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**REPORT TO
PHYSICIANS**

**FEBRUARY 1998
VOL. 43, NO. 2**

THE UNIVERSITY OF TEXAS
**MD ANDERSON
CANCER CENTER**

Making Cancer History

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Radiotherapy Protocols

Therapies combat head and neck cancers, Hodgkin's disease, breast cancer, and other tumors.

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Is your family cancer in the genes or in the stars?



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**Refusing To Give
Cancer a Chance**

Reason for surgery:
"I want to be there
for my children."

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DiaLog

Genetic testing introduces new twists and turns to medical evaluation labyrinth.

MD Anderson Oncology



A recent treatment review in the **Division of Radiation Oncology** included these X-rays (above, left to right), indicating cancers of the supraglottic larynx, parotid gland, lung, and tonsils.

Radiation Oncology: Targeting Effective Treatment

by Beth W. Allen

The questions fly from all quarters of the room: What's the performance status? What's the risk of pneumonitis? Did the surgery help? What were the surgical margins? How does the protocol account for lung motion? What's the morbidity?

This scene, charged with the vitality of a public meeting and the intensity of courtroom testimony, plays out four days a week in the M. D. Anderson Cancer Center Division of Radiation Oncology.

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How M. D. Anderson Does It

This article introduces How M. D. Anderson Does It, a series of occasional reports about the ways M. D. Anderson physicians approach cancer treatment and patient care.

Radiation Oncology

(Continued from page 1)

Standing before division colleagues, physicians present cases under their care and their plans for curative treatment. With this method, patients get not only a second opinion but also a third, fourth, and a fifth—make that a 25th.

“Every new potentially curable patient is reviewed by a roomful of physicians, staff, residents, and trainees—on the average, 25 physicians—who review every case,” said Division of Radiation Oncology head James D. Cox, M.D.

Meeting four mornings every week, the physicians learn each patient’s basic health statistics, the history of diagnosis along with the presenting symptoms and signs, the histology and pathology reports, pertinent positive findings, disease stage, other treatment, and radiotherapy plan. Then the questions start.

Thus the division practices what is its 30-year treatment-defining and -refining process: patients are

assessed, treated, evaluated; outcomes analyzed; and treatment revised to improve outcomes.

“This has been ongoing for more than three decades,” says Dr. Cox. “Nobody else does it—every morning, four days a week. It’s totally unique.” Dr. Cox credits the process with ensuring evolution of the best treatment because it is based on outcomes of the more than 3,000 patients treated in the division annually.

To Dr. Cox, providing excellent treatment means paying attention to what you don’t want to do—cause harm to normal tissues—as well as what you do want to do—eliminate or reduce cancer. Using the latest dose-response data, selectively employing chemotherapy as an adjuvant therapy, and implementing three-dimensional conformal radiation therapy make it possible for physicians in the division to reduce radiation volume. The division’s efforts to protect normal structures from radiation also involve technological advancement.

The division’s creation—a miniature multileaf collimator—is helping physicians more carefully define treatment fields. The collimator, for which the division is seeking a patent, permits very precise application of computer-assisted treatment planning and three-dimensional conformal radiation therapy (3-D CRT). A tissue-sparing advance over conventional radiotherapy, 3-D CRT is associated with fewer side effects and less posttherapy morbidity. Dr. Cox points to this work as an example of the division’s ability to create new applications from technical advances.

Another technical development, sprung from laboratory work with fibroblast cultures, is genetic testing to identify patients with ultrasensitivity to radiation.

“Although this ultrasensitivity is rare, 3%–5% of people treated with high doses exhibit it,” according to Dr. Cox, who says such ultrasensitivity can produce more severe scarring than normal and long-term consequences in treatment areas, such

PROTOCOLS

Radiotherapy Protocols Offer Treatment for Range of Sites and Types of Cancer

The following list is only a sample of the radiotherapy protocols open to patients with many types and stages of cancer. Contact the New Patient Referral Office or the M. D. Anderson clinical trials listing on the World Wide Web (see numbers and addresses below) for more information.

- Extended-field radiation therapy for favorable Hodgkin’s disease (ID95-162). *Physician: James D. Cox, M.D.*

Patients who are 16 years of age but less than 50 who have a histologic diagnosis of stage IA or IIA Hodgkin’s disease with a mediastinal-to-thoracic

ratio of <0.35 are eligible for participation in this study of treatment. Patients must have no more than three regions of involvement if the disease is supra-diaphragmatic. Prior chemotherapy or radiotherapy makes a patient ineligible, and patients will not have chemotherapy or immunotherapy with the radiotherapy. The platelet count must be $>175,000/\text{mm}^3$ and the absolute granulocyte count $>2,800/\text{mm}^3$.

- A phase I/II trial to evaluate brachytherapy as the sole method of radiation therapy for stage I and II breast carcinoma (RTOG95-17). *Physician: Eric Strom, M.D.*

“Usually I see candidates for this feasibility study before definitive surgical management,” said principal investigator Dr. Eric Strom, associate professor of radiation oncology. This helps ensure that patients’ surgical treatment meets specific requirements in this brachy-

therapy regimen open to patients with American Joint Committee on Cancer stage I or II breast cancer (T1N0, T2N0, T1N1, or T2N1). Disease must be confirmed by histology, and the lesion, which must be ≤ 3 centimeters, must be confirmed by pathology. “The margins of resection must be clear, and an extensive intraductal component must not be present,” he said. Treatment must have been tylectomy with axillary dissection, which must have included sampling at least six nodes and finding fewer than four positive. Dr. Strom said that at least six clips must be used to mark the tylectomy cavity. Absence of microcalcifications must be proved by mammography after surgery if they were present before surgery. Patients with distant metastases or a diagnosis of invasive in situ lobular carcinoma, ductal carcinoma in situ, or nonepithelial breast malignancy (sarcoma or lymphoma) are ineligible.



Dr. James D. Cox (front row) listens to comments from **Dr. Ritsuko Komaki** (second from left on second row) in a Division of Radiation Oncology morning review session. Left to right on second row are **Dr. Moshe Maor**, **Dr. Komaki**, **Dr. Tahir Ijaz**, and **Dr. Scott Lankford**.

as skin, subcutaneous tissues, bones, and nerves.

All patients with breast cancer undergo this testing, as do patients in whom a reaction has occurred in treatment and others suspected of greater susceptibility to injury.

The research program also encompasses one of the longest-running federal grants in radiotherapy in the United States. A recently approved renewal will

add five years to the 35-year research endeavor.

Dr. Cox said there may be only one other radiation oncology division in the country that treats as many patients. High patient volume means radiation oncologists accumulate broad experience within a specialty or subspecialty. Physicians within the division specialize in treating one or two of the following cancers: cancer of the breast, central nervous system,

gastrointestinal tract, genitourinary tract, head and neck, or skin; gynecologic, pediatric, or thoracic cancers; or lymphoma or sarcoma.

"The experience of a faculty member with a specific disease is vastly greater than would be expected anywhere else," says Dr. Cox. He estimates that each radiation oncologist at M. D. Anderson sees as many patients within his or her specialty as other radiation oncologists see across the spectrum of diverse cancers in any given year. As Dr. Cox explains, this experience provides "tremendous specialization expertise and technical experience with all kinds of variations."

Of the patients who come to M. D. Anderson for radiotherapy, about

(Continued on page 4)

PROTOCOLS

- Phase III intergroup randomized comparison of radiation alone vs. preradiation chemotherapy for pure and mixed oligodendrogliomas (RTOG94-02). *Physician: W. K. Alfred Yung, M.D.*
"The incidence of oligodendroglioma appears to be increasing," said Dr. W. K. Alfred Yung, professor and deputy chairman of the Department of Neuro-Oncology and principal investigator of this phase III study. For that reason, Dr. Yung said, "It is important to establish the role of chemotherapy in the treatment of this tumor." Eligible are patients 18 years or older whose unifocal or multifocal supratentorial pure or mixed oligodendrogliomas have been confirmed by pathology and are not predominantly located in the posterior fossa. Patients should not have had radiotherapy or chemotherapy previously. Karnofsky performance status should ≥ 60 . Required blood counts are as follows: platelet counts $\geq 150,000/$

mm^3 ; absolute granulocyte count $\geq 1,500/\text{mm}^3$; a serum creatinine count ≤ 1.5 times normal; and bilirubin, serum aspartate aminotransferase, and alkaline phosphatase values ≤ 2 times normal.

- Stereotactic fractionated radiotherapy using a mini multileaf collimator and a relocatable frame for brain tumors (ID97-011). *Physician: Moshe Maor, M.D.*
Patients older than 16 years with a recurrent primary brain tumor or new and recurrent brain metastasis well defined by magnetic resonance imaging are eligible for this study. They must have a Zubrod performance status of ≥ 2 and a life expectancy of three months. Any primary or metastatic tumors outside the brain must be stable.
- A randomized phase II trial of concurrent radiation and chemotherapy for advanced squamous cell carcinoma of the head and neck (RTOG97-03).

Physician: Adam Garden, M.D.

To be included in this study, patients must be 18 years or older and have histologically proved squamous cell carcinoma of the oral cavity, oropharynx, or hypopharynx (stage III or IV), without metastasis. Life expectancy must be ≥ 6 months, and Karnofsky performance status must be ≥ 70 . Metastatic disease at a distant site or clinically significant heart disease makes patients ineligible for participation.

FOR MORE INFORMATION about these clinical trials, physicians or patients should call the M. D. Anderson Information Line. Those within the United States, please call (800) 392-1611; those in Houston or outside the United States, please call (713) 792-6161. Visit the M. D. Anderson Cancer Center clinical trials Web site at <http://www.clinicaltrials.org> for a more complete listing of treatment research protocols and inclusion and exclusion criteria.

TALK BACK for the Last Time

Interest Survey Concludes in This Issue

This is your last opportunity to complete this interest survey. Please fill out the survey if you haven't before. Return it to *Oncology* Survey, Scientific Publications—234, M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030. Or fax it to (713) 794-1370. In thanks, we'll send you a copy of the award-winning *M. D. Anderson's Road Map to Cancer Prevention*.

■ Indicate the degree of your interest in the following topics by circling the corresponding number.

NOT AT ALL VERY MUCH

- | | | | | | | | | | | |
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| 1. Impact of cancer on your geographic region | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
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| 4. One- or two-paragraph news stories about cancer treatment or research | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 5. Ethical issues related to cancer care | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
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| 7. Patient education sheet that could be photocopied and passed to patients | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 8. Treatment protocols at M. D. Anderson | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

■ Rank the following within each column (1 = Most important).

<input type="checkbox"/> Brevity of articles	<input type="checkbox"/> Relevance to general practice	<input type="checkbox"/> Understanding oncology practice in general
<input type="checkbox"/> Timeliness of articles	<input type="checkbox"/> Relevance to patient	<input type="checkbox"/> Understanding Anderson's approach to treatment
<input type="checkbox"/> Depth of reporting	<input type="checkbox"/> Relevance to practice at Anderson	

■ Check one of the options to complete the following sentences.

- I do do not currently read *Oncology*.
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■ Complete the following sentences by filling in the blank.

The cancer-related topic I am most interested in is _____

My favorite periodical for cancer information is _____

■ (Optional) Complete to receive your copy of *M. D. Anderson's Road Map to Cancer Prevention*.

Name _____

Address _____

432A

Radiation Oncology

(Continued from page 3)

85% are referred by their physician, and the remainder come by self-referral. Patients need not undergo other therapy at M. D. Anderson to have radiotherapy here.

Curative radiotherapy is the focus of the division's efforts, although palliative therapy is practiced. "We support the idea that patients being treated palliatively should be treated very close to home," said Dr. Cox.

David Bolling, deputy administrator of the division, reports that a quarterly survey taken by an external firm shows that patients give high marks to the division's work. In the 1996-1997 academic year, 97% of patients reported overall satisfaction with their treatment. When asked about the division's physicians, therapists, nursing, environment, and commitment/teamwork, 96%-99% reported satisfaction in each category. Eighty-six percent said they would definitely recommend treatment at M. D. Anderson. The annual ratings were based on postdischarge responses of 398 interviewees. Ratings at the top of a 10-point scale (7-10) were identified as indicating satisfaction.

Education is also a part of the division's mission. Training in the department at any time are about 16 residents and one or two fellows, who come from across the country. Trainees are likely to already be familiar with faculty even before coming to M. D. Anderson through textbooks or the 200-plus articles produced annually by departmental faculty.

The Division of Radiation Oncology includes the Department of Experimental Radiation Oncology, the Department of Radiation Physics, and the Department of Radiation Oncology. The division faculty includes 36 physicians and 21 scientists. ●

FOR MORE INFORMATION, contact Dr. Cox at (713) 792-3411 or the M. D. Anderson Information Line at (800) 392-1611. Those outside the United States should call (713) 792-6161 to reach the information line.



Cancer: Is it in the Genes or in the Stars?



Now that hundreds of hereditary disorders can be detected even before a baby is born, the expression "It's in the genes" has largely replaced "It's in the stars" as a common explanation for events.

It is true that physicians and geneticists know dramatically more than they did a decade ago. Nonetheless, the meaning of phrases like *genetic code* and *genetic mutation* remain as remote in meaning to most of us as the stars are distant.

But though their precise meaning may be remote, their implications are not. Just as a pregnant woman is acutely aware of the consequences to her unborn child of genes gone wrong, so adults with genetic mutations know that their family's genetic legacy can transform or even end their lives.

In cancer care, physicians and others are working to ensure that genetic information not only identifies those at risk, but also leads to better treatment and prevention. Let's examine how cancers occur and how to assess risk.

Ways Cancers Occur

Cancers occur in three ways. Most cancers are not hereditary. These are called *sporadic cancers*, and they occur randomly. *Familial cancers* are those that occur because of a genetic predisposition to cancer in certain families. These are also affected by such nongenetic factors as environmental exposures or lifestyle. *Hereditary cancers* are associated with specific genetic mutations and are governed by genetic principles of inheritance. About 5%–10% of cancers are inherited genetically.

Assessing Risk

What is your risk? Here are four ways to assess it. Specially trained professionals can also help.

Evaluate your family's medical history. Look at first-degree relatives (mother, father, siblings, children), second-degree relations (grandparents, aunts, uncles, nieces, nephews, and grandchildren), and third-degree relatives (cousins).

Identify cause of death. If a relative had cancer, try to find out how old your relative was when he or she was diagnosed, the location of the tumor, and whether smoking was part of the relative's medical history.

Look for patterns that suggest hereditary disease:

- Determine if the cancer occurred in your relative earlier than is typical.
- Find out if cancer has occurred in more than one close relative.
- Enlist your physician's help in determining whether there is a pattern—cancer in both organs in organs that are paired, a cancer syndrome, or multiple primary tumors in one person.

Ask your physician to help classify your risk. If it is higher than normal, your physician may suggest that you gather more specific information on your relatives or undergo genetic testing and counseling.

If you need to gather more information, obtain pathology reports from the medical records of your relatives. These are statements by a physician-scientist who studied a sample of your relation's tumor or other tissue or blood in a laboratory. Autopsy reports, hospital records, or death certificates also provide clues.

For genetic testing and counseling, consult a cancer center or hospital that is part of a university or contact a genetics counselor. A list of such counselors, which can be searched by state, is posted on the World Wide Web site of the National Cancer Institute (<http://cancernet.nci.nih.gov/wwwprot/genetic/genersch.html>).

High Stakes, High Anxiety

Counseling is important in determining if genetic testing is necessary, and it is fundamental to successfully navigating the choppy waters of fear and anxiety associated with testing. The stakes are high, and findings can bring conflict within the family and worries about confidentiality, hiring discrimination, and insurability outside the family.

Unfortunately, genetic test findings don't foretell the future conclusively. Identifying a gene mutation associated with a specific cancer doesn't mean that cancer will inevitably occur; it means risk is higher. Similarly, if no cancer-associated mutation is found, it doesn't ensure a cancer-free life; it means the person tested has the same risks as the general population. In addition, sometimes scientists discover genetic alterations whose significance is unknown.

Science has crafted exquisite tools for examining human genetics, and highly trained physicians and counselors are prepared to help wield those tools in cancer genetic screening. It remains, however, a matter of intensely personal choice whether—as well as how—to put those tools to use.

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 outside the United States.

February 1998

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Genetic Findings Prompt Cancer Survivor To Elect Surgery

by Alison Ruffin

Redacted

Clinic Decodes Genetic Risks, Prevention Options

With the knowledge that about 5%–10% of all cancers can be attributed to inherited genetic changes, more people are becoming interested in learning whether they carry altered genes that may place them at higher risk of cancer.

To meet the need for genetic risk assessment and counseling, The University of Texas M. D. Anderson Cancer Center established the Human Clinical Cancer Genetics Clinic to study heritable genetic mutations that predispose individuals to cancer. It focuses on mutations that cause breast, ovarian, endometrial, bowel, and endocrine cancers. Genes related to colon cancer susceptibility are also a particular interest.

“This has the potential to revolutionize our approach to cancer,” says Gordon Mills, M.D., who emphasizes the decision-making role patients play in health care, especially those who know the risks associated with their genetic profile. Dr. Mills chairs the Department of Molecular Oncology and is acting medical director of the Breast and Ovarian Risk Assessment Clinic at M. D. Anderson Cancer Center.

“Risk counseling, genetics counseling, and treatment counseling are important in communicating information to individuals, allowing them to make appropriate health care decisions,” he said.

Two other physicians, in addition to Dr. Mills, direct program aspects. Heading the high-risk bowel program is Patrick Lynch, M.D., J.D., and heading the endocrine program is Robert Gagel, M.D.

A strong family history of cancer is the primary reason for consultations, which may be requested by physicians for their patients or by patients themselves.

“The basis of our program is cancer prevention,” said Dr. Mills. “Our goal is to help individuals

assess their risk for breast and ovarian cancer so that they will be able to consider the merits of potential prophylactic interventions. When prevention is not possible, however, the next goal is to initiate early detection and curative interventions.”

The clinic Dr. Mills heads advises individuals about risks related to mutations in the genes *BRCA1* and *BRCA2* (the breast cancer 1 and breast cancer 2 genes). *BRCA1* was first associated with breast and ovarian cancer occurrence about six years ago. Subsequently, scientists successfully cloned *BRCA1* and *BRCA2*, thus allowing study and providing better understanding of their activity.

“This has the potential to revolutionize our approach to cancer.”

—Gordon Mills, M.D.



About 10%–30% of individuals with a mutation of the *BRCA1* gene will eventually have ovarian cancer, and about 40%–60% will have breast cancer. Risk of colon and prostate cancer is elevated in these individuals three to four times above that for the normal population. For this reason, people with these gene mutations should be counseled about screening options for all types of cancer.

Dr. Mills reminds those with mutations that an inherited abnormality in one or more genes does not guarantee a cancer diagnosis, but he advises, “Someone who inherits an abnormality will essentially be at increased risk for his or her entire life.”

Understanding inherited genetic changes that can lead to cancer is an important step in developing new, more effective cancer prevention, diagnostic, and treatment strategies, according to Dr. Mills.

—Alison Ruffin

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DiaLog

Genetic Tests Demand New Answers

Rebecca D. Pentz, Ph.D.
Clinical Ethicist

In the near future, genetic testing will be a standard part of every oncologist's practice. For the physician, this advance will entail not only being familiar with genetics but also informing patients adequately about new tests, including nonmedical risks and benefits.



Adequately informing patients about diagnostic test findings and treatments has never been easy. The barriers are substantial. Complex issues are difficult to explain in lay terms. Some patients don't want to be informed; they want physicians to make the decisions. Other patients want information, but they may be overwhelmed and unable to understand a physician's explanations. Or a quick decision about treatment may be so important that a leisurely discussion of risks and benefits may actually increase the patient's risk.

Genetic tests introduce new twists to this labyrinth. Discovering a gene mutation is information not just about an individual but about an entire family. Add to this that genetic results are probabilistic. Highly symbolic, genetic results seem to reveal more of our essence as individuals than our cholesterol count does. Furthermore, the history of genetics includes the disturbing chapter on eugenics. Even in this

country we sterilized without consent thousands of "feeble-minded" women in an attempt to purify the American germ plasm.

Properly informing people about genetic testing is thus a daunting task. The consensus statement published in *JAMA* (1997;277:1467-74) suggests a two-stage approach. The first stage includes counseling about risks, benefits, and alternatives and is followed by a waiting period for time to think. Only after the waiting period are candidates asked whether they want to proceed with testing.

The ethics consultation service recently reviewed a case exemplifying the complexity of genetic testing. It involved a woman who had agreed to give a blood sample for an epidemiological study. In studying her sample, the laboratory scientist detected an abnormality that had reproductive implications. Should she be told even though she had consented to give blood for an entirely different study? The ethics team judged she should and devised a plan to tell her in the most helpful manner.

Based on our experience and that of other genetics centers, M. D. Anderson has constructed an informed consent—that includes many related issues as well as this unusual circumstance. We are not Pollyannaish about the difficulty of obtaining consent for genetic testing, but using the staged approach and guided by the informed consent document, we think our process is improving.

The University of Texas
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