

Abdelhamid H. Elgazzar

# Orthopedic Nuclear Medicine

Second Edition

 Springer

---

# Orthopedic Nuclear Medicine

---

Abdelhamid H. Elgazzar

# Orthopedic Nuclear Medicine

Second Edition

 Springer

Abdelhamid H. Elgazzar  
Department of Nuclear Medicine  
Kuwait University  
Safat, Kuwait

ISBN 978-3-319-56165-3      ISBN 978-3-319-56167-7 (eBook)  
DOI 10.1007/978-3-319-56167-7

Library of Congress Control Number: 2017945675

© Springer-Verlag Berlin Heidelberg 2004; © Springer International Publishing AG 2017

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Printed on acid-free paper

This Springer imprint is published by Springer Nature  
The registered company is Springer International Publishing AG  
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

---

## Foreword

Technetium-99m-labeled bone imaging agents were introduced to the nuclear medicine community almost 50 years ago, and the resultant literature has become a vast web of knowledge concerning the pathophysiology, diagnosis, and therapy of skeletal (and marrow) disorders. Many authors have attempted to organize and structure this information to produce an interactive heuristic approach to skeletal scintigraphy, pathologic soft tissue uptake, and the therapy of painful osteoblastic metastases. This writer is among those who have attempted to produce such a volume, and I know from this arduous experience how difficult is the task.

It is therefore an honor and a pleasure to write a foreword to the second edition of *Orthopedic Nuclear Medicine*, by Abdelhamid H. Elgazzar, MD, an internationally recognized nuclear medicine specialist, researcher, and highly productive author, whose analytic, incisive, and inquisitive mind gave early promise of an outstanding career.

Dr. Elgazzar has produced the finest monograph on skeletal imaging to date, an encyclopedic work, beautifully illustrated with planar and tomographic (SPECT and PET) scintigraphs and excellent correlative radiographs. Impressive histologic illustrations are an important part of the author's approach to explaining the basic science and pathophysiology behind scintigraphic findings. The book focuses on, and updates, its coverage of simultaneously imaging with SPECT or PET and computed tomography/magnetic resonance. Besides the technetium-99m bisphosphonates, there are thorough discussions of other important radiopharmaceuticals and their clinical applications, including fluorine-18-FDG of course, sodium fluoride-F-18, and gallium-68 (as the citrate and as a label for PMSA). The text is further complemented by a wise tabular approach to differential diagnosis, as well as by clear illustrative diagrams. The bibliography and index have been appropriately and extensively updated as well.

This second edition of *Orthopedic Nuclear Medicine* should receive the accolades of the international nuclear medicine/radiology community: practitioners, researchers, teachers, trainees, and students. Dr. Elgazzar has written a remarkable, updated, beautifully produced book.

Cincinnati, OH, USA

Edward B. Silberstein, M.A., M.D.  
Eugene L. and Sue R. Saenger  
Professor of Radiological Sciences  
Professor of Medicine, Emeritus  
University of Cincinnati Medical Center

---

## Preface to the Second Edition

Nuclear medicine and molecular imaging have continued to develop with impressive advances in recent years. With the introduction of newer radiotracers and the use of hybrid imaging, the role of nuclear medicine in orthopedics has further grown in diagnosis and treatment of various bone and joint diseases.

This new edition of the book has accordingly been significantly updated with newer applications of hybrid imaging and the use of positron emission tracers in bone diseases. This text with the update and addition of two new chapters provides students and medical professionals with a comprehensive and clearly presented update on nuclear medicine and molecular imaging applications in orthopedic medicine. Global vision was considered however, given the limited resources in some communities which necessitates keeping presentation of certain modalities and procedures with their updates. The book begins with a chapter presenting fundamental anatomic, physiologic, pathologic, and technical concepts relevant to understanding orthopedic functional imaging and its use in clinical practice. Subsequent chapters cover diagnosis of skeletal infections, trauma, vascular disorders, metabolic bone diseases, neoplastic bone diseases, soft tissue calcifications, and joint disorders. A chapter on bone marrow imaging and another on hybrid imaging in musculoskeletal disorders have been added in this edition. The final chapter is devoted to the use of radionuclides in the treatment of bone and joint diseases.

This text continues to be unique in its brief, yet comprehensive and in-depth, approach to clarity through the creative use of numerous illustrations and figures; many have been added and updated. Because an understanding of both normal pathophysiology and morbid pathophysiology is a prerequisite for the successful use of orthopedic nuclear medicine, necessary pathophysiological aspects are presented at the beginning of each chapter, followed by a description of the use of scintigraphy for the various disease processes as well as correlative imaging.

The book is intended for all those interested in orthopedics, including radiologists, orthopedic surgeons, internists, pediatricians, other clinicians, and nuclear medicine professionals at all levels. My aim is to advance knowledge in orthopedic nuclear medicine, clarify and increase awareness of its important impact on the management of benign and malignant conditions, and hence improve its use for patients with various bone and joint disorders.

---

## Acknowledgment

My thanks and appreciation go to Dr. Khattab Khaled, Dr. Salwa Shams, Mrs. Heba Issam, Dr. Ismet Sarikaya, Prof. Abdullatif Al-Bader, Mrs. Reham Al-Hajji, Mr. Junaid Ziaee, Prof. Edward Silberstein, Prof. Medhat Osman, Prof. Mehraj Sheikh, Dr. Saud Enezi, Prof. Isabel Roca, Dr. Dia Shehab, Dr. Charito Love, Mrs. Aseel Alkandari, Dr. Sakr Assad, Dr. Sherif Haiba, Dr. Abdelmonem Omar, Mr. Talal Albanai, Mr. Attia Alsheshtawi, Dr. Ali Zankawi, Miss Samar Almutairi, Mr. LS Spencer and Dr. Jehan Alshammari for their sincere and valuable support.

Contributor to Chapter 11

Dr. Ismet Sarikaya,

Associate Professor, Department of Nuclear Medicine,

Kuwait University,

Kuwait



---

# Contents

<b>1</b>	<b>Basic Sciences of Bone and Joint Diseases</b>	1
1.1	Introduction	2
1.2	Anatomy and Physiology of Bone	2
1.2.1	Bone Development	2
1.2.2	Bone Anatomy	3
1.2.3	Bone Physiology	7
1.3	Anatomy and Physiology of Bone Marrow	11
1.4	Anatomy and Physiology of Joints	11
1.5	Spectrum of Bone and Joint Disease	13
1.6	Modalities for Imaging Bone and Joint Diseases	14
1.7	Diagnosis of Bone and Joint Diseases by Nuclear Medicine Techniques	15
1.8	Technical Considerations	18
1.8.1	Pre-imaging Considerations	18
1.8.2	Imaging Considerations	22
1.8.3	Post-Imaging Considerations	29
1.8.4	Sources of Diagnostic Errors	30
	References	35
<b>2</b>	<b>Diagnosis of Inflammatory Bone Diseases</b>	37
2.1	Introduction	38
2.2	Pathophysiology	38
2.2.1	Inflammation	38
2.2.2	Skeletal Infections	41
2.3	Imaging Skeletal Infections	49
2.3.1	The Need for Diagnostic Imaging	49
2.3.2	Imaging Modalities for Skeletal Infections	50
2.4	Diagnosis of Skeletal Infection by Imaging	50
2.4.1	Diagnosis Using Morphologic Imaging Modalities	50
2.4.2	Diagnosis by Scintigraphic Methods	52
2.4.3	Imaging Using Combined Modalities	63
2.5	Diagnosis of Specific Forms of Skeletal Infections	63
2.5.1	Diabetic Foot Osteomyelitis	63
2.5.2	Vertebral Osteomyelitis (Spondylodiscitis)	70
2.5.3	Chronic Active Osteomyelitis	73
2.5.4	Periprosthetic Infection	77

2.5.5	Posttraumatic Osteomyelitis . . . . .	83
2.5.6	Osteomyelitis in Patients with Sickle Cell Disease . . . . .	84
2.5.7	Neonatal Osteomyelitis . . . . .	84
2.5.8	Epiphyseal Osteomyelitis . . . . .	84
2.6	Follow-Up of Response to Therapy . . . . .	85
2.7	Differentiating Osteomyelitis from Infectious Arthritis . . . . .	85
2.8	Differentiating Infection from Tumors . . . . .	85
2.9	Noninfectious Inflammatory Conditions . . . . .	86
2.9.1	Chronic Nonbacterial Osteomyelitis . . . . .	86
2.9.2	Osteitis Condensans Ilii . . . . .	88
2.9.3	Osteitis Pubis . . . . .	88
2.9.4	Infantile Cortical Hyperostosis (Caffey-Silverman Disease) . . . . .	88
2.9.5	Sternoclavicular Hyperostosis . . . . .	88
2.9.6	Osteitis Condensans of the Clavicle . . . . .	88
2.10	Scintigraphic Patterns of Skeletal Manifestations of Poliomyelitis . . . . .	90
	References . . . . .	90
<b>3</b>	<b>Diagnosis of Metabolic, Endocrine, and Congenital Bone Disease . . . . .</b>	<b>101</b>
3.1	Introduction . . . . .	101
3.2	Paget's Disease (Osteitis Deformans) . . . . .	102
3.3	Osteoporosis . . . . .	109
3.4	Osteomalacia and Rickets . . . . .	114
3.5	Hyperparathyroidism . . . . .	116
3.6	Renal Osteodystrophy . . . . .	119
3.7	Complex Regional Pain Syndrome I (Reflex Sympathetic Dystrophy) . . . . .	122
3.8	Hypertrophic Osteoarthropathy . . . . .	127
3.9	Fibrous Dysplasia . . . . .	128
3.10	Other Metabolic and Endocrine Conditions . . . . .	131
3.10.1	Hypothyroidism . . . . .	131
3.10.2	Hyperthyroidism . . . . .	131
3.10.3	Fluoride Toxicity . . . . .	131
3.10.4	Aluminum Toxicity . . . . .	131
3.10.5	Hypervitaminosis A . . . . .	131
3.11	Osteopetrosis . . . . .	132
3.12	Medullary Diaphyseal Sclerosis (Medullary Diaphyseal Stenosis or Hardcastle Syndrome) . . . . .	132
3.13	Gorlin's Syndrome . . . . .	132
3.14	Progressive Diaphyseal Dysplasia (Camurati-Engelmann Disease) . . . . .	134
3.15	Infantile Cortical Hyperostosis (Caffey-Silverman Syndrome) . . . . .	136
3.16	Madibular Condylar Hyperplasia . . . . .	136
	References . . . . .	138

<b>4</b>	<b>Diagnosis of Traumatic Disorders</b> . . . . .	147
4.1	Introduction . . . . .	147
4.2	Pathophysiology . . . . .	148
4.2.1	Acute Fractures . . . . .	148
4.2.2	Stress Fractures . . . . .	149
4.2.3	Spondylolysis . . . . .	150
4.2.4	Spondylolisthesis . . . . .	150
4.2.5	Fracture Healing . . . . .	150
4.2.6	Trauma to Bone-Adjacent Structures . . . . .	153
4.3	Scintigraphic Diagnosis of Acute Fractures . . . . .	153
4.3.1	Role of Scintigraphy in Acute Fracture . . . . .	153
4.3.2	Scintigraphic Appearance of Acute Fractures . . . . .	154
4.3.3	Scintigraphic Imaging of Specific Fractures . . . . .	155
4.4	Scintigraphic Diagnosis of Stress Fractures . . . . .	168
4.4.1	Role of Scintigraphy in Stress Fractures . . . . .	168
4.4.2	Scintigraphic Appearance of Stress Fractures . . . . .	169
4.4.3	Scintigraphic Diagnosis of Specific Stress Fractures . . . . .	172
4.5	Scintigraphic Evaluation of Fracture and Bone Graft Healing . . . . .	180
4.5.1	Evaluation of Fracture Healing . . . . .	180
4.5.2	Evaluation of Bone Graft Viability . . . . .	180
4.5.3	Evaluation of Metallic Implants for Removal . . . . .	181
4.6	Scintigraphic Diagnosis of Injuries to Bone-Adjacent Structures . . . . .	182
4.6.1	Avulsion Injury . . . . .	182
4.6.2	Skeletal Muscle Injury . . . . .	182
4.6.3	Post-Traumatic Soft Tissue Calcification . . . . .	183
4.6.4	Meniscal and Ligament Tears . . . . .	183
4.6.5	Enthesopathies . . . . .	183
4.6.6	Impingement Syndromes . . . . .	183
	References . . . . .	184
<b>5</b>	<b>Diagnosis of Circulatory Disorders</b> . . . . .	191
5.1	Introduction . . . . .	191
5.2	Pathophysiology . . . . .	192
5.3	General Scintigraphic Features and Staging . . . . .	193
5.4	Distinctive Forms of Osteonecrosis . . . . .	195
5.4.1	Post-traumatic Osteonecrosis . . . . .	195
5.4.2	Osteonecrosis of the Femoral Head in Children (Legg-Calvé-Perthes Disease) . . . . .	195
5.4.3	Osteonecrosis of the Femoral Head in Adults . . . . .	199
5.4.4	Spontaneous Osteonecrosis of the Knee . . . . .	201
5.4.5	Multifocal Osteonecrosis . . . . .	204
5.4.6	Sickle Cell Disease Osteonecrosis . . . . .	205
5.4.7	Dysbaric Osteonecrosis . . . . .	206
5.4.8	Osteochondroses Featuring Osteonecrosis . . . . .	206
	References . . . . .	209

<b>6</b>	<b>Neoplastic Bone Diseases</b> .....	213
6.1	Introduction .....	214
6.2	Pathophysiology .....	215
6.2.1	Primary Bone Tumors .....	215
6.2.2	Metastatic Bone Disease .....	225
6.3	Imaging of Primary Bone Tumors .....	232
6.3.1	Overall Role of Imaging .....	232
6.3.2	Imaging of Major Specific Primary Tumors .....	236
6.4	Scintigraphy and Correlative Imaging of Metastatic Bone Disease .....	249
6.4.1	Scintigraphic Patterns of Bone Metastases on Bone Scans .....	251
6.4.2	Scintigraphic Evaluation of Metastases of Certain Tumors .....	257
6.5	Follow-Up of Malignant Bone Disease .....	269
	References .....	272
<b>7</b>	<b>Diagnosis of Joint Disorders</b> .....	281
7.1	Introduction .....	282
7.2	Classification .....	282
7.3	Rheumatoid Arthritis .....	283
7.4	Crystal Deposition Arthropathies .....	286
7.4.1	Gouty Arthritis .....	286
7.4.2	Calcium Pyrophosphate Dihydrate Deposition Disease .....	287
7.5	Infectious Arthritis .....	288
7.6	Osteoarthritis .....	288
7.7	Sacroiliitis .....	293
7.8	Neuroarthropathy .....	296
7.9	Spondyloarthropathies .....	296
7.9.1	Ankylosing Spondylitis .....	297
7.9.2	Psoriatic Arthritis .....	297
7.9.3	Reactive Arthritis (Reiter's Disease) .....	298
7.9.4	Enteropathic Spondylitis .....	299
7.10	Other Arthropathies and Related Conditions .....	299
7.10.1	Behçet's Syndrome .....	299
7.10.2	Costochondritis (Tietze's Syndrome) .....	299
7.10.3	SAPHO Syndrome .....	299
7.10.4	Synovitis .....	300
7.11	Periarticular Soft Tissue Syndromes .....	301
7.11.1	Diffuse Idiopathic Skeletal Hyperostosis (DISH) .....	301
7.11.2	Septic Bursitis .....	302
7.11.3	Septic Tenosynovitis .....	302
7.11.4	Plantar Fasciitis .....	302
	References .....	303

<b>8</b>	<b>Bone Marrow Imaging</b> .....	307
8.1	Introduction .....	307
8.2	Development and Structure of Bone Marrow .....	307
8.3	Conversion and Reconversion .....	310
8.4	Alterations to Bone Marrow .....	311
8.5	Imaging of Bone Marrow .....	311
8.6	Bone Marrow Scintigraphy .....	312
8.7	Clinical Uses of Bone Marrow Scintigraphy .....	314
8.7.1	Diagnosis of Skeletal Infections .....	314
8.7.2	Assessment and Follow-Up of Gaucher's Disease .....	317
8.7.3	Treatment Planning in Cancer Patients .....	318
8.7.4	Paget's Disease .....	319
8.7.5	Bone Marrow Tumors and Bone Marrow Extension .....	320
8.7.6	Other Uses .....	320
	References .....	320
<b>9</b>	<b>Diagnosis of Soft Tissue Calcification</b> .....	323
9.1	Introduction .....	324
9.2	Dystrophic Calcification .....	324
9.3	Metastatic Calcification .....	325
9.4	Heterotopic Bone Formation .....	331
9.4.1	Pathophysiology .....	331
9.4.2	Scintigraphic Evaluation .....	334
9.4.3	Correlative Imaging .....	339
9.4.4	Special Forms of Heterotopic Bone Formation .....	339
9.5	Calcinosis Cutis .....	344
9.5.1	Calcinosis Cutis Universalis .....	344
9.5.2	Calcinosis Cutis Circumscripta .....	345
9.6	Rhabdomyolysis .....	345
	References .....	345
<b>10</b>	<b>Hybrid Imaging in the Diagnosis of Bone Diseases</b> .....	349
10.1	Introduction .....	349
10.2	SPECT/CT .....	349
10.2.1	Uses of SPECT/CT in Neoplastic Diseases .....	350
10.2.2	Uses of SPECT/CT in Nonneoplastic Diseases .....	353
10.3	PET/CT .....	372
10.3.1	F-18 FDG PET/CT .....	372
10.3.2	F-18 Sodium Fluoride PET/CT .....	374
10.3.3	Combined F-18 NaF and F-18 FDG PET/CT .....	376
10.3.4	Ga-68-Citrate PET/CT .....	378
10.3.5	Ga-68 PSMA PET/CT .....	378
10.4	PET/MR .....	378
	References .....	382

<b>11 Therapeutic Use of Radionuclides in Bone and Joint Disease.</b> . . . . .	387
11.1 Introduction . . . . .	388
11.2 Treatment of Cancer-Related Bone Pain . . . . .	388
11.2.1 Rationale . . . . .	388
11.2.2 Radiopharmaceuticals . . . . .	389
11.2.3 Mechanism of Action. . . . .	392
11.2.4 Choice of Radiopharmaceutical. . . . .	393
11.2.5 Clinical Use . . . . .	394
11.3 Radionuclide Synovectomy. . . . .	397
11.3.1 Rationale . . . . .	397
11.3.2 Radiopharmaceuticals . . . . .	397
11.3.3 Choice of Radiopharmaceutical. . . . .	400
11.3.4 Clinical Uses . . . . .	401
11.4 Other Radionuclide Therapies . . . . .	407
11.4.1 Treatment of Primary Osteogenic Sarcoma. . . . .	407
11.4.2 Metastatic Prostate Carcinoma . . . . .	408
11.4.3 Multiple Myeloma . . . . .	408
11.4.4 Treatment of Neuroblastoma . . . . .	409
11.4.5 Bone Marrow Ablation . . . . .	410
References. . . . .	410
<b>Glossary</b> . . . . .	417
<b>Index</b> . . . . .	421

## Contents

1.1	<b>Introduction</b> .....	2
1.2	<b>Anatomy and Physiology of Bone</b> .....	2
1.2.1	Bone Development.....	2
1.2.2	Bone Anatomy.....	3
1.2.3	Bone Physiology.....	7
1.3	<b>Anatomy and Physiology of Bone Marrow</b> .....	11
1.4	<b>Anatomy and Physiology of Joints</b> .....	11
1.5	<b>Spectrum of Bone and Joint Disease</b> .....	13
1.6	<b>Modalities for Imaging Bone and Joint Diseases</b> .....	14
1.7	<b>Diagnosis of Bone and Joint Diseases by Nuclear Medicine Techniques</b> .....	15
1.8	<b>Technical Considerations</b> .....	18
1.8.1	Pre-imaging Considerations.....	18
1.8.2	Imaging Considerations.....	22
1.8.3	Post-Imaging Considerations.....	29
1.8.4	Sources of Diagnostic Errors.....	30
	<b>References</b> .....	35

The bone develops by intramembranous and endochondral ossification. Intramembranous ossification occurs through the transformation of mesenchymal cells into osteoblasts, while in endochondral ossification, a pre-existing cartilage forms first and then undergoes ossification. Two types of bone tissues form the skeleton, compact or cortical bone and cancellous, trabecular, or spongy bone. The spongy bone has a turnover rate approximately eight times greater than that of cortical bones. The bone is formed of three types of cells: osteoblasts, which produce the organic bone matrix; osteocytes, which produce the inorganic matrix; and osteoclasts, which are responsible for bone resorption. The bone marrow converts into yellow, or inactive, marrow, gradually reaching an adult pattern by the age of 25 years. The yellow marrow may revert due to the stress associated with several pathological and physiological processes. Joints develop in the mesenchyme between the ends of bones and are classified into several types according to their functional features as well as the nature of the adjoining tissue. The principal response of the bone to injury, and disease, is reactive bone formation; this is the basis of increased uptake of bone-specific radiopharmaceuticals, namely, Tc-99m diphosphonates and F-18 sodium fluoride. Other specific bone and joint pathological changes define the patterns of uptake of other radiopharmaceuticals used for imaging such diseases [e.g., gallium-67, labeled leukocytes, thallium-201, Tc-99m methoxyisobutylisonitrile (MIBI), and F-18 fluorodeoxyglucose (FDG)]. The factors that ensure the best possible