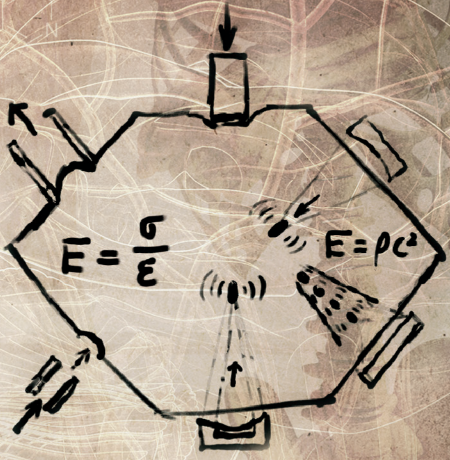
Measurement of Soft Tissue Elasticity *in Vivo*

Techniques and Applications



Yong-Ping Zheng
Yan-Ping Huang

CRC Press
Taylor & Francis Group

Measurement of Soft Tissue Elasticity *in Vivo*

Techniques and Applications

Measurement of Soft Tissue Elasticity *in Vivo*

Techniques and Applications

Yong-Ping Zheng
Yan-Ping Huang

CRC Press
Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

Version Date: 20150724

International Standard Book Number-13: 978-1-4665-7629-2 (eBook - PDF)

Visit the Taylor & Francis Web site at
http://www.taylorandfrancis.com

and the CRC Press Web site at
http://www.crcpress.com

To our families
Sally Ding, Jenny, Winnie and Linnie Zheng
Amy Chen and Vicent Huang
For their love and support

Contents

Preface, xiii

Acknowledgements, xvii

Authors, xix

CHAPTER 1 ▪ History and Recent Development in Soft Tissue Elasticity Measurement 1

CHAPTER 2 ▪ Conventional Methods for Soft Tissue Elasticity Measurement *in Vitro* 7

2.1 INTRODUCTION 7

2.2 METHODS FOR MEASUREMENT OF SOFT TISSUE ELASTICITY 10

2.2.1 Compression (Unconfined and Confined) 10

2.2.2 Extension 13

2.2.3 Inflation 14

2.2.4 Shear 15

2.2.5 Bending 18

2.2.6 Spinning 19

2.2.7 Osmotic Swelling 20

2.3 SUMMARY 22

CHAPTER 3 ▪ Indentation Measurement of Soft Tissue Elasticity 23

3.1 INTRODUCTION 23

3.2 ANALYSIS METHODS FOR TRADITIONAL INDENTATION 32

3.2.1 Single-Phase Analysis of Indentation Test 33
3.2.1.1 Effect of Thickness and Poisson's Ratio 34
3.2.1.2 Effect of Finite Deformation 36
3.2.2 Biphasic Analysis of Indentation Test 37
3.2.3 Indentation on Tissues with Curved Substrate 40
3.2.4 Indentation on Tissues with Curved Surface 41
3.2.5 Nonlinear Viscoelasticity and Finite Element Analysis 42
3.3 ENDING REMARKS 42

CHAPTER 4 ▪ Novel Indentation Measurement of Tissue Elasticity *in Vivo* 45

4.1 INTRODUCTION 45
4.2 NOVEL INDENTATION MEASUREMENT 48
4.2.1 Methods 48
4.2.1.1 Ultrasound Indentation 48
4.2.1.2 Ultrasound Water-Jet Indentation 56
4.2.1.3 Optical Indentation 58
4.2.2 Indentation Analysis 64
4.2.3 Reliability and Accuracy Analysis of Measurement 70
4.2.4 Related Measurement of Multiple Tissue Properties 72
4.3 NANOINDENTATION 73
4.4 FUTURE DEVELOPMENT OF INDENTATION 76

CHAPTER 5 ▪ Suction Measurement of Tissue Elasticity *in Vivo* 79

5.1 INTRODUCTION 79
5.2 ANALYSIS OF SUCTION TEST 84
5.2.1 Macroscopic Suction 84
5.2.2 Microscopic Suction 89
5.3 SUMMARY 91

CHAPTER 6 ▪ Indirect Methods for Soft Tissue Elasticity Measurement *in Vivo* 93

6.1 INTRODUCTION 93
6.2 RESONANT FREQUENCY SHIFT MEASUREMENT 94
6.3 VIBRO-ACOUSTIC SPECTROGRAPHY AND HARMONIC MOTION IMAGING 95
6.4 DYNAMIC HOLOGRAPHY 98
6.5 SHEAR WAVE PROPAGATION METHOD 99
6.5.1 Basic Principle of Shear Wave Method 99
6.5.2 Measurement Techniques of Shear Wave Propagation 102
6.5.2.1 Sonoelastography 102
6.5.2.2 Transient Elastography 105
6.5.2.3 Acoustic Radiation Force-Based Elasticity Imaging Techniques 109
6.6 ADVANTAGES, PROBLEMS AND FUTURE PERSPECTIVES 115

CHAPTER 7 ▪ Elasticity Imaging and Elasticity Measurement 119

7.1 INTRODUCTION 119
7.2 ELASTICITY IMAGING TECHNIQUES 120
7.2.1 Quasi-Static Compression and Strain Imaging 120
7.2.2 Dynamic Shear Wave Elastography 123
7.3 SUMMARY 124

CHAPTER 8 ▪ Elasticity, Nonlinearity and Viscoelasticity of Soft Tissues 125

8.1 INTRODUCTION 125
8.2 ORIGINS OF NONLINEARITY AND VISCOELASTICITY 128

8.3 MODELLING OF TISSUE NONLINEARITY AND VISCOELASTICITY 129
8.3.1 Direct Stress–Strain Analysis 129
8.3.2 Lump Element Analysis 130
8.3.3 Quasilinear Viscoelastic (QLV) Model 131
8.4 METHODS FOR MEASUREMENT OF VISCOELASTICITY *IN VIVO* 133
8.5 SUMMARY 133

CHAPTER 9 ■ Finite Element Methods and Inverse Solutions for Elasticity Measurement 135

9.1 INTRODUCTION 135
9.2 PHYSICS FOUNDATION 136
9.3 MODELLING AND SIMULATION 139
9.3.1 Inverse Problem on Quasi-Static Elastography 139
9.3.2 Modelling Wave Propagation 140
9.3.3 Consideration of Acoustic Radiation Force 140
9.3.4 Modelling Indentation 141
9.4 CONCLUSION AND FUTURE RESEARCH DIRECTIONS 143

CHAPTER 10 ■ Clinical Applications of Soft Tissue Elasticity Measurement 145

10.1 INTRODUCTION 145
10.2 APPLICATIONS IN UNDERSTANDING TISSUE PHYSIOLOGY AND COMPUTER MODELLING 146
10.2.1 Skeletal Muscles 146
10.2.2 Surgical Simulation 148
10.3 APPLICATIONS IN DISEASE DIAGNOSIS AND TREATMENT MONITORING 150
10.3.1 Liver Fibrosis 150
10.3.2 Cancer 153
10.3.3 Tissue Degeneration 154

10.4 APPLICATIONS IN DIFFERENT TISSUE PARTS 155
10.5 RELATED DEVICES IN THE MARKET 156
10.6 SUMMARY 158

CHAPTER 11 ▪ Conclusions and Future Perspectives 159

11.1 SUMMARY AND TECHNICAL PERSPECTIVE 159
11.2 APPLICATION PERSPECTIVE 160

REFERENCES, 163

Preface

An important motivation for us to write this book was the lack of a standardised method for tissue elasticity measurement *in vivo*, in spite of so many different techniques available. These techniques have been developed based on different physical principles mainly over the past 30 years, although the first indentation device for the assessment of skin *in vivo* can be traced back to 1912. Researchers working on technological developments tend to focus on the techniques they initiated and make efforts to find more applications. On the other hand, clinicians or researchers working on the applications may either stick to a technique familiar to them or face a challenge of how to select a suitable technique for their applications. For researchers working on mechanics, it is well known that only two independent mechanical parameters are required to describe a homogenous, isotropic, linear and elastic material, which can be any two of Young's modulus, shear modulus and Poisson's ratio. Every material possesses intrinsic mechanical parameters. However, when different techniques are developed by different research groups based on different physical principles for measuring mechanical properties of different soft tissues, highly different parameters are used to represent tissue elasticity. One aim of this book is to provide both engineers interested in developing new methods and clinicians using techniques with an overview of the existing *in vivo* tissue elasticity measurement methods, their physical principles, advantages, disadvantages and assumptions.

Since Prof. Y.C. Fung published his classic textbook on biomechanics, *Biomechanics: Mechanical Properties of Living Tissues*, in 1993, there have been limited techniques available for the measurement of soft tissue elasticity *in vivo*. If readers aim to form a systematic understanding of the fundamental biomechanics of different body tissues, this is the right book to read. The entire field of ultrasound-assisted tissue elasticity measurement and imaging techniques has been rapidly developing since the early 1990s with the representative paper of Prof. J. Ophir and coworkers, 'Elastography: a quantitative method for imaging the elasticity of biological tissues'. *Ultrasound Imaging* 13(2):111–134, in 1991. Later, magnetic resonance imaging (MRI) and optical imaging-assisted techniques were developed. Since then, researchers all over the world have proposed many innovative methods aiming to provide more accurate, intrinsic and convenient measurement of tissue elasticity *in vivo*, including sonoelastography, transient elastography (TE), intravascular elastography, vibro-acoustography, supersonic shear imaging (SSI), harmonic motion imaging, acoustic radiation force impulse imaging (ARFI), magnetic resonance elastography (MRE), optical elastography, etc. More names are generated when the techniques go to commercial domains, such as vibration-controlled transient elastography (VCTE)™, Fibroscan™, Fibrotouch™, Virtual Touch™, real-time tissue elastography™ and shear wave elastography (SWE)™. These techniques have all been described in Chapter 6. As different techniques and devices provide different parameters to indicate tissue elasticity with numerous assumptions, it is almost impossible for end-users to understand the fundamentals. When clinicians use an ultrasound scanner to measure blood flow, they clearly know what the value means. However, when the same clinicians obtain a parameter about tissue elasticity, they have to understand much more about tissue biomechanics, which is often beyond what they have been trained. For many end-users, knowledge about tissue elasticity measurement and imaging may come from a salesperson of a specific device, which requires that the salesperson be very knowledgeable and not be biased with the different techniques available.

In 1993, the authors' team began work on the development of novel techniques for measuring tissue elasticity *in vivo*, starting from ultrasound indentation. Since then, the team has developed a series of methods, including ultrasound indentation, water-jet ultrasound indentation, air-jet indentation, vibro-ultrasound shear wave propagation, real-time image-guided transient elastography, ultrasound compression, ultrasound swelling and optical coherence tomography (OCT)-based indentation and suction. They have become one of the many teams, globally, in generating new terms related to tissue elasticity measurement. During substantial collaborations with collaborators working in many different medical and health care fields, they realised the huge gap between the techniques development engineers and health care professionals use. The users tended to simply accept whatever quantitative parameters a device provided and seldom spent time understanding the principle and assumption behind such parameters. In addition, it is very unique that the author's team has been working on techniques to bridge modern ultrasound and optical imaging with conventional elasticity measurement techniques, including indentation, compression and suction tests. This gives an opportunity for them to appreciate even more the huge diversity of tissue elasticity measurement techniques. There are many devices available using indentation, suction, resonant frequency shift, etc., including Myotonometer™, Myoton™, Cutometer™, Ocular Response Analyzer™, Artscan and tissue ultrasound palpation system (TUPS). The principles of these devices are discussed in related chapters in this book together with the constraints and assumptions used.

In addition to the diversity of measurement techniques and devices, tissue elasticity measurement can be further complicated by the complex mechanical behaviours of soft tissues, particularly measured *in vivo*. Soft tissues are actually inhomogeneous, anisotropic, nonlinear, viscoelastic and time dependent (dynamic). Handling complicated behaviours during the measurement of tissue elasticity is a very important topic. If they are not considered carefully, the reliability of measurement results will be questionable. Again, this kind of knowledge is beyond the understanding of many end-users, such as clinicians who want to use elasticity value of tissues for disease diagnosis or tissue assessment. In this book, we briefly discuss the origins of nonlinearity and viscoelasticity of tissues and how to reduce the influence of such behaviours on the measurement. For more comprehensive understanding of the fundamental knowledge about the topic, the readers may refer to Prof. Fung's book.

While the authors focus on a comprehensive review of tissue elasticity measurement *in vivo*, they also give introductions to many techniques available for *in vitro* studies. These *in vitro* methods are not only important for readers to form an overall understanding of tissue elasticity measurement, but also for validating any newly developed measurement techniques. This book covers topics from measurement techniques to clinical applications. Some typical clinical applications are discussed in Chapter 10, but they are by no means exhaustive. The field of tissue elasticity measurement is still rapidly growing, and the future is difficult to predict. The authors propose two future directions for research in this field. One is to standardise the terms and parameters, or even the test protocols used in different fields in the near future. Currently, when describing tissue elasticity, people in different fields and devices based on different techniques may use different parameters, including modulus, Young's modulus, shear modulus, effective modulus, elastic modulus, shear wave speed, stiffness, hardness, firmness, compliance, tenderness, pliability, etc. Each of these parameters can also be defined differently by different research teams. The second is that one technique can be standardised to dominate the field, while devices can be adapted to fit the measuring requirements for different tissues. In this way, the results obtained for the same tissue by different clinicians at different places can be comparable and a standardised protocol can be established.

Acknowledgements

It would have been impossible for the authors to complete this book without all the research and development work conducted by the PhD and MPhil students: Minhua Lu, Qing Wang, Congzhi Wang, Clare Chao, Shanica Hon, Shuzhe Wang, Alex Choi, Tak-Man Mak, Sushil Patil, Jiawei Li and Connie Cheng; the authors are grateful for their help.

A group of postdoctoral fellows have also contributed to the research work, including Drs. Tianjie Li, Jiaying Zhang, Match Ko, Lei Tian, Haijun Niu, Carrie Ling, Queeny Yuen, Yongjin Zhou and Jun Shi, together with a group of engineers, including Like Wang, Junfeng He, Zhengming Huang, Louis Li, William Chiu, Jiangang Chen, Guohua Pan and Zhongle Wu. Dr. Tianjie Li also directly contributed to Chapter 9.

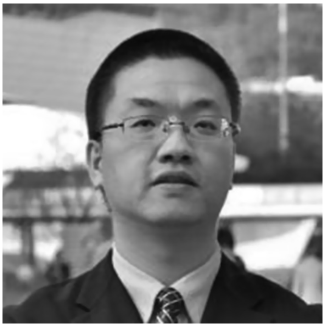
Other team members have also made different kinds of contributions to the field, including Dr. Xin Chen, Dr. Jingyi Guo, Dr. Hongbo Xie, Wentao Liu, Jinsheng Fung, Chunhong Ji, Timothy Lee, Dr. Guangquan Zhou, Dr. Weiwei Jiang, Dr. Haris Begovic, Dr. James Cheung, Yi Wang, Kelly Lee, Jinxin Zhao and Yen Law.

The authors also express their sincere thanks to all their collaborators in different fields, and all these collaborations have inspired them to continue improving techniques for tissue elasticity measurement *in vivo*. They are also thankful to Professor Arthur Mak, their mentor in the field of tissue biomechanics, and to Sally Ding, who has contributed her time and efforts in editing the majority of theses and papers generated by the team. Finally, the authors thank the editorial and production staff of CRC Press for their patience, care and cooperation in producing this book and the supports from colleagues of PolyU Technology and Consultancy Company Limited (PTeC) and Interdisciplinary Division of Biomedical Engineering of the Hong Kong Polytechnic University.

Yong-Ping Zheng
Yan-Ping Huang
Hong Kong

Authors

Professor Yong-Ping Zheng earned BSc and MEng degrees in electronics and information engineering from the University of Science and Technology of China, Hefei, Anhui, P.R. China. He earned his PhD in biomedical engineering from the Hong Kong Polytechnic University (PolyU) in 1997. After a postdoctoral fellowship at the University of Windsor, Canada, he joined PolyU as an assistant professor in 2001 and was promoted to associate professor and professor in 2005 and 2008, respectively. He served as the associate director of the Research Institute of Innovative Products & Technologies in PolyU from 2008 to 2010 and has been serving as the head of the Interdisciplinary Division of Biomedical Engineering since its establishment in 2012. Prof. Zheng's main research interests include tissue elasticity measurement and imaging, biomedical ultrasound imaging and wearable sensors for health care. He has published a large number of papers in the field of ultrasound for soft tissue assessment. As chief supervisor, he has supervised 10 PhD students, 6 MPhil graduates and more than 10 postdoctoral fellows. He is on the editorial boards of a number of journals, including *Ultrasound in Medicine and Biology*, *Physiological Measurement* and *Journal of Orthopaedic Translation*. He is a senior member of the IEEE, a fellow of the Hong Kong Institution of Engineers, and secretary-elect of the World Association of Chinese Biomedical Engineers. He holds 7 U.S. and 10 Chinese patents and has another 8 patents pending, many of which have been licensed to industry for commercialisation.



Dr. Yan-Ping Huang is now a teaching fellow at the Interdisciplinary Division of Biomedical Engineering, Faculty of Engineering, the Hong Kong Polytechnic University, Hung Hom, Hong Kong. He earned his bachelor's degree (2002) in electronic engineering and information science from the University of Science and Technology of China (USTC) in Hefei, and MPhil (2005) and PhD (2013) both in biomedical engineering (BME) from the Hong Kong Polytechnic University. After this, he completed one-year postdoctoral training in the Department of Bioengineering, University of Washington (Seattle), before serving in his current position. His main research interests include the measurement and imaging of soft tissue elasticity, using high-resolution medical imaging techniques such as high-frequency ultrasound and optical coherence tomography, in both instrumental development and preclinical investigations, targeting the early diagnosis of diseases of small-scale tissues, including skin, articular cartilage and the microvascular network. He has abundant experience in research and collaboration in the field of BME related to the measurement of soft tissue elasticity *in vivo* and has published quite a number of internationally peer-reviewed papers in the field.

CHAPTER 1

History and Recent Development in Soft Tissue Elasticity Measurement

Using soft tissue elasticity for the assessment of different pathological conditions has been a clinical approach for thousands of years. The most common technique is referred to as 'palpation', i.e. using fingers to feel tissue elasticity (Figure 1.1). The elasticity of soft tissues can be referred to as hardness, stiffness and so on, which represents how much a tissue can be deformed under a certain loading condition. For example, when a tissue is undergoing fibrosis, it becomes stiffer; when there is an oedema, it may become softer. In ancient Greece, palpation was recommended as a method to detect stiffening or pain of the abdomen by Hippocratic physicians (Nicolson 1993). For example, palpation was used as part of the practice for differentiating between ascites and tympanites. Because of the difference in internal fluids, the operator would feel quite differently for the two different pathologies. In the eighteenth century, palpation was also used as a bedside practice for the detection of tumour as recorded in Mogagni's classic work *The Seats and Causes of Diseases as Investigated by Anatomy*: 'and being asked to feel the man's belly, I scarcely perceiv'd any particular tumor elsewhere than in the scrobiculus cordis'.