NEWYORK–PRESBYTERIAN
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Spring 2007

Update: Novel Therapies for Pancreatic Cancer

Pancreatic cancer remains among the most lethal cancers in adults, with a mortality rate of 90% within the first year following diagnosis. Still, new treatments have provided much hope, and Columbia and Weill Cornell researchers at NewYork-Presbyterian Hospital have been spearheading investigations into new compounds being developed and tested for specific molecular targets that may ultimately contribute to the fund of knowledge about which elements are critical to malignant growth.

"One agent is a virus that infects and kills pancreatic cancer cells with the RAS mutation, which is the most common mutation observed in pancreatic cancer," said Allyson J. Ocean, MD, who works with coinvestigators Maureen E. Lane, PhD, gastroenterologists Mark Pochapin, MD, and Felice Schnoll-Sussman, MD; and oncologist Joseph T. Ruggiero, MD. "We have been heavily involved in the preclinical work in cell lines and animals, and we are now working on the protocol for a clinical trial. There has already been some preliminary clinical work in other solid tumors, and we are very excited about its potential in pancreatic cancer."

NewYork-Presbyterian/Weill Cornell is part of the Pancreatic Cancer Research Team (PCRT), a national consortium created for both basic research and multicenter trials under the direction of Daniel Von Hoff, MD, of the Arizona Health Sciences Center. The PCRT, with which

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MammoSite's Results Present New Options, Opportunities

Case Study

The advantages of partial-breast radiation have long been recognized at NewYork-Presbyterian Hospital, where investigators have been leaders in developing and testing options for its delivery. Few other cancer centers in the world have comparable experience with this technique. Weill Cornell oncologists at NewYork-Presbyterian Hospital have a long history of using brachytherapy with iridium sources implanted at the time of surgery.

In 2002, a device called MammoSite, with a refined method of delivering brachytherapy, was approved by the FDA. Physicians at NewYork-Presbyterian/Weill Cornell began using the device soon after FDA approval. Such extensive experience with MammoSite has led to a clear understanding of which women are the best candidates for this or other forms of adjuvant therapy with

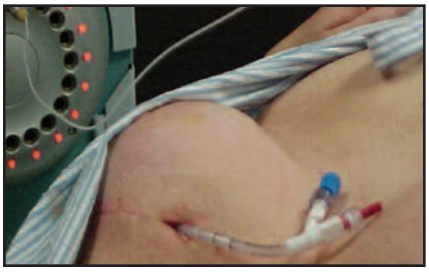

Photo courtesy of Dattatreyadu Nori, MD

In the MammoSite procedure, a balloon catheter is inserted into the surgical cavity left after removal of the tumor.

partial-breast radiation and which should still be treated with external-beam irradiation of the whole breast. Rather than just 1 or 2 approaches, oncologists at the Hospital consider a very broad array of options for each patient, including those within a clinical trial, which is possible at a leading treatment center.

"Our interest in partial-breast radiation is actually part of an overall approach to minimally invasive treatments for early-stage breast cancers,"

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INSIDE

Current Trends in Genitourinary Malignancies: Third Annual Conference
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UPDATES

NewYork-Presbyterian
The University Hospital of Columbia and Cornell

Hospital Explores Minimally Invasive Surgery in Ovarian Cancer

Although gynecologic cancers such as cervical and uterine are often treated with minimally invasive laparoscopy surgery, the technique remains an experimental procedure in selected patients with early-stage ovarian carcinoma, according to oncologists at NewYork-Presbyterian Hospital.

"Minimally invasive surgery is possible in a subset of carefully selected women," said Thomas Caputo, MD. For example, older patients with early-stage disease who cannot tolerate open surgery because of a higher likelihood of adverse events may be candidates for a laparoscopic procedure.

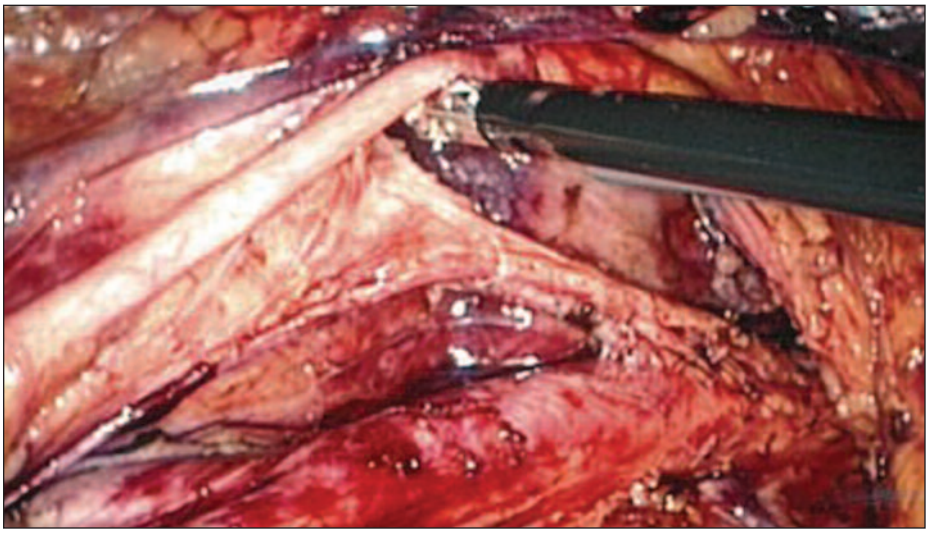

Photo courtesy of Thomas Herzog, MD.

Doctors perform paraaortic lymph node dissection for ovarian cancer using a laparoscope.

With early-stage disease, it is still possible to remove cancerous tissue through small incisions using a laparoscope if staging has been completed, said Dr. Caputo.

However, the majority of surgery in these patients is still performed using an open procedure. "Right now, the goal is to try and remove as much tumor as possible and we recommend being as aggressive as possible," he said.

Increasing the use of minimally invasive surgery for ovarian cancer may require more effective adjuvant chemotherapies to treat the remaining disease, noted Dr. Caputo. Better chemotherapies could be used to debulk tumors, the remainder of which could be removed with laparoscopy. "Researchers need to be looking for more active chemotherapy drugs and compounds," he said.

Although minimally invasive surgery is an option for early-stage disease, it is not well established for advanced cancer, said Thomas Herzog, MD. Most advanced cases require extensive surgery and debulking, which is performed using open incisions. Managing advanced ovarian tumors through a laparoscope can be difficult because organs such as the peritoneum and bowels need to be stripped, he explained.

Other areas of the body to which advanced disease may spread include the abdomen, diaphragm, and the pelvic region, added Dr. Caputo.

Performing debulking of these organs often would take too many hours through a laparoscope, said Dr. Herzog. However, with future technologic advances, physicians may one day be able to utilize laparoscopy for women with advanced ovarian cancer.

"We've seen tremendous improvement in minimally invasive surgical technologies," said Dr. Herzog. For example, cameras and equipment are better, as is the understanding of what physicians see through the scope, he said.

Although debulking late-stage ovarian cancer may not currently be a widely used option, laparoscopy is sometimes a useful tool for staging the disease in select patients, said Dr. Caputo. For diagnostic purposes, the laparoscope allows surgeons to determine whether patients should proceed with a debulking surgery, followed by chemotherapy, or whether the cancer is not debulkable, he explained.

"With a laparoscope you can look around and decide how much you can or cannot do," he said. However, he emphasized that using laparoscopy for staging patients with ovarian cancer is still experimental.

Gynecologic oncologists generally use laparoscopy to examine pelvic masses up to 10 cm, said Dr. Herzog. These masses are removed through laparoscopic ports and a frozen section examination is performed to determine whether or not the growth is cancerous, he explained. If results are malignant, the physician can determine the extent of the patient's disease by using laparoscopy and taking biopsies of the omentum, peritoneum, and pelvic lymph nodes.

Minimally invasive laparoscopy surgery is more often used to remove endometrial, uterine, and some cervical cancers—situations in which the tumor is not bulky and surrounding lymph nodes are small enough to come through port sites, said Dr. Caputo.

Physicians are able to accomplish the same lymph node yield through minimally invasive techniques as with open surgery, said Dr. Herzog. "Laparoscopy is usually the first option for many patients with endometrial and cervical cancers, and they are often able to go home the next day," he added.

"How much you really gain from robotics as compared to traditional laparoscopic gynecological surgery needs to be evaluated in a scientifically rigorous forum."

Thomas Herzog, MD

Improvements in treating gynecologic cancers with minimally invasive surgery may occur with new developments in robotics. In patients with ovarian cancer, minimally invasive robotic surgery, "might be used in some cases where precise dissection is required," said Dr. Herzog.

Regardless of the cancer type, 1 drawback of robotic laparoscopic surgery is that the physician loses tactical sensation, said Dr. Herzog. Benefits include the generation of 3-dimensional computer images and very little tremor.

"How much you really gain from robotics as compared to traditional laparoscopic gynecological surgery needs to be evaluated in a scientifically rigorous forum," said Dr. Herzog.

This type of study has already occurred in prostate cancer, and researchers found that robotics had advantages over traditional laparoscopy in certain cases, he said.

Ultimately, the type of surgery chosen for gynecologic cancers, whether open or minimally invasive, is based on each patient's individual needs, concluded Drs. Caputo and Herzog.

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NewYork-Presbyterian Oncology

is a publication of the Cancer Centers of NewYork-Presbyterian Hospital. The Cancer Centers are at the forefront of cancer screening and diagnosis, basic science, and clinical research. The Cancer Centers serve more than 6,500 new cancer patients each year, who receive state-of-the-art multidisciplinary care. The Cancer Centers include the NCI-designated Herbert Irving Comprehensive Cancer Center at NewYork-Presbyterian Hospital/Columbia University Medical Center and the Weill Cornell Cancer Center at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, which are respectively comprised of faculty from the Columbia University College of Physicians and Surgeons and the Weill Cornell Medical College.

NewYork-Presbyterian Oncology Editorial Board

NewYork-Presbyterian Hospital's Cancer Prevention Newsletter and Web site offer information for professionals on the latest developments in the field of cancer prevention and screening. Visit www.nypcancerprevention.org.

Pancreatic
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Robert L. Fine, MD and his team at NewYork-Presbyterian/Columbia also collaborate, provides access to a tumor bank that will increase resources for tissue samples; it also leads in studies of the broad array of agents that are coming forward in clinical development.

"The list of targeted agents with promise in pancreatic cancer is long and getting longer. In the PCRT, some of the agents in clinical development include aurora kinase inhibitors, polo-like-kinase-1 inhibitors, imidazoline small molecule compounds, Rav-12 monoclonal antibodies, angiogenesis inhibitors, and Src kinase inhibitors," Dr. Ocean said.

"We have developed 6 new regimens for pancreatic and neuroendocrine cancers that have been or will be translated to the clinic, and several are very promising," added Dr. Fine. "In studies that were recently completed with a new regimen, we anticipate the highest rates of response and survival ever achieved in patients with metastatic and inoperable non-metastatic pancreatic cancer." Although he cautioned results must be duplicated in large, Phase III studies, "the most encouraging aspect of this research is that it was conceived in our lab, so we understand the molecular and biochemical mechanisms, and this provides us with insight for modifying regimens for greater activity or safety.

"This work heavily depends upon experts in many fields," said Dr. Fine. According to Dr. Fine, surgeons John Chabot, MD; John D. Allendorf, MD; and Beth Shrope, MD; gastroenterologists Peter D. Stevens, MD; Harold Frucht, MD; and Stravos N. Stravopoulos, MD; pathologist Helen Remotti, MD; scientists Paul Brandt-Rauf, MD, PhD, ScD, and Gloria Su, PhD; and medical oncologists William H. Sherman, MD, and Michael J. Hall, MD; and other multidisciplinary research scientists have made vital contributions to this research.

"Without our laboratory scientists and the clinical expertise of my peers, the success of the translational research and clinical achievements would not be possible," Dr. Fine added. "Close collaborations of our cancer center scientists under the leadership of Ricardo Della-Favora, MD, facilitates the development of novel therapeutics at Columbia."

> **"The list of targeted agents with promise in pancreatic cancer is long and getting longer."**
>
> *—Allyson J. Ocean, MD*

The regimen providing the greatest activity so far observed is known as GTX (gemcitabine, docetaxel, and capecitabine), which demonstrated synergistic in vitro and substantial antitumor effects clinically in late-stage metastatic pancreatic cancers and is now being studied for earlier use in shrinking nonresectable tumors. The GTX work was presented at this year's annual meeting of the American Society of Clinical Oncology and the American Association of Cancer Researchers, but there are other exciting new therapies being developed and patented in Dr. Fine's lab. These include a new specific gene therapy that only kills cells with mutant ras/mutant p53; a peptide that only kills cancer cells with mutant p53; and a new form of chemotherapy that does not utilize the conventional toxic agents. Importantly, the gene therapy and the peptide also kill premalignant pancreatic, breast, and colon cells before they become cancers. All are moving forward toward clinical development.

At NewYork-Presbyterian Hospital, interdisciplinary collaboration is considered essential to the efforts to increase the ratio of cures to transient remissions. The primary goal of this collaboration is to increase the number of tumors that can be resected, which is the only treatment associated with significant rates of relapse-free survival. At NewYork-Presbyterian/Columbia, Dr. Fine works closely with Dr. Chabot, who has worked to expand the definitions of resectability. At NewYork-Presbyterian/Weill Cornell, Michael D. Lieberman, MD, has also been actively involved in collaborative efforts.

"We have recently been working to combine chemotherapy with therapeutic radiation in the neoadjuvant setting to increase the number of pancreatic cancers that can be made resectable," Dr. Ocean noted. Her team works in collaboration with radiation oncologist David Sherr, MD. "The question we are attempting to address is what is the best sequence and combination of modalities to achieve a maximum reduction in tumor size."

Understanding the pathophysiology and the vulnerabilities of pancreatic cancer is a recurring theme. At NewYork-Presbyterian/Weill Cornell, through collaboration with clinical investigators at the Jay Monahan Center for Gastrointestinal Health, there is a project to study pancreatic cystic neoplasms, which are premalignant lesions that may provide insight into the pathogenesis of pancreatic cancer. At NewYork-Presbyterian/Columbia, new mouse models for pancreatic cancer as well as cystic neoplasms of the pancreas developed by Dr. Su and the molecular and biochemical studies in pancreatic cancer have been fundamental to the progress in bringing new lab-based treatments to the clinic.

"This research provides a platform for a very novel and directed approach in which we hope that our therapies will be increasingly capable of killing malignant cells with minimal effects on normal tissues," noted Dr. Fine. "We are firmly dedicated to eradicating this formidable disease. The close collaboration between the scientists and clinicians at the Hospital will help us remain at the forefront of translational research in pancreatic cancer. The lessons learned will also be applicable to other malignancies with similar genetic defects such as lung, breast, and colon cancers."

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New Hematology/Oncology Chief Encourages Bi-Campus Collaboration at NewYork-Presbyterian

Edward P. Gelmann, MD, recently joined NewYork-Presbyterian Hospital/Columbia University Medical Center as the new Chief of the Division of Hematology and Oncology and the Deputy Director for Clinical Research of the Herbert Irving Comprehensive Cancer Center (HICCC).

Part of Dr. Gelmann's responsibilities is to facilitate collaboration between NewYork-Presbyterian/Columbia and NewYork-Presbyterian Hospital/Weill Cornell Medical Center. He is working with the Co-Chiefs of NewYork-Presbyterian/Weill Cornell's Hematology/Oncology Department, Barbara L. Hempstead, MD, and David M. Nanus, MD.

"The working relationship between the 2 campuses is a big priority," said Dr. Gelmann. As part of this relationship, both Hematology/Oncology Departments are working together to conduct joint clinical trials and to provide Web-based clinical trial information for patients and referring physicians. In addition, the HICCC is working to develop more interactive relationships with satellite research institutions and private practices.

Dr. Gelmann also has a number of goals in mind for the HICCC. "We plan to build a centralized infrastructure to support the conduct of clinical trials," he said.

This includes development of a comprehensive staff with uniform training, establishment of institutional guidelines, and use of information technology to make the clinical trial process more consistent throughout the Center.

Also on the agenda is expanding the HICCC's relationship with sponsors of clinical trials. "Sponsors need to know that the Center is responsive and a fertile ground for conducting research," Dr. Gelmann said. "They need to know that trials can be done expeditiously."

The HICCC is developing a more user-friendly interface with sponsors, various review agencies, and the Institutional Review Board (IRB). "Agencies and the IRB can be made more responsive, so turnaround time on clinical trial review is faster and the process is more transparent," he said.

> "Some of the more recent dramatic developments in cancer therapy have been based on findings in basic science."
>
> —*Edward P. Gelmann, MD*

Dr. Gelmann also has several objectives in mind for his role as Chief of Hematology/Oncology. For example, the division needs to develop clinical research programs that interface with and take advantage of the already high academic standards and accomplishments of NewYork-Presbyterian/Columbia, he said.

Specifically, Dr. Gelmann plans to establish a developmental therapeutics program, that will test new cancer agents at the earliest phases of clinical trials in humans. New cancer drugs and treatments are increasingly based on cancer genetics. Scientists are identifying specific genetic errors that cause a normal cell to become cancerous and then can develop drugs that block the function of the cancer-causing proteins. "Some of the more recent dramatic developments in cancer therapy have been based on findings in basic science," said Dr. Gelmann. "Developing new therapies will take a lot of astute experimentation because each type of cancer is unique."

Dr. Gelmann will also continue to pursue his own research interests. His laboratory at Georgetown University School of Medicine, in Washington, DC where he was most recently Chief of the Division of Clinical Sciences in the Department of Oncology, will be moving to NewYork-Presbyterian/Columbia. In this new location, he will collaborate with other leaders in genitourinary malignancies such as NewYork-Presbyterian's Daniel P. Petrylak, MD, Mitchell C. Benson, MD, and Carlos Cordon-Cardo, MD, PhD.

Dr. Gelmann's laboratory studies the prostate-specific homeodomain protein NKX3.1, a tumor suppressor that is commonly downregulated in prostate cancer in humans. In a recent publication, Dr. Gelmann and colleagues reported their finding that NKX3.1 can modify the activity of the DNA-resolving enzyme topoisomerase I, which may have implications for organ-specific DNA replication, transcription, or repair (*Cancer Res* 2007;67:455-467).

Another research interest is the androgen receptor gene. In the *Journal of Biological Chemistry* (2005;280:37853-37867), Dr. Gelmann and a colleague recently proposed that the multifunctional oncoprotein β-catenin "may play an integral role in formation of the androgen-receptor transcriptional complex."

Dr. Gelmann received his medical degree from Stanford University School of Medicine in Palo Alto, Calif, in 1976 and completed his internship and residency in the Department of Internal Medicine at the University of Chicago Hospitals and Clinics in 1978. He pursued a clinical fellowship in oncology at the Medicine Branch of the National Cancer Institute (NCI), which he completed in 1980. He was a medical staff fellow in the Institute's laboratory of tumor cell biology from 1979 to 1983.

In the years since, some of Dr. Gelmann's many academic appointments have included Senior Investigator in the Medicine Branch at the NCI; Professor of Medicine and Professor of Cell Biology at Georgetown University School of Medicine; and Director of the Lombardi Cancer Center Growth Regulation of Cancer Program at Georgetown University.

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Investigators Awarded Breast Cancer Research Grants

The Breast Cancer Research Foundation (BCRF) and the Susan G. Komen for the Cure Foundation have awarded research grants to study breast cancer to several Columbia and Weill Cornell investigators from NewYork-Presbyterian Hospital.

Four researchers from NewYork-Presbyterian were among 115 distinguished investigators from around the world selected to receive the 2006-2007 BCRF grants, which generally range from $225,000 to $250,000. A record-breaking $24.3 million in grants were awarded at the Foundation's annual symposium and luncheon held at the Waldorf Astoria in New York City in October.

The Foundation awarded 3 co-investigators, Regina Santella, PhD, Ruby Senie, PhD, and Mary Beth Terry, PhD, a grant to study environmental exposures and genetic susceptibility to breast cancer.

"We're finding that women who are unable to properly repair DNA damage have an increased risk of developing the disease," said Dr. Santella.

Genotyping has revealed that genes that remove bulky DNA adducts and damage from oxidative stress influence how diet and smoking impact breast cancer, she explained.

An important part of their research involves looking at patterns of mammographic density and how these are associated with various tumor characteristics, said Dr. Terry.

"We currently don't fully understand how density is associated with clinical and pathological factors," she said.

Over the next year, the researchers will use biospecimens and data from more than 500 women with breast cancer, in addition to more than 500 sisters who do not have the disease. They will expand research on how the ability to repair damaged DNA impacts breast cancer risk by investigating a repair pathway that fixes double-strand breaks in DNA.

Another part of this research will be to investigate the role of DNA methylation and its impact on breast cancer risk, and whether environmental exposures are associated with epigenetic changes.

The Foundation also awarded a BCRF 2006-2007 grant to Andrew Dannenberg, MD, who is co-investigating with Cliff Hudis, MD, of Memorial Sloan-Kettering Cancer Center. The doctors are studying the effect of nonsteroidal anti-inflammatory drugs (NSAIDs) on estrogen, a cause and promoter of growth of hormone-receptor–positive breast cancer.

"Ultimately, this research should both increase our understanding of how NSAIDs reduce the risk of breast cancer and provide insights into approaches for both preventing and treating breast cancer," said Dr. Dannenberg.

NSAIDs may impact breast cancer because they inhibit cyclooxygenase (COX) enzymes—COX-1 and COX–2—said Dr. Dannenberg. COX enzymes contribute to the production of prostaglandins that increase aromatase activity, thereby stimulating estrogen synthesis. Inhibitors of COX proteins block prostaglandin production and thereby reduce estrogen synthesis. This effect may contribute to the reduction in breast cancer incidence in women who take NSAIDs, but other anti-breast cancer effects are likely, said Dr. Dannenberg.

One of the goals of the 2006-2007 research project is to evaluate the relative importance of COX-1 and COX-2 as determinants of aromatase activity, he said. Inhibition of either enzyme results in a significant reduction in aromatase activity in cultured cells.

Consequently, NSAIDs that inhibit both COX enzymes, such as aspirin or ibuprofen, may be more effective than selective COX-2 inhibitors in suppressing estrogen production, explained Dr. Dannenberg. He and his co-investigator are comparing aspirin with COX-2 inhibitors to examine its ability to delay the development of experimental breast cancer.

Another research goal is to explore the

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> "This research should both increase our understanding of how NSAIDs reduce the risk of breast cancer and provide insights into approaches for both preventing and treating breast cancer."
>
> *—Andrew Dannenberg, MD*

MammoSite

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noted Alexander J. Swistel, MD. "The movement toward lumpectomy, which provides a similar degree of protection from recurrence when compared to mastectomy in node-negative tumors, was an early event to preserving quality of life. We have seen the same concept extend to lymph node dissection and now adjuvant radiation. The question arose, 'Why radiate the whole breast if partial-breast radiation can produce the same outcome of lowering recurrences?'"

In appropriate candidates, MammoSite and other partial-breast radiation strategies offer advantages over external-beam radiation to the whole breast. Primarily, the duration of therapy is shorter. Whereas a course of external-beam radiation to the whole breast is administered over 7 weeks on a daily basis, MammoSite therapy is administered over 5 days. The device is essentially a small balloon catheter inserted by the surgeon at the time of lumpectomy. Because MammoSite delivers radiation to the interior of the breast at the site where the tumor was resected, the risk for skin reactions or discoloration, often associated with external-beam radiation, is reduced. Other approaches to partial-breast irradiation have been tested, each with advantages and disadvantages. One approach is to deliver radiation to the tumor site at the time of resection. A risk of intraoperative treatment, however, is that it is delivered before the pathology report is completed. If the patient has positive margins, intraoperative treatment may complicate subsequent re-excision of the radiated lumpectomy bed.

"MammoSite is ideal for small tumors, and it is well tolerated," Dr. Swistel noted. "It can be used in much older women with good results. It avoids a lot of the side effects, such as fatigue, associated with higher doses of radiation over longer periods."

Appropriate candidates for the technique are selected in consultation with Mary Katherine Hayes, MD. Among the criteria used are distance from the lesion to the skin, symmetry of the balloon within the lesion cavity, and distance from the balloon to the chest wall.

"There must be at least 5 mm to 7 mm between the surface of the balloon and the skin," said Dattatreyudu Nori, MD. "We also have very firm criteria for defining the conformation volume of the inflated balloon on CT scan at the time of treatment relative to the conformation reported intraoperatively. We have performed more than 2,000 MammoSite treatments, and we have used our expertise to create guidelines to identify the optimal candidates for this procedure. We also offer patients 3-dimensional conformal radiation, which, like MammoSite, is delivered twice per day over 5 days. This is also a partial-breast radiation approach, but it is not as localized as MammoSite."

The Case

A 63-year-old high school principal with an abnormal result on mammography was diagnosed with a 0.5-cm invasive ductal carcinoma in the upper outer quadrant of her left breast. The patient was considered an excellent candidate for breast conservation and sentinel node dissection. When margins of the lumpectomy specimen prove negative and the node is clear, the next step to minimize the risk for recurrence is adjuvant whole-breast irradiation. Recently, in cases in which the tumor size is relatively small and the disease is diagnosed early, the concept of whole-breast irradiation has come under question, especially because local recurrence appears to arise within the same area of the breast as the original tumor.

In this case, the patient had heard about partial-breast radiation and expressed a preference for this treatment over whole-breast treatment; however, she wanted to know her options. Based on her pathology report, she was a candidate for partial-breast irradiation, which not only reduces the duration of treatment but is likely to achieve a better cosmetic result.

In the procedure, a balloon catheter is inserted into the surgical cavity left after removal of the tumor. The catheter can be placed at the time of resection or in a separate procedure. Before radiation is delivered, the balloon is inflated with saline and a contrast agent. This allows the tissue to conform to the balloon and permits more consistent irradiation to the target tissue. When the patient returns for treatment, which is delivered on an outpatient basis, a computerized radiation machine is used to insert a radioactive seed into the inflated balloon, providing a precise dose of radiation to the target tissue for a short period, after which it is removed. This treatment is repeated each day for up to 5 days. When node-negative women with breast cancer who undergo lumpectomy are given their options for adjuvant radiation, they generally prefer MammoSite, according to Dr. Nori. "Working women are especially enthusiastic because they can continue in their jobs due to the fact that treatment is so convenient and well tolerated," he added. "There is minimal to no pain or discomfort associated with the procedure."

Result

In this case, the treatment was indeed effective, and to date, the patient's cancer has not recurred.

Because of successes such as these, the MammoSite procedure is becoming more widely available. The American College of Radiology and the Radiation Oncology Treatment Group have opened a prospective randomized study to examine the efficacy of the methods used to deliver partial-breast irradiation. NewYork-Prebyterian/Weill Cornell was previously 1 of only 10 centers in the country that successfully completed a trial in which MammoSite was used to treat patients with ductal carcinoma in situ. Results continue to be encouraging, and this technique may eventually become the standard of care for patients with breast cancer who require adjuvant radiation therapy.

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connections between the several growth-promoting pathways contributing to breast cancer. For example, the researchers have shown that the receptor HER-2 causes increased amounts of aromatase activity and that this can be prevented with a COX inhibitor.

Similar work is being conducted to explore the link between COX enzyme activity and angiogenesis. Inhibiting COX can help reduce the formation of new blood vessels in experimental breast cancer, explained Dr. Dannenberg.

In addition to the BCRF grants, the Susan G. Komen for the Cure Foundation awarded Linda Vahdat, MD, $250,000 during its 2005-2006 funding cycle.

Dr. Vahdat and her colleagues will conduct a Phase II study of a copper-depletion compound called tetrathiomolybdate, an antiangiogenic agent, in 50 patients at high risk for breast cancer recurrence.

"We're hoping to understand factors that contribute to the breast tumor being dormant and occult for up to 15 to 20 years and then, all of a sudden, becoming active again," said Dr. Vahdat. Researchers also hope to discover whether they can interrupt this activation process with tetrathiomolybdate.

"We're hoping to understand factors that contribute to the breast tumor being dormant and occult for up to 15 to 20 years and then, all of a sudden, becoming active again."

—Linda Vahdat, MD

In the study, patients will orally ingest tetrathiomolybdate daily for 2 years. They will be evaluated with physical examinations and routine laboratory studies on a monthly basis, while imaging studies will be performed every 4 months.

Researchers will also evaluate circulating surrogate markers of angiogenesis at baseline, 1 month, and every 6 months for the trial duration.

Plasma angiogenic activity will be evaluated using an angiogenic assay and assessment and quantification of circulating endothelial and pro-angiogenic hematopoietic progenitor cells by flow cytometry and TUNEL assay. Researchers will also evaluate plasma vascular endothelial growth factor (VEGF)-A, VEGF-C, VEGF-D, thrombospondin-1, and histidine-rich glycoprotein.

"One day it may be possible for women to take a copper-depletion pill as part of their overall treatment plan, when they are diagnosed with breast cancer and keep the tumor dormant and occult forever," concluded Dr. Vahdat.

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NEWYORK-PRESBYTERIAN ONCOLOGY

Important news from the Cancer Centers of NewYork-Presbyterian Hospital, at the forefront of cancer prevention and screening, diagnosis, treatment, basic science, and clinical research.

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