Bone Quantitative Ultrasound

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Editors

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Introduction

Pascal Laugier and Guillaume Haïat

Ask yourself what makes the strength of a building such as the Eiffel tower, i.e., its ability to withstand bending and shearing forces of the wind. The quantity of scrap used to build it? The intrinsic strength of each iron beam? The structure (i.e., size, shape, orientation of the beams, overall shape of the building)? All these factors contribute to the strength would answer the engineer. The Eiffel tower was surprisingly inspired by the work in early 1850s of the anatomist Hermann von Meyer on the anatomy of the femur (thighbone). Like engineers who control the integrity and the strength of buildings (towers, bridges), physicians scrutinize the strength of our bones, specifically to detect fragile bones and identify subjects at fracture risk and in need for treatment.

Fragile bones are commonly, but not exclusively, encountered in a disease called osteoporosis characterized by a decrease in bone mass and structural and material deterioration of bone, leading to increased susceptibility to fractures. Osteoporosis is most common in women after menopause, but may also develop in men, and may occur in anyone in the presence of particular hormonal disorders and other chronic diseases or as a result of medications. Osteoporosis may significantly affect life expectancy and quality of life. Osteoporosis is a major public health threat with extremely high costs to health care systems. Approximately one in two women and one in four men over age 50 will have an osteoporosis related fracture in their remaining lifetime. The costs measure in billions of dollars annually and these numbers are expected to increase, with as many as 6.3 million hip fractures predicted annually, around the world, by 2050. Clinicians and researchers alike are emphasizing the importance of early detection of osteoporosis and fracture prevention.

Today, X-ray measured bone mass serves as a surrogate for bone fragility, but fails to take into account other important aspects like material strength or microstructure. Mechanical waves such as ultrasound are intrinsically suited to probe

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mechanical properties and may perhaps have the best chances of all modalities to yield non-invasively an improved estimation of bone fragility combined with advantages like lack of ionizing radiation and cost-effectiveness.

Although the clinical potential of ultrasound for the investigation of bone fragility was recognized as early as in the 1950s where an ultrasound method was described for monitoring fracture healing [1], ultrasound was used episodically to investigate bone properties until the 1990s. The reason why ultrasound techniques were not used before this date was because of immature technology and poor understanding of the interaction mechanisms between ultrasound and bone. In 1984, Chris Langton et al. took a step forward by discovering that the transmission of ultrasound through the heel could discriminate osteoporotic from non-osteoporotic women [2]. He demonstrated that the heel of osteoporotic patients could transmit ultrasound waves with less attenuation than that of age-matched normal subjects. Since then many advances have been achieved and a variety of different sophisticated technologies capable of measuring different skeletal sites such as the heel, fingers, wrist, leg or hip have been introduced and evaluated. The evidence that ultrasound is a valid (radiation free and inexpensive) method for fracture risk assessment is first class. Several devices received FDA approval that further opened the door to clinical acceptance and use. Bone ultrasound technology, termed QUS (Quantitative Ultrasound), gained a place in the armamentarium of modalities used to assess the skeleton.

While the concept of measuring attenuation and velocity of ultrasound in bone has changed little since its inception, technology has evolved. Quantitative ultrasound imaging of the skeleton was first applied to image the heel [3]. Technological advances have provided clinicians with smaller, lighter, and portable equipment such as an inexpensive device operated with four AAA batteries [4].

An important limitation of QUS today is their limited access to peripheral skeletal sites only. One of the most significant recent technological advances is the new QUS scanner developed for direct assessment of skeletal properties at the proximal femur (hip) [5]. For X-ray based techniques, measurements directly at the main osteoporotic fracture sites have proved to be superior to measurements in the peripheral skeleton. It is reasonable to also expect better hip fracture risk prediction for QUS assessment at the proximal femur compared to the heel. However, the complexity of the anatomy and the presence of soft tissues make measurements at this site quite challenging.

More recently, the emphasis of innovative QUS basic research has shifted towards cortical long bone measurements, such as the tibia (leg) or the radius (forearm). Like tube or pipelines inspected by non destructive ultrasonic testing methods, long bones can be probed by ultrasound waves produced in response to an impact (the ultrasound impulse) transmitted by a source to the bone through soft tissues. Interestingly, long bones support the propagation of different kind of waves, such as surface or guided waves, which contain relevant information on micro-structural and material properties. Judicious choice of propagation modes over a suitable frequency range can be achieved and subsequent measurements of their velocities can reflect distinct aspects of bone quality [6], hoping that they would appropriately reflect the bone quality status at the main fracture sites (e.g., hip or spine) and its changes associated with disease or treatment.

QUS techniques could find widespread clinical use to predict bone fragility not only in osteoporotic patients, but also in a wider context of bone diseases in female, male and pediatric populations. For example, preliminary studies suggest that this technique may be a useful method of assessing changes in bone health in preterm infants for whom X-ray technologies are unsuitable. An ultrasound wearable system for remote monitoring of the healing process in fractured long bones has also been reported [7].

QUS techniques and implementations have been introduced into clinical practice despite the fact that the interpretation of QUS data is hampered by the structural complexity of bone. Interaction mechanisms between ultrasound and bone are still poorly understood. Modeling can be seen as a major need in order to drive future experiments, to optimize measurements, to integrate multiscale knowledge, and to relate QUS variables to relevant bone biomechanical properties. Ultrasound propagation through bone is complex. It may involve different wave types, each with its own propagation characteristics. An accurate 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. The complex and multiscale nature of bone significantly complicates the task of solving equations, though.

Recently developed computer simulation tools offer a fertile alternative to intractable theoretical formulations. Computer simulation will likely have its greatest impact by allowing the researcher to visualize the propagation of ultrasound through the complex three-dimensional bone structures and by providing insight into the interaction mechanisms between ultrasound and bone. Simulators and computers may well become the primary tool for investigators to answer questions such as: how is the wave transmitted through the bone, what is the path followed by the wave? How does it interact with bone? What kind of wave is propagating? Computer simulations have been applied to the problem of transmission through pieces of spongy bone (such as that found in the femur at the hip), and along or across long cortical bones such as the radius [8–10]. In every case, the computer simulations provided valuable insight into the properties (e.g., nature and pathway) of the propagating waves. Computer simulation therefore resembles experiments in a virtual laboratory with independent control over each bone parameter. Virtual scenarios of osteoporosis for instance can be easily implemented and used to form a comprehensive understanding of bone ultrasonic properties and their relation to bone biomechanical competence [11], help validate or refute theoretical approaches, and probe new experimental configurations.

Although the methodology for assessing bone properties using ultrasound is much less developed to date than with X-rays, the potential of ultrasound extends far beyond the currently available techniques and is largely unexploited. Many new areas of investigation are in preliminary stages, though. Most active research is carried out in QUS to develop new measurement modes, access to the central skeleton (hip), exploit multiple propagation modes or extend the frequency range of the measurements. All these new developments should result in new QUS variables and systems able to provide information on material or structural properties other than density and ultimately on osteoporotic fracture risk.

Quantitative ultrasound (QUS) of bone is a relatively recent research field. The research community is steadily growing, with interdisciplinary branches in acoustics, medical imaging, biomechanics, biomedical engineering, applied mathematics, bone biology and clinical sciences, resulting in significant achievements in new ultrasound technologies to measure bone and develop models to elucidate the interaction and the propagation of ultrasonic waves in complex bone structures. The present book will offer the most recent experimental results and theoretical concepts developed so far and would be intended for researchers, graduate or undergraduate students, engineers and clinicians who are involved in the field.

The **first chapter** is intended for readers who do not have a background in bone biomechanics. It gives a description of bone, highlighting the complex and hierarchical structure of bone, pointing to bone properties that determine bone strength. Then basic definitions and concepts of biomechanics are given. The clinical context (osteoporosis) in which quantitative ultrasound (QUS) has been developed is described. The first chapter can be skipped by readers who have a good knowledge of bone biomechanics. The **second chapter** offers an ultrasound overview which is intended for readers who do not have a background in the physics of ultrasound and may be skipped by those readers who already have a good knowledge of ultrasound wave propagation. Basic definitions of acoustics and equations of ultrasound wave propagation in homogeneous media are given. The **third chapter** is devoted to the generic measurement and signal processing methods implemented in bone clinical ultrasound devices. The section describes the devices, their practical use and clinical performance measures. The potential of QUS for a clinical application in osteoporosis management, the status today and its future perspectives are described in Chap. 4.

Chapters 4 to 9 cover the physical principles of ultrasound propagation in heterogeneous media such as bone and the interaction between an ultrasound wave and bone structures. Our goal is to give the reader an extensive view of the interaction mechanisms as an aid to understand the QUS potential and the types of variables that can be determined by QUS in order to characterize bone strength. The propagation of sound in bone, bone marrow and surrounding soft tissue is still subject of intensive research and a unique conclusive theory does not exists yet. Ultrasonic wave propagation in cancellous bone and cortical bone obeys different theories. For example, the Biot theory modeling bone as a poroelastic medium and the theory of scattering have been extensively used to describe wave propagation in cancellous bone, whereas propagation in cortical bone falls in the scope of guided waves theories. In these chapters, we intend to present in details the models that are used to solve the direct problem and strategies that are currently developed to solve the inverse problem. These developments will include analytical theories (Biot theory of poroelasticity, theory of scattering, guided wave theory) and numerical approaches that have grown exponentially in recent years. We assume that the reader is familiar with the theory of elastic wave propagation in homogeneous media as well as with the underlying physical concepts of elastic wave interaction with heterogeneous media. This part of the book covers many advanced physical and mathematical concepts used to model ultrasound propagation in bone. Also, in order to differentiate the numerous variables used in ultrasound measurements it is important to better understand the complexity of the underlying physical concepts.

Chapters 10 to 14 review research findings of in vitro and in vivo ultrasound studies of bone and highlights some useful concepts that may lead to a better insight into the relationships between characteristics of ultrasound propagation and bone properties. This part of the book refers as much as possible to the theoretical developments presented in Chaps. 4–9. Clinically available QUS techniques rely on the quantitative measurement of linear acoustic parameters. Therefore much of the discussion is dedicated to these parameters (e.g., attenuation, speed of sound, backscatter coefficient) and to their relationship to bone mechanical and structural properties. The goal is to highlight the foundations for the clinical use of QUS technologies for fracture risk prediction and bone status assessment. Chapter 14 presents the state of the art and provides an extensive review of studies in the literature dealing with bone healing monitoring by ultrasonic means.

Intensive research is ongoing in many different areas of applications of ultrasound to characterize bone. The three last chapters (**15 to 17**) cover these cutting-edge researches (non-linear ultrasonics, ultrasound tomography, and acoustic microscopy) although they are still at an early development stage. The goal is to give a flavour of new areas of investigation that are currently investigated with the aim of measuring a variety of material and structural properties at several descriptive levels of bone structure from the tissue to the organ level.

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