

# **LUNG CANCER**

**A COMPREHENSIVE  
TREATISE**

Edited by

Jacob D. Bitran, M.D.

Harvey M. Golomb, M.D.

Alex G. Little, M.D.

Ralph R. Weichselbaum, M.D.

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## **A Comprehensive Treatise**

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# Lung Cancer

## A Comprehensive Treatise

*Edited by*

**Jacob D. Bitran, M.D.**

Associate Professor of Medicine  
Pritzker School of Medicine  
Director, Clinical Research Development  
Joint Section of Hematology/Oncology  
University of Chicago Medical Center  
Michael Reese Medical Center  
Chicago, Illinois

**Harvey M. Golomb, M.D.**

Professor of Medicine  
Pritzker School of Medicine  
Director, Joint Section of Hematology/Oncology  
University of Chicago Medical Center  
Michael Reese Medical Center  
Chicago, Illinois

**Alex G. Little, M.D.**

Associate Professor of Surgery  
Pritzker School of Medicine  
Chief, Section of Thoracic Surgery  
Department of Surgery  
University of Chicago Medical Center  
Chicago, Illinois

**Ralph R. Weichselbaum, M.D.**

Professor and Chairman  
Department of Radiation Oncology  
Pritzker School of Medicine  
Michael Reese/University of Chicago Center for Radiation Therapy  
Chicago, Illinois



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## Editorial Method

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We have attempted to incorporate the proposed new staging system into our book with the editors' comments at the end of each chapter. In addition, the chapter on staging describes both the previous and new staging system. In fact, the proposed system appears to be similar to the previous staging system in terms of stage grouping. That is,  $T_1N_0M_0$  and  $T_2N_0M_0$  tumors constitute stage I under the new system, and we regarded them in this fashion under the old system. Similarly, stage II consists of  $T_1N_1M_0$  and  $T_2N_0M_0$  lung cancers

The major impact of the new staging system is that locally extensive primary tumors are classified as either  $T_3$  or  $T_4$ , and metastases to regional lymph nodes can be classified as either  $N_2$  or  $N_3$ . Patients with  $T_4$  tumors or involvement of  $N_3$  nodes constitute a stage IIIB group, and patients with distant organ metastases are in stage IV.

JACOB D. BITRAN, HARVEY M. GOLOMB  
ALEX G. LITTLE, RALPH R. WEICHELBAUM

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## Contributors

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**Martin D. Abeloff, M.D.**

Chief, Medical Oncology, The Johns Hopkins Oncology Center; Professor of Oncology, The Johns Hopkins University School of Medicine, Baltimore, Maryland

**Joseph Aisner, M.D., F.A.C.P.**

Professor of Medicine, Oncology, Pharmacology, and Experimental Therapeutics, Department of Medicine, University of Maryland School of Medicine; Deputy Director for Clinical Affairs, University of Maryland Cancer Center; University of Maryland Medical Systems, Baltimore, Maryland

**Mario Albertucci, M.D.**

Department of Surgery, Creighton University School of Medicine, Omaha, Nebraska

**Azhar M. Awan, M.D.**

Assistant Professor, Department of Radiation Oncology, University of Chicago Medical Center, Chicago, Illinois

**John C. Baldwin, M.D.**

Assistant Professor of Cardiovascular Surgery, Department of Cardiovascular Surgery, Stanford University School of Medicine, Stanford, California

**Carlos Bekerman, M.D.**

Associate Professor, Department of Radiology, Michael Reese Hospital and Medical Center, Chicago, Illinois

**Jacob D. Bitran, M.D.**

Associate Professor of Medicine, Pritzker School of Medicine; Director, Clinical Research Development, Joint Section of Hematology/Oncology, University of Chicago Medical Center, Michael Reese Medical Center, Chicago, Illinois

**Paul A. Bunn, Jr., M.D.**

Professor of Medicine and Head, Division of Medical Oncology, Department of Medicine, University of Colorado Health Sciences Center, Denver, Colorado

**George T. Y. Chen, Ph.D.**

Professor and Director, Medical Physics, Department of Radiation Oncology, University of Chicago, Chicago, Illinois

**Tom R. DeMeester, M.D.**

Professor and Chairman, Department of Surgery, Creighton University School of Medicine, Omaha, Nebraska

**David G. Dienhart, M.D.**

Instructor, Division of Medical Oncology, University of Colorado Health Sciences Center, Denver, Colorado

**Stephen R. Ell, M.D., Ph.D., F.A.C.P.**

Associate Professor, Department of Radiology, University of Chicago Medical Center, Chicago, Illinois

**David S. Ettinger, M.D., F.A.C.P.**

Associate Professor of Oncology and Medicine, The Johns Hopkins Oncology Center, The Johns Hopkins University School of Medicine, Baltimore, Maryland

**Mark K. Ferguson, M.D.**

Assistant Professor, Department of Surgery, University of Chicago Medical Center, Chicago, Illinois

**Thomas J. Fitzgerald, M.D.**

Assistant Professor, Department of Radiation Oncology, University of Massachusetts Medical Center, Worcester, Massachusetts

**Harvey M. Golomb, M.D.**

Professor of Medicine, Pritzker School of Medicine; Director, Joint Section of Hematology/Oncology, University of Chicago Medical Center, Michael Reese Medical Center, Chicago, Illinois

**F. Anthony Greco, M.D.**

Director and Professor of Medicine, Division of Oncology, Department of Medicine, Vanderbilt University, Nashville, Tennessee

**Joel S. Greenberger, M.D.**

Professor and Chairman, Department of Radiation Oncology, University of Massachusetts Medical Center, Worcester, Massachusetts

**Hermes C. Grillo, M.D.**

Chief, General Thoracic Surgery, Massachusetts General Hospital; Professor of Surgery, Harvard Medical School, Boston, Massachusetts

**Philip C. Hoffman, M.D.**

Associate Professor of Clinical Medicine, Joint Section of Hematology/Oncology, Department of Medicine, The University of Chicago Medical Center, Chicago, Illinois

**Daniel C. Ihde, M.D.**

Head, Clinical Investigations Section, NCI-Navy Medical Oncology Branch, National Cancer Institute and Naval Hospital; Professor of Medicine, Department of Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland

**Renee H. Jacobs, M.D.**

Clinical Instructor, Section of Hematology/Oncology, Department of Medicine, University of Chicago and Michael Reese Medical Center, Chicago, Illinois

**David H. Johnson, M.D.**

Assistant Professor of Medicine, Division of Oncology, Department of Medicine, Vanderbilt University, Nashville, Tennessee

**Thomas Lad, M.D.**

Associate Professor of Clinical Medicine, University of Illinois College of Medicine; Chief, Medical Oncology Section, Veterans Administration West Side Medical Center, Chicago, Illinois

**Allen S. Lichter, M.D.**

Professor and Chairman, Department of Radiation Oncology, University of Michigan Medical Center, Ann Arbor, Michigan

**R. Ilona Linnoila, M.D.**

Pathologist, Human Tumor Biology Section, NCI-Navy Medical Oncology Branch, Naval Hospital, Bethesda, Maryland

**Alex G. Little, M.D.**

Associate Professor of Surgery, Pritzker School of Medicine; Chief, Section of Thoracic Surgery, Department of Surgery, University of Chicago Medical Center, Chicago, Illinois

**Heber MacMahon, M.D.**

Associate Professor, Department of Radiology, University of Chicago Medical Center, Chicago, Illinois

**James B. D. Mark, M.D.**

Johnson & Johnson Professor of Surgery; Head, Division of Thoracic Surgery, Stanford University School of Medicine, Stanford, California

**Douglas J. Mathisen, M.D.**

General Thoracic Surgical Unit, Massachusetts General Hospital; Assistant Professor of Surgery, Harvard Medical School, Boston, Massachusetts

**Mary J. Matthews, M.D. (deceased)**

Pathologist, Department of Anatomic Pathology and NCI-Navy Medical Oncology Branch, Naval Hospital, Bethesda, Maryland

**F. Griffith Pearson, M.D., F.R.C.S (C), F.A.C.S.**

Professor of Surgery, University of Toronto; Surgeon-in-Chief, Toronto General Hospital, Toronto, Ontario, Canada

**James A. Radosevich, Ph.D.**

Assistant Professor of Medicine, Section of Hematology/Oncology, Department of Medicine, Northwestern University; Staff Research Scientist, Veterans Administration Lakeside Medical Center, Chicago, Illinois

**Steven T. Rosen, M.D., F.A.C.P.**

Associate Professor of Medicine, Section of Hematology/Oncology, Department of Medicine, Northwestern University, Veterans Administration Lakeside Medical Center, Chicago, Illinois

**John C. Ruckdeschel, M.D.**

Professor of Medicine and Head, Division of Medical Oncology, Albany Medical College; Executive Officer, Lung Cancer Study Group, Albany, New York

**James W. Ryan, M.D.**

Associate Professor, Department of Radiology, Nuclear Medicine Division, University of Chicago Medical Center, Chicago, Illinois

**Eric J. Seifter, M.D.**

Assistant Professor of Medicine, Department of Medicine, Uniformed Services University of the Health Sciences; Investigator, NCI-Navy Medical Oncology Branch, National Cancer Institute, Bethesda, Maryland

**David B. Skinner, M.D., F.A.C.S.**

Dallas B. Phemister Professor and Chairman, Department of Surgery, Pritzker School of Medicine, University of Chicago, Chicago, Illinois

**Ralph R. Weichselbaum, M.D.**

Professor and Chairman, Department of Radiation Oncology, Pritzker School of Medicine; Michael Reese/University of Chicago Center for Radiation Therapy, Chicago, Illinois



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# \_\_\_\_ PART I \_\_\_\_

## **Basic Principles**



Jacob D. Bitran, Harvey M. Golomb  
Alex G. Little, Ralph R. Weichselbaum

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# 1

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## The Multimodality Approach to Lung Cancer

The title of this book reflects its goals: to be both reasonably comprehensive and serve as a textbook. With regard to the first goal, we have attempted to address the important issues of lung cancer biology, diagnosis, staging, and treatment by all three therapeutic modality groups. Regarding the second goal, our aim is to present the state of the art regarding lung cancer in a fashion that is useful to residents, fellows, and practicing physicians. Where there is controversy or an important difference of opinion, we have attempted to present all sides. Authors have been selected from many places, but the editorial board is from the Chest Oncology Group at The University of Chicago Medical Center. We stress throughout the philosophy that has emerged from our joint endeavors over the decade that this group has been in existence.

In particular, we want to emphasize the value of a prospective, multimodality approach to patients with lung cancer. The stress is on the word "approach." All physicians involved in the care of lung cancer patients in any institution should take part in the important decision-making steps involved in diagnosis, staging, and long-term follow-up of these patients, as well as therapy. In addition, there should be a disease- and patient-oriented approach, not a procedure-oriented approach for surgical and radiation therapy oncologists or a chemotherapy-oriented approach for medical oncologists. These desiderata can best be achieved through a group, multimodality approach such as has been utilized by the Chest Oncology Group at The University of Chicago Medical Center. We would like to offer a description of our group's interactions as an archetype to be used in considering the benefits, practicalities, and logistics of this approach.

Our weekly Chest Oncology conference is attended by representatives from the Medical Oncology, Thoracic Surgery, and Radiation Oncology sections who combine to form the Chest Oncology Group. Also present is a radiologist for interpretation of radiologic examinations, a nuclear medicine representative for nuclear scan readings, and a pathologist who reviews material pertinent to the patients to be discussed. Three groups of patients are reviewed and discussed. First, new patients with suspected or newly diagnosed lung cancer are presented in detail and clinical information is re-

viewed. Diagnostic and staging alternatives are discussed with the referring physician and appropriate strategies developed. Treatment strategies based on the potential outcomes of diagnostic and staging plans are also evaluated at that time. The referring physician leaves the conference knowing the recommended plan and having contributed to its formulation. The second group of patients presented are those in the hospital who have been previously discussed by the Chest Oncology Group. New results of diagnostic or staging evaluations are reviewed, as well as results or complications of ongoing treatment. A group plan is formulated for further evaluation or therapy and alternatives are developed. Feedback to the responsible physicians is instantaneous as most of the patients are on the Medical Oncology or Thoracic Surgery Services; physicians treating patients on other services are present and participate in discussions and decisions. The third group of patients discussed are those being followed in the outpatient clinic for whose care a decision must be made or for whom a change in management needs to be considered. The responsible physician can succinctly present the pertinent information and immediately receive multimodality consultation in an integrated fashion.

This group approach can be threatening to an individual physician who fears the potential loss of control over his or her patients. It is always clear, however, that when patients are presented by a physician outside the Chest Oncology Group that the group is acting in a consultative capacity. It is only by utilizing this approach, with experienced physicians representing the three modalities presently used to treat lung cancer, that decisions can be made and strategies planned that afford the patient the optimal approach. For example, a referring physician is able to hear and participate in an open discussion of therapeutic options and the rationales for their selection. Discussions can take place regarding a patient's physiologic status and ability to withstand surgery or tolerate chemotherapy or radiation therapy. Only in this fashion can the three modalities be integrated to achieve their maximum benefits for therapy; the full treatment plan is decided together and a coordinated therapeutic schedule devised. It is a system of checks and balances; with an open discussion among representatives of three therapeutic modalities, diagnostic, staging, and therapeutic plans are developed in a balanced manner to the patient's benefit. Patients referred to any member of the Chest Oncology Group are presented and discussed by the group, except for occasional patients requiring urgent intervention prior to any therapy. This prevents the possibility of patients referred to one specialty automatically receiving that particular modality prior to consideration of other options. The prospective and group approach encourages the development of an integrated plan in which the three modalities are combined to maximize their joint efforts.

Another important benefit from this organized multimodality approach is that of the ability to jointly develop therapeutic and/or investigative protocols and subsequently to maintain control over patients entered into them. With the opportunity to participate prospectively in the design of clinical protocols, the odds of adherence to protocol aspects by each therapeutic group are maximized. The "tunnel vision" that can result when any one therapeutic modality group alone treats a patient is prevented by prior agreement between groups, and this is supported by the joint discussion and review of patients in the weekly conference.



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## 2

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# Pathology of Lung Cancer—An Update

## DEFINITION AND PROBLEMS

Lung tumors include a wide spectrum of benign and malignant neoplasms, predominantly of epithelial type and entodermal derivation. This chapter is limited to discussion of the major types of epithelial tumors (squamous cell, small cell, adenocarcinoma, and large cell carcinoma) and carcinoids, which constitute over 90–95 percent of all primary pulmonary neoplasms.

It is paradoxical and possibly prophetic that many concepts concerning lung cancer proffered 10 years ago as gospel have been challenged and found inappropriate. Simple, relatively benign techniques such as fiberoptic bronchoscopy and guided fine-needle aspirates have permitted diagnoses of central, peripheral, and apical lung tumors.<sup>73,82</sup> Cytology has been raised to a fine art in the interpretation of these aspirates.<sup>36,42,45,74,105</sup> Staging procedures to define regional or extensive disease have been profoundly altered by computed tomographic (CT) scans and by magnetic resonance (MR) imaging. Restaging procedures utilizing these techniques have altered impressions concerning the complete or partial response of the tumor to therapy. Operability of small cell lung cancer (SCLC), once considered an exercise in futility, has become feasible for the small number (5 percent) of these patients who present with a T<sup>1</sup>N<sup>0</sup>M<sup>0</sup> pulmonary mass.<sup>97</sup> Treatment policies and protocols based on older concepts thus become problematic.

## CHALLENGE TO LIGHT-MICROSCOPIC CONCEPTS

Electron microscopy (EM), immunohistochemistry (IHC), and basic experimental research techniques have profoundly altered and immensely improved our understanding of the embryogenesis, histogenesis, and morphogenesis of all lung cancers. The entodermal rather than neural crest origin of SCLC is currently accepted by almost all serious students of the disease.<sup>27</sup> It is likewise recognized from a number of reports that some non-small cell lung cancers (NSCLC) demonstrate, by one or all of the techniques mentioned above, distinct neuroendocrine (NE) features.<sup>5,8,29,46,54,67,114</sup> Because of the relative paucity of data to date, there is no clear indication of the extent of this problem, whether NSCLC with NE features respond to