


High Risk Lung Assessment Program

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intensive X-ray screening for lung cancer detected more cancers than were found in patients who were not screened intensively, but that there was no difference in mortality rates between the two groups after five years. This apparent contradiction might be explained by the theory that the screenings preferentially detected cancers that were slow-growing and less likely to cause death in patients than more aggressive forms of cancers that grow faster.

Some recent studies suggest that CT screening does improve survival outcomes, while others conclude the opposite. To determine the answer to this critical question, a large trial funded by the National Cancer Institute, currently in its fourth year, is studying over 50,000 smokers. Half will receive screenings by CT scan, and the other half by X-ray (based on the 1970s trials, X-ray screening is considered equal to no screening, or the negative control group). 

For more information, please call 800.543.2782.

PANCREATIC CANCER AWARENESS DAY

Are you or your family at risk?

This important program discusses the latest in screening, early detection, treatment options, and sources of support for patients and their families. Topics include:

- ❖ Risk Factors
- ❖ Breakthroughs in Minimal Access Detection, Screening, and Therapeutics
- ❖ New Imaging Techniques
- ❖ Surgical Options
- ❖ Chemotherapy Treatment

November 10, 2007, 1:00-3:00 pm

NewYork-Presbyterian/Columbia Faculty Club
630 West 168th St. 4th Floor, New York, NY


For information, contact Christine Rein at 201.346.7014.

Accelerated Partial Breast Irradiation

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lumpectomy,” Dr. Russo continues. “This could make it possible for more women to undergo breast preservation surgery (lumpectomy) instead of mastectomy, especially in areas where radiation facilities are not available.”

Although standard irradiation and APBI should both reduce the risk of local recurrence at the lumpectomy cavity, one concern with APBI is the risk of ‘elsewhere’ breast recurrence (i.e., in locations other than the lumpectomy cavity). A Phase III multicenter randomized clinical trial comparing whole breast irradiation to APBI is currently underway to evaluate the risk of local recurrence, acute and chronic toxicities, and quality of life associated with APBI compared to whole breast irradiation.

It should be noted that APBI is not offered to women with BRCA gene mutations, because of their increased risk of developing breast cancer. 

For more information, visit breastmd.org or call 800.543.2782.

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The **Breast Cancer in Women of Color** annual symposium took place Saturday September 22, 2007 in midtown Manhattan. Over 200 attendees participated and received the most up-to-date information about prevention, screening, and treatment of breast cancer in women of color. Columbia breast cancer faculty and visiting keynote speakers made for a wonderful and successful day of learning and sharing.




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“Together with colleagues at the Comprehensive Breast Center, we are making excellent progress in advancing the care of patients and women at risk. I am proud of these achievements.”

Mahmoud B. El-Tamer, MD, FACS
*Acting Chief, Breast Cancer Section
NewYork-Presbyterian Hospital/
Columbia University Medical Center*

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Breast Cancer


Innovations in Prevention, Detection, and Treatment

Breast Cancer. Striking women of all backgrounds, breast cancer exacts an enormous toll throughout our society. It is the second most common cancer affecting women (after skin cancer) and the second leading cause of death in women (after lung cancer). Some figures help to sketch its impact in this country:

- ❖ Approximately one in eight, or 13% of women, will develop invasive breast cancer;
- ❖ In 2007, about 178,000 women will be diagnosed with invasive breast cancer;
- ❖ About 40,000 women will die of the disease;
- ❖ There are over two million breast cancer survivors today;
- ❖ Over \$8 billion is spent on treatment every year.

These numbers tell just part of the story. Major strides are being made against this disease, both in research laboratories and in clinical practice. Public education has kept pace to the extent that one can hardly leave home without encountering a campaign to encourage annual mammography, or a local walk or run to raise funds for breast cancer research.

These efforts are clearly having effect. More women are undergoing screenings earlier, resulting in more cancers being detected at earlier stages. Many effective new therapies are now available, with still others right behind in the pipeline. The horizon holds promise of even better therapies, thanks to advances in genetic research that have enabled researchers to identify previously unidentified types of breast cancer with distinct biological characteristics and responses to therapy.

October is Breast Cancer Awareness Month. This special issue is dedicated to every person touched by breast cancer, and it salutes their physicians and caregivers who go beyond the call of duty every day. It aims to highlight some of the current advances in screening, prevention, treatment, and research at Columbia University, where the Breast Cancer Program stands at the forefront of some of the most exciting and promising work in the field today. 



John Baxendale

Screening for Breast Cancer

Understanding mammogram, ultrasound, and MRI

Most women wish to be responsible about screening for breast cancer, especially as incidence of the disease increases and virtually everyone is touched by it, either directly or indirectly. Routine breast screening can detect abnormal masses before symptoms appear, and before cancers have a chance to spread – often facilitating treatment early enough to save lives. Yet in the age in which “sound bite” health information can be superficial, unclear, and contradictory, it is easy to become confused about the correct way to proceed. Should one get a mammogram? Should one insist on newer tests such as MRI? What about ultrasound?

The goal of screening is to detect cancers at an early stage, before they are palpable and before they have spread. Mammography is the gold standard of breast screening and is the only screening tool that meets the criteria for what constitutes an efficacious screening tool, according to **Elise Desperito, MD**, *Director*

of Mammography, Columbia University Medical Center. In use for over 30 years, mammography involves a series of X-rays of the breast. Mammography has been proven in randomized controlled trials to produce statistically significant reductions in death, and women over age 40 should have a screening mammogram every year.

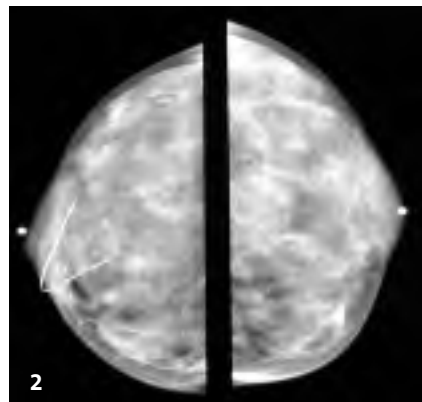
In light of the availability of other imaging tools, it is important to consider how sensitive mammography is, says Dr. Desperito, and to understand its benefits and limitations. “The sensitivity of mammography decreases as the density of the breast increases,” she says. Mammograms reveal the density of breast tissue, which is graded on a four-stage scale. Category 1 tissue consists of mostly fat, while category 4 tissue contains little fatty tissue, and almost all fibroglandular tissue. Mammography is 98% sensitive in women with fatty breasts, and 84% sensitive in women with dense breasts. “In women under age 50 with a family history

of breast cancer, studies have shown that the sensitivity of mammography can be as low as 70%.”

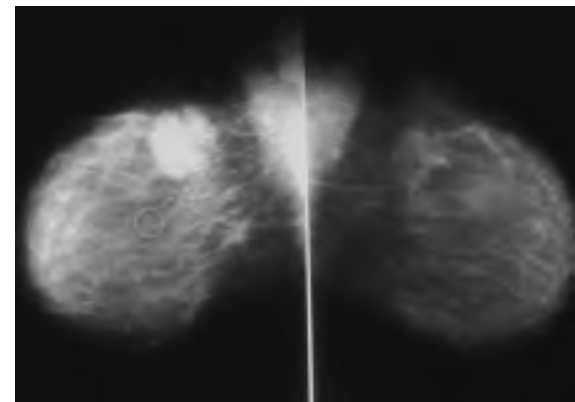
On the other hand, mammography has the ability to detect microcalcifications. Microcalcification can indicate the presence of ductal carcinoma in situ (DCIS), a very early stage of breast cancer. Microcalcifications are not detected by MRI or by ultrasound.

THE ROLE OF ULTRASOUND

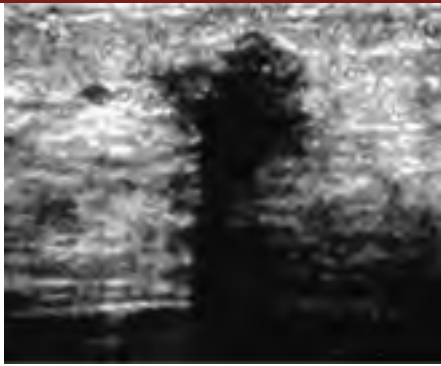
Some studies have shown that ultrasound can enhance cancer detection rates when used in addition to mammography. Ultrasound uses sound waves to create an image of the breast tissue. If an abnormality (such as an area of increased density) appears on a mammogram, ultrasound may be warranted for further evaluation, according to Dr. Desperito. If a woman has a palpable mass but nothing is detected by mammography, particularly in women with dense breast tissue,



The mammogram in figure 1 shows a fatty breast, with very little fibroglandular tissue. Figure 2 shows a very dense breast. The linear metallic marker indicates where this patient had previous surgery.



This mammogram shows a large mass at the top of the breast. The cancerous area (in white) is obvious in this patient because she has a relatively fatty breast. If the breast was very dense, it would be far more difficult to see the cancer because the breast tissue would also appear white rather than gray.



The dark area in this ultrasound image is a classic appearance of a cancerous mass, marked by its irregular borders and posterior shadowing.

ultrasound should be performed.

“Ultrasound is traditionally used to ‘problem-solve,’ such as to define a mass found by mammography. In these cases, ultrasound can differentiate between a simple cyst or solid mass,” Dr. Desperito explains. “In women at high risk for breast cancer, our experience tells us that ultrasound can detect cancers that we can’t see in mammography.”

Ultrasound is not yet considered a routine screening tool because studies have not determined its efficacy compared to mammography. A very large multicenter trial is currently underway to perform this comparison.

THE ROLE OF MRI

Over the last ten years, MRI has increasingly been used for evaluation of breast tissue. MRI, or magnetic resonance imaging, entails the use of intravenous contrast, which is taken up very quickly by cancer cells and shows up as bright areas on the computer screen. MRI is a very sensitive examination, Dr. Desperito explains: “Once a woman has a biopsy-proven breast cancer, we are using MRI to help us evaluate the extent of disease in that breast. It can help determine whether there are other areas of abnormal tissue near the biopsy-proven cancer, areas of abnormal tissue in other quadrants of the breast, or cancer in the other breast.”

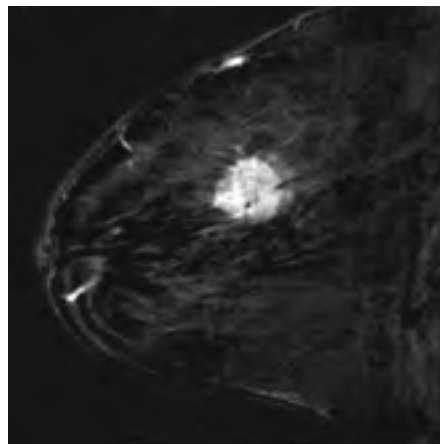
Nevertheless, even MRI has its limitations. “The enhancement we see in the breast tissue after the contrast is administered intravenously is not limited to abnormal or cancerous tissue. Normal

breast tissue can enhance just like abnormal tissue. As a result, there is a high false positive rate, which can lead to unnecessary biopsies and patient anxiety, and multiple follow-up exams.”


As a screening tool, MRI is most appropriate for patients at high risk. This category includes women who have at least a 20-25% chance of developing breast cancer:

- those with mutations of BRCA1/2 genes;
- women who have Hodgkins disease and have had radiation to the thorax;
- women with a family history of breast cancer (mother, daughter, sister);
- women who have had breast cancer; and
- in some cases, women with biopsy-proven high-risk lesions, atypia, or lobular carcinoma in situ may be considered for MRI.

The bottom line, says Dr. Desperito, is that breast imaging and breast screening can be complex and must involve dialogue with one’s physicians. Mammography may be sufficient for one patient, but not for another. There is often no simple answer, and no ‘cookie



A large mass is clearly enhanced (appears brightly) in this magnetic resonance image, compared to the surrounding normal tissue.

cutter’ approach. “As we have more tools available, it becomes more complex to use the right tools. Research is unfolding as we speak about how to best use these tools in order to best care for each patient,” she explains. 

To learn more, please visit breastmd.org or call 800.543.2782.

STAGES OF BREAST CANCER

Stage 0 (early stage): Includes findings of DCIS or Paget’s disease, but no actual tumor.

Stage I (early stage): Tumor no more than 2 cm across, with no spread to lymph nodes.

Stage II (early stage): Tumor 2 to 5 cm across, and cancer has spread to underarm lymph nodes.

Stage IIA: Tumor less than 2 cm with lymph node involvement, or cancer between 2 and 5 cm with no lymph node involvement.

Stage IIB: Tumor larger than 2 cm with lymph node involvement.

Stage III: Also called *locally advanced cancer*, tumor larger than 5 cm, with extensive cancer in underarm lymph nodes, or that has spread to other lymph node areas or tissues near the breast (such as above or below the clavicle).

Stage IIIA: Tumor larger than 5 cm with involvement of underarm lymph nodes. Any tumors fitting the description above.

Stage IIIB: As in IIIA, and associated with chest wall or skin involvement, or with spread to lymph node above the clavicle.

Stage IV: Cancer has spread to another organ in the body (also called metastatic cancer).

Prevention of Breast Cancer

Effective therapies for breast cancer are available and most women who develop breast cancer enjoy a very long survival. “But taking steps to lower the risk of its development remains the most effective way of decreasing the incidence of breast cancer and the mortality it causes,” according to **Katherine Crew, MD**,

Strategies for breast cancer prevention

First, all women at higher risk for breast cancer receive more intensive screenings than women without high risk factors. These screenings may include mammograms, ultrasound, and breast magnetic resonance imaging (MRI) exams. Equally important preventive measures include

drug, raloxifene, is approved for the treatment of osteoporosis and has fewer side effects than tamoxifen; this drug is currently pending FDA approval as an agent to reduce risk of breast cancer. “Within the next year, we will probably have two drugs approved for prevention,” says Dr. Crew.

PREVENTION RESEARCH

The Breast Cancer Program is conducting studies of several agents that may help to reduce the risk of breast cancer. Current studies include oral green tea extract, vitamin D, and others.

Oral Green Tea Extract

An antioxidant found in green tea may have antitumor effects, suggest epidemiologic and animal studies. Columbia is the lead center in a study funded by the National Cancer Institute to 1) determine the safety and appropriate dosage of the compound, and 2) examine the biologic effects of green tea in breast tissue. Eligible women include those who have already been treated for hormone receptor-negative breast cancer and who are at high risk of developing cancer in the opposite breast.

According to **Dawn L. Hershman, MD, MS**, Principal Investigator, the researchers will begin the study by conducting mammograms on each participant. After patients take oral green tea extract for six months, they will have a second mammogram. The researchers will look at changes in cell structure to see whether density of the breast tissue has been reduced, because lowering the breast density may reduce the risk of breast cancer.

Dr. Crew, Co-investigator of the green
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Katherine Crew, MD, consults with a patient.

Assistant Professor of Medicine and medical oncologist.

The Breast Cancer Program researches and administers a series of interventions to prevent breast cancer. Its efforts are directed primarily at women who do not have cancer, but who are at higher risk of developing breast cancer. These include women with atypical ductal hyperplasia, or abnormal growth of the cells lining the milk ducts; lobular carcinoma in situ (LCIS); and family history of breast cancer.

lifestyle changes such as a low fat diet, regular exercise, limiting alcohol intake to less than one drink per day, and maintaining an ideal body weight (obesity increases the risk of breast cancer).

Chemoprevention is the use of systemic agents to lower the risk of developing cancer. Tamoxifen is approved for use in prevention, but it is not used commonly for this purpose because of its side effects (including hot flashes, increased risk of uterine cancer, and blood clots). A similar

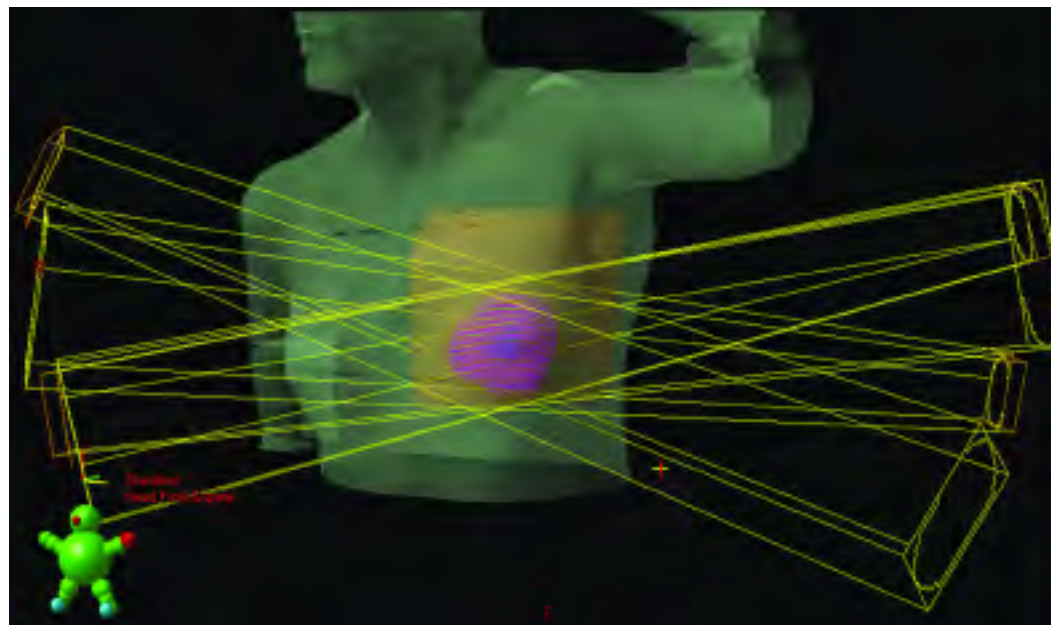
Accelerated Partial Breast Irradiation

Investigational procedure may make radiation therapy accessible to more women.

After undergoing a lumpectomy to remove the part of the breast affected by breast cancer, most women must undergo radiation therapy treatments to eliminate microscopic cancer cells that might remain undetected by clinical examination or breast imaging. The standard course delivers radiation to the entire breast, and consists of six to seven weeks of therapy, five days a week. For women who live far from their radiation facilities, the burden associated with daily trips for almost two months can be too much to bear. As a result, some women have curtailed therapy, or even foregone radiation therapy altogether, despite the increased risk of their cancers recurring.

A new kind of radiation therapy may now alleviate this travel burden and allow more women to complete this highly important therapy, according to **Sandra Russo, MD, PhD, MPH, Attending Radiation Oncologist**. Accelerated partial breast irradiation, or APBI, is a new form of radiation therapy under investigation for preventing recurrences in women who have undergone surgery for breast cancer. “APBI may be able to shorten the course of radiation from six or seven weeks to just one week,” Dr. Russo explains.

APBI is delivered directly to the cavity from which the breast cancer was removed rather than to the entire breast, and at a much higher daily dose compared to that used during the standard whole breast radiation therapy. Because the cumulative amount of radiation given during one week of high dose APBI is approximately equal to that delivered during six to seven weeks of daily low dose irradiation therapy, it is believed that the two methods may be equally



This figure shows the three-dimensional conformal radiation therapy (3D-CRT) APBI technique. This noninvasive method of delivering APBI uses multiple beams arranged to assure the optimal dose to the lumpectomy cavity while minimizing acute and chronic toxicity.

effective overall at decreasing the risk of recurrence at the lumpectomy cavity.

There are several methods by which radiation oncologists may deliver APBI to the lumpectomy site. These include an intracavity balloon brachytherapy (MammoSite®), multicatheter interstitial brachytherapy, intraoperative radiation therapy (IORT), and three-dimensional conformal external beam radiation (3D-CRT), which involves targeting external beam radiation therapy towards the lumpectomy cavity. All four methods may be used to deliver APBI and are under investigation to determine the optimal dose of radiation needed to achieve the lowest risk of recurrence with the least toxicity. Currently, the radiation oncologists at Columbia University are using 3D-CRT as part of a national clinical trial that is comparing lumpectomy followed by whole breast irradiation to APBI.

Acute effects after external beam radiation include local redness, swelling and tenderness, and occasionally, fatigue, while chronic side effects may include skin changes in the treated area, scar tissue formation in the treated area, and the risk of a local recurrence. According to Dr. Russo, most women undergoing either whole-breast radiation therapy or APBI continue their normal activities during their treatments since the acute side effects are well tolerated. “Although the chronic side effects of whole breast irradiation are well known, it will take years to assess the long term side effects of each APBI technique and the risk of ‘elsewhere’ recurrences.”

“It is hoped that by alleviating the time burden associated with breast irradiation, more women will complete the recommended course of radiation after

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Treating Breast Cancer

Quality of care — from survival to cosmetics

In treating breast cancer, the first priority is to provide treatments that will ensure patients' long-term survival. The next priority, says **Mahmoud El-Tamer, MD, FACS, Acting Chief, Breast Surgery Section**, is to prevent recurrences of the disease,

and third, to address quality of life issues such as cosmetic outcomes after surgery.

SURVIVAL

The **Comprehensive Breast Center**, part of Columbia University Medical Center's

Herbert Irving Comprehensive Cancer Center, is a multidisciplinary team comprised of breast surgeons, plastic and reconstructive surgeons, diagnostic radiologists, medical oncologists, pathologists, radiation oncologists, gynecologists, geneticists, psychiatrists, physical therapists, and nutritionists, as well as physician assistants and specialized nurses. These specialists are committed to providing the best care possible to women with breast disease. Their dedication, combined with academic and research capabilities and the full spectrum of diagnostic and therapeutic technology, result in the superior care that patients have come to expect from the center.

The center's survival rates testify to the depth of this team's commitment: compared to national and state averages, survival rates of patients treated at the Comprehensive Breast Center are consistently and significantly higher.

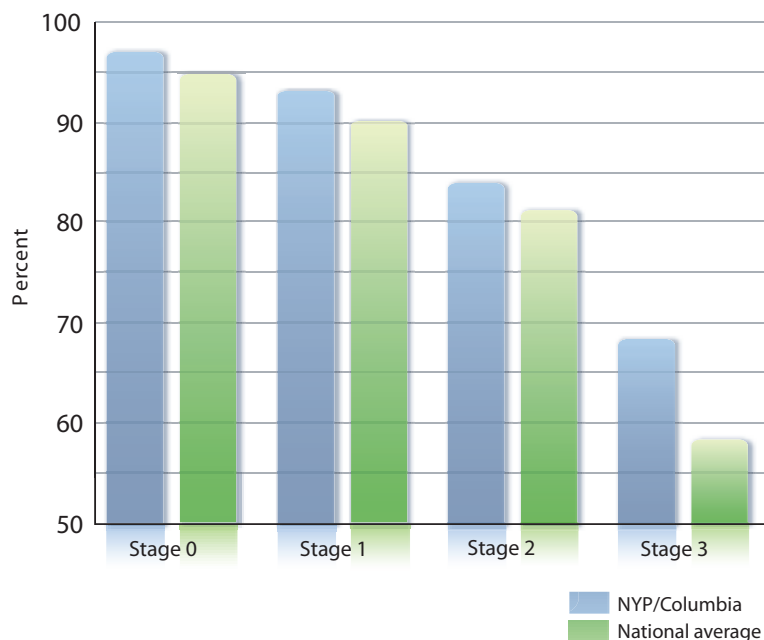
PREVENTING RECURRENCES

Patients who receive treatment at earlier stages of disease have a lower rate of recurrent disease than those who are diagnosed at later stages. On average, about 10-15% of women treated for breast cancer may have a recurrence in the breast, according to Dr. El-Tamer. Local recurrences occur at the site of the original cancer, while 'elsewhere' recurrences involve a different part of the breast, or the other breast.

The center uses surgery, radiation, and chemotherapy or hormonal therapy to help decrease the incidence of local recurrence. Since chemotherapy improves survival rates in patients with tumors that are one cm in size or larger, the center strives to give chemotherapy to the great-

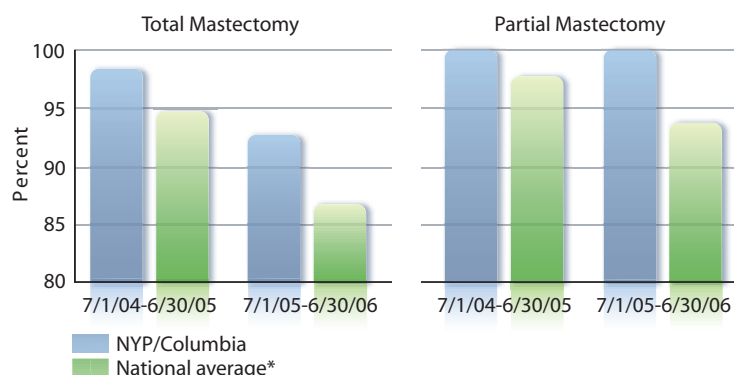
**Five-Year Survival Rate
Columbia Compared To National Average**

Patients were diagnosed with breast cancer in 1998.



* Stage 4 data not shown above; the number of cases is too low for confident analysis. National Average: data obtained from 296 teaching/research hospitals across the U.S.

Freedom From Post-Operative Complications



* Data obtained from 296 teaching/research hospitals across the U.S.

est percentage of women possible. Similarly, radiation therapy prevents cancer cells from progressing, replicating, and spreading. The Comprehensive Breast Center now offers partial breast irradiation (PBI), a new form that requires just one week rather than two months of daily therapy. PBI, also called APBI (accelerated partial breast irradiation), limits the application of radiation to the precise area in which a tumor was removed, rather than the entire breast. “In some centers, patients are not consistently offered these options,” explains Dr. El-Tamer.

Despite these therapies, some cancers are resistant to treatment, and some women are prone to developing recurrences. According to **Kathie-Ann Joseph, MD, MPH**, *Assistant Professor of Surgery and Director of Breast Cancer Surgical Research*, “If a patient has a recurrence after having had a lumpectomy and radiation, she will likely have to have a mastectomy. In addition to survival, this is another reason why it is so important to prevent recurrences through optimal treatment the first time.”

QUALITY OF LIFE

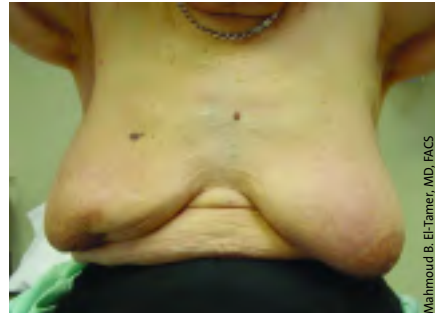
The Comprehensive Breast Center places paramount importance on its commitment to quality-of-life issues, according to Dr. El-Tamer. These issues include patients’ comfort and well-being during

SURGERY:

Mastectomy — removal of the whole breast, with or without removal of the underarm lymph nodes.

Lumpectomy — surgery to remove the tumor and a small amount of normal tissue around it.

This patient had cancer in both breasts. The right side was operated on at another institution and left the patient with visible indentation and deformity. Years later, Dr. El-Tamer removed cancer from her left breast using oncoplastic techniques, which resulted in the excellent appearance visible in the photo below.



This patient underwent oncoplastic surgery to remove a cancer from her right breast. The picture above shows the excellent cosmetic result three years later.

every stage of treatment, and satisfaction with cosmetic results in the long term.


“As a woman discusses treatment with her physician, she will want to know what kind of surgery will give her the best cosmetic results and leave her feeling whole,” says **Laura A. Klein, MD**, *Instructor in Clinical Surgery*. Patients who are able to retain their breasts adapt better than those who do not. Moreover, it is important that the breast be preserved in an acceptable shape and appearance. “When we perform breast preservation surgery, we aim not just to keep the breast, but to keep a breast that is cosmetically acceptable to the patient,” says Dr. Klein.

An emerging discipline called *oncoplastic surgery* combines the goals of eliminating the cancer and simultaneously

delivering a good cosmetic result.

One key technique in this approach is the *local advancement flap*, long used during breast reduction surgery. With this technique, the surgeon removes the cancer, then rotates the remaining tissue to reconstruct the breast. “This gives the woman an optimal appearance and leaves no indentations or defects,” according to Dr. Klein. “Thanks to creative oncoplastic techniques such as this, more women now have the option of lumpectomy with immediate local reconstruction, rather than mastectomy,” she says. In some cases, the surgeon may also reduce the size or alter the shape of the opposite breast in order to maintain a balanced appearance.

Women with DCIS (ductal carcinoma in situ), a noninvasive cancer, can also benefit from oncoplastic techniques. Because DCIS is distributed through the breast’s ductal system, sometimes it can be difficult to excise. Removal of DCIS may require removal of a substantial amount of breast tissue, and some patients have traditionally had to undergo mastectomy. Now, the creative use of oncoplastic methods is allowing many women with DCIS to keep their breasts intact and with excellent results.

“Many other centers do not offer these options,” says Dr. El-Tamer, in part because they require unique expertise, and in part because they require more time in the operating room to perform. The extra effort is worth it, however. “A very large percent of patients we operate on have a very good cosmetic result and are very satisfied,” he says. 

For more information, please visit breastmd.org or call 800.543.2782.

Imaging Breast Cancer

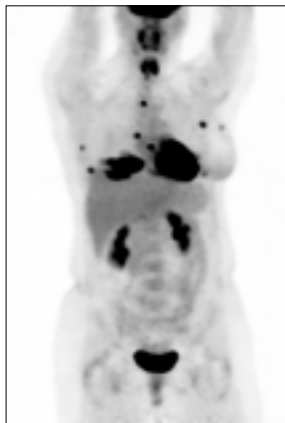
Role of PET and PET/CT in diagnosis and treatment

Although mammogram is the most commonly performed method of screening the breast, other imaging modalities such as ultrasound, magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) may be used to provide additional information to better locate and define abnormal findings. Among these, PET, and more recently PET/CT, fills certain imaging needs that the other modes cannot meet.

Unlike diagnostic imaging studies such as CT, which show the anatomical structures, PET scans reveal metabolic activity in the body. Bright hot spots can indicate the presence of tumors, which metabolize excess glucose and take up more of the radiolabeled tracer used during PET scans than areas that do not metabolize excess glucose.

Along with lung cancer, lymphoma, and colorectal cancer, breast cancer is among the top indications for which a PET scan is ordered, according to **Ronald Van Heertum, MD**, Director, Columbia Kreitchman PET Center. Although PET is not commonly used to evaluate breast lesions at early stages, it is very useful for patients whose tumor markers in the blood are increasing, which may indicate recurrent disease. “Rising cancer markers suggest the likelihood of a new tumor, but they don’t tell where in the body a new tumor may be located,” Dr. Van Heertum says. “PET and PET/CT can be used in such situations to define the presence of a new tumor or confirm the location of a suspected tumor.”

CT scans can reveal the size of lymph nodes, and usually nodes larger than 10 mm are considered abnormal. But



1) PET



2) CT



3) fused PET/CT

These scans were taken in April 2007, before the patient underwent chemotherapy.

The patient shown in these scans underwent a lumpectomy to remove a cancerous growth in her right breast in 2006. In the spring of 2007, a tumor recurrence was suspected and she was referred for a PET/CT study.

The bright areas on the initial PET/CT study (figure 3) and dark areas on the PET study (figure 1) reveal extensive disease recurrence in the right breast, with additional localized areas of spread in the left breast, bones, and left axilla (armpit).

After chemotherapy, the patient was referred back for a follow-up PET/CT study (figure 6). This revealed significant decrease in the extent of the cancer in the right breast and skeleton, but increased spread of disease in the left breast and left axilla. These changes can also be seen in the darkened areas on the post-chemotherapy PET scan (figure 4). These findings are consistent with a mixed response to treatment, according to Ronald Van Heertum, MD.

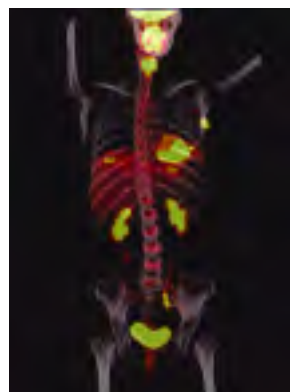
Although the CT scans (figures 2 and 5) were useful to help localize the patient's disease, they did not reveal the extent of disease.



4) PET

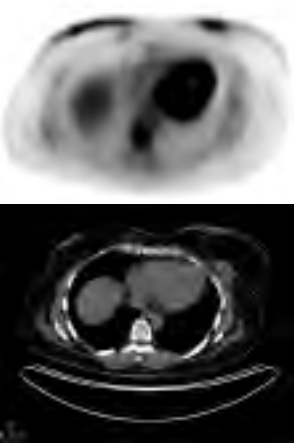


5) CT



6) fused PET/CT

These scans were taken in July 2007, after chemotherapy.




nodes can enlarge for reasons other than cancer, and CT can not distinguish the cause. PET can detect whether there is uptake caused by a tumor, regardless of size, and is more specific than CT.

GAUGING RESPONSE TO TREATMENT

Moreover, PET is highly useful in showing the extent of disease and a patient's response to treatment. Early on, patients with a new tumor may undergo PET after surgery in order to establish a baseline prior to treatment by chemotherapy or hormonal therapy. As treatment progresses, sequential PET scans can determine whether therapy is working, and how well. "PET is now proving to be a great way to follow patients to see if they are responding to treatment," says Dr. Van Heertum. "PET can be very effective in picking up recurrent disease and residual disease when a patient is undergoing treatment by chemotherapy or radiation."

Combined PET/CT scans are particularly useful for monitoring response to therapy, and the addition of anatomical information from CT defines the location of a mass very precisely for the purposes of performing biopsy or radiation therapy. According to Dr. Van Heertum, "Someone may have no evidence of disease on a CT scan but clearly increased metabolic activity on PET. Or, there may be no change on the CT scan, but a dramatic increase or decrease in metabolic activity on PET. This information affects patients' treatment very significantly."

In some cases, the combination of PET/CT can define lesions that would be impossible to clarify by PET or CT alone. For instance, a mass appearing on a CT scan could be a tumor, or it could be fibrosis (scarring) from radiation and surgery. There is no non-surgical way to identify which it is, short of monitoring over time to see whether it grows larger (which would indicate it is cancerous). Instead of waiting, the combined PET/CT scan provides a reliable indication of whether the mass is cancerous or not, without exploratory surgery.

Most insurers and Medicare reimburse for PET scans in the treatment of patients who have recurrent breast cancer. 

For referrals or more information about PET for breast cancer, call 212.923.1555.

APPLICATIONS OF PET AND PET/CT IMAGING

Cancer

PET and PET/CT offer an extremely high level of accuracy in detecting, staging, restaging, or monitoring treatment of nearly all types of cancer, including breast and ovarian cancer, as well as brain, colorectal, esophageal, liver, lung, lymphoma, kidney, pancreatic, thyroid, and many other cancers. In children, PET is particularly useful in the diagnosis of Hodgkin's disease and lymphoma.

Cardiology

PET can delineate blood-flow patterns and assess heart-muscle viability for cardiology patients, helping to establish the optimal treatment plan.

Neurology

PET can reveal abnormal patterns in the brain, helping to localize regions causing epileptic seizures, as well as differentiating among various dementia disorders, including Alzheimer's disease.

The Columbia Kreitchman PET Center works with referring physicians to verify benefits, including enrollment of patients in Medicare's National Oncologic PET Registry (NOPR), which is required for Medicare reimbursement of certain cancers.

For more information, please call 212.923.1555.

DETECTING AND DIAGNOSING OVARIAN CANCER

There is a correlation between breast and ovarian cancer: both are associated with abnormalities in the BRCA1 and BRCA2 genes.

As is the case with breast cancer, tumor markers are monitored after treatment of ovarian cancer for indications that treatment is successful. If these markers rise, the challenge is to discover why — false positives can occur, and if the patient has no symptoms, it can be difficult to determine the location of a new tumor. The use of PET can help to determine the presence of a localized mass, or if there is diffuse systemic disease. Because these types of cancer require very different treatments, the use of PET is extremely important.

PET is also invaluable in determining response to therapy in patients with ovarian cancer. "The only other way to determine whether treatment is effective is to perform surgery," says Dr. Van Heertum. "With PET, we can often see how well therapy is working without surgery."

Adjuvant Breast Cancer Treatment

Chemotherapy and hormonal therapies help to prevent recurrences in women diagnosed with early stage breast cancer

After surgery for breast cancer, the use of chemotherapy and/or hormonal therapy is an important part of strategies to prevent recurrences of the disease.

Adjuvant therapy is the use of these drugs after surgery to prevent the growth of cancer cells that may remain. Studies have

shown that adjuvant chemotherapy and/or hormonal therapy significantly increase women's chances of long-term survival.

cancer, according to **Dawn L. Hershman, MD, MS**, *Florence Irving Assistant Professor of Medicine & Epidemiology*, and *Co-Director of the Herbert Irving Cancer Center Breast Program*. "These systemic agents work either by blocking estrogen from stimulating the cancer cell (i.e. tamoxifen), or by reducing the amount of estrogen produced in the body (i.e. the aromatase inhibitors)," she explains.

Recent clinical trials have demonstrated that AIs are more effective than tamoxifen at reducing breast cancer recurrences in post-menopausal women, "but for pre-menopausal women, tamoxifen is the treatment of choice."

TREATMENT OPTIONS: CHEMOTHERAPY

Like hormonal therapies and AIs, chemotherapy refers to systemic drug therapies given either in pills or intravenously to shrink the size of existing tumors in patients with advanced disease, or to prevent recurrences in patients with early stage cancer.

According to Dr. Hershman, professional guidelines dating back to the early 1990's recommend that chemotherapy drugs be considered for all women with invasive breast cancer, especially those with positive lymph nodes or estrogen receptor (ER) negative tumors. "Nevertheless, despite its ability to help prevent recurrences among women with early stage breast cancer, chemotherapy is not appropriate for every patient." Dr. Hershman explains that determining who should receive chemotherapy is a complex question that involves many factors.

To navigate this challenging territory, the Breast Cancer Program uses many tools to guide treatment decisions.

A series of tests helps to gauge each

patient's risk based on the size of her tumor, its grade (how aggressive it is), whether or not it has spread to lymph nodes, and whether the tumor is hormone-receptor positive or not.

Among the more recently available tools is a new genetic test. This test assesses tumors for the expression of genes that are associated with risk of recurrence. Studies have shown that based upon the expression patterns of these genes, some patients are more likely to experience breast cancer recurrences. "Combined with evaluation of the tumor's physical characteristics, the profile of gene expression gives a more accurate assessment of a patient's risk of having recurrent cancer," explains Dr. Hershman. This added information provides valuable guidance during treatment decisions, particularly when the need for chemotherapy may be difficult to determine.

According to **Kathie-Ann Joseph, MD, MPH**, *Assistant Professor of Surgery and Director of Breast Cancer Surgical Research*, "This test is especially valuable for patients with hormone receptor positive, lymph node negative breast cancer – women who have traditionally been seen as low risk."

CANCER SURVIVORSHIP

Despite the known survival benefits of early breast cancer treatment, toxicity and side effects lead some women to avoid, curtail, or delay these treatments. Because dose reductions, treatment delays, or stopping treatment early can affect survival, it is critical to understand and predict which patients may be more susceptible to either the acute or late effects of cancer therapy.



Dawn L. Hershman, MD, MS

TREATMENT OPTIONS: HORMONAL THERAPY

The increase in breast cancer survival seen since 1990 is largely due to the benefits of hormonal therapies, such as tamoxifen and aromatase inhibitors (AIs), for the treatment of hormone-sensitive breast

Estrogen receptor (ER) negative cancer (also called *hormone receptor negative*) — cancer cells that do not need estrogen to grow, and are not affected by hormonal drugs.

Estrogen receptor (ER) positive cancer (also called *hormone receptor positive*) — cancer cells that need estrogen to grow, and may be treated by drugs that block estrogen from binding to them.

Neoadjuvant chemotherapy — chemotherapy administered before surgery. The purpose of neoadjuvant chemotherapy is to shrink a large tumor so that it can then be removed with a less extensive operation, or can be treated more effectively with radiation.

Adjuvant chemotherapy — chemotherapy administered after surgery to prevent the growth of any remaining cancer cells.

A multidisciplinary team of researchers led by Dr. Hershman is focused on understanding and preventing short-term and long-term effects of chemotherapy and hormonal therapy. The program is actively studying ways to reduce the side effects related to cancer treatments, improve quality of life, and improve adherence to life-saving treatment. Examples of their

According to results from the Study of Tamoxifen and Raloxifene, or STAR trial, both tamoxifen and raloxifene are equally effective at preventing breast cancer in post-menopausal women, but raloxifene has fewer side effects. Raloxifene has not been studied in pre-menopausal women.



research include the following:

- Understanding and treating bone loss associated with cancer treatment;
- Understanding cognitive side-effects associated with cancer treatment;
- Understanding and treating neurologic side effects associated with cancer treatment;
- Understanding and treating joint pain associated with the use of AIs;
- Interventions to improve exercise in minority breast cancer survivors;
- Understanding dental consequences of cancer therapies; and
- Evaluations of complementary and alternative medicines, and studies on post-treatment symptoms.

ADVANCED BREAST CANCER TREATMENT

Columbia's efforts to advance breast cancer treatment also include testing novel therapeutic agents to target cancer cells more directly, in efforts to increase efficacy and reduce toxicity. At this time, the program is studying chemotherapy in combination with drugs such as vorinostat, bevucizumab, tipifarnib, and others. In addition, the researchers are studying many drugs in early stages of development to evaluate their potential for the treatment of breast cancer.

Many patients treated at Columbia University Medical Center have participated in national clinical trials to study hormonal therapies and chemotherapies, and to better understand the optimal duration of their use. Appropriate candidates may participate in trials evaluating the newest chemotherapy treatments for early stage breast cancer. In addition, eligible patients may participate in national clinical trials to determine the efficacy of using genetic risk profiles to predict benefits from chemotherapy in addition to hormonal therapy. [!\[\]\(173968034f6ca6c36e25dcb8a274badd_img.jpg\)](#)

Prevention

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tea study, explains that the capsule form provides a pharmacologic dose of the antioxidant compound without the caffeine that would be present if one were to drink the equivalent dosage in liquid form. "A therapeutic dose would require drinking more than ten cups of green tea per day," she says.

Vitamin D

Most large randomized studies conducted to date on prevention have focused on hormonal agents (such as tamoxifen). But hormone receptor negative breast cancer, which does not need estrogen to grow, does not respond to tamoxifen and is associated with a poorer prognosis than hormone receptor positive breast cancer, says Dr. Crew. "To reduce the risk this type of cancer, agents that work by non-hormonal mechanisms must be developed." Approximately one third of breast cancers are hormone receptor negative.

A pilot study at Columbia will be the first to assess the feasibility of studying high dose vitamin D as an agent for chemoprevention. This is based on evidence from a recent Women's Health Initiative (WHI) that suggested calcium and vitamin D were beneficial in reducing breast cancer incidence in a subgroup of healthy postmenopausal women. After an initial safety study, a larger multicenter study is expected to follow. [!\[\]\(45eb3fe9227bffd7b122069000f27d4d_img.jpg\)](#)

SURGICAL PREVENTION

For women at very high risk of breast cancer, prophylactic surgery may be the appropriate choice for prevention. Surgical removal of both breasts offers the highest risk reduction. Learn more about options in surgical prevention at www.columbiasurgery.org.

To learn more about prevention and chemotherapy, call 212.305.1945 or 212.305.1732.

Breast Cancer Research Reports

Understanding the Biology of Tumors

In popular health news today, the word inflammation is gaining increasing publicity, thanks to the tremendous progress researchers have made in identifying its importance in a host of disease processes. Indeed, inflammatory processes play a critical role in a wide range of conditions including heart disease, diabetes, Alzheimer's disease, and even cancer.

In the Department of Surgery, **Ann Marie Schmidt, MD**, *Division Chief, Surgical Science*, and **John D. Allendorf, MD**, *Assistant Professor of Surgery*, have made significant strides in understanding how inflammatory processes may be linked to the development of tumors.

At root is a complex process that involves the immune system and the way its components work to keep the body healthy. In health, pro- and anti-inflammatory components maintain a balance so that the body recognizes and resists foreign invaders without destroying its own cells. The ability of cancer cells to

grow and migrate through the body indicates that something in this balance is amiss.

In order to proliferate, cancer cells must go through a number of steps and interactions with molecules in the body. One of these is a receptor called RAGE (receptor for advanced glycation end products), which is very active in cancer cells.

By blocking this receptor in animal studies, Drs. Schmidt and colleagues were able to slow the growth and spread (metastases) of tumors. They used several methods to block RAGE, and in each case, the approach was effective: pro-tumor mechanisms were blocked, and the animals' tumors grew much smaller.

"We are seeing profound suppression of tumor metastases and tumor growth," says Dr. Schmidt.

Based on the striking results of these laboratory and animal studies, they believe that suppression of RAGE could be a promising target for future clinical research in people. Nevertheless, more work remains to be done before RAGE-based therapies may be tested in clinical trials in human subjects with

First Study of Trovax for Breast Cancer to Begin

Since 1997, the Tumor Immunotherapy Program has been at the forefront of efforts to beat cancer through the development of new vaccines. Led by **Howard L. Kaufman, MD**, *Chief, Division of Surgical Oncology*, the program conducts laboratory research and offers vaccines to patients with melanoma, colon cancer, kidney cancer, and other types of cancer including breast cancer.

Tumor vaccines work by activating components of the patient's natural immune response. By coaxing the immune system to produce antibodies or T-cells against cancer cells, tumor vaccines may be able to slow or stop the progression of disease.

The Trovax vaccine has been studied in the treatment of colon and kidney cancers. Trovax targets a protein called 5T4, which was originally found expressed in these types of cancer. According to Dr. Kaufman, "5T4 is also expressed in virtually every breast cancer, and so there is great interest in applying Trovax to patients with breast cancer."

The first study of Trovax for breast cancer will begin early in 2008 in women who have been treated with surgery or chemotherapy for stage IIIB or stage IV breast cancer and have



Howard L. Kaufman, MD, FACS, Chief, Division of Surgical Oncology and Director, Tumor Immunotherapy Program

no detectable disease remaining. Participants will receive Trovax monthly for six doses, and be monitored for signs of recurrence. "We will be looking closely at the response of the immune system," says Dr. Kaufman. "If there is a strong immune response to the vaccine, it will likely be protective against recurrent breast cancer."

This study is based on clues revealed by earlier trials in colon and other cancers, according to Dr. Kaufman. "In studying



Ann Marie Schmidt, MD, Chief, Division of Surgical Science, Department of Surgery

cancer. In their studies, Drs. Schmidt and Allendorf are testing the effects of eliminating RAGE either in the blood cells and immune cells, or in tumor cells themselves, as experimental strategies to probe the cell-specific roles of RAGE in tumor biology. “Before we can aim toward a therapy based on RAGE, we must identify which cells RAGE is involved in that might be key.” [👑](#)

To learn more about RAGE research in the Surgical Science Division, go to www.columbiasurgery.org and search on “Surgical Science.”

Trovax for colon cancer, we learned that we probably have to give vaccines fairly often. When colon cancer patients received the vaccine monthly for four months, a large number of patients had stable or improved disease. When we reduced vaccinations to once every three months, more frequent recurrences were seen.”

Although the breast cancer study will be done in women with no evidence of disease, Dr. Kaufman explains that cancer cells can still lurk unseen. “Low numbers of cancers cells can be present in the body, but go undetected. By the time we are able to detect cancer cells, patients have billions of them.” Based on the program’s experience in previous studies, Dr. Kaufman expects that those who receive the vaccine will not have as many recurrences, or will have delayed recurrences, compared to women who do not receive the vaccine.

The study will be conducted through the Southwest Oncology Group, a national cooperative organization that conducts studies across multiple U.S. institutions. As a member and leading study participant, Columbia will be serving as the immunology center in the breast cancer study. [👑](#)

The Tumor Immunotherapy Program conducts basic and translational research to develop new vaccines in the laboratory, evaluate them in mouse models, and to rapidly bring them to the clinic.

For more information, visit www.tumovaccines.com or call 212.342.0232.

referrals • 1.800.227.2762

Heart Health

Emerging field combines cardiac surgery and interventional cardiology

Intricate repairs to the heart can now be performed through flexible catheters threaded into blood vessels in the groin or arm. Using this method, physicians can repair or replace heart valves, open blockages in the blood vessels, gently ablate the surface of the heart to stop atrial fibrillation, and perform a host of other diagnostic and therapeutic procedures. In comparison to open surgery, catheter techniques can mean less pain and faster recovery for patients. For some patients who may be too sick to undergo surgery, the availability of catheter techniques can sometimes mean the only chance to receive treatment.

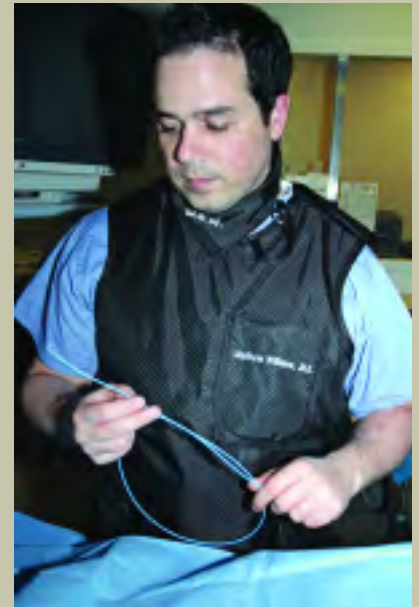
Yet open surgery is still the only option in certain cases, and the skill of experienced surgeons remains indispensable.

There are simply some procedures that are better performed through traditional methods.

“Surgeons tend to have a set of skills and think a certain way about how to approach a patient’s problem, while interventional cardiologists have a different set of skills and take a different approach,” says **Mathew R. Williams, MD, Surgical Director, Cardiovascular Transcatheter Therapies**. He chose to pursue both paths so that he could “combine the best of both worlds.” As the first U.S. physician to have joint training and appointments in interventional cardiology and cardiac surgery, Dr. Williams performs an increasing number of what he calls “hybrid” procedures — procedures that use the best of both surgical and less invasive methods to achieve optimal solutions.

“We can make complicated procedures safer and perhaps more effective by utilizing hybrid approaches,” he says.

One such example is the transapical catheter procedure for replacing the aortic valve, which may be an option for select



Mathew R. Williams, MD

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High Risk Lung Assessment Program

Every year, hundreds of thousands of people are diagnosed with lung cancer, mesothelioma, emphysema, or another serious lung disease.

A new program at Columbia University Medical Center aims to turn the tide on both genetic and acquired lung diseases by helping people who are at high risk to get the care they need in the earliest stages of disease progression. New this year, the **High Risk Lung Assessment Program** is directed by **Joshua Sonett, MD**, *Chief, General Thoracic Surgery*, and **Charles A. Powell, MD**, *Director of Thoracic Oncology Research, Division of Pulmonary and Critical Care Medicine*.

“Many individuals have a family history of lung disease, or have been exposed to substances such as smoke, asbestos, or even dust from the World Trade Center,” says Dr. Powell. “It is important that they receive screening for lung diseases, and that after initial screening, that any abnormalities are followed up appropriately.”

Many people do receive an initial CT scan, either from their primary care physicians or at the hospital. Up to 50% of patients will have some abnormality on these screenings. In many cases, such abnormalities are harmless, according to Dr. Sonett. But it is critical that suspicious

lesions be carefully assessed and closely monitored, so that those requiring intervention can be treated earlier than later. “Although many centers treat cancer, not all institutions are experienced in screening and treating patients with non-cancerous conditions. For instance, Alpha-1 Antitrypsin 1 deficiency is an important cause of Chronic Obstructive Pulmonary Disease,” says Dr. Powell. The genetics department at Columbia University has extensive experience in identifying individuals at risk for this and for other genetic diseases.

The High Risk Lung Assessment Program uses an algorithm-driven approach to provide comprehensive, thorough care to two main groups of people. The first group, the “worried well,” includes those at risk for pulmonary disease due to family history or exposures. The program helps to define the risk each patient faces, and to try to mitigate risk factors by referring them to Columbia’s Smoking Cessation Program, or conducting further screening through lung function tests or additional CT scans. This group of patients includes many New York firefighters who responded to the attack on 9/11, as well as people who have been exposed to chemicals, paint, or other toxic substances.

The second group targeted by the program includes people who have begun a screening protocol, or who have been found to have an abnormality on a CT scan. For these patients, the program uses the best available evidence to manage the results of screenings and provide comprehensive follow-up care.

The program’s algorithm-based approach includes a series of steps to help determine the probability that a nodule may be malignant or benign. This assessment incorporates both patient characteristics and features of the lesion itself, according to Dr. Powell. Patient characteristics include age, smoking history, family history of lung cancer, and the presence of other diseases such as chronic obstructive pulmonary disease. Characteristics associated with the nodule include features such as calcification, size, and shape. Using the algorithm to assess both kinds of factors, the physicians derive the probability that a lesion may be malignant or not.

Results fall into three categories, with abnormalities identified as high-, intermediate-, and low-risk for cancer. An example of a high risk lesion would be a three cm, spiculated (unevenly edged) nodule in a 65-year-old smoker, whereas a one cm, smooth, calcified lesion in a 34-year-old non-smoker would be considered at low-risk for cancer.

The determination of risk is then used to guide treatment decisions. For low-risk lesions, Drs. Powell and Sonett typically recommend follow-up imaging at algorithm-specified intervals. All imaging and follow-up appointments are coordinated by the program. If a lesion is highly likely to be cancerous, the program may recommend biopsy or removal of the

KEY PERSONNEL AT THE MULTIDISCIPLINARY HIGH RISK LUNG ASSESSMENT PROGRAM

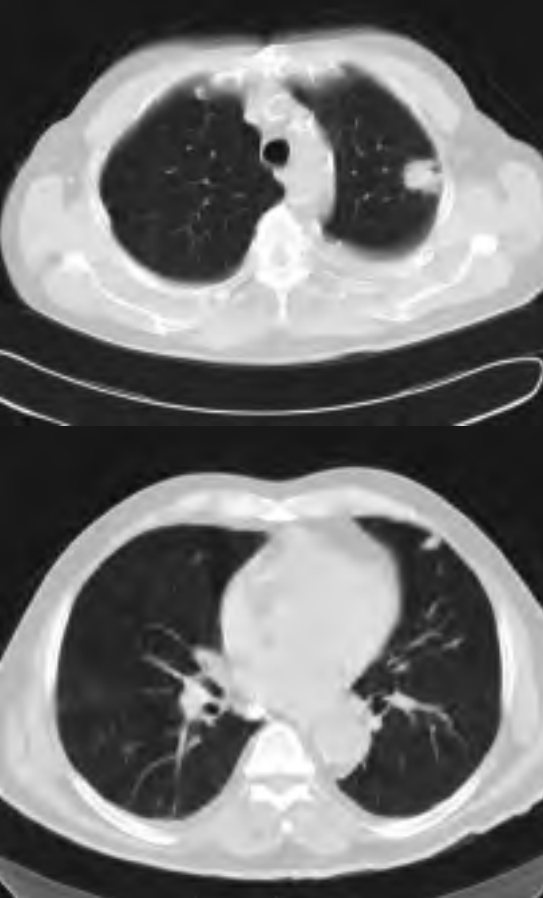
Joshua Sonett, MD, Chief, Section of General Thoracic Surgery

Charles A. Powell, MD, Assistant Professor of Clinical Medicine, Department of Medicine, Division of Pulmonary, Allergy, & Critical Care Medicine, and Director of Thoracic Oncology Research

John H. M. Austin, MD, Professor of Radiology

Roger A. Maxfield, MD, Associate Clinical Professor, Department of Medicine, Division of Pulmonary, Allergy, & Critical Care Medicine

Mark Stoopler, MD, Associate Clinical Professor, Department of Medicine, Division of Hematology and Oncology



(top) In this CT scan, the white area indicates a lesion with irregularly shaped borders partially attached to the pleura (outer lining of the lung) in a patient with emphysema. This is likely a malignant cancer.

(bottom) The lesion in this scan is small, regularly shaped, smooth and rounded, indicating it is likely benign.

lesion. In most cases, the program uses minimally invasive surgical methods. For those patients with lung cancer, the program uses endobronchial ultrasound, which provides sophisticated staging of lesions in patients with lung cancer. In addition, the program includes thoracic oncology evaluation for consideration of chemotherapy when appropriate.

For intermediate lesions, the team uses other tools to try to refine the probability of malignancy. One is to follow the lesion over time, because malignant nodules tend to grow, whereas benign ones do not. Sequential CT scans at three-month intervals may be recommended to monitor for signs of change. Another strategy is to use PET/CT scanning to determine whether a nodule may be metabolically active, because malignant lesions tend to be

metabolically active while benign nodules do not. It is important for patients to understand that even PET/CT, which detects metabolic activity in the body, is not 100% accurate, and it is possible to have false positives and false negatives due to several factors.

The program's systematic approach to assessing risk and to providing follow-up care helps both patients and their physicians, says Dr. Sonett. Furthermore, by marshalling NewYork-Presbyterian/Columbia University Medical Center's extensive resources, it facilitates rapid referral to other experts when needed, including the lung failure team, the interstitial lung disease program, and others.

SCREENING FOR LUNG CANCER: WHAT THE RESEARCH SAYS

The story of screening for lung cancer is complicated. Early detection of cancers is clearly important to patients' survival. But if a nodule is detected, the course of monitoring and treatment is often not straightforward. "Not all cancers grow aggressively," says Dr. Powell, "and today's tests are not able to reliably distinguish non-invasive from aggressive lung cancers."

Many researchers are now working to develop tools to differentiate the types of nodules; at Columbia, Dr. Powell is working to develop molecular tests to distinguish aggressive from noninvasive cancers. With funding from the National Institutes of Health, his team performs translational research studies to identify the mechanisms and biomarkers associated with the progression of lung cancer. The research team includes experts in cancer biology research, pathology, thoracic oncology, thoracic surgery, pulmonary medicine, and radiology.

In the meantime, physicians must rely on the data that is available to guide their screening and treatment decisions. Three large trials in the 1970s concluded that

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Heart Health

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patients who are too sick to undergo traditional surgery. In one experimental procedure, interventional cardiologists thread a catheter through the femoral artery up to the heart, and with imaging of the interior of the vessels and heart, replace a diseased aortic valve with a new tissue valve. In some patients, however, the vessels in the leg are too small for the catheter to be inserted. So in the transapical approach, Dr. Williams makes a small incision in the chest, inserts a short catheter into the tip of the heart, and through this catheter replaces the aortic valve. "This requires surgical skills to access the heart, and it requires catheter skills to replace the valve," he explains. This method avoids having to stop the heart or use the heart-lung machine, steps that are usually necessary during open surgery, but that carry risks.

For patients who are at high risk for surgery, or are not eligible for open surgery, this hybrid approach offers an important alternative. "If not for this approach, some of our patients would have undergone very high risk surgery. A few patients would not have been able to undergo surgery or receive any treatment for their aortic disease," he says.

The catheter aortic valve procedure is available to select patients as part of the PARTNER study. Led by the Center for Interventional Vascular Therapy at Columbia University Medical Center and the Division of Cardiothoracic Surgery, this trial is investigating the safety and efficacy of percutaneous replacement of the aortic valve. [👑](#)

Learn more about interventional cardiology at www.crf.org, and heart surgery at www.columbiasurgery.org.