jansons et al 1984, Oranov et al 1988, Tatarinov et al 1990). Comparing the \((r, t)\) diagrams for acrylic and tibial measurements, the same qualitative features were observed (a small-amplitude first arriving signal and a larger amplitude second slower wave) which suggests that the same phenomena were involved. The values for the velocity of the second wave \textit{in vivo} fell in the range that would be expected for a Lamb A0-type wave in bone. The ability to discriminate osteoporotics suggests that it is indeed a wave propagating through bone, not soft tissue. Nevertheless, there is, as yet, no direct evidence confirming the nature of the second wave \textit{in vivo}, and further work is needed to validate our hypothesis that it is indeed a Lamb A0 wave in bone.

Our tibial data indicated that the velocity of the second wave differed significantly between normal and osteoporotic women, showing a mean reduction of 15% in osteoporotics. There are at least two possible explanations for the enhanced sensitivity of the second wave for
osteoporosis compared to the first wave. Firstly, it may be due to the greater sensitivity of
the velocity of the second wave to the thickness of the tibial cortex, compared to the first
arriving signal. Osteoporotics are likely to have a thinner tibial cortex than normals and
the second wave may better reflect this. The acrylic data (figure 4) show that the second
wave exhibits greater thickness sensitivity that the first arriving wave. Secondly, it may be
that the velocity of the second wave is more sensitive to the material properties throughout
the whole of the cortical thickness, rather than just the periosteal region, and thus captures
pathological changes that the first wave cannot.

Our study has some important limitations. The number of subjects in the in vivo study
was very small. The study was not blinded, and hence operator bias could potentially have
influenced the results. Further blinded studies with larger numbers are needed, and the studies
should be extended to investigate bone changes associated with other pathologies, and with
normal growth and ageing. The human tibia is neither an infinite plate nor a cylindrical tube,
but is rather an irregular hollow shell. It does not exist in a vacuum, but is surrounded by
tissue and is filled with bone marrow. All of these considerations have been neglected in this
initial study. Nevertheless, the Lamb wave theory appears to provide a satisfactory framework
to explain the behaviour we have observed. We suggest that when studied axially over the
relatively short distance scales used in this study (20–50 mm) under pulsed excitation, the tibia
can be approximated to a plate with relatively constant thickness. Previous work suggests that
the effects of fluid-loading tend to be modest, at least for the fundamental modes (Cheeke et al
1999), and the axial Lamb-like modes in a cylindrical tube are similar in behaviour to those
in a plate provided the wall thickness is small compared to the tube diameter (Graff 1991).
Bone is anisotropic (Hoffmeister et al 2000), and anisotropy affects Lamb wave behaviour
(Dayal and Kinra 1989, Li and Thompson 1990, Castaings and Hosten 2001). However, the
A0 mode, in contrast to other Lamb modes, has been shown to be relatively insensitive to
anisotropy (Li and Thompson 1990, Castaings and Hosten 2001).

Acrylic was used as a bone phantom in this study, but it has different acoustic properties
from bone. The longitudinal and shear velocities are approximately 30% lower than cortical
bone (the latter measured in the axial direction). The velocities of the Lamb A0 mode in
acrylic measured in our study (900–1300 m s$^{-1}$) were lower than that of soft tissue or water
(approximately 1500 m s$^{-1}$), and this should prevent the A0 wave from radiating from a water-
or tissue-loaded acrylic plate. Hence, acrylic may not be an appropriate bone phantom in
seeking to understand the role of the mediating tissue layer in guided wave excitation and
detection.

The numerical simulations and the phantom measurements used transducers in direct
contact with the solid, whereas a thin tissue layer was present in vivo. Hence, in vivo there
may be additional waves present in the received signals, including a directly transmitted
wave travelling through tissue alone, waves reflected from the bone surface, and, conceivably,
Stonely waves. Some of these waves can be expected to arrive at approximately the same
time as the A0 wave. The greater complexity of the in vivo $(r, t)$ plots compared to the acrylic
measurements (figure 5) is likely to be due to the presence of these additional waves, and
further work is needed to investigate the role of the tissue layer and to enhance discrimination
between specific guided waves and undesired signals.

We used a relatively crude method for exciting guided waves, namely excitation and
detection through low-frequency, small-diameter transducers placed in contact at normal
incidence. Under these conditions, the transducers behave as point-like omni-directional
sources or receivers, and our results suggest that it is overwhelmingly the A0 mode that
is preferentially excited. Selective guided mode can be achieved by using more directional
transducers and choosing specific frequency and incident angle combinations (Chimenti 1990).
Guided ultrasonic waves in long bones

There are many potential advantages in being able to use, selectively, a range of Lamb modes. Each mode has a unique mode shape and pattern of energy flow as a function of depth in the layer, implying that depth-specific information may be obtained. Information from different modes can also be used in inversion schemes for estimating the elastic constants and/or geometry of the structure under test.

In conclusion, we have demonstrated the feasibility of measuring ultrasonic guided waves in the tibia, and have obtained results suggesting enhanced sensitivity to osteoporosis compared to the current ultrasonic methodology based on the first arriving signal alone. Guided waves open up many novel opportunities for bone characterization and their utilization in this context is in its infancy.

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Publication II
Assessment of the tibia using ultrasonic guided waves in pubertal girls

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Abstract The purpose of this study was to compare low frequency ultrasonic guided wave measurements with established ultrasound and bone density measurements in terms of their ability to characterize the tibia in pubertal girls. Subjects were 12–14-year-old girls (n = 106) who were participating in a calcium and vitamin D intervention study. A prototype low frequency pulse transmission device consisting of a uniaxial scanning mechanism and low frequency transducers orientated perpendicularly to the limb was used to measure two ultrasound velocities in the tibia. The first velocity, V1, was that of the first arriving signal, similar to that measured by existing commercial tibial ultrasound devices. The second velocity, V2, was that of a slower wave propagating at 1,500–2,000 m/s, which has been shown elsewhere to be consistent with the lowest order antisymmetric guided mode in the bone. In addition, commercial ultrasound devices (Omnisense, Sunlight Ltd.; QUS-2, Quidel Corp.) were used to measure the speed of sound (SOS) in the tibia and the radius and attenuation (BUA) in the calcaneus. Cortical bone cross-sectional area (CSA), mineral density (BMD) and cortical thickness (cTh) of the tibia were measured using pQCT, site-matched to the ultrasound measurements. Both V1 and V2 correlated significantly with cortical BMD and with cTh and CSA. On the other hand, tibial SOS correlated with BMD, but not with cTh and CSA. These results indicate that the prototype device using guided waves captures aspects of tibial cortical bone geometry in addition to bone density, thereby potentially offering increased diagnostic information compared to existing tibial ultrasound devices.

Keywords Bone mineral density and cortical thickness · Tibia · Ultrasonic guided waves · Ultrasound velocities

Introduction

Osteoporosis is a serious and growing public health concern in many developed countries with aging populations [1, 2, 3]. Thus, the assessment of bone mechanical condition is a clinically important issue in the pre-emptive diagnosis of osteoporosis and the prediction of fracture risk [4].

In recent years quantitative ultrasound (QUS) measurements have become an attractive tool for assessment and management of osteoporosis [5]. In comparison to conventional X-ray-based peripheral bone densitometry, ultrasound has the potential to reflect bone elasticity, microarchitecture, geometry and mass density, whereas X-ray absorption is inherently limited to information about bone density and geometry alone. Ultrasound has a number of additional attractive features, including the absence of ionizing radiation and lower cost compared to many X-ray devices.

There are a number of QUS devices available for laboratory research and clinical use today. However, they vary considerably with respect to site-measured and physical principles adopted in the measurement itself [4]. In calcaneal QUS, broadband ultrasound attenuation (BUA) and speed of sound (SOS) are determined in calcaneal cancellous bone from ultrasound transmission measurements across the foot. Calcaneal QUS measurements are predictive of fracture risk in postmenopausal women and correlate with the strength of the...
proximal femur [6, 7, 8]. In contrast to calcaneal QUS, ultrasonic measurement of long bones has historically been achieved by transmitting ultrasound along, and not across, the limb [9, 10, 11, 12]. This so-called axial transmission technique [9] involves transducers placed perpendicularly to the limb and the transmission of an ultrasonic pulse along the long axis of the bone. The apparent velocity (often termed SOS) is determined from the transit time of the first arriving signal and the propagation distance. At least two commercial devices using this approach have been approved for use in clinical measurements [13]: the Soundscan 2000/Compact (Myriad Ultrasound Systems Ltd., Rehovot, Israel) and the Omnisense (Sunlight Medical Corp., Rehovot, Israel), of which only the latter is currently commercially available.

The in-vivo results from the tibia [14, 15, 16, 17, 18] indicate that the measured SOS correlates significantly with cortical bone mineral density (BMD) and to a lesser extent with BMD at other skeletal sites. In addition, a significant correlation between SOS and cortical bone elastic modulus has been established by in-vitro measurements [15]. However, tibial ultrasound is a poor discriminant of osteoporotic fracture [19] and is only weakly associated with femoral strength and BMD [4]. Experimental studies using bone phantoms demonstrate that, under certain conditions, the wave measured with the above approach propagates at the longitudinal (bulk) wave velocity [9]. However, there is also evidence indicating that the velocity decreases when the bone thickness is less than the acoustic wavelength of the propagating pulse [20, 21]. Nevertheless, the clinical results regarding thickness effects are inconclusive, which may be due to differences in the ultrasonic frequencies used by the different commercial systems or other methodological factors.

Diaphyseal cortical bone exists as an irregular tubular layer typically 3–8 mm thick in the human tibia. Solid layers support the propagation of guided waves—waves that arise from the reflection and mode conversion of longitudinal and shear waves at the boundaries of the layer [22, 23]. In a uniform solid plate these guided waves are called Lamb waves and have been the subject of extensive theoretical work and experimental investigation [24, 25, 26, 27]. The attraction of guided waves lies in the fact that their propagation characteristics reflect both the material and geometrical properties of the layer. Furthermore, it is generally possible to excite a number of different modes, or types, of guided wave in a given layer. Guided waves therefore potentially offer more diagnostic information than afforded by techniques based on using longitudinal or shear waves alone.

Recent preliminary studies [28, 29, 30] indicate that ultrasonic guided waves can be observed and measured in acrylic bone phantoms and in human cortical bone in vivo. In these studies, axial transmission measurements were made at low frequencies using a prototype device, and the velocities of two propagating waves were measured. The velocity of the faster wave was measured from the first arriving signal, as in the existing tibial ultrasound devices. In thick layers, the velocity of this wave was close to the longitudinal velocity, but velocity decreased with decreasing thickness towards that of a guided wave termed the Lamb S0 wave. This thickness-related velocity change has been reported in other studies [20, 21]. The slower wave had a velocity approximately half that of the faster wave, and its velocity decreased strongly with decreasing thickness, behavior that was consistent with another guided wave: the Lamb A0 wave. A small pilot study suggested that the velocity of the second wave was a more sensitive discriminate of osteoporosis than either tibial SOS (measured using a commercial device) or tibial cortical BMD (measured using pQCT).

Given the promising results obtained in the preliminary studies described above, the present study aimed to apply ultrasonic guided wave measurements in a large group of human subjects for the first time. To this end we investigated the performance of low frequency ultrasonic guided wave measurements of the tibia in pubertal girls. This was achieved by comparing the results obtained using the guided wave device to site-matched measurements of volumetric cortical BMD, cortical thickness (cTh), cortical cross-sectional area (cCSA) and tibia SOS, and also with measurements of radius SOS and calcaneal BUA.

Materials and methods

Subjects

The subjects were a hundred and six girls aged 12–14 years with Tanner stage II–V maturational status who were participating in an intervention study to evaluate the effects of calcium, vitamin D and milk product supplementation on the acquisition of bone mass during puberty [31]. Tanner stage was assessed by a public health nurse according to the pattern of development of pubic hair and breasts. All of the participants and their legal guardians provided informed consent in accordance with the Ethical Committees of the University of Jyväskylä, the Central Hospital of Central Finland and the Finnish National Agency of Medicines. The physical characteristics of the subjects were measured as described elsewhere [31].

Anthropometrical measurements

Height and weight were determined with the subjects wearing light clothing only and no shoes. Height was determined using a fixed wall scale. Weight was determined within 0.5 kg for each subject using an electronic scale, calibrated before each measurement session. Body mass index (BMI) was calculated as weight/height² (kg/m²).

Ultrasound assessments

Ultrasound velocity at the medial tibia mid-shaft was measured using a prototype low frequency QUS device (University of Jyväskylä, Finland). The system and measurement procedure have been described in more detail previously [30]. Briefly, the device
consisted of one transmitter and one receiver mounted in an automatic uniaxial scanning mechanism. Both transducers had a diameter of 5 mm and a center frequency of approximately 200 kHz. The transducers were set-up perpendicularly to the lower left limb in gel-coupled contact with the skin at a site two-thirds of the way up the tibia. The receiver was scanned in 0.75-mm steps along the tibia such that the transducer separation increased from 20 to 50 mm (Fig. 1). The response was recorded at 40 discrete distances during the scan. A gray-scale-mapped distance-time \((r,t)\) diagram was then produced from the recorded data [9, 28] (Fig. 1). An \((r,t)\) diagram allows the propagating wave packets to be visualized, and velocity may be determined simply by fitting lines to the wave packets and calculating the slopes. Such an approach is not affected by the soft tissue layer between the transducers and the tibia, provided that the thickness of the tissue layer can be assumed to be constant over the scanned distance [32]. A semi-automatic method was applied to determine the velocities of the first arriving wave (wave 1) and an additional slower wave (wave 2), with the resulting velocities termed \(V_1\) and \(V_2\), respectively. To determine \(V_1\), a linear fit was made to points on the rising edge of the first arriving signal at 25% of the amplitude of the first maxima. To determine \(V_2\), linear fits were applied over the corresponding successive maxima of the slower wave packet. One of the resulting lines was observed to cross the linear fit to wave 1 at approximately the origin of the \((r,t)\) diagram (Fig. 1). This line was assumed to represent a well-defined mode of ultrasound propagation, termed wave 2 in the following, and its corresponding velocity \(V_2\) was determined. In some cases a reliable assessment of \(V_2\) was difficult due to the small amplitude of the wave of interest and the presence of interfering waves, for example. These cases were noted to allow potentially unreliable results to be excluded at a later stage. The in vivo reproducibility, expressed as RMS coefficient of variation [33] of these measurements, as assessed by three repeated measurements in six different subjects, was 1.8% for \(V_1\) and 2.3% for \(V_2\).

In addition, a commercial QUS device, Omnisense (Sunlight Technologies, Rehovot, Israel), was used to measure the speed of sound (SOS) in the left radius (at a site one-third of the way up the radius) and tibia (at the same location at which \(V_1\) and \(V_2\) were recorded). Broadband ultrasound attenuation (BUA) was recorded from the calcaneus using the QUS-2 device (Quidel corporation, Santa Clara). In our experience, the in vivo reproducibility (RMS CV) of these techniques was 1.0, 0.9 and 1.5% for tibial SOS, radial SOS and calcaneal BUA, respectively.

Bone geometry and density assessments

Peripheral quantitative computed tomography (pQCT, Norland/Stratec XCT 2000, Stratec Medizintechnik, Pforzheim) was performed at the tibial midshaft at the site where the ultrasound assessments were also performed. The voxel size of the pQCT was 0.59 mm. Cortical volumetric bone mineral density (cBMD), cross-sectional area (cCSA) and cortical wall thickness (cTh) were determined from the pQCT scans using Bonalyse software (Geanie 2.0, Bonalyse Oy, Jyväskylä). Cortical thickness was obtained using a circular ring model (Norland/Stratec pQCT software), in which the tibial shaft was assumed to be an ideal cylinder with the same total cross-sectional area and medullary area as the real bone. Then, the difference between the outer and inner radius was taken to be the average whole cortical wall thickness.

Table 1 Anthropometrical characteristics of subjects \((n=106)\)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Range</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>13.4 (0.8)</td>
<td>12.0–15.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159 (7)</td>
<td>140–174</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>50 (11)</td>
<td>32–99</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>20 (4)</td>
<td>14–37</td>
</tr>
</tbody>
</table>

Table 2 Recorded variables in terms of the mean, standard deviation and range

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>(n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>(V_1) (m/s)</td>
<td>3,713 (182)</td>
<td>3,390–4,356</td>
<td>106</td>
</tr>
<tr>
<td>(V_2) (m/s)</td>
<td>1,720 (92)</td>
<td>1,542–1,978</td>
<td>106</td>
</tr>
<tr>
<td>SOS(_{\text{tibia}}) (m/s)</td>
<td>3,650 (114)</td>
<td>3,366–3,911</td>
<td>102</td>
</tr>
<tr>
<td>SOS(_{\text{radius}}) (m/s)</td>
<td>3,837 (97)</td>
<td>3,563–4,071</td>
<td>103</td>
</tr>
<tr>
<td>BUA (dB/MHz)</td>
<td>75 (11)</td>
<td>55–110</td>
<td>106</td>
</tr>
<tr>
<td>pQCT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cBMD (mg/cm(^3))</td>
<td>1,048 (39)</td>
<td>935–1,145</td>
<td>104</td>
</tr>
<tr>
<td>cCSA (mm(^2))</td>
<td>253 (31)</td>
<td>186–321</td>
<td>104</td>
</tr>
<tr>
<td>cTh (mm)</td>
<td>4.1 (0.4)</td>
<td>3.1–5.1</td>
<td>104</td>
</tr>
</tbody>
</table>

Fig. 1 A schematic diagram of the low-frequency scanning and measuring system. RF waveforms are mapped on gray-scale in a personal computer and \((r,t)\) diagrams are produced. The linear fits of wave 1 and wave 2 cross at the origin of the \((r,t)\) diagram and the corresponding velocities \(V_1\) and \(V_2\) are obtained as the slopes of the linear fits.

Statistical analysis

Univariate linear regression was performed to assess the associations of the measured variables. Pearson’s correlations of \(V_1\), \(V_2\), \(\text{SOS}_{\text{tibia}}\), \(\text{SOS}_{\text{radius}}\) and BUA with pQCT measurements were determined, and a \(P\) value less than 0.05 was considered statistically significant. A paired \(t\)-test was applied to test the difference be-
tween the V1 and SOS of the tibia. Forward stepwise multivariate linear regression models were used to determine which of the bone geometry, bone density and anthropometric variables contributed to the variation in ultrasound measurements. Multiple regression analysis was also used to test the ability of combinations of ultrasound measurements to predict particular bone properties. One-way ANOVA was used to compare QUS and pQCT results in different Tanner stages, and Tukey HSD was applied for multiple comparisons.

**Results**

The girls measured in this study had a mean age of 13.4 years (Table 1). The maturation status of the 106 girls was as follows: 28 at Tanner Stage II, 49 at Tanner Stage III and 29 at Tanner Stage ≥IV.
Table 2 provides the results of the QUS, bone density and bone geometry assessments. Two subjects were missing from the pQCT and SOS assessments. In addition, one radial and two tibial SOS measurements were failures. Mean tibial SOS was significantly lower \((P < 0.001)\) than V1, although the difference (approximately 60 m/s, or 1.5%) was relatively small. The second guided wave velocity, V2, was, on average, less than half the value of either V1 or tibial SOS.

Figure 2 depicts the measured ultrasound and pQCT variables by Tanner stage. V1 and V2 were significantly different between Tanner stages II and IV \((P < 0.001)\) for both), and between Tanner stages III and IV \((P = 0.006\) and \(P = 0.028\), respectively), whereas SOS\(_{\text{tibia}}\) differed significantly only between Tanner stages II and IV \((P = 0.020)\). BUA, cBMD and cTh were significantly different between all Tanner stages (II, III and IV), showing the same trends as V1 and V2.

Both V1 and V2 correlated significantly with cBMD and cTh (Table 3). In addition, V1 correlated with cCSA, and there was also a trend between V2 and cCSA \((r = 0.163, P = 0.097)\). SOS of the tibia and radius was significantly correlated with cBMD only. Calcaneal BUA was correlated with cBMD and, interestingly, with cTh and cCSA. V1 and V2 were also interrelated, and both V1 and V2 correlated with tibial and radial SOS, and with calcaneal BUA (Table 3).

Excluding those subjects for whom measurements of V2 were judged potentially unsatisfactory yielded a group of \(n = 82\). Repeating the regression analyses in this subset of the whole group yielded a pattern of relationships very similar to what was seen before (Fig. 3). However, the correlations with cTh were slightly improved to \(r = 0.31\) and \(r = 0.35\) for V1 and V2, respectively. Correlations between cCSA and V1 and V2 were also improved to \(r = 0.27\) and \(r = 0.26\) (both are significant), respectively.

In the stepwise multiple regression models for the subset \((n = 82)\), cBMD was a significant predictor for all of the ultrasound measurements, with the exception of BUA (Table 4). Cortical cross-sectional area was an independent predictor for V2 only, and we found that the combination of cCSA and cBMD could explain 22% \((P < 0.001)\) of the variance in V2. In addition, height and weight together in the model with cBMD could explain 49% \((P < 0.001)\) of the variance in SOS\(_{\text{tibia}}\).
Multiple regression was also used to test our hypothesis that V1 and V2 should reflect both bone thickness and bone material properties as captured by SOS\textsubscript{tibia}. To do this we used cTh and SOS\textsubscript{tibia} as independent variables, again in a forward stepwise fashion. We found that both V1 and V2 were predicted by a combination of cTh and SOS\textsubscript{tibia}, with a total \( r^2 \) for the models of 0.162 and 0.173, respectively.

Multiple regression models to determine optimal combinations of ultrasonic measurements to predict bone and anthropometric variables showed that 22\% \((P < 0.001)\) of the total variance in cTh was predicted by the combination of V2 and BUA, and 48\% \((P < 0.001)\) of the total variance in cBMD was explained by the model having SOS\textsubscript{tibia}, V2 and BUA as independent predictors. In addition, we found that BUA was a significant predictor for all of the included bone and anthropometric variables.

**Discussion**

This study represents the first full in vivo investigation of a new method for ultrasonic assessment of the tibia. Features distinguishing this method from existing devices are the use of low frequencies, the scanning of the receiving transducer and, most importantly, the ability to measure the velocities of two distinct propagating waves. The faster of these two waves measured with the prototype low frequency device had a velocity (V1) close to, but slightly higher than, the velocity measured using the Omnisense device (tibial SOS\textsubscript{tibia}), despite the fact that in both cases the wave measured was the first arriving signal. Data from bone phantom studies \cite{30, 21} and numerical simulations \cite{20} indicate that the velocity of the first arriving signal decreases when the acoustic wavelength is greater than the cortical thickness. Based on this, we would have expected V1 to be lower than tibial SOS, since the new device operated at lower frequencies (hence longer wavelengths) than the commercial system, but in fact the opposite trend was seen. One possible explanation for this is that differences in the method used to define the arrival of the propagating signal can have significant effects on the derived velocities \cite{20}, and such methodological effects may mask other underlying trends.

When looking at the results in different Tanner stage groups (Fig. 2), the pQCT results clearly reflected the expected growth-related increases associated with bone size and density with increasing Tanner stage. The same trend was observed in the ultrasound results V1, V2 and BUA, but the trend was much weaker or absent for the SOS measurements. This suggests that V1, V2 and BUA are more sensitive to bone changes in growing girls than are SOS measurements.

The results demonstrated that the velocity of the first arriving ultrasonic signal, as reflected in both the V1 and tibial SOS measurements, was related to cortical BMD. However, the correlation of V1 with cBMD was slightly lower than the corresponding correlation between SOS and cBMD. This could be due to the poorer in vivo precision of the new device compared to the Omnisense. The correlation with cBMD for both V1 and tibial SOS were lower than previously reported \cite{16}, which may reflect the subject group used in this study. Previous studies have generally investigated adults, whereas we have studied prepubertal girls with a narrow age range. Consequently, the variation in bone properties within our subject group may have been more limited, reducing the strength of the correlations.

### Table 4

Stepwise multiple regression models for predicting ultrasound and bone properties \((n = 82, \text{unsatisfactory results excluded})\)

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Predictors</th>
<th>Total ( r^2 )</th>
<th>Beta</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Models predicting ultrasound measurements*</td>
<td>cBMD</td>
<td>0.151</td>
<td>0.388</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>V1</td>
<td>cBMD</td>
<td>0.225</td>
<td>0.388</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>V2</td>
<td>cCSA</td>
<td>0.208</td>
<td>0.044</td>
<td></td>
</tr>
<tr>
<td>SOS\textsubscript{tibia}</td>
<td>cBMD</td>
<td>0.489</td>
<td>0.508</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ht</td>
<td>BUA</td>
<td>0.434</td>
<td>0.434</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wt</td>
<td>-0.472</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOS\textsubscript{radius}</td>
<td>cBMD</td>
<td>0.153</td>
<td>0.391</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BUA</td>
<td>Wt</td>
<td>0.487</td>
<td>0.044</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>b. Models predicting bone and anthropometric properties**</th>
<th>cTh</th>
<th>V2</th>
<th>0.221</th>
<th>0.271</th>
<th>0.013</th>
</tr>
</thead>
<tbody>
<tr>
<td>V1</td>
<td>BUA</td>
<td>0.315</td>
<td>0.004</td>
<td></td>
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</tr>
<tr>
<td>cCSA</td>
<td>BUA</td>
<td>0.188</td>
<td>0.434</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>cBMD</td>
<td>V2</td>
<td>0.486</td>
<td>0.239</td>
<td>0.010</td>
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</tr>
<tr>
<td>SOS\textsubscript{tibia}</td>
<td>BUA</td>
<td>0.327</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ht</td>
<td>SOS\textsubscript{tibia}</td>
<td>0.208</td>
<td>0.379</td>
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<tr>
<td>Wt</td>
<td>BUA</td>
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<td>0.11</td>
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<td></td>
</tr>
<tr>
<td>V2</td>
<td>BUA</td>
<td>0.222</td>
<td>0.236</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>BUA</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The independent variables used were cTh, cCSA, cBMD and body height (Ht) and weight (Wt).

**The independent variables used were V1, V2, SOS\textsubscript{tibia}, SOS\textsubscript{radius} and BUA.
Using simple linear regression, $\text{SOS}_{\text{tibia}}$ measured with the Omnisense did not correlate with cortical thickness and cross-sectional area, but V1 did. This can be explained by considering that, as discussed earlier, a thickness-related velocity decrease can be expected only when the wavelength is greater than the thickness [20]. The Omnisense operates at 1.25 MHz, corresponding to a wavelength of approximately 3 mm in bone, whereas the new device operating at approximately 200 kHz produces wavelengths of typically 20 mm. The cortical thickness in our subject group ranged from 3 to 5 mm, and hence the ability to reflect thickness was restricted to the low frequency device.

The new ultrasound device measured the velocity of a second, slower wave (V2), which earlier studies [28, 29, 30] have indicated to be consistent with the fundamental antisymmetric guided wave (also known as the Lamb A0 wave). This type of guided wave is essentially a flexural wave, and its velocity is predicted to be strongly dependent on the thickness. The excitation and measurement of this wave in pubertal girls extends our original observations in a pilot study of elderly women and suggests that this type of measurement may be applicable across diverse patient groups. A correlation between V2 and cortical thickness (cTh) was indeed observed in the data, in agreement with theoretical expectations. The correlation with thickness was stronger for V2 than for V1, although this difference was very small and not statistically significant. Our earlier studies have shown a more profound thickness effect for V2 compared to V1 in acrylic bone phantoms [30], but an in vivo confirmation of this trend must await further data. In addition, V2 correlated with cBMD, which was again expected since the velocity of guided waves depends on material properties (as represented by cBMD) in addition to thickness.

The results from the multiple regression analyses indicated, not unexpectedly, that cortical BMD was an independent predictor of all site-matched ultrasound measurements. However, an independent relationship with cortical bone cross-sectional area was observed only for V2. This agrees with our expectations that the cortical bone growth is more strongly related to guided wave velocity V2 than to any other velocities discussed here.

In addition, multiple regression results supported our hypothesis that V1 and V2 reflect both cortical bone material properties (as captured by $\text{SOS}_{\text{tibia}}$) and cortical thickness, though we should note that the total variance in V1 or V2 explained by a combination of $\text{SOS}_{\text{tibia}}$ and cTh was less than 20%. Consistently, multiple regression results to determine optimal combinations of ultrasonic measurements to predict bone variables indicated that V2 indeed predicts aspects of both the bone cortical thickness and cBMD.

Heel BUA correlated more strongly with tibial cortical thickness and cross-sectional area than did V1 or V2. This suggests that the new tibial ultrasound measurement provides less reliable estimates of tibial geometry than does an established method measuring at a different skeletal location. However, BUA is not adjusted for heel thickness, and so reflects bone size as well as bone material properties. Tibial cortical thickness and area clearly reflect bone size, too, and hence a correlation between these variables and BUA is not unexpected. The significant correlations between V1 and V2 on the one hand and cTh and cCSA on the other indicate the ability of the new method to capture aspects of tibial geometry, but do not necessarily represent the full potential of the new measurement approach, for reasons that are discussed below.

This work was subject to a number of limitations. The ultrasonic guided wave measurements were made using a prototype device that has not been optimized or fully validated for clinical use. Indeed, this technology is still under development. The reproducibility of the new device was poorer than the commercial tibial ultrasonometers. Nevertheless, we felt that the promising initial results with this approach [29, 29, 30] justified a rapid larger scale in vivo evaluation as described in this present work. It is important to note that in some subjects there were difficulties in making measurements of the second wave with the new device, and 22% of the measurements were judged potentially unreliable. Clearly, this needs to be addressed if the method is to be clinically useful. One important factor is the role of the soft tissue overlying the bone, which may impede the excitation and detection of the second wave in bone. Ultrasound velocity in tissue (approximately 1,500 m/s) is close to that of the second wave in bone (1,542–1,978 m/s in this study), so that signals propagating through tissue could be mistaken for a second wave in bone. We are engaged in studies to clarify these questions and improve our methodology and analysis techniques. For example, recently we have applied a more advanced analysis approach (not described here) to the data acquired in this study, allowing us to identify a sub-group of n = 38 in whom the second wave can be identified unambiguously as a Lamb A0 wave propagating in bone. In this sub-group the correlation between V2 and cTh was $r = 0.494$, and between V2 and cBMD was $r = 0.652$, substantially higher than reported here. This demonstrates that while the associations reported in this present study are generally weak, improvements with regard to the performance of the low frequency ultrasound technique can be expected.

The partial volume effect could be a source of error in the BMD measurements. However, this would have tended to introduce a systematic error in BMD estimations and would therefore not have affected the correlations between BMD and other variables.

In this study, cortical thickness was an average measured for the whole cross-section rather than locally in the bone region directly under the ultrasound transducers. Our reasoning for doing this was that our prototype device used low ultrasonic frequencies (long wavelengths) and is therefore likely to be more sensitive to average rather than local cortical thickness.
In summary, the results reported here indicate that velocities measured using a prototype ultrasonic guided wave device in prepubertal girls correlate with cortical geometry. This supports the hypothesis that guided wave measurements can offer increased diagnostic information compared to existing tibial ultrasound measurements.

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References

Publication III
THICKNESS SENSITIVITY OF ULTRASOUND VELOCITY IN LONG BONE PHANTOMS

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Abstract—One approach to bone disease diagnosis such as osteoporosis is to measure the velocity of ultrasound propagating axially along long bones. In this study, the variation in velocity as a function of radial position was assessed using two polyvinyl chloride (PVC) bone phantoms with cross-sectional geometry similar to the human tibia but differing in medullary cavity diameter. Two ultrasonometers were used; these were a commercial device operating at a relatively high frequency (HF) of 1.25 MHz and a prototype low frequency (LF) device operating at approximately 200 kHz. The LF measurements showed a larger variation with radial position, with changes in velocity of up to 20% occurring around the phantom compared with changes of only 4% at most for HF. The LF velocity correlated strongly with local thickness ($r^2 = 0.81$) but HF velocity did not. The results demonstrate that LF measurements have a greatly enhanced thickness sensitivity. Using LF, it may therefore be possible to assess bone thickness as a function of radial position and hence to determine the distribution of bone around the long axis. (E-mail: pemoilan@cc.jyu.fi) © 2004 World Federation for Ultrasound in Medicine & Biology.

Key Words: Axial transmission, Bone, Cortical thickness, Osteoporosis, Phantom, Tibia.

INTRODUCTION AND LITERATURE

The axial transmission technique for determining the velocity of ultrasound along a long bone was first described over four decades ago in the context of fracture healing (Siegel et al. 1958, Gerlanc et al. 1975). With this method, two or more transducers are placed at the limb surface over a bone and signals are transmitted along the bone. The velocity of the first arriving signal is determined knowing the transit time and the distance between the transducers. Attempts to reduce errors associated with overlying soft tissue have included multiple transmitter/receiver schemes (Saulgozis et al. 1996, Bossy et al. 2004a) and methods in which receiver and transmitter are moved relative to each other (Lowet and Van der Perre 1996). The axial transmission method has been used in at least two commercial bone ultrasonometers, although only the Omnisense (Sunlight Medical Ltd., Tel Aviv, Israel) is currently available (Hans et al. 1999).

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A satisfactory description of the physical basis of the method has only emerged recently. Camus et al. (2000) demonstrated that, when the wavelength is less than the bone thickness, the measured wave corresponds to a so-called “lateral” (or “head”) wave propagating at the longitudinal velocity for bone. When the wavelength is comparable or greater than the thickness, a more complex situation ensues and the first arriving wave is made up of contributions from reflected waves and/or guided waves, yielding an apparent velocity lower than the longitudinal velocity (Bossy et al. 2002). This trend for a decrease in velocity when thickness is below a certain threshold value has been reported both in experimental studies of simple bone phantoms and animal bones (Njeh et al. 1999) and in numerical simulations of wave propagation (Bossy et al. 2002, Bossy et al. 2004b, Nicholson et al. 2002). Clinical data also support the idea of a relationship between tibial axial transmission velocity and bone thickness (Prevrhal et al. 2001).

Whilst previous work has confirmed that thickness can influence the velocity measured axially along the bone, it remains unclear how these effects are likely to manifest in practice or whether they could be of use diagnostically. Bones are complex 3-D objects in which cortical thickness is not constant but varies with radial...
position and axial position. This current study therefore aimed to assess thickness effects on axial ultrasound velocity in anatomically representative bone phantoms manufactured from PVC. Since the ratio of wavelength to thickness is an important factor, the study used two different ultrasonic devices operating at different frequencies.

MATERIALS AND METHODS

Two bone phantoms were manufactured from PVC. These phantoms were tubular structures with a circular central hole and an outer cross-sectional profile chosen to mimic that of the human tibia. A “thick” and “thin” phantom were manufactured, having medullary canal diameters of 15 and 19 mm, respectively. The cross-sectional profiles of the two phantoms are shown in Figure 1. A series of 10 measurement sites were marked around each phantom (Fig. 1). At each measurement site, the thickness of the phantoms along a line normal to the surface of the inner circle was measured using calipers three times and the mean value taken. In the “thick” phantom local thickness determined in this way varied from 5.2 to 13.3 mm and, in the “thin” phantom, it varied from 2.6 to 10.2 mm.

Ultrasonic velocity measurements using the axial transmission technique were made using two devices. High frequency (HF) measurements were made using a commercial bone ultrasoundometer, the Omnisense (Sunlight Medical Ltd., Tel Aviv, Israel), which operates at a nominal center frequency of 1.25 MHz. Transducers were mounted inside a single handheld probe. In clinical measurements, the probe is coupled to the skin using gel and the probe is scanned manually at a chosen anatomical site perpendicularly to the long axis of the bone. Axial transmission velocity is calculated using proprietary algorithms and it is claimed that the effects of overlying soft tissue are accounted for. For measuring the phantoms, the so-called “CS” probe, usually used for clinical measurements on the phalanges, was used. This probe was used because the larger probes failed to give a velocity measurement in some cases with these phantoms. The bone phantoms were measured by holding the phantom at one end using a laboratory clamp, applying gel to the chosen site and applying the probe to that site. Unlike clinical measurements, the probe was not moved during the measurement.

Low frequency (LF) ultrasonic velocity measurements were made using a prototype axial transmission device that has been described elsewhere (Nicholson et al. 2002). Briefly, it consisted of a pair of LF transducers (center frequency approximately 200 kHz, diameter 5 mm) mounted perpendicularly to the long axis of the bone phantom. The transducers were coupled to the bone phantoms using gel. The transmitter was driven by a commercial pulse generator (model 5077, Panametrics Inc., Waltham, MA), and ultrasonic pulses were propagated from transmitter to receiver. The receiver was moved progressively away from the transmitter, along the long axis of the bone phantom, under computer control, and the received signals were amplified and digitized. The digitized signals were analyzed as grey-scale plots of amplitude as a function of time (t) and transmitter-receiver distance (r), (so-called “r,t diagrams”), allowing the first arriving wave to be visualized. The velocity of this wave was determined by automatically fitting a line to the first zero-crossing points of this wavefront.

For each of the 10 locations around each phantom, three repeated measurements were made with each device and the means and standard deviations were calculated. This mean was taken as the velocity value for that location. The variation in velocity with location in each phantom was expressed as a percentage as (100 * (MaxV–MinV)/MeanV), where MaxV was the maximum velocity and MinV was the minimum velocity and MeanV was the overall mean velocity. Linear regression analysis was used to investigate the relationship between local thickness and velocity.

RESULTS

In both the thick and thin bone phantoms, the LF velocity measurements varied much more around the phantom than did the HF measurements (Fig. 2). Minimum velocities were seen for sites 4 to 8, where the local thickness of the phantoms was also a minimum (Fig. 1). The variation in velocity around the “thick” phantom was 2.2 and 17.1% for HF and LF measurements, re-
spectively. The corresponding values for the velocity variation around the “thin” phantom were 4.0 and 21.4%, respectively. The HF measurements did not correlate significantly with local thickness (Fig. 3). On the other hand, LF measurements were strongly correlated linearly with local thickness ($r^2 = 0.81$, $p < 0.001$) (Fig. 3).

A different perspective on the relationship between velocity and thickness was obtained by calculating the ratio of the acoustic wavelength, $\lambda$, to local thickness, $d$. The wavelength was calculated as $\lambda = c/f$, where $c$ was the measured velocity and $f$ was the frequency (1.25 MHz for HF and 200 kHz for LF). Plotting velocity as a function of $d/\lambda$ demonstrated that thickness effects only occurred when the thickness was comparable with or less than the wavelength (Fig. 4).

Discussion and Summary

Previous studies of the relationship between bone thickness and axial transmission ultrasound velocity have been limited to experimental measurements of bone phantoms with simple plate or tube geometries (Njeh et al. 1999) or numerical simulations using 2-D and 3-D...
measurements were not (Figs. 2 and 3). This agreed with measurements were sensitive to local thickness, but HF results of this present study demonstrated that LF velocity fundamental behavior due to cortical thickness. The re-

porosity of cortical bone have an impact on ultrasound velocity, but these effects do not change completely the fundamental behavior due to cortical thickness. The results of this present study demonstrated that LF velocity measurements were sensitive to local thickness, but HF measurements were not (Figs. 2 and 3). This agreed with earlier experimental and theoretical work indicating that thickness effects are expected only when the thickness is comparable with, or less than, the wavelength in bone (Njeh et al. 1999, Bossy et al. 2002) (Fig. 4). When \( \lambda_{\text{bone}} \) is less than thickness, and using the appropriate transmitter-receiver distance, the first-arriving signal represents a lateral or head wave propagating at the bulk velocity in bone and thickness has no impact on velocity (Camus et al. 2000, Bossy et al. 2002). When \( \lambda_{\text{bone}} \) is of the same order or greater than the bone thickness, the first-arriving signal no longer represents a lateral wave, but arises from a combination of reflected waves and/or plate modes (Bossy et al. 2002) and the apparent velocity decreases.

In vivo studies support the idea that low frequency ultrasound velocity measurements are sensitive to bone thickness. Prevrhal et al. (2001) measured velocity in the tibia using a commercial device operating at 250 kHz and found a correlation between velocity and thickness, whereas Sievanen et al. (2001), using a higher frequency device (as used in this current study), found no correlation in the tibia and only a modest correlation in the radius.

Looking more closely at our results from the HF device, there was, in fact, some evidence for a relationship between thickness and velocity, even though this was not apparent in the correlation results for the pooled data from all 10 radial measurement positions in the two phantoms. At measurement site 1, located on the tibial ridge (Fig. 1), the lowest HF velocity measurements were recorded (Fig. 2), but the local thickness was actually greatest here. This anomaly, that stands in contradic-
tion to the other results given here, may be explained by considering that the sharp ridge is locally thin when considering the “tangential” direction. It can be seen as, in effect, a side-on measurement of a thin plate. In general, it may be that the HF device is affected by the rapidly changing surface geometry at this particular site and that the measurement is unreliable on such sharply curved surfaces. Excluding the velocity measurements for this site resulted in a significant positive correlation between thickness and velocity \( (r^2 = 0.41, p < 0.001) \).

It should be noted that the frequency quoted for the LF ultrasound system (200 kHz) is an approximate value, since the transducers had a bandwidth extending from 50 kHz to approximately 300 kHz. Similarly, the quoted frequency of the commercial HF device (1.25 MHz) is simply the nominal central frequency quoted by the manufacturer. For both devices, the effective frequency may vary from measurement to measurement, dependent on the attenuation and coupling conditions.

Measurement reproducibility was much poorer for the LF device compared with the commercial HF device, as can be seen by the relatively large standard deviation error bars in Figure 2. The HF device calculates velocity based on several hundred sequential measurements and has been optimised for maximum reproducibility in vivo. The relatively poor reproducibility of the LF device is due to a number of reasons. The main reason is that the LF device is designed to measure both the first-arriving signal and the higher amplitude, but slower, flexural wave (not dealt with in this present study). Conse-

qently, the full dynamic range is not used in recording the first arriving signal. Also, the transducers are orien-
tated normal to the surface to maximize excitation of the flexural wave, but better excitation of the first arriving longitudinal wave would be expected if the transducers were angled, as in the HF device. In addition, precision in determining time-of-flight for the LF device is ex-
pected to be worse than that of the HF device, simply because of to the longer wavelengths employed.

The velocity of longitudinal waves in PVC (approximately 2400 m/s) is lower than that for cortical bone (approximately 4000 m/s). The higher velocity in bone means that wavelengths in bone will be longer and this means that thickness effects will tend to be more pronounced than those observed here. For example, with the HF device, velocity reduction begins in PVC when the thickness is 1.9 mm or lower, whereas, for bone, we would expect the corresponding critical thickness to be approximately 3.2 mm. According to in vivo peripheral quantitative computed tomography (pQCT) measurements in postmenopausal women (Sievänen et al. 2001), the cortical thickness of the human tibia ranged from 2.1 mm to 5.4 mm (mean 3.6 mm). The corresponding figures for the radius were 1.6 to 3.6 mm (mean 2.6 mm). Using a slightly different approach to cortical thickness measurement, Prevrhal et al. (2001) reported a significant reduction in tibial cortical thickness in postmenopausal women with fractures compared to premenopausal women \((5.1 \pm 0.7 \text{ mm versus } 6.1 \pm 0.6 \text{ mm}, p < 0.001)\). Based on these data, our results suggest that HF
measurements should reflect cortical thickness in the radius in the majority of subjects, but will only do so at the tibia for those subjects with relatively thin cortex. On the other hand, LF measurements should be sensitive to thickness for all subjects at both radius and tibia.

It should be noted that the commercial HF device may be accurate, precise and clinically useful, even if it is not sensitive to changes in cortical thickness seen in vivo. Indeed, this device may have been designed to minimize thickness effects and, therefore, to provide information mainly on bone material properties without the confounding effects of cortical thickness.

The results show that LF velocity measured at different radial positions reflects the variation in local bone thickness. This represents a potential source of error in single site measurements, since, if the radial position of the measurement site is not accurately controlled, then repeated measurements may vary due to measuring at slightly different positions with differing local thicknesses. In the commercial HF device, this problem is addressed by scanning the probe by hand back and forth at the selected site, with the software seeking the highest values using a proprietary algorithm. On the other hand, the thickness sensitivity of LF velocity measurements could possibly form the basis of a noninvasive clinical technique for determining the cross-sectional profile of a bone, which is information usually obtained via techniques such as X-ray computed tomography. However, to do this, it would be necessary to make low frequency axial transmission measurements at many points around the bone using transducers at the limb surface and it is difficult to see how this could be achieved with the current technology.

This study did not consider the effects of the underlying soft tissue on the ultrasound results, although it is an important factor in the clinical application. Camus et al. (2000) demonstrated that the soft tissue must be thin enough compared with the axial distance between the emitter and receiver to provide the fastest propagation path via bone. Secondly, the soft tissue thickness must be fairly constant over the scanning range, to obtain valid velocities. However, a gradual change in the soft tissue thickness can be successfully eliminated using so-called bidirectional measurement (Bossy et al. 2004a). In addition, the soft tissue attenuates the signal slightly but also it provides a fairly good coupling medium. Thus, the results given for the free bone phantom can be applied to the clinical bone measurement, provided that the two different soft tissue thickness conditions are satisfied or under control.

For simplicity, this study only considered the fastest first-arriving signal, ignoring the potential of the flexural guided waves that can also be measured using the same LF device. These flexural waves have been shown to correspond to the fundamental antisymmetric (A0) Lamb waves and to yield velocities strongly related to cortical thickness (Nicholson et al. 2002, Moilanen et al. 2003). Combining measurements of these two types of wave in a single multimode ultrasound measurement could potentially yield increased diagnostic power.

Whilst LF measurements are more sensitive to bone thickness, HF measurements reflect primarily the longitudinal ultrasound velocity in the solid which is, in turn, indicative of bone material properties. Multifrequency measurements could, therefore, result in an improved clinical measurement, capable of differentiating between material and geometrical bone changes.

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REFERENCES


Publication IV
COMPARISON OF THREE ULTRASONIC AXIAL TRANSMISSION METHODS FOR BONE ASSESSMENT

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Short title:
Ultrasonic assessment of bone
COMPARISON OF THREE ULTRASONIC AXIAL TRANSMISSION METHODS FOR BONE ASSESSMENT

Abstract

This study compared three approaches to bone assessment using ultrasonic axial transmission. Velocity $V$ of the first arriving signal was measured with a commercial device ($V_1$, Sunlight Omnisense$^\text{TM}$) operating at 1.25 MHz, a prototype based on 1MHz bi-directional axial transmission ($V_2$) and a low frequency (200 kHz) prototype ($V_3$), also measuring the velocity of a slower wave ($V_4$). Bone properties were determined by peripheral Quantitative Computed Tomography. Significant but modest correlation between velocities reflects differences in the nature of the propagating waves and methodological differences. Of the higher frequency devices, the bidirectional measurements provided stronger correlations with bone properties than conventional measurements. High-frequency devices were less sensitive to cortical thickness than the low-frequency device because high-frequency waves interrogates a thinner cortical layer than low-frequency waves. The results suggest that different axial transmission approaches reflect different bone properties. Therefore, a multi-frequency technique might be useful in probing different bone properties.

Keywords: cortical bone, ultrasound axial transmission, in vitro, bone properties
Introduction

In recent years, quantitative ultrasound (QUS) has proved a useful technique for the assessment of bone fragility and osteoporosis. The ability of QUS to discriminate osteoporotic patients from healthy patients and fractured from non-fractured subjects has been demonstrated in several studies (Frost et al. 2002, Hans et al. 2003, Njeh et al. 1997). Portable, inexpensive, ionising radiation-free, and clinically validated, QUS is now playing a role as a diagnostic tool in the detection of osteoporosis. The propagation characteristics of ultrasonic waves through bone are related to bone mechanical properties (elastic coefficients) as well as to other bone characteristics, such as density and macro- or micro-architecture, which are themselves associated with biomechanical properties. Because all these characteristics are important determinants of bone fragility, QUS is generally considered as being a promising tool for the assessment of bone material and structural properties in addition to bone mass (Chaffai et al. 2002).

The axial transmission technique has been specifically designed for the assessment of cortical bone. It has been applied to the measurement of different skeletal sites such as the radius, tibia, metatarsus, and finger phalanges (Bossy et al. 2004c, Moilanen et al. 2003, Nicholson et al. 2002, Njeh et al. 2000). The generic term “axial transmission technique” indicates a measurement configuration in which emitters and receivers are placed on the same side of the skeletal site, along the bone axis, and the speed of sound (SOS) is determined for an ultrasonic signal transmitted along the cortex. The first commercially-produced axial transmission device for bone measured SOS used a 250 kHz pulse transmitted along the cortical layer of the mid tibia (Foldes et al. 1995b). A later commercial system, the Sunlight Omnisense™, operates at 1.25 MHz and can measure the distal one-third radius site, and potentially other skeletal sites including the ulna, finger phalanges, metacarpal or metatarsus. With this device, multisite axial transmission has been proposed as the direct successor to tibial axial transmission (Barkmann et al. 2000, Hans et al. 1999). Bossy and colleagues have developed a bi-directional axial transmission probe (1 MHz) in which an ultrasonic pulse is transmitted along the bone surface in two opposite directions from two sources placed at both ends of a unique group of receivers (Bossy et al. 2004a). A simple combination of the time delays derived from waves propagating in opposite directions efficiently corrects automatically for soft tissue.
In the approaches described above, the time-of-flight of the first arriving signal is measured and used to calculate velocity. Other axial transmission devices have been developed based on a different approach, which is to use low frequencies and, in some cases, special transducers or coupling conditions, in order to excite and measure surface or guided waves propagating in the bone at relatively low velocities. These waves arrive, in general, after the first arriving signal. One such device uses 200 kHz broadband transducers (Nicholson et al. 2002) and another uses specially-designed 110 kHz needle transducers (Lefebvre et al. 2002). In general, several modes propagate but the first antisymmetric mode \( (A_0) \) (plate mode in a simple plate theory) tends to dominate the received signal and its velocity is measured (Nicholson et al. 2002). Considering that velocity measurements on tubular cortical shells agree closely with those measured on cortical plates of equal thickness (Bossy et al. 2004b), plate theory terminology has been adopted for the purposes of this study, as in earlier studies.

Although all axial transmission approaches are based on the same basic measurement principles, different waves may contribute to the measured signal. For example at 1.25 MHz, different waves may contribute to the fastest part of the signal depending on the ratio \( d/\lambda \), \( d \) being the cortical thickness and \( \lambda \) being the wavelength. Compressional waves propagating in cortical bone at \( \sim 4000 \text{ m/s} \) have a wavelength \( \lambda \sim 3.2 \text{ mm} \). If \( \lambda \ll d \), the fastest signal corresponds to a lateral wave (Camus et al. 2000), guided by the interface between bone and soft tissue, emitted from the surface at the critical angle and propagating at the bulk wave velocity. On the other hand, for \( \lambda > d \), the velocity measured is lower than the longitudinal velocity, and tends towards that expected for the \( S_0 \) wave (first symmetric plate mode) (Bossy et al. 2002, Njeh et al. 1999). In contrast, with the device using 200 kHz waves with \( \lambda \sim 20 \text{ mm} \), which is much larger than the tibial cortical thickness, the \( S_0 \) mode should always arrive first. In other approaches, the \( A_0 \) mode is preferentially measured resulting in much lower velocity. This emphasizes the necessity to carefully consider the experimental conditions in order to correctly interpret the data. To our knowledge, there is no report on the comparison of different axial transmission techniques. This is the reason why the objective of this study was to compare three different approaches using ultrasonic axial transmission in vitro.

Ultrasound measurements were performed on a set of human radii, using three different devices: a commercial ultrasound device (Omnisense™, Sunlight Ltd, Rehovot, Israel) measuring the first arriving signal at 1.25 MHz; a prototype measuring the first arriving signal using bidirectional axial transmission at 1MHz (Laboratoire d’Imagerie Paramétrique, Paris, France); and a low frequency prototype (200kHz)
device (Department of Health Sciences, University of Jyväskylä, Finland) measuring the velocity of both the first arriving signal and a slower guided wave. All the velocity estimates were compared and related to site-matched material and structural properties of bone, obtained by peripheral quantitative computed tomography (pQCT). The ability of the three devices to reflect bone properties was then compared.

Materials and Methods

Specimens

Forty one fresh human radii obtained from cadavers (17 female and 24 male donors, of mean age 73 years, SD=10 yrs, range 45 – 90 yrs) were assessed in this study. Soft tissue was removed and the fresh specimens were kept frozen at –20°C between measurement sessions. Specimens were shipped between Finland and France on dry ice. Prior to measurements, specimens were thawed overnight and were then measured at room temperature. Ultrasound velocities were measured by the three devices at a region of interest corresponding to 45% of the radius length from the distal end, close to the “1/3 distal radius” region used clinically (Fig. 1). The location was marked on the bone using permanent ink providing a fixed point to which all subsequent measurements were site-matched. It should be noted that, as part of a previous study (Bossy et al. 2004c), the distal part of the radius, corresponding to the distal 30%, was removed by a single cut across the shaft (Fig.1). In terms of circumferential position, measurements were made on the postero-lateral aspect of the bone (Fig.2), corresponding approximately to the location usually measured in vivo at the distal radius using the axial transmission technique.

Devices

Both high frequency devices basically exploit the same propagation phenomenon. A probe contains a set of transmitters and receivers. The probe is placed in contact with the cortical surface (or the skin surface in clinical measurements). A water-based gel is used for obtaining an ultrasonic coupling between the probe and the specimen. The measurement consists of transmitting an ultrasonic pulse from a transmitter and recording the signal radiated from the cortical bone surface using receivers. The propagation has been described in depth in several recent studies (Bossy et al. 2004c, Camus et al. 2000, Nicholson et al. 2002). When the incident wave impinges on cortical bone at a certain angle, a part of the incident wave will be reflected directly and a part of it will excite either a lateral wave, or guided modes or other surface acoustic waves, depending on experimental conditions (e.g. incidence angle, values of critical angles,
ratio of wavelength in bone to cortical thickness). Guided modes, or surface acoustic waves, propagate through bone or along its surface, but reradiate a wave in soft tissue provided their velocity in bone is greater than the longitudinal velocity in soft tissue. Therefore, several types of waves potentially contribute to the total pressure field sensed by the receiver. The nature of the first arriving signal is determined by the ratio of wavelength in bone to cortical thickness and the geometrical arrangement of the transducers (Bossy et al. 2002). Speed of sound is derived from the time of flight of the first arriving signal.

The Sunlight Omnisense ™ operates at 1.25 MHz and uses a proprietary probe containing several ultrasonic transmitters and receivers. To increase the amplitude of the transmitted and received signals, the transducers are mounted at an angle close to the critical angle relative to the surface of the probe. The exact transducer arrangement and algorithm used to determine time of flight remain undisclosed, but the manufacturer claims that the device is able to correct for effects of varying soft tissue thickness in vivo. The precision of this device in our hands is better than 0.5%. For this study, the so-called Omnisense “CS” probe was used, which is approximately 25mm long. The axial transmission velocity measured using the Omnisense was termed $V_1$.

Bi-directional axial transmission measurements of velocity ($V_2$) were made using a prototype device that has been described elsewhere (Bossy et al. 2004a). This device operates at 1MHz and is composed of a linear array of transducers, with two emitters placed at either end of a single group of 14 receivers. The bidirectional feature of the transmission allows an automatic compensation for soft tissue and for probe inclination with respect to bone surface (Bossy et al. 2004c, Bossy E. 2004). The velocity $V_2$ is that of the first arriving signal and is derived from the inverse slope of the time-of-flight measured on the 14 consecutive receivers as a function of the source-receiver distance. The time-of-flight here was defined as the arrival time of the maximum of the first detectable peak above noise. With this device, SOS is measured along a 1 cm fixed longitudinal distance (Bossy et al. 2004c). In our hand, the precision, assessed by measuring 3 times 10 specimens with intermediate repositioning of the probe resulted in a standard error of 20 m/s and a mean coefficient of variation of 0.4%.
Velocity measurements were also made using a prototype low frequency axial transmission device with a pair of custom-made unfocused contact transducers with a centre frequency of approximately 200kHz (Nicholson et al. 2002). The transmitter was excited using a short pulse, and the bandwidth of the acoustic signal was approximately 50 to 350 kHz (at -16 dB). The receiver was moved progressively away from the transmitter in steps, and the ultrasonic signal was recorded at discrete locations along a 3 cm axial scanning range. The recorded signals were stored as a distance-time matrix, which was used for determining the velocities of two distinct waves: the first arriving wave and a slower guided wave corresponding to the fundamental antisymmetric (A0) plate mode in the cortical layer. The velocity ($V_3$) of the first arriving wave was determined from time-of-flight as a function of receiver position, with time-of-flight defined using a 25% threshold of the amplitude of the first detectable peak. The velocity ($V_4$) of the A0 guided wave was determined by applying a strong band-pass filter with a centre frequency of 100 kHz, determining the time-of-flight for the slower wavefront using a zero-crossing method, and then calculating velocity, as before, from a linear fit to the time-of-flight data as a function of receiver distance. Precision was assessed by 3 repeat measurements in the 41 specimens, and resulted in standard errors of 140 m/s and 36 m/s and mean coefficients of variation of 3.8% and 2.7% for $V_3$ and $V_4$ respectively.

Assessment of bone properties

Cortical and trabecular bone mineral density (cort.BMD, trab.BMD), cross-sectional area (CSA) and cortical thickness (cort.Th) were measured by peripheral quantitative computed tomography (pQCT) (Norland/Stratec XCT 2000, Stratec Medizintechnik, Pforzheim, Germany). A single slice scan with a thickness of 1 mm was obtained in a region site-matched to the ultrasound measurement site. The voxel size was 0.2 mm. A typical radius pQCT image from this site is shown in Fig. 3 along with images from sites 25mm distal and proximal to this site. Bone properties were determined using the manufacturer's default threshold values to separate bone from soft tissue. In all cases the pQCT measurements reflected average values for the whole radius section.

Ultrasound velocity measurements with the Sunlight Omnisense ($V_1$) and the low frequency prototype device ($V_3, V_4$), and pQCT measurements, were performed in Finland, in the Department of Health
Sciences of the University of Jyväskylä. Velocity measurements with the bi-directional device ($V_3$) were performed in France, at the Laboratoire d’Imagerie Paramétrique (Paris).

**Statistical analysis**

Univariate linear regression was used to assess correlations among the four ultrasound velocities measured. Differences between velocities were assessed using a paired two-sided $t$-test. Pearson’s correlation of SOS with bone properties was calculated by linear regression. Correlations were considered statistically significant for $p$ values lower than 0.05. Optimal combinations of bone properties for predicting ultrasound velocity were evaluated using multifactorial stepwise regression. All statistical computations were made using the Matlab Statistics Toolbox (The Mathworks Inc., Natick, MA, USA).

**Results**

**Descriptive statistics**

Mean values for velocity decreased in the following order: $V_1 > V_2 > V_3 >> V_4$ (Table 1, Fig. 3). Note that $V_4$ is not shown in Fig. 4 because the mean value ($1280 \pm 142$ m.s$^{-1}$) is much lower than the mean values (approximately 4000 m.s$^{-1}$) for the first arriving signal velocities. A significant statistical difference existed between all velocities ($V_1$ compared to $V_2$, $p<0.05$; all other comparisons, $p<0.0001$).

**Correlations between the different devices**

All velocities correlated significantly with each other, except $V_1$ with $V_4$ (Table 2). The highest correlation value was obtained between $V_1$ and $V_2$ ($r=0.74$, $p<10^{-4}$). The lowest significant correlation values were observed between $V_3$ and $V_4$, both of which were measured with the same device ($r=0.32$, $p<0.05$).

**Correlations between ultrasound velocities and bone material properties**

Table 3 summarises the correlation coefficients between the different velocity measurements and pQCT determined bone properties, and Figures 5 - 7 illustrate the most significant relationships. The best correlations with cort.BMD (Fig. 5) were found with $V_2$ ($r=0.72$, $p<10^{-4}$) and $V_4$ ($r=0.67$, $p<10^{-4}$). In contrast, $V_1$ and $V_3$ were only moderately correlated to cort.BMD. The best correlation with trab.BMD (Fig. 6) was found with $V_4$ ($r=0.74$, $p<10^{-4}$). Of the other velocities, $V_2$ was only moderately correlated to
trab.BMD, and no correlation of trab.BMD with $V_1$ or $V_3$ was found. Correlations with CSA and cort.Th were strongest for $V_4$ (Fig. 7), and were weak or non-significant for the other velocity measurements. A strong correlation existed between CSA and cort.Th ($r=0.87$ $p<10^{-4}$), and, as a consequence, the correlation between $V_4$ or $V_3$ and CSA was not significant after adjustment for cort.Th.

Using step-wise regression, the optimal combination of bone properties for predicting velocities was investigated. Two equivalent models were identified for $V_4$. In the first model, $V_4$ was determined best by a combination of cort.BMD and trab.BMD ($r^2=0.62$, RMSE = 89.4 m/s, $p < 10^{-4}$). In the second model, $V_4$ was determined best by a combination of cort.BMD and cortical thickness ($r^2=0.62$, RMSE = 90 m/s, $p < 10^{-4}$). $V_1$, $V_2$ and $V_3$ were determined best by cort.BMD alone and no combination could improve significantly their determination. In summary, 25% (RMSE = 104 m/s) of the variability of $V_1$, 52% (RMSE = 51 m/s) of the variability of $V_2$, and 16% (RMSE = 167 m/s) of the variability of $V_3$ could be explained.

**Discussion**

The axial transmission of ultrasound along cortical bone has been studied by a number of researchers and given rise to various technical implementations (Bossy et al. 2004a, Foldes et al. 1995a, Gerlanc et al. 1975, Lefebvre et al. 2002, Lowet et al. 1996, Nicholson et al. 2002, Siegel et al. 1958). This technique was developed early in the 1950s to study cortical bone status during fracture healing (Siegel et al. 1958) and has subsequently been used in bed rest studies (Tatarinov et al. 1990), for skeletal status assessment in osteoporosis (Foldes et al. 1995a), in healthy pubertal girls (Moilanen et al. 2003), in newborns (Nemet et al. 2001, Pereda et al. 2003) and in children with chronic diseases (Damilakis et al. 2004, Levine et al. 2002).

The nature of the information on bone properties conveyed by ultrasonic measurements has been a central question since many years and several experimental studies have looked at the relationships of these bone characteristics with ultrasound velocity (Moilanen et al. 2003, Njieh et al. 1999, Prevrhal et al. 2001, Sievanen et al. 2001). However, discrepancies were frequently observed between different studies. The *in vivo* observed correlation between tibial or radial cortical density and velocity was generally found to be around $r = 0.5$ (range 0.46 – 0.66) in different studies using the low frequency first arriving signal
(Moilanen et al. 2003, Prevrhal et al. 2001), the low frequency A0 mode (Moilanen et al. 2003) or the high frequency first arriving signal (Sievanen et al. 2001). Inconsistent results have been reported for the relation between cortical thickness and velocity: a non significant or weak correlation only was observed with high frequency measurements (Moilanen et al. 2003, Sievanen et al. 2001) while a significant correlation to cortical thickness was found with low frequency measurements (r ranging from 0.24 to 0.62 with tibial or radial cortical thickness (Moilanen et al. 2003, Prevrhal et al. 2001). A direct comparison between these studies is difficult because substantial variations can be found between the various axial transmission techniques, including differences in the frequency, in the algorithm used to calculate sound velocity, in the practical implementation of compensation methods for soft tissues effect, design of the in vivo study, etc. Most importantly, the interaction between the incident ultrasonic field and bone results in different type of waves, depending on the experimental excitation conditions such as, for example, the thickness-to-wavelength ratio (d/λ) (Bossy et al. 2002, Nicholson et al. 2002) that has been mentioned earlier. Consequently, the sensitivity of the measured sound velocity to different bone properties will depend on the type of wave which has been excited. These difficulties, and the confusion raised by the use of a single term (“SOS”) to designate the speed of sound of different types of wave, have prevented an accurate interpretation on what exactly is being measured using axial transmission. A correct interpretation of ultrasound measurement results requires first a detailed understanding of ultrasound propagation with clear identification of the different waves and their exact propagation paths that contribute to analyzed signals (Bossy et al. 2002, Camus et al. 2000, Lowet et al. 1996, Nicholson et al. 2002). Only then can a face to face comparison between different techniques be performed.

A dependence of the SOS on cortical thickness is expected from theoretical considerations and from simulation studies. Finite difference simulation studies (Bossy et al. 2002; 2004b, Nicholson et al. 2002) showed that the thickness of the cortical layer strongly influences the value of the velocity of the first arriving signal. Indeed, for a given frequency, the thickness will determine the nature of the wave generated in bone. It is predicted that the first arriving signal corresponds to a lateral wave if d/λ is greater than ½, whereas the slower S0 wave arrives first when the thickness-to-wavelength ratio is much less than ½ (Bossy et al. 2004b).
Typical bone thickness varies from 1 to 5 mm in human radius. For frequencies around 1 MHz (i.e. for $V_1$ and $V_2$), the wavelength is approximately 4 mm and therefore the thickness dependence of sound velocity is determined by the change in nature of the first arriving signal from a lateral wave to a S0 mode as explained above. For $d/\lambda$ greater than 1/2, the velocity does not depend on the cortical thickness. Under this limit, the sound velocity gradually changes from the sound velocity of the lateral wave (~4000 m/s) to the velocity of the anisotropic S0 mode (~3650 m/s for a 1 mm thick cortical layer) as $d/\lambda$ decreases (Bossy et al. 2004b). This explains the positive relationship between $V_2$ and thickness observed experimentally. To help understand this and other results, Fig. 8 shows velocity as a function of $d/\lambda$ for the finite difference simulations performed by Bossy et al (Bossy et al. 2002) and for the fundamental plate (Lamb) modes assuming a transverse isotropic medium. The regions of the curves corresponding to the different velocity measurements of this present study are superimposed.

The failure to observe a relationship between $V_1$ and thickness could be due to several factors. Firstly, $V_1$ was measured at a slightly higher frequency than $V_2$, so $d/\lambda$ will be greater (Fig. 8), and hence the influence of thickness will be reduced compared to $V_2$. Secondly, $V_1$ may be subject to errors associated with bone heterogeneity (discussed below) which will reduce the ability to observe significant correlations with other bone properties.

A further question relates to the positive association observed between $V_3$ and thickness. Measurements of $V_3$ were made at 200 kHz centre frequency, corresponding to $d/\lambda = 0.2$, where dispersion is minimal (Fig. 8). In fact, if $V_3$ represents the phase velocity of the S0 plate mode then a modest negative association with thickness would be expected (Fig. 8). The experimental data can be explained by considering that $V_3$ was measured using a broadband pulse, and that frequencies considerably higher than the 200 kHz centre frequency will have been present in the transmitted signal. Measurement of the first arriving signal will, by definition, measure the fastest propagating signal, and, these will have been the higher frequency components subject to the same phenomena as $V_2$, i.e. a positive association with thickness due to the transition from lateral wave to S0 plate mode (Fig. 8).

$V_4$ is the sound velocity of a slower second wave whose behaviour has been shown elsewhere to be consistent with the lowest order Lamb antisymmetrical (A0) mode (Nicholson et al. 2002) and its
thickness dependence is also determined by the geometrical dispersion of $A_0$. From Fig. 8 it can be understood that the velocity of this wave shows the strongest correlation with thickness because it is strongly dispersive over the full range of $d/\lambda$ studied.

The main novelty of this study was to focus on the comparison of three different devices operating at different frequencies by measuring the same set of bone specimens. $V_1$ was found to be higher than $V_2$ which was itself higher than $V_3$ (Fig. 4). The difference in velocity values was more pronounced between $V_3$ and $V_2$, than between $V_1$ and $V_2$. These results are consistent with numerical studies that predict different type of waves at high frequency ($V_1$ and $V_2$) and low frequency ($V_3$). As mentioned above, $V_1$ and $V_2$ values should fall between the velocity of the bulk compressional wave (lateral wave) and that of the $S_0$ mode, whereas $V_3$ might be expected to reflect mostly the slower $S_0$ mode. The difference between $V_1$ and $V_2$ is also in agreement with the finite difference simulations that predicts a slightly higher velocity for a slightly higher $d/\lambda$ ratio in the frequency range and the range of thickness values found in this study (Fig. 8) (Bossy et al. 2002, Nicholson et al. 2002). Other effects can also play a role in the difference in estimated velocity with different devices such as the distance between emitters and receivers, the signal processing algorithms used to measure speed of sound and the calibration methods. Further work will be necessary for a detailed analysis of these effects.

In spite of the fact that the three devices did not measure the same velocity values, correlations were expected between the results given by the different devices. The highest, but still modest, correlation was obtained between $V_1$ and $V_2$ ($r=0.74$). That $V_1$ and $V_2$ exhibited the best correlation was expected since the two devices measure the velocity of the first arriving signal at similar frequencies. However, a better correlation could have been expected for similar techniques measuring the first arriving signal in the 1 – 1.25 MHz frequency range on the same bone specimens. Several reasons may have had an adverse effect on the correlation. First, bone is dramatically heterogeneous. In the course of this study, it was observed that a shift of 1 cm in the longitudinal position of the bi-directional probe along the long axis of the bone could result in a variation of sound velocity of approximately 50m/s [data not reported here]. Thus, any failure in perfectly matching the measurement sites may have produced unwanted variability in the measurements. Some variability may also come from the difference in the emitter-receiver geometrical configuration in the probe and the measurement of slightly different regions. Most notably, the difference
in the acquisition procedures may have been at the primary source of the moderate correlation between $V_1$ and $V_2$. Remember that the bi-directional probe consists in a linear arrangement of transducers with two sources placed on both sides of a unique group of receivers such that sound velocity is deduced from a combination of the arrival times on the receivers of waves propagating in opposite directions. Since the cortical thickness determines the nature of the first arriving signal and its velocity, uneven thickness of the cortex under the probe may result in slightly different waves propagating in opposite directions and thus in slightly different time delays. An increase in cortical thickness was observed on the longitudinal cross-section X-ray images of the 41 radius as the distance from the distal extremity of the bone increases. In some cases, the relative increase could reach values up to 100%. When we processed the data from the bi-directional axial transmission to calculate the velocity of the signal arriving on the receivers from both transmission directions ($V_{2+}$ and $V_{2-}$) we found significant different velocity values ($V_{2+}=4013\pm121$ m.s$^{-1}$ and $V_{2-}=3876\pm147$ m.s$^{-1}$; paired t-test $p<10^{-4}$). The combined experimental bidirectional transmission approach circumvented partly the difficulty of measuring the velocity due to the uneven thickness of the cortex in the bone specimens and reduced the directional dependence of $V_2$. Considering that the orientation of the Sunlight Omnisense probe was not controlled, it is suspected that an additional variability caused by uncontrolled directional dependence of $V_1$ impaired the correlation coefficients between $V_1$ and $V_2$. Unexpected moderate to low correlations were also found between high frequency measurements $V_1$ and $V_2$ and low frequency measurements $V_3$ and $V_4$ (Table 1). Besides the reasons previously mentioned, the difference in nature of the signal measured with low and high frequency and their potentially different sensitivity to bone properties might explain such low correlation.

Most important is the ability of a non-invasive technique to reflect bone properties that are affected by bone disease, such as BMD and structural parameters. All velocities were significantly correlated to cortical BMD, but the highest correlation was found for $V_2$ compared to the others (Table 3). Surprisingly, the correlation of $V_1$ to cortical or trabecular BMD was much lower compared to the analogous velocity $V_2$. More generally, the bi-directional transmission ($V_2$) resulted in higher correlation with bone properties compared to unidirectional axial transmission ($V_1$) (note: the Sunlight Omnisense is assumed to operate in a unidirectional fashion but the manufacturer does not explicitly state this) suggesting that averaging the velocities from two opposite transmission directions reduces the variability due to the directional dependence, produces more reliable velocity estimate and strengthens the
relationship between velocity and bone properties compared to unidirectional axial transmission. The absence of correlations between $V_1$ and bone properties other than cortical BMD is most likely due to these uncertainties on the measurements.

As expected, the high-frequency devices ($V_1$ and $V_2$) were less sensitive to CTh, CSA and trabecular BMD than the low-frequency device ($V_3$ and $V_4$) (Table 3) because high frequency waves reflect preferentially the bone properties in the periosteal region of approximately 1 to 1.5 mm in depth as shown by the finite difference simulation results (Bossy et al. 2004b). In contrast, the low frequency approach excites guided waves ($A_0$ or $S_0$) that propagate within the total thickness of the cortical layer. The characteristics of these propagating modes are therefore affected by bone properties across the entire cortical layer. This may explain why $V_4$ is strongly related to both cortical BMD and trabecular BMD, while $V_2$ is only moderately correlated to trabecular BMD. As explained above, the situation for $V_3$ is complicated by the probable presence of frequency components considerably above the 200 kHz centre frequency. This may explain why $V_3$ did not correlate with trabecular BMD. Given the low penetration depth of the wave generated at 1 MHz, it is likely that only the thinner bone specimens contributed to the correlation of $V_2$ with trabecular BMD.

The two equivalent multiple linear regression models combining cort.BMD and trab.BMD (model 1) or cort.BMD and cort.Th (model 2) improved the prediction of $V_4$ ($r^2 = 0.62$) over a simple linear regression model with cort.BMD only ($r^2 = 0.45$). This demonstrates that $V_4$ captures independent information on different bone properties, and, as explained above, this occurs because the $A_0$ mode is highly dispersive over the $d/\lambda$ range studied.

There are some limitations associated with this study. Firstly, bones were studied with soft tissue removed. The Sunlight Omnisense is a clinical device presumably optimized for measurements of bone overlaid with soft tissue, and the absence of soft tissue may have affected the results in some way. However, the precision of the Omnisense measurements on the in vitro radius specimens was good, which would suggest that no fundamental problems were occurring. Measurements of $V_4$ with the low frequency device are strongly affected by soft tissue, with practical problems in exciting and detecting the $A_0$ wave, and possibly changes to the $A_0$ wave velocity due to fluid loading. The trends observed here for
V₂ may therefore not necessarily be reproducible in clinical studies. Further work is required to confirm this. In addition, the bone specimens were cut relatively near the measurement site, and this could have affected results, particularly at low frequencies.

In summary, three axial transmission devices measuring four different ultrasound velocities in cortical bone have been compared. The various approaches yield different velocity values, well explained by the difference in nature of propagating signals. Our results suggest that bone properties may be reflected differently in different axial transmission measurements. The most important results were (1) the good performance of a bidirectional axial transmission at high frequency reflected in the correlation of V₂ with several bone properties (cort.BMD, Trab.BMD and cort.Th) and the 52% of the variability of V₂ explained by cort. BMD alone, and (2) the ability of the low frequency slower A₀ mode (V₄) to reflect material and geometrical properties with an even higher percentage of the variability of V₄ explained by a combination of bone properties. Because the thickness of the cortical layer probed by waves is limited by the ultrasonic frequency, different information on bone status will be given by different approaches. Low frequency (~250 kHz) may be useful for the investigation of changes occurring in bone at the endosteal surface such e.g., trabecularization caused by endosteal resorption, while the MHz range might be used to characterize specifically the periostal layer and its changes occurring during periosteal apposition in elderly for example. Further work is required to explore the potential of a multiple frequency approach to separate the effects of changes in external layer or deeper layers of bone. Another interesting avenue of research might be to adopt the bidirectional approach for low frequency measurements in an attempt to increase the reliability of the measurements.

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Table 1. Descriptive statistics of ultrasound velocity measured by axial transmission and bone properties measured with pQCT

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<th>Mean±SD (m/s)</th>
<th>Min-Max (m/s)</th>
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<tr>
<td><strong>Velocity</strong></td>
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<tr>
<td>$V_1$ (m/s)</td>
<td>4010 ± 119</td>
<td>3759 - 4283</td>
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<tr>
<td>$V_2$ (m/s)</td>
<td>3953 ± 72</td>
<td>3822 - 4122</td>
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<td>$V_3$ (m/s)</td>
<td>3799 ± 179</td>
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<tr>
<td>$V_4$ (m/s)</td>
<td>1280 ± 142</td>
<td>1009 - 1587</td>
</tr>
<tr>
<td><strong>Bone properties</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical BMD (g.cm$^{-3}$)</td>
<td>1272 ± 45</td>
<td>1167 – 1364</td>
</tr>
<tr>
<td>Trabecular BMD (g.cm$^{-3}$)</td>
<td>413 ± 202</td>
<td>70 - 808</td>
</tr>
<tr>
<td>Cross sectional area (mm$^2$)</td>
<td>80 ± 20</td>
<td>46 - 113</td>
</tr>
<tr>
<td>Cortical thickness (mm)</td>
<td>2.5 ± 0.5</td>
<td>1.45 – 3.41</td>
</tr>
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</table>

Table 2: Correlation between velocities measured at the radius with three devices

<table>
<thead>
<tr>
<th></th>
<th>V2</th>
<th>V3</th>
<th>V4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r$</td>
<td>$p$</td>
<td>$r$</td>
</tr>
<tr>
<td>$V_1$</td>
<td>0.74</td>
<td>&lt;10$^{-4}$</td>
<td>0.50</td>
</tr>
<tr>
<td>$V_2$</td>
<td></td>
<td></td>
<td>0.46</td>
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<tr>
<td>$V_3$</td>
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n.s.: non significant
<table>
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<tr>
<th></th>
<th>cort.BMD</th>
<th>Trab.BMD</th>
<th>CSA</th>
<th>cort.Th</th>
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<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>$V_1$</td>
<td>0.5</td>
<td>$&lt;10^{-4}$</td>
<td>0.23</td>
<td>n.s.</td>
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<td>$V_2$</td>
<td>0.72</td>
<td>$&lt;10^{-4}$</td>
<td>0.47</td>
<td>$&lt;0.005$</td>
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<tr>
<td>$V_3$</td>
<td>0.4</td>
<td>$&lt;0.01$</td>
<td>0.21</td>
<td>n.s.</td>
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<tr>
<td>$V_4$</td>
<td>0.67</td>
<td>$&lt;10^{-4}$</td>
<td>0.74</td>
<td>$&lt;10^{-4}$</td>
</tr>
</tbody>
</table>

n.s. : non significant
Fig. 1: Location of measurement site on the radius specimens. The site corresponded to 45% of the radius length from the distal end, close to the “1/3 distal radius” region used clinically. The distal portion of the radius was removed as part of another study.

Fig. 2. The ultrasound measurements were performed at the postero-lateral location, corresponding to the clinical evaluation.
Figure 3. Typical peripheral Quantitative Computed Tomography images of the distal radius (b) at the measurement site situated 45% of the length of the radius from the distal end, (a) 25 mm distal to this site, and (c) 25 mm proximal to this site.
Fig. 4: Velocity distributions for the first arriving signal measured by the three probes. A statistical difference exists between the distributions.

Fig. 5: Scatter plots showing $V_2$ and $V_4$ (m.s$^{-1}$) versus cortical bone mineral density (mg.cm$^3$). The central line is the linear regression curve.
Fig. 6: Scatter plots showing $V_2$ and $V_4$ (m.s$^{-1}$) versus trabecular bone mineral density (mg.cm$^3$). The central line is the linear regression curve.

Fig. 7: Scatter plots showing $V_4$ (m.s$^{-1}$) versus cortical thickness (mm) and CSA (mm$^2$). The central line is the linear regression curve.
Figure 8. Dispersion curves for a bone plate. The top continuous curve shows data for the first arriving signal predicted by finite difference simulation from the study of Bossy et al (2004). The lower two curves are the two fundamental plate modes, S0 and A0. The regions corresponding to the four different velocity measurements are indicated schematically by the shaded boxes. Note that for V3, the box is extended with dashed lines to represent the influence of higher frequency components in the measured signal (see text).
Publication V
Measuring the phase velocity of guided waves
in free and immersed plates as bone phantoms

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Running title: Guided waves in bone phantoms

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Abstract

Previously we have reported the possibility of observing a guided wave, consistent with the fundamental antisymmetric (A0) Lamb mode, propagating in bone phantoms as well as in the human tibia and radius bones. Our previous methodology has relied on a coarse line fitting over the observed wave fronts which, however, has limited ability to assess the dispersion and is subject to errors due to strong interference by other wave modes. In order to provide a more robust tool for identifying individual wave modes and determining their phase velocities, signal processing techniques based on the two dimensional Fast Fourier Transform (2D-FFT) were investigated. Particularly, we attempted to reduce the limitations of spatial FFT resolution in terms of improving the precision of measurement of the A0 mode. Experiments were performed on free and immersed plates. We found that, when using specific time domain filtering, and controlling the signal processing parameters according to analytical theory for the Lamb A0 mode, we were able to assess the phase velocities and thicknesses of the bone phantoms reliably. Using these methods was essential for the immersed plates in particular.

Keywords

axial transmission, ultrasonic velocity, guided waves, cortical bone, phantom

PACS numbers

43.20.Mv, 43.40.Dx, 43.80.Ev, 43.80.Vj
Introduction

Human long bones are effectively hollow tubes, and thus support the propagation of guided wave modes within the bone layer in addition to the first arriving signal (FAS) measured by existing clinical devices. When the thickness is greater than the wavelength, the FAS signal represents a lateral (head) wave propagating at the bone surface at the longitudinal velocity [2,3]. This may not be a very useful clinical assessment since important pathological changes, such as reduced bone thickness and increased porosity at the endosteal (inner) surface, may remain undetected. Guided waves are more attractive because they propagate throughout the bone thickness, and have the potential to give additional diagnostic information related to bone material and geometrical properties. The possibility of measuring guided waves in bone using an axial transmission technique has recently been proposed and demonstrated by our group and others [1,4]. It has been shown that Lamb wave theory for plates can closely predict the results for phantoms [1] and for bones measured in vitro [4].

Previously we have reported measurements made with a low frequency axial transmission device using a fixed transmitting transducer and a receiving transducer that can be scanned along the axis of the bone or phantom [1]. Our previous velocity results for bone phantoms and bones have relied on a relatively crude line fitting to the wave fronts that are observed in the distance-time-intensity matrix obtained with this method. This kind of line fit provides a velocity that is affected by interfering wave modes across all the frequencies present. The difficulties arise, especially, when measuring human bones in vivo, as the velocity of the measured guided wave (1300-2000 m/s) overlaps that of soft tissue (1400-1600 m/s), and it is therefore possible that signals propagating through soft tissue may be mistaken for a guided wave in bone.

With advanced signal processing techniques, such as 2-D spectrum analysis, it may be possible to identify the propagating wave modes and to determine the corresponding
phase velocities with regard of frequency or wave number. 2-D fast Fourier transform (2D-FFT) has been used in several studies for successfully identifying guided wave modes from such of multi-mode signals that have been simulated or measured by means of axial transmission method in free and multilayered plate and tube structures [5-11]. In addition, Lefebvre et al used 2D-FFT for measurements in bone specimens [4].

We have found, however, that there are limitations in reliably discriminating and identifying wave modes when the conventional 2D-FFT is applied to our measurements. When considering an assessment of human long bone, the length of relatively flat bone available near the bone surface is typically only a few centimetres. The spatial scanning length is thus limited, e.g. to 30 mm, whereas the propagating wavelengths are typically >> 1mm. This yields a very flat wave number spectrum with a low resolution. Joint wave number maxima may occur between the recorded wave modes and the reliable determination of the individual peak locations is not possible. These problems are especially difficult in the case of in vivo bone measurements, as strong interfering wave modes are present due to signals that propagate in the surrounding soft tissue.

The objective of this work was to develop and introduce an improvement to the conventional 2D-FFT based spectrum analysis. It was shown that the novel approach enabled more reliable identification of guided wave modes from recorded distance-time-intensity matrices and more precise determination of the phase velocities for the identified wave modes than the ordinary 2D-FFT. In particular, we concentrated on improving the measurement of the fundamental antisymmetric Lamb mode (A0).

**Analytical theory for plate waves**

Lamb waves are two-dimensional elastic waves that propagate in a solid elastic plate of finite thickness. They arise from the multiple reflection and mode conversion of longitudinal and shear waves from the upper and lower surfaces of the plate [12-14].
They exist in the form of resonant modes where the combination of frequency and phase velocity corresponds to standing waves in the thickness direction.

The motion of a homogeneous, linear elastic solid can be modelled by Navier’s displacement equations of motion

\[(\lambda + \mu)u_{j,ij} + \mu u_{i,ij} = \rho \ddot{u}_i ,\]  

where \(u_i\) is the displacement vector,

\[u_{k,j} = \frac{\partial^2}{\partial x_i \partial x_j} u_k ,\]

\(\rho\) is the mass density and \(\lambda\) and \(\mu\) are the Lamé constants. Summation over a repeated index is assumed. The displacement vector can be expressed via Helmholtz decomposition

\[u_i = \frac{\partial \phi}{\partial x_i} + e_{ijk} \frac{\partial \psi_j}{\partial x_j} ,\]

where \(\phi\) and \(\psi_j\) are scalar and vector potentials, respectively, and \(e_{ijk}\) is a permutation symbol. Substitution of Eq. (2) into Eq. (1) yields two uncoupled wave equations

\[\left(\nabla^2 - \frac{1}{(c_L)^2} \frac{\partial^2}{\partial \tau^2}\right) \phi = 0 ,\]

\[\left(\nabla^2 - \frac{1}{(c_T)^2} \frac{\partial^2}{\partial \tau^2}\right) \psi = 0 ,\]

where \(\nabla^2 = \partial^2/\partial y^2 + \partial^2/\partial z^2\), \(c_L\) is the bulk longitudinal velocity and \(c_T\) the bulk shear velocity. According to the partial wave technique (Fig 1) [14], the solutions of Eq. (3) are sought in forms

\[\phi = C_1 e^{ik_L[z \sin(\theta_L) + y \cos(\theta_L)]} + C_2 e^{ik_L[z \sin(\theta_L) - y \cos(\theta_L)]}\]

\[\psi = C_3 e^{ik_T[z \sin(\theta_T) + y \cos(\theta_T)]} + C_4 e^{ik_T[z \sin(\theta_T) - y \cos(\theta_T)]} ,\]

where
\[ \theta_L = \arcsin \left( \frac{k}{k_L} \right), \quad \theta_T = \arcsin \left( \frac{k}{k_T} \right), \]

and \( k_L \) is the wavenumber of a longitudinal wave component, \( k_T \) the wavenumber of a shear wave component and \( k \) the wavenumber of a guided wave (in the direction of propagation). The constants \( C_1, C_2, C_3 \) and \( C_4 \) are arbitrary unknowns and will be determined by the boundary conditions.

Both of the potentials in Eq. (4) now consist of two terms, one representing a downward propagating plane wave (positive \( y \) in the exponential term) and one representing an upward propagating plane wave (negative \( y \) in the exponential term).

The physical correspondence to this is assuming four plane bulk waves in the solid, two longitudinal and two shear (Fig 1).

Displacements \( u_i \) can now be obtained by Eq. (2), and stresses \( \sigma_{ij} \) by

\[ \sigma_{ij} = \lambda \delta_{ij} \varepsilon_0 + 2\mu \varepsilon_{ij}, \quad (5) \]

where \( \delta_{ij} \) is Kronecker delta, dilation \( \varepsilon_0 = \varepsilon_{11} + \varepsilon_{22} + \varepsilon_{33} \), and strains

\[ \varepsilon_{ij} = \frac{1}{2} \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right). \quad (6) \]

By requiring traction free boundary conditions \( \sigma_{xy} = \sigma_{yx} \equiv 0 \) at free plate surfaces \( y = 0 \) and \( y = h \), where \( h \) is the plate thickness, and ignoring shear horizontal displacements \( (u_s \equiv 0) \), four equations will be obtained,

\[ \begin{aligned}
    \left( \lambda k_L^2 + 2\mu K_L^2 \right)[C_1 + C_2] + 2\mu k K_T^2 [C_3 - C_4] &= 0, \\
    -2\mu k K_T^2 [C_1 - C_2] + \mu \left( K_T^2 - 2k_T^2 \right) [C_3 + C_4] &= 0, \\
    \begin{aligned}
    \left( \lambda k_L^2 + 2\mu K_L^2 \right)[C_1 e^{ik_L h} + C_2 e^{-ik_L h}] + 2\mu k K_T^2 [C_3 e^{ik_T h} - C_4 e^{-ik_T h}] &= 0, \\
    -2\mu k K_T^2 [C_1 e^{ik_L h} - C_2 e^{-ik_L h}] + \mu \left( K_T^2 - 2k_T^2 \right) [C_3 e^{ik_T h} + C_4 e^{-ik_T h}] &= 0,
    \end{aligned}
\end{aligned} \quad (7a) \]

\[ \begin{aligned}
    \left( \lambda k_L^2 + 2\mu K_L^2 \right)[C_1 + C_2] + \mu \left( K_T^2 - 2k_T^2 \right) [C_3 - C_4] &= 0, \\
    -2\mu k K_T^2 [C_1 - C_2] + \mu \left( K_T^2 - 2k_T^2 \right) [C_3 + C_4] &= 0, \\
    \begin{aligned}
    \left( \lambda k_L^2 + 2\mu K_L^2 \right)[C_1 e^{ik_L h} + C_2 e^{-ik_L h}] + 2\mu k K_T^2 [C_3 e^{ik_T h} - C_4 e^{-ik_T h}] &= 0, \\
    -2\mu k K_T^2 [C_1 e^{ik_L h} - C_2 e^{-ik_L h}] + \mu \left( K_T^2 - 2k_T^2 \right) [C_3 e^{ik_T h} + C_4 e^{-ik_T h}] &= 0,
    \end{aligned}
\end{aligned} \quad (7b) \]
where

\[ K_{LT} \equiv k_{LT} \cos(\theta_{LT}) = \left( k_{LT}^2 - k^2 \right) = \left[ \frac{\omega}{c_{LT}} \right]^2 - k^2, \]

and \( \omega \) is the angular frequency.

This system of equations (7a to 7d) can be expressed in a matrix form

\[ \mathbf{AC} = 0, \tag{8} \]

where matrix

\[ \mathbf{A} = \begin{bmatrix}
\lambda k_L^2 + 2\mu K_L^2 & \lambda k_L^2 + 2\mu K_T^2 & 2\mu k_T & -2\mu K_T \\
-2\mu k_L & 2\mu K_L & \mu(K_T^2 - 2k_T^2) & \mu(K_T^2 - 2k_T^2) \\
(\lambda k_L^2 + 2\mu K_L^2) e^{iK_L h} & (\lambda k_L^2 + 2\mu K_T^2) e^{iK_T h} & 2\mu k_T e^{iK_T h} & -2\mu k_T e^{-iK_T h} \\
-2\mu k_L e^{iK_L h} & 2\mu k_T e^{-iK_T h} & \mu(K_T^2 - 2k_T^2) e^{iK_T h} & \mu(K_T^2 - 2k_T^2) e^{-iK_T h}
\end{bmatrix}, \]

and vector \( \mathbf{C} \) contains the four unknown constants \( C_1 \) to \( C_4 \). The matrix equation (8) is satisfied when the determinant of matrix \( \mathbf{A} \) vanishes. The characteristic equation for a plate in vacuum (with given wavenumber \( k \), angular frequency \( \omega \), bulk velocities \( c_L \) and \( c_T \), and plate thickness \( h \)) can thus be written as

\[ |A(\omega, k, c_L, c_T, h)| = 0. \tag{9} \]

The roots of this characteristic (or dispersion) equation provide the dispersion relations of the given structure, and can be solved numerically [14, 15].

The above described method, though not as elegant as the classical solution for Lamb waves [11-14], is powerful as it is easily extendable also to multilayered plate and tube structures. This is a useful property, for instance, if attempting to model the coupling effects of soft (e.g., liquid) overlayer on top of bone phantoms.
Experimental measurements

Materials

Twelve free acrylic plates, thickness ranging from 2.0 to 24.0 mm, and one aluminium plate (thickness 4.0 mm) were measured in air. The aluminium plate was, in addition, measured in various immersion depths in water, ranging from 0 to 12 mm. The thickness of the water layer on top of the plate was determined from the volume of water added to the container. Transducers were placed in contact with the upper surface of the water.

Experimental setup

An axial transmission device, consisting of one custom-made piezoceramic transmitter and one receiver, orientated normal to the plate, was used to measure ultrasound velocities. Ultrasonic gel or water was used as coupling medium. The transducers were excited using a Panametrics 5077PR pulser and the pulse excitation had a band-width from 50 to 350 kHz. The receiver was moved progressively away from the transmitter, and the ultrasonic signal was recorded at 40 discrete locations 20 to 50 mm apart from the transmitter. A computer based digital oscilloscope was used for data acquisition using a sampling rate of 10 MHz. The recorded signals were stored as a distance (r) - time (t) matrix, which was then displayed as a grey scale intensity plot, hereafter called as the (r,t) diagram. From the (r,t) diagram we observed two distinct wave fronts, the weak first arriving signal, generally consistent with the lateral wave (or head wave), and a slower second wave which we have shown elsewhere to be consistent with the fundamental antisymmetric Lamb wave (A0) [1].
Signal processing

Selective time domain filtering

Selective filtering was used to extract a region of interest from the rest of the signal in the time domain. To achieve this the (r,t) matrix is multiplied by a Hanning window mask (Fig 3a) which has a specified slope (or group velocity) $c_g$, time width $t_w$ (half width of the Hanning window), and time delay $t_d$. The time delay is measured at distance $r = 0$ from time $t = 0$ to the top of the window (Fig 3b). Thus, the top of the mask window crosses the time axis at point $t = t_d$. The time delay is $t_d = t_{dd} + t_{ad}$, where $t_{dd}$ is device delay due to excitation and $t_{ad}$ is additional delay due to other factors (e.g. a soft overlayer on top of the solid substrate). The actual delay at given $r$ is given by $\text{delay} = t_d + r/c_g$.

2D-FFT

A 2D-FFT was used to produce a phase velocity - frequency spectrum of the measured distance-time-intensity matrix. A one-dimensional FFT was first performed in the time domain, and a distance-frequency-intensity matrix was thus obtained. Then, the FFT was performed in the spatial domain, yielding wave-number spectra for given frequencies. Corresponding phase velocities were determined by $c_p = 2\pi f/k$ (where $f$ is the frequency and $k$ the wave number), and thus a phase velocity spectrum was obtained. Quantisation of the phase velocity spectrum, due to limited spatial resolution, was reduced by using spline interpolation. The highest local maximum of the phase velocity spectrum was then sought within a specified range of interest $c_{p1} < c_p < c_{p2}$. The minimum ($c_{p1}$) or maximum ($c_{p2}$) of the range was not accepted as a result.

The phase velocity spectra, obtained at a number of frequencies within a frequency range of interest, were then separately normalised and merged as columns into a phase velocity – frequency - intensity matrix, hereafter called as $(c_p,f)$ spectrum.
Correspondingly, the obtained peak locations can be represented as functions of phase velocity and frequency, yielding a \((c_p, f)\) diagram.

**Selective 2D-FFT**

We then combined the selective time domain filtering with the 2D-FFT to provide a powerful tool that enhanced the ability to discriminating wave modes. Selective filtering was used to define the region of interest of the recorded signal, and hence the undesired parts of the time domain signal did not affect the phase-velocity-frequency spectrum. With this approach, the choice of processing parameters now provided different ways to target the measurement of particular wave modes. The first parameter, \(c_g\), was chosen such that it corresponds to the calculated group velocity for the given material, structure, and wave mode. This yielded a group velocity filter that enables the measurement of the phase velocity of the corresponding wave mode. The parameter \(c_g\) could either be chosen as a constant with regard to frequency, or could be varied functionally according to a given calculated theoretical group velocity dispersion curve. Only the choice of constant \(c_g\) will be discussed in this work.

The effects of selective filtering parameters on the \((c_p,f)\) spectrum and diagram will be discussed in detail in a later section.

**Theory fitting**

Let \(V_{\text{exp}}(f_i, t_d)\) be the experimental and \(V_c(f_i, h)\) calculated phase velocity for a given frequency \(f_i\), plate thickness \(h\) and time delay \(t_d\). The optimal parameters \(h\) and \(t_d\) will then be obtained from

\[
\min \left( \sum_{i=1}^{N} \left| V_{\text{exp}}(f_i, t_d) - V_c(f_i, h) \right| \right).
\]  

(10)

As described above, the experimental velocity \(V_{\text{exp}}(f_i, t_d)\) is also a function of filtering parameters \(c_g\) and \(t_w\), in addition to \(f\) and \(t_d\). Correspondingly, the calculated phase
velocity $V_c(f,h)$ is also a function of material parameters $c_L$, $c_T$ and $\rho$ in addition to $f$ and $h$. It depends on the choice that which parameters are given as constants and which will be adjusted by the minimisation routine Eq. (10). We chose to perform the fit in terms of $h$ and $t_d$, and thus to obtain an estimate to the thickness of the plate of which material properties are known.

Whereas the curves were fitted according to minimum absolute mean error in Eq. (10), the quality of the curve fits were evaluated in terms of a relative mean squared error

$$E_{rel} = \frac{1}{N_{rel}} \sum_{n=1}^{N} \left( \frac{V_{exp}(f_n) - V_c(f_n)}{V_c(f_n)} \right)^2.$$  \hspace{1cm} (11)

Relative error $E_{rel}$ was used as it yields an independent estimate of the fitting quality and thus enables the direct comparison of measurements.

**Results**

**Free plates**

Figure 3 illustrates the parameters of selective time domain filtering and shows the effect of masking on an (r,t) diagram from a 3.6 mm acrylic plate. In the (r,t) diagram the high-intensity wave packet with a slow phase velocity has previously been shown to be consistent with the A0 Lamb mode [1].

**Identification of A0 mode**

Figure 4a illustrates a $(c_p,f)$ spectrum and corresponding $(c_p,f)$ diagram obtained for a raw (r,t) intensity matrix (i.e. without using selective time domain masking) for a 3.6 mm acrylic plate. The experimental phase velocities, determined as peak values of each phase velocity spectrum, are shown by diamond markers. Calculated phase velocities for the fundamental antisymmetric (A0) and symmetric (S0) Lamb modes with the given plate parameters are shown as dotted lines. As the A0 mode was clearly observed
already on an (r,t) diagram, the corresponding (c_p,f) diagram quite precisely follows the A0 mode, though an exception is seen at 270 kHz as a confusion with S0 mode. The relative fitting error Eq. (11) between experimental velocities and A0 within the given frequency range was 14%.

When choosing the prediction $c_g$ between Rayleigh velocity ($c_R$) and shear velocity ($c_T$) (Fig 2), and thus fixing the filtering parameters as $c_g = 1280$ m/s and $t_w = 5.0$ µs, and then performing the 2D Fourier analysis, we obtained Fig. 4b. Time delay and plate thickness were fitting parameters, as will be described later. Now, the energy was clearly concentrated on the A0 mode. Confusion with S0 or any other modes no longer occurs, and the obtained (c_p,f) diagram looks smooth and clear. The error between the obtained phase velocities and expected A0 within the given frequency range was 1.7%.

**Sensitivity analysis**

The effects of selective filtering parameters on the obtained experimental phase velocities are illustrated in Fig 5. For a free plate the choice of $c_g$, $t_d$ or $t_w$ did not have a large effect on the result. Thus, the constant $c_g$ (=1280 m/s for acrylic, chosen to be between the Rayleigh and shear velocities) was a fairly good choice when measuring a free plate. However, we noticed that when decreasing $t_w$, the choice of $t_d$ began to have a greater effect on the resulting phase velocities at low frequencies (Fig 5d), which was related to the alignment of the narrow time window on the wave fronts observed in the distance-time plane. While properly aligned, the closest match between calculated and experimental phase velocities was obtained.
Plate theory fitting

When fitting the calculated phase velocity of A0 mode (material parameters: \(c_L = 2730 \text{ m/s}, c_T = 1325 \text{ m/s}, \rho = 1.20 \text{ kg/dm}^3\)) to experimental results (filtering parameters \(c_g = 1280 \text{ m/s}, t_w = 3 \mu\text{s}\) in terms of \(t_d\) and plate thickness, we obtained an excellent relationship between an obtained and actual plate thickness in the range of 2 to 8 mm (Fig 6a). In the plates with greater thickness than 8 mm, the dispersion of A0 mode became small within the given frequency range, and thus the dispersion-based thickness estimation was less accurate than in thin plates. The error of the obtained thickness estimate was at about \(\pm10\%\) (Fig 6b).

Immersed plate

Identification of A0 mode

When filtering the raw distance-time matrix measured from an immersed aluminium plate, in the most of the cases we were not able to identify the A0 mode at all (Fig 7a). Only some messy signs of some higher, potentially fluid borne modes could be seen.

However, if assuming that the free plate A0 mode could also be measured from an immersed plate, and performing the selective 2D-FFT analysis, we were able to reduce the effect of interfering wave modes and identify A0 (Fig 7b). The relative fitting error Eq. (11) between expected A0 and obtained phase velocities now was 2.8%.

Sensitivity analysis

For an immersed plate, the choice of selective filtering parameters was found to have much greater effect than for free plates. When increasing the immersion depth, the effect of interfering wave modes increased rapidly as the number of artefacts on the obtained phase velocities increased (Fig 8). However, the proper alignment of the filtering mask allowed us to minimise the effect of these artefacts and to obtain genuine guided wave velocities (Fig 7b).
**Free plate theory fitting**

Assuming that the free plate A0 mode could also be measured in an immersed plate, we again fitted the calculated A0 phase velocities (material parameters: $c_L = 5950$ m/s, $c_T = 3120$ m/s, $\rho = 2.70$ kg/dm$^3$) with experimental results in terms of thickness and time delay. As a result, the thickness of a 4 mm aluminium plate could roughly be measured until 6 mm immersion depth (Fig 9a). In addition we found that the obtained time delay increased with increasing overlayer thickness (i.e. immersion depth) $a$ (Fig 9b), the slope being $\frac{dt}{da} = (1.4 \pm 0.1) \mu$s/mm.

**Discussion and conclusions**

Ordinary and selective 2D-FFT approaches were used to attempt to identify the Lamb A0 mode and to measure its phase velocity in free and immersed plates. It was shown that the selective time domain filtering enhanced the reliability of mode identification and determination of phase velocities over the conventional 2D-FFT method. The experimental velocities were in excellent agreement with corresponding theoretical predictions suggesting that the A0 Lamb mode can be measured in immersed plates as well as in free plates. In addition, it was shown that the developed theory fitting scheme enabled the successful estimation of the plate thickness in both free and immersed plates.

If considering the conventional 2D-FFT in free plates, we found that rapid jumps in the signal peak intensity may occur, apparently from A0 to S0 or some other higher mode at certain frequencies (Fig 4a). This may seem an odd effect, but it is to be remembered that the given phase velocity - frequency - intensity diagrams have been scaled at each given frequency to their maximum within the given phase velocity range. In figure 4a, for instance, the chosen phase velocity range (300 to 2000 m/s) limits the effect of S0 intensities that appear outside of this range. If limiting the phase velocity up
to 1300 m/s, the effect of S0 became eliminated and the precision of experimental A0 phase velocity (compared with the theory prediction) improved from 14% to 4.3%. However, it still did not achieve the quality of the corresponding selective 2D-FFT result (1.7% error). This indicates that the selective 2D-FFT method is more robust than the conventional method in reliably identifying and measuring the A0 mode in free plates.

The power of the selective time domain filtering method truly does itself justice in immersed plates. The ordinary 2D-FFT yielded only negligible signs of the plate A0 mode, and the dominant signal intensities were due to some interfering wave modes. As A0 is a leaky wave mode with a low velocity, compared to that of water, it is expected that the intensity of A0 decreases rapidly with increasing immersion depth. Simultaneously with increasing immersion depth, the intensity of the direct lateral wave or guided waves in the fluid overlayer may increase. In figure 7b, one may observe confusion patterns suggestive of higher order guided modes that saturate close to 1500 m/s at higher frequencies. It could be expected that these are guided modes in the fluid overlayer. However, when using the selective 2D-FFT with the assumption that A0 can be measured, all the interfering wave modes essentially disappeared. The A0 mode became strong and evident, and its phase velocity was reliably determined. Looking at the signal through a narrow selective time filter thus removes the interfering wave modes that appear at clearly different times than A0. On the other hand, as the immersion depth is increased, the portion of interfering wave modes’ energy increases within the time window, and measurement of A0 becomes difficult (Fig 8). Figure 9a indicates that the immersion depth of 5 to 6 mm is the limit for measuring A0 mode in a 4mm aluminium plate.

We used a relatively narrow Hanning window half time widths, $t_w = 3 \mu s$ for free and $t_w = 5 \mu s$ for immersed plates. These values we found to work the best by practice, as
slightly different values of \( t_w \) were tested within the range 3 to 10 \( \mu s \). However one might criticise this since such window lengths are of the same order or shorter than the periods of the measured wave modes (frequencies 30 to 350 kHz correspond to periods of approximately 33 to 3 \( \mu s \), respectively). This issue we cannot fully justify, and it remains as a subject for further investigation. However, it can be said that the spectrum analysis was being performed in 2-D and the slope of the filtering mask \((c_g)\) was chosen according to reasonable expectations for the group velocity. We were analysing a region of near constant phase and, we suggest, a full period was not required for satisfactory interpretation. Indeed we found, however, that the use of too short time window shifted the obtained phase velocities slightly away from their correct positions. Thus, a compromise needs to be made between the mode selecting power and decreasing frequency resolution, when the window is being shortened.

If considering the first fitting parameter \((t_d)\), we did not obtain any clear relationship between \( t_d \) and actual plate thickness in free plates. This may be explained by the fact that there was more than one parallel wave front corresponding to one single wave mode (Fig 3c,d) and that a narrow selective time window (especially a narrow one) may pick up any one of these when an optimal fit between theory and experimental result is warranted.

In the case of immersed plates there was a clear relationship between the obtained \( t_d \) and overlayer thickness \( a \) \((dt_d/da = 1.4 \ \mu s/mm \pm 0.1 \ \mu s/mm)\). Let us consider the following bilayer configuration: aluminium plate (thickness \( h \), \( c_g = 3000 \ m/s \)), water overlayer (thickness \( a \), \( c_w = 1500 \ m/s \)), and two transducers on top of water layer, within the distance \( r \) from each other. The time that it takes for a classical wave to travel back and forth through the overlayer is \( t = 2a/(c_w\cos(\theta )) \), where \( \theta = \text{asin}(c_w/c_g) = \text{asin}(1500/3000) = 30^\circ \) (according to Snell’s law), yields \( dt/da = 1.54 \ \mu s/mm \). This assumption is slightly higher but in rather good agreement with the experimental result.
suggesting that the expected time delay of A0 Lamb mode in immersed plate could be estimated according to classical wave theory.

In this work it was successfully assumed that the free plate A0 mode could be measured also in an immersed plate. According to theory, it is actually expected that the immersion does not affect much the phase velocity dispersion of Lamb modes, but only introduces an attenuation mechanism as wave modes leak from plate to surrounding liquid [16, 17]. However, the wave modes that reflect down from the upper surface of a thin overlying water layer cause mode coupling between fluid overlayer and solid plate. This phenomenon may affect strongly the dispersion characteristics of the guided waves and can be analytically modelled by the fluid-solid bilayer theory [17, 18]. The group velocity of bilayer A0-like mode (termed mode 1 by Yapura or M0 by Simonetti) has much greater dispersion than that of A0 in a free plate. Therefore the constant $c_g$ assumption, as used in this work, may not be adequate when measuring bilayer modes. According to our initial investigations, the group velocity assumption could be varied as a function of frequency, on the basis of calculated prediction. This yields a possible method for measuring the bilayer modes, at the cost of increased computing time.

As the objective of this study was to reduce the limitations of the poor spatial FFT resolution (due to short scanning interval length), we only explored the ability of selective time domain filtering to help with this problem. However, the approach described in this work cannot truly increase the resolution but it can only reduce the confusion with other wave modes that appear at the same frequency but different times. As this reduces the risk for joint peaks, it is a subject to greatly help with the resolution problems. In fact, another interesting approach is available (spatial linear prediction or a Prony method) that has been reported to truly increase the spatial resolution in quite similar applications [10, 19]. This method might further improve the methodology discussed in this work.
In conclusion, selective 2D-FFT provides a useful tool for identifying particular wave modes in the axial transmission data and determining phase velocities. Particularly, the ability of determining the phase velocity for A0 Lamb mode and estimating the thickness of a plate was shown. In addition, it was shown that A0 mode could also be measured through an overlying layer of liquid without being strongly affected by the dispersion of coupled bilayer wave modes or lateral wave through the water layer. Therefore, it is seems worthwhile for testing the applicability of this method also with real bone measurements, in vitro and in vivo.

It remains to be assessed how the tubular shape of long bone affects the dispersion of the measured wave modes. According to our initial results in tubes, the plate theory assumption works relatively well in thin-walled tubes, but in thick-walled tubes it yields a systematic error which significantly reduces the precision of the results and may thus yield misinterpretations. Therefore, the tubular shape needs to be taken into account with the analytical model of guided waves. In addition, it remains to be studied how the presence of an overlying layer of soft tissue affects the dispersion of measured guided waves, and again to assure whether these coupling effects could yield misinterpretations if not under control. It is also to be clarified that whether modelling with coupled wave modes would yield a more complete or precise picture about the bone and soft tissue structure, though we believe that in certain cases it is appropriate to only use free plate or tube models as shown in this work.

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References


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