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# BIOLOGICAL AND MEDICAL PHYSICS, BIOMEDICAL ENGINEERING

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Wolfgang Drexler
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(Eds.)

# Optical Coherence Tomography

## Technology and Applications

With 758 Figures

Springer

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Library of Congress Control Number : 2007943142

ISSN 1618-7210

ISBN 978-3-540-77549-2 Springer Berlin Heidelberg New York



Springer is a part of Springer Science+Business Media.

springer.com



Typesetting: Camera-ready by SPi Publisher Services, Pondicherry
Cover: eStudio Calamar Steinen

Printed on acid-free paper SPIN 10912041 57/3180/SPi - 5 4 3 2 1 0

# Preface

New medical imaging technologies can improve the diagnosis and the clinical management of disease. Furthermore, they can also contribute to a better understanding of disease pathogenesis and therefore advance the development of novel therapies. These new technologies thus have a powerful impact in medical research and clinical practice. Minimally invasive imaging techniques, e.g. X-ray computed tomography (CT), magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), radioisotope imaging (position emission tomography PET and SPECT), and diffuse optical tomography (DOT) have revolutionized diagnostic medicine during the last decades. These techniques permit three-dimensional visualization; however, their spatial resolution is typically limited to a few millimeters in standard clinical practice. Optical imaging techniques such as conventional microscopy as well as confocal, fluorescence, and multiphoton microscopy enable high axial and transverse ($\leq 1\,\mu$m) resolution imaging, but have limited penetration in biological tissue. Excisional biopsy and histopathology remain the gold standard for cancer diagnostics. However, information is not available in real time and diagnostics based on biopsies can suffer from unacceptable false-negative rates because of sampling errors.

An imaging modality that enables noninvasive, simultaneous imaging of both three-dimensional cellular resolution tissue morphology as well as assessment of depth resolved function could significantly improve early medical diagnosis, contribute to a better understanding of disease pathogenesis, and enhance the monitoring of therapy. Optical coherence tomography (OCT) is an emerging, noninvasive optical medical diagnostic imaging modality, which enables in vivo cross-sectional tomographic visualization of the internal microstructure in biological systems. Since its invention in the late 1980s and early 1990s, the original concept of OCT was to enable noninvasive optical biopsy, i.e. the real time, in situ imaging of tissue microstructure with a resolution approaching that of histology, but without the need for tissue excision and postprocessing. To accomplish – or to approach – this challenging goal, recent research in OCT has achieved quantum advances in resolution, data acquisition speed, optimization of tissue penetration, as well as contrast enhancement. Development of state-of-the-art delivery systems, facilitated the application of OCT in a variety of medical fields, enable the imaging of internal body organs. Furthermore, extensions of OCT have been developed that enable non-invasive *depth resolved* functional imaging, providing spectroscopic, polarization-sensitive, blood flow or physiologic tissue information. These new OCT technologies promise to not only improve image contrast but should also to enable the differentiation of pathologies via localized metabolic properties or functional (physiologic) state.

As a consequence, there have been numerous recent developments in OCT technology and considerable interest in this topic – especially in the field of ophthalmology, gastroenterology, and cardiology. Objectively this is evidenced by a tremendous increase in publications (≈90 in 1998, to 900 in 2006, for a total of ≈5,000), patents (≈9 granted patents in 1998, to more than 90 in 2006), and companies involved in the field of OCT (≈3 in 1998, to more than 20 in 2006). It is noteworthy that about 50% of all OCT publications (≈2,500) so far have been published in ophthalmic journals, demonstrating the significant impact of this OCT in this field. Another 25% (≈1,250) have been published in optics journals, reflecting the numerous technical advances that have been accomplished. In the year 1998, OCT publications were cited ≈700 times, where as in the year 2006, more than 10,000 publications citations referred to OCT research. The market for OCT equipment is predicted to grow at a compound annual rate of over 30% in the next four years reaching €200 million by the year 2011. The clinical impact of OCT, especially in ophthalmology, is also demonstrated by the fact that several fourth generation of commercial instruments have recently been introduced and that, worldwide, there are more than one half dozen companies commercializing this technology for ophthalmic diagnosis.

These significant recent advances in OCT technology as well as the successful OCT applications in a variety of medical fields initiated the idea for this book. The objective of this book is to comprehensively summarize and critically highlight the state of the art of OCT technology and its applications by leading international experts in the specific fields. The chapters presented herein have been grouped into 5 themes:

- Two chapters give an overview, history, as well as basic theory of OCT. The modeling of light tissue interactions in OCT systems is described in Chap. 3.
- In Part I, eleven chapters summarize the state-of-the-art *OCT Technology*, including Spectral/Fourier, Frequency Domain OCT, Ultrahigh Resolution OCT, superluminescent diodes, ultrashort pulse and tuneable light sources for OCT, as well as optical designs, linear OCT systems, and OCT signal and image processing.
- In Part II, six chapters focus on *En face OCT and Optical Coherence Microscopy* including flying spot and acoustic optic modulation-based

en face OCT, scanning OCM, second harmonic OCT, and combined multiphoton microscopy with OCT, full field and holographic OCT.
- In Part III, eight chapters introduce *extensions of OCT* describing Doppler flow, polarization sensitive, spectroscopic, molecular contrast, phase-resolved OCT as well as OCT combined with fluorescence, elastic scattering spectroscopy combined with OCT, and optical tissue clearing for OCT.
- In Part IV, the final fourteen chapters summarize the broad spectrum of *medical OCT applications* including tissue engineering, developmental biology, ophthalmology, gastrointestinal endoscopy, intravascular imaging, dermatology, laryngology, as well as applications in the oral cavity, pulmonary area, gynaecology, urology, and other hollow organ systems. A final chapter describes the development of technology for clinical imaging.

Because of the recent advances in OCT performance, e.g. resolution, scanning/data acquisition speed, sensitivity and penetration, many new applications of this technology are now becoming possible. In the future, OCT will likely continue to grow with the development of new applications in different medical specialties as well as new applications to fundamental science. OCT is in a unique position not only to perform non-invasive visualization of microstructural morphology, but also to enable unprecedented, depth-resolved functional assessment of tissue – ideally performed with a single measurement. OCT can now be considered as an optical analogue to CT or MRI, but with microscopic resolution. In addition to functional extensions of OCT, this technique might have the potential to revolutionize medical diagnosis in the very near future. It is unlikely, though, that OCT will replace excisional biopsy and histology or other existing diagnostic modalities. However, from the viewpoint of screening and diagnosis of diseases, OCT might enable significantly new insight in the pathogenesis and therapy control of several diseases. The unique features of this developed technology would enable a broad range of research and clinical applications, which might not only complement many of the existing imaging technologies available today, but also will potentially reveal previously unseen morphological, dynamic, and functional changes in different biological tissues and medical fields.

This book would not have been possible without the participation of many leading international researchers and their groups. The editors are especially grateful to the numerous contributors for their significant and indispensable efforts that resulted in this comprehensive and state-of-the-art review of OCT and its applications. We are also especially grateful to Claus Ascheron (Springer) and the publication staff, Adelheid Duhm, Elke Sauer, and others at Springer for their efforts to make this book possible.

On behalf of all the co-authors we hope you find this book interesting, enlightening, and stimulating.

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March 2008 *James G. Fujimoto*

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