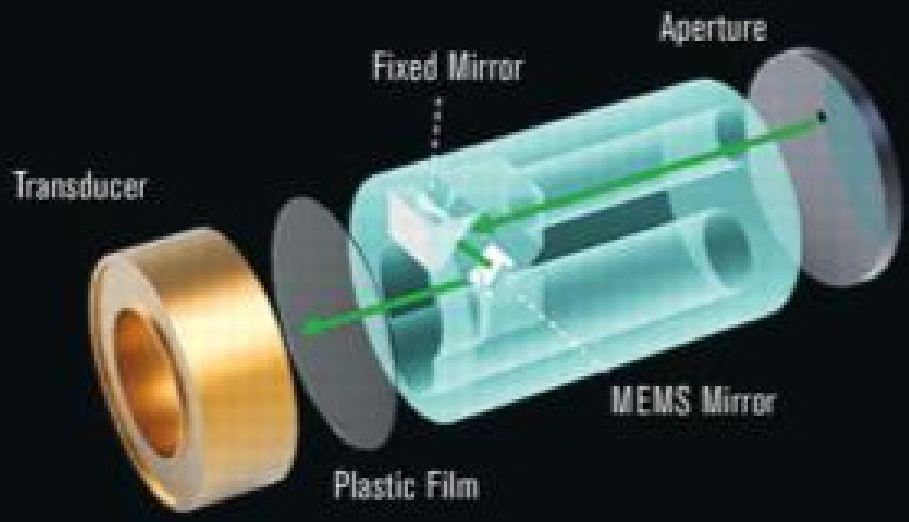

Photoacoustic Tomography

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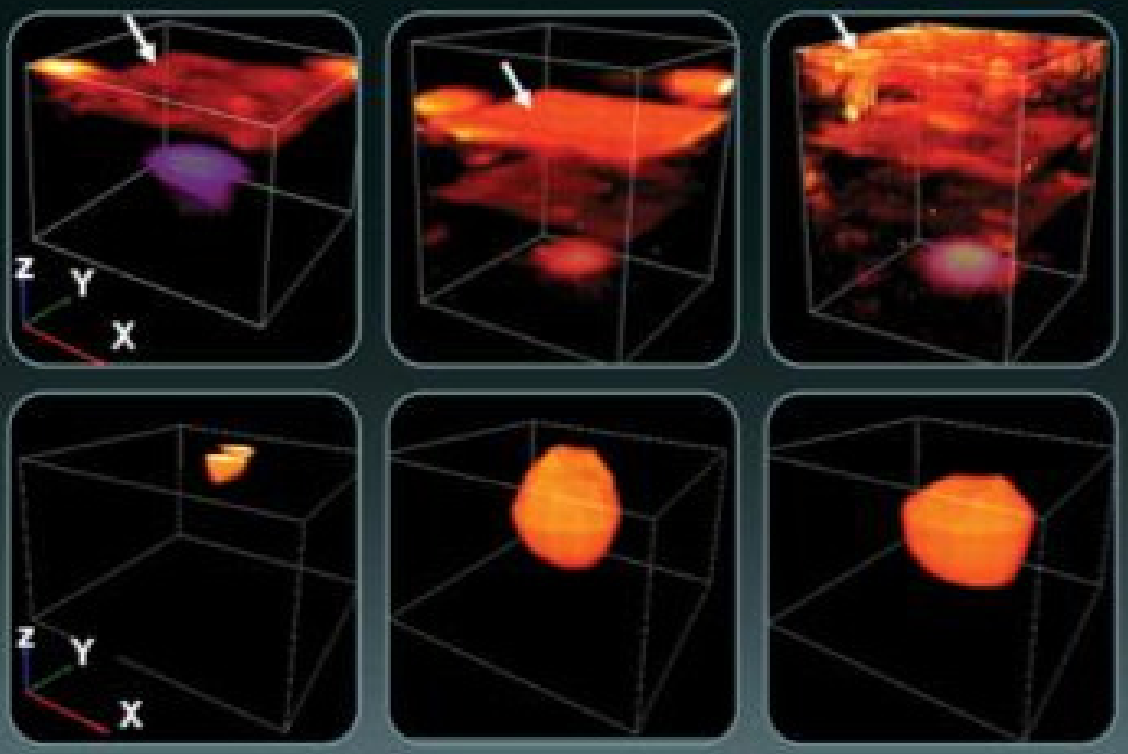

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To Yonghong, Max, and Michael

Contents

Preface

Photoacoustic tomography (PAT) is an emerging biomedical imaging modality that combines the high-contrast and spectroscopic-based specificity of optical imaging with the high spatial resolution of ultrasound imaging in a single modality. By listening to light, PAT detects tissue-absorbed photons ultrasonically through the photoacoustic effect. Since ultrasonic scattering is two to three orders of magnitude weaker than optical scattering in tissue, PAT breaks the 2–4 mm spatial resolution limit associated with pure optical tomography such as diffuse optical tomography (DOT) for deep tissue imaging, or the ~1 mm depth limit associated with confocal and multiphoton microscopy and optical coherent tomography (OCT). In PAT, tissue is excited with a short (typically a few nanoseconds) laser pulse (focused or unfocused); the subsequent laser-induced transient photoacoustic waves in the range of 1–100 MHz, due to the transient thermoelastic expansion of light-absorbing components in tissue, are detected by wideband unfocused or focused ultrasound transducer(s). Unique advantages of PAT are that functional or biochemical parameters such as deoxy-hemoglobin (HbR), oxy-hemoglobin (HbO_2), water (H_2O), lipids, and so forth along with vasculature and blood flow can be imaged in high resolution. In addition, highly specific molecular PAT can be realized through the use of molecular contrast agents. Finally, PAT can be made portable for bedside applications, is economical, and uses non-ionization radiation.

PAT has found its potential clinical applications in several areas. In breast imaging, PAT offers the submillimeter-resolution ability to quantitatively image the high optical contrast generated through the presence of blood, water, and lipid, which are the predominant transformations associated with malignancy. Clinical studies conducted at multiple institutions and countries have repeatedly shown that 2-to-11 and higher absorption contrasts exist in breast cancers that can be imaged by PAT. These studies suggest that PAT has the potential to detect breast tumors at early stages. Application of PAT to joint imaging has been recently explored, offering an opportunity for early detection and monitoring of progressive diseases including osteoarthritis and rheumatoid arthritis. In this case, the optical contrast is produced through the degraded articular cartilage and the increased water content and turbidity in the synovial cavity. Other clinical applications of PAT also are *starting to appear*, including intravascular imaging and intraoperative imaging during cancer treatment.

While brain imaging and electrophysiology play a central role in neuroscience research and in the evaluation of neurological disorders, a single noninvasive modality that offers both high spatial and temporal resolution is currently not available. PAT may become such a neuroimaging modality at least in animals. In Chapter 8, I show an acute epilepsy rat model in which PAT can noninvasively track seizure brain dynamics with both high spatial and temporal resolution and at a depth that is clinically relevant. The noninvasive yet whole surface and depth capabilities of PAT actually seeing what is happening during ictogenesis in terms of seizure onset and spread.

The concept of PAT emerged in the mid-1990s, and the field of PAT is now rapidly moving forward. Several reviews and edited books on PAT have been published. However, I have decided to write a book that presents a detailed and comprehensive treatment of PAT. It appears timely to produce such a book for the first time in this field. The book is essentially a collection of the research work that the author and his colleagues have been pursuing over the past decade. This actually presents a unique feature of the book as it allows the principles of PAT and its applications to be treated in a systematic way. In addition, the collection covers almost every aspect on PAT from mathematics, image reconstruction methods, instrumentation, and phantom/animal experiments to clinical applications. I believe this book will be particularly useful for graduate students and researchers who wish to enter the field of PAT.

In Chapter 1, the fundamentals of PAT are presented including the theory on photoacoustic effect, various image reconstruction methods, and instrumentation. Chapter 2 describes various advanced methods for quantitative PAT, which allow the recovery of tissue optical absorption coefficients and/or acoustic properties. Experimental validations of the reconstruction methods are also presented here. The development of several image-enhancing schemes including both software and hardware approaches are discussed in Chapter 3. Chapter 4 describes array-based PAT systems that are the foundation for the realization of 2D, 3D, and 4-D PAT. Photoacoustic microscopy (PAM), a variation of PAT, is detailed in Chapter 5. The recent development of multimodality methods is presented in Chapter 6. These works describe the combinations of PAT/PAM with other imaging methods including DOT, fluorescence molecular tomography (FMT), ultrasound imaging and OCT, which represent new directions in the field of PAT. Chapter 7 focuses on the discussion of contrast agents–based molecular PAT where both nontargeted and cell receptor–targeted methods are included. Chapter 8, the final chapter, describes the clinical applications and animal studies in the areas of breast cancer detection, osteoarthritis diagnosis, seizure localization, intravascular imaging, and image-guided cancer therapy.

I wish to thank my previous and current colleagues whose contributions to the works presented have made this book possible. I would also like to thank the staff at CRC Press, especially associate editor Ashley Gasque and project coordinator Jill Jurgensen, who have worked diligently at bringing this book to fruition. Finally, my wife, Yonghong, and my family made it all worthwhile.

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