

**REPORT TO
PHYSICIANS**

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THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER
Making Cancer History™

4

Liver Tumors
Clinical trials help
physicians reevaluate
role of intra-arterial
therapies.

6

CME

**Educational
Opportunities**
M. D. Anderson
to sponsor several
conferences in
coming months.

7

Patient Education
Is hormone
replacement therapy
right for you? House
Call looks at the risks
and benefits of HRT.

8

99-402

CA 125 Assay
Improved sensitivity
could lead to early
detection of ovarian
cancer.

MD Anderson Oncology

New MRI Techniques Pinpoint Brain Tumors, Reveal Brain Functions in Real Time

by Dawn Chalaire

Using a new, faster, and more powerful magnetic resonance imaging (MRI)

scanner, researchers at The University of Texas M. D. Anderson Cancer Center are delving deep into the brain anatomy to see where thoughts and actions originate. Their aim—to better characterize brain lesions and develop more effective but less neurologically damaging treatments for them.

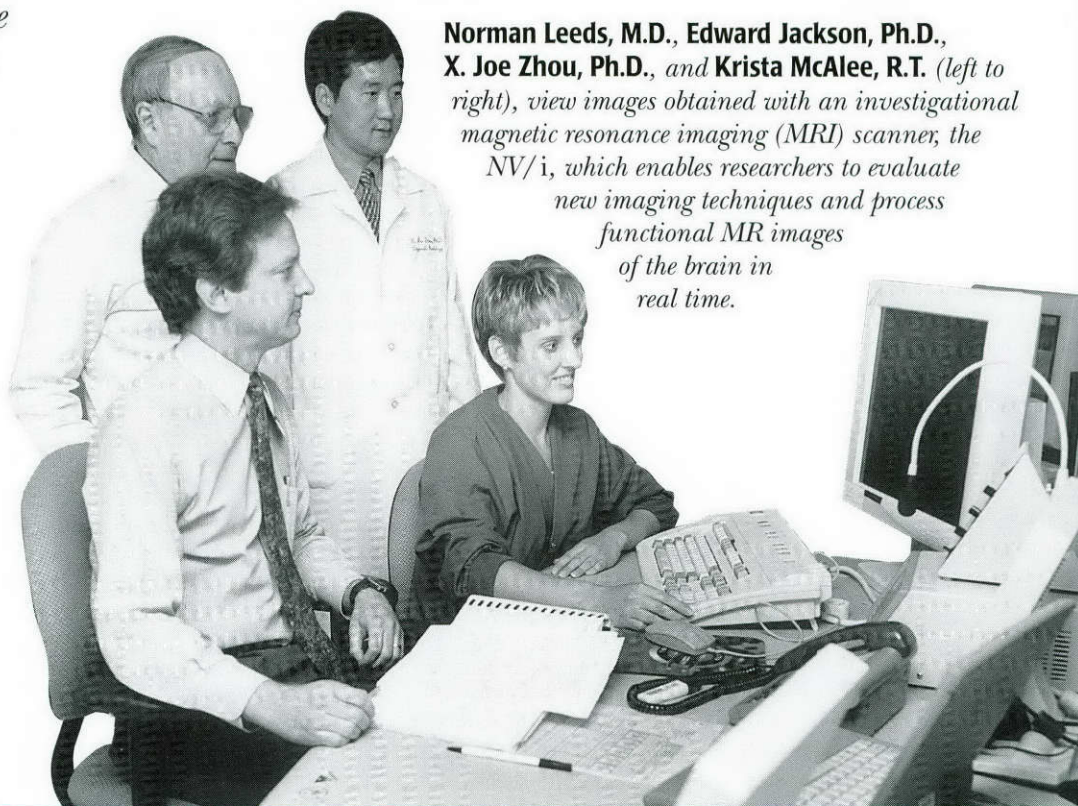
The investigational neurovascular interactive (NV/i) scanner developed by GE Medical Systems, with its faster data acquisition and greater processing power, is enabling researchers to evaluate new

imaging techniques and process functional MR images in real time. The NV/i is one of three high-speed MRI scanners acquired by the Department of Diagnostic Radiology earlier this year. “The major advantage of the NV/i is that it allows us to assess the newer

imaging techniques of diffusion and perfusion, as well as stimulated brain function imaging, to better comprehend how the brain functions,” said Norman E. Leeds, M.D., a professor in the Department of Diagnostic Radiology.

(Continued on next page)

Norman Leeds, M.D., Edward Jackson, Ph.D., X. Joe Zhou, Ph.D., and Krista McAlee, R.T. (left to right), view images obtained with an investigational magnetic resonance imaging (MRI) scanner, the NV/i, which enables researchers to evaluate new imaging techniques and process functional MR images of the brain in real time.



New MRI Techniques

(Continued from page 1)

Dr. Leeds and several physicists, neuro-oncologists, neurosurgeons, and neuropsychologists from M. D. Anderson Cancer Center and Rice University are designing and conducting studies using the new scanner while working with the manufacturer to evaluate and refine the NV/i's capabilities.

"This work is not simple. It requires a very knowledgeable team," Dr. Leeds said, "but it should allow us to provide patient services that most other centers can't."

Though researchers at M. D. Anderson have been able to do functional MRI since 1997, the NV/i scanner greatly improves the image quality they can achieve and allows them to image, in real time, changes in the brain as it activates functions such as speech, memory, and movement. While functional areas of the brain are generally found in the same places in all humans, the specific sites may vary slightly between individuals and are often significantly affected by the presence of tumors.

At M. D. Anderson, functional MRI is being developed primarily to help neurosurgeons plan resections of brain tumors. The images provided by functional MRI techniques could not only reveal the exact location of brain tumors but also enable surgeons to precisely locate adjacent functional areas so as to allow surgery without damaging critical structures.

Before functional MRI can be used clinically, however, its accuracy must be proved. To do this, the researchers at M. D. Anderson are studying functional task activation paradigms designed to determine where motor activity, expressive and receptive speech, and memory are activated in the brain. During a regularly scheduled MRI scan, patients are asked to perform an activity such as tapping a finger or silently generating words or sentences while the NV/i scanner records changes in the area of the brain that controls the activity in real time.

"While the patient's in the scanner, we ask them to perform these

tasks and then on a separate monitor from the console where we normally sit, we can actually see the buildup of signal intensity in the areas of task activation occurring in real time. In the past when we did these functional studies we acquired the data, then went away and processed it for a couple of hours while crossing our fingers in hopes that we got what we needed," said Edward Jackson, Ph.D., an assistant professor in the Department of Diagnostic Radiology.

To validate the functional MRI

"This work should allow us to provide patient services that most other centers can't."

studies, control studies have been done in 30 normal subjects. Also, when the patients undergo surgery for their tumors, neurosurgeons test the accuracy of the functional MR images by stimulating the brain to be sure the corresponding electrical activity in the brain occurs in the same location that is indicated on the functional MR image.

"We're still at the stage of making sure that what we see with the new technique agrees with what we see with established but more invasive techniques," Dr. Jackson said.

Unlike positron emission tomography and surgical brain mapping, functional MRI is completely non-invasive. Therefore, it could be repeatedly used to assess the effects of cancer treatments on brain function, thus allowing oncologists to more accurately weigh the benefits and risks of surgical resection, radiation therapy, and chemotherapy. Functional MRI could also determine whether brain deficits are the result of treatment or tumor recurrence. Charles S. Cleland, Ph.D., of the Pain Research Group, is using functional MRI to look at where the brain processes painful stimuli in order to understand how to target those areas for pain relief.

The improved image quality and faster acquisition rates of the NV/i

scanner have also made it possible to highlight changes in cerebral blood volume and flow. With proper manipulation of the data obtained, such perfusion-weighted MRI scans could distinguish necrosis caused by radiation from tumor and possibly determine tumor grade.

"The goal of radiation therapy and chemotherapy is to control the tumor by damaging it, which reduces blood flow and results in some degree of necrosis. Sometimes, however, it's very difficult to separate tumor from necrosis," Dr. Leeds said. "Perfusion imaging should enable us to do so. It should also permit us to evaluate tumor activity and determine the effects of treatment on the tumor to better predict outcomes."

Dr. Leeds and his team are investigating the use of perfusion-weighted MRI to determine the physical effects on the brain of the cancer drug interferon-alpha, which can cause psychological changes in some patients. Perfusion-weighted MRI is also being used to look for changes in blood volume and flow that correspond to the clinical symptoms of anemia and fatigue.

Moreover, in collaboration with physicist X. Joe Zhou, Ph.D., the NV/i scanner is being used to evaluate another imaging technique that could prove useful for delineating areas of tumor, necrosis, and edema within the brain. Unlike perfusion-weighted MRI, diffusion-weighted MRI does not require a contrast agent. Instead, it relies on high-speed imaging techniques to measure the random motion of water protons within the brain; areas of restricted motion produce a bright signal. The technique has been used extensively to study areas of restricted motion in the brains of stroke patients. Its potential applications in patients with brain tumors include better characterizing brain lesions, identifying their extent, and visualizing changes in the brain's white matter tracts caused by tumor growth. ●

FOR MORE INFORMATION, contact Dr. Leeds at (713) 745-0562 or Dr. Jackson at (713) 745-0559.

Liver Cancer Clinical Trials

Clinical trials currently in progress at The University of Texas M. D. Anderson Cancer Center include the following for patients with liver cancer or liver metastases.

- A phase I dose-escalation trial of hepatic artery infusion with an EF1B-attenuated adenovirus, ONYX-015, alone and in combination with intravenous 5-fluorouracil/leucovorin, into patients with intrahepatic metastases from gastrointestinal carcinoma (ID98-184). *Physician: James L. Abbruzzese, M.D.*

Study participants must have histologically or cytologically confirmed colorectal, gastric, or pancreatic carcinoma that has metastasized to the liver. Their tumor must not be curable with surgery but must be treatable with perfusion via a hepatic artery catheter. Participants must also be above 18 years old and have a life expectancy of greater than 3 months and preserved organ function. The participants will return to M. D. Anderson up to 15 times to receive an infusion of the adenovirus ONYX-015 alone and combined with an intravenous infusion of the drugs 5-fluorouracil and leucovorin.

- A phase II trial of subcutaneous (SC) recombinant human interferon alpha (RIFNA2b) and continuous intravenous (IV) 5-fluorouracil (5-FU) for the treatment of hepatocellular carcinoma (HCC) (DM97-040). *Physician: Yehuda Z. Patt, M.D.*

Patients with histologically proven primary hepatocellular carcinoma confined to the liver or that has metastasized are eligible for this study. Patients who have never received treatment or

have received one higher priority therapeutic regimen may participate. Patients who have already received RIFNA and 5-FU may not take part in the study. Patients with tense ascites or brain metastases or who are pregnant or lactating also may not take part. Patients will return to M. D. Anderson on an outpatient basis to receive infusions of 5-FU. Subcutaneous injection of RIFNA2b, which will be done three times a week, may be given by a family physician. A family physician may also perform weekly laboratory tests.

- Phase II trial of gemcitabine in the treatment of metastatic or recurrent cholangiocarcinoma/gall bladder cancer (ID98-360). *Physician: Yehuda Z. Patt, M.D.*

To participate in this study, patients must have biopsy-proven, measurable, unresectable, locally advanced adenocarcinoma of the biliary ducts or gall bladder. Patients also must be 18 years of age or older and must not have received prior chemotherapy for metastatic disease. Patients who had basal or squamous cell skin cancer or cervical carcinoma *in situ* that has been treated or cured or whose malignancy has been in remission for more than 2 years may take part in the study. If patients previously underwent surgery that required general anesthesia and enteral feedings, it must have been at least 3 weeks prior to the beginning of the study. Patients who are pregnant or have a severe coexisting illness (*i.e.*, poorly controlled diabetes mellitus, oxygen-supplemented chronic obstructive pulmonary disease, unstable angina, poorly controlled arrhythmia, infection) may not participate. The chemotherapeutic drug gemcitabine will be given to patients on an outpatient basis.

- Phase II study of radiofrequency ablation of colorectal cancer liver metastases combined with post-ablation hepatic arterial infusion of floxuridine alternating with 5-fluorouracil (ID98-035). *Physician: Lee Ellis, M.D.*

To be eligible for this study, patients must have histologically proven colorectal cancer that has metastasized to the liver. Patients who unsuccessfully received systemic chemotherapy or intra-arterial chemotherapy that did not include 5-fluorouracil or fluoropyrimidine may participate. Patients with clinical or radiographic evidence of extrahepatic metastasis, liver tumors greater than 4 cm in diameter, or more than six liver tumors or who received prior liver irradiation are ineligible. In addition, patients with gross ascites, evidence of cirrhosis, or active duodenal or gastric ulcers may not participate. Women who are pregnant or breast-feeding are also ineligible. Patients will return to M. D. Anderson twice a month to undergo radiofrequency ablation. After ablation, patients will remain at M. D. Anderson on an inpatient basis for 5 to 7 days. In addition to radiofrequency ablation, patients will receive alternating infusions of the chemotherapeutic drugs floxuridine and 5-fluorouracil on an outpatient basis. ●

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://www.clinicaltrials.org> for a broader listing of treatment research protocols.

Correction to Compass

We regret that in the June 1999 issue of *Compass*, the last sentence of the "Screening Recommendations" section contained an error. We here reprint the entire "Screening Recommendations" section. The last sentence contains the correction.

Screening Recommendations

Screening to detect early, treatable prostate cancers is recommended. According to all of our experts, it is important to help patients understand that current treatment approaches for localized prostate cancer are very

favorable, based on survival data. Patients with early-stage disease have very good prognoses and a choice of treatments with low complication rates, suggesting that detecting early-stage disease is important.

According to Dr. Grossman, physicians at M. D. Anderson endorse the approach of annual screening (DRE and serum PSA) for men between the ages of 50 and 70. Where there is a family history of prostate cancer, screening should begin at age 40. Screening is unnecessary when there are other conditions limiting life expectancy and no symptoms of prostate cancer. ●

Aggressive Regional Therapies Offer Some Promising Results for Patients with Liver Tumors

by Dawn Chalaire

In treating liver tumors with agents administered by hepatic arterial infusion (HAI), Yehuda Patt, M.D., keeps a phrase from Hamlet in mind: “Diseases desperate grown, by desperate appliance are relieved, or not at all.”

“Regional therapy such as HAI is an attempt to extract the extra mile from marginally effective drugs,” explained Dr. Patt, chief of the Regional Therapy Service in the Department of Gastrointestinal Oncology and Digestive Diseases at The University of Texas M. D. Anderson Cancer Center. “If we had drugs that were concentration independent—that taken as a pill would accomplish the same thing—nobody would bother with HAI.”

For years, HAI has been a source of controversy among gastrointestinal oncologists. It effectively delivers high concentrations of cancer drugs directly to liver tumors through the hepatic artery while, in theory at least, minimizing the drugs’ systemic effects on normal tissue. Yet, despite evidence that HAI produces higher local response rates than intravenous chemotherapy, studies have failed to convincingly show that HAI therapy increases survival or improves quality of life—until now.

At the American Society of Clinical Oncology (ASCO) meeting in May, Nancy Kemeny et al. reported significantly better survival after HAI and systemic chemotherapy than after systemic chemotherapy alone in patients with colorectal cancer following resection of liver

metastases. Another study by the Eastern Cooperative Oncology Group and Southwest Oncology Group showed that patients who received a combination of HAI and systemic chemotherapy after hepatic resection of liver metastases had fewer liver recurrences and a longer time to recurrence compared with patients treated with hepatic resection alone.

“The ASCO meeting has stimulated us to reconsider the role of intra-arterial therapy, probably in the adjuvant setting, and to come up with new trials that will address this role and reduce some of the controversies, even within our own group, over the best way to use this technology,” said James Abbruzzese, M.D., chairman of the Department of Gastrointestinal Medical Oncology and Digestive Diseases.

The studies presented at the ASCO meeting are significant, Dr. Patt said, because it is impossible to design a study to show the full extent of HAI’s survival benefits in patients with liver metastases since patients are enrolled into HAI therapy only after frontline systemic therapy fails. He predicted that these studies will revive the use of HAI regimens.

“I definitely think HAI will be used in adjuvant therapy after liver resections or together with radio-frequency ablation, but I also believe that we will see a surge in the use of this therapy in patients with established liver metastases that have not been resected,” Dr. Patt said.

Currently, HAI is used at M. D. Anderson to treat patients with primary and metastatic liver tumors—most commonly hepatocellular carcinoma (HCC) and colon cancer metastatic to the liver. HCC accounts for about 250,000 deaths worldwide each year but is relatively

uncommon in the United States, although its incidence is rising. Approximately 20% of colon cancer deaths occur in patients with metastases confined to the liver. Because recurrence is high and long-term survival low for both diseases, HAI is often used in clinical trials to administer new agents or new combinations of drugs.

“Our approach to treating metastatic colon cancer, as well as HCC, is to start with systemic therapies. If they work, that’s fantastic because then they work not only in the liver but elsewhere also, and we can resort to HAI in patients who are marginally responsive or not responsive to systemic or other drugs,” Dr. Patt said.

At M. D. Anderson, the preferred method of extended HAI is to place a pump about 3 inches in diameter half an inch beneath the skin of the abdomen and connect it to a catheter implanted in the hepatic artery. Drugs injected into the pump are infused into the hepatic artery at a constant rate. Although surgically implanted, the pump still requires a shorter hospital stay and creates fewer complications than percutaneous therapy, which requires continuous hospitalization during infusion and insertion of a new catheter before each treatment. The pump model used at M. D. Anderson for several years was recently discontinued, and now all patients who receive HAI therapy for the first time must enroll in a trial of an investigational Medtronic pump led by Dr. Patt.

While most clinicians agree that flaws in the methodologies of the previous studies of HAI were at least partly to blame for their lack of definitive answers regarding patient survival, it has been the risks associated with HAI that have fueled the



“... we can resort to HAI in patients who are marginally responsive or not responsive to systemic or other drugs.”

– Yehuda Patt, M.D.,
chief of the Regional Therapy Service, Department
of Gastrointestinal Oncology and Digestive Diseases

Yehuda Patt, M.D.,
holds one of the implantable Medtronic pumps used to administer high concentrations of chemotherapy drugs, as well as other agents such as the adenovirus ONYX-015, directly to liver tumors through the hepatic artery.

controversy. Attaching a catheter to the hepatic artery, with or without an implantable pump, can lead to a variety of complications, especially if the procedure is done by an inexperienced surgeon. The high concentrations of drugs delivered intra-arterially can also be harmful to a patient's biliary tree.

Dr. Patt said that the toxicities seen in some early trials of HAI have led to more careful patient selection and a wider selection of drugs and drug combinations used with HAI.

“The advantage of using the pump is that if the patient's tumor stops responding to frontline HAI therapy, we always have access to the hepatic artery for studying new agents,” Dr. Patt said. “It gives us that many more therapeutic and investigational options.”

One example of the investigational options made possible by HAI is a novel phase I study led by Dr. Abbruzzese in which ONYX-015, an adenovirus that targets tumor cells lacking the *p53* tumor suppressor gene, is delivered via HAI. Stanford University and the Mayo Clinic are also participating in the multi-institutional study of ONYX-015 with or without intravenous fluorouracil and leucovorin in patients with liver metastases

from gastrointestinal cancers.

“Right now, we think the best way to deliver the adenoviral compound is locally or regionally. In a number of studies, it has been delivered locally to other organs, and so a logical extension is to try to deliver it regionally, which is where the intra-arterial approach comes into play,” Dr. Abbruzzese said. “This new ONYX-015 study is not so much a study of intra-arterial therapy as it is a way to try to show the capabilities of this particular adenovirus. It's still premature to know if this is going to revolutionize intra-arterial therapy.”

Highlighting the trend toward using HAI in adjuvant settings is a phase II study led by Lee Ellis, M.D., in the Department of Surgical Oncology. The study is combining radiofrequency ablation of colorectal cancer liver metastases with post-ablation HAI of floxuridine alternating with fluorouracil. Dr. Ellis said that eligible patients must have no more than six liver lesions, all smaller than 4 cm in diameter, and no extra-hepatic metastases.

“Giving a higher dose of chemotherapy directly to the liver and a lower dose to the body makes us think HAI would be good to use in the adjuvant setting when there is no

known gross disease in the liver,” Dr. Ellis said.

Combining HAI with systemic therapy is critical to treating liver tumors, said Dr. Patt, who is conducting a pair of such clinical trials.

“Even though you can control the disease in the liver for a certain length of time, the disease will change its natural course and eventually pop up outside the liver,” he said.

In one such trial, Dr. Patt is alternating HAI of floxuridine with systemic i.v. CPT-11 in patients with colon cancer metastatic to the liver and refractory to systemic fluorouracil and leucovorin. In another trial, patients with HCC are being given systemic i.v. platinum, interferon, Adriamycin (doxorubicin), and fluorouracil (PIAF). If disease recurs or is confined to the liver only, the same combination is given by HAI to eliminate residual disease in the liver and possibly make the patient a candidate for resection. So far, according to Dr. Patt, one in four patients has responded to systemic PIAF, and the addition of HAI administration has increased the response rate to 46% and resulted in three complete histologic remissions among 15 registered patients.

“I must stress, though, that some of these treatments, in hepatoma especially, may be lethal if you do not choose your patients meticulously or misapply treatment to poor candidates,” Dr. Patt said. “So, it's extremely important to know who you treat.”

In carefully selected patients, however, aggressive HAI therapies such as these offer promising results against diseases that can seldom be relieved by any other means. ●

FOR MORE INFORMATION, contact Dr. Patt at (713) 792-2828.

Upcoming Conferences Explore Many Topics

by Kimberly JT Herrick

The chart below lists the conferences sponsored by M. D. Anderson Cancer Center's Office of Continuing Medical Education and Conference Services from mid-September 1999 to April 2000.

Continuing education credit hours, including American Medical Association/Physicians Recognition Award Category 1 (AMA/PRA Cat. 1) and other professional certifications, are listed for those conferences for which such certification has been approved according to criteria of the Accreditation Council for Continuing Medical Education.

Additional and updated information about these and other confer-

ences and in-house educational events at M. D. Anderson can be obtained from the Conferences and Educational Events links on the M. D. Anderson home page on the World Wide Web (www.mdanderson.org). Contact M. D. Anderson Conference Services by phone at (713) 792-2222, facsimile at (713) 794-1724, or electronic mail (meetings@www.mdacc.tmc.edu) for any additional information. ●

Conferences Sponsored by The University of Texas M. D. Anderson Cancer Center

Mid-September 1999
to April 2000

Date	Conference (Location)	Chairpersons (Contact)	Continuing Education Credit (Credit Hours)
Sept. 18, 1999	Breast Cancer Update (Houston)	Gabriel N. Hortobagyi, M.D.	AMA/PRA Category 1 (4.5)
Sept. 24-25, 1999	Living Fully with Cancer Conference (Houston)	Judy Gerner	
Sept. 24-25, 1999	Adolescent and Young Adult Issues in Oncology (Houston)	Sima Jeha, M.D.	AMA/PRA Category 1 (12.5)
Oct. 2-5, 1999	21st Annual Pharmacy Symposium (Houston)	Sharon Bronson, M.S., and William Dana, Pharm.D.	
Oct. 4-8, 1999	Practical Training in Interventional Radiology (Houston)	Contact Erlinda Alabastro at 713-792-2714.	
Oct. 8-9, 1999	Anderson's Alumni Conference, "Cancer Care—UT M. D. Anderson Approach" (Houston)	Ralph Freedman, M.D.	AMA/PRA Category 1 (14.5)
Oct. 19-21, 1999	New Drugs in GI Malignancies (Paris, France)	Contact Jaffer Ajani, M.D., at 713-792-2828.	
Oct. 21, 1999	Healthy Woman's Symposium (Houston)	Diane Bodurka-Bevers, M.D., and Michelle Gershenson	
Oct. 29-30, 1999	Issues in Prostate Cancer: A Conference for Patients and Families (League City, TX)	Andrew von Eschenbach, M.D., Christopher Logothetis, M.D., and D. A. Swanson, M.D.	
Nov. 13, 1999	LMA Hands-on Workshop & Seminar for Training, Education, and Research (Houston)	David Ferson, M.D. Contact Mary Ann Schneider at 713-792-6911.	AMA/PRA Category 1 (6.5)
Nov. 16-22, 1999	Cancer in the Middle East: Current Status and Future Collaborative Opportunities (Cairo and Sharm El-Sheikh, Egypt)	Contact Amr Soliman, M.D., Ph.D., at 713-792-4533.	
Nov. 18-21, 1999	Society for Neuro-Oncology Annual Meeting (Scottsdale, Arizona)	Victor Levin, M.D. Contact Jan Esenwein at 713-745-2344.	AMA/PRA Category 1 (25.5)
Jan. 9-12, 2000	Cancer Research at the Millenium: 42nd Annual Clinical Conference and 52nd Annual Symposium on Fundamental Cancer Research (Houston)	John Mendelsohn, M.D., and Margaret Kripke, Ph.D.	AMA/PRA Category 1 (22.5)
Feb. 6-9, 2000	Hawaii Endoscopy Conference, "A Practical Approach to Gastrointestinal, Pancreatobiliary, and Hepatic Diseases" (Maui, Hawaii)	Isaac Rajjman, M.D.	
Feb. 16-19, 2000	Radiation Oncology: RadOnc 2000 (Houston)	James D. Cox, M.D.	2/19/2000—Nursing (7.4)
Feb. 19-20, 2000	1st Annual Conference on Cancer-Related Fatigue (Houston)	Charles Cleeland, Ph.D.	
March 23-24, 2000	8th Annual Genitourinary Oncology Conference (Houston)	Christopher Logothetis, M.D., and Randall Millikan, M.D.	
April 29, 2000	Houston Society of Clinical Pathology (Houston)	Elvio Silva, M.D.	



Hormone Replacement Therapy: End to Hot Flashes or Fuse for New Cancers?

Weighing the benefits and the risks of hormone replacement therapy (HRT) is an important concern for middle-aged women. On the one hand, HRT's documented payoffs include relief of menopausal symptoms and prevention of osteoporosis. On the other, women who receive hormone treatment may be increasing their risks of breast and uterine cancers.

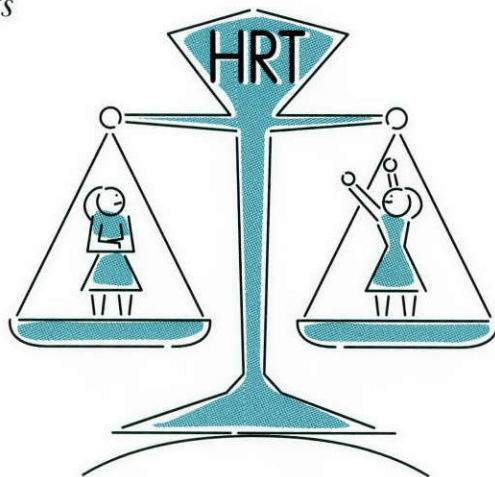
Hormones and Menopause

Menopause, the absence of menstrual periods for one year, typically occurs in women between the ages of 45 and 55. It may be induced surgically by removal of the uterus and ovaries. At menopause, a woman's ovaries stop producing the female sex hormone estrogen. This lower level of estrogen then may cause such menopausal symptoms as hot flashes, night sweats, and vaginal dryness. The lack of estrogen also contributes to a woman's developing osteoporosis or thinning of the bones, which may lead to fractures.

The severity of menopausal symptoms varies greatly among women. About 80% of menopausal women experience some symptoms, but according to The Women's Fund for Health Education and Research, only 10% to 30% have complaints serious enough to make them seek help from a physician.

Payoffs of HRT

Hormone replacement therapy consists of estrogen with or without progesterone. These hormones may be prescribed in the form of a pill, patch, implant, or cream.



HRT has been shown to relieve hot flashes, night sweats, insomnia, and vaginal dryness in menopausal women. It also helps prevent osteoporosis by promoting the absorption of calcium, which slows down bone loss.

Although some studies suggest that HRT may reduce or postpone a woman's risk of suffering a heart attack or stroke, more research must be done before this can be confirmed. This is true also for indications that HRT improves the verbal memory skills of postmenopausal women, decreases urinary incontinence and urinary tract infections, and possibly reduces the risk of developing colon cancer.

HRT and Endometrial Cancer

But hormone replacement therapy also carries significant health risks for some women. Estrogen used alone in women who still have their uterus has been linked to an increased risk of endometrial cancer, the most common gynecologic malignancy. Estrogen overstimulates the growth of the lining of the uterus, called the endometrium.

Adding the hormone progesterone to the estrogen replacement decreases the risk of endometrial cancer. The progesterone causes the endometrium to slough off cells every month. Estrogen now is rarely

prescribed alone in women who have not had a hysterectomy.

As protection against endometrial cancer, M. D. Anderson physicians advise that progesterone be added to estrogen in either continuous or cyclic fashion.

HRT and Breast Cancer

Breast cancer is another concern for women on HRT. Some studies suggest an increased risk of breast cancer among women who have used high doses of estrogen or have used estrogen for 10 years or more. The American Cancer Society reports that this risk applies only to current or recent users. A woman's breast cancer risk returns to that of the general population within five years of stopping estrogen replacement therapy, the ACS says.

HRT generally is not recommended for women with known or suspected cancer of the breast or uterus.

HRT: Is it for You?

Whether or not to have hormone replacement therapy is a decision a woman should discuss with her doctor. Issues to be considered are the severity of the woman's menopausal symptoms, her family history of cancers of the breast or uterus, and her risk factors for heart disease and osteoporosis. Only then can she decide whether HRT is the right choice for her. ●

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.

July/August 1999

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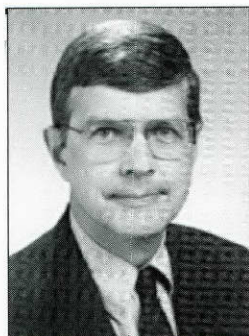


DiaLog

CA 125: The Past and the Future

Robert C. Bast, Jr., M.D.
Head, Division of Medicine

When it was first developed, the cancer antigen (CA) 125 assay provided the first generally available test for monitoring the courses of patients with epithelial ovarian cancer.



Over the last 15 years, we have learned a great deal about its potential and limitations. More than 2,000 papers have been published concerning laboratory and clinical studies of CA 125. The original CA 125 assay utilized the OC 125 antibody that recognizes the CA 125 epitope on a high-molecular weight glycoprotein. Despite repeated attempts, the gene encoding the peptide component has not yet been cloned. Monoclonal antibodies have been raised against other epitopes expressed by this molecule, leading to the development of the CA 125-II assay, which exhibits less day-to-day variation. Using either assay, elevated levels of CA 125 are detected in a number of benign conditions. CA 125 can be expressed in gynecologic and nongynecologic cancers, but it is most consistently elevated in epithelial ovarian cancer and is well established as its best monitor.

The rate of decline in CA 125 during primary chemotherapy has been an important independent prognostic factor in several multivariate analyses. Persistent elevation of CA 125 at the time of

second-look surgical surveillance procedures predicts residual disease with >95% specificity. Rising CA 125 values have preceded clinical detection of recurrent disease by at least three months in most, but not all, studies. Given the modest activity of salvage chemotherapy, this information has not yet had an impact on survival. Rising CA 125 values during subsequent chemotherapy have been associated with progressive disease in more than 90% of cases. CA 125 levels can also aid in distinguishing malignant from benign pelvic masses, permitting effective triage of patients for primary surgery.

Early detection of ovarian cancer remains the most promising application of CA 125. An algorithm has been developed that estimates the risk of ovarian cancer based upon the level and trend of CA 125 values. This early detection strategy should provide adequate specificity, but sensitivity may not be optimal.

In the future, improved sensitivity may be attained using multiple markers and neural network analysis. Most serum tumor markers have been proteins or carbohydrates, but such lipid markers as lysophosphatidic acid deserve evaluation. Genomic and proteomic technologies should identify additional novel markers.

Adapted, with permission, from Bast RC, Xu FJ, Yu S, Barnhill S, Zhang Z, Mills GB: International Journal of Biological Markers 1998;13(4):179-87.

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