Part IV

Therapeutic Modalities
Principles of Surgical Oncology

Raphael E. Pollock, MD, PhD
Donald L. Morton, MD

Surgery is the oldest modality of cancer therapy and still forms the mainstay of treatment in solid tumors. It remains a paradigm that more patients are cured by surgery when it is used as a single treatment in comparison with any other individual form of cancer therapy. Even in the contemporary multimodality cancer therapy milieu, it is the rare solid-tumor patient whose care does not include a surgical component. To be maximally effective, the cancer surgeon must function as a member of the oncology team, and is frequently the first oncology specialist that a patient will consult. The cancer surgeon is commonly charged with the responsibility to establish a tissue diagnosis for a suspicious lesion, where it will be the surgeon’s decision whether an operative procedure is needed versus an image-directed or other biopsy approach. The cancer surgeon will usually bear the responsibility for communicating the biopsy findings to the patient, completing the procedures needed to stage the patient, and initiating the interaction between the now diagnosed and staged patient and other members of the multimodality oncology team. Because of these responsibilities, it is most often the cancer surgeon who initially explains to the patient the sequence and rationale of the various treatment components that will be used to manage their specific malignancy. To be maximally effective, the cancer surgeon must therefore be aware of the different therapeutic options, the natural history of a given malignancy, and how these factors will be integrated into a well-conceived and appropriate multimodality treatment algorithm. It is also usually the cancer surgeon’s responsibility to provide initial information about prognosis and to make decisions about follow-up care and surveillance to detect tumor recurrence. In these regards, the cancer surgeon is unlike almost any other surgical specialist, in that the commitment to a given patient is for both the acute and the long-term components of the patient’s disease process.

Over the years, the practice of surgical oncology has come full circle. Originally, surgeons attempted to treat cancer conservatively by removing only the gross lesion. Unfortunately, this led to extremely high rates of local recurrence and subsequent patient mortality. In the late nineteenth century, surgeons began to undertake complete en bloc resections and amputations to treat patients with malignant lesions. These techniques yielded improved results, but the procedures were ablative and mutilating. With the advent of complementary and effective treatment modalities, notably radiation therapy in the 1920s and chemotherapy after the 1940s, the orientation of surgical resection is once again becoming conservative.

Adjuvant chemotherapy, alone or in combination with radiation therapy, has improved disease-free survival and prolonged quality life for patients who have been rendered free of gross disease by surgery but who still have a high likelihood of recurrence as a consequence of microscopic residual metastases. Randomized clinical trials have demonstrated the benefit of adjuvant chemotherapy in a variety of tumors, including breast cancer, colon cancer, osteogenic sarcoma, testicular cancer, ovarian cancer, and certain lung cancers. In some cancers (eg, sarcoma), the benefit of adjuvant therapy is modest; however, in other tumor systems, such as testicular and bone cancer, it has resulted in two- and threefold improved overall survival rates.

Surgery is most effective in the treatment of localized primary tumor and associated regional lymphatics. This is accomplished by en bloc surgical procedures that attempt to encompass gross and microscopic tumor in all contiguous and adjacent anatomic locations. Intuitively, it appears logical that surgery should have little role in disease management once a neoplasm has spread from the primary location to a distant site. However, prolonged survival is possible following the surgical resection of some metastases in the lung, liver, or brain. For example, a 5-year survival rate up to 40% can be anticipated after surgical resection of solitary colorectal metastasis in the liver.

Surgery operates by zero-order kinetics, in which 100% of excised cells are killed. In contrast, chemotherapy and radiation therapy operate by first-order kinetics, and only a fraction of tumor cells are killed by each treatment. These zero- and first-order processes are complementary. Surgical resection reduces the tumor burden, which hopefully increases the efficacy of nonsurgical adjuvant therapies intended to eliminate microscopic residual disease, thereby decreasing the risk of recurrence.

During the past two decades, major improvements in both operative technique and the use of combined modality therapy have significantly reduced the morbidity and mortality associated with the surgical treatment of solid neoplasms. For example, breast-preserving surgery has become an alternative to mastectomy in patients with breast carcinoma; limb salvage is often possible in patients with bone and soft-tissue sarcomas; and sexual potency/urinary continence can frequently be preserved for patients with prostate cancer. Because surgery is increasingly combined with other treatment modalities, it is essential that most patients with solid neoplasms have their treatment planned by a multidisciplinary team, which includes radiation and medical oncologists as well as surgical oncologists. Manifestly, the successful surgical oncologist must be able to coordinate and integrate the efforts of the entire oncologic team if the oncologist is to retain a primary role in the management of the cancer patient.
HISTORICAL CONSIDERATIONS

Oncology (from the Greek words onkos, meaning mass or tumor, and logos, meaning study) is the study of neoplastic diseases. Early authors suggested that certain families, races, and working classes were predisposed to neoplastic transformations. In 1862, Edwin Smith, an American Egyptologist, discovered the apparently earliest recordings of the surgical treatment of cancer. Written in Egypt circa 1600 B.C., this treatise was based on teachings possibly dating back to 3000 B.C. The Egyptian author advised surgeons to contend with tumors that might be cured by surgery but not to treat those lesions that might be fatal.

Hippocrates (460–375 B.C.) was the first to describe the clinical symptoms associated with cancer. He advised against treating terminal patients, who would enjoy a better quality of life without surgical intervention. He also coined the terms carcinoma (crab legs tumor) and sarcoma (fleshy mass). In the second century A.D., Galen published his classification of tumors, describing cancer as a systemic disease caused by an excess of black bile. Galen cautioned that as a systemic disease, cancer was not amenable to cure by surgery, which was often promptly followed by patient death. This strong admonition against surgery persisted for more than 1,500 years until the eighteenth century pathologists discovered that cancer often grew locally before spreading to other anatomic sites. Prior to the advent of safe general anesthetics, surgery was used primarily to manage trauma or severe infectious problems such as abscess drainage. In that era, cancer surgery consisted primarily of amputation or cauterization of surface tumors of the trunk or extremities. Patients were usually unwilling to submit to the pain of tumor surgery, when there was so little likelihood of positive survival impact.

During the eighteenth and nineteenth centuries, advances in anatomic pathology led to an increase in autopsies, which, in turn, resulted in a better understanding of human physiology. The early work of Morgagni, Le Dran, and Da Salva established that there was an initial period of local tumor growth prior to distant dissemination. This led to the understanding that not all tumors were systemic, and that certain lesions cause death solely by local invasive growth. Percival Pott (1714–1788) was the first to describe a specific etiologic factor associated with cancer development. In 1775, Pott demonstrated a high incidence of cancer of the scrotum in chimney sweeps who had reached puberty, and recommended wide local resection for cure. In 1829, the French Surgeon Joseph Récamier (1774–1852) first described the complicated process of tumor dissemination. The first recorded elective tumor resection was performed in 1809 by Ephraim McDowell, an American surgeon. He successfully removed a 22-pound ovarian tumor from a patient, who subsequently survived 30 years. McDowell’s work, which included 12 more ovarian resections, stimulated greater interest in elective surgery for cancer patients.

Surgeons were initially hindered by the extreme discomfort that patients experienced during surgical procedures, as well as the lack of agents that could reduce the incidence of infection. Crawford Long (1815–1878) was the first to use ether for general anesthesia in 1842, but it was the reported work of John Collins Warren (1778–1856) and William T.G. Morton (1819–1868) that brought the potential of anesthesia to public attention. The surgical procedure in Warren’s first published account of ether anesthesia (1846) was the elective removal of a tongue carcinoma for which submaxillary gland resection and partial glossectomy were performed. Warren was also responsible for the first American-authored textbook of tumor surgery, Surgical Observations on Tumors, published in 1838. Joseph Lister (1827–1912) was the first to report the successful use of antiseptics during elective surgery. In 1867, Lister applied Pasteur’s concept that bacteria cause infection, when he introduced the use of carbolic acid as an antiseptic agent in conjunction with heat sterilization of surgical instruments. Lister is also credited with the introduction of absorbable ligatures, as well as the placement of drainage tubes to control secretions and dead space in surgical wounds. Robert Wood Johnson developed the individual sterile dressing pack in 1876, which also remarkably improved postoperative wound-contamination problems.

Even with the advent of antiseptics and general anesthesia, surgical oncology in the second half of the nineteenth and early twentieth centuries was still associated with high patient mortality rates. Cancer was rarely diagnosed in the early stages; consequently, few patients were considered candidates for curative surgery. Those surgeons who did attempt surgical excision of malignant lesions were hindered by rudimentary anesthetics, which was also independently associated with high patient mortality. Antibiotics were not yet available, and surgical instruments were crude. The importance of the microscope to evaluate frozen tissues for surgical margins was not yet appreciated, and surgeons had great faith in their own unaided gross visual assessment of the tumor perimeter. However, several important developments in this era led to rapid advancements in surgical oncology. Emphasizing meticulous surgical technique, gentle tissue handling, and applications of listeriae principles, pioneers such as Albert Theodore Bilroth (first gastrectomy, laryngectomy, and esophagastrectomy), William Stewart Halsted (en bloc resection, radical mastectomy), as well as many other more contemporary surgeons defined and advanced the boundaries of surgical oncology, as summarized in Table 38-1.2,3

Ongoing innovations continue to advance effective surgical primary tumor control linked to improved surgical outcomes and better quality of life. Advances in microvascular surgery now permit the free transfer of complex autologous tissues, such as free jejunal grafts to reconstitute the upper aerodigestive system or osteomyocutaneous flaps to reconstruct extremities and other mobile body parts such as the jaw. Automatic stapling devices, as well as endoscopic instrumentation coupled with high-resolution fiberoptics, has remarkably advanced intraabdominal and pelvic tumor surgery, resulting in less-morbid procedures that require significantly less patient recuperation time and effort (Figure 38-1). Enhanced biomedical monitoring and the emergence of critical care medicine have made it possible to safely undertake increasingly complicated surgical procedures. A more sophisticated awareness of the patterns of tumor progression have made possible less-invasive surgical approaches. Examples include sentinel node biopsy as a replacement for formal lymphadenectomy in early stage carcinoma of the breast, and the introduction of radiofrequency ablation with ultrasonography guidance, which has markedly enhanced surgical cancer control of multifocal liver disease while minimizing patient morbidity.

THE CONTEMPORARY ROLE OF SURGICAL ONCOLOGY

Surgical oncologists are surgeons who devote most of their time to the study and treatment of malignant neoplastic disease. They must possess the necessary knowledge, skills, and clinical experience to perform both the standard as well as extraordinary surgical procedures required for patients with cancer. Surgical oncologists must be able to diagnose tumors accurately and to differentiate aggressive neoplastic lesions from benign reactive processes. In addition, surgical oncologists should have a firm understanding of radiation oncology, medical oncology, and hematology. They must also be capable of organizing interdisciplinary studies of cancer. Surgical oncologists should also be trained in pathology, because they will be called on to excise appropriate tumor samples for pathologists and make decisions about adequacy of surgical margins. Surgical oncologists have a shared role with medical oncologists as the “primary care physicians” of cancer treatment. Almost all cancer patients will initially be managed by one of these two specialists who will bear the ultimate responsibility for coordinating appropriate multimodality care for the individual patient.

Not surprisingly, given the complexity of contemporary multidisciplinary approaches to the cancer patient, free-standing cancer centers have developed facilities to provide the needed planning expertise, clinical care, patient support services, and access points to clinical trials. Cancer center professional staff share the exclusive goal of eradicating neoplastic disease. Comprehensive cancer centers are frequently (but not invariably) affiliated with academic medical institutions and offer the complete spectrum of oncology therapies, clinical trials, rehabilitation, and social services, as well as basic and translational research programs to move new knowledge from the laboratory bench to the patient bedside. In this contemporary oncology milieu, the role of the surgical oncologist has expanded, while the overall impact of noncancer surgical specialists has declined.
Surgical oncology is more of a cognitive than a technical surgical specialty. With the exception of a small cluster of index operations, such as regional pancreatectomy, limb salvage and retroperitoneal sarcoma surgery, isolated limb perfusion, and multisegment liver resection, most of the surgical procedures that are performed by surgical oncologists are similar to those performed by a surgeon not oncologically trained. What frequently differentiates these two types of surgeons is not merely knowledge about how to do a specific operation, but an awareness of how and when to do that operation; that is, the cognitive knowledge of contemporary multimodality cancer care. A broad knowledge of cancer in its presenting and recurring forms, as well as an awareness of the molecules driving tumor proliferation and dissemination, is an integral part of the special cognitive database of the surgical oncologist.

As part of the larger surgical community, the surgical oncologist is a critical conduit of cancer information to colleagues in general surgery and other surgical specialties. This function is performed by academic presentations at large surgical meetings, such as those of the American College of Surgeons or the Society of Surgical Oncology, as well as by service in directing hospital-based tumor boards and direct consultation on behalf of individual cancer patients. Because of their leading role in the initial diagnosis of cancer, it is not surprising that surgical oncologists are also frequently in leadership roles in cancer prevention and screening programs. Nationally based multimodality clinical trial groups also depend on surgical oncology expertise to help in trial design, establishing the criteria of surgical quality control, educating trial participants regarding standards of surgical care (including indications for procedures), as well as assistance in accurate data collection, analysis, and presentation of trial results.

**COMBINED MODALITY THERAPY**

Pediatric oncologists pioneered the use of combined modality therapy (radiation in combination with chemotherapy and surgery) as effective management of childhood neoplasms. Control of localized retinoblastoma in children has been dramatically increased by using multimodality therapy. The cure rate for patients with Wilms tumor is 75%, if surgical therapy is followed by chemotherapy and, in some cases, radiation, an increase of 40% over operation alone. Embryonal rhabdomyosarcoma responds best to combinations of radiation, chemotherapy, and operation. Until recently, the effectiveness of multimodality therapy was only occasionally demonstrable for adult neoplasms. A striking example is the approach to skeletal and soft-tissue sarcomas. Surgical therapy, the accepted method for local management of most skeletal and soft-tissue sarcomas of the extremities, is associated with frequent treatment failure if used alone. In the past, approximately 50% of patients with soft-tissue sarcomas and 80% of those with bone sarcomas eventually succumbed to distant metastases, even after amputation of the extremity bearing the primary tumor. Consequently, multimodality treatment regimens were developed to improve these results. Preoperative chemotherapy with intraarterial doxorubicin followed by radiation resulted in extensive tumor cell necrosis in as many as 75% of patients. The effectiveness of this preoperative therapy permitted local resection of the sarcoma and salvage of a viable functional extremity. Local recurrence rates were as low as with amputation, and long-term results were functionally and psychologically superior. In addition, there was no decrease in overall or disease-free survival rates. Multimodality therapy is also effective for localized breast cancers. In clinical trials, radiation and minimal surgery were demonstrably as effective as mastectomy in the control of small breast cancers. Survival and local recurrence rates were the same for both groups, and patients treated with multimodality therapy were spared the physical deformity and psychological problems of mastectomy.

In selecting appropriate therapy, surgery and radiation are still the most successful means of treating cancer localized to the primary site and/or regional lymph nodes. Because these forms of

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<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Surgeon</th>
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<tr>
<td>1775</td>
<td>Etiologic basis of cancer</td>
<td>Percival Pott</td>
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<td>1809</td>
<td>Elective oophorectomy</td>
<td>Ephraim McDowell</td>
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<td>1829</td>
<td>Metastatic process</td>
<td>Joseph Récamier</td>
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<td>1846</td>
<td>Ether as anesthesia</td>
<td>John Collins Warren</td>
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<td>1867</td>
<td>Carboilic acid as antisepsis</td>
<td>Joseph Lister</td>
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<td>1873</td>
<td>Laryngectomy</td>
<td>Albert Theodore Billroth</td>
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<td>1878</td>
<td>Resection of rectal tumor</td>
<td>Richard von Volkman</td>
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<td>1880</td>
<td>Esophagectomy</td>
<td>Albert Theodore Billroth</td>
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<tr>
<td>1881</td>
<td>Gastrectomy</td>
<td>Albert Theodore Billroth</td>
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<td>1890</td>
<td>Radical mastectomy</td>
<td>William Stewart Halstead</td>
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<td>1896</td>
<td>Oophorectomy for breast cancer</td>
<td>G.T. Beatson</td>
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<td>1904</td>
<td>Radical prostatectomy</td>
<td>Hugh H. Young</td>
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<td>1906</td>
<td>Radical hysterectomy</td>
<td>Ernest Wertheim</td>
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<td>1908</td>
<td>Abdominoperineal resection</td>
<td>W. Ernest Miles</td>
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<td>1909</td>
<td>Thyroid surgery (Nobel Prize)</td>
<td>Theodore Emil Kocher</td>
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<td>1910</td>
<td>Craniotomy</td>
<td>Harvey Cushing</td>
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<td>1912</td>
<td>Cordotomy for the treatment of pain</td>
<td>E. Martin</td>
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<td>1913</td>
<td>Thoracic esophagectomy</td>
<td>Franz Torek</td>
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<td>1927</td>
<td>Resection of pulmonary metastases</td>
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<td>1933</td>
<td>Pneumonectomy</td>
<td>Evarts Graham</td>
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<td>1935</td>
<td>Pancreaticoduodenectomy</td>
<td>Allen O. Whipple</td>
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<td>1945</td>
<td>Adrenalectomy for prostate cancer</td>
<td>Charles B. Huggins</td>
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<td>1957</td>
<td>Isolated limb perfusion</td>
<td>Oliver Creech</td>
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<tr>
<td>1958</td>
<td>Organization of National Adjuvant Breast and Bowel Project (NSABP) to conduct prospective randomized trials</td>
<td>Bernard Fisher</td>
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<tr>
<td>1965</td>
<td>Hormonal therapy of cancer</td>
<td>Charles Huggins</td>
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<tr>
<td>1971</td>
<td>Free tissue transfer with microvascular anastomosis</td>
<td>Harry Buncke</td>
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therapy exert their effects loco-regionally, neither is usually considered curative once the disease has metastasized beyond these sites. However, both methods are frequently useful as palliative treatments, and occasional long-term survival follows surgical resection of single-organ metastases.

An emerging component of the multimodality approach is tumor immunotherapy. The concept of immunostimulation with biologic response modifiers or nonspecific immunomodulators is not new in cancer therapy. Nearly a century ago, William B. Coley developed the basis for nonspecific cancer immunotherapy using mixed bacterial vaccines (Coley toxin). Since then, whole-cell or cell-fragment tumor vaccines have been introduced for active specific immunotherapy of neoplastic disease, and some of these have reached clinical applications maturity. In melanoma, which is the focus of most cancer vaccine research, immunochemotherapy is now used as an adjuvant to surgery for treatment of local and regional neoplastic disease, as well as to prolong the survival of patients with distant metastases. Cytokines such as interferon are being used to modulate the immune response and have proved effective in some diseases, such as chronic myeloid leukemia and hairy cell leukemia. Use of the colony-stimulating factor (CSF) is invaluable in accelerating hematopoietic recovery from high-dose chemotherapy, as well as a comparison of bone marrow transplantation protocols.

Unlike surgery and radiation therapy, systemic therapies, such as chemotherapy, immunotherapy, and hormonal therapy are treatments that can kill tumor cells that have already metastasized to distant sites. These systemic modalities have a greater chance of cure in patients with minimal (or even subclinical) tumor burden, as compared to those patients with clinically evident disease. Consequently, surgery and radiation therapy may be useful in decreasing a given patient’s tumor burden, thereby maximizing the impact of subsequent systemic approaches.

Whether the goals of therapy should be cure or palliation depends on the stage of a specific cancer. If the cancer is localized without evidence of spread, it may be possible to eradicate the cancer and cure the patient. When the cancer has spread beyond the possibility of cure, the goal is to control symptoms and maintain maximum activity and quality of life for as long as possible (Figure 38-2). Patients are generally judged incurable if they have distant metastases or evidence of extensive local infiltration of critical structures adjacent to tumor. However, some patients are potentially curable even though they have distant metastases. For example, patients with solitary pulmonary, hepatic, or cerebral metastases may still be curable by resection, and patients with widespread choriocarcinoma or ovarian carcinoma metastases may still be cured using chemotherapy. Histologic proof of distant metastases should be obtained before the patient is deemed incurable. Occasionally, an exploratory celiotomy or thoracotomy may be necessary to determine the histology of ambiguous lesions in the lungs or liver. In rare situations, the clinical situation may point so overwhelmingly to distant metastases that the patient may be considered incurable without biopsy. For each anatomic site, there are certain local criteria that place the patient unequivocally in an incurable status, whereas other anatomic constraints may imply a poor prognosis but are not an absolute indication of incurability per se. In equivocal situations where extensive studies fail to demonstrate metastatic or incurable local extension, the patient deserves the benefit of the doubt and should be treated for cure.

The selection of therapeutic modalities depends not only on the type and extent of cancer, but also on the patient’s general condition and the presence of any coexisting disease. For example, surgery may be contraindicated in a patient who has had a recent myocardial infarction. A patient with preexisting diabetes will be much more susceptible to the toxic effects of hormonal therapy with corticosteroids. Renal disease may increase the toxicity of some of the chemotherapeutic agents, such as methotrexate or ifosfamide. In addition, acute or chronic infection or bleeding may make any form of cancer therapy dangerous and must be addressed before initiating definitive oncology treatment.

The patient’s psychologic make-up and life situation also must be considered. A patient who is unable to accept the realities of a given treatment should be offered other treatment options, if possible. Consultation with a psychiatrist experienced in cancer (a psycho-oncologist) may help the patient deal with the reality of the disease and its treatment. This is particularly true for surgical procedures that significantly alter the patient’s appearance, such as mastectomy, or those that involve a change of organ function, such as colostomy. Experimental forms of therapy should also be avoided in some patients whose potential noncompliance might jeopardize both themselves as well as the clinical trial. For example, patients who are unwilling to tolerate the inconvenience of an intraarterial catheter (and might therefore remove it themselves) should not undergo treatment that depends on this form of angioaccess.

Extensive staging procedures may indicate that a tumor is localized to a primary site and/or regional lymph nodes, and hence curable by local therapy (surgery and/or radiation). However, approximately 60% of localized malignant tumors ultimately recur, suggesting that many such patients must have had subclinical metastases at the time of initial diagnosis. The probability of cure may be improved if systemic approaches are coupled with the local treatments. Chemotherapeutic drugs must be given when the number of tumor cells is low enough to permit their destruction at doses that can be tolerated by the patient. The opportunity for cure is most likely during the early stage of disease or immediately after surgery when the tumor burden has been minimized.

Figure 38-2 Palliative surgery. A, A patient with a large fungating tumor occupying the lumbar triangle and superior buttock region. This patient had already developed lung metastases and was suffering from intractable pain. The tumor itself created a socially unacceptable situation, and prevented her from interacting with her family. Systemic therapy for her metastatic disease could be initiated. (Four-color version of figure on CD-ROM)

B, The same patient several weeks after a negative margin wide local excision with skin graft closure. The patient’s pain problem was eliminated, and she was able to fully interact with her family. Systemic therapy for her metastatic disease could be initiated.
Adjuvant chemotherapy has remarkably improved surgical results in some malignancies, primarily because of cytotoxic effects on clinically undetectable neoplastic cells outside the operative field. Neoadjuvant or induction chemotherapy that is initiated prior to local and regional treatments also can affect micrometastatic distant disease while significantly cytoreducing the primary tumor. After a course of neoadjuvant chemotherapy, the tumor may be surgically resected with or without concomitant preoperative or postoperative radiotherapy.

Classically, surgery has been first in the sequence of therapies for solid neoplasms, but increasing evidence suggests that it should perhaps be the last. Chemotherapy and radiation therapy both work by first-order kinetics. However, because of tumor cell heterogeneity, it can be anticipated that resistant clones of viable neoplastic cells may persist in the primary tumor after these therapies. Such clonal heterogeneity is more likely in large tumors that are both poorly perfused by chemotherapeutic agents and are also relatively hypoxic and therefore resistant to radiation therapy. Because surgery works by zero-order kinetics, it effectively removes the local residual primary tumor cells that are resistant to these other modalities. In addition, this sequence of preoperative therapies can cause shrinkage of tumor mass because of the destruction of chemo- and radiosensitive tumor cells (Figure 38-3). The frequent possibility of less ablative surgery resulting in tissue (and function) preservation is a major dividend of this preoperative cytoreduction by neoadjuvant treatment. There have been promising results from clinical trials that have applied these concepts in bone and soft-tissue sarcomas, locally advanced breast cancer, and other neoplasms.

A growing neoplasm can evade immune attack by producing specific and nonspecific immunosuppression. Specific immunosuppression can be caused by antigens shed from the tumor into the blood. These antigens, which circulate alone or as antigen–antibody complexes, can inhibit the lymphocyte-mediated destruction of tumor cells in vitro and may play a similar role in vivo. Nonspecific or generalized immunosuppression is attributed to humoral factors produced by or in response to the neoplasm. Any therapeutic maneuver that lowers tumor burden may reverse specific and nonspecific immunosuppression, thereby altering the immune balance in favor of the patient. In this respect, cancer surgery may be thought of as immunotherapy, in that it effectively removes the immunosuppressive cancer cell mass. Once the tumor mass has been removed, the patient’s immune system then may be able to destroy subclinical micrometastases. This premise suggests that local disease should be considered as a manifestation of systemic illness, whether or not the patient has clinically overt metastases. Surgery for apparently localized tumors can thus favorably affect the host–tumor relationship and may even cure the patient with subclinical distant metastases.

**SURGICAL COMPONENTS OF CANCER MANAGEMENT**

**PREVENTION** The old adage that an ounce of prevention is worth a pound of cure certainly applies in solid-tumor oncology. As the role of genetic mutations that predispose to subsequent cancer development expands, one can anticipate that prophylactic surgery will be extended to encompass these conditions. In these situations, it is imperative that the surgical oncologist become intimately knowledgeable about the indications, limitations, and ethical considerations regarding genetic counseling, if only because it will be the responsibility of the surgeon to alert other family members at risk and arrange for appropriate testing. The above emerging indications are being added to an already established role for prophylactic surgery in predisposing conditions such as cryptorchidism associated with subsequent testicular carcinoma, long-standing ulcerative colitis or familial polyposis associated with colon carcinoma, multiple endocrine neoplasia syndromes associated with the development of medullary carcinoma of the thyroid, and oral leukoplakia associated with subsequent development of squamous cell carcinoma. Assessing the risk/benefit ratio of prophylactic surgery is critical yet is frequently difficult to accomplish with precision. With the future advent of inexpensive and reliable genetic screening technologies, coupled with emerging insights derived from the new field of molecular epidemiology, one can anticipate more definitive understanding of prophylactic surgery benefits regarding cancer prevention in populations at risk.

**BIOPLAY AND DIAGNOSIS OF TUMORS** The diagnosis of solid tumors depends on locating and performing a biopsy of the lesion. Biopsy evidence will be used to determine the histology and/or grade of a tumor, which is a prerequisite for planning definitive therapy. Significant therapeutic errors have been made when biopsy confirmation of malignancy was not obtained prior to treatment, as in the radical mastectomies that were performed for nodular fat necrosis. Even when biopsy reports from another hospital are available, the slides of the previous biopsy must be obtained and reviewed prior to the institution of therapy. This is essential because all too often (and particularly in rare neoplasms) an erroneous interpretation may have been made in the initial pathology assessment.

Biopsy is easiest when the tumor is near the surface or involves an orifice that can be examined with appropriate visualizing instruments, such as the bronchoscope, colonoscope, or cystoscope. Carcinomas of the breast, tongue, or rectum can be seen or palpated and a portion can be excised for definitive diagnosis. In contrast, deep-seated lesions may grow to quite a large size before causing symptoms. Ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) are all useful techniques for localizing such lesions at the time of invasive biopsy (Figure 38-4). However, while image-directed needle biopsy may be useful in some patients, exploratory surgery is often required to obtain a definitive biopsy that establishes the exact histologic diagnosis. Fortunately, such procedures can now be frequently performed on an outpatient basis by using minimally invasive technology such as laparoscopic surgical approaches.

Three methods are commonly used to biopsy suspicious lesions: needle biopsy and open incisional or excisional biopsy. Regardless of the method used, the pathologic interpretation of the tumor mass will be valid only if a representative section of tumor is obtained. The surgical oncologist must be aware that a sampling error can occur with needle and incisional biopsies where only small portions of the total tumor mass is submitted for pathologic examination. It is the surgeon’s task to provide adequate tissue for diagnosis. Orientation of the specimen, as may be necessary, is also the responsibility of the surgeon. It is axiomatic that adequate tissue can provide the basis for diagnosis by an adequate pathologist, whereas inadequate tissue will be insufficient for diagnosis by an adequate or inadequate pathologist.

**Figure 38-3** Neoadjuvant chemotherapy. A patient with a large perinephric malignant fibrous histiocytoma located in the left side of the abdomen and retroperitoneum. A, Before treatment with neoadjuvant chemotherapy. B, After four courses of doxorubicin-based multidrug chemotherapy. Note the approximate 50% reduction in overall tumor size. At the time of surgery it was possible to save the left kidney while achieving a negative margin resection. Pathologic analysis demonstrated nearly 100% necrosis of this neoadjuvantly treated tumor.
Tumor staging is a system used to describe the anatomic extent of a specific malignant process in an individual patient. Staging systems cluster relevant prognostic factors about the primary tumor, such as size, grade, and location, as well as information about dissemination to regional sites, such as lymph nodes or distant metastatic loci. Accurately staging a cancer is absolutely essential in designing an appropriate therapeutic program and advising about prognosis.

Fine-needle aspiration (FNA) is a cytologic technique in which cells are aspirated from a tumor using a needle and syringe with the application of negative pressure. The technique can also be performed using image-directed guidance and is particularly helpful in the diagnosis of relatively inaccessible lesions, such as deep visceral tumors. The aspirated tissue consists of disaggregated cells rather than intact tissue. Diagnosis of malignancy, therefore, usually depends on detection of abnormal intracellular features, such as nuclear pleomorphism, and so the margin of error in diagnosis of many tumor types is higher than with other biopsy techniques. In addition, because of the lack of intact tumor architecture, FNA cannot distinguish invasive from noninvasive malignancy. Consequently, other types of biopsy may be more appropriate, depending on the clinical context, such as distinguishing carcinoma in situ from an infiltrating malignancy.

Cutting-core biopsy is the simplest method of histologic (as opposed to cytologic) diagnosis and may be useful for biopsy of subcutaneous masses and muscular masses, as well as some internal organs, such as liver, kidney, and pancreas. The added benefit is that this method is inexpensive and causes minimal disturbance of the surrounding tissue. Cutting-core biopsies are performed with a large-bore needle, such as the Vim Silverman or Tru Cut. This technique retrieves a small piece of intact tumor tissue, which allows the pathologist to study the invasive relationship between cancer cells and the surrounding microenvironment. The danger of implanting tumor cells in a needle track during biopsy is extremely small. This risk can be avoided altogether if the needle track is positioned so that it can be excised en bloc at the time of the definitive surgical procedure. Needle biopsy may be less appropriate if the specimen is small, which increases the likelihood of the needle missing the lesion or the biopsy not being representative of the entire tumor. Consequently, a needle biopsy report that is negative for malignant disease should be viewed with skepticism if it is inconsistent with the clinical presentation and should be followed by incisional or excisional biopsy.

Incisional biopsy for pathologic examination involves removal of a small portion of the tumor mass. It is best performed in circumstances where the incisional wound can be totally excised in continuity with the definitive surgical resection, in the event that any tumor cells are spilled at the time of biopsy. Incisional biopsy is indicated for deeper subcutaneous or intramuscular tumor masses when initial needle biopsy fails to establish a diagnosis. Incisional biopsy includes the instrument removal of tumor portions during endoscopic examination of the bronchus, esophagus, rectum, or bladder, and also includes suction or curettage of the endometrium, as well as laparoscopic biopsy.5

An incisional biopsy is also appropriate when a tumor is so large that total local excision would violate wide tissue planes and negatively impact on a subsequent wide local resection for curative purposes. If possible, an incisional biopsy should retrieve a deep section of tumor, as well as a margin of normal tissue. Incisional biopsies suffer from the same disadvantages as needle biopsies in that the removed portion may not be representative of the entire tumor. Consequently, a negative biopsy does not preclude the possibility of cancer in the residual mass.

Excisional biopsy completely removes the local tumor mass. It is used for small, discrete masses that are 2 to 3 cm in diameter, where complete removal will not interfere with a subsequent wider excision that may be required for definitive local control. Excisional biopsy allows the pathologist to examine the entire lesion. However, this method is contraindicated in large tumor masses because the biopsy procedure could scatter tumor cells throughout a large surgical field that would need to be widely and totally encompassed by the ultimate surgical resection. For this reason, excisional biopsy is usually contraindicated for skeletal and soft tissue sarcomas, whereas it is very useful for superficial squamous or basal cell carcinomas or malignant melanomas.

The excisional method is also used for polyoid lesions of the colon, for thyroid and breast nodules, for small skin lesions, and when the pathologist cannot make a definitive diagnosis from tissue removed by incisional biopsy. An unbiopsied lump is also surgically removed when the suspicious character of the lesion, the need for its removal (whatever the diagnosis), and the nonmutating nature of the operation render such an approach feasible. Examples of such procedures include hemithyroidectomy for thyroid nodules after inconclusive fine needle aspiration and a right hemicolecction for a cecal mass that might be either inflammatory or neoplastic. In the latter instance, colonoscopic biopsy is informative only if positive for neoplasm.

Surgeons should always mark the excisional biopsy margins with sutures or metal clips so that if removal is incomplete and further excision is needed the positive margin can be accurately identified in situ. Orientation of biopsy incisions is also extremely important. Ill-conceived incisions can unnecessarily open up additional tissue planes, necessitating subsequent wider radiation fields or more extensive ultimate surgical resections. For example, tumors of the extremities are best biopsied by using incisions that run parallel to the long axis of that limb. This facilitates a definitive en bloc resection that encompasses the biopsy track (Figure 38-5). Biopsy incisions should be closed using meticulous hemostasis because a hematoma can lead to widespread dissemination of tumor cells with contamination of tissue planes. Instruments, gloves, and drapes should be discarded and replaced with unused substitutes if the definitive surgical resection immediately follows the biopsy procedure.

Lymph nodes should be carefully selected for biopsy. Axillary nodes may be preferable to groin nodes if both are enlarged because of a decreased likelihood of postoperative infection. Other caveats are also noteworthy. For example, lymph node specimens preserved in formaldehyde cannot be analyzed for cytogentic or flow cytometric immunophenotyping. The laboratory work-up for lymphoma usually requires unfixed sterile tissue. Cervical lymph nodes should not be biopsied until a careful search for a primary tumor has been made using nasopharyngoscope, esophagoscope, and bronchoscope because enlargement of the upper cervical nodes by metastases is usually caused by laryngeal, oropharyngeal, and nasopharyngeal primary neoplasms. In contrast, supraclavicular nodes are more frequently enlarged as a result of metastases from primary tumors of the thoracic or abdominal cavities or breast.

The tumor specimen may be prepared for pathologic examination by either frozen or permanent section. Frozen sections are made at the time of biopsy, and pathologic diagnosis can be obtained within 10 to 20 min. Frozen sections are used when the diagnosis is required to assess resectability at the time of major surgery, or to check tumor margins intraoperatively. Frozen-section biopsy-proven carcinomatosis may mandate abandoning a procedure with a curative intent in favor of a palliative approach. Occasionally, mediastinoscopy, laparoscopy (peritoneoscopy), thoracoscopy, exploratory thoracotomy, or even laparotomy is necessary to obtain adequate representative tissue samples for microscopic examination to confirm diagnosis or tumor stage.

STAGING Tumor staging is a system used to describe the anatomic extent of a specific malignant process in an individual patient. Staging systems cluster relevant prognostic factors about the primary tumor, such as size, grade, and location, as well as information about dissemination to regional sites, such as lymph nodes or distant metastatic loci.
In general, a malignancy (cancer) may spread by more than one route, and an orderly course of metastasis is not predictably certain. For example, patients with breast cancer or melanoma can manifest distant metastatic disease in the lungs, liver, or skeleton without ever developing evidence of lymph node metastases. Table 38-2 summarizes the metastatic patterns of various human tumors.

Cancer cells may also spread by direct extension through tissue spaces and planes. Some neoplasms, such as soft-tissue sarcomas and adeno- carcinosomas of the stomach or esophagus, may extend for a considerable distance (10 to 15 cm) along tissue planes beyond the palpable tumor mass. Other neoplasms, such as a basal cell carcinoma of skin, rarely extend for more than a few millimeters beyond the visible margin. Even though most central nervous system (CNS) tumors infrequently metastasize, they may penetrate nearby brain tissue, and their location can cause death by interfering with vital CNS functions.

Tumor cells can readily enter the lymphatics and extend through these channels by permeation or embolization to the lymph nodes. Permeation is the growth of a colony of tumor cells along the course of the lymphatic vessel. This commonly occurs in the skin lymphatics in carcinoma of the breast and in the perineural lymphatics in carcinoma of the prostate. Lymphatic involvement is extremely common in malignant epithelial neoplasms of all types, except basal cell carcinoma of the skin, which metastasizes to regional lymphatics in less than 0.1% of cases, or mesenchymal neoplasms, such as sarcomas, which metastasize to lymph nodes in only 2% to 5% of cases.

Spread along the lymphatics by embolization to regional or distant lymph nodes is of great clinical importance. Tumor cells travel within anastomosing lymphatics and can spread to proximal nodal basins via the collateral lymphatic channels. Lymph node metastases are first confined to the subcapsular space; at this stage, the node is not enlarged and may appear normal to the naked eye. Gradually, the tumor cells permeate the sinusoïds and replace the nodal parenchyma. There is little direct spread from node to node, because the nodal capsule is not penetrated until a late stage. However, when an involved lymph node is more than 3 cm in diameter, tumor has usually extended beyond the capsule into the perinodal fat, indicating an ominous prognosis.

Lymph from the abdominal organs and lower extremities drains into the cisterna chyli, and then into the thoracic duct, which finally opens into the left jugular vein. By using this route, tumor cells can pass freely from the lymphatic system into the bloodstream. Oncologists originally believed that solid neoplasms first involved regional lymph nodes and then spread into the bloodstream by drainage into the thoracic duct and then to other parts of the body. An alternative explanation now favored by most oncologists assumes that the presence of cancer cells in regional lymph nodes indicates an unfavorable host-tumor relationship and the concomitant high likelihood of distant (albeit subclinical) metastases.

**Patterns of Tumor Spread** In general, a malignant tumor may spread (1) by infiltrating surrounding tissue, (2) via the lymphatics, (3) by vascular invasion, or (4) by implantation in serous cavities. However, many cancers spread by more than one route, and an orderly course of metastasis is not predictably certain. For example, patients with breast cancer or melanoma can manifest distant metastatic disease in the lungs, liver, or skeleton without ever developing evidence of lymph node metastases. Table 38-2 summarizes the metastatic patterns of various human tumors.

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Cancer cells may reach the bloodstream either through the thoracic duct or by direct invasion of blood vessels. Capillaries offer no resistance to tumor cell transgression. Small veins are frequently invaded, whereas thick-walled arteries are rarely violated. Veins frequently form a plexus extending to the subendothelial regions, which provide a portal of entry through the thin vein wall. When the vascular endothelium is destroyed, a thrombus can form that is quickly invaded by tumor. This combination of thrombus and tumor may detach to form large tumor emboli. Vascular invasion is common in both carcinomas and sarcomas and is associated with a poor prognosis. Some types of neoplasms have a remarkable tendency to grow as a solid column along the course of neovessels. Neoplasms have a remarkable tendency to grow as a solid column along the course of neovessels, whereas others of the same type and in the same organ tissue may remain localized for years. Metastases may dominate the presenting clinical picture while the primary tumor remains latent and asymptomatic or even undetectable. For example, cerebral metastases from silent cancers in the bronchus or the breast are often mistaken for primary benign CNS neoplasms.

A surgical oncology resection is designed to remove the primary neoplasm and the usual contiguous lymphatic and vascular routes of tumor spread with the intent to ablate every cancer cell in the body. According to this view of surgical therapy, cure is achieved by the mechanical removal of all cancer cells. However, cancer cells are frequently found in operative wound washings or in the drainage from postoperative wounds. In that many of these patients never develop recurrent cancer, host immune defenses must be effective in destroying any tumor cells missed at the time of resection. Similarly, the demonstrably viable tumor cells that are frequently found in the blood or lymphatics of cancer patients seldom lead to metastatic implants. Prolonged remission is also evidence of effective immune defenses. Rapidly progressive cancer sometimes recurs 10 or more years after successful treatment of the primary tumor. During the preceding long period of clinical remission, the growth of tumor cells has presumably been inhibited by host defenses. Host immune mechanisms may also have a role in the salvage of patients undergoing resection of metastases in distant organs, such as the lung or liver. It is likely that these patients have other subclinical metastases, which presumably are destroyed by host immune mechanisms in that subset of postresection patients who subsequently become disease-free long-term survivors.

**Preoperative Preparation**

The preoperative patient is frequently in relatively poor physical condition. This is because many malignant tumors have toxic effects on the host that are disproportionate to the size of the lesion. Patients may have a poor nutritional status because of interference with normal alimentary function, as is often encountered with cancers of the mouth, pharynx, esophagus, intestinal tract, and appended glandular organs, such as the pancreas. Pain may contribute to anorexia and consequent severe electrolyte disorder. Every effort should be made to correct nutritional deficiencies, restore depleted blood volume, and correct hypoproteinemia prior to extensive surgical procedures. Total parenteral nutrition (TPN) can be used to prepare the malnourished patient for a major operation, although reconstitution is a slow process, and TPN may chiefly serve to interrupt further deterioration by restoring positive nitrogen balance. Surgical morbidity and mortality following extensive cancer operations will predictably be problematic if critical physiologic and biochemical deficiencies are not corrected in advance.

Determining the risk inherent in a given operation is a complicated and inexact assessment based on a number of factors. The physical status of the patient, including cardiopulmonary reserve, comorbid conditions, debility inherent to a specific operation, hepatic and renal function, and the intent of surgical procedure (curative versus palliative) are all pertinent to this assessment. The technical complexity of an operation, the type of anesthetic used, and the relative experience of the involved healthcare personnel can all impact on the complications of a procedure. Various schema for risk assessment, such as the five-level physical status classification of the American Society of Anesthesiologists (Table 38-3) and the Eastern Cooperative Oncology Group five-step performance scale (Table 38-4) may be useful in assessing the appropriateness of a given operation for a specific patient.

Operative mortality is defined as mortality that occurs within 30 days of an operative procedure. In cancer patients, the underlying disease is a major determinant of operative mortality. While it is true that comparable operations are usually more morbid in the geriatric age group as compared with other adults, advanced age per se should not disqualify a patient from a potentially curative surgical procedure. Because of their high-risk nature, decisions about the indications for palliative surgical procedures are particularly difficult. For example, palliative surgery in the contexts of florid metastatic disease or to relieve patients who are suffering from intestinal obstruction secondary to carcinomatosis has a 20% to 30% perioperative mortality. In such circum-

### Table 38-2 Patterns of Neoplastic Spread for Common Human Cancers

<table>
<thead>
<tr>
<th>Neoplasm Hematogenous</th>
<th>Neoplasm Lymphatic</th>
<th>Local Infiltration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma Breast</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Endometrium</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Ovary</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Stomach</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Colon</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Kidney</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Prostate</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Liver</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Epidermoid carcinoma</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Lung</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Larynx</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Cervix</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Transitional cell carcinoma</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Bladder</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Melanoma</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Basal cell carcinoma</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bone</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Brain neoplasm</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Does not occur: 0 = < 1%; 1 = 1%–5%; 2 = 15%–30%; 3 = 30%; 4 = 50%.
A patient with a recurrent synovial...manipulation of the tumor. There are...operative procedure and local recurrence. This possibility could be secondary to perioperative tumor cell implantation, which, in turn, may be facilitated by immunosuppression induced by surgery and anesthesia.8

**Operative Considerations** Once a decision has been made to proceed with surgical therapy, the operative procedure itself must be carefully planned for the specific surgical patient. It is essential to realize that the best (and often the only) opportunity for cure is with the first resection, at the time of initial tissue plane, lymphatic, and blood vessel potential exposure to tumor cells that may be dislodged within the operative field (see Figure 38-4). A subsequent recurrence may be difficult to distinguish from the normal postsurgical inflammatory reaction and scarring.

When a preliminary biopsy has been performed, the entire operative field should be repre...and the tumor mass may also act as a protective barrier against intraoperative tumor cell traversal into severed lymphatics and vessels. Tumor cells may have been implanted in the incision when an incisional biopsy alone had been previously performed. To encompass potentially contaminated tissues, it is extremely important to remove a wide segment of skin and underlying muscle, fat, and fascia beyond the limits of the original incision (Figure 38-6).

Malignant neoplasms are usually not truly encapsulated. The tumor is commonly encased by a pseudocapsule that is composed of a compression zone of normal tissue interspersed with neoplastic cells. This pseudoencapsulation offers a great temptation for simple enucleation, in that the tumor may be easily dislodged from its bed. However, this approach must be resisted because microscopic extensions of tumor from the primary through the pseudocapsule will be left behind after simple enucleation, dooming the patient to a local recurrence. Ideally, the surgeon should operate through normal tissues at all times and never encounter or even directly visualize the neoplasm during its removal. Dissection should proceed with meticulous care to avoid surgical procedure can greatly increase the number of cancer cells recovered from the bloodstream. Likewise, it is also important to use an appropriately large incision so as to minimize unnecessary manipulation of the tumor. There are reports of a correlation between the presence of tumor cells in the bloodstream during the operative procedure and local recurrence. This possibility could be secondary to perioperative tumor cell implantation, which, in turn, may be facilitated by immunosuppression induced by surgery and anesthesia.8

**Types of Cancer Operations** Wide local resection with removal of an adequate margin of normal peritumoral tissue may be adequate treatment for low-grade neoplasms that very rarely metastasize to regional nodes or widely infiltrate adjacent tissues. Basal cell carcinomas and mixed tumors of the parotid gland are examples of such tumors. In contrast, neoplasms that spread widely by infiltration into adjacent tissues, such as soft-tissue sarcomas and esophageal and gastric carcinomas, must be excised with a wide margin of normal tissue. This wide tissue margin between the line of excision and the tumor mass may also act as a protective barrier against intraoperative tumor cell traversal into severed lymphatics and vessels. Tumor cells may have been implanted in the incision when an incisional biopsy alone had been previously performed. To encompass potentially contaminated tissues, it is extremely important to remove a wide segment of skin and underlying muscle, fat, and fascia beyond the limits of the original incision (Figure 38-6).

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---

**Table 38-3** American Society of Anesthesiologists: Physical Status Classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-1</td>
<td>A normal healthy patient.</td>
</tr>
<tr>
<td>P-2</td>
<td>A patient with mild systemic disease.</td>
</tr>
<tr>
<td>P-3</td>
<td>A patient with severe systemic disease.</td>
</tr>
<tr>
<td>P-4</td>
<td>A patient with severe systemic disease that is a constant threat to life.</td>
</tr>
<tr>
<td>P-5</td>
<td>A moribund patient who is not expected to survive without the operation.</td>
</tr>
<tr>
<td>P-6</td>
<td>A declared brain-dead patient whose organs are being removed for donor purposes.</td>
</tr>
</tbody>
</table>


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**Table 38-4** Eastern Cooperative Oncology Group: Performance Scale and Corresponding Karnofsky Rating

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all disease activities without restriction (Karnofsky 100)</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, for example, light housework/office work (Karnofsky 80–90)</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours (Karnofsky 60–70)</td>
</tr>
<tr>
<td>3</td>
<td>Capable of limited self-care, confined to bed or chair 50% or more of waking hours (Karnofsky 40–50)</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled; cannot carry on any self-care; totally confined to bed or chair (Karnofsky 30 or less)</td>
</tr>
</tbody>
</table>

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**Figure 38-6** Surgical strategies to encompass all potential tissues at risk. A, A patient with a recurrent synovial sarcoma previously resected through a transverse scar that lies perpendicular to the long axis of the extremity. The recurrent tumor is enclosed within the black dotted circle. The entire field, including the previous scar, is at risk for harboring tumor cells; therefore an appropriate surgical strategy must be created to remove tissues at risk. The recurrent nature of this tumor suggests that radiation therapy may be necessary after resection; consequently, avoiding skin grafting or flap reconstruction is important. B, A double Z-plasty technique was used to encompass the entire recurrent tumor as well as previous resection scar, thereby avoiding the use of tissue transfer or skin grafting, but necessitating creation of a wide surgical field. It would have been preferable for this patient to have had an initial tumor excision through a scar placed parallel with the long axis of the extremity at the time of the first resection. (Four-color version of figure on CD-ROM)
tumor cell spillage. Surprising amounts of skin, subcutaneous fat, and muscle can usually be sacrificed with little functional loss. However, tumor involvement of major vessels, nerves, joints, or bones may require sacrifice of these structures. Occasionally, even amputation may be necessary as an initial surgical procedure, if a curative result is to be obtained. The extent of operation must be based solely on the extent of resection needed to achieve negative margins and not by plans for subsequent surgical reconstruction. The problem of reconstruction should be approached as a separate surgical procedure. This usually requires the participation of plastic and reconstructive surgeons and other surgical specialists who have been consulted prior to the resection so that an appropriate reconstructive strategy can be articulated (Figure 38-7).

During the operation, enhanced awareness of tumor extent and/or pathologic evaluation of resected margins may indicate that an alteration is needed in the initial operative plan. Decisions regarding the extent of resection are difficult and require experienced judgment. It is usually better to proceed with a potentially curative extirpation of the tumor mass, unless there is unequivocal histologic confirmation that the lesion has extended beyond the boundaries of curative surgical resection.

Many neoplasms metastasize via the lymphatics, and operations have been designed to remove the primary neoplasm and draining regional lymph nodes in continuity with all intervening structures. The role of reconstructive surgery as a part of the multimodality care of the oncology patient. A. A CT scan of patient with multiply recurrent high-grade sarcoma of the proximal thigh, groin, and pelvis referred for radical hemipelvectomy. This patient had never received neoadjuvant chemoradiation; an aggressive course of same was the initial form of treatment for this patient. B. The surgical field after tumor resection. Note that all of the soft tissue of the lower abdominal wall, proximal thigh, and groin have been resected, and the iliofemoral vasculature can be seen in the depths of the wound. C. Reconstruction of this defect is accomplished by creation of a new inguinal ligament using Gortex mesh (white material). Note that the Gortex mesh can be tailored to accommodate the iliofemoral vasculature, thereby avoiding vessel constriction. A contralateral rectus abdominis musculocutaneous flap based on the intact inferior epigastric vascular system is mobilized and rotated into the surgical defect. D. Upon completion of the surgical procedure the patient is rendered free of disease with an intact and fully functional extremity. (Four-color version of figure on CD-ROM)
tissues. Circumstances favor this type of operative approach when the lymph nodes draining the neoplasm lie adjacent to the tumor bed or when there is a single avenue of lymphatic drainage that can be removed without sacrificing vital structures. It is important to avoid cutting across involved lymphatic channels, which markedly increases the possibility of local recurrence.

At the present time, it is generally agreed that en bloc regional lymph node dissection is indicated for clinically demonstrable nodal involvement with metastatic tumor. However, in many cases, the tumor has already spread beyond regional nodes. Although the cure rates following resection in such circumstances may be quite low (20% to 50%), undue pessimism should not prevent such patients from receiving appropriate surgical treatment. En bloc removal of the involved lymph nodes may offer the only chance for cure and can at least provide significant palliative local control. Regional lymph node involvement should therefore not be viewed as a contraindication to surgery but as a possible indication for adjuvant therapies, such as radiation or chemotherapy.

The routine dissection of regional nodes in close proximity to the primary malignancy is recommended for most cancer types even when these structures are not clinically involved with tumor. This recommendation is based on the high rate of locoregional recurrence following surgical resection when multiple lymph nodes are microscopically involved and the high error rate when palpation alone is used to assess possible lymph node involvement with tumor. Microscopic tumor dissemination to regional lymph nodes can be detected in 20% to 40% of clinically node-negative carcinomas and melanomas.

The validity of elective or prophylactic lymph node dissection has been challenged because it is not clear whether cure rates are improved if subclinically positive lymph nodes are removed before they become clinically palpable. Actively accruing prospective randomized clinical trials are currently addressing this question for many types of neoplasms. Regardless of direct therapeutic benefit, knowledge of regional node tumor status can impact on staging and subsequent treatment. In many neoplasms, prognosis depends on the status of the lymph node basin draining the primary tumor. Some breast cancer patients with metastases to regional nodes derive significant survival benefit from adjuvant chemotherapy or hormonal therapy. Some patients with melanomas may become eligible for investigational adjuvant trials only if lymph node metastases can be demonstrated. Finally, a comparison of experimental results from different institutions depends on accurate staging at the time when therapy is initiated.

In addition to questions of timing, the extent of lymph node dissection is also controversial. Sentinel lymphadenectomy is a promising new technique for detection of early nodal disease and is currently under investigation in multicenter trials. Detection of the sentinel node (ie, the first lymph node draining a primary tumor) was introduced by Morton for melanoma and is now being applied to breast carcinoma and other neoplasms. Initially, the technique relied on the injection of a vital blue dye at the tumor site and visual tracking of this dye along the lymphatics draining to the nodal basin. Subsequently, sentinel node mapping has been facilitated by adding a radiolabeled isotope to the dye and monitoring its path using a handheld gamma probe.

Advances in surgical technique, anesthesia, and supportive care (blood transfusion, antibiotics, and fluid and electrolyte management) permit more radical, extensive, and lengthy operative procedures. Such procedures offer a chance for a cure that cannot be achieved by other means and are justified in selected situations, if there is no evidence of distant metastases. For example, some slow-growing primary tumors may reach an enormous size and widely infiltrate locally without metastasizing to distant sites. Supradistal operative procedures should be considered for these extensive and nearly inoperable tumors because the occasional patient is cured. However, such operations should be undertaken only by experienced surgeons who can select those patients most likely to benefit. As an example of carefully indicated radical surgery, pelvic exenteration is a well-conceived operation capable of curing patients with radiation-treated recurrent cancer of the cervix and certain well-differentiated and locally extensive adenocarcinomas of the rectum. This operation removes all pelvic organs (bladder, uterus, and rectum) and soft tissues within the pelvis. Bowel function is restored with colostomy. Urinary tract drainage is established by anastomosis of the ureters into a segment of the bowel (ileum or sigmoid colon). The 5-year relapse-free survival is 25% when pelvic exenteration is used to manage these problems. It is also imperative that the surgical oncologist be willing to accept responsibility for helping to optimize the postoperative emotional and psychological rehabilitation of the patient prior to embarking on extensive resections, such as hemipelvectomy, forequarter amputation, mutilating operations for head and neck carcinomas, or total pelvic exenteration.

Surgical resection of selected localized recurrent neoplasms may produce a long period of remission. Surgical procedures are frequently successful in controlling recurrent soft-tissue sarcomas, anastomotic recurrences of colon cancer, certain basal and squamous cell carcinomas of skin, and local breast cancer recurrence following segmental mastectomy. However, surgical resection of locally recurrent tumors in patients with synchronous metastatic disease is usually not indicated unless the entire local recurrence can be completely excised and there is also some form of not previously used (yet effective) therapy available to control the metastases.

Historically, routine second-look operations to detect early recurrence of colon cancer were advocated by Gilbertsen and Wangensteen. However, the improvement in outcome after these second-look procedures has not been sufficient to justify their routine use. In contrast, more recent longitudinal follow-up strategies using tumor markers such as carcinoembryonic antigen (CEA) have been more useful in selecting patients likely to benefit from reoperation.

Although logic might suggest that once a neoplasm has metastasized to a distant site, it is no longer curable by surgical resection, experience shows otherwise. The removal of metastatic lesions in the lung, liver, or brain occasionally produces a clinical cure. Resection of disseminated tumor may be indicated in selected patients with slowly growing metastasis, especially if the lesion is solitary. Even multiple metastases may be successfully resected if their growth rate is slow, or if regional or systemic chemotherapies administered before surgery have resulted in disease stabilization or tumor shrinkage. Prior to undertaking resection, an extensive work-up should be performed to rule out metastatic spread to other body sites outside of the proposed operative field.

Some patients with isolated liver metastases may benefit from surgical resection. Resection is recommended for the patient whose primary tumor has been controlled, who has no evidence of extrapatic metastases, and who has a solitary liver metastasis or metastases located in one hepatic lobe. While only a minority of patients with colon cancer metastatic to the liver will meet these requirements of operability, approximately 25% of these operable patients will survive more than 5 years after resection. In certain circumstances, the results for resection of pulmonary metastatic lesions have also been very satisfactory. For example, resection of a solitary or limited pulmonary metastasis for some tumor types, such as osteogenic sarcoma, results in a higher survival rate than does resection of primary bronchogenic carcinoma of the lung. Resection of pulmonary metastases may be indicated even when more than one metastatic lesion is present, particularly if the metastases have been demonstrably responsive to systemic or regional therapies prior to surgery, or the tumor has a long doubling time.

Surgical procedures are sometimes indicated to palliate symptoms without attempting to cure the patient, thereby prolonging a useful and comfortable life. A palliative operation may be justified to relieve pain, hemorrhage, obstruction, or infection when it can be done without untoward risk to the patient. Palliative surgery may also be applicable when there are no better nonsurgical means of palliation, or when the procedure will improve the quality of life, even if it does not result in prolonged survival. In contrast, surgery that only prolongs a miserable existence is not of benefit to the patient. Examples of indicated palliative surgical procedures include (1) colostomy, enterointerostomy, or gastrojejunosotomy to relieve obstruction; (2) cordotomy to control pain; (3) cystectomy to control hemorrhagic tumors of the bladder; (4) amputation for intractably painful tumors of the extremities; (5) simple mastectomy for carcinoma of the breast, when the tumor is infected, large, ulcerated, and locally resectable,
(even in the presence of distant metastases); (6) potentially obstructing colon resection in the presence of hepatic metastases; and (7) destruction of liver metastases by using radiofrequency ablation. Surgery for residual disease is a special application of palliative surgery. In some patients, extensive yet isolated local spread of malignancy precludes gross total resection of all disease. In these patients, cytoreductive surgery may be of benefit provided that (1) other forms of effective treatment are available for use after surgery, and (2) that reduction of tumor bulk will enhance the effectiveness of these postsurgical therapies.

Problems with exsanguinating hemorrhage, perforated viscus, abscess formation, or impending obstruction of a hollow viscus, such as gastrointestinal organs, critical blood vessels, or respiratory structures, are sometimes amenable to emergency surgical intervention. Emergency surgery may also be indicated to decompress tumors that are invading the CNS or that are destroying critical neurologic components by exerting pressure in closed spaces. The cancer patient being evaluated for emergency surgery may be neutropenic or thrombocytopenic as a consequence of recent myelosuppressive chemotherapy. Sometimes a potential catastrophe can be avoided by operating on such patients expectantly just after they have gone through the nadir of their most recent myelosuppressive chemotherapy. Because of the high risks involved, each patient and the patient's family must be made aware of the dangers and benefits of the proposed surgery, as well as of other potentially effective treatments that might be available if the patient survives this emergency operation.

Reconstructive surgery after tumor resection has remarkably improved the quality of life for many cancer patients. The routine application of microvascular anastomotic techniques has enabled the free transfer of composite grafts containing skin, muscle, and/or bone to surgically created bodily defects. Breast reconstruction after mastectomy, tissue transfers as part of extremity surgery for sarcoma or mandible reconstructible, and aerodigestive reconstruction using jejunal free grafts (Figure 38-8) are examples of these dramatic improvements in the combined surgical management of complex cancer problems. In the future, applications of the new discipline of tissue engineering will remarkably extend the reconstructive armamentarium. Using these approaches in the future, it may be possible to custom grow nerve, fat, muscle, bone cartilage, or other body components as replacements for tissues that will need to be resected as part of a composite cancer procedure (Figure 38-9). After resection, the tissue-engineered prostheses will then be implanted, thereby avoiding the constraints of only having dispensable autologous body parts available for reconstructive purposes.

SPECIAL SITUATIONS

Vascular Access Vascular access for nutritional as well as hematologic support, intraoperative monitoring, and the administration of systemic therapies frequently falls under the purview of surgical oncologists. Development of catheter technology over the past 35 years has led to the use of a large variety of vascular access devices, including percutaneous versus subcutaneous (transcutaneous needle access), single versus double or triple lumen, and so on, depending on the intended use. Multilumen catheters allow simultaneous administration of otherwise incompatible agents, such as some blood products, antibiotics, and chemotherapies.

Catheter placement, whether accomplished at the bedside, in the radiology procedure suite, or in the operating room, must be performed as a sterile surgical procedure. Postcatheter placement chest radiographs are mandatory to rule out the presence of iatrogenic hemopneumothorax, as well as to confirm catheter-tip location. Previous central catheterization is associated with venous thrombosis, and a nuclear venous flow study performed prior to subsequent catheterizations may detect chronic subclinical occlusion in a potential candidate recipient vessel (Table 38-5).

There is little information available upon which to base a decision to use percutaneous venous access versus a subcutaneously implantable venous access system. Results of a recently published Canadian randomized trial suggest that the majority of participants can receive satisfactory venous access percutaneously, with the added expense of an implantable system reserved for those patients who fail percutaneous access strategies. This latter approach has been the standard of practice at the University of Texas MD Anderson Cancer Center or more than a decade with comparably satisfactory results.

EMERGING TECHNOLOGIES Several new and/or maturing technologies are finding their way into standard surgical oncology care. Some recent approaches, such as laparoscopic surgery, have been in existence for a relatively longer time and are now matured to the point of clinical trials-defined specific applications as standard of care. Other newer technologies, such as breast ductal lavage, are still in the evaluation phase and it remains to be determined whether they will have a future permanent role.

Breast Ductal Lavage Breast ductal lavage is an emerging minimally invasive surgical procedure that is used to identify cellular abnormalities in the epithelial lining of the breast ductal system. The procedure consists of identifying...
most important single known prognostic factor for subsequent melanoma recurrence. The role of sentinel lymph node biopsy also continues to mature in carcinoma of the breast. Recent refinements in technique have rendered application of this technology less cumbersome. For example, the radiolabeled sulfur colloid which is used to identify the sentinel node can be reliably administered 24 h before the biopsy is performed, which relieves the time constraints inherent in immediate preoperative injection. Intraoperatively, sentinel node status can be as accurately assessed by using touch preparation as compared to frozen-section analysis. This both shortens the overall duration of the surgical procedure and preserves nodal tissue for other clinical and research applications.

These technical improvements have led to expanded application for sentinel node biopsy in malignant disease of the breast. The use of neoadjuvant chemotherapy was recently shown not to affect sentinel node biopsy accuracy, rendering surgical consolidation less morbid in patients so treated. Other new applications, such as in ductal carcinoma in situ (DCIS), are apparent in results from recent studies suggesting a 12% positive rate in the higher risk patients with DCIS, such as those with microinvasion. It can be anticipated that sentinel node biopsy technology will continue to develop as new uptake markers are applied and as analytic schema such as microarray technology are coupled with this minimal surgical approach, thereby further increasing prognostic accuracy which in turn will impact on therapy and surveillance decisions.

Radiofrequency Ablation Radiofrequency ablation (RFA) is a technology in which tumor tissue is selectively destroyed by the transfer of heat energy from an electrode placed within the tumor and then delivered as an alternating current (Figure 38-12). This approach has been used extensively in the context of unresectable primary and secondary hepatic malignancy. In some patients, RFA has been successfully used as an initial treatment in bilobar liver disease in conjunction with synchronous or sequential hepatic resection. It is particularly effective in the treatment of hepatocellular carcinoma in patients with cirrhosis, a finding that augers well in areas such as Southeast Asia where this clinical scenario is particularly prevalent.

Based on these successes in malignancy of the liver, RFA has been used experimentally in the treatment of unresectable pancreatic carcinoma, retroperitoneal sarcoma, and other malignant diseases. A recent report has demonstrated the utility of RFA in early stage breast carcinoma where the need to preserve tissue may be a paramount concern to many patients. In this experience, the ability to totally ablate the breast tumor was achieved in 25 of 26 patients, an approach that is now being further tested in clinical trials in which patients will be core-needle biopsied for residual viable tumor 4 weeks after RFA and then undergo sequential or modified mastectomy only if the core-needle biopsy is positive. Patients with negative core biopsies will receive radiation therapy without mastectomy. Approaches such as these, if validated in clinical trials, point to the future possibility of eliminating the malignant biologic threat of a given tumor without the necessity of surgical resection with concomitant normal tissue loss.

Surgical Oncology in the Future Within the next decade, cancer is predicted to replace cardiovascular disease as the leading cause of death among Americans. Given that there are no more than approximately 30 to 40 surgical oncologists produced yearly in the United States, it is clear that the traditional surgical oncology educational roles in academic medical centers, as well as in the larger healthcare community, will continue and perhaps come under increasing pressure to expand.

As multimodality care grows in complexity and chemotherapy/radiotherapy move more prominently into the neoadjuvant position, surgical oncologists will have to become increasingly involved in clinical trial design. To be effective in this arena, understanding the natural history of specific malignancies will require an expanded knowledge base about the mutated genes and their cognate proteins that drive solid-tumor proliferation and metastasis. Surgical oncologists will have to become more knowledgeable about these factors, both during training and as a lifelong commitment to self-education.
Figure 38-11  Contemporary double-detection method of sentinel node biopsy.  
A, Injection of isosulfan dye in the peritumoral position.  
B, Gamma probe being used to detect and cal- 
ibrate the peritumoral radioactivity draining via the breast lymphatics up to the axilla. The injection of unfiltered radioactive technetium sulfur colloid occurs 90 min prior to the biopsy procedure.  
C, The sentinel node is readily identified by the three staining afferent ducts draining into the staining lymph node. After removal of this lymph node, the surgical defect is scanned with the gamma probe to confirm the removal of tissues containing the injected radioactivity. Courtesy of Jeffrey Gershenwald, MD, Department of Surgical Oncology, University of Texas M.D. Anderson Cancer Center. (Four-color version of figure on CD-ROM)

Figure 38-12 Radiofrequency ablation (RFA) of liver tumors.  
A, Radiofrequency needle used to deliver topical heat.  
B, Intraoperative open placement of RFA needle.  
C, Ultrasound demonstrating RFA needle (dense white line) placement into tumor (dark mass; cen-
ter).  
D, Preoperative computed tomography (CT) scan in a patient with bilobar colorectal cancer liver metastases. The patient had a large tumor in the left lateral segment of the liver (central arrow) and four smaller tumors (one of which is seen at the arrow on the left side of the image) in the right lobe of the liver.  
E, CT scan 2 months after resection of the left lateral segment of the liver combined with intraopera-
tive RFA of the right lobe tumors. Note that the RFA defect (arrow) is larger than the treated tumor. RFA is planned to treat the tumor and a surrounding zone of hepatic parenchyma to ensure complete thermal necrosis of malignant tissue. Courtesy of Steven Curley, MD, Department of Surgical Oncology, University of Texas M.D. Anderson Cancer Center. (Four-color version of figure on CD-ROM)
In light of these changing demographics and increasing pressures for knowledge, it is perhaps unfortunate that the Accreditation Council for Graduate Medical Education (ACGME) has not yet granted formal subspecialty status to surgical oncology. This inaction may temporarily impede the growth of surgical oncology by discouraging some from entering the specialty. This prospect is unfortunate, given the emerging need for an expanded cadre of trained surgical oncologists who will be committed to working with other cancer specialists in developing new combined modality treatment programs.

It is also certain that surgical oncologists will be unable (and do not desire) to perform all of the increasing number of cancer resections that will be needed by the United States population in the future. In the final analysis, the most important consideration may be the willingness of surgical oncologists to think innovatively about surgery as part of multimodality care, while preserving, and even improving, the quality of the surgical product that is being offered. Fortunately, many of the most talented surgical trainees being produced in the United States have embraced this challenge and are gravitating to postresidency surgical oncology fellowship training. Surgical fellowship programs focusing on oncology are now available in nearly all of the surgical specialties. This favorable state of surgical oncology as a “superspecialty” bodes well for the future. Our patients and our medical colleagues expect this of us (and the solid-tumor challenge demands this of us) if we are to work together and succeed in eliminating cancer as the major public health hazard that it currently represents.

REFERENCES
