

# NEW YORK-PRESBYTERIAN

## ONCOLOGY

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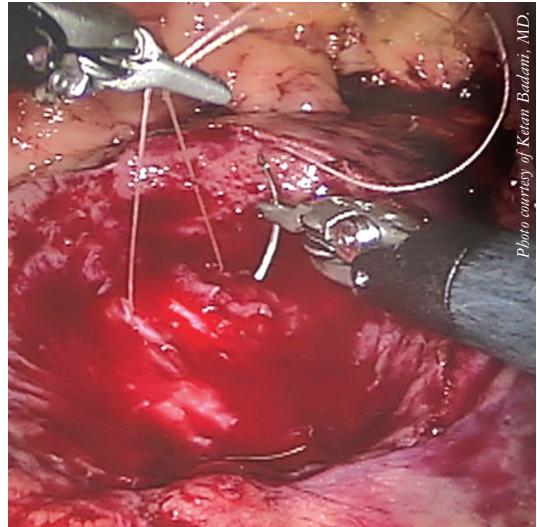
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## Novel Uses of Robotics for Bladder and Kidney

**R**obotic surgery, largely pioneered in surgery of the prostate, is rapidly being adapted for use in other organs. Columbia and Weill Cornell researchers at NewYork-Presbyterian Hospital now have significant experience with robotics for radical cystectomy—led by Douglas S. Scherr, MD—and groundbreaking work is also being done with robotics in partial nephrectomies under the direction of Ketan Badani, MD. The use of robotics in these procedures is providing the same advantages as in prostate resection, including dramatically faster recoveries with equal or better surgical precision.

"Robotic cystectomy allows a patient to receive the maximal treatment for bladder cancer through a minimally invasive approach," said Dr. Scherr. "In our series, the average length of stay is 5 days, versus 8 days for the standard, open technique. Although we are only beginning to collect long-term data, important oncologic end points, such as the number of lymph nodes removed and the margin status, indicate that the outcomes with robotic surgery are at least equivalent." In a recently conducted cost-benefit analysis, the reduction in recovery times yielded "substantial" costs savings as well.

Now, the experience in cystectomy, built from the success of prostate excisions, is accumulating rapidly. More than 100 robotic cystectomies for bladder cancer have been performed at NewYork-Presbyterian Hospital/Weill Cornell Medical Center and Mitchell C. Benson, MD, and James M. McKiernan, MD, at NewYork-Presbyterian Hospital/Columbia University Medical Center have had similar experiences. Robotic surgery has proved versatile and is easily adapted to different types of procedures, such as urinary diversions and



Robotic partial nephrectomy: The technology offers enhanced precision over laparoscopic approaches.

ileal conduit reconstructions. One of the advantages of the precision provided by robotics has been a reduction in complications, particularly blood loss. In a study published by Dr. Scherr and his co-investigators in the *British Journal of Urology*, the average transfusion requirement was reduced by 75% (0.5 vs 2.0 units;  $P=0.007$ ). To date, this is the only published data on transfusion requirements with robotic surgery.

"Robotics appears to be superior to the standard open technique in selected cases of bladder cancer," noted Dr. Scherr. "Based on the results so far, there is every reason to expect the long-term data to support the perioperative advantages. The reduction in

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## Studies Identify New Options for Breast Cancer

**A**t NewYork-Presbyterian Hospital, the treatment of breast cancer involves a comprehensive approach that includes reducing toxicities as well as improving outcomes. Initiatives designed to improve outcomes for patients with breast cancer are focused on an ambitious drug development program that often allows patients access to therapies not available outside of clinical trials, as well as an active prevention program that focuses on both

drugs and nutrients with the potential to inhibit the mechanisms of malignant transformation.

Among the most important recent advances for the treatment of metastatic breast cancer is a drug called ixabepilone, which was approved in late 2007. The drug is indicated for metastatic or locally advanced cancer resistant to taxane or anthracycline, and it can be combined with capecitabine or

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# Hospital Leading Studies of Myeloma, Related Diseases

**C**olumbia and Weill Cornell researchers at New York-Presbyterian Hospital are leading ongoing clinical studies of novel therapies for multiple myeloma that are setting new standards for treatment outcomes and patient quality of life during therapy. The researchers are carrying on a long tradition of therapeutic innovation at the Hospital, which historically has served as a key site for the development of agents with activity against this complex disease. Current initiatives include studies of targeted agents such as monoclonal antibodies as well as new options for treatment-naïve patients.

At New York-Presbyterian Hospital/Columbia University Medical Center, for example, research focuses on treatments for a wide spectrum of lymphoproliferative malignancies—not just multiple myeloma. Owen A. O'Connor, MD, PhD, who joined the Herbert Irving Comprehensive Cancer Center at New York-Presbyterian/Columbia last year as Director of the Lymphoid Development and Malignancy Program, has led clinical testing of several drugs that have now been approved for the treatment of hematologic malignancies, including vorinostat, which has become an important option in T-cell lymphomas. Vorinostat (also known as SAHA) was actually synthesized by Ronald Breslow, PhD, and his col-

leagues in the Department of Chemistry at Columbia University College of Physicians and Surgeons. Prior to joining New York-Presbyterian/Columbia, Dr. O'Connor also performed seminal work at Memorial Sloan-Kettering Cancer Center on the use of bortezomib in the treatment of mantle cell lymphoma; bortezomib had already been found to be effective in the treatment of multiple myeloma.

"We have a very large and highly active program for the development of new drugs in hematologic malignancies," noted Dr. O'Connor. "This ranges from drug discovery to preclinical testing and to evaluating novel agents and combinations for future clinical study. Our preclinical work provides the basis for understanding the underlying mechanisms of action for these agents, which becomes critical as we think about the best strategies for their future development. We have a team that has had experience guiding numerous drugs from the chemists' lab to the preclinical and clinical settings. Right now, there is no shortage of exciting targets or drugs for the treatment of these challenging cancers."

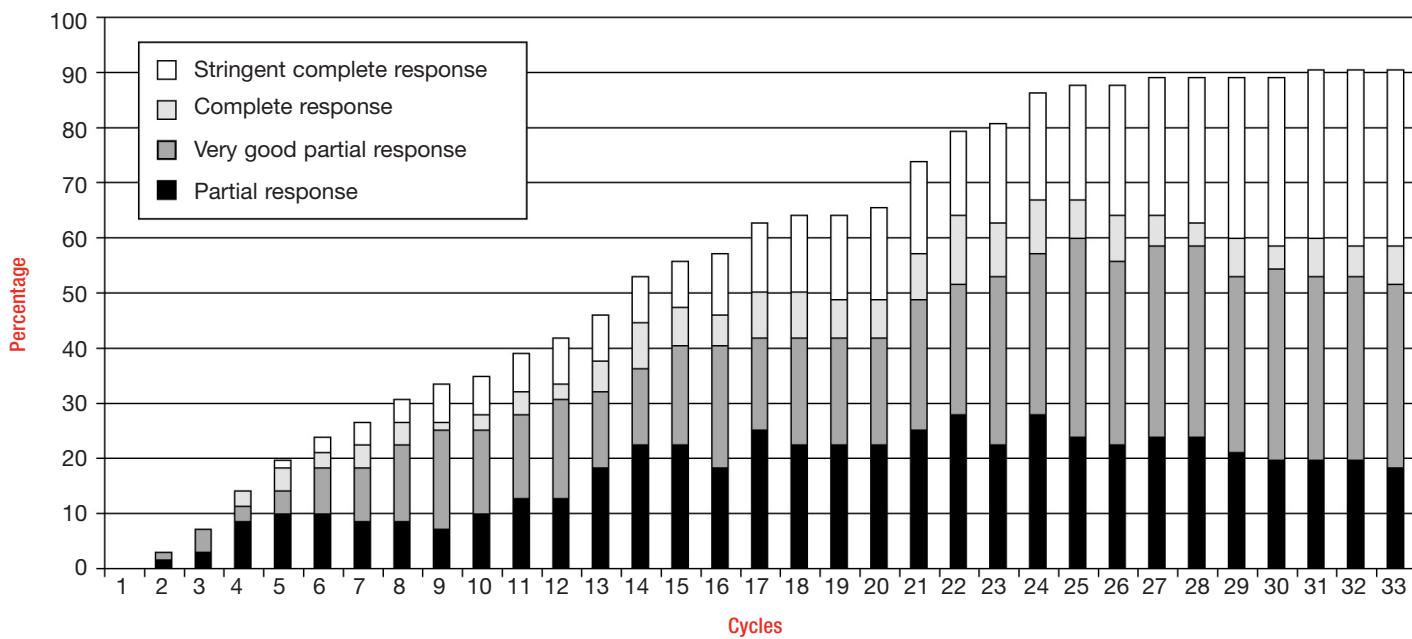
For example, based on preclinical studies conducted by Jill Mastrella in Dr. O'Connor's laboratory, the drug noscapine, used in Europe as a narcotic, emerged as a highly

active agent against multiple myeloma cell lines. "The drug is attractive because it is orally bioavailable and the activity against myeloma was very impressive in the preclinical animal models," Dr. O'Connor explained. "In addition to its activity, there has been no evidence of neuropathy so far. This has been an important toxicity for many drugs that work in the way we believe noscapine works."

Weill Cornell researchers at New York-Presbyterian Hospital, meanwhile, led clinical trials studying the efficacy of The BiRD (Biaxin [clarithromycin]/Revlimid [lenalidomide]/dexamethasone) regimen, now a standard for treatment-naïve patients with multiple myeloma (Figure). "In results we published in the February 2008 issue of *Blood*, the BiRD regimen achieved an impressive objective response of 90%, with a complete response rate of 39%," said Ruben Niesvizky, MD. "These are the highest response rates so far achieved in previously untreated patients, and it has provided a new benchmark."

Weill Cornell researchers are studying targeted therapies such as monoclonal antibodies that attach to cell surface markers on malignant cells or inhibitors of cyclin-dependent kinase, an enzyme that controls cell division and tumor survival. In the development of targeted therapies, according to

see **Myeloma**, page 6



**Figure.** Response to BiRD regimen.

Source: *Blood*. 2008;111(3):1101-1109.

**BiRD**, Biaxin (clarithromycin)/Revlimid (lenalidomide)/dexamethasone

# Dannenberg Appointed Head of New Cancer Center

NewYork-Presbyterian Hospital/Weill Cornell Medical Center has established a new Cancer Center—headed up by Andrew J. Dannenberg, MD—to further develop, coordinate, and advance basic, translational, and clinical research efforts, as well as enhance overall patient care.

NewYork-Presbyterian/Weill Cornell's Cancer Program is already a leader in cancer research, with renowned initiatives at the Arthur and Rochelle Belfer Institute of Hematology and Oncology, the Lehman Brothers Lung Cancer Research Center, and the Multiple Myeloma Center. According to Herbert Pardes, MD, President and CEO of NewYork-Presbyterian Hospital, the goal of the new Center is to transform what is already an excellent cancer program into a renowned cancer center, investing in both historically strong areas (ie, lymphoma, lung cancer, genitourinary cancer, and preventive oncology) while "establishing new programs that can be uniquely identified with NewYork-Presbyterian/Weill Cornell." As part of the Center's formation, Weill Cornell Medical College has committed 10 new positions for the recruitment of cancer biologists.

"The key to the success of this initiative will be collaboration and team science," noted Dr. Dannenberg. "Our program will facilitate interactions between physicians and scientists from a wide variety of fields—everything from hematology and oncology to radiology, surgery, urology, genetics, pediatrics, immunology, pharmacology, even communication sciences—helping them to create synergies that might not otherwise exist. These multidisciplinary collaborations should extend to our colleagues at Cornell University—Ithaca, Weill Cornell Medical College—Qatar, and the Methodist Hospital in Houston, TX. We also aim to improve our physical infrastructure, with additional lab space and shared resources to stimulate advances that are so badly needed."

Dr. Dannenberg is Director of Cancer Prevention at NewYork-Presbyterian/Weill Cornell and Henry R. Erle, MD—Roberts Family Professor of Medicine at Weill Cornell Medical College. He has received the Upjohn Achievement Award for scientific research, the American Liver Foundation Scholar Award, and the International Life Sciences Research

Foundation Award. He has authored more than 100 scientific articles and edited several books and journals, including *COX-2: A New Target for Cancer Prevention and Treatment*. Dr. Dannenberg is also a member of the American Society for Clinical

Investigation, the American Association for Cancer Research, the American Gastroenterological Association, the American Association for the Study of Liver Diseases, and the International Society of Cancer Chemoprevention.

## 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.

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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](http://www.nypcancerprevention.org).

## “Tailored” Radiation Improves Outcomes in Breast Cancer

**M**ajor initiatives are under way at NewYork-Presbyterian Hospital to tailor radiation therapy (RT) for patients with breast cancer with the goal of preserving efficacy but minimizing the burden to patients.

There are now a number of RT options available as part of breast-conserving therapy (Table, page 6). Some include more limited exposure of normal structures, such as the heart and lungs, to RT. There are also tools in development for assessing the RT-induced adverse late toxicities and cosmetic effects. One initiative has produced a reproducible and objective measure of late effects of radiation, such as a degree of fibrosis and change in skin color. These are crucial steps toward improving functional and aesthetic outcomes, as well as the overall quality of life of the growing population of breast cancer survivors.

Columbia and Weill Cornell physicians at NewYork-Presbyterian Hospital are taking a leading role in pursuing strategies to reduce the adverse sequelae of therapeutic irradiation to the normal tissues while reducing the overall length of the entire treatment. Radiation to the lumpectomy cavity alone, called partial breast irradiation (PBI), limits irradiation of the majority of the breast unaffected by cancer.

One example of PBI is treatment with MammoSite balloon brachytherapy (internal radiation), which has been employed by clinicians at the Stich Radiation Center at NewYork-Presbyterian Hospital/Weill Cornell Medical Center since its inception. So far, nearly 300 patients have been treated, and this approach has been associated with excellent local control rates, acceptable toxicities, and good to excellent cosmetic results. An alternative form of PBI, using external beam radiation therapy (EBRT), will soon be available in clinical studies. It is a noninvasive approach to targeting the lumpectomy cavity and has normal tissue-sparing advantages for carefully selected candidates.

“While brachytherapy has had an over a decade-long track record of good local control and cosmetic outcomes, as reported in randomized Phase III multicenter studies, partial breast irradiation with EBRT remains a subject of research investigation, with some promising results in terms of excellent control rates, a safe toxicity profile, and good to excellent cosmetic results as demonstrated

**“I think it is well recognized that there is an important need for an objective method to evaluate changes in the skin and soft tissues of the breast after radiation therapy.”**

—Shermian Woodhouse, MD



A physician measures fibrosis in the breast following radiation therapy.

by the Phase I/II studies,” said A. Gabriella Wernicke, MD. “In a clinical research protocol under way involving premenopausal women, a 1-week course of MammoSite brachytherapy is delivered in 10 treatments. In another, EBRT is being employed in postmenopausal women as a means to further reduce invasive procedures.”

Meanwhile, at NewYork-Presbyterian Hospital/Columbia University Medical Center, among the most significant recent initiatives is to assess the toxicity of radiation to the skin. The goal is to further minimize the impact of disease in breast cancer survivors.

“With breast conservation treatments, such as lumpectomy and partial breast radiation, we have the opportunity to reduce the impact of breast cancer, but many women experience significant changes in the quality of their skin at the site of radiation,” said Shermian Woodhouse, MD. “This can be an unwanted reminder of their cancer and can impose a negative psychological effect. In comparing treatments, one

of the problems we have had is the inability to objectively measure relative changes in skin color and quality. This is now an area of interest.”

Specifically, Dr. Woodhouse and her colleagues have developed tools that reproducibly measure the degree of erythema and change in melanin, which determine the color change, as well as edema and fibrosis, which contribute to the change in breast texture. The data testing the methods have been presented at several recent meetings, including the Radiological Society of North America in 2007. Although several previous methods have been proposed for grading skin after irradiation, none offers the same degree of reproducibility.

“Our methodology was very well received. I think it is well recognized that there is an important need for an objective method to evaluate changes in the skin and soft tissues of the breast after RT. Improving or preventing acute and chronic changes of the skin cannot be adequately addressed without

see **Radiation**, page 6

*Photo courtesy of A. Gabriella Wernicke, MD.*

# Surgeons Customize Therapy for Esophageal Cancer

National data show that only 15% to 25% of patients with esophageal cancer are likely to be alive at 5 years after initial surgical removal of their tumors. This is not so at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, where the cure rate at 5 years approaches 50% following surgical resection.

"For patients with premalignancies and those with very small tumors, we favor using endoscopic approaches to remove the tumor, with the goal of avoiding more radical surgery and retaining the native esophagus," explained Nasser Altorki, MD. "Such procedures are particularly useful in patients who are too old or too sick to have surgery."

Esophageal cancer is a rare disease in the United States, with only 12,000 new cases diagnosed annually. However, its incidence, and particularly the incidence of adenocarcinomas of the distal esophagus, has doubled since the 1970s. Reasons for this increase include a rise in the incidence of obesity and of gastroesophageal reflux disease, both of which are established risk factors for esophageal cancer.

According to Jeffrey L. Port, MD, minimally invasive and endoscopic techniques are important tools for the diagnosis and treatment of early esophageal cancer. They are particularly useful in screening patients with Barrett's esophagus, a condition that can be a

**"For patients with premalignancies and those with very small tumors, we favor using endoscopic approaches ... [and] avoiding more radical surgery."**

—Nasser Altorki, MD

precursor to esophageal carcinoma. In addition to the diagnostic role of endoscopy, endoscopic mucosal resection (EMR) and radio-frequency (RF) ablation may also be used to eliminate focal lesions in Barrett's esophagus patients who are found to have focal dysplastic lesions. Because EMR strips the esophagus of mucosal layers, Dr. Port also uses it to rule out invasive carcinoma. "These techniques have increased our diagnostic accuracy and hold the promise of controlling the progression of Barrett's esophagus to cancer," Dr. Port noted.

Although some carcinomas are detected early in patients with Barrett's esophagus, many are not preceded by that condition. Still others are not detected until they have already penetrated through to the esophageal submucosa and possibly metastasized to nearby lymph nodes.

"Minimally invasive procedures are perfect for early, small tumors but not for locally advanced cancers with full-thickness tumors or nodal spread, where conventional surgery works best in the long run," Dr. Altorki asserted. "Indeed, as the tumor grows deeper into the esophageal wall and lymph nodes

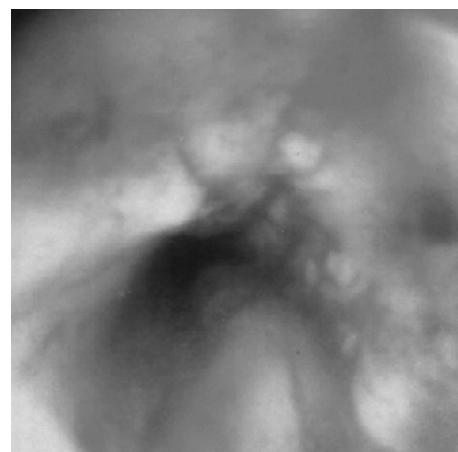
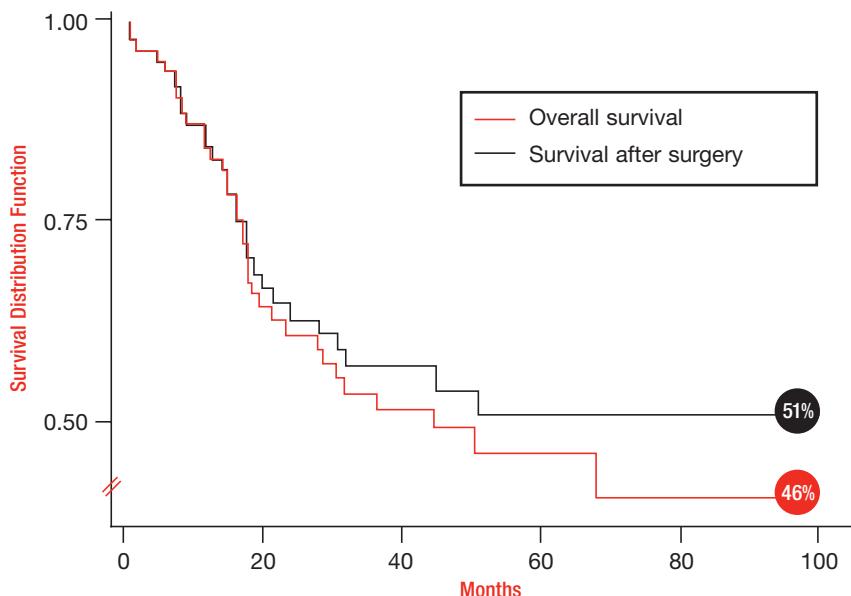


Image of esophageal cancer.

become involved, endoscopic techniques become ineffective and surgery becomes the only hope for a possible cure."

Drs. Altorki and Port have reported the most favorable outcomes—in terms of applicability, efficacy, and safety—in subgroups of advanced esophageal cancer patients following en bloc radical esophagectomy and 3-field lymph nodal dissection. The procedure is performed widely in Japan and is slowly gaining recognition in North America. They established the rationale for nodal dissection when they reported that 36% of esophageal cancer patients had clinically unsuspected cervicothoracic nodal involvement, regardless of cell type (*Ann Surg* 2002;236(2):177-183). Results from that prospective, longitudinal study of 111 esophageal cancer patients also revealed that 32% of those who underwent the surgery had their cancer upstaged as a result of operative findings. However, their most significant finding from that trial was that 51% of patients who underwent the surgery were alive 5 years postoperatively (Figure).

"Between endoscopic outpatient procedures, minimally invasive surgery, and conventional radical surgery, we maintain a number of viable options to suit the needs and stage of each individual patient," emphasized Dr. Altorki. "It is important to keep an open mind and have multiple tools in your tool bag to treat this disease."



**Figure.** Overall and disease-free survival following en bloc radical esophagectomy and 3-field lymph nodal dissection.

Adapted from *Ann Surg*. 2002;236(2):177-183.

Contributing faculty for this article:  
Nasser Altorki, MD; Jeffrey L. Port, MD

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Dr. Niesvizky, there may be an opportunity for not only more effective therapy, but better tolerated therapy.

"We have been accruing patients with relapsed or refractory multiple myeloma in a Phase II study with VEGF [vascular endothelial growth factor] trap, a recombinant human fusion protein that binds VEGF to prevent angiogenesis," he said. Like another clinical trial with a humanized monoclonal antibody targeted against CD-74, a cell surface receptor that is found on myeloma cells and is known to induce apoptosis, the results are not expected to yield a cure but may extend survival with a relatively low risk for significant adverse events.

Similarly, Ajai Chari, MD, who leads clinical trial efforts in plasma cell dyscrasias at New York-Presbyterian/Columbia, has launched a Phase I/II trial of noscapine in relapsed/refractory myeloma. Another agent under Phase I investigation is the novel selective and highly potent proteasome inhibitor carfilzomib, which, unlike bortezomib, does not appear to be associated with neuropathy. Further along in drug development is the novel heat shock protein inhibitor tanespimycin. The potential benefit of adding this agent to bortezomib is being investigated in a multicenter Phase III study.

Efforts are also ongoing to provide optimal high-dose therapy followed by autologous stem cell rescue for patients with multiple

myeloma. Although the timing of such transplants is controversial, even previously treated patients can achieve excellent responses with high-dose therapy. For patients from whom stem cells cannot be harvested with granulocyte-colony stimulating factor alone, the novel CXCR4 receptor antagonist AMD3100 has been successful.

"We are also comparing various methods of screening for residual disease after transplant to better select patients that may require consolidation therapy, and hopefully identify pathogenetic markers that might serve as targets for novel therapy," said Dr. Chari.

Contributing faculty for this article:  
**Ajai Chari, MD; Ruben Niesvizky, MD;**  
**Owen A. O'Connor, MD, PhD**

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accurate and objective means of measuring these changes," Dr. Woodhouse reported. "Hopefully, our work will lead to better ways to not only assess but also treat the toxicity from these various treatment options and accurately inform patients about differences between treatments."

The leadership taken by investigators at New York-Presbyterian Hospital means patients will have access to all treatment modalities years before the results of the ongoing national randomized clinical trial become available. "We believe that, for women meeting the eligibility criteria, PBI offers an enhanced quality of life during

treatment through a more convenient schedule," Dr. Wernicke noted. "As the principal investigator of the above-mentioned trials, I am convinced that we offer a team effort of careful screening and follow-up, state-of-the-art treatment planning, and cutting-edge technology so as to ensure delivery of high-quality therapy to eligible patients."

Dr. Wernicke's clinical and research interest in RT-induced fibrosis (RIF) as a late sequela of RT has led her to develop a more precise and objective methodology of its early detection and assessment. Her work on RIF was presented at the 49th research meeting at the American Society for Therapeutic

Radiology and Oncology and at an American Society of Clinical Oncology Breast Cancer Symposium in 2007, and it has been accepted for presentation at the American College of Radiology meeting in 2008.

"The key to precise and early detection of RIF is the ability to provide an early intervention for functional and cosmetic outcomes prior to RIF's stabilization and transformation into the irreversible state," said Dr. Wernicke. "Potentially, we will strive to identify patients who have a genetic predisposition to developing RIF with the goal of preventing its occurrence."

Contributing faculty for this article:  
**A. Gabriella Wernicke, MD; Sherman Woodhouse, MD**

**Table. Techniques of RT Delivery as Part of Adjuvant Therapy of Breast Cancer**

RT Option	Technique of RT	Equipment/Device	Planning System	Duration of Therapy	Number of Treatments Per Day	Level of Evidence
1	Conventional EBRT to the whole breast tangents	Linear accelerator EBRT	CT-based	6-7 wk	1	I
2	PBI to the lumpectomy cavity (interstitial brachytherapy)	Remote afterloading of interstitial catheters	CT-based	1 wk	NA	I
3	PBI to the lumpectomy cavity (intracavitary brachytherapy)	MammoSite balloon	CT-based	1 wk	2	I
4	PBI to the lumpectomy cavity (EBRT)	Trilogy/linear accelerator EBRT/IMRT	CT-based	2 wk	1	II

Note: Option 3 for selected premenopausal women and option 4 for post-menopausal women are available through clinical research protocols at New York-Presbyterian/Weill Cornell. An ongoing national multicenter randomized clinical trial (NSABP B-39) compares RT option 1 with RT options 2-4.

**CT**, computed tomography; **EBRT**, external beam radiation therapy; **IMRT**, intensity-modulated radiation therapy; **NA**, not applicable; **PBI**, partial breast irradiation; **RT**, radiation therapy

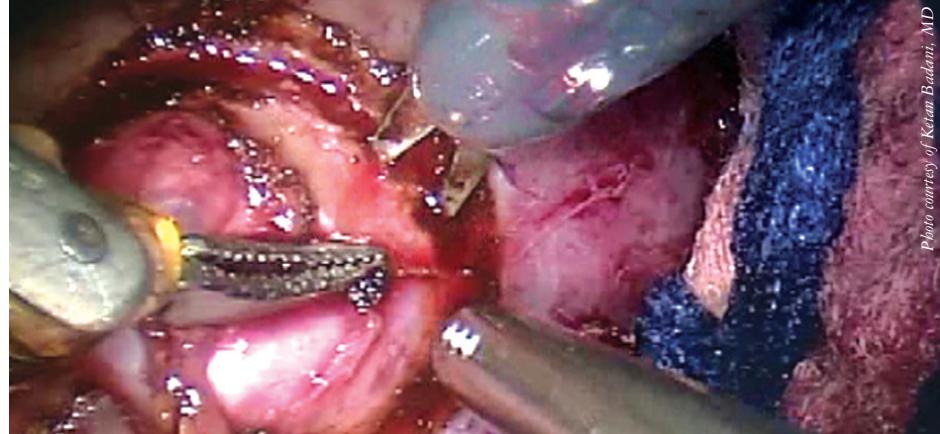
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recovery time is a major advantage for patients."

In cancer of the kidney, the use of robotic surgery is in an earlier stage of development, but the results of work being performed by Dr. Badani at New York-Presbyterian Hospital/Columbia University Medical Center are also very encouraging. Dr. Badani developed his robotic skills in prostate surgery, primarily at Henry Ford Hospital in Detroit, with which he was affiliated before coming to the Hospital. In fact, New York-Presbyterian Hospital is the only hospital in New York City with the latest-generation da Vinci S Surgical System, which has been instrumental in developing partial nephrectomy techniques. Robotic partial nephrectomy is also offered at New York-Presbyterian/Weill Cornell, although it is more commonly done with a laparoscopic minimally invasive approach.

"With robotics, there is a much greater opportunity for complex reconstruction of the kidney than can typically be achieved with a standard laparoscopic approach," said Dr. Badani. "This means that, hopefully, we have an opportunity not only to reduce the need for patients to require a kidney transplant, but also their need for dialysis later in life." As in cystectomy, robotic surgery in the kidney is associated with a reduction in blood loss and a faster recovery. Some patients are discharged the day after surgery.

"Robotics provides better visualization



Robotics provides better visualization and better surgical planning.

and better surgical planning," he continued. "The current instrumentation provides a very good range of motion, permitting complex surgeries that would be difficult to perform laparoscopically."

Although he cautioned that a robotic technique is not appropriate for all patients who are candidates for partial nephrectomy, he believes that robotics will become a gold standard in those who are. Some of the same relative advantages observed in prostatectomy, notably decreased blood loss and faster recovery time, make it likely that outcomes will be better with robotics, but even a similar outcome would favor a robotic approach.

To date, there is little published data on the efficacy of robotics in partial nephrectomy; however, small studies have indicated that the precision of robotic systems is particularly useful in the resection of smaller

tumors (<2 cm) and that suturing is easier.

The work in cystectomy and partial nephrectomy is an extension of the successful robotic surgeries performed in the prostate, but they are only the next stage in a program that is likely to continue to expand. Dr. Badani cited work being undertaken with robotics in pelvic floor reconstruction and repair of vaginal wall prolapse. For cases in which robotics is feasible, there appear to be no disadvantages so far.

"In the prostate, data suggest that the robotic surgery is more precise and permits better preservation of sexual function and less risk of urinary incontinence," he said. "As we develop more experience and improve on instrumentation, there are likely to be similar advantages in other organs."

Contributing faculty for this article:  
**Ketan Badani, MD; Douglas S. Scherr, MD.**

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used as monotherapy. It induces cell apoptosis by binding to tubulin and promoting tubulin polymerization and microtubule stabilization.

"It is a very effective drug in a population for which there have been limited options. We have been working with this agent in the clinic for 6 years, so many of our patients were able to benefit from this agent before it was widely available," said Linda Vahdat, MD, lead investigator on the Phase III trial. "I believe we have one of the most active clinical trials programs in breast cancer in the country, and several other drugs coming forward look promising."

One group of agents is called the epothilones, a new class of cytotoxic agents that have a mechanism similar to taxanes but are more soluble in water and have a dis-

similar resistance profile. A Weill Cornell research team led by Dr. Vahdat at New York-Presbyterian Hospital will serve as principal investigators in a registration trial of epithelone (ZK-Epo) that is now beginning to accrue patients.

"Our group published a paper in the *Journal of Clinical Oncology* a few months ago that evaluated joint symptoms in postmenopausal women taking adjuvant aromatase inhibitors," said Dawn L. Hershman, MD, MS. "It demonstrated that 47% of patients on one of these agents had joint pain, which is more than previously reported. When we conducted a multiple logistic regression analysis to identify risk factors, prior exposure to taxanes increased the risk of joint pain 4-fold. Understanding the risks as well as the benefits of breast cancer therapy is the first step toward

improving compliance with therapy. With more women surviving breast cancer and living longer, active lives, it is essential that we understand and try to avoid complications that will diminish the quality of that life."

In both the treatment of early-stage breast cancer and in cancer prevention, several novel agents show promise, but one of the challenges is the difficulty of confirming efficacy of these agents. Trials often require several thousand women and include 5 to 10 years of follow-up, which can be prohibitively expensive. Katherine Crew, MD, MS, reported that one of her areas of investigation is identifying intermediate markers that might be surrogates of clinical benefit.

"One example is breast density," she said. "Having dense breasts on a mammogram is

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a strong predictor of cancer risk. So this may be a useful marker in intervention trials to test novel agents for breast cancer prevention. Other markers we can look at include the rates of cell proliferation and apoptosis within the breast tissue." She added that some of their initiatives involve novel chemopreventive agents, such as high-dose vitamin D and the use of green tea extract, a study that is being supported by the National Cancer Institute.

"We are now moving into an area where we can individualize therapy based on the molecular genetics of each patient's cancer and target therapies to patients in a more sophisticated and rational way," added Dr. Hershman. "The Columbia clinical and basic science translational research teams at Herbert Irving Comprehensive Cancer Center at NewYork-Presbyterian/Columbia work hand-in-hand to exploit the findings from the large cadre of outstanding laboratory researchers. We use these findings to design novel therapeutic trials that we can offer our patients, and move the field forward for all women."

Another major interest of Dr. Vahdat involves the use of a copper-depletion compound, called tetrathiomolybdate, to prevent

angiogenesis; a trial is under way in women with breast cancer at high risk for relapse who have completed standard therapy but are looking for additional strategies that might help reduce the risk for tumors returning.

"We do not know what reignites malignant growth, but we do know that tumors cannot grow without a blood supply," she

said. "In a breast cancer animal model, copper depletion was highly effective in preventing metastases from forming. What was interesting in these studies was that when copper was restored, the growth of metastases began almost immediately."

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