Personalized Pathway-Activated Systems Imaging in Oncology

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Editors

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Principal and Instrumentation

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Foreword

In the past 40 years, there has been an enormous increase in the range of imaging techniques available to investigate patients with cancer. Imaging modalities including computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, optical imaging, and gamma scintigraphy have been used to diagnose cancer. Although CT and MRI provide considerable anatomic information about the location and the extent of tumors, they do not adequately provide optimal staging and differentiate residual or recurrent tumors from edema, radiation necrosis, or gliosis. Ultrasound images demonstrate local regional abnormalities, but they are operator-dependent. The optical imaging showed promising results; however, its ability to detect deep tissue penetration still has rooms to improve. Radionuclide imaging modalities (positron emission tomography, PET; single photon emission computed tomography, SPECT) are diagnostic cross-sectional imaging techniques that map the location and concentration of radionuclide-labeled compounds. Beyond knowing precisely where a tumor is and its size, shape, and viability, PET and SPECT are making it possible to target the molecular makeup of the tumor and its metabolic activity. Whereas PET and SPECT can provide a very accurate picture of metabolically active areas, its ability to show anatomic features is limited. As a result, new imaging modalities have begun to combine PET and SPECT images with CT scans used for treatment planning. PET-CT or SPECT-CT scanners combine anatomic and functional images taken during a single procedure, without having to reposition the patient between scans. PET-CT or SPECT-CT becomes a tool for image-guided pathway-directed precision therapy.

^{18}F-fluorodeoxyglucose (FDG) has been used to diagnose and stage tumors, myocardial infarction, and neurological disease by PET. Although tumor metabolic imaging using ^{18}F-FDG has been studied in the last two decades, its clinical practice is still hampered by factors such as differentiation of infection/tumor recurrence and low-grade/high-grade tumors. To improve the diagnosis, prognosis, planning, and monitoring of the cancer treatment, the characterization of tumor tissue is extensively determined by the development of more tumor-specific radiopharmaceuticals. The novel molecular imaging agent enables the comprehensive characterization of therapeutic intervention due to their specificity in molecular targets. Molecular

imaging agents have potential application in patient selection, pharmacokinetic, dosage-finding, and proof-of-concept studies. To improve the diagnosis and prognosis and the planning, monitoring, and predicting of the cancer treatment, novel PET or SPECT imaging agents as well as higher-resolution PET-CT or SPECT-CT scanners are needed that would allow precise measurement of molecular pathways on a whole-body image upon administration of a functional molecular imaging agent. These mechanism-based agents provide image-guided therapy that may discontinue ineffective treatment of diseases in the earlier phase and benefit patients. The development of a compounded single kit for clinical imaging was reviewed in this book. The kit formulation fulfills cGMP compliance for standardization and optimization of the drug product; meets quality assurance of sterility, pyrogenicity, and other analyses; and could shorten manufacturing time and reduce production cost by using generator-produced isotopes. This book seeks to bridge the gap from translational science to bedside.

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Preface

The development of molecular biology and genetics over the past 50 years has provided medical science with unprecedented chances to study the molecular basis of diseases. Imaging becomes involved in the age of molecular medicine by creating new contrast media and radiopharmaceuticals. New classes of contrast agents based on tissue-specific uptake were developed. Molecular imaging science has been focused on imaging guidance in the areas of targeting epigenetic abnormalities and tumor microenvironment in overcoming resistance in cancers. The use of image-guided technologies to select patient for personalized therapy and to monitor therapeutic outcomes is the focus of this book.

Nuclear and optical imaging agents could play major roles in the move from imaging of structure and morphology to the visualization of the individual biologic processes underlying disease and could contribute to more accurate diagnostics and improved treatment efficacy. In the chapter, the progress in the translation of macroscopic optical imaging and applications—including fluorescence imaging, FISH and optical tomography, and flow cytometry—was reviewed. The trends in nuclear imaging agent development were reviewed. Regulatory compliance of an imaging agent from bench to bedside was reviewed. The emergence of novel imaging agents in conjunction with specialized reconstruction algorithms can provide not only high-quality and high-resolution MRI or CT-like images but also functional information. This improvement in imaging technology allows quantitative target assessment of microenvironmental hemodynamics and subsequently in the imaging session.

The topics covered in this book are advances in molecular imaging both in radioactive and nonradioactive applications in preclinical drug discovery, drug development, regulatory compliance, and instrumentation for better management of cancer patients.

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