

Contents

Authors and Co-Authors of Volume 5	vii
Preface	xv
Introduction	xvii
Contents of Volumes 1, 2, 3, and 4	xix

Part I Liver Cancer

A. Diagnosis

1. Applications of Positron Emission Tomography in Liver Imaging: An Overview	5
Amir H. Khandani	
Introduction.....	5
Metastatic Liver Disease.....	7
Cholangiocarcinoma.....	10
Gall Bladder Carcinoma.....	11
Hepatocellular Carcinoma.....	12
Therapy Monitoring.....	14
References.....	15
2. Localized Fibrous Tumor of the Liver: Imaging Features	17
Thomas Moser and Tereza S. Nogueira	
References.....	19

3. A Radial Magnetic Resonance Imaging Method for Imaging Abdominal Neoplasms.....	21
Maria I. Altbach	
Introduction.....	21
Techniques for T2-Weighted Imaging	22
Lesion Characterization with T2-Weighted Imaging.....	22
Radial Magnetic Resonance Imaging Methods:	
An Alternative for Reducing Motion Artifacts and Improving Image Quality	24
Radial Fast Spin-Echo, A New Alternative for T2 Mapping of the Liver	27
Conclusions.....	30
References.....	30
4. Liver: Helical Computed Tomography and Magnetic Resonance Imaging.....	33
Yuji Baba, Yasuyuki Yamashita, Kazuo Awai, and Koichi Kawanaka	
Introduction.....	33
Dynamic Computed Tomography Using Multi-Detector Computed Tomography.....	33
Tumors Arising in Liver Cirrhosis	35
Tumor Arising in Noncirrhotic Liver or in Oncologic Patients	36
Computed Tomography Angiography	36
Angiography-Assisted Computed Tomography.....	36
Computed Tomography During Arterial Portography	37
Computed Tomography During Hepatic Angiography.....	39
Magnetic Resonance Imaging.....	39
Dynamic Magnetic Resonance Imaging	39
Superparamagnetic Iron Oxide	40
References.....	42

Part II Resectable Liver Cancer

A. Diagnosis

5. Selection of Patients for Resection of Hepatic Colorectal Metastases: 18F-Fluorodeoxyglucose/Positron Emission Tomography	49
Rebecca Auer and Yuman Fong	
Introduction.....	49
Positron Emission Tomography Scanning as a Staging Modality to Complement Conventional Imaging	50
Positron Emission Tomography Scan for the Detection of Extrahepatic Disease.....	50

Positron Emission Tomography Scan for the Detection of Intrahepatic Disease.....	51
Value of Positron Emission Tomography Correlated to Prognostic Clinical Risk Score (CRS).....	52
Positive Impact of Positron Emission Tomography on the Management of Patients with Liver Metastases.....	53
Negative Impact of Positron Emission Tomography on the Management of Patients with Liver Metastases.....	54
Outcome of Patients Selected for Hepatic Resection Following [¹⁸ F]Fluorodeoxyglucose-Positron Emission Tomography (FDG-PET)	54
Standard Uptake Value and Predicting Prognosis or Response to Therapy	55
Positron Emission Tomography Scanning for Surveillance and Follow-Up.....	57
The Role of Positron Emission Tomography in Evaluating an Elevated Carcinoembryonic Antigen (CEA)	57
The Role of Positron Emission Tomography in Follow-Up Post Hepatic Resection.....	58
Algorithm to Include Positron Emission Tomography Scanning in Work-Up of Hepatic Colorectal Metastases.....	58
Conclusion	59
References.....	59
B. Treatment	
6. Ultrasonography During Liver Surgery	63
Guido Torzilli	
Introduction.....	63
Technical Aspects	63
Liver Exploration	64
Resection Guidance	69
Hepatocellular Carcinoma	69
Liver Metastases	73
References.....	74
Part III Unresectable Liver Cancer	
A. Treatment	
7. Intraoperative Magnetic Resonance Imaging for Radiofrequency Ablation of Hepatic Tumors.....	81
Oliver F. Bathe and Houman Mahallati	
Introduction.....	81
Radiofrequency Ablation as a Treatment for Liver Tumors	81

Principles of Radiofrequency Ablation.....	81
Indications.....	83
Outcomes Associated with Radiofrequency Ablation	84
Alternative Ablative Techniques.....	85
Problems Associated with Monitoring the Ablative Endpoint	86
Impedence and Temperature.....	86
Ultrasound.....	86
Defining the Extent of Thermal Injury by Magnetic Resonance Imaging.....	86
Magnetic Resonance Imaging Characteristics of Thermal Injury	86
Enhancing the Definition of Extent of Thermal Injury	88
Potential Utility of Functional Magnetic Resonance Imaging.....	89
Intraoperative Magnetic Resonance Imaging as an Adjunct to Radiofrequency Ablation.....	90
Rationale	90
Technical Developments.....	90
Potential Indications.....	92
Conduct of Intraoperative Magnetic Resonance Imaging for Radiofrequency Ablation	92
Future Developments	96
References.....	98
8. Surgically Unresectable and Chemotherapy-Refractory Metastatic Liver Carcinoma: Treatment with Yttrium-90 Microsphere Followed by Assessment with Positron Emission Tomography	103
Ching-Yee Oliver Wong	
Introduction.....	103
Assessment Using Positron Emission Tomography.....	104
Y-90 Microsphere Radioembolization	105
Clinical Results	109
Illustrations	111
References.....	112
B. Prognosis	
9. Unresectable Liver Metastases from Colorectal Cancer: Methodology and Prognosis with Radiofrequency Ablation	117
Junji Machi	
Introduction.....	117
Methodology of Radiofrequency Ablation	118
Prognosis Using Radiofrequency Ablation: Our Study	120
Patients and Methods	120

Unresectability of Tumors	120
Preoperative and Intraoperative Evaluation	121
Radiofrequency Ablation Methods	121
Postoperative Follow-Up.....	122
Statistical Analyses	122
Short-Term Results	123
Long-Term Results.....	123
Current Role of Radiofrequency Ablation	124
Future Perspective.....	128
References.....	129

Part IV Hepatocellular Carcinoma

A. Diagnosis

10. Screening with Ultrasonography of Patients at High-Risk for Hepatocellular Carcinoma: Thrombocytopenia as a Valid Surrogate of Cirrhosis	137
Sheng-Nan Lu, Jing-Houng Wang, Kwong-Ming Kee, and Po-Lin Tseng	
Introduction.....	137
Epidemiology of Hepatocellular Carcinoma and Liver Cirrhosis	137
Benefit of HCC Screening	138
Surrogate Tests for Liver Cirrhosis and Fibrosis	139
Ultrasonographic HCC Screening on the Thrombocytopenic Adult	141
References.....	142
11. Hepatocellular Carcinoma: Contrast-Enhanced Sonography.....	145
Byung Ihn Choi and Se Hyung Kim	
Introduction.....	145
Physics of Microbubbles.....	146
Contrast-Enhanced Color Doppler Sonography	146
Contrast-Enhanced Power Doppler Sonography	147
Contrast-Enhanced Harmonic Power Doppler Sonography	147
Contrast-Enhanced Pulse-Inversion Harmonic Sonography.....	148
Contrast-Enhanced Coded Harmonic Sonography	150
Contrast-Enhanced Agent Detection Imaging	151
Low Mechanical Index Imaging	153
Contrast-Enhanced Sonography in Assessing the Therapeutic Response of Hepatocellular Carcinomas	153
References.....	156

12. Focal Liver Lesion: Nonlinear Contrast-Enhanced Ultrasound Imaging	159
Vincenzo Migaletto and Giuseppe Virgilio	
Introduction.....	159
Harmonic Imaging: Basic Principles	160
Physical and Technological Background	162
Nonlinear Contrast Enhancement of Focal Liver Lesions	163
(A) Characterization of Focal Liver Lesions	163
(B) Detection of Focal Liver Lesions.....	171
(C) Monitoring of Percutaneous Ablative Treatment	174
Conclusion	176
References.....	177
13. Hepatocellular Carcinoma: Magnetic Resonance Imaging	183
Bachir Taouli	
Introduction.....	183
Magnetic Resonance Imaging Technique	183
Magnetic Resonance Imaging Appearance of Hepatocellular Carcinoma	184
Gadolinium Enhancement of Hepatocellular Carcinoma	186
Magnetic Resonance Imaging Tissue-Specific Contrast Agents	187
Combined Use of Superparamagnetic Iron Oxide and Gadolinium	187
Atypical Appearances of Hepatocellular Carcinoma.....	188
New Perspectives	189
References.....	190
14. Expression of Vascular Endothelial Growth Factor in Hepatocellular Carcinoma: Correlation with Radiologic Findings	193
Masayuki Kanematsu, Richard C. Semelka, and Shinji Osada	
Introduction.....	193
History of Radiologic Diagnosis of Hepatocellular Carcinoma	194
Development of Hepatocellular Carcinoma, Its Vasculature, and Vascular Endothelial Growth Factor Expression	196
Correlation of Vascular Endothelial Growth Factor Expression and Radiologic Findings in Hepatocellular Carcinoma in Prior Reports	199
Our Previous Research with Immunohistochemistry.....	200
Magnetic Resonance and Computed Tomographic Data Correlated to Vascular Endothelial Growth Factor Measured Using Western Blotting	202
Summary	209
References.....	210

15. Detection of Small Hepatic Lesions: Superparamagnetic Oxide-Enhanced Diffusion-Weighted T2 FSE Imaging	213
Shigeru Kiryu and Kuni Ohtomo	
Introduction.....	213
Superparamagnetic Iron Oxide-Enhanced Magnetic Resonance Imaging.....	213
Diffusion-Weighted Imaging for Suppression of Signals from Hepatic Vessels	214
Periodically Rotated Overlapping Parallel Lines with Enhanced Reconstruction Technique.....	215
SPIO-Enhanced DWI T2 FSE Imaging Using Propeller	216
References.....	218
 16. Diagnosis of Hepatocellular Carcinoma: Multidetector-Row Computed Tomography and Magnetic Resonance Imaging.....	 221
Hiromitsu Onishi, Takamichi Murakami, and Hironobu Nakamura	
Introduction.....	221
Multidetector-Row Helical Computed Tomography.....	221
Multidetector-Row Helical Computed Tomography Scanning Technique	222
Contrast Administration for the Dynamic Multidetector-Row Helical Computed Tomography Study	222
Administration Dose of Contrast Material.....	222
Iodine Concentration of Contrast Material	223
Injection Flow Rate and Duration of Contrast Material	223
Optimal Scanning Delay	223
Scanning Timing	224
Image Processing	224
Magnetic Resonance Imaging.....	225
Magnetic Resonance Scanning Technique.....	225
Contrast-Enhanced Dynamic Magnetic Resonance Imaging	226
Tissue-Specific Contrast-Enhanced Magnetic Resonance Imaging.....	226
Computed Tomography Imaging Features of Hepatocellular Carcinoma	227
Computed Tomographic Angiography.....	228
Magnetic Resonance Imaging Features of Hepatocellular Carcinoma	229
Superparamagnetic Iron Oxide-Enhanced Magnetic Resonance Imaging Feature of Hepatocellular Carcinoma	230
Staging of Hepatocellular Carcinoma.....	231
Accuracy for the Diagnosis of Hepatocellular Carcinoma	232

Hepatocellular Carcinoma After Transcatherter Arterial Chemoembolization.....	232
Hepatocellular Carcinoma After Percutaneous Radiofrequency Ablation Therapy.....	232
Limitations and Prospects.....	233
Summary.....	233
References.....	233
17. Hepatocellular Carcinoma: Effect of Injection Rate/Injection Duration of Contrast Material on Computed Tomography.....	237
Tomoaki Ichikawa and Tsutomu Araki	
Introduction.....	237
Fixed Injection Rate and Injection Duration of Contrast Material.....	237
Fixed Injection Rate of Contrast Material.....	238
Fixed Injection Duration of Contrast Material.....	239
References.....	239
18. Detection of Combined Hepatocellular and Cholangiocarcinomas: Enhanced Computed Tomography.....	241
Akihiro Nishie and Kengo Yoshimitsu	
Introduction.....	241
Pathogenesis.....	242
Enhanced Computed Tomographic Findings.....	243
References.....	247
19. Hepatocellular Carcinoma and Adenomatous Hyperplasia (Dysplastic Nodules): Dynamic Computed Tomography and a Combination of Computed Tomography and Angiography.....	249
Kenichi Takayasu	
Introduction.....	249
Classification of Nodular Hepatocellular Lesions.....	249
Multistep Progression of Hepatocarcinogenesis.....	250
Needle Biopsy.....	252
Methods of Multidetector Computed Tomography.....	253
Methods of a Combination of Computed Tomography and Angiography.....	253
CT Images of Advanced Hepatocellular Carcinoma.....	253
CT Images of Early Hepatocellular Carcinoma.....	254
Computed Tomography Images of Adenomatous Hyperplasia and Atypical Adenomatous Hyperplasia.....	255
Computed Tomography Images of Nodule-in-Nodule Hepatocellular Carcinoma.....	255

Natural Outcome of Hypo-Attenuating Nodular Lesions	256
Critical Consideration to Treat Hypoattenuating Lesions.....	257
References.....	257
20. Hepatocellular Cancer in Cirrhotic Patients:	
Radiological Imaging.....	261
Francesca Lodato, N. Davies, D. Yu, and Andrew K. Burroughs	
Introduction.....	261
The EASL Consensus Statements and AASLD Guidelines	262
Surveillance for HCC: Radiological Techniques	263
Ultrasonography (US), Doppler-Ultrasonography, Power Doppler-Ultrasonography and Contrast-Enhanced Ultrasonography	264
Spiral Computed Tomography	265
Magnetic Resonance Imaging.....	267
The Problem of Small Nodules.....	268
Conclusions.....	270
References.....	271
B. Treatment	
21. Treatment of Hepatocellular Carcinoma	
with Thalidomide: Assessment with Power Doppler Ultrasound.....	277
Chiun Hsu, Chiung-Nien Chen, and Ann-Lii Cheng	
Summary	277
Introduction.....	277
Evaluation of Tumor Vascularity Using Power Doppler Sonography	279
Evaluation of Vascular Response of HCC to Thalidomide by Power Doppler Ultrasound: A Prospective Study.....	279
Future Perspectives of Imaging Studies for Evaluation of Anti-angiogenesis Therapy.....	282
References.....	284
22. Perfusion Scintigraphy with Integrated Single	
Photon Emission Computed Tomography/Computed	
Tomography in the Management of Transarterial	
Treatment of Hepatic Malignancies	287
Timm Denecke, Bert Hildebrandt, and Enrique Lopez-Hänninen	
Introduction.....	287
Current Status of Hepatic Arterial Chemotherapy and Radioembolization	287
Intraarterial Chemotherapy	287
Transarterial Radioembolization.....	289

Technique of Transarterial Treatment	289
Hepatic Arterial Infusion Chemotherapy	289
Radioembolization	290
Visualization of Perfusion Territories of Hepatic Intraarterial Catheters in Planning and Control of Transarterial Treatment.....	291
Imaging Techniques	291
Single Photon Emission Computed Tomography with Integrated Computed Tomography for Port Perfusion Scintigraphy.....	291
Image Analysis.....	293
Therapeutic Consequences.....	297
Discussion	298
References.....	300
23. Postoperative Interferon Alpha Treatment of Patients with Hepatocellular Carcinoma: Expression of p48 Using Tissue Microarray	303
Hui-Chuan Sun	
Introduction.....	303
Materials and Methods.....	304
Tissue Microarray and Immunohistochemistry	304
Scoring of P48 Immunohistochemistry	304
Statistical Analysis.....	305
Results.....	305
Clinicopathological Data	305
Survival	306
Prognostic Factors for Disease-Free Survival and Overall Survival in Group 1	306
Discussion	307
References.....	309
C. Prognosis	
24. Hepatocellular Carcinoma: Overexpression of Homeoprotein Six 1 as a Marker for Predicting Survival	313
Kevin Tak-Pan Ng and Kwan Man	
Introduction.....	313
Materials and Methods.....	314
Cell Lines	314
Clinical Samples	314

Reverse Transcription-Polymerase Chain Reaction.....	314
Western Blot.....	315
Statistical Analysis.....	315
Results.....	315
Six1 Expression in HCC Cell Lines.....	315
Six1 Expression in HCC Patients and Normal Donors.....	317
Six1 Protein Expression Correlated with Advanced Tumor Stage	317
Six1 Protein Expression Correlated with Poor Survival	318
Discussion.....	319
References.....	322
25. Hepatocellular Carcinoma:	
KiSS-1 Overexpression as a Prognostic Factor	325
Katharina Schmid, Isabella Mosberger, and Fritz Wrba	
Introduction.....	325
Materials	327
Methods.....	327
Tissue Preparation.....	327
Immunohistochemistry	328
Evaluation of Immunohistochemical Result	328
Results and Discussion	328
Patients and Tissue Samples	328
References.....	330
26. Hepatocellular Carcinoma: Prognosis	
Using Hepatoma-Derived Growth Factor	
Immunohistochemistry	333
Hideji Nakamura, Kenya Yoshida, and Yasuhiko Tomita	
Hepatoma-Derived Growth Factor.....	333
Developmentally Regulated Expression of Hepatoma-Derived	
Growth Factor	334
Role in Hepatocarcinogenesis.....	334
Role in Cancer Progression and Angiogenesis	335
Immunohistochemical and Analytical Methods	336
Materials	336
Method	337
Evaluation of Hepatoma-Derived Growth Factor	
Expression in Hepatocellular Carcinoma.....	337
Prognostic Significance of Hepatoma-Derived	
Growth Factor in Hepatocellular Carcinoma	338
References.....	340

27. Hepatitis C Virus-Related Human Hepatocellular Carcinoma: Predictive Markers Using Proteomic Analysis (Methodology)	343
Yasuhiro Kuramitsu and Kazuyuki Nakamura	
Hepatitis C Virus-Related Human Hepatocellular Carcinoma (HCV–HCC).....	343
Proteomics.....	343
Proteomics for Hepatocellular Carcinoma Tissues.....	344
Proteomics for Sera from Hepatocellular Carcinoma Patients.....	344
Proteomics for Hepatitis C Virus-Related Hepatocellular Carcinoma Tissues.....	345
Preparation of HCV–HCC Tissue Samples.....	345
Two-Dimensional Gel Electrophoresis (2-DE).....	345
Sodium Dodecyl Sulfate-Polyacrilamide Gel Electrophoresis (SDS-PAGE).....	345
Image Analysis of the Gels.....	346
Mass Spectrometry Analysis.....	346
Amino Acid Sequencing by Liquid Chromatography–Tandem Mass Spectrometry (LC-MS/MS).....	346
Proteins Whose Expression Was Increased in HCV–HCC Tissues.....	346
Proteins With Decreased Expression.....	347
Proteomics for Auto-Antibodies in the Sera of Hepatocellular Carcinoma Patients.....	348
References.....	349

Part V Metastases

A. Diagnosis

28. Liver Metastases from Colorectal Cancer: Ultrasound Imaging	355
Søren R. Rafaelsen	
Introduction.....	355
Ultrasound Scanning Technique.....	356
Advantages of Diagnostic Hepatic Ultrasound.....	357
Grayscale Echo Pattern.....	357
Detection of Liver Metastases.....	358
Doppler Flow Pattern.....	359
Ultrasound in Postoperative Follow-Up.....	363
Future Potential Advancements.....	363
References.....	364

29. Preclinical Liver Metastases: Three-Dimensional High-Frequency Ultrasound Imaging	369
Kevin C. Graham, Lauren A. Wirtzfeld, James C. Lacefield, and Ann F. Chambers	
Introduction.....	369
Method: High-Frequency Ultrasound	373
Three-Dimensional Imaging and Volume Calculation.....	374
High-Frequency Ultrasound Imaging of Preclinical Liver Metastases	376
Other Applications of High-Frequency Ultrasound Imaging to Preclinical Cancer Research	379
Future Developments – Ultrasound Contrast Agents	380
Conclusions.....	383
References.....	383
 30. Colorectal Liver Metastases:	
¹⁸F-Fluorodeoxyglucose-Positron Emission Tomography	387
Stéphanie Truant, Damien Huglo, and François-René Pruvot	
Introduction.....	387
Principle of FDG-PET and General Pitfalls.....	388
Colorectal Liver Metastases: Yield of ¹⁸ F-Fluoro- Deoxyglucose-Positron Emission Tomography	389
Preoperative Staging of Patients with Colorectal Liver Metastases.....	389
Detection of Liver Metastases.....	389
Detection of Extrahepatic Metastases	391
Abdominal Cavity	392
Extra-Abdominal Organs	395
Impact of FDG-PET Findings on Patient’s Management	397
Additional Disease and Change of Management.....	398
Survival Impact.....	399
Postoperative Follow-Up After Resection of Colorectal Liver Metastases and Rising Carcinoembryonic Antigen (CEA)	400
FDG-PET for Monitoring the Response to Systemic or Regional Therapy of Colorectal Liver Metastases	401
Anticancer Systemic Therapy	401
New Targeted Therapies (Monoclonal Antibodies).....	402
Regional Therapies	403
Hepatic Arterial Chemotherapy	403
Other Regional Therapies	404
Conclusion	404
References.....	404

Part VI Biliary Cancer

A. Diagnosis

31. Biliary Cystic Tumors: Clinicopathological Features	411
Yasuni Nakanuma, Hiroko Ikeda, Yasunori Sato, Kenichi Harada, Koichi Nakamura, and Yoh Zen	
Introduction.....	411
Anatomical Classification of the Biliary Tree.....	412
Non-Neoplastic Biliary Cystic Lesions	412
Peribiliary Cysts.....	412
Hepatic Foregut Cyst	414
Biliary Hamartoma.....	415
Biliary Cystic Neoplasm.....	416
Hepatobiliary Cystadenoma and Cystadenocarcinoma	417
Intraductal Papillary Neoplasm of the Bile Duct (IPNB)	419
Other Types of Neoplastic Cystic Diseases	426
References.....	426
32. Cholangiocarcinoma: Intraductal Sonography	429
Kazuo Inui, Hironao Miyoshi, and Junji Yoshino	
Introduction.....	429
Methods.....	429
Instruments.....	429
Insertion Methods	430
Indications.....	431
Images and Clinical Utility	432
Intraductal Sonography.....	432
Three-Dimensional Intraductal Sonography.....	432
Discussion	434
Conclusions.....	436
References.....	436
B. Prognosis	
33. Extrahepatic Bile Duct Carcinoma: Role of the p53 Protein Family	441
Alexander I. Zaika and Seung-Mo Hong	
Introduction.....	441
Epidemiology.....	441
Etiology.....	441
Diagnosis.....	442
Pathology	442
Prognosis.....	443

Role of p53 in Malignant Tumors of the Bile Duct	443
Analysis of p53 Mutations	444
Roles of p73 and p63 in Malignant Tumors of the Bile Duct	444
Analyses of p63 and p73 in Tumors	447
References	448
34. Extrahepatic Bile Duct Carcinoma:	
Mucin 4, a Poor Prognostic Factor	451
Michiyo Higashi, Shugo Tamada, Kohji Nagata, Masamichi Goto, and Suguru Yonezawa	
Introduction	451
Mucin Characteristics	451
MUC4 Mucin	452
Antibodies Against MUC4	453
MUC1 Mucin	453
Antibodies Against MUC1	455
Methods	455
Tissue Sample Management	455
Immunohistochemistry	458
References	458
C. Treatment	
35. Hilar Cholangiocarcinoma: Photodynamic Therapy and Stenting	463
Marcus Wiedmann, Joachim Mössner, and Helmut Witzigmann	
Summary	463
Introduction	463
Preoperative Biliary Drainage	464
Palliative Bile Duct Stenting	464
Palliative Stenting of Malignant Duodenal Obstruction	469
Photodynamic Therapy (PDT)	470
Mechanism of Action	470
Contraindications for Photodynamic Therapy	471
Photosensitizers	472
Photodynamic Therapy for Palliation of Hilar Cholangiocarcinoma	472
Photodynamic Therapy for Neoadjuvant and Adjuvant Treatment of Hilar Cholangiocarcinoma	478
Future Directions of Photodynamic Therapy for Hilar Cholangiocarcinoma	478
References	479

Part VII Splenic Cancer**A. Diagnosis**

36. Splenic Metastases: Diagnostic Methods	489
Eva Compérat and Frédéric Charlotte	
Introduction.....	489
Epidemiology.....	489
Pathologic Features.....	489
Pathogenesis.....	490
Clinical Features	491
Diagnostic Procedures	493
Differential Diagnosis.....	494
References.....	496
Index	499