Specialized Training and Techniques of Pathologists Lead to Targeted Therapies

by Sunni Hosemann

Solving cancer's puzzle requires both a sharp eye for detail and the ability to see the whole picture. The discoveries of cellular—and even molecular—differences between cancers once thought to be identical make the distinctions made by clinical pathologists more critical, even as their clues become smaller.

"It's important," said Armand Glassman, M.D., professor of hematopathology at The University of Texas M. D. Anderson Cancer Center, "that we get it right."

Determinations made by pathologists have a profound impact on clinical decisions about treatment, on the patient's quality of life, and sometimes on survival itself. Consider a biopsy sample from a suspicious mass or lesion. The pathologist's interpretation of the cells he or she sees is often a treating physician's most critical guide in determining the best course of treatment for a patient. The first judgment to be made is whether the sample reflects cancer at all, and this is not always clear-cut.

"We do see patients who have been told they have cancer, and they don't," said Dr. Glassman.

For those specimens that do represent cancer, the task is to determine its exact nature. For example, all breast cancers are not alike: some are biologically more aggressive than others; some are receptive to hormones and others are not; and some are responsive to specific chemotherapy agents that have no effect on others. This means that an inaccurate interpretation of the cytology or genetic makeup of a patient's tumor could lead to an ineffective treatment or at the very least

(Continued on next page)
Techniques of Pathologists Lead to Targeted Therapies
(Continued from page 1)

to a missed opportunity to administer the most effective treatment. The same is true of many other cancers, and most treating physicians at M. D. Anderson are quick to cite the importance of having a pathologist who is expert and experienced in analyzing specific neoplasms as a member of the treatment team.

“We do think that the fact that ‘cancer is all we do’ is a fortunate thing for our patients and also for community physicians and pathologists who use us as a resource for their patients,” said Janet Bruner, M.D., who chairs the Department of Pathology at M. D. Anderson.

Identifying disease subtypes

In many forms of cancer, pathologic analysis of cytogenetic characteristics and tumor behavior are brought to bear to distinguish important disease subtypes that can be targeted for specific treatment. One example involves the HER2/neu oncogene, which is overexpressed in some pancreatic and breast tumors. These tumors are responsive to the monoclonal antibody trastuzumab (Herceptin). In the hematologic cancers (leukemias and lymphomas), molecular genetics and biological techniques have revolutionized diagnosis and treatment. In acute myelogenous leukemia (AML), for example, several important subsets have been identified that correspond to specific genetic abnormalities. The inversion 16 genetic abnormality in AML is one of the better known examples. Patients who have this type of AML may benefit from targeted treatment with the monoclonal antibody gemtuzumab ozogamicin (Mylotarg). Similarly, the presence of CD20 in certain lymphocytic leukemias or lymphomas is treated with another monoclonal antibody, rituximab.

Treatment guidelines for almost all cancers begin with disease stage or grade. In the treatment of melanoma, for example, this is the crucial distinction, and all further treatment is based on it. Thus, the role of pathologists in cancer care is fundamental. “I like to think of pathology as a keystone,” said Dr. Glassman, “that provides information to supplement or expand the treating physician’s approach to the patient.”

— Armand Glassman, M.D., professor, Department of Hematopathology

“I like to think of pathology as a keystone that provides information to supplement or expand the treating physician’s approach to the patient.”

Specialized techniques

Dr. Glassman, a hematopathologist, is ad interim chief of M. D. Anderson's cytogenetics lab, which analyzed more than 8,000 individual specimens in 2000, including hematologic and solid tumor specimens. Analysis, he said, starts with cell morphology, where the experience of a trained eye that has seen many, many specimens is paramount. M. D. Anderson hematopathologists analyzed more than 15,000 bone marrow samples and 3,500 lymph node samples during the past year.

In addition, there are specialists in new techniques such as fluorescence in situ hybridization (FISH), which is an analytically more sensitive way of determining chromosomal abnormalities, particularly in the leukemias and lymphomas. FISH is also used to monitor cellular response to chemotherapy agents and to look for recurrence of disease. “Cytogenetic studies have become increasingly important in the leukemias and lymphomas, and we look for that to become increasingly true overall as more genetic markers are discovered,” said Dr. Bruner. In breast cancer specimens, FISH is used to identify genetic markers, such as HER2/neu, which are linked to prognostic factors and therapeutic directions.

Other important techniques include immunohistochemical analysis, which reveals the origins and behavior of cells and how they respond to various agents, and immunophenotyping, the study of cells and the proteins they are expressing. In addition to analyzing more than 150 frozen-section specimens a day, surgical pathologists also participate in the intraoperative analysis of sentinel lymph node biopsy specimens, which figure prominently in melanoma, breast cancer, and other cancers. Bone tumor mapping helps treating physicians monitor response to therapy, which has both prognostic and treatment implications by helping to indicate changes needed in therapy or the need for additional tests. Pathologists at M. D. Anderson work with radiologists in performing fine-needle aspiration biopsy procedures, and their direct involvement ensures that samples are complete and reduces the need for repeat procedures.

Translational research in pathology at M. D. Anderson is focusing on emerging technologies that will make it possible to have smaller and smaller biopsy samples and enable diagnoses to be confirmed before surgery in more cases, so that surgeons will know more about the nature of a patient’s cancer preoperatively, and surgery can be used more for treatment than for diagnosis.
Consultations and second opinions

For community pathologists, relying on M. D. Anderson's laboratories and faculty is a way to extend the services they offer without having to invest in resources they don't use every day.

"About 60% of the samples we analyze are sent to us by physicians (both clinicians and pathologists) outside of this institution for confirmation, differential diagnosis, specialized analysis, or second opinion, and we are very happy to provide this kind of support," Dr. Bruner said.

Besides providing affirmation for the treating physician who is making clinical decisions, there is also economic benefit in avoiding unnecessary or ineffective testing or treatment measures. And partnering with M. D. Anderson often helps physicians meet licensing and accreditation requirements as well.

Pathologists at M. D. Anderson are all specialists in one or more types of cancer, and the Section of Surgical Pathology includes eight subspecialties: breast cancer, dermatopathology, gastrointestinal cancer, genitourinary cancer, head and neck cancer, neuropathology, sarcoma/unknown primary tumor, and thoracic/mediastinal cancer. A separate department is devoted to hematopathology.

"Here, we are very fortunate," said Dr. Glassman, "to be able to provide our clinical colleagues with the expertise of pathologists who specialize in specific types of cancer." ●

For a complete listing of pathologists and their specialties, log on to the M. D. Anderson Web site at http://www.mdanderson.org (http://www3.mdanderson.org/depts/pathology). To obtain a consultation or second opinion from M. D. Anderson pathologists, contact the Department of Pathology at (713) 792-3111.

---

Study Reveals Types of Diagnostic Errors and Their Costs

by Sunni Hosemann

The fact that diagnostic errors sometimes occur would not surprise most physicians. Sometimes, the consequences are mainly academic—a particular variant is distinguishable, but the distinction lacks clinical impact. A recent study has found, however, that diagnostic errors can also have serious consequences for both patients and physicians.

Janet Bruner, M.D., a neuropathologist and chairman of the Department of Pathology at The University of Texas M. D. Anderson Cancer Center, led a 1997 study of diagnostic discrepancies and their clinical impact in cases where brain and spinal cord biopsy specimens were reviewed for second opinions. Dr. Bruner's group classified discrepancies according to their seriousness. "Very serious" errors were those that would have substantially altered a patient's treatment and prognosis, caused unnecessary expenses through ineffective application of resources (such as tests or treatment), or possibly resulted in medical malpractice liability issues for the treating physician. This group included cases in which the diagnosis of malignant or benign was changed (in one case, a pineal mass thought to be a germinoma or ganglioglioma was found to be a benign pineal cyst; in another, a diagnosis of cerebral vasculitis was found to be a central nervous system lymphoma); cases in which the initial diagnosis was one cancer, but a different one was confirmed; and cases in which noncancers were involved in serious ways (as when a case submitted as a cerebral infarct was found to be an infection caused by toxoplasmosis instead). The implications of these types of distinctions are obvious: in one case a patient had undergone brain radiation for glioblastoma that was rediagnosed as a benign central neurocytoma, which is a surgically curable condition.

A second type of discrepancy included cases where the type or grade of disease was changed. These types of errors were classified as "less serious" by Dr. Bruner and her colleagues in the study, although they still had substantial implications for treatment decisions and the quality of life of patients. In one instance, reexamination revealed that the biopsy sample was most likely taken from the periphery of the tumor, which placed the tumor in a lower-grade category than it actually was. The correction in this case may not have changed the outcome, but it prevented the treating physician from giving the patient misleading prognostic information and inadequate treatment. Distinctions of this nature might eliminate a patient from entering a clinical trial and can skew results of clinical studies and experimental protocols and affect statistics that are the basis for clinical decisions.

Errors found in the study that were classified as "minor" were those in which the second opinion added important information or clarified a doubtful diagnosis. In one example, a diagnosis of brain lymphoma was further distinguished as a large cell B-type lymphoma. The consequences of these types of discrepancies may not seem great in terms of treatment or outcome, but such distinctions can give the treating physician more confidence to make decisions about initiating or withholding specific kinds of therapies. ●

Dr. Janet Bruner, a neuropathologist who chairs the Department of Pathology, led a study of diagnostic errors and their clinical consequences.
High-Dose Chemotherapy for Breast Cancer:

by Kerry L. Wright

While public opinion has been quick to both celebrate and denigrate high-dose chemotherapy (HDCT) and autologous hematopoietic stem cell transplantation for breast cancer, researchers say that the final verdict on the controversial treatment may still be years away and can only be reached if phase III clinical trials are continued and completed.

"Of the many experimental approaches under investigation, some make it and become standard treatment; others don't, and they end up in the dustbin of history," said Gabriel N. Hortobagyi, M.D., professor and chairman of the Department of Breast Medical Oncology at The University of Texas M. D. Anderson Cancer Center. "And it is too early to tell where high-dose therapy for breast cancer will be."

Clinical trials of HDCT have been hampered by encouraging results early on as well as by more sobering data recently. In the 1970s and 1980s, phase II trials of HDCT showed that 20% to 40% of patients who had a response to standard-dose chemotherapy (SDCT) had a complete response to HDCT, said Naoto T. Ueno, M.D., Ph.D., director of Blood and Marrow Transplantation in breast cancer and an assistant professor in the Department of Blood and Marrow Transplantation at M. D. Anderson. According to Dr. Ueno, these encouraging phase II results raised hopes to such an extent that it became difficult to recruit patients for randomized phase III trials in the 1990s because patients were reluctant to be randomized into a control group. Now the tables have turned: Many patients no longer want to be randomized into experimental groups, said Dr. Ueno, who watched recruitment rates for HDCT trials throughout the country plummet after preliminary results from nine phase III trials were reported in 1998 and 1999.

Of the first five randomized studies comparing HDCT with variations of SDCT in patients with primary breast cancer, only one study showed a survival advantage for HDCT, but it was later determined to contain falsified data. One of four studies in patients with metastatic breast cancer showed a significantly longer response duration and a higher overall survival rate for patients treated with HDCT compared with SDCT. (However, that study, which was led by the same investigators who reported fraudulent data in the study of patients with primary breast cancer, was the subject of an on-site audit, the results of which are scheduled to be published in the Journal of Clinical Oncology.)

Because HDCT is more expensive than SDCT and has more severe toxic effects, some have questioned whether it should be continued in light of these phase III trial results. But many of the phase III trials were insufficient in follow-up, duration of observation, and number of participants, said Dr. Hortobagyi, who was the principal investigator of one of the smaller primary breast cancer trials. And according to Dr. Ueno, the study design and size also varied from trial to trial.

"There are important ongoing trials that need to be completed as expeditiously as possible."

— Gabriel N. Hortobagyi, M.D., professor and chairman, Department of Breast Medical Oncology

Naoto T. Ueno, M.D., Ph.D., an assistant professor in the Department of Blood and Marrow Transplantation, and Rosemarie Hontiveros, a patient access coordinator in the Department of Blood and Marrow Transplantation Business Services, discuss ways to facilitate insurance approval for a patient enrolled in a trial of high-dose chemotherapy and hematopoietic stem cell transplantation for breast cancer.
Completion of Clinical Trials Necessary

Physicians at M. D. Anderson perform HDCT by first administering SDCT to shrink the tumor, followed by a high-dose regimen that includes cyclophosphamide, carmustine (BCNU), and thiopeta. The patient’s bone marrow or peripheral blood progenitor cells are removed before treatment, stored, and replaced after high-dose treatment to provide support to the immune system. Most patients recover from any toxic side effects within four to six weeks, at which time the response of their disease is evaluated.

After word of the positive results from the early phase II trials spread throughout the country, many patients were treated with HDCT off-protocol, but M. D. Anderson’s position continues to be that “this type of treatment should be done only in the context of clinical trials,” said Dr. Ueno.

Several multi-institutional phase III clinical trials are accruing patients or have completed accrual, and investigators are performing follow-up until the results can be analyzed and reported. The largest of these studies is National Cancer Institute (NCI)-sponsored trial S9623, which is examining HDCT in patients whose disease is less advanced than that of patients from previous trials. (This study was recently closed to new patient registration.) In addition, a Dutch study presented at the 2000 annual meeting of the American Society of Clinical Oncology (ASCO) reported statistically significant advantages in overall and progression-free survival rates in patients who underwent transplantation, although data from only 289 of 885 patients had been analyzed. Many of the remaining multicenter trials, as well as smaller trials such as those currently recruiting patients at M. D. Anderson (see Protocols on next page), are addressing problems of the earlier phase III studies and have been designed to look at groups of patients who have not previously been examined.

NCI director Richard Klausner, M.D., recently wrote an open letter to members of ASCO, urging them to consider HDCT clinical trials as options for their patients. “Whether or not high-dose chemotherapy is a useful therapy for [women at high risk of recurrence] can only be determined if clinical trials testing this question appropriately are successfully completed,” Dr. Klausner wrote.

The NCI has recommended that studies continue to determine if high-dose chemotherapy can improve the outcome of breast cancer treatment.

“There are important ongoing trials that need to be completed as expeditiously as possible,” said Dr. Hortobagyi. He added that only then should physicians consider the available data and form an opinion about the clinical usefulness of HDCT.

“Some of the early individual trials of adjuvant chemotherapy and many of the early trials of adjuvant tamoxifen were not terribly promising,” said Dr. Hortobagyi. “But when we put them together in a meta-analysis, which gives much greater statistical power, it became apparent that they had a very substantial effect in reducing the mortality rate and risk of recurrence,” he said.

It took randomized trials of nearly 32,000 patients with primary breast cancer to convince oncologists that tamoxifen was an effective drug. And, said Dr. Hortobagyi, even though some of the early reports of adjuvant chemotherapy were encouraging, it took another 10 years and 30,000 patients to prove its worth. So far, Dr. Hortobagyi said, only about 2000 patients with breast cancer have been treated on protocol with HDCT.

The importance of conducting a large number of trials is also illustrated by studies of nonspecific immunotherapy for breast cancer in the early 1970s. According to Dr. Hortobagyi, initial results were promising for a variety of agents, but large comparative trials eventually showed no benefits.

“So these are tricky issues, and it’s important for all of us to understand that there is a very good reason why one needs to conduct these slow, painstaking clinical trials because those are the ones that actually give us the final answers,” he said.

FOR MORE INFORMATION, contact Dr. Hortobagyi at (713) 792-2817 or Dr. Ueno at (713) 794-5745.

See page 6 for Protocols.
Studies Examine High-Dose Chemotherapy for Breast Cancer

Clinical trials of high-dose chemotherapy with autologous bone marrow or peripheral blood progenitor cell transplantation in progress at the University of Texas M. D. Anderson Cancer Center include the following for patients with breast cancer.

- A phase II study of high-dose chemotherapy and autologous blood progenitor cell rescue for patients with primary breast cancer that is refractory to preoperative chemotherapy (DM95-046). Physician: Richard Champlin, M.D.
  
  Patients 18 to 60 years old with histologically confirmed, stable or progressive stage IIb, stage III, or stage IV breast cancer without distant metastases are eligible. Patients must also have a primary lesion that is accessible for tissue collection prior to beginning treatment, and their tumors must be refractory to standard preoperative chemotherapy. Patients with resectable breast cancer will undergo surgery followed by high-dose chemotherapy and stem cell transplantation. Patients with unresectable tumors will be treated first with the high-dose chemotherapy regimen, followed by surgery for those who are eligible. All patients will subsequently receive radiation therapy.

- A phase III randomized comparison of high-dose chemotherapy and granulocyte colony-stimulating factor (G-CSF) with G-CSF alone for mobilization of peripheral blood stem cells for autologous transplantation in patients with responsive metastatic breast cancer or high-risk stage II-III disease (DM95-047). Physician: James L. Gajewski, M.D.
  
  This study is designed for patients with stage II, stage III, or stage IV breast carcinoma who have received no more than two chemotherapy regimens for metastatic disease and whose disease is responsive to chemotherapy at the time of study entry. Patients with metastases must have a documented reduction in metastatic disease of at least 50% in all sites (except bone). Patients with ≥ 10 positive axillary nodes after primary surgery or ≥ 4 positive axillary nodes after neoadjuvant chemotherapy and primary surgery are eligible. Exclusion criteria include allergies to murine protein or eggs, active infections, and previous treatment with carmustine (BCNU).

- Multi-institutional phase II study of combined trastuzumab and paclitaxel after high-dose chemotherapy with autologous peripheral blood progenitor cell transplantation for patients with metastatic breast cancer that overexpresses HER2/neu (DM99-004). Physician: Naoto T. Ueno, M.D., Ph.D.
  
  Patients enrolled in this study must have stage IV breast cancer that overexpresses HER2/neu, as determined by immunohistochemical staining. Patients cannot have received more than four cycles of paclitaxel-containing regimens before high-dose chemotherapy is administered, and their disease must have had a complete or partial response to pretransplantation chemotherapy. Treatment will include high-dose chemotherapy with cyclophosphamide, carmustine, and thiotepa followed by weekly administration of trastuzumab and paclitaxel. Participants are required to stay in Houston during treatment.

- Mini-allogeneic peripheral blood progenitor cell transplantation for recurrent or metastatic breast cancer (DM97-268). Physician: Naoto T. Ueno, M.D., Ph.D.
  
  Patients with newly diagnosed invasive carcinoma of the breast who have not received any prior chemotherapy are eligible. Patients will be randomized to receive high-dose chemotherapy or six cycles of standard chemotherapy with doxorubicin and docetaxel.

Immunosuppressants and donor lymphocyte infusions will be terminated if residual disease is detected 100 days after allogeneic transplantation.

  
  This study is designed for patients with stage IV invasive breast carcinoma with low HER2/neu expression who do not have an HLA-matched sibling. Participants must be 18 to 62 years old and must have had at least a partial response to pretransplantation standard-dose chemotherapy. Patients will undergo an autologous transplant with stem cells that have been stimulated with G-CSF and interleukin-2, followed by high-dose chemotherapy and posttransplantation stimulation with interleukin-2 and granulocyte-macrophage colony-stimulating factor (GM-CSF).

- Randomized trial of high-dose chemotherapy versus standard-dose chemotherapy for patients with inoperable primary breast cancer (ID00-226). Physician: Naoto T. Ueno, M.D., Ph.D.
  
  Patients with newly diagnosed invasive carcinoma of the breast who have not received any prior chemotherapy are eligible. Patients will be randomized to receive high-dose chemotherapy or six cycles of standard chemotherapy with doxorubicin and docetaxel.

For more information about these clinical trials, physicians or patients may call the M. D. Anderson Information Line. Those within the United States should call (800) 392-1611; those in Houston or outside the United States should call (713) 792-6161. Visit the M. D. Anderson Cancer Center clinical trials Web site at http://clinicaltrials.org for a broader listing of treatment research protocols.
The experience of dealing with their illness leaves many patients with cancer feeling overwhelmed, afraid, and alone. Sometimes, the kind of help these patients need most comes from other patients. One way that patients help one another is through support groups, which allow patients to share their concerns with people who have had similar experiences and to learn new ways of handling problems.

Support groups have helped thousands of patients with cancer cope with their illness. Several recent studies indicate that besides improving quality of life, support groups may actually prolong the survival of patients with cancer.

In a support group, patients are able to share their feelings in a confidential setting with people who face many of the same issues, discuss the emotional needs created by cancer, and exchange information about their disease. Some support groups are designed for family members and friends of patients with cancer. These groups help the family deal with such problems as how best to help the patient, disruptions in family routines, and financial worries.

Several types of cancer support groups are available. Some groups are led by a mental health professional, some by other patients. A group may be for people with a particular disease, such as breast cancer, for teens or young adults, for family members, or for general support. Many groups are free, but some require a fee (insurance will sometimes cover the cost). Groups also vary in size, approach, and how frequently they meet. It's a good idea to check out different groups to find the one you're most comfortable with.

How do you find the right support group?
Most hospital social service departments have information about groups in the area. Your doctor, nurse, or social worker also can help you find the right group.

Here are a few resources you might want to check out:

The American Cancer Society offers several support groups. Man to Man is a support and education group for men with prostate cancer and their families. Coping with Breast Cancer offers emotional support and education for patients with breast cancer. Dialogue is a group geared to help patients, their families, and their friends learn to live with cancer. Life After Loss helps people deal with the death of a loved one from cancer. For information about the availability of these groups near you, call 1-800-ACS-2345.

M. D. Anderson Cancer Center sponsors a wide variety of support groups in Houston for patients with cancer and their families. These include For Men Only, Cancer Patients and Families, Centering Prayer Group, Life After Loss (a bereavement group), Radiation Oncology Support and Education Group, Women with Metastatic Cancer, Families Living with Cancer (separate groups for adults, teens, and children), and Well Wives, a group for women whose husbands have cancer. For more information on these groups and many others, call 1-800-392-1611 or go online at www.mdanderson.org.

For support groups outside the Houston area, the Anderson Network sponsors Texas Community Outreach Support Groups in several cities. For information, call 1-800-345-6324.

Some national organizations that have cancer support groups include:
- The American Brain Tumor Association (1-800-886-ABTA)
- Cancer Care, Inc. (1-800-813-HOPE)
- Candlelighters Childhood Cancer Foundation (1-800-366-CCCF)
- Cure for Lymphoma Foundation (1-800-CFL-6848)
- Kidney Cancer Association (1-800-850-9132)
- Leukemia and Lymphoma Society (1-800-955-4572)
- Lymphoma Research Foundation of America (1-800-500-9976)
- National Alliance of Breast Cancer Organizations (1-888-80-NABCO)
- National Ovarian Cancer Coalition (1-888-OVARIAN)
- US Too International (prostate cancer support groups at 1-800-80-US-TOO)
- The Wellness Community (1-888-793-WELL)

The Anderson Network has a national telephone hot line that patients with cancer can call to speak with a cancer survivor (1-800-345-6324 or 713-792-2553 in Houston). Within 48 hours, an Anderson Network member with the same diagnosis and treatment will call back and offer support.

For more information, contact your physician or contact the M. D. Anderson Information Line:
- (800) 392-1611 within the United States, or
- (713) 792-6161 in Houston and outside the United States.

February 2001

©2001 The University of Texas M. D. Anderson Cancer Center
Many Specialties, One Goal

Janet M. Bruner, M.D.
Chairman, Department of Pathology

The pathologist has been called "the doctor's doctor" because we primarily communicate with other physicians, rather than directly with patients. Our role at M. D. Anderson is not only to provide an accurate diagnosis of a patient's tissue specimen obtained through a biopsy or through surgery but also to give the clinician treating that patient as much information about the patient's tumor as possible. Besides the standard techniques of immunohistochemistry and electron microscopy, we also use state-of-the-art molecular diagnostic and cytogenetic studies and image analysis to make our diagnostic interpretations.

The training that our pathologists receive is extensive. All have completed medical school and a four- to five-year residency in pathology. Many also have doctoral science degrees. Most have also completed an additional one- to three-year fellowship in their chosen field of specialized pathology, and some have subspecialty board certification in the areas of dermatopathology, neuropathology, hematopathology, or cytopathology.

But what makes our Department of Pathology unique among other cancer institutions and hospitals is its organization. Each of the 40 pathologists within the institution has chosen, according to his or her interests and expertise, one of the following areas of tissue or organ subspecialty: breast, gastrointestinal/liver, gynecologic, brain and spinal cord (neuropathology), genitourinary, sarcoma/bone, pulmonary, endocrine, head and neck, skin (dermatopathology), and cytopathology. A separate Department of Hematopathology specializes in the diagnosis of malignancies of the blood and lymphoid organs.

We began implementing this subspecialty model in September 1999. Until then, most of our pathologists had provided patient care in every area. Many pathologists, several in each clinical area, are required to make this type of subspecialization work. Fortunately, at M. D. Anderson we have the dual mission of providing patient care and conducting collaborative clinical and basic science research. This permits us to employ many pathologists, as we all participate in both patient care and research. Therefore, we have some experience with this organizational model through our collaborative research with both other clinical and basic science departments here at M. D. Anderson. The formal organization into subspecialty services for patient care simply reinforced and extended this to our clinical work. This arrangement permits us to contribute more efficiently to multidisciplinary patient care and educational conferences.

Having such a large and uniquely organized department allows us to provide diagnostic and prognostic information not only to our own clinical colleagues here at M. D. Anderson but also to physicians in hospitals across the United States and around the world.