Engineering Materials

The “Engineering Materials” series provides topical information on innovative, structural and functional materials and composites with applications in optical, electronical, mechanical, civil, aeronautical, medical, bio and nano engineering. The individual volumes are complete, comprehensive monographs covering the structure, properties, manufacturing process and applications of these materials. This multidisciplinary series is devoted to professionals, students and all those interested in the latest developments in the Materials Science field.

More information about this series at http://www.springer.com/series/4288

Zhe Liu
Editor

Advances in Functional Micro-/Nanoimaging Probes

Springer

Editor
Zhe Liu
Academy of Medical Engineering and
Translational Medicine
Tianjin University
Tianjin, People's Republic of China

ISSN 1612-1317 ISSN 1868-1212 (electronic)
Engineering Materials
ISBN 978-981-10-4803-6 ISBN 978-981-10-4804-3 (eBook)
https://doi.org/10.1007/978-981-10-4804-3

Library of Congress Control Number: 2018950929

This Springer imprint is published by the registered company Springer Nature Singapore Pte Ltd.
The registered company address is: 152 Beach Road, #21-01/04 Gateway East, Singapore 189721, Singapore

This book is dedicated to people who endeavor to develop molecular imaging technologies, materials, and bridge them with bio-engineering and clinical uses.

It is also presented to my lovely daughter, who always conceives wonderful ideas and embraces the unknown nature with curiosity.

Zhe Liu

Foreword I

With the emerging techniques of biomedical imaging and imaging probes, molecular imaging has become a useful tool to investigate the mechanisms of disease occurrence and metastasis. The innovations of functional imaging materials or molecular probes help enhance image contrast and make invisible bioprocesses visible. Imaging techniques come into a multimodal era, and more and more technologies have fused into place. Therefore, the combination of imaging devices and probes will reinforce the significance of biomedical imaging in both research and clinical studies. This book provides a systematic description of molecular imaging history, current status, and advanced developments on micro-/nanofunctional imaging probes for both basic research and biomedical applications. It will be a useful handbook for newcomers to learn basic knowledge in this area, and also to provide professionals to keep an eye on such frontiers.

Meanwhile, artificial intelligence (AI) has rapidly changed the mode of medical diagnosis and therapy to improve human health care. AI has also found applications along with medical imaging for precision medicine, and individualized treatments. To this end, AI engineers are currently working together with clinical doctors to boost their translations to bedside use in the field of early stage assessment, meta-image diagnosis, big data analysis, etc. It can be expected that multidisciplinary studies powered by AI will shed a new perspective on future medicine.

Hangzhou, China

Pintong Huang, M.D. and Ph.D.
Professor and Chief of Department
of Ultrasound in Medicine;
The 2nd Affiliated Hospital,
School of Medicine, Zhejiang University;
Director of the Molecular Imaging and Artificial
Intelligence Committee,
Chinese Ultrasound Doctor's Association;
Director of Zhejiang Society of Ultrasonics
Medical Engineering Association

Foreword II

Medical imaging has witnessed rapid advancements in the last century, and various imaging techniques have been widely applied for the diagnoses of human diseases. This book, Edited by Dr. Zhe Liu, summarized the recent developments in the fields of molecular imaging, brand-new imaging devices, and their mechanisms. Multimodality imaging techniques and image-based surgery (or therapy) described in this book will facilitate people to understand life sciences and find optimized treatment strategies for important human diseases.

On the other hand, multifunctional imaging biomaterials especially the imaging probes have been actively developed in the past decades, and many of them have been approved for clinical trials in Europe or the United States. With the aid of imaging probes or contrast agents, molecular imaging has been endowed with higher resolution and sensitivity with which biological or pathological processes were monitored and detected precisely at the molecular or cellular level. This book pays much emphasis on the innovations of imaging probes and using their dual or multimodal imaging properties for biological applications. Thus, for scientists in both academic and industry, they will find usefulness in this book which will help them to step into the molecular imaging world and make relevant investigations. Now is the right time to take this book into the market, bridging the connections between imaging techniques, biomaterials, basic biology, and material sciences.

Besides that, the functional micro-/nanoimaging probes have found clinical applications in MRI, PET, ultrasound, etc. The real translation of functional imaging materials from bench to bed will revolutionize the theranostic styles to a large extent and accelerate our understanding of brain sciences and disease mechanisms. It will also give birth to an unprecedented opportunity for human health improvements. Hopefully, this book can play multiple roles in the abovementioned areas and help molecular imaging with an ever-fast development in the near future.

Hefei, China

Prof. Gaolin Liang, Ph.D.
Department of Chemistry, University
of Sciences and Technology of China

Foreword III

This book provides a valuable resource for a comprehensive understanding of the field of micro- and nanotechnology-based materials for enhancing the functionality of medical imaging modalities. It is written as a set of five chapters providing independent viewpoints of the broad subject matter. In comparison, each chapter offers both common and unique contributions to the theory and practice of the field.

Chapter 1 provides an explanation of each major imaging modality and the importance of micro- and nanoparticle probes within a rich historical context. Single and multi-modality strategies are introduced for diagnosis alone and combined therapeutic/diagnostic ("theranostic") purposes. A valuable contribution comprises a list of commercial probes.

Chapter 2 addresses design parameters and fabrication protocols for micro- and nanoparticles with properties required for the appropriate performance such as biocompatibility, specificity, signal strength, and clearance. Material selection, chemical conversions, and physical production techniques are addressed in depth. Principles provided have both specific and general product development ramifications.

Chapter 3 takes each imaging mode separately (MRI, US, OI, PET, X-Ray, and CT), and describes, in extensive detail, the compositions and actions of their function-enhancing probes. Clinical applications and issues are addressed, even to the detail of specific organs being imaged and products being used. Dual and multiple modalities such as image-guided controlled drug delivery and dual instrumental analysis are described as advanced technologies being implemented.

Chapter 4 focuses on current, commercially available, imaging probes, and those in clinical development for disease prognosis. It goes into the most detail of the book chapters in correlating: manufacturer/materials/imaging modality/targeted organs. A valuable compendium of tables containing such information is provided.

Chapter 5 provides a forward-looking picture of developing imaging techniques, therapeutic targets, and treatment approaches. A prominently highlighted and explained technique yielding enhanced fluorescence imaging involves "aggregation-induced emission". Complex, micron-scale composite materials for image-guided and targeted therapy in conjunction with irradiation, thermal, or ultrasonic energy are

emerging for treating cancer and other lesions. Finally, imaging probes for the detection of bacteria and modified nanoparticles that kill bacteria when subjected to near-infrared radiation show promise for treating infections.

Maximum benefit from this book can be derived as an introduction to the field of nanoscale and microscale probes for medical imaging by reading it in detail. Alternatively, the book chapters can be perused for information on particular topics such as specific imaging modalities, particle compositions, commercial products, etc. Every chapter may contain information on a particular subject and can be "mined" for valuable content with unique perspectives.

It is finally noted that the references provided are both extensive and current. They represent the most advanced stages of the field being addressed, and a substantive proportion of the publications referenced represent the work of the authors of this book.

Respectfully submitted,

Boston, MA, USA

Arthur J. Coury, Ph.D.
University Distinguished Professor
Northeastern University

Preface

Today is the 123rd anniversary since people obtained the first X-ray image of humans, and from then on we have learned more about the body's anatomical structures and functions.

Today is the nineteenth anniversary since the concept of molecular imaging was proposed, and from then on we have witnessed fast development of imaging technologies, and their successful medical application for disease diagnosis.

We are entering a new era that people seek to know more about themselves, from brain sciences to health care and from disease treatment to body examinations. Molecular imaging is far more than an isolated subject but has become a powerful tool to make predictions for people's health, provide golden standards for molecular diagnosis, and integrate relevant medical techniques into efficient and painless therapies. Right in front of us, a milestone is set where we need to reflect on past proceedings, and boost enduring advances for interdisciplinary and eventual clinical translation.

In particular, visualized medicine is a new innovation area that provides disease diagnosis, treatment, and surgery with an intuitive approach and an online evaluation methodology. Among them, functional micro-/nanoimaging probes make visualized medicine more convenient and accessible to use. Unprecedented opportunities beyond such challenges can be expected to give birth to a roaring revolution in this field, and this was our motivation to start writing this book, and also the destination in which we present it to readers.

Kind regards,

Tianjin, China

Zhe Liu Ph.D.
Academy of Medical Engineering and
Translational Medicine
Tianjin University

Acknowledgements

We authors appreciate for the kind help and valuable assistance in the composition of the book from our colleagues of Tianjin University, Institute of Chemistry, Chinese Academy of Sciences (ICCAS), Beijing National Laboratory for Molecular Sciences (BNLMS), The Second Affiliated Hospital of Zhejiang University, Wenzhou Institute of Biomaterials and Engineering, Chinese Academy of Sciences, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Hangzhou Red Cross Hospital, Northeastern University (USA) and Kyushu University (Japan). Special thanks should be addressed to Profs. Thomas J. Webster and Arthur J. Coury for their elaborate English editing for the book manuscript.

Three distinguished scholars in the fields of material research, basic biological sciences, and clinical doctors have been invited to write Foreword. They provided readers with different insights and forward-looking ideas from their viewpoints, and this will help us acquire an overall understanding and keep pace with their advances.

This contribution was financially supported by the National Natural Science Foundation of China (21575106), Joint Research Fund of Beijing National Laboratory of Molecular Sciences, Joint Research Fund of Key Laboratory of Analytical Chemistry for Living Biosystems, Chinese Academy of Sciences, the Scientific Research Foundation for Returned Scholars, Ministry of Education of China and Zhejiang Qianjiang Talents Program.

In the end, I would like to thank all the authors' arduous contributions and close collaborations with Springer editors for the book production. This work is challenging, but enjoyable and fulfilling indeed.

Contents

Contributors

Run Chang Department of Chemical Engineering, Northeastern University, Boston, MA, USA

Kai Chen The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Waner Chen Wenzhou Institute of Biomaterials and Engineering, Chinese Academy of Sciences, Wenzhou, People's Republic of China

Yueyue Cheng The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Yanyan Dong The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Ming Gao Department of Chemical Engineering, Northeastern University, Boston, MA, USA

Xuemei Gu The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Chunchun He The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Jianle Huang The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Daren Liu The Second Affiliated Hospital of Zhejiang University, Hangzhou, People's Republic of China

Li Liu Institute of Chemistry, Chinese Academy of Sciences, Beijing, People's Republic of China; Beijing National Laboratory for Molecular Sciences, Beijing, People's Republic of China

Xiangjun Liu Beijing National Laboratory for Molecular Sciences, Key Laboratory of Analytical Chemistry for Living Biosystems, CAS Research/Education Center for Excellence in Molecular Sciences, Institute of Chemistry, Chinese Academy of Sciences, Beijing, People's Republic of China

Zhe Liu Academy of Medical Engineering and Translational Medicine, Tianjin University, Tianjin, People's Republic of China; Wenzhou Institute of Biomaterials and Engineering, Chinese Academy of Sciences, Wenzhou, People's Republic of China; The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China; Wenzhou Institute of Biomaterials and Engineering, Wenzhou Medical University, Wenzhou, People's Republic of China

Wei Ma Institute for Materials Chemistry and Engineering (IMCE), Kyushu University, Fukuoka, Japan

Xianwei Ni The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Dihua Shangguan Beijing National Laboratory for Molecular Sciences, Key Laboratory of Analytical Chemistry for Living Biosystems, CAS Research/Education Center for Excellence in Molecular Sciences, Institute of Chemistry, Chinese Academy of Sciences, Beijing, People's Republic of China

Qiuming Su School of Medicine, Zhejiang University, Hangzhou, People's Republic of China

Linlin Sun Department of Chemical Engineering, Northeastern University, Boston, MA, USA

Chengfang Wang The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Doudou Wang Wenzhou Medical University, Wenzhou, People's Republic of China

Liping Wang The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Pengfei Wang The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Thomas J. Webster Department of Chemical Engineering, Northeastern University, Boston, MA, USA

Beibei Wu The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Senmin Wu The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Shunlong Xu The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Gaoyi Yang Hangzhou Red Cross Hospital, Hangzhou, People's Republic of China

Yan Yang The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Jinmin Ye The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Fangfang Yu The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Hui Zhu The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Chunpeng Zou The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China

Abbreviations

2PM	Two-photon microscopy
ACPP	Activatable cell penetrating peptide
ACQ	Aggregation-caused quenching
AD	Alzheimer's disease
AIE	Aggregation-induced emission
AMO	Amoxicillin
ATO	Antimony-doped tin oxide
BBB	Blood–brain barrier
BFCs	Bifunctional chelators
BL	Bladder
BLI	Bioluminescence imaging
BMA	Bis-methylamine
BMEA	Bis (methoxyethylamide)
$CaCO_3$-MNP	Calcium carbonate mineralized nanoparticle
CAs	Contrast agents
CCD	Charge-coupled device
CDs	Carbon dots
CE US	Contrast-enhanced US
CE-Gd	Core-encapsulated Gd
CE-MRA	Contrast-enhanced magnetic resonance angiography
CMC	Critical micelle concentration
CNS	Central nervous system
CNTs	Carbon nanotubes
CS	Chitosan
CT	Computed tomography
DAPTA	D-Ala1-peptide T-amide
DBCO	Azadibenzocyclooctyne
DO3A	Dodecane-1,4,7-triacetate
DOT	Diffuse optical tomography
DOTA	Dodecane-1,4,7,10-tetraacetic acid

DOX	Doxorubicin
DSWC	Dorsal skinfold window chamber
DTPA	Diethylenetriaminepentaacetic acid
DTX	Docetaxel
EBD	Endocardial border delineation
ECD	Ethylcysteinate dimers
ECL	Electrochemiluminescence
EDC	1-ethyl-3-(3-dimethylaminopropyl) carbodiimide
EGFP	Enhanced green fluorescent protein
EGFR	Epidermal growth factor receptor
EOB	Ethoxybenzyl
EPR	Enhanced permeability and retention
FA	Folic acid
FCH	Fluoromethylcholine
FDA	Food and Drug Administration
FDG	Fluoro-2-deoxy-D-glucose
FMT	Fluorescence-mediated tomography
FPT	Fluorescence protein tomography
FR	Folate receptor
FRI	Fluorescence reflectance imaging
FUS	Focused ultrasound
GABA	Gamma-aminobutyric acid
GB CAs	Gd-based contrast agents
Gd	Gadolinium
Gd-BOPTA	Gadobenatedimeglumine
GFP	Green fluorescent protein
GGPNPS	Gas-generating polymeric nanoparticle system
GI	Gastrointestinal
GTA	Glutaraldehyde
HAIs	Healthcare-associated infections
HCC	Hepatocellular carcinoma
HIFU	High-intensity focused ultrasound
HMONs	Hollow mesoporous organosilica nanoparticles
HMPAO	Hexamethylpropyleneamine oxime
HMRG	Hydroxymethyl rhodamine green
HP	Hydroxypropyl
HPS	Hexaphenylsilole
HR-FRI	High-resolution FRI
HSA	Human serum albumin
HS-MBs	Hard-shelled MBs
HT	Hyperthermia
i.v.	Intravenous
IBD	Inflammatory bowel disease
ICG	Indocyanine green
IONP	Iron oxide nanoparticle

LBL	Layer by layer
LECs	Lymphatic endothelial cells
LGE	Late Gd enhancement
LN	Lymph node
LN-MRI	Lymphotropic nanoparticle-enhanced MRI
LSPR	Localized surface plasmon resonance
LTSL	Lyso-thermosensitive liposomal
LVO	Left ventricular opacification
MB	Methylene blue
MBs	Microbubbles
MDR	Multidrug resistance
MI	Mechanical index
MMR	Macrophage mannose receptor
MPM	Multiphoton microscopy
mpMRI	Multiparametric MRI
MRgFUS	MR-guided FUS
MRI	Magnetic resonance imaging
MRR	MR renography
MRSA	Methicillin resistance *S. aureus*
MRU	MR urography
MSCT	Multislice CT
MSOT	Multispectrum optoacoustic tomography
MWCNTs	Multi-walled carbon nanotubes
NBs	Nanobubbles
NHS	*N*-hydroxysuccinimide
NIH	National Institute of Health
NIR	Near infrared
NP	Nanoparticle
NSF	Nephrogenic systemic fibrosis
OATP1B3	Organic anion-transporting polypeptide 1B3
OCT	Optical coherence tomography
OFDI	Optical frequency-domain imaging
OI	Optical imaging
PA	Photoacoustic
PAA	Polyacrylic acid
PAMAM	Polyamidoamine
PBLG	Poly (γ-benzyl L-glutamate)
PBT	Poly (butylene terephthalate)
PCL	Poly-ε-caprolactone
PCR	Polymer chain reaction
PDT	Photodynamic therapy
PEG	Polyethylene glycol
PEO	Poly (ethylene oxide)
PET	Positron emission tomography
PFC	Perfluorocarbon

PL	Photoluminescence
PLL	Poly-L-lysine
PpIX	Protoporphyrin
PSA	Prostate-specific antigen
PSMA	Prostate-specific membrane antigen
PTT	Photothermal therapy
PTX	Paclitaxel
PVA	Polyvinyl alcohol
PVP	Polyvinylpyrrolidone
QDs	Quantum dots
RES	Reticuloendothelial system
RF	Radio frequency
RFP	Red fluorescent protein
RGD	Arg-Gly-Asp
rGO	Reduced grapheme oxide
RIR	Restricted intramolecular rotation
ROI	Region of interest
SCC	Squamous cell carcinoma
SCF	Stem cell factor
SC-Gd	Surface-conjugated Gd
SDF	Stromal cell-derived factor
SDT	Sonodynamic therapy
SEM	Scanning electron microscopy
SERS	Surface enhance Raman scattering
SGC	Scirrhous gastric cancer
SiNP	Silica-based nanoparticle
SLNs	Sentinel lymph nodes
SNR	Signal-to-noise ratio
SPECT	Single-photon emission computed tomography
SPION	Superparamagnetic iron oxide nanoparticle
SS-MBs	Soft-shelled MBs
SSPIO	Standard SPIO
TEM	Transmission electron microscopy
THF	Tetrahydrofuran
TMEDA	Tetramethylethylenediamine
TNBC	Triple-negative breast cancer
TOP	Trioctylphosphine
TOPO	Trioctylphosphine oxide
TPE	Tetraphenyl ethane
TPE	Tetraphenylethylene
TRUS	Transrectal ultrasound
TSPO	Translocator protein
UCAs	Ultrasound contrast agents
UDI	Ultrasound dispersion imaging
UR	Urine

US	Ultrasound
USPION	Ultrasmall SPION
UTMD	Ultrasound-targeted microbubble destruction
UV	Ultraviolet
VAN	Vancomycin
VCAM	Vascular cell adhesion molecule
VEGFR	Vascular endothelial growth factor receptor
ZA	Zoledronic acid