

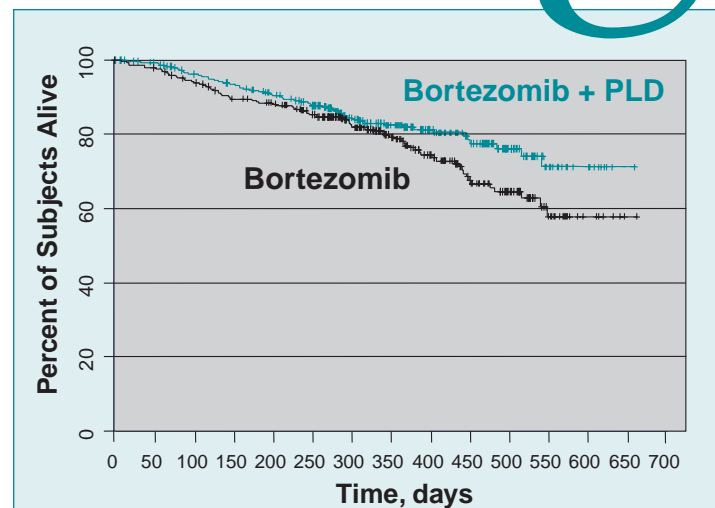
Oncology

Multiple Myeloma: Increasing Response, Remission, and Survival Rates in a Complex Disease

By John LeBas

Fifty years ago, a diagnosis of multiple myeloma meant the patient could expect a short survival period plagued by pain from bone lesions, disability, and fatigue. Progress against this plasma cell cancer was slow for several decades, and the few clinical breakthroughs sometimes proved dangerous and were suitable for only a minority of patients.

Yet in recent years, novel drugs and rational combinations of therapeutic agents have yielded better response and remission rates with less toxicity, and the end result has been longer overall survival. "The median overall survival duration was less than 2 years 50 years ago, before we had any chemotherapy for multiple myeloma. Now, the median overall survival duration is about 5 years for all patients, with perhaps 20% living for more than 10 years," said Raymond Alexanian, M.D., a professor in the Department of Lymphoma and Myeloma at The University of Texas M. D. Anderson Cancer Center. "And the longer we can



Overall survival of patients taking bortezomib (Velcade) or bortezomib plus pegylated liposomal doxorubicin (PLD, Doxil) for treatment of multiple myeloma. In this study, patients taking bortezomib plus PLD were more likely to survive than patients taking bortezomib alone. Recent success against multiple myeloma is credited to novel combinations involving newer agents such as bortezomib and PLD. These combinations often produce more effective results with less toxicity than older agents.

control these patients' disease, the greater chance they have of outliving it."

Developing successful treatments has been an exercise in perseverance, and although specialists at M. D. Anderson are happy about the progress, they are quick to explain that much work remains. A cure is still elusive, and current therapies are focused on inducing partial or complete remission and sustaining that remission as long as possible.

"Just about all multiple myeloma patients who achieve remission will relapse. And the next time we give them treatment, the disease is usually a little bit more resistant to therapy," said Robert Orłowski, M.D.,

(Continued on page 2)

Multiple Myeloma

(Continued from page 1)

Ph.D., an associate professor and chief of the Myeloma Section in the Department of Lymphoma and Myeloma at M. D. Anderson. “Also, therapy that is effective against myeloma cells must sometimes be given at doses that are somewhat damaging to healthy tissues. Therefore, our goal is always to reduce the amount of myeloma cells in the bone marrow, hopefully to undetectable levels, with a minimum overall amount of therapy. Fortunately, we have identified combinations of agents that are increasing the effectiveness of both frontline and later-line therapy.”

Better therapeutic agents

In the past 5 years, the U.S. Food and Drug Administration has approved four therapeutic agents for multiple myeloma: bortezomib (Velcade), thalidomide (Thalomid), lenalidomide (Revlimid), and a combination of doxorubicin encapsulated in a liposome (pegylated liposomal doxorubicin, Doxil) and bortezomib. These agents’ mechanisms of action vary. Bortezomib is a proteasome inhibitor that induces apoptosis (death) of myeloma cells; thalidomide and lenalidomide are immunomodulatory agents that can slow or stop myeloma reproduction; and doxorubicin inhibits the DNA functions of cancer cells and induces apoptosis.

While each of these agents has individual activity against multiple myeloma, it’s the enhanced activity gained by combining them with older, established agents, such as the glucocorticoid dexamethasone and the alkylating agents melphalan and cyclophosphamide, that has produced the most headway against the disease in recent years. “Such combinations produce more effective anti-myeloma activity with less added toxicity,” Dr. Alexanian said. Also, the newer agents can sometimes resensitize myeloma that has become refractory to previously administered drugs. And both lenalidomide and bortezomib, relatively new drugs, yielded such positive results as second-line therapies that they are rapidly becoming part of standard frontline treatment combinations.

Safer stem cell transplantation

To be most effective against multiple myeloma, some agents, especially melphalan, must be given at high doses that are likely to damage or destroy the bone marrow. In the past, the aggressive nature of this approach decreased the



Dr. Raymond Alexanian

proportion of patients to whom it could be applied. But today, because of improvements in supportive care and a better understanding of which patients benefit most, about two-thirds of patients are candidates for intensive therapy supported by autologous stem cell transplantation, also known as stem cell rescue. Stem cells harvested from patients’ bodies before the beginning of therapy are reintroduced after therapy to generate new marrow.

When autologous stem cell transplantation was first introduced, it was very risky. Now, techniques allow stem cells to be separated from other blood components and counted to ensure an adequate number have been collected. Thus, the risk has been greatly diminished; death from autologous stem cell transplantation now occurs in less than 2%–3% of patients.

Treatment strategies

When pain or dangerous side effects are present, as they are in about 80%–85% of newly diagnosed patients, it is important to rapidly achieve complete remission, or as close to it as possible, Dr. Alexanian said. Not only does a quick and complete remission help the patient avoid repeated cycles of potentially toxic therapy, but remission status after initial therapy is also a predictor of how long the patient will live. Complete remission is associated with a median overall survival of 10 years, while patients who achieve partial remission or no remission have median overall survival durations of 5 years and 2.5 years, respectively.

Usually, the first step in treatment is to try to induce remission through several rounds of chemotherapy at the highest dose acceptable for the patient. If the patient is a candidate for autologous stem cell transplantation, more intensive therapy can be given. Recently, combinations of bortezomib and lenalidomide with older drugs (bortezomib plus dexamethasone, bortezomib plus thalidomide and dexamethasone, and lenalidomide plus dexamethasone) have been shown to produce the best rates of complete remission in patients who also received a stem cell transplant, Dr.

Characteristics of Multiple Myeloma

Multiple myeloma (plasma cell cancer) progresses slowly, with the time from first cancer cell to diagnosis typically about 20 years. However, the disease is usually considered advanced and is causing serious health problems by the time it is discovered.

Diagnosis usually occurs between the ages of 55 and 80 years. As many as 65,000 patients in the United States are living with the disease, and more than 17,000 new cases are expected to be diagnosed this year.

Major symptoms include:

- Bone pain, generally in the spine or ribs. Myeloma cells cause bone reabsorption, which weakens bones and results in multiple lytic lesions (hence the name “multiple myeloma”)

- Constipation or changes in mental status caused by high levels of calcium being reabsorbed into the body
- Kidney damage or failure caused by high levels of calcium in the blood as well as high levels of monoclonal immunoglobulin produced by myeloma cells
- Anemia resulting from myeloma cells crowding out the bone marrow or from renal damage
- Immune system dysfunction
- Peripheral neuropathy

The disease can also manifest silently; 1 of 5 patients doesn’t have symptoms at the time of diagnosis, and the cancer is detected through screening blood tests or x-rays.

“Our goal is always to reduce the amount of myeloma cells in the bone marrow, hopefully to undetectable levels, with a minimum overall amount of therapy.”

– Dr. Robert Orlowski



Orlowski said. Complete remission can be achieved in at least 35%–40% of patients who receive both drug therapy and a transplant, and partial remission is seen in up to 95% of patients.

Unfortunately, not every patient is a candidate for stem cell transplantation. About 30% of multiple myeloma patients cannot undergo a transplant because their age or other medical problems increase the risk of the procedure beyond a safe range or because of socioeconomic factors. For this “nontransplant” population, less toxic drug combinations are available, Dr. Orlowski said. They include a melphalan-prednisone-bortezomib combination and a melphalan-prednisone-thalidomide (MPT) combination. In a recent clinical trial, treatment with MPT in the nontransplant population increased overall survival by 1.5 years over the old standard, melphalan plus prednisone. Without a stem cell transplant, complete remission can be achieved in 15%–30% of patients.

For the 15%–20% of patients who are not experiencing symptoms at the time of diagnosis, no immediate treatment may be needed. Rather, these patients may be monitored closely for several years, with therapy delayed until a risk of complications from the disease arises, at which point new, more effective therapies may be available.

Future directions

Despite the recent advances against multiple myeloma, there is much room for improvement, said Dr. Orlowski, who believes more widespread clinical testing is key to identifying future standard therapies. He cites bortezomib as an example of a breakthrough agent that first was tested in patients with relapsed and treatment-refractory multiple myeloma and then was found to be

effective against newly diagnosed disease. Without clinical trials, researchers would not have known whether it was worth the risk to make bortezomib a frontline therapy.

“When we move these active experimental drugs such as bortezomib into the front line, what we don’t know is whether they will still be as effective once the disease relapses,” said Dr. Orlowski. “The question is always, are we burning some bridges by using these therapies up front, in newly diagnosed multiple myeloma? I generally think it’s important to take that chance, because that’s when we have the best possibility of achieving a durable remission and a

longer survival.”

Clinical trials are also needed to help validate research into multiple myeloma’s genetic signature. It is now believed that the disease comprises seven or eight distinct subtypes defined by different genetic abnormalities. For example, up to half of all cases are associated with chromosome 13 monosomy, which predicts poor outcome in multiple myeloma patients. “Even though patients with chromosome 13 monosomy and certain translocations benefit less from the current standard therapies, they might benefit from having novel therapies such as bortezomib and lenalidomide in their treatment regimens,” Dr. Orlowski said. “We want to identify appropriate therapy for patients based on the genetic subtype of their myeloma. Doing so could help us achieve greater response and remission rates with initial therapy, which will then lead to longer survival for more patients.” ●

For more information, call Dr. Orlowski or Dr. Alexanian at 713-792-2860.

Clinical Trials in Multiple Myeloma

- **A Phase III Randomized, Double-Blind Study of Maintenance Therapy with CC5013 or Placebo Following Autologous Stem Cell Transplantation for Multiple Myeloma (CALGB100104).** Principal investigator (PI): Muzaffar H. Qazilbash, M.D. The goal of this clinical trial is to determine whether lenalidomide therapy and autologous stem cell transplantation can help control multiple myeloma better than transplantation alone.
 - **A Phase I Clinical Trial of Oral Vorinostat (MK-0683) in Combination with Bortezomib in Patients with Advanced Multiple Myeloma (2005-0438).** PI: Donna M. Weber, M.D. Vorinostat, or suberoylanilide hydroxamic acid (SAHA), has already been approved by the U.S. Food and Drug Administration to treat cutaneous T-cell lymphoma; this trial will study its use in multiple myeloma.
 - **A Randomized Phase II Trial of Two Stem Cell Doses to Reduce Transplant-Induced Symptom Burden in High-Risk Patients with Multiple Myeloma or Amyloidosis (2005-0601).** PI: Sergio A. Giralt, M.D. The goal of this clinical trial is to learn whether higher doses of stem cells can help decrease the symptoms that occur after treatment with high-dose melphalan.
 - **A Phase II Multicenter Study of CNTO 328 (Anti-IL-6 Monoclonal Antibody) in Subjects with Relapsed or Refractory Multiple Myeloma (2007-0479).** PI: Sheeba K. Thomas, M.D. This trial will study the effectiveness of CNTO 328 administered with or without dexamethasone for relapsed or refractory multiple myeloma. ●
- For more information on trials at M. D. Anderson, visit www.clinicaltrials.org.

Beyond Images: Advances in Interventional Radiology

By Sunni Hosemann

Today, interventional radiologists working in oncology consider few cancers inaccessible. These specialists use image guidance to treat tumors and tumor-related complications—often in the most difficult-to-reach places.

Like angioplasty, which was the first medical treatment to incorporate real-time image guidance, many interventional radiology procedures in oncology were developed as alternatives for when conventional treatments such as surgery were not possible. But some of these techniques have become so refined that they are now the convention rather than the alternative.

On any given day, medical and surgical oncologists at M. D. Anderson call on interventional radiologists not only to obtain biopsy samples but to relieve

obstructions, drain ducts and abscesses, ablate tumors nonsurgically, and embolize hemorrhaging vessels. These procedures often require extraordinary collaboration. “We bring an additional set of tools or options for the multidisciplinary team to consider as they tailor individual patients’ care,” said Ravi Murthy, M.D., an associate professor in the Section of Interventional Radiology at M. D. Anderson. More than four decades after the advent of interventional radiology, those options are being applied in increasingly inventive and beneficial ways.

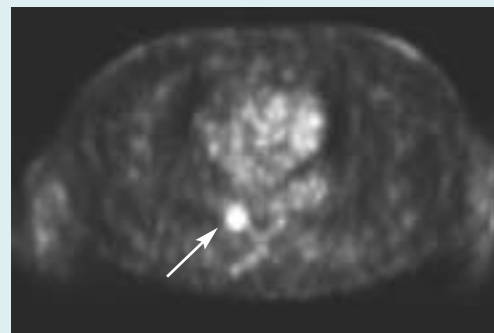
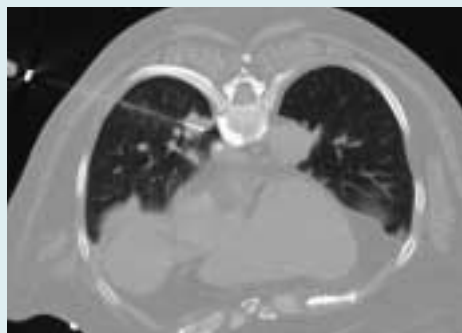
Diagnosis

Image-guided tumor sampling, such as needle biopsy, is perhaps the most common cancer-related procedure performed by interventional radiologists. This longtime staple of the field continues to evolve. Current techniques allow interventional radiologists to sample lesions that were once considered inaccessible. Tumors in the mediastinum, for example, were traditionally difficult to access without an open thoracotomy. Without image guidance, probing the

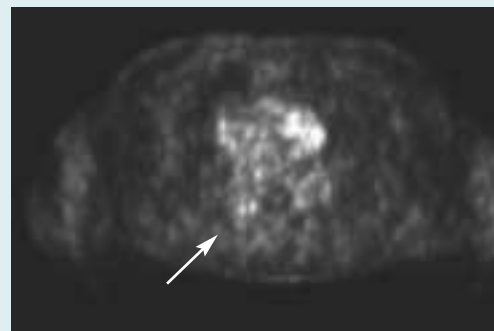
mediastinum with a needle can be perilous because of the high density of vital structures, including nerves, blood vessels, and the lungs. But with image guidance, percutaneous transthoracic needle biopsy allows relatively safe access to virtually all of the mediastinum, including areas that cannot be seen with endoscopic procedures such as bronchoscopy and mediastinoscopy.

Interventional radiologists must consider innovative approaches to avoid complications when directing a biopsy needle through the mediastinum to a lesion, according to Sanjay Gupta, M.D., an associate professor in the Section of Interventional Radiology. One such approach was developed after it was discovered that passing the needle through a loculated pleural effusion could reduce the risk of lung puncture. If an effusion is not present, the interventional radiologist can create such a “window” by injecting saline into the pleural space or positioning the patient in a way that allows pleural fluid to move into the necessary location.

Interventional Radiology Used to Treat a Lung Tumor



Radiofrequency ablation was used to treat this recurrent non-small cell lung cancer, which was initially treated with radiation therapy. Above, computed tomography shows the needle electrode inserted into the neoplasm. The electrode delivers a therapeutic dose of heat energy into the tumor. At right, positron emission tomography shows the metabolic activity of the tumor (designated by arrows) before (top) and after (bottom) the ablation therapy.



Treatment

As interventional radiologists have developed better techniques to access tumors for sampling, they have also developed new ways to treat neoplasms. Many of these treatments are adapted from traditional surgical techniques yet are typically less invasive and often as effective.

Nonsurgical ablation

Interventional radiology frequently is used to perform nonsurgical ablative therapies, including radiofrequency (heat) ablation, cryoablation (freezing), and the delivery of tumoricidal substances such as ethanol and acetic acid. Such ablative procedures were first used to treat liver metastases and were done during open surgery. “Now we can perform many ablative therapies without taking the patient to surgery,” said Kamran Ahrar, M.D., an associate professor in and medical director for the Section of Interventional Radiology. “This results in fewer complications, less morbidity, and less cost.”

Interventional radiologists now use radiofrequency ablation to treat primary and metastatic lesions in the lungs, kidneys, and bones, as well as the liver. Such procedures generally involve guiding a needle electrode into a growth and then delivering thermal energy through the electrode to kill the tumor.

In many cases, radiofrequency ablation is used as the primary treatment for a tumor—in osteoid osteoma, for example. This small, benign but painful tumor occurs in children, adolescents, and young adults and traditionally was treated with surgical resection. “Now, we place a needle inside the nidus of the tumor under computed tomography guidance and are able to ablate it in one treatment,” Dr. Ahrar said. The procedure is done on an outpatient basis, and patients are able to return to their normal activities immediately.

Embolization therapies

Some of the first interventional radiology procedures were developed in emergency settings for when no other treatment was available. For example, arterial embolization to stop upper gastrointestinal bleeding was first done

under emergency conditions. “Today, arterial embolization to control hemorrhage in patients with neoplastic disease is often a lifesaving procedure,” said Marshall Hicks, M.D., a professor in and deputy chair ad interim of the Department of Diagnostic Radiology. The same technique can be applied in similar situations to treat vascular problems that would otherwise preclude surgery, radiation, or chemotherapy, Dr. Hicks said.

One such example is partial splenic embolization, which is used to treat cancer patients who have developed thrombocytopenia that precludes chemotherapy. When the portal venous system is compromised by disease, as in liver cancer, or as a result of chemotherapy, hypersplenism develops. This causes platelets to sequester in the spleen, resulting in thrombocytopenia. Not only does platelet sequestration in the spleen make platelets unavailable, but there is evidence that these trapped cells contribute to the degradation of thrombopoietin, which further reduces already low platelet counts.

According to Michael Wallace, M.D., an associate professor in and chief of the Interventional Radiology Section, partial splenic embolization has been used to palliate these effects by reducing the volume of the spleen, thereby raising platelet counts and enabling patients to begin or resume chemotherapy. This procedure, performed while the patient is under intravenous sedation, is an acceptable alternative to splenectomy for managing hypersplenism in the context of hematologic abnormalities, portal hypertension, and venous congestion, as well as for treating malignancies that directly involve the spleen. “This is a reasonably tolerated, reasonably low-risk procedure,” Dr. Wallace said. “Patients typically go home in 4 days or so, and 95% of them are able to resume chemotherapy.”

In addition, embolization can be used to occlude the blood supply of a tumor, causing it to shrink and possibly die. Reducing a tumor’s size can also reduce symptoms and facilitate surgical resection of the tumor. Depending on the tumor site and the aims of the procedure, interventional radiologists can stop a

Interventional radiologists have developed ways to deliver therapy to a tumor via its blood supply.

tumor’s blood supply in a variety of ways. They can use metallic coils or gel foam to occlude large vessels or use particulate materials or liquid embolic agents to close small vessels. Furthermore, the advent of microcatheter technology has enabled interventional radiologists to access the necessary vessels without embolizing non-target tissues.

Other therapies

Being able to access a tumor’s blood supply means that interventional radiologists are also able to deliver chemotherapy infusions directly into neoplasms. And more recently, interventional radiologists have developed ways to deliver radiation to a tumor via its blood supply, providing an option for treating unresectable liver neoplasms, including hepatocellular carcinomas and metastatic colon, lung, and breast cancers, among others. Oncologists have had little success in treating these lesions once chemotherapy fails, and the use of external beam radiation has been limited by the liver’s sensitivity to radiation. (*Editor’s note: Please see the related story, “Radioembolotherapy Using Yttrium 90,” on page 6.*)

Future innovation and invention in interventional radiology will provide further novel options for multidisciplinary approaches in the treatment of cancer. “Imaging technology is becoming more sophisticated and refined all the time, and as a result, so is our ability to adapt image-guided procedures from medical, surgical, and radiation oncology,” Dr. Hicks said. “This growing range of therapeutic options ultimately results in better care for our patients.” ●

For more information, call M. D. Anderson’s Division of Diagnostic Imaging at 713-745-4794.

Radioembolotherapy Using Yttrium 90

By Sunni Hosemann

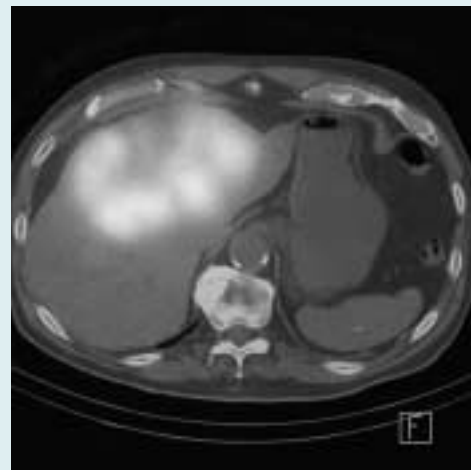
One of the newer applications of interventional radiology is a form of brachytherapy for unresectable liver neoplasms that uses glass or resin microspheres to carry yttrium 90 (^{90}Y), a high-energy, beta particle-emitting isotope. The microspheres, about the diameter of a human hair, are administered via a catheter by intra-arterial hepatic injection guided by fluoroscopy.

Once injected, the particles embed in the capillary network of the tumor. "The fact that this is not gamma radiation but short-penetrating beta radiation is of critical importance," said Ravi Murthy, M.D., an associate professor in the Section of Interventional Radiology at M. D. Anderson. "Because the radiation is effective on adjacent tissue but does not 'travel' beyond the tumor, there are minimal effects outside the tumor itself." Once placed, ^{90}Y emits therapeutic doses of radiation for the next few days.

This procedure takes advantage of the fact that liver neoplasms are highly vascular and receive their blood supply via the hepatic artery, whereas the liver parenchyma receives its blood supply primarily through the portal vein. Since the blood supplies are independent, the injection can target tumor tissue and spare normal tissue.

A detailed arteriogram of the vessels leading to the tumor is done prior to the procedure to detect anatomic variations and aberrant vessels. An important part of this interrogation is to identify potential ways for the radioactive microspheres to disperse to locations other than the intended target, such as the gastrointestinal tract. Variations in anatomy are not unusual. For example, the gastric arteries may branch from the left hepatic artery in some patients and from the common, proper, or right hepatic arteries in other patients. A detailed study of vessels branching from the hepatic artery to supply various other organs is therefore essential before delivering radioactive microspheres into the hepatic vasculature. When potential outflow vessels are found, they are occluded by small coils.

Liver tumors also have a tendency to cause arteriovenous shunting. In such cases, there is a danger that the



These images were taken in a 73-year-old man who underwent radioembolotherapy for an unresectable hepatocellular carcinoma. An intravenous contrast-enhanced computed tomography scan (left) shows the hypervascular tumor mass (designated with arrows). In an outpatient procedure, resin microspheres carrying a therapeutic dose of yttrium 90 were delivered via the hepatic artery under angiographic guidance. A post-implantation non-contrast-enhanced single photon emission computed tomography scan (right) demonstrates radioactivity (soft glow) confined to the tumor.

^{90}Y microspheres could pass through the tumor to the lung, causing radiation pneumonitis. To avoid this complication, a diagnostic dose of like-sized but harmless "surrogate" particles, technetium-99m-labeled macroaggregated albumin, is injected prior to radioembolotherapy. The distribution of the technetium-99m-labeled macroaggregated albumin will predict the distribution of the ^{90}Y microspheres, allowing the radiologist to detect any risks from arteriovenous shunting.

At M. D. Anderson, ^{90}Y radioembolotherapy of the liver is done with the patient under sedation, on an outpatient basis. Most patients experience mild side effects (fatigue and mild abdominal pain) for about 2 weeks following the procedure. Initially, treatments were given to half of the liver at a time, separated by a period of about 4 weeks, but with improvements in technique and supportive care, patients now generally receive only one treatment.

Currently, this procedure is offered only when other treatments have failed or are not feasible, but Dr. Murthy believes it has greater potential. "This treatment has a theoretical advantage in that it may significantly augment the benefits seen with systemic treatments

when administered early in the disease process in select patients. Furthermore, the mild toxicities associated with radioembolotherapy may offer an effective alternative to diseases that are traditionally combated with other more toxic embolotherapies," he said. And for that reason, he is eager to see it integrated into mainstream therapy.

To that end, two trials are approved to start this year. Dr. Murthy and colleagues Cathy Eng, M.D. (Gastrointestinal Medical Oncology) and Rodolfo Nuñez, M.D. (Nuclear Medicine) have designed a randomized, phase II clinical trial in which ^{90}Y microspheres will be combined with cetuximab and irinotecan to treat liver metastases in colon cancer patients. It is a hybrid treatment requiring an unusual level of collaboration for a study, but Dr. Murthy believes it has the potential to offer patients "the best of three worlds—medical oncology, nuclear medicine, and interventional radiology." The second trial is a pilot study of ^{90}Y radioembolotherapy in hepatocellular carcinoma patients, done in collaboration with Thomas Jefferson University and the University of Pittsburgh. Experiences from this study will be used to refine the cohort for an anticipated larger randomized trial. ●



A Guide to Radiation Therapy

More than half of everyone diagnosed with cancer will receive some form of radiation therapy. That's because radiation therapy is relatively safe and effective, and it may result in fewer physical side effects than other treatments, such as chemotherapy and surgery.

How radiation therapy works

Simply put, radiation is energy that travels as waves or extremely small particles. In radiation therapy, high doses of these invisible waves or particles are directed at cancer cells. The radiation damages the cells' DNA, causing them to eventually die or stop multiplying.

Sometimes cancer can be cured using radiation therapy alone or combined with chemotherapy or surgery. In other cases, radiation therapy cannot kill all the cancer cells, but it can shrink the tumor to relieve cancer-related symptoms. If radiation therapy cannot cure or shrink a tumor, it may be able to at least stop or slow the tumor's growth.

Radiation therapy can be external beam (delivered from the outside by a machine) or internal (delivered by a radioactive material embedded in or near the tumor). Both treatment methods are considered "local" because they take place at the site of the cancer, rather than throughout the body. The type of radiation therapy used depends on the type of cancer, its size and location, and other factors.

External beam radiation therapy

In *external beam radiation therapy*, a radiation-generating machine aims a beam of radiation at the cancer. The beam, which is painless, passes through the skin and hits the tumor.

Traditional radiation therapy uses

Radiation damages cancer cells' DNA, causing them to eventually die or stop multiplying.

multiple beams of energy that come from different directions and intersect at the tumor. Ideally, only the tumor receives the damaging dose of energy delivered by these intersecting beams, but the radiation can also harm healthy tissue nearby.

A newer technology called *intensity modulated radiation therapy* uses a three-dimensional map of the cancer to deliver the energy more precisely. Based on this map, a computer calculates different beam intensities and directions that allow the energy to be concentrated inside the tumor. Another newer technology is *proton beam radiation therapy*, which uses a beam of energy that goes into the tumor and then stops. Both intensity modulated radiation therapy and proton beam radiation therapy have much less potential for damaging the healthy tissue surrounding a tumor.

Usually, external beam radiation therapy is given in short, daily sessions for 2–10 weeks. The therapy itself is painless, and it doesn't make the patient radioactive.

Internal radiation therapy

Unlike external beam therapy, *internal radiation therapy* typically requires a small incision so the doctor can place small bits of radioactive material in or near the tumor. Those radioactive implants—often referred to as "seeds"—give off a cancer-killing dose of radiation for a few days or weeks (depending on the type of seed used) and then become harmless. The doctor may or may not have to remove the seeds after therapy.

Since internal radiation therapy involves an invasive procedure, a local anesthetic may be used to reduce discomfort. The radiation itself cannot be felt. However, depending on the dose, a brief hospital stay may be required while the radioactivity subsides.

Side effects

Doctors are getting better all the time at avoiding damage to healthy cells from radiation therapy. However, there is still a chance that healthy tissues will be harmed. This can cause a wide range of side effects, depending on the type of treatment:

- External beam radiation can cause skin irritation wherever the radiation enters the body. This side effect is common and usually temporary. Fatigue is another common side effect of radiation therapy, regardless of the site being treated.
- Radiation for head and neck cancers can result in mouth irritation, loss of taste, discomfort, and hair loss.
- Radiation for cancers in the pelvic area may cause reduced fertility, bladder problems, and digestive problems.
- Radiation for cancers in the breast and chest area can result in shortness of breath, problems swallowing, and changes in the breast.
- Radiation for cancers in the abdomen may cause vomiting, nausea, and diarrhea.

There is also a small chance that radiation therapy may cause a new cancer to develop years later. Patients considering radiation therapy should discuss with their doctors how this risk and others compare to the potential benefits. ●

Sources: *The National Cancer Institute and the American Cancer Society*

For more information, talk to your physician, or:

- call askMDAnderson at 1-877-632-6789
- visit www.mdanderson.org

OncoLog, July/August 2008
J. LeBas

©2008 The University of Texas
M. D. Anderson Cancer Center

Address Service Requested

IN BRIEF

Researchers Enhance Anticancer Activity of Natural Killer Cells in Laboratory

Histone deacetylase (HDAC) inhibitors and proteasome inhibitors increased the activity of natural killer (NK) cells against certain pediatric cancers, according to recent laboratory studies at M. D. Anderson. Researchers say the findings could lead to treatments that stimulate an effective immune response against cancer with less-toxic doses of therapeutic agents.

In their studies, researchers from the Children's Cancer Hospital at M. D. Anderson exposed NK cells and cancer cells to the HDAC inhibitors MS-275 and sodium valproate and the proteasome inhibitors bortezomib (Velcade) and NPI-0052. NK cells showed greater activity against cancer cells after exposure to the inhibitors in the lab, most often because the inhibitors increased the signaling activity of the cancer cells. As a result, the NK cells were better able to detect the cancer cells and then kill them. Additionally, MS-275 made the NK cells more sensitive to signaling from the cancer cells while simultaneously increasing the signaling activity.

The research team found that the HDAC therapy increased NK cells' effectiveness against osteosarcoma, while the

proteasome inhibitor therapy heightened the NK cells' activity in acute myelogenous leukemia and neuroblastoma cell lines.

Dean Lee, M.D., Ph.D., an assistant professor in Pediatrics and the senior investigator on the study, said enhancing the immune system's targeting of tumor cells offers the hope of not only killing more cancer but also allowing more healthy cells to survive, which would lessen toxicity. "We hope to develop therapies that don't rely on us administering

Enhancing the immune system's targeting of tumor cells offers the hope of not only killing more cancer but also allowing more healthy cells to survive.

more NK cells or more toxic chemotherapy but that marry the two to provide a synergistic, less toxic effect," Dr. Lee said.

Dr. Lee and co-investigators Shiguo Zhu, Ph.D., a postdoctoral fellow in Pediatrics, and Laurence Cooper, M.D., Ph.D., an associate professor in Pediatrics, presented their findings in May at the annual meeting of the American Society of Pediatric Hematology/Oncology. The team is currently researching NK cell-enhancing therapies in acute lymphocytic leukemia and medulloblastoma. ●

OncoLog

The University of Texas
M. D. Anderson Cancer Center

President

John Mendelsohn, M.D.

Provost and Executive Vice President

Raymond DuBois, M.D., Ph.D.

Senior Vice President for Academic Affairs

Stephen P. Tomasovic, Ph.D.

Director, Department of Scientific Publications

Walter J. Pagel

Managing Editor

John LeBas

Assistant Managing Editors

Joe Munch Maude Veech

Contributing Editors

Melissa G. Burkett Lionel Santibañez
Sunni Hosemann Ann M. Sutton

Design

The Very Idea®

Photography

Jim Lemoine

Editorial Board

Michael Fisch, M.D., Chair
Lyle Green, Vice Chair
Therese Bevers, M.D.
Robert Gagel, M.D.
Beverly Handy, M.D.
Patrick Hwu, M.D.
Charles Koller, M.D.
Maurie Markman, M.D.
Shreyaskumar Patel, M.D.
David Schwartz, M.D.
Rena Sellin, M.D.
Randal Weber, M.D.
Christopher Wood, M.D.

Physicians: To refer a patient or learn more about M. D. Anderson, please contact the Office of Physician Relations at 713-792-2202, 1-800-252-0502, or www.mdanderson.org/departments/physrelations.

Patients: To refer yourself to M. D. Anderson or learn more about our services, please call 1-877-632-6789 or visit www.mdanderson.org.

For questions or comments about *OncoLog*, please e-mail scientificpublications@mdanderson.org or call 713-792-3305. Current and previous issues are available online in English and Spanish at www.mdanderson.org/oncolog.

Made possible in part by a gift from the late Mrs. Harry C. Wiess.



A Comprehensive Cancer
Center Designated by the
National Cancer Institute