Pocket Guide to Radiation Oncology
Pocket Guide to Radiation Oncology

EDITORS

DANIEL D. CHAMBERLAIN, MD
Adjunct Assistant Professor
University of Texas MD Anderson
Banner MD Anderson Cancer Center
Gilbert, Arizona

JAMES B. YU, MD, MHS
Associate Professor
Department of Therapeutic Radiology
Yale University School of Medicine
Cancer Outcomes, Public Policy, and Effectiveness Research (COPPER) Center at Yale
New Haven, Connecticut

ROY H. DECKER, MD, PhD
Associate Professor
Residency Training Program Director
Department of Therapeutic Radiology
Yale University School of Medicine
New Haven, Connecticut
“For our children"
CONTENTS

Contributors xi
Abbreviations xvii
Preface xxi

1: Brain Metastasis 1
   Sabin B. Motwani

2: Glioblastoma Multiforme 7
   Ahmet Tunceroğlu and Sabin B. Motwani

3: Low-Grade Glioma 13
   Sabin B. Motwani

4: High-Grade Glioma 17
   Ahmet Tunceroğlu and Sabin B. Motwani

5: Meningioma 23
   Trevor Bledsoe and Sameer Nath

6: Pituitary Tumors 29
   Trevor Bledsoe and Sameer Nath

7: Nasopharynx Cancer 33
   Arti Parekh and Ana Kiess

8: Nasal Cavity and Paranasal Sinus 37
   Sarah Nicholas and Ana Kiess

9: Oropharynx Cancer 41
   Zach Guss and Ana Kiess

10: Oral Cavity and Lip Cancers 45
    Colette Shen and Ana Kiess

11: Major Salivary Gland Tumors 51
    Adam Ferro and Ana Kiess

12: Larynx and Hypopharynx Cancers 55
    Linda Chen and Ana Kiess

13: Thyroid Cancer 61
    Ana Kiess

14: Occult Primary Cancer of the Head and Neck 65
    Omar Mian and Ana Kiess

15: Nonsmall Cell Lung Cancer 69
    Daniel D. Chamberlain

16: Small Cell Lung Cancer 73
    Brandon R. Mancini and Roy H. Decker
CONTENTS

17: Mesothelioma 77
   Brandon R. Mancini and Roy H. Decker

18: Thymoma 81
   Brandon R. Mancini and Roy H. Decker

19: Early Stage Breast Cancer 85
   Adam Kole and Meena Moran

20: Locally Advanced Breast Cancer 91
   Adam Kole, Sanjay Aneja, and Meena Moran

21: Esophageal Cancer 97
   Charles Rutter and Kimberly Lauren Johung

22: Gastric Cancer 101
   Charles Rutter and Kimberly Lauren Johung

23: Hepatobiliary 105
   Charles Rutter and Kimberly Lauren Johung

24: Pancreatic Cancer 111
   Charles Rutter and Kimberly Lauren Johung

25: Rectal Cancer 117
   Charles Rutter and Kimberly Lauren Johung

26: Anal Cancer 123
   Charles Rutter and Kimberly Lauren Johung

27: Ovarian Cancer 129
   Jacqueline Kelly and Shari Damast

28: Endometrial Cancer 133
   Brandon R. Mancini and Shari Damast

29: Cervical Cancer 139
   Skyler Johnson and Shari Damast

30: Vaginal Cancer 145
   Debra Nana Yeboa and Shari Damast

31: Vulvar Cancer 149
   Trevor Bledsoe and Shari Damast

32: Prostate Intact 155
   Gary Walker and Deborah A. Kuban

33: Adjuvant/Salvage Prostate Cancer 159
   Rachit Kumar and Deborah A. Kuban

34: Bladder Cancer 163
   Rachit Kumar and Deborah A. Kuban

35: Seminoma 167
   Gary Walker and Deborah A. Kuban
36: Hodgkin Lymphoma 171
   Neil Taunk and Rahul R. Parikh

37: Non-Hodgkin Lymphoma 175
   Neil Taunk and Rahul R. Parikh

38: Multiple Myeloma/Plasmacytoma 181
   Jerry T. Liu and Rahul R. Parikh

39: Cutaneous Lymphoma 185
   Neil Taunk and Rahul R. Parikh

40: Sarcoma 189
   Andrew Bishop and B. Ashleigh Guadagnolo

41: Non Melanoma Skin Cancer 195
   Anna Likhacheva

42: Malignant Melanoma 199
   Anna Likhacheva

43: Merkel Cell Carcinoma 203
   Anna Likhacheva

44: Ependymoma 207
   James Y. Rao, Sahaja Acharya, and Stephanie M. Perkins

45: Medulloblastoma 211
   James Y. Rao, Sahaja Acharya, and Stephanie M. Perkins

46: Neuroblastoma 215
   James Y. Rao, Sahaja Acharya, and Stephanie M. Perkins

47: Wilms’ Tumor 219
   James Y. Rao, Sahaja Acharya, and Stephanie M. Perkins

48: Rhabdomyosarcoma 223
   James Y. Rao, Sahaja Acharya, and Stephanie M. Perkins

49: Ewing’s Sarcoma 227
   James Y. Rao, Sahaja Acharya, and Stephanie M. Perkins

50: Leukemia 231
   James Y. Rao, Sahaja Acharya, and Stephanie M. Perkins

51: Palliative Radiation 237
   James B. Yu

Appendix 1: Radiation Therapy Symptom Management 243
   Aida Amado

Appendix 2: Normal Tissue Tolerances 249
   Tomasz Bista

Index 255
CONTRIBUTORS

Sahaja Acharya, MD
Department of Radiation Oncology
Washington University School of Medicine
St Louis, Missouri

Aida Amado, ACNP-BC
Banner MD Anderson Cancer Center
Gilbert, Arizona

Sanjay Aneja, MD
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

Andrew Bishop, MD
Department of Radiation Oncology
The University of Texas MD Anderson Cancer Center
Houston, Texas

Tomasz Bista, MS
Banner MD Anderson Cancer Center
Gilbert, Arizona

Trevor Bledsoe, MD
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

Daniel D. Chamberlain, MD
University of Texas MD Anderson
Banner MD Anderson Cancer Center
Gilbert, Arizona

Linda Chen, MD
Department of Radiation Oncology
The Johns Hopkins School of Medicine
Baltimore, Maryland

Shari Damast, MD
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

© Demos Medical Publishing
CONTRIBUTORS

Roy H. Decker, MD, PhD
Department of Therapeutic Radiology
Yale University School of Medicine
New Haven, Connecticut

Adam Ferro, MD, MS
Department of Radiation Oncology
The Johns Hopkins School of Medicine
Baltimore, Maryland

B. Ashleigh Guadagnolo, MD
Department of Radiation Oncology
The University of Texas MD Anderson Cancer Center
Houston, Texas

Zach Guss, MD, MSc
Department of Radiation Oncology
The Johns Hopkins School of Medicine
Baltimore, Maryland

Skyler Johnson, MD
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

Jacqueline Kelly, MD, MSc
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

Ana Kiess, MD, PhD
Department of Radiation Oncology
The Johns Hopkins School of Medicine
Baltimore, Maryland

Adam Kole, MD, PhD
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

Deborah A. Kuban, MD
Department of Radiation Oncology
The University of Texas MD Anderson Cancer Center
Houston, Texas

Rachit Kumar, MD
Banner MD Anderson Cancer Center
Gilbert, Arizona
CONTRIBUTORS

Anna Likhacheva, MD
Banner MD Anderson Cancer Center
Gilbert, Arizona;
Department of Radiation Oncology
The University of Texas MD Anderson Cancer Center
Houston, Texas

Jerry T. Liu, MD
Department of Radiation Oncology
Icahn School of Medicine at Mount Sinai
New York, New York

Kimberly Lauren Johung, MD, PhD
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

Brandon R. Mancini, MD
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

Omar Mian, MD, PhD
Department of Radiation Oncology
The Johns Hopkins School of Medicine
Baltimore, Maryland

Meena Moran, MD
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

Sabin B. Motwani, MD
Rutgers Cancer Institute of New Jersey
New Brunswick, New Jersey

Sameer Nath, MD
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

Sarah Nicholas, MD
Department of Radiation Oncology
The Johns Hopkins School of Medicine
Baltimore, Maryland
Arti Parekh, MD
Department of Radiation Oncology
The Johns Hopkins School of Medicine
Baltimore, Maryland

Rahul R. Parikh, MD
Department of Radiation Oncology
Robert Wood Johnson Medical School
New Brunswick, New Jersey

Stephanie M. Perkins, MD
Department of Radiation Oncology
Washington University School of Medicine
St Louis, Missouri

James Y. Rao, MD
Department of Radiation Oncology
Washington University School of Medicine
St Louis, Missouri

Charles Rutter, MD
Department of Therapeutic Radiology
Yale School of Medicine
New Haven, Connecticut

Colette Shen, MD
Department of Radiation Oncology
The Johns Hopkins School of Medicine
Baltimore, Maryland

Neil Taunk, MD
Department of Radiation Oncology
Memorial Sloan Kettering Cancer Center
New York, New York

Ahmet Tunceroğlu, MD, PhD
Department of Radiation Oncology
Robert Wood Johnson Medical School
New Brunswick, New Jersey

Gary Walker, MD
Banner MD Anderson Cancer Center
Gilbert, Arizona
Debra Nana Yeboa, MD  
Department of Therapeutic Radiology  
Yale School of Medicine  
New Haven, Connecticut

James B. Yu, MD, MHS  
Department of Therapeutic Radiology  
Yale University School of Medicine  
Cancer Outcomes, Public Policy, and Effectiveness Research (COPPER) Center at Yale  
New Haven, Connecticut
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3DCRT</td>
<td>3D conformal radiation therapy</td>
</tr>
<tr>
<td>4DCT</td>
<td>4 Dimensional computed tomography</td>
</tr>
<tr>
<td>ABS</td>
<td>American Brachytherapy Society</td>
</tr>
<tr>
<td>ABVD</td>
<td>Adriamycin Bleomycin Vinblastine Dacarbazine</td>
</tr>
<tr>
<td>ADT</td>
<td>Androgen deprivation therapy</td>
</tr>
<tr>
<td>AFP</td>
<td>Alpha fetoprotein</td>
</tr>
<tr>
<td>ALCL</td>
<td>Anaplastic large cell lymphoma</td>
</tr>
<tr>
<td>AP</td>
<td>Anterior posterior</td>
</tr>
<tr>
<td>APR</td>
<td>Abdominoperitoneal resection</td>
</tr>
<tr>
<td>BCG</td>
<td>Bacillus Calmette-Guerin intravesicular therapy</td>
</tr>
<tr>
<td>BEACOPP</td>
<td>Bleomycin Etoposide Adriamycin Cyclophosphamide Oncovin (Vincristine) Procarbazine Prednisone</td>
</tr>
<tr>
<td>BID</td>
<td>Twice per day</td>
</tr>
<tr>
<td>BUN/Cr</td>
<td>Blood urea nitrogen/Creatinine</td>
</tr>
<tr>
<td>bPFS</td>
<td>Biochemical Progression Free Survival</td>
</tr>
<tr>
<td>C/A/P</td>
<td>Chest / Abdomen / Pelvis</td>
</tr>
<tr>
<td>CA125</td>
<td>Cancer antigen 125</td>
</tr>
<tr>
<td>CA19-9</td>
<td>Carbohydrate antigen 19-9 (also called cancer antigen 19-9)</td>
</tr>
<tr>
<td>CBC</td>
<td>Complete blood count</td>
</tr>
<tr>
<td>CBCT</td>
<td>Cone beam computed tomography</td>
</tr>
<tr>
<td>CEA</td>
<td>Carcinoembryonic antigen</td>
</tr>
<tr>
<td>ChemoRT</td>
<td>Chemoradiation therapy</td>
</tr>
<tr>
<td>CLL/SLL</td>
<td>Chronic lymphocytic leukemia / small lymphocytic lymphoma</td>
</tr>
<tr>
<td>CMP</td>
<td>Comprehensive metabolic panel</td>
</tr>
<tr>
<td>CR</td>
<td>Complete response</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebrospinal fluid</td>
</tr>
<tr>
<td>CSI</td>
<td>Cranial spinal radiation therapy</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>CTV</td>
<td>Clinical target volume</td>
</tr>
<tr>
<td>CXR</td>
<td>Chest X-ray</td>
</tr>
<tr>
<td>D&amp;C</td>
<td>Dilation and curettage</td>
</tr>
<tr>
<td>DFS</td>
<td>Disease free survival</td>
</tr>
<tr>
<td>DLBCL</td>
<td>Diffuse large B cell lymphoma</td>
</tr>
<tr>
<td>DM</td>
<td>Distant metastasis</td>
</tr>
<tr>
<td>DMFS</td>
<td>Distant metastasis free survival</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>DRE</td>
<td>Digital rectal exam</td>
</tr>
<tr>
<td>DSS</td>
<td>Disease specific survival</td>
</tr>
<tr>
<td>DVH</td>
<td>Dose volume histogram</td>
</tr>
<tr>
<td>D2cc</td>
<td>Dose for the most exposed 2cc of an organ</td>
</tr>
<tr>
<td>D90</td>
<td>Minimum dose covering 90% of target</td>
</tr>
<tr>
<td>EBRT</td>
<td>External beam radiation therapy</td>
</tr>
<tr>
<td>EBV</td>
<td>Epstein-Barr Virus</td>
</tr>
<tr>
<td>ECE</td>
<td>Extracapsular extension</td>
</tr>
<tr>
<td>EFS</td>
<td>Event free survival</td>
</tr>
<tr>
<td>EGD</td>
<td>Esophagogastroduodenoscopy</td>
</tr>
<tr>
<td>EQD2</td>
<td>Equivalent dose in 2 Gray per fraction</td>
</tr>
<tr>
<td>ERCP</td>
<td>Endoscopic retrograde cholangiopancreatography</td>
</tr>
<tr>
<td>ER/PR</td>
<td>Estrogen receptor / progesterone receptor</td>
</tr>
<tr>
<td>EUA</td>
<td>Exam under anesthesia</td>
</tr>
<tr>
<td>EUS</td>
<td>Endoscopic ultrasound</td>
</tr>
<tr>
<td>FFF</td>
<td>Freedom from failure</td>
</tr>
<tr>
<td>FFS</td>
<td>Failure free survival</td>
</tr>
<tr>
<td>FISH</td>
<td>Fluorescence in situ hybridization</td>
</tr>
<tr>
<td>FL</td>
<td>Follicular lymphoma</td>
</tr>
<tr>
<td>FNA</td>
<td>Fine needle aspiration</td>
</tr>
<tr>
<td>FOLFIRI</td>
<td>Folinic acid, Fluorouracil, Irinotecan</td>
</tr>
<tr>
<td>FOLFOX</td>
<td>Folinic acid, Fluorouracil, Oxaliplatin</td>
</tr>
<tr>
<td>fx</td>
<td>Fractions</td>
</tr>
<tr>
<td>GE</td>
<td>Gastroesophageal</td>
</tr>
<tr>
<td>GI</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>GTR</td>
<td>Gross total resection</td>
</tr>
<tr>
<td>GTV</td>
<td>Gross tumor volume</td>
</tr>
<tr>
<td>Gy</td>
<td>Gray</td>
</tr>
<tr>
<td>H&amp;P</td>
<td>History and physical</td>
</tr>
<tr>
<td>HCC</td>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>HDR</td>
<td>High dose rate (brachytherapy)</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>HLA</td>
<td>Human leukocyte antigen</td>
</tr>
<tr>
<td>HPV</td>
<td>Human papilloma virus</td>
</tr>
<tr>
<td>HT</td>
<td>Hormonal therapy</td>
</tr>
<tr>
<td>IBTR</td>
<td>Ipsilateral breast tumor recurrence</td>
</tr>
<tr>
<td>ICRT</td>
<td>Intra-cavitary radiation therapy</td>
</tr>
<tr>
<td>IFRT</td>
<td>Involved field radiotherapy</td>
</tr>
<tr>
<td>IG-SRS</td>
<td>Image guided stereotactic radiosurgery</td>
</tr>
<tr>
<td>IGRRT</td>
<td>Image guided radiation therapy</td>
</tr>
<tr>
<td>IHC</td>
<td>Immunohistochemistry</td>
</tr>
<tr>
<td>IMRT</td>
<td>Intensity modulated radiation therapy</td>
</tr>
<tr>
<td>IORT</td>
<td>Intraoperative radiotherapy</td>
</tr>
</tbody>
</table>
ITV  Internal tumor volume
IV    Intravenous
IVC   Inferior vena cava
IVRT  Intra-vaginal radiation therapy
KPS   Karnofsky Performance Status
LAR   Low anterior resection
LC    Local control
LDH   Lactate dehydrogenase
LDR   Low dose rate (brachytherapy)
LFTs  Liver function tests
LN    Lymph node
LP    Lumbar puncture
LRR   Local regional recurrence
LVSI  Lymphovascular invasion
MALT  Mucosa associated lymphoid tissue
MCL   Mantle cell lymphoma
MF    Mycosis fungoides
MRI   Magnetic resonance imaging
MZL   Marginal zone lymphoma
NED   No evidence of disease
NLPHL Nodular lymphocyte-predominant Hodgkin lymphoma
NK    Natural killer
OAR   Organ at risk
OBS   Observation
OS    Overall survival
PA    Posterior anterior
PCFCL Primary cutaneous follicular center lymphoma
PCMZL Primary cutaneous marginal zone lymphoma
PCNSL Primary CNS lymphoma
PCSS  Prostate cancer specific survival
PCTCL Primary cutaneous T-Cell Lymphoma
PCV   Procarbazine CCNU and Vincristine
PET   Positron emission tomography
PFS   Progression free survival
PMBL/GZL Primary mediastinal B-cell lymphoma / Gray zone lymphoma
PNET  Primitive neuroectodermal tumor
PO    By mouth
PSA   Prostate-specific antigen
PTCL  Peripheral T-cell lymphoma
PTV   Planning tumor volume
QD    Once per day
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>QoL</td>
<td>Quality of life</td>
</tr>
<tr>
<td>RANO</td>
<td>Response assessment in neuro-oncology</td>
</tr>
<tr>
<td>RCHOP</td>
<td>Rituximab cyclophosphamide doxorubicin vincristine prednisone</td>
</tr>
<tr>
<td>RFA</td>
<td>Radiofrequency ablation</td>
</tr>
<tr>
<td>RFS</td>
<td>Relapse free survival</td>
</tr>
<tr>
<td>RTOG</td>
<td>Radiation therapy oncology group</td>
</tr>
<tr>
<td>RP</td>
<td>Radical prostatectomy</td>
</tr>
<tr>
<td>RT</td>
<td>Radiation therapy</td>
</tr>
<tr>
<td>s/p</td>
<td>Status post</td>
</tr>
<tr>
<td>SBRT</td>
<td>Stereotactic body radiotherapy</td>
</tr>
<tr>
<td>SRS</td>
<td>Stereotactic radiosurgery</td>
</tr>
<tr>
<td>SRT</td>
<td>Stereotactic radiotherapy</td>
</tr>
<tr>
<td>SS</td>
<td>Statistically Significant</td>
</tr>
<tr>
<td>SSD</td>
<td>Source to surface distance</td>
</tr>
<tr>
<td>SV</td>
<td>Seminal vesicles</td>
</tr>
<tr>
<td>TACE</td>
<td>Transcatheter arterial chemoembolization</td>
</tr>
<tr>
<td>TAH/BSO</td>
<td>Total abdominal hysterectomy / Bilateral salpingo-oophorectomy</td>
</tr>
<tr>
<td>TH/BSO</td>
<td>Total hysterectomy / Bilateral salpingo-oophorectomy</td>
</tr>
<tr>
<td>TID</td>
<td>Three times per day</td>
</tr>
<tr>
<td>TME</td>
<td>Total mesorectal excision</td>
</tr>
<tr>
<td>TSEBT</td>
<td>Total skin electron beam therapy</td>
</tr>
<tr>
<td>VEGF</td>
<td>Vascular endothelial growth factor</td>
</tr>
<tr>
<td>VMAT</td>
<td>Volumetric modulated arc therapy</td>
</tr>
<tr>
<td>VP</td>
<td>Ventriculoperitoneal</td>
</tr>
<tr>
<td>WART</td>
<td>Whole abdominal radiation therapy</td>
</tr>
<tr>
<td>WBRT</td>
<td>Whole brain radiation therapy</td>
</tr>
<tr>
<td>WHO PS</td>
<td>World Health Organization Performance Status</td>
</tr>
<tr>
<td>WPRT</td>
<td>Whole pelvis radiation therapy</td>
</tr>
<tr>
<td>32P</td>
<td>Phosphorus-32</td>
</tr>
</tbody>
</table>
We first conceived of this project years ago when we were all residents putting together study sheets in preparation for eventual board certification exams. We imagined taking our painstakingly created study sheets and distributing them to our fellow residents and medical students, passing them out with a wink and a nod to colleagues around the country. As trainees, the idea of a “little black book” of radiation oncology that could be surreptitiously looked at before walking into a patient’s room, or before being questioned by an attending physician in chart rounds, held great appeal.

Now that we are all older, grayer, and specialized, a rapid reference that allows for quick review of the existing standard of care and most relevant literature promises to save us time and energy, and reassurance that we won’t put our feet in our mouths when covering tumor boards we don’t normally cover, or staff satellites for our colleagues and see patients we don’t usually see. In the era of quick curbside conversations and multitasking, this quick pocket-sized reference can be carried for a quick review between our children’s activities instead of heavy textbooks often filled with esoteric topics and unnecessarily minutiae.

We hope that this text, Pocket Guide to Radiation Oncology will indeed reside in the pockets of our colleagues, trainees, and staff. We are indebted to the authors who have contributed their expertise to this text.

Daniel D. Chamberlain, MD
James B. Yu, MD, MHS
Roy H. Decker, MD, PhD
WORKUP

All Cases
- H&P (include weight loss and performance status)
- Smoking cessation assistance
- Pulmonary function tests
- PET/CT
- Bronchoscopy
- Consider pathologic evaluation of mediastinal nodes
- Pathologic confirmation

If Stage >IA
- Pathologic evaluation of mediastinal nodes
- MRI brain

If Superior Sulcus Tumor Abutting Spine or Subclavian Vessels
- MRI spine and thoracic inlet

If Stage IV
- Genomic testing (e.g., EGFR, ALK, ROS1) particularly for adenocarcinoma, but may include squamous cell carcinoma in patients with minimal tobacco history

TREATMENT RECOMMENDATIONS BY STAGE

<table>
<thead>
<tr>
<th>Stage</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Surgery (lobectomy + node dissection preferred)</td>
</tr>
<tr>
<td>IA inoperable</td>
<td>SBRT is an alternative to limited (sublobar)surgery</td>
</tr>
<tr>
<td>IB</td>
<td>Surgery → ± chemo (in select cases)</td>
</tr>
<tr>
<td>IB inoperable</td>
<td>SBRT → ± chemo (in select cases)</td>
</tr>
<tr>
<td>IIA</td>
<td>Surgery → chemo</td>
</tr>
<tr>
<td>IIA inoperable</td>
<td>ChemoRT</td>
</tr>
<tr>
<td>IIB</td>
<td>Surgery → chemo</td>
</tr>
<tr>
<td>IIB inoperable</td>
<td>ChemoRT</td>
</tr>
<tr>
<td>IIIA</td>
<td>Neoadjuvant chemoRT → Surgery → Chemo OR chemo → Surgery → RT OR definitive ChemoRT</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Stage</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIIA Resectable T3-4, N0-1</td>
<td>Surgery ➔ Chemo</td>
</tr>
<tr>
<td>IIIA Unable to tolerate concurrent treatment</td>
<td>Sequential radiation and chemotherapy</td>
</tr>
<tr>
<td>IIIB</td>
<td>ChemoRT</td>
</tr>
<tr>
<td>IIIB Tumor too large for RT</td>
<td>Chemo ➔ reevaluate for ChemoRT</td>
</tr>
<tr>
<td>IIIB Unable to tolerate concurrent tx</td>
<td>Sequential therapy or systemic therapy alone</td>
</tr>
<tr>
<td>IV</td>
<td>Systemic therapy</td>
</tr>
<tr>
<td>IV (M1a) effusion</td>
<td>Systemic therapy. In cases where the fluid is repeatedly path negative may consider definitive therapy</td>
</tr>
<tr>
<td>IV (M1b) single brain or adrenal met</td>
<td>Consider definitive treatment to the met and thoracic disease</td>
</tr>
<tr>
<td>IV (M1a) Solitary contralateral lung</td>
<td>Treat as separate primaries</td>
</tr>
<tr>
<td>Multiple lung cancers (&gt;2)</td>
<td>Local therapy if symptomatic, at risk of becoming symptomatic, or solitary metachronous lesion. Otherwise chemo.</td>
</tr>
<tr>
<td>Superior sulcus T3N0-N1 resectable</td>
<td>Neoadjuvant chemoRT ➔ Surgery ➔ Chemo</td>
</tr>
<tr>
<td>Superior sulcus T4 NO-N1 borderline resectable</td>
<td>ChemoRT ➔ rapid evaluation ➔ (surgery if resectable ➔ Chemo) versus finish definitive chemoRT</td>
</tr>
<tr>
<td>Superior sulcus unresectable</td>
<td>Definitive chemoRT</td>
</tr>
<tr>
<td>Post-op pN0-N1 margins</td>
<td>Chemotherapy as appropriate per stage</td>
</tr>
<tr>
<td>Post-op pN2</td>
<td>Chemotherapy ➔ Post-op radiation</td>
</tr>
<tr>
<td>Post-op Margin +</td>
<td>ChemoRT</td>
</tr>
</tbody>
</table>

**TECHNICAL CONSIDERATIONS**

**Simulation**
- Supine, arms up, immobilization
- Simulate and treat with respiratory motion assessment and management strategy (e.g., 4DCT and ITV or gating)
15: NONSMALL CELL LUNG CANCER

Dose Prescription
- SBRT: BED$_{10} > 100$ $54$ Gy in 3 fx, $50$ Gy in 4 fx, $50$ Gy in 5 fx
- Definitive chemo-RT: 60 to 66 Gy in 30 to 33 fx
- Pre-op chemo-RT: 45 to $50$ Gy in 25 fx
- Post-op RT: $50$ to $54$ Gy in 25 to 30 fx at 1.8 to 2 Gy/fx

Target Delineation
- Contour parenchymal lesions on lung window, lymphnodes on a soft tissue window.
- GTV based on imaging and biopsies
- ITV = GTV contoured in all phases of respiration to obtain iGTV, then + 8 mm for clinical target volume (CTV) expansion OR GTV+ 8 mm to obtain CTV and then contour CTV in all phases of respiration
- PTV = ITV + 0.3 to 0.5 cm depending on localization method and reproducibility
- Limiting treatment to tumor and involved nodal stations is preferred over radiation of elective (uninvolved) nodal areas.
- In post-op cases include the hilar stump in the CTV.
- For SBRT PTV= iGTV (GTV on all phases of respiration) + 5 mm (no CTV expansion)
- Daily CBCT

Planning
- 6- to 10-MV photons
- Heterogeneity corrections used
- Intensity-modulated radiation therapy (IMRT) may improve patient reported quality of life.

FOLLOW UP
If asymptomatic: CT chest and H&P Q6 months × 2 years then annually.

SELECTED STUDIES
RTOG 0236 (Timmerman, JAMA 2010; DOI: 10.1001/jama.2010.261)
59 patients with NSCLC T1-2N0 tumor <5 cm treated with 54 Gy in 3 fx. Three-year LC 97.6%, 3-year overall survival (OS) =55.8%

Intergroup 0139 (Albain, Lancet 2009; DOI: 10.1016/S0140-6736(09)60737-6)
369 patients with T1-3N2 NSCLC randomized to concurrent chemoRT 45 Gy then surgery (if no progression) then chemo
× 2 cycles versus concurrent chemoRT 61 Gy. No difference in OS. Progression-free survival (PFS) improved in surgery arm. In exploratory analysis, OS improved in patients randomized to surgery if they underwent lobectomy, but not pneumonectomy.

**SEER PORT study (Lally, J Clin Oncol 2006)**
SEER review of 7,400 stage II to III NSCLC patients s/p lobectomy or pneumonectomy. Increased use of PORT correlated to T3 to T4, tumor size, node stage, number of involved nodes, and ratio involved nodes to sampled nodes. Subset analysis for patients with N2 disease ([HR] 0.855; 95% CI, [0.762, 0.959]; \(P = .0077\)), PORT was associated with a significant increase in survival. Survival worse for N0 patients treated with PORT

**RTOG 0617 (Bradley, Lancet Oncology 2015; DOI: 10.1016/S1470-2045(14)71207-0)**
Randomized 464 stage III patients to concurrent chemoRT to either 60 Gy of 74 Gy. MS (28.7 vs. 19.5 months) and OS at 18 months (66.9% vs. 53.9%) favored 60 Gy. Fewer local regional failures (35.3% vs. 44%) in the 60 Gy arm. Patient reported QOL better in patients treated with IMRT in both arms.

**LAMP (Belani, J Clin Oncol 2005)**
Patients with stage III NSCLC randomized to: induction chemo × 2 cycles then RT 63 Gy, versus induction chemo × 2 cycles then concurrent chemoRT 63 Gy, versus concurrent chemoRT 63 Gy then paclitaxel/carboplatin × 2 cycles consolidation. Median OS (13.0, 12.7, and 16.3 months) favored upfront concurrent chemoRT.

Stage III NSCLC patients treated with concurrent chemoRT 59.4 Gy then if no progression randomized to consolidation docetaxel versus observation. Stopped early after analysis of 203 patients. Increased toxicity but no survival benefit from consolidation chemo.

**Intergroup 0160 (Rusch, J Clin Oncol 2007)**
110 patients with T3to T4, N0-1 Superior sulcus NSCLC treated with concurrent chemoRT45 Gy then (if no progression) surgery, then chemo × 2 cycles. Eighty percent underwent surgery and 76% had R0 resection. Unresectable patients had completion chemoRT to 63 Gy total. 5-year OS.
21: ESOPHAGEAL CANCER
Charles Rutter, MD
Kimberly Lauren Johung, MD, PhD

WORKUP

All Cases
- H&P (dysphagia, weight loss, performance status)
- Esophagogastroduodenoscopy (EGD) with biopsy (human epidermal growth factor receptor 2 [HER2] testing if adenocarcinoma)
- Endoscopic ultrasound (evaluates depth of invasion, nodes)
- CT chest/abdomen with PO and IV contrast
- PET/CT
- Bronchoscopy (if at/above carina)
- Counseling on nutrition and smoking cessation
- Consider gastrostomy tube for nutrition if obstructed

TREATMENT RECOMMENDATIONS BY STAGE

<table>
<thead>
<tr>
<th>Stage</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis/T1aN0</td>
<td>Endoscopic resection ± ablation OR Esophagectomy</td>
</tr>
<tr>
<td>T1bN0 Operable</td>
<td>Esophagectomy</td>
</tr>
<tr>
<td>T1bN0 Inoperable or Cervical Esophagus</td>
<td>Definitive chemoRT</td>
</tr>
<tr>
<td>T1bN+ or T2-T4aN0-N+ and Operable</td>
<td>Neoadjuvant chemoRT ➔ Esophagectomy</td>
</tr>
<tr>
<td>T1bN+ or T2-T4aN0-N+ and Inoperable or Cervical Esophagus</td>
<td>Definitive chemoRT</td>
</tr>
<tr>
<td>T4b AnyN, M0</td>
<td>Definitive chemoRT</td>
</tr>
<tr>
<td>M1</td>
<td>Systemic therapy ± palliative RT or palliative/supportive care</td>
</tr>
<tr>
<td>pT3-T4, pN+, or positive margins</td>
<td>Post-op chemoRT (if no neoadjuvant RT was delivered)</td>
</tr>
</tbody>
</table>

TECHNICAL CONSIDERATIONS

Simulation
- Simulate supine with custom immobilization
- Assessment and management of respiratory motion (e.g., 4DCT + ITV, gating)
Dose Prescription

Definitive ChemoRT
- 45 Gy in 1.8 Gy/fx to esophagus and elective regional nodes
- Sequential boost to primary tumor and involved nodes to 50.4 Gy in 1.8 Gy/fx or
- Dose painted IMRT with 45 Gy in 1.8 Gy/fx to esophagus and elective regional nodes; 50 Gy in 2 Gy/fx to primary tumor and involved nodes

Pre-Op ChemoRT
- 41.4 to 50.4 Gy in 1.8 Gy/fx to esophagus and elective regional nodes
- Sequential boost to primary tumor and involved nodes to 50.4 Gy in 1.8 Gy/fx or
- Dose painted IMRT as noted previously for definitive chemoRT

Post-Op RT
- 45 to 50.4 Gy in 1.8 to 2 Gy/fx

Target Delineation
Contour on soft tissue windows
- See Expert Consensus contouring guidelines for IMRT (Wu, IJROBP 2015; DOI: 10.1016/j.ijrobp.2015.03.030)
- GTV = Gross tumor and involved nodes based on EGD and imaging
- ITV = GTV contoured throughout respiratory cycle
- CTV = ITV + 3.5-cm to 4-cm superior and inferior expansion along the esophagus and 1-cm radial expansion; consider elective treatment of bilateral supraclavicular and mediastinal nodes for tumors above the carina and celiac and gastrohepatic nodes for tumors below the carina
- PTV = CTV + 0.5 cm using daily IGRT

Treatment Planning
- 3DCRT or IMRT
- 6-MV to 10-MV photons
- Use heterogeneity corrections

FOLLOW UP
If asymptomatic: H&P every 3 to 6 months × 2 years, then every 6 to 12 months × 3 years, then annually. Imaging and EGD as clinically indicated.
SELECTED STUDIES

Modern trial comparing surgery alone to neoadjuvant chemoRT to 50.4 Gy with Cisplatin/Fluorouracil (5-FU), followed by surgery in T1-3N0-1 patients (75% adenocarcinoma). At 5 years, neoadjuvant chemoRT improved overall survival (OS) (39% vs. 16%) and progression-free survival (PFS) (28% vs. 15%), without operative mortality in the neoadjuvant therapy arm.

CROSS Trial (Shapiro, Lancet Oncol 2015 Long-Term Results; DOI: 10.1016/S1470-2045(15)00040-6)
A second modern trial of surgery ± neoadjuvant chemoRT. The chemoRT regimen used lower RT doses (41.4 Gy in 1.8 Gy fractions) and different chemotherapy (weekly Carboplatin/Paclitaxel), but still demonstrated improved OS (47% vs. 33% at 5 years, median 48.6 vs. 24.0 months), PFS, locoregional and distant control, and greater margin-negative resection rates in a population of patients with T1N1 or T2-3N0-1 disease, predominantly (80%) of the distal esophagus/gastroesophageal (GE) junction.

German Trial (Stahl, J Clin Oncol 2005; DOI: 10.1200/JCO.2005.00.034)
Compared trimodality therapy (chemoRT + surgery) to definitive chemoRT in a cohort of patients with T3-4N0-1 squamous cell carcinoma of the esophagus. Both arms received three cycles of induction Cisplatin/5-FU/Etoposide before undergoing Cisplatin/Etoposide x one cycle + 40 Gy RT then surgery (trimodality arm) versus Cisplatin/Etoposide x one cycle + 64 to 65 Gy RT (definitive arm). There was no difference in OS with the addition of surgery (40% vs. 35% at 2 years), although cancer-specific survival and local control were improved in the trimodality arm.

Trial of definitive RT versus definitive chemoRT among patients with nonmetastatic thoracic esophageal cancer (88% squamous cell carcinoma). On the chemoRT arm, four cycles of Cisplatin/5-FU
were given concurrently with RT to 50 Gy, while the RT-alone arm received 64 Gy. ChemoRT improved OS at 5 years (26% vs. 0%), as well as local and distant control, compared to patients treated with RT alone. Importantly, there were no long-term survivors on the RT-alone arm, underscoring the fact that definitive RT alone has no role in curative-intent therapy.

**Intergroup 0123 (Minsky, J Clin Oncol 2002; DOI: 10.1200/JCO.20.5.1167)**
Comparison of standard-dose (50.4 Gy) versus dose-escalated (64.8 Gy) Cisplatin/5-FU chemoRT in T1-4N0-1 esophageal cancer. Dose-escalation achieved using 14.4 Gy boost to GTV + 2 cm after initial 50.4 Gy. There were no differences in OS or control at locoregional or distant sites between arms, and there were more treatment-related deaths on the dose-escalated arm (11 vs. 2), although the majority of these deaths (7 of 11) occurred before 50.4 Gy.

**Contouring Guidelines (Wu, Int J Radiat Oncol Biol Phys 2015; DOI: 10.1016/j.ijrobp.2015.03.030)**
Expert consensus contouring guidelines for IMRT in esophageal and GE junction cancer.

Propensity score-based comparison of long-term outcomes with 3DCRT versus IMRT for esophageal cancer.
46: NEUROBLASTOMA
James Y. Rao, MD
Sahaja Acharya, MD
Stephanie M. Perkins, MD

WORKUP

All Cases
- H&P
- CT or MRI primary, CT chest, abd, pelvis, MIBG scan
- Labs: CBC, CMP, UA, urinary VMA/HMA
- Bilateral bone marrow biopsy

Considerations
- Most commonly arises in the adrenals
- Neuroblastoma (NB) patients have constitutional sx (“sick appearing”)
- Tumors commonly have calcifications
- Skull and orbit bones are common sites of metastasis
- N-myc amp or DI = 1 associated with poorer prognosis
- Significant portion of infants have spontaneous regression

TREATMENT RECOMMENDATIONS

Based on COG Risk Groups

Low Risk (as Defined in ANBL00B1)
- Stage 1, Any
- Stage 2, N-myc not Amp, and Resection ≥50%
- Stage 4S, N-myc not Amp, DI >1, FH, and Asymp

Intermediate Risk (as Defined in ANBL0531)
- Stage 2, N-myc not Amp, and Bx/Resection <50%
- Stage 3 and Age <547 days
- Stage 3, Age ≥547 days, and FH
- Stage 4 and Age <365 days
- Stage 4, Age ≥365 days, DI >1, and FH
- Stage 4S, N-myc not Amp, and not low risk

High Risk (as Defined in ANBL0532)
- Stage 2, N-myc Amp
- Stage 3, N-myc Amp
- Stage 3, Age ≥547 days, N-myc not Amp, and UH
- Stage 4, N-myc Amp
Stage 4, Age 365 to 546 days, and DI = 1
Stage 4, Age 365 to 546 days, and UH
Stage 4, Age ≥547 days
Stage 4S, N-myc Amp

FH: favorable histology; UH: unfavorable histology; Amp: amplified; DI: DNA Index; Asymp: asymptomatic

<table>
<thead>
<tr>
<th>Low risk</th>
<th>Surgery, then observation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Observation after bx for stage 4S patients</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>Maximum safe resection</td>
</tr>
<tr>
<td></td>
<td>Chemotherapy based on biology</td>
</tr>
<tr>
<td></td>
<td>Second-look surgery considered for patients with initial unresectable disease or incomplete resection.</td>
</tr>
<tr>
<td></td>
<td>RT is controversial.</td>
</tr>
<tr>
<td></td>
<td>RT to residual or recurrent tumor not recommended in ANBL0531, which prefers additional chemo.</td>
</tr>
<tr>
<td>High risk</td>
<td>Induction chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Surgical resection</td>
</tr>
<tr>
<td></td>
<td>Consolidation chemo/transplant</td>
</tr>
<tr>
<td></td>
<td>RT to primary site and to viable met</td>
</tr>
<tr>
<td></td>
<td>Maintenance cis-retinoic acid</td>
</tr>
<tr>
<td>Cord compression</td>
<td>Consider up-front chemo</td>
</tr>
<tr>
<td></td>
<td>RT or surgery for unresponsive disease</td>
</tr>
<tr>
<td>Symptomatic hepatomegaly</td>
<td>Whole liver radiation</td>
</tr>
<tr>
<td>Metastatic sites</td>
<td>Evaluate for MIBG positive met after induction chemotherapy. RT to be delivered after transplant.</td>
</tr>
</tbody>
</table>

**TECHNICAL CONSIDERATIONS**

**Simulation**
- Simulate and treat with general anesthesia if necessary.
- Consider 4DCT for tumor locations in the thorax or upper abdomen susceptible to motion.

**Dose Prescription**
- High Risk: 21.6 Gy in 1.8 Gy/fx if GTR and 36 Gy in 1.8 Gy/fx if gross residual (21.6 Gy + 14.4 Gy boost)
- Cord Compression: <3 years old: 9 Gy in 1.8 Gy/fx, ≥3 years old: 21.6 Gy in 1.8 Gy/fx
Whole Liver Radiation: 4.5 Gy in 1.5 Gy/fx
Metastasis: 21.6 Gy in 1.8 Gy/fx

**Target Delineation**

*For High-Risk Disease*

- GTV1 = disease on imaging prior to surgery, + LN defined on path, corrected volumetrically after surgical resection but not at the point of attachment.
- GTV2 = volume of residual tumor after surgery and chemotherapy
- CTV1 = GTV1- + 1.5-cm anatomically confined expansion
- CTV2 = GTV2 + 1.0-cm anatomically confined expansion
- PTV1 = CTV1 + 0.5- to 1.0-cm expansion, this receives 21.6 Gy
- PTV2 = CTV2 + 0.5- to 1.0-cm expansion, this receives 14.4 Gy boost

For tumors located in the thorax or upper abdomen, an assessment should be made to determine the extent of motion. PTV margins should include motion as a component.

**Treatment Planning**

- Conventional planning reasonable for lateraled tumors
- Consider 3D or intensity-modulated radiation therapy (IMRT) to reduce dose to normal structures

**FOLLOW UP**

If asymptomatic: H&P with labs and catecholamines q3 months for 1 year, q6 months for 5 years, and afterward. Bone scan and MIBG at 3 months, then q6 months for 3 years.

**SELECTED STUDIES**


379 high-risk neuroblastoma patients treated induction chemotherapy and surgical resection, then randomized to myeloablative chemo, 10 Gy TBI, autologous bone marrow transplant versus intensive chemo. Patients then randomized to cis-RA versus no further therapy. Improved overall survival with ABMT/cis-RA 59% versus ABMT/no cis RA 41%, chemo/cis-RA 38%, and chemo/no cis-RA 36%.

For patients on CCG 3891, combined external beam radiation therapy (EBRT) 10 Gy to primary tumor site and addition of 10 Gy TBI resulted in improved local control of 52% compared to 10 Gy EBRT to primary tumor alone 22%. Suggests dose-response relationship for local RT.


IMRT reduced kidney doses for midline tumors. IMRT not superior to AP/PA fields for lateralized tumors.