

DIAGNOSIS AND STAGING OF CANCER

A Radiologic Approach

Foreword by Leo G. Rigler, M.D.

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Foreword

Despite extensive efforts to eliminate human exposure to substances that may prove to be carcinogenic, the incidence of cancer in the population is steadily increasing. The reduction or elimination of environmental factors that contribute to the causation of cancer ultimately may prove to be the best approach for controlling this group of diseases, but as long as such a large percentage of the population is or will be affected by malignant tumors, every physician will be confronted for many years to come with problems in the early diagnosis, staging, and treatment of neoplasms. The sophistication of new diagnostic and treatment methods puts an increasing burden upon the physician, but it does give him a great potential for making early diagnoses and for instituting effective therapy. Considering the nature of the disease and the history of certain types of cancer, it is not surprising that some investigators have come to believe that in treating cancer we are merely postponing the inevitable; the disease will finally overcome its host if he has not already succumbed to another disorder. Even if this *were* true, the effective prolongation of life and relief of symptoms are extraordinarily worthwhile and should be approached with as high a level of expertise as can be achieved.

The importance of diagnostic radiology in the detection of cancer in its earlier stages, or while the neoplasm is still minimal in size, has long been recognized but is not yet universally accepted. Since a malignant tumor is microscopic in origin there is no doubt that the majority of its lifespan has already been spent by the time the lesion is sufficiently large to be detected by even the most accurate roentgenographic or other diagnostic procedure. Nevertheless, all the evidence indicates that even with such locally "advanced" lesions, if they are relatively small at the time of detection, the outlook for survival of the host with proper treatment may still be satisfactory. Unfortunately, even small, grossly evident lesions in the lungs, stomach, colon, and other organs may escape detection in a substantial percentage of cases because of inadequacies in our techniques of examination as well as in our ability to interpret the roentgen findings. The detection of a carcinoma when it is small is of such importance that it must not be left to chance, nor should detection be open to the possibilities of error that may be a consequence of inexperience or inadequate training in the interpretation of roentgenograms. A fallacy common among non-radiologists who perform and interpret their own radiographic examinations is that they can be saved from error by obtaining consultation on those cases in which they actually find an abnormality but are uncertain of its nature or significance. This is the converse of the actual situation: the diagnostic radiologist is especially trained and his experience is attuned to detect the small

variations from the normal that may be in the first sign of a malignancy. Of course, the determination of the nature of a specific abnormality, once detected, may require the combined wisdom, experience, and facilities of many medical specialists.

The great value of radiographic examinations has led to their extensive use, but unfortunately has caused *abuse*, as well. Unnecessary examinations are prevalent in practice, partly because of excessive caution on the part of the physician and partly because of his ignorance of the possibilities, as well as the limitations, of a radiologic procedure. We are inclined to order radiologic examinations far too mechanically, often without proper consideration. This increases the cost to the patient, in terms of both money and radiation hazard.

Radiologic examinations encompass much more than the detection of abnormality; they may permit positive identification of the nature of a malignant process, determination of its stage or extent, and monitoring of the results of treatment. From the latter, the best course for future management can be derived. Direct roentgenographic visualization of the effects of radiation or chemotherapy upon one or more lesions may be the most important factor in effecting disease control or palliation.

With most cancers, the complexity of the disease process inevitably requires the involvement of a number of specialists. Nothing is more important than the quality of the dialogue between them. In this context the radiologist should be considered a consultant whose opinion should be sought not only in the interpretation of the roentgenographic findings after an examination but also *before* the roentgenographic study is performed in order to determine its value in a particular clinical situation and to select the proper methodology that should be used.

Newer methods of imaging, especially computer-assisted technology, may open new horizons in the diagnosis of cancer throughout the body, as has already been accomplished in the detection and identification of brain lesions. Other procedures, such as the improvement and enhancement of the roentgenographic image by television conversion and manipulation, improved methods of contrast angiography, the expansion of nuclear scanning methods, and the further development of ultrasonic echography, all give promise that the future will bring improvements in our ability to detect cancer early in its course.

The editors have assembled in this unusual book some highly authoritative and complete chapters covering most tumors by their anatomical sites. While using a unique and informative organizational approach, the material brings together the clinical, diagnostic, and staging aspects of most tumors, with particular reference to the contributions of radiology in reaching treatment decisions. The necessary correlations between various specialists are further exemplified by the organization of each chapter, which juxtaposes a brief description of the clinical problem with the potential radiologic contribution. Clearly this book brings to oncology, in all its aspects, many new ideas as well as a comprehensive view of how to achieve the best possible results from roentgenographic investigation of the cancer patient.

The great potential that the conventional diagnostic and the newer special imaging procedures have brought us may well be wasted because of small errors in technique or the improper application of available methods. The purpose of this book is to minimize the possibility of such errors of omission or commis-

sion, by bringing to the oncologist, and in fact to any physician confronted by the problems of malignancy, as much information as possible so that we may exploit our current potential for healing to the fullest. The reader of these chapters will be well rewarded.

LEO G. RIGLER, M.D.

Preface and Introduction

This book is intended for the guidance of *clinicians* who treat cancer patients. It is not a radiologic text, but it may give the practicing radiologist or trainee a consultative framework for answering specific clinical questions about radiologic techniques. The emphasis is upon solving *practical clinical problems in patient diagnosis and management*, with particular attention given to the contribution of diagnostic radiology. Radionuclide scanning techniques and diagnostic ultrasound have been addressed superficially and only in the context of ways in which they might fit into the total constellation of clinical, laboratory, and pathologic findings that are considered, together with diagnostic radiologic information, in clinical decision making.

Unfortunately, there is sometimes a lack of forethought and meaningful communication between the clinician (including the radiation therapist, the medical oncologist, and the surgical oncologist) and the diagnostic radiologist, mixed occasionally with an uncritical enthusiasm for certain types of radiologic examinations. This enthusiasm may result in the repeated and inflexible use of some radiologic studies for tumor diagnosis or staging, which may waste valuable departmental resources and place unnecessary burdens upon the patient. *Cost-effectiveness* has not been addressed in this volume as such; the editors feel it is inappropriate (even if it were feasible) to assign a value to a diagnostic procedure that may affect the quality or the duration of a human life. Individual diagnostic and management decisions must be made by the patient together with his family and his "significant others," including those whom he has entrusted with his care.

The recent era of enhanced interest in cancer management (including prevention and diagnosis) has also been a time of exciting new developments in diagnostic radiology. No longer must we ask, "Do we possess an appropriate radiologic imaging study to elucidate the patient's problem?" Instead, we must be concerned with the question, "Have we controlled appropriately the choice and the sequence of radiologic studies in a given patient to maximize the clinically useful information derived from each examination?" This book addresses itself to the limitations of diagnostic radiology as well as its strengths; it is essential that the clinician perceive both the situations in which radiology will be of assistance, and those in which it has little to offer the patient. The practicing physician and the radiologist must appreciate fully the limitations in sensitivity and specificity of a diagnostic radiologic examination in the

context of a given patient's problem. Patient comfort and the medical contraindications to performing certain radiologic examinations must also be considered carefully.

Demonstrable *facts* are different from clinical judgments that ostensibly are based upon these facts. A radiologic imaging procedure may demonstrate a specific finding that is "fact," but its impact on the individual patient's care clearly depends upon a physician's judgment and the quality and relevance of the factual material that is obtained. Radiographs of poor quality, inappropriate radiographic views, inadequate correlation with other diagnostic observations, and inaccurate radiologic or clinical interpretations can all lead to faulty treatment conclusions. Consider the following examples:

1. A premenopausal patient with a history of cancer of the breast had an oöphorectomy for bilateral pulmonary nodules, which later were found to have been caused by histoplasmosis.
2. A patient with a "positive" bone scan and cancer of the prostate had a bilateral orchiectomy; the cause for the abnormal scan later was shown to be osteoarthritis.

Positive bone scans are not specific for cancer. Many benign diseases that cause a "positive" scan can be diagnosed accurately if roentgenograms are also taken of the corresponding region.

3. A 38-year-old woman with amenorrhea and galactorrhea had been followed clinically for eight years and was almost totally blind. Radiologic studies had been limited to plain skull films, which were correctly interpreted through the years as "normal." A chromophobe adenoma was found at subsequent craniotomy.

This example demonstrates the acknowledged limitations of plain skull radiographs in diagnosing small sellar tumors. The clinician should have been aware that skull films alone are an insensitive means of screening for this condition; he should have been much more aggressive diagnostically, given the persistence and worsening of the patient's clinical symptoms in the face of negative skull roentgenograms.

These brief examples illustrate treatment (or non-treatment) decisions based upon observed "facts." However, clinical judgments were made without the availability of sufficient information, essential steps in decision making were overlooked, and false conclusions were drawn from unwarranted diagnostic assumptions. Patient care decisions must never be predicated upon roentgenologic observations alone, nor on any isolated laboratory or physical finding.

Diagnostic radiology is capable of making important contributions at several intervention points in the clinical management of patients with cancer.

(1) Radiologic studies may contribute to cancer screening and early detection in selected situations; (2) diagnostic radiology may be invaluable for assisting the clinician in differential diagnosis; (3) radiologic examinations may contribute to staging the extent of a known malignancy, and thereby also may assist in planning appropriate therapy and in estimating the patient's prognosis; and (4) radiologic methods are an invaluable means for following the treated patient in order to monitor the therapeutic response, as well as to detect tumor persistence or recurrence.

The editors have encouraged the contributing authors to address each of these four major areas of practical clinical concern. Most chapters therefore consist of a clinical introduction to define the problem broadly, followed by a

detailed radiologic discussion addressing actual clinical problems that are encountered in the detection, differential diagnosis, staging, treatment, and post-treatment follow-up of cancer patients. Each of the contributing authors has been asked to develop a personal overview of his subject, and many legitimate areas of controversy will remain. For example, Steckel and Kagan (Chapter 1—Hodgkin's Disease) have promulgated the "classic" view in favor of obtaining an inferior venacavagram, intravenous urogram, and lymphogram in most patients with Hodgkin's disease *before exploratory laparotomy*. Although the latter view is still widely held in the United States, recent experience in Britain has suggested that these studies often may not be required.¹ Greene (Chapter 3—Lung and Mediastinum) makes the contention that most pulmonary carcinomas are centrally located, in or near the major bronchi (and hence are difficult to detect radiographically when they are small), which means that periodic chest roentgenograms for screening purposes are of limited usefulness. Rigler, on the other hand, has maintained that most pulmonary carcinomas arise peripherally but are overlooked until central (mediastinal or hilar) adenopathy, pneumonia, or atelectasis supervenes.² He concluded that roentgenographic screening in high-risk patients is worthwhile and that research (including improved radiologic imaging) should be directed toward enhancing the detection of small peripheral carcinomas.

Rösch (Chapter 9—Liver, Gallbladder, Biliary Ducts, Pancreas, and Spleen) is enthusiastic about the radiologic contribution to earlier diagnosis and improved cure rates in malignancies of the pancreas and hepatobiliary region. In surgical circles, however, consistent enthusiasm for earlier diagnosis exists only with carcinoma of the gallbladder.³⁻⁴ It is the editors' view that Rösch's technical and interpretative skills are matched in relatively few centers and that improved results will follow the widespread application of more exacting visceral angiographic techniques. On the other side of the spectrum, Gilbert (Chapter 12—Female Genital Tract) shows pessimism about the potential contribution of special radiologic studies such as venograms, lymphograms, or hysterosalpingograms for gynecologic malignancies; he feels these studies cannot be relied upon to reach treatment decisions for patients with gynecologic tumors. However, Gilbert's opinion is not shared by several other investigators who have taken a special interest in these radiologic studies.⁵⁻⁹ Gold's viewpoint (Chapter 13—Breast) on the importance of mammography for detecting early breast carcinoma has the support of many other investigators. However, it must be emphasized that in order to achieve 90 per cent diagnostic accuracy, the radiologist doing mammography must take a special interest in each patient (including a personal examination of the patient), and he must employ exacting radiographic techniques. There must also be a continued interchange of pertinent information between the radiologist, the breast surgeon, and the pathologist. In his approach to bone tumors (Chapter 14—Bone and Soft Tissues Sarcomas), Gold correlates the appearance of bone lesions with their clinical behavior using a roentgenographic-morphologic classification. This classification differs from the traditional radiologic terminology in describing these tumors, but we feel it will provide more practical assistance to the pathologist as well as to the clinician in determining a patient's prognosis and management. In all chapters, extensive bibliographies are provided for those readers who wish to pursue certain topics, including the more controversial issues, in greater depth.

A specific illustration concerning the use of diagnostic radiology in cancer staging might serve to underline the philosophy of *interdisciplinary consultation*, which is a major premise of modern cancer diagnosis and management (a philosophy that has also prompted this book). Radiologic examinations are integral to determining the stage of many malignancies, prior to the institution of treatment. Despite acknowledged limitations, the editors have adopted the "TNM system" for cancer staging because of its practical utility and its increasingly widespread use (see accompanying table). However, the precise application of the TNM system still varies from institution to institution and (even within the same institution) from one organ to another. The TNM classification system is defined briefly as follows: T represents local tumor extent; N, regional lymph node status; and M, distant metastasis. Confusion in the use of this system still exists because some clinicians regard the TNM system solely as a means for clinical description; others use it to effect treatment decisions; and still others regard it principally as an instrument for predicting patient survival. Furthermore, in many patients (such as those with deeply situated metastatic lymph nodes from primary tumors of the breast, cervix, respiratory tract, digestive tract, colon, or prostate, with microscopic bladder wall invasion, or with splenic lymphomatous infiltration) only pathologic staging has any demonstrable validity, since clinical and roentgenographic examinations both have a wide range of error.

Proposed originally as a *clinical staging device*, the TNM system has in fact come to connote to many oncologists the employment of a much broader range of diagnostic studies beyond physical examination, including roentgenologic studies, laboratory determinations, radionuclide scanning, and (occasionally, but with increasing frequency) biopsy or surgical exploration. The editors also have favored a broader or interdisciplinary definition for TNM staging of cancer in this book. All useful diagnostic modalities, when employed judiciously and with a potential for practical benefit to the individual patient, are recommended to reach an accurate pretreatment assessment of the stage of the disease. Therefore, tumor staging maneuvers recommended here usually will include the use of one or more roentgenologic techniques, often with the addition of endoscopic, radionuclide, pathologic, or other contributory studies.

TNM Staging System

Tumor	
T0	No evidence of primary tumor.
TIS	Carcinoma in situ.
T1 T2 T3 T4	Progressive increase in tumor size and involvement.
TX	Tumor cannot be assessed.
Nodes	
N0	Regional lymph nodes not demonstrably abnormal.
N1 N2 N3 etc.	Increasing degrees of demonstrable abnormality of regional lymph nodes. For many primary sites the subscript "a," e.g., N1 _a , may be used to indicate that metastasis to the node is not suspected; and the subscript "b," e.g., N1 _b , may be used to indicate that metastasis to the node is suspected or proved.)
NX	Regional lymph nodes cannot be assessed clinically.
Metastasis	
M0	No evidence of distant metastasis.
M1 M2 M3	Ascending degrees of distant metastasis, including metastasis to distant lymph nodes.

As in the example of interdisciplinary cooperation offered by current cancer staging procedures, the repeated emphasis in this book is upon two-way communication between the diagnostic radiologist and the medical or surgical oncologist, endoscopist, radiotherapist, and pathologist. With clinical and laboratory correlation, appropriate radiologic imaging techniques may establish the correct diagnosis and tumor stage, upon which a treatment decision can then be made. In other situations, the radiologist can pinpoint a suspicious area for biopsy in the lung, bone, bronchus, mediastinum, peritoneum, retroperitoneum, liver, pleura, stomach, or colon, in order to establish the histologic diagnosis or tumor stage.

No diagnostic examination should ever be performed (or subsequently interpreted) by a radiologist in the absence of pertinent clinical information about the patient. The attitude of "let's see what the radiologist observes first without prejudicing him with our clinical findings" has absolutely no redeeming value. The diagnostic radiologist, like the radiation therapist, the medical oncologist, the surgeon, and the pathologist, is a physician first and a specialist second. He can only be expected to propose a hierarchy of *differential diagnoses* in close consultation with the patient's physician and with a full knowledge of all other pertinent physical, historic, laboratory, and pathologic findings. Like the pathologist who may be unable to interpret the significance of cytologic or histologic observations in the absence of related clinical, laboratory, and radiologic data, the radiologist is not a Delphian oracle who extracts occult meanings from stars in the heavens or from shadows on a viewbox. He is a medical consultant with a practical need for communication with the patient's physician and other consultants, to determine the need for (and the proper sequence of) individual radiologic examinations, as well as to reach a clinically useful interpretation of the results. In arriving at clinical judgments that require the use of radiologic imaging, neither the clinician nor the diagnostic radiologist is ever justified in failing to consult the other.

Finally, it should be pointed out that diagnostic radiology is undergoing rapid technical evolution at this moment. Those who surmised that the major technical advances in radiology had already been made when the fluoroscopic image amplifier was invented and the percutaneous catheter (for angiography) was adopted for clinical use had several surprises waiting for them. Computerized axial tomography ("EMI scanning") and gray-scale ultrasound techniques virtually unknown and unappreciated as clinical imaging modalities until recently, are achieving their full stature as this book goes to press. There is little question that these and perhaps other new imaging techniques will have a revolutionary impact upon the detection, diagnosis, staging, and post-treatment follow-up of patients with cancer. In some instances the editors and contributing authors have attempted to *project* the influence of these newer technical modalities over the next several years from relatively limited data now on hand, but the situation is changing too rapidly now even for the best prognosticators. We believe that these newer imaging techniques, including "whole-body" computerized tomography, will enable the physician to visualize pathologic changes in the soft tissues and parenchymal organs that heretofore were undetectable or exceedingly difficult to demonstrate by noninvasive means. Extravagant claims that arteriography and conventional radiography are now "on their way out" are not supportable. These established radiologic methods will continue to serve essential functions in our diagnostic armamentarium and will be complementary to the newer technologies that are now on

the horizon. With parallel recent technical advances in clinical endoscopy, it would seem that "in vivo" imaging is at a new crossroads and that beneficial effects upon cancer patient management will be felt strongly over the next two to three years. It is therefore incumbent upon all of us, clinical oncologists as well as diagnosticians, to remain current with the rapid advances which are taking place in imaging techniques.

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