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M. D. Anderson Cancer Center
*Is Celebrating Its 60th Anniversary*



REPORT TO PHYSICIANS

APRIL 2001 Vol. 46, No. 4

# OncoLog

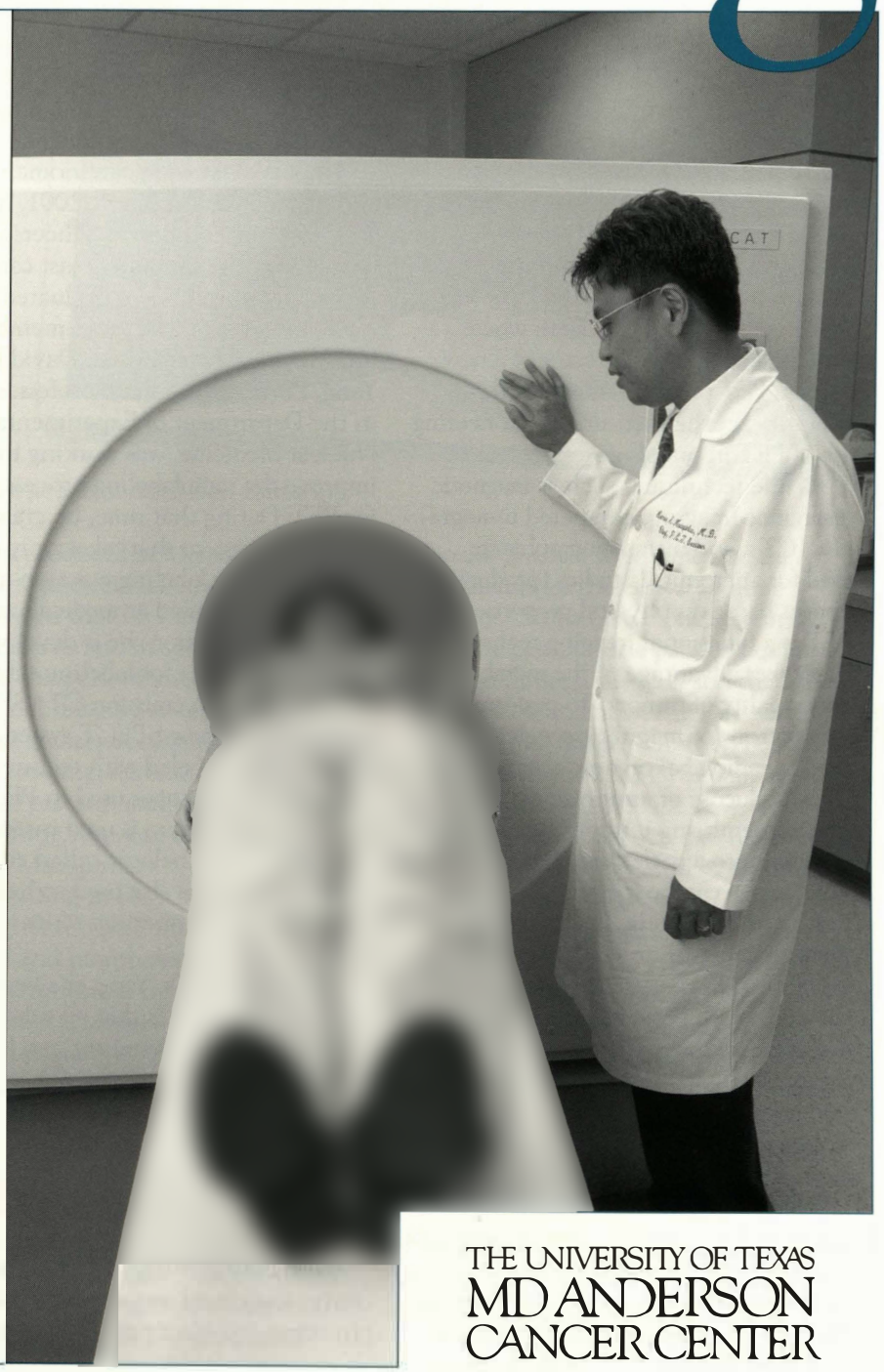
# Clinical PET Facility Returns to M. D. Anderson

## *Nuclear Physicists Continue Work Begun During Camera's Absence*

**by Kerry L. Wright**

*From 1994 until late last year, The University of Texas M. D. Anderson Cancer Center did not have a working positron emission tomography (PET) camera, but that did not stop its nuclear physicists from making theoretical advances in PET technology. Now, after years of working behind the scenes, their perseverance is beginning to pay off.*

*(Continued on* **next page***)*



*After more than five years without a positron emission tomography (PET) camera, M. D. Anderson will soon open a new clinical PET center directed by* **Dr. Homer Macapinlac** *(pictured), an associate professor in the Department of Nuclear Medicine.*

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

# PET Facility Returns to M. D. Anderson

*(Continued from* **page 1***)*

The Department of Nuclear Medicine recently forged a bond with Russian scientists who are supplying them with the rare earth materials they need to make their theoretical improvements a reality. At the same time, a new state-of-the-art clinical PET center is being established.

The very first clinical PET camera was constructed in the early 1970s at the Mallinckrodt Institute of Radiology at Washington University. According to Edmund Kim, M.D., a professor in the Department of Nuclear Medicine at M. D. Anderson (and a nuclear medicine fellow at Washington University in the 1970s), PET showed good promise at the time, but its images were crude, its use was mostly limited to imaging the head, and its resolution was only about 20 mm. In 1987, the first PET camera appeared at M. D. Anderson, where Dr. Kim became the director of a new clinical PET program, marking the beginning of the institution's pioneering use of PET in oncology.

While techniques such as magnetic resonance imaging, computed tomography (CT), and ultrasonography are used for anatomical studies (producing images based on physical properties), PET is a functional imaging technique that takes advantage of the metabolic abnormality of tumors. To perform PET, a cyclotron (or magnetic accelerator) is used to radiolabel organic compounds, such as glucose or amino acids, with positron-emitting isotopes that are then injected into a patient so that a metabolic image can be formed via a computer. Unfortunately, the metabolic imaging center that M. D. Anderson established in the 1980s closed in the mid-1990s because operating the cyclotron was very expensive, and insurance companies often refused to reimburse patients for clinical studies.

"Now there are almost 80 medical centers with one or two PET scanners," said Dr. Kim. This huge boom has been due in part to improvements in technology. For example, the computers of today are smaller, cheaper, and more efficient. In addition, the government now allows reimbursement for clinical PET studies: Three years ago, PET was approved by Medicare for imaging pulmonary nodules, lung cancer, lymphoma, colorectal carcinoma, and melanoma. On July 1, 2001, head and neck and esophageal cancers will be added to the list, and breast cancer is the next disease to be evaluated.

> ***"Our goal is to develop really high-resolution systems at low cost."***
>
> **– Wai-Hoi (Gary) Wong, Ph.D., professor, Department of Nuclear Medicine**

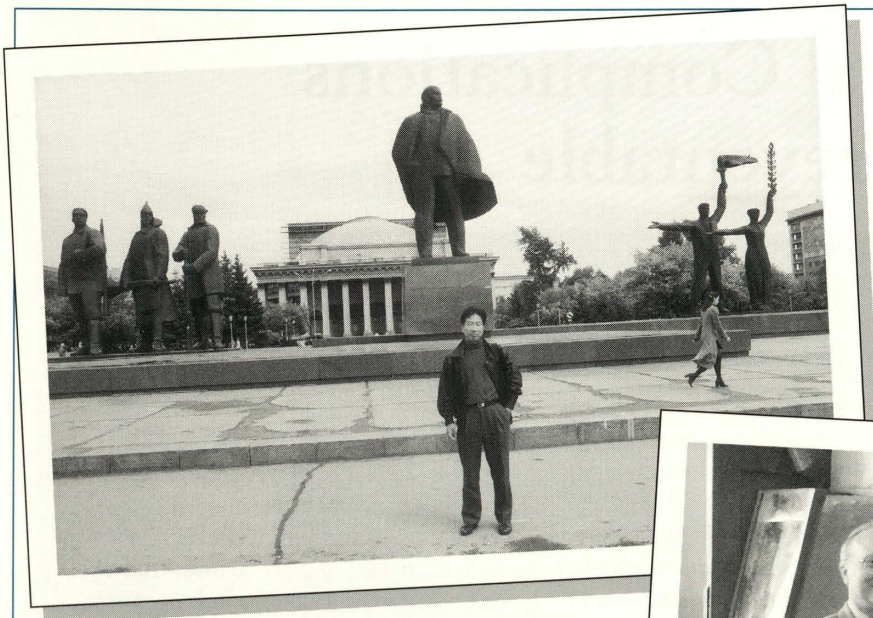
While M. D. Anderson's metabolic imaging center was closed, David J. Yang, Ph.D., an associate professor in the Department of Experimental Nuclear Medicine, was working to improve the radiolabeling process used for PET. During that time, he created an automated system that takes only 10 to 20 minutes per labeling reaction and is currently being used at medical centers in Japan. In addition, he is developing a novel technique for labeling substrates for single-photon emission CT (SPECT) studies. In the new SPECT system, substrates are labeled with technetium instead of the isotopes used in PET, and a gamma camera is used instead of a PET camera. A chelator called ethylene cysteine, or EC, is also used to help conjugate the technetium to its substrate.

According to Dr. Yang, the beauty of this new technique is that all substrates, regardless of their chemistry, can be labeled in the same way (which isn't always the case for PET) using EC as a common constituent in each reaction. "So now we will have a universal rule for looking at molecular targets," said Dr. Yang.

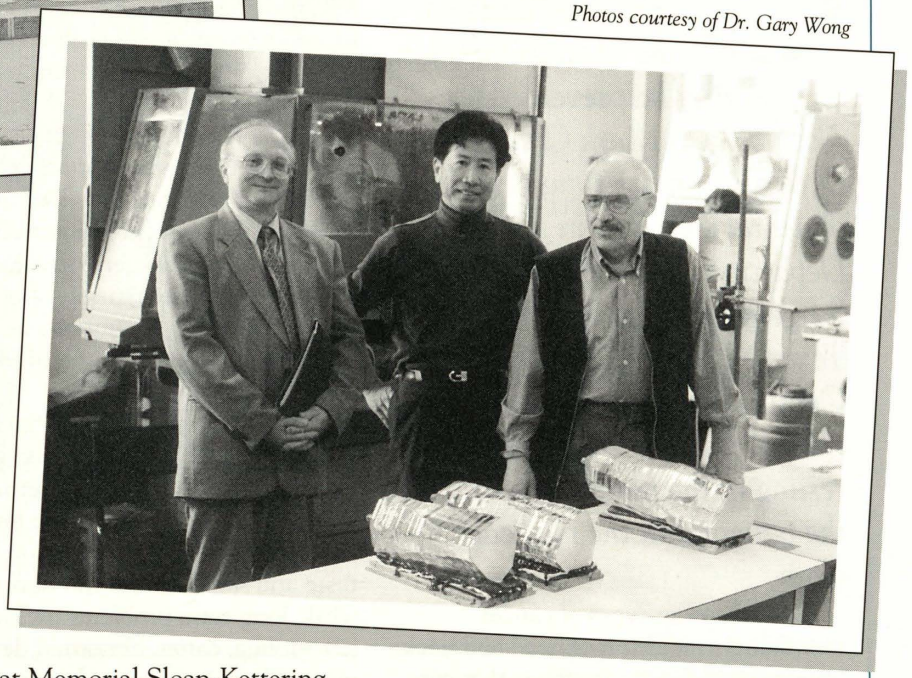
Also busy at work while the PET center was closed was a team of nine physicists and electronic engineers led by nuclear and PET physicist Wai-Hoi (Gary) Wong, Ph.D., a professor in the Department of Nuclear Medicine, who was conducting research to develop cameras even more powerful than those that were commercially available. The team's most recent project is the development of an eight-module clinical camera designed to image not only the head and whole body, as current commercial cameras do, but also the breast.

"Our goal is to develop really high-resolution systems at low cost," said Dr. Wong. The resolution, or the size of a structure or lesion that can be seen, is actually determined by the size of the gamma ray detectors in the camera. When positron-emitting isotopes enter the body, they collide and react with electrons to produce gamma ray photons that strike the detectors. The detectors then turn the light that is created into electrical signals that are registered by the computer to form an image. Whereas cameras 15 years ago had only 500 to 700 detectors, the model Dr. Wong is working on has nearly 40,000 much smaller detectors and a resolution of 2 mm for the head and breast modes and 2 to 3 mm for the whole-body mode, the highest resolution of any camera in the world. (The most advanced commercial cameras today have resolutions of 4 to 6 mm.)

According to Dr. Wong, one way to reduce the cost of PET machines (though possibly at the expense of resolution) would be to reduce the number of gamma ray detectors, which are each made up of about 50 tiny crystals resembling small jewels and are the most expensive part of the machine. "The second thing is to lower the price of the crystals," he said. The crystals are composed of rare earth materials found predominantly in China and Russia. As Russia is still in a state of perestroika, the materials are much cheaper there, said Dr. Wong, who recently traveled to St. Petersburg, Moscow, and Siberia in search of materials for his new model. The nine-day trip resulted in an agreement with the Russian Academy of



Photos courtesy of Dr. Gary Wong



**Dr. Wai-Hoi (Gary) Wong**, *a professor in the Department of Nuclear Medicine, recently traveled to the city of Novosibirsk in Siberia (above) in search of rare earth materials to build a new high-resolution, low-cost clinical PET camera. While there, Dr. Wong met with representatives from the Institute of Inorganic Chemistry at the Russian Academy of Science (right), from whom he eventually purchased $100,000 worth of bismuth germinate crystals.*

Science in Siberia to purchase $100,000 worth of bismuth germinate, currently the most common material from which the crystals are made. According to Dr. Wong, if his team is satisfied with the quality of the crystals and their model camera is eventually produced, they hope to create a long-standing relationship with their new partners in Russia.

As the efforts of Dr. Yang and Dr. Wong continue, the Department of Nuclear Medicine is also working hard to reinstate its once-flourishing PET facility. For the first time since the close of the previous facility, a high-resolution PET camera is in operation at M. D. Anderson. The camera became active in November 2000, and a new clinical PET center will formally open on May 10, 2001. According to Homer Macapinlac, M.D., an associate professor and chief of the Section of Positron Emission Tomography in the Department of Nuclear Medicine, about six patients per day undergo PET imaging in the facility, and its capacity has not yet been reached. Dr. Macapinlac, who is both developing and directing the new center, recently joined M. D. Anderson after spending the past five years as clinical director of the PET program at Memorial Sloan-Kettering Cancer Center.

Data produced at Memorial Sloan-Kettering and several other institutions have shown that PET effectively complements and in some ways even exceeds the performance of other traditional imaging systems. "PET provides greater accuracy in diagnosing disease, staging, determining the extent of tumor present, and especially in determining response to therapy," said Dr. Macapinlac.

According to Dr. Kim, conventional imaging techniques often show abnormalities and morphological changes in tumors after initial treatment, and PET is particularly useful for differentiating between posttreatment changes and possible recurrences or irregular tumors. To facilitate combining PET with traditional imaging, a hybrid camera will soon be purchased for M. D. Anderson's new imaging center.

"The unit we're currently looking at is actually a combined PET/CT unit," said Janet Champagne, the administrative manager of the Department of Clinical Nuclear Medicine and the coordinator for the center's formal opening. "So you have one system with one bed that the patient lies on. They go through the CT, and then they continue on and have the PET scan," she said. The images can then be fused to display the functional and anatomical data simultaneously.

The center is expected to have three PET cameras in operation by the end of 2001, and additional growth will be scheduled as necessary. "We're carefully mapping the demand for PET images so that we will have enough scanners and cyclotrons to accommodate the projected clients," said Champagne. The cameras will be available for any patient within the institution and also for patients outside the institution, upon the request of their physicians. ●

**FOR MORE INFORMATION**, *contact Dr. Kim at (713) 794-1052, Dr. Yang at (713) 794-1053, Dr. Wong at (713) 792-5847, or Dr. Macapinlac at (713) 792-7126.*

# Postirradiation Oral Complications Are Serious but Preventable

**by Don Norwood**

*Considering the threat of postirradiation oral complications, the obvious question is: Can they be prevented? According to Mark Chambers, D.M.D., an assistant professor of dental oncology in the Department of Head and Neck Surgery at The University of Texas M. D. Anderson Cancer Center, they can be, to a certain extent, with the responsibility resting in the hands of both the patient and the medical team.*

As with other types of cancer treatment, irradiation of head and neck cancers produces toxic effects that can be troublesome for patients and are often serious enough to limit further cancer treatment. One such effect is dental deterioration, specifically complications in the oral cavity of patients who undergo irradiation of head and neck cancers. While these complications vary according to the patient's oral status, type of malignancy, and therapy combination (radiation therapy with or without surgery, chemotherapy, or both), they are a common problem.

"In most patients with cancer, problems in the oral cavity mirror those in the general population: moderate to advanced periodontal disease, poorly restored dentition, and soft tissue pathologies associated with tobacco use, alcohol use, nutritional neglect, and general hygiene neglect," said Jack Martin, D.D.S., professor and chief of the Section of Oncologic Dentistry and Prosthodontics in the Department of Head and Neck Surgery. "Evaluation, treatment, and prevention of oral and dental pathology are important in the overall treatment outcome of patients with cancer."

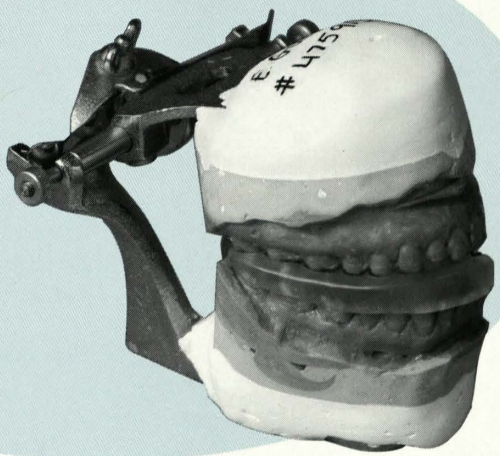
The oral complications that occur after radiation therapy are divided into two classes: acute and long term. Acute complications include mucositis, infectious stomatitis, alteration of taste and smell acuity, and dermatitis, while long-term problems include xerostomia, caries, abnormal development, fibrosis, trismus, photosensitivity, and osteoradionecrosis. The severity of these problems depends on many factors, including the radiation dose, the energy source, the volume of irradiated tissue, and the patient's periodontal condition and performance status.

"Irradiation can permanently destroy cellular elements of bone, which can limit the ability to heal after a traumatic event," Dr. Chambers explained. "Further, the risk of complications following trauma or oral surgical procedures in an irradiated field can be highly significant, although some authors claim this risk is low up to a predetermined threshold of irradiation. For these reasons, elective oral surgical procedures such as extractions and soft tissue surgery are contraindicated within an irradiated field because of hypovascularity and hypocellularity. However, nonsurgical procedures that can be safely performed include routine restorative procedures, oral prophylaxis, radiography, and endodontic and prosthodontic procedures."

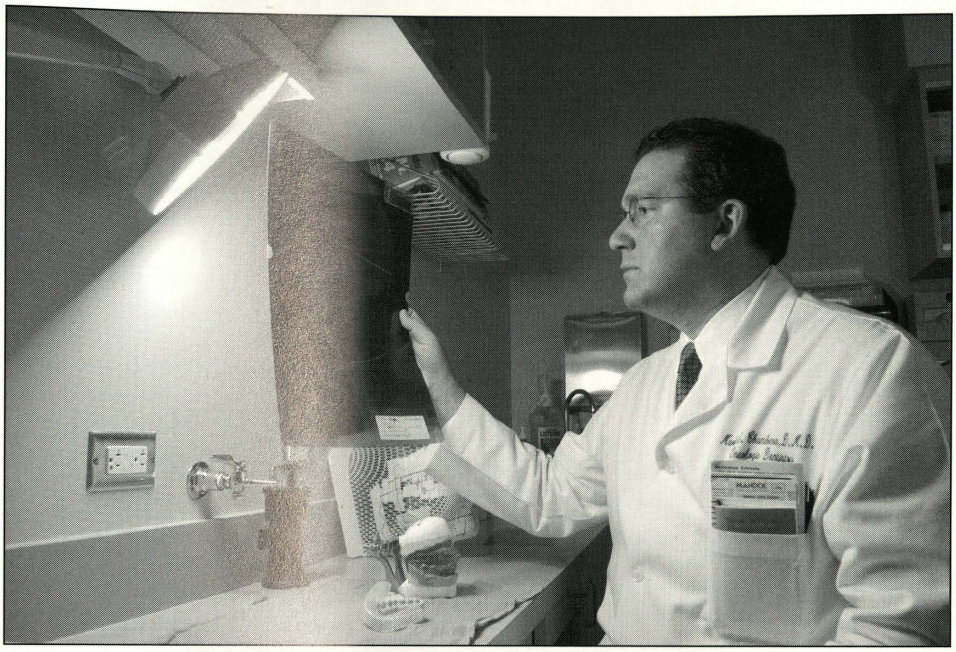
Because certain surgical procedures are not advised after radiation therapy, dental oncologists examine patients before treatment and remove and document any preexisting acute or chronic pathologic conditions—dental abscesses, teeth with advanced periodontal disease, dental calculus causing gingivitis, partially erupted teeth with potential for pericoronitis, and soft tissue tooth trauma—that could affect the cancer treatment strategy selected by the treating physician.

One particularly troublesome aspect of radiation therapy for head and neck cancers is the effect it has on the salivary glands. When these glands are included in the volume of irradiated tissue, the radiation causes atrophy of the glands' secretory cells, leading to a decrease in the quality and quantity of salivary secretions. It has also been postulated that radiation-induced damage to the glands' vascular and connective tissues causes the decrease in salivary secretions. Whatever the cause, the effect is preventable.

"Salivary hypofunction can increase the risk of dental caries, compromise mucosal integrity, impair chewing and swallowing, and reduce the quality of life of irradiated patients," said Dr. Chambers. "Therefore, when the salivary glands are irreversibly damaged from radiation therapy, the patient can benefit from a well-documented anticaries preventive regimen. This regimen consists of a daily application of 0.4% stannous fluoride gel or 1.0%



*Fluoride carriers such as this customized fluoride chamber are used to apply a fluoride gel to the teeth of patients whose salivary glands have been damaged by radiation treatments and who are susceptible to developing dental caries.*



**Dr. Mark Chambers**, *an assistant professor of dental oncology in the Department of Head and Neck Surgery, evaluates a simulation radiation film in preparation for oral surgery on a patient with several oral abscesses who has completed radiation therapy.*

***"If oral care guidelines are followed, oral tissues can be maintained in a healthy state following radiation therapy."***

**– Mark Chambers, D.M.D., assistant professor, Department of Head and Neck Surgery**

sodium fluoride gel onto the dentition using a brush-on technique or a vehicle known as a fluoride carrier."

The 0.4% stannous fluoride gel (which was invented in a joint collaboration between M. D. Anderson and the Veterans Administration Hospital in Houston more than 40 years ago) or 1.0% sodium fluoride gel is placed in a custom-fabricated polypropylene fluoride carrier, Dr. Chambers said. The carrier is then placed onto the dentition, completely covering and slightly extending beyond the tooth surface, for 10 minutes; this is repeated daily. Patients who receive low radiation doses and are expected to have slight xerostomia can apply the gel using a toothbrush.

In addition to dental caries, irradiation of the salivary glands is associated with other oral complications, particularly oral infections. "Changes in salivary flow induced by radiation are worrisome because saliva protects the oral mucosa from dehydration and assists in removing food and microbial debris from the oral cavity," said Dr. Martin.

With guidance from the medical team, however, patients can take measures to prevent these complications, as well.

"To avoid oral infections and reduce mucositis, the patient must frequently rinse the oral cavity to reduce the number of oral microorganisms and maintain mucosal hydration. This can be done with a solution of 1 teaspoon of sodium bicarbonate in 1 quart of water. This concoction should be used frequently during each day to alkalinize the oral cavity and keep the oral/oropharyngeal tissues moist," said Dr. Chambers.

Agents that promote the flow of saliva, such as cholinergic agonists, have been investigated and shown to have clinically significant benefits when given for the symptomatic treatment of postirradiation xerostomia. Other rinses that are being investigated, such as those containing cytokines, aloe vera derivatives, and antibiotics, may prove to be less irritating and more effective in reducing the symptoms that occur after radiation therapy.

Dr. Chambers noted that an exciting development in the field of head and neck cancer irradiation is intensity-modulated radiation therapy (IMRT). Currently used in the M. D. Anderson Department of Radiation Oncology, IMRT may reduce the total radiation dose delivered to major salivary glands in certain treatment schedules, which would result in a reduction in the incidence of postirradiation xerostomia.

While the advances in the treatment of postirradiation oral complications are encouraging, Dr. Martin stressed that prevention remains the goal, the fulfillment of which should be a priority for both patient and practitioner.

"If oral care guidelines are followed, oral tissues can be maintained in a healthy state following radiation therapy," Dr. Chambers said. "Cooperation and compliance are essential and are the result of education and motivation ... By fostering communication and compliance among the multidisciplinary team, the practitioner can ensure that patients with cancer of the head and neck receive quality care." ●

**FOR MORE INFORMATION**, *contact Dr. Chambers at (713) 792-2672 or Dr. Martin at (713) 745-2512.*

# Trial Shows Pill Is as Effective as Intravenous Chemotherapy for Advanced Colon Cancer

**by Julie Penne and Dawn Chalaire**

*Patients with advanced colorectal cancer may soon have a less toxic, more convenient option for the treatment of their disease—in the form of a small pink tablet.*

In a study led by The University of Texas M. D. Anderson Cancer Center, researchers found that oral capecitabine (Xeloda) is an acceptable option to the intravenous chemotherapy regimen of fluorouracil (5-FU) plus leucovorin for the treatment of metastatic colon cancer.

Investigators suggest, however, that the oral drug is most appropriate for patients who are highly motivated and able to take multiple pills (usually three or four) twice a day as recommended.

Results of the phase III trial, conducted at M. D. Anderson and 60 other sites throughout the United States, Canada, Brazil, and Mexico, are published in the April 15 issue of the *Journal of Clinical Oncology*. More than 600 patients were enrolled in the trial, all with colon cancer that had spread to other organs.

According to the comparative study, tumors in approximately 25% of patients who took the oral capecitabine responded, compared with those in about 16% of patients receiving intravenous chemotherapy. Median survival times were 12.5 months for the oral drug and 13.3 months for the intravenous therapy, and median time to disease progression was 4.3 months for the pill and 4.7 months for intravenous chemotherapy. These differences were not statistically significant. Patients who took capecitabine experienced a significantly lower incidence of diarrhea, stomatitis, nausea, hair loss, and neutropenia—symptoms commonly associated with intravenous chemotherapy. They also required fewer trips to the hospital for adverse reactions than those taking 5-FU plus leucovorin.

But researchers say the trade-off for convenience is that patients must take responsibility for taking the pills as directed and for communicating regularly with their health care team. For that reason, the pill remains an option, rather than a new standard treatment, for patients with metastatic colon cancer.

"The encouraging results of this trial give physicians additional latitude in recommending to each patient the optimal course of treatment. It is especially important to remember that this oral drug was found to be equal to, not superior to, the intravenous chemotherapy regimen of 5-FU plus leucovorin," said Robert Wolff, M.D., an assistant professor in the Department of Gastrointestinal Medical Oncology and a colon cancer specialist who enrolled many patients in the trial. "While the oral drug is much more convenient for patients and produces fewer side effects, this treatment depends on the patient's willingness and ability to take the pills as prescribed."

In the randomized study, half of the patients took oral capecitabine in three-week cycles: twice daily for two weeks, followed by one week of no treatment. The pills were taken approximately 12 hours apart, with water, within 30 minutes of breakfast and dinner. The remaining patients received 5-FU plus leucovorin by rapid intravenous injection daily for five days every four weeks.

"This treatment is definitely more convenient and less toxic than the intravenous chemotherapy," said Dr. Wolff. "But it literally puts the treatment in the hands of the patient. It is a consideration that physicians must acknowledge when devising a treatment plan."

At the time the study was designed, intravenous 5-FU and leucovorin was the standard first-line therapy for advanced colorectal cancer. Since then, a combination of 5-FU, leucovorin, and irinotecan has become widely accepted as the new standard therapy.

"However, this three-drug combination has more potential for toxicity than 5-FU and leucovorin alone. Therefore, some physicians, in discussions with their patients, may elect to proceed with oral therapy as first-line treatment," Dr. Wolff said.

Capecitabine, an oral fluoropyrimidine carbamate that is converted to 5-FU in tumor tissue, is also being investigated in combination with irinotecan in several clinical trials. Other studies are examining capecitabine combined with oxaliplatin, and phase I trials of irinotecan, oxaliplatin, and capecitabine are being planned. ●

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

# PET Facility Returns to M. D. Anderson

*(Continued from* **page 1***)*

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# After Cancer: A Survivor's Diary

*Cancer survivors often walk a fine line between trying to return to a "normal" life and coping with the legacy of their disease. The following diary entries illustrate some of the joys and challenges encountered by cancer survivors, followed by helpful tips.*

*Going for my first checkup at the hospital today. Feeling pretty nervous—*

**It's common for patients to feel anxious about every checkup**, and this can last for several years. Arriving at the appointment with a list of questions can help you feel more in control. Cancer checkups are a good time to ask about the symptoms of recurrence, the kind of diet that should be observed, other treatment options, and other concerns such as sexual problems, care instructions, and general fitness.

*Went to hairdresser's for first time in over a year—celebrated afterward with a chocolate sundae!!*

**Do things that you enjoy once your treatment is over**, even if you don't always feel your best. Pleasure is a powerful tool!

*Woke up with funny pain in my side today. Made an appointment to see doctor. Now what?*

**Be on the watch for symptoms** that may indicate the return of your cancer. Ask your physician what these symptoms are, and be sure to follow your oncologist's recommendations for cancer screening tests.

*Got a letter from my insurance company today saying they were cancelling my health insurance policy because of the cost of all my cancer care. Also got a bill for costs not covered by insurance. What a day.*

**There are many ways around the cancellation of health insurance.** Many states sell comprehensive health insurance to state residents with serious medical conditions who can't find a company that will insure them. You may also be able to enroll in a group plan. Be careful about changing jobs until you know whether you'll be covered under the new company's group plan.

*Trudy called tonight to ask if I would help her host a Spring Bazaar luncheon for 100. I had to turn her down. I hated to do this, but I just don't feel up to such demands yet.*

**It is important to pace yourself**, especially right after cancer treatment. Don't hesitate to say no to anything that may be too demanding for you. Be kind to yourself; focus on what you can do and not on what you can't do.

*Everyone has been so nice to me, but I still feel so alone. I'm the only person I know who's had my kind of cancer.*

**Consider joining a cancer survivors' group**; it is a good place to learn how to cope with problems unique to your cancer or to the treatment you received. M. D. Anderson's Life After Cancer Care program (www.mdanderson.org/departments/lacc/) offers a Cancer Survivor Message Board where cancer survivors and their caregivers can communicate, share concerns, and offer encouragement.

*Today was my first day back to work, and my boss told me this afternoon that they might have to let me go because of my cancer. She told me that they were afraid that I would be out of work a lot, and they can't work around my being absent anymore.*

**Eighty percent of people with cancer return to work** after diagnosis and treatment. Research has also shown that cancer survivors are as productive on their jobs as other workers, and they aren't absent from work any more frequently. Organizations such as the Job Accommodation Network, the National Coalition for Cancer Survivorship, and the Patient Advocate Foundation can also help survivors faced with employment issues.

*My first grandchild was born today. She is beautiful—not surprising! I never thought a year ago when I was going through all those cancer treatments that I could feel such happiness again. Or that I'd even be here! Every day is a gift now.*

**There is life after cancer!**

*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.*

**April 2001**

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## Staff Publications in April

*Below is a partial list of staff publications appearing this month.*

Azuma A, Huang P, Matsuda A, Plunkett W. 2'-C-cyano-2'-deoxy-1-beta-D-arabino-pentofuranosyl-cytosine: a novel anticancer nucleoside analogue that causes both DNA strand breaks and G(2) arrest. *Mol Pharmacol* 2001;59(4): 725-31.

Buchholz TA, Tucker SL, Erwin J, Mathur D, Strom EA, McNeese MD, Hortobagyi GN, Cristofanilli M, Esteva FJ, Newman L, Singletary SE, Buzdar AU, Hunt KK. Impact of systemic treatment on local control for patients with lymph node–negative breast cancer treated with breast-conservation therapy. *J Clin Oncol* 2001;19(8):2240-6.

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