

# FOX CHASE CANCER CENTER forward

Fall 2010



What's in a  
**word?**

*The changing  
language of cancer*

Radiation Safety: Risk vs. Reality | Getting a Clear Read on Screening | A Surgeon's Quest to Be Forgotten

NEWS, VIEWS, AND STORIES, FROM HEARTS AND MINDS UNITED AGAINST CANCER

## for•ward:

1. situated in the front
2. moving ahead
3. pertaining to the future

## FOX CHASE CANCER CENTER


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Fox Chase Cancer Center is one of the leading cancer research and treatment centers in the United States. Founded in 1904 as one of the first cancer hospitals in the nation, it holds the prestigious comprehensive cancer center designation from the National Cancer Institute—an honor that recognizes excellence in the full range of cancer science and medicine, as well as community outreach.

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 A Comprehensive Cancer  
Center Designated by the  
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### *If You Say So*

*Sticks and stones may break my bones, but words will never hurt me.*

I remember chanting that time-honored adage at schoolyard bullies like an incantation, as if it cast a web of protection over me. The funny thing is, it kind of did.

From the perspective of adulthood, that statement seems woefully inaccurate. Fractured femurs aside, I suspect that by the time we step foot on the rocky ground of adolescence, most of us bear the invisible scars of sibling torment, classmate teasing, parental criticism. But in speaking the words I believed at 5 to be true, I created that truth. I was, indeed, protected.

Such is the power of language.

Powerful, and mysterious. After all, there isn't much to these things, words—little black marks on the page, or with the spoken version, vibrations that strike the eardrum and are gone. And yet. More than concrete or steel, words create and define our realities. They introduce us to possibility. They can even be the connective tissue between the world of body, cell, medicine and that of mind, spirit, will.

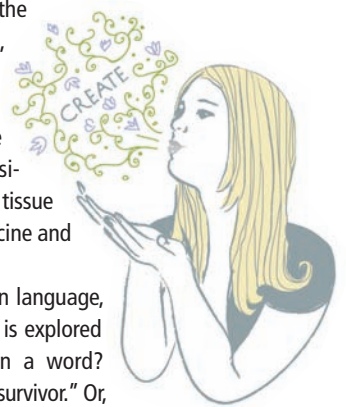
The impact of even subtle shifts in language, the choice of one word over another, is explored in the story on page 10. What's in a word? The difference between "victim" and "survivor." Or, for one patient, a seemingly minor but critical distinction: During treatment, she opted for the term "chemotherapy"—emphasis on *therapy*—over "chemo," which she found harsh. Her choice brought her a feeling of greater control.

Which may be the point. We do control our words, and through them more power and potential than we may realize. We should perhaps consider carefully, then, how we use them—consider not only their potential to harm but also to uplift and inspire, connect and create.

What possibilities await our invention? We need only name them. Recall the unassailable authority of another childhood echo, that popular parental refrain:

***Because I said so.***

—Abbey J. Porter, Editor



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 When it comes to prevailing against cancer, we've come a long way, baby. A message from the president.

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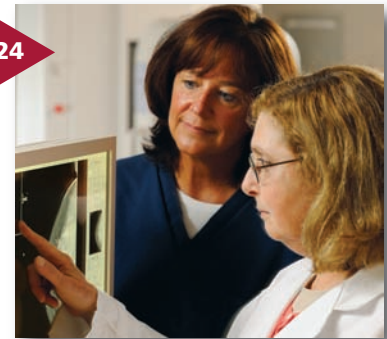
### Restoration Artist

The proudest moments for reconstructive surgeon Neal Topham are when he restores patients to the point that they go back to living and forget all about him.



### Getting a Clear Read

Screening helps detect and prevent cancer, and save lives. But it's not always clear who should get tested for what, and when. Experts at Fox Chase weigh in.



### Science at Sea

Some of the earliest research linked to Fox Chase was carried out far from Philadelphia by scientists with sand between their toes and the waves of the Cape Cod Bay rolling in their ears.



*The Marine Experimental Station, which operated in the 1930s and '40s in North Truro, Massachusetts, is depicted in this painting, believed to be by scientist Stanley P. Reimann, a prominent figure in Fox Chase's founding. The painting hangs in the Center's Talbot Research Library.*

## ON THE COVER



**Take a closer look** at the language used to talk about cancer, and it's clear that it can play an important role for patients, their loved ones, professional caregivers—anyone affected by the disease. How people talk about cancer can empower or disempower, clarify or confuse. Read why it's worth choosing your words carefully.

*Story on page 10*

## Cancer, light and dark

In this issue's cover story, writer Nancy Ross-Flanigan recalls a time when people were afraid even to utter the word "cancer." When they might instead have referred to "the big C" or made up a story to explain the disease that was affecting them or their father or wife or sister.

However dire the disease itself, it surely gained even greater power through this silent reign of fear.

Those growing up today, amid proudly displayed pink and teal and lavender ribbons and campaigns with names like "Cancer Schmancer" and "Stand Up to Cancer," might assume those dark days were eons ago. They weren't. Like many of us, I remember them well.

How far we have progressed, in such a relatively short time, in our quest to escape

cancer's shadow. This issue of *Forward* highlights some of the advances—in technology, understanding, and outlook—that continue to fuel new hope in our quest.

Progress also has brought new challenges. In the case of cancer screening, our ability to detect more cancers earlier—a potential lifesaver—also has raised questions about when and whether to treat—and screen. And while technological advancements have given us more effective, efficient radiation therapy, it's also more critical than ever for care providers to ensure patient safety. The value of expert care in navigating these issues cannot be overstated, and I'm proud to be part of an institution at the leading edge of cancer detection and prevention, as well as safe and effective radiation therapy.

Plastic surgeon Neal Topham talks about the Center's leadership in another rapidly evolving area: computer modeling that is allowing surgeons like him to rebuild and restore patients more quickly and accurately than ever before.

Dr. Topham also speaks candidly to the undeniable challenge inherent in this work: the difficult days and nights and conversations, the times when even the best efforts of the best doctors are not enough. What helps him get through is reminding himself of the other days, when he helps patients push away from the hospital bed, away from cancer, and step back into life.

Those whose lives and work are touched by cancer know well the struggle to maintain such a balance. The same holds true for the "big picture" of our quest to prevail against this disease. We have great distances to travel, to be sure, but let's not lose sight of how far we've come. Each success shines a light on the complex problem of cancer, bringing us one step closer to finally dispelling its shadow.

Michael V. Seiden, M.D., Ph.D.  
President and Chief Executive Officer



KARL SEIFERT

forward  
FALL 2010

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## Healthcare Reform to Expand Access to Services, Increase Research Funding

Increased funding for biomedical research and improved patient access to clinical trials and other services are among the anticipated effects of landmark health-care legislation signed into law in March.

The Patient Protection and Affordable Care Act, whose provisions will be phased in over several years, aims to reshape the U.S. healthcare system by providing coverage to more people, improving healthcare services, and making the healthcare delivery system more efficient.

"The reform also advocates more transparency—not only in costs, but in patient outcomes," says Rob Davis, director of regulatory and government affairs at Fox Chase, who notes the law will require non-profit healthcare providers like Fox Chase to begin publicly reporting patient outcomes by 2014.

"Healthcare reform is still in its infancy, and its overall ramifications are still being considered," Davis says, "but it looks to be beneficial, overall, to cancer care."



DAVID DEBALIKO

Rob Davis, director, regulatory and government affairs

Among the good news: Additional grant funding will be available for research in a number of areas, including the comparative effectiveness of treatments for diseases including cancer. The law establishes a Center for Comparative Effectiveness Research in the Department of Health and Human Services

that's designed to better inform physicians' treatment decisions by providing evidence of the effectiveness, benefits, and potential harms of various treatments. The center's funding priorities include improving imaging technologies for diagnosing and monitoring cancer and reducing racial, ethnic, and socioeconomic disparities in cancer care.

In addition, Davis says, more patients will have access to clinical trials. Starting in 2014, private insurers will be required to cover patients' routine costs associated with participation in such trials. The law also makes preventive services, including some screening tests, a requirement of all insurance plans.

Cancer patients will be among those who benefit from the overall expansion in health-care coverage provided by the reform: Insurers no longer will be permitted to deny coverage based on pre-existing conditions, and lifetime spending limits will be lifted. The law is projected to reduce the number of uninsured Americans from the current 54 million to 23 million by 2020.

## Center Appoints New Chief Scientific Officer

In August, Fox Chase appointed molecular oncologist Jonathan Chernoff to be senior vice president and chief scientific officer. The role was formerly occupied by Jeff Boyd, who has been named executive director of the Institute for Personalized Medicine, as well as chief of the division of molecular pathology.

A molecular oncologist, Chernoff will coordinate and chart the course of research at Fox Chase. He has been with the center since 1991 and most recently held the role of deputy chief scientific officer.

As executive director of the Institute for Personalized Medicine, Boyd will work to match emerging targeted drug therapies to the genetic profiles of individual patient tumors on a larger scale than previously possible. He has been the principal architect in launching the institute.

## Physicians Named 'Top Docs'

Thirty Fox Chase physicians representing a range of specialties are highlighted in *Philadelphia* magazine's annual "Top Doctors" issue, published in May. The list is designed to serve as a guide to expert medical care in the Philadelphia region.

Featured doctors were selected through a national survey of professional peers, with nominees screened by physician-led research teams based on criteria such as education and experience. One in four of the Center's physicians are included.

Two Fox Chase physicians also appear in the section "Physicians, Healing Themselves," which details the health and fitness habits of featured doctors: surgeons Andrew A. Gumbs, a cyclist, and John A. Ridge, who fences. "You can trace the demise of civilizations to sugar," says Gumbs, who advocates a diet free of sugar and processed food.



### ON THE WEB

For more information on *Philadelphia* magazine's "Top Doctors," visit [www.fccc.edu/topics/topdocs](http://www.fccc.edu/topics/topdocs).

## Clinic to Treat Rare Form of Breast Cancer

In May, Fox Chase opened the region's first clinic dedicated to treating patients with a rare and aggressive form of breast cancer. The Inflammatory Breast Cancer Clinic is led by Massimo Cristofanilli, who joined the Center in January as chairman of the department of medical oncology.

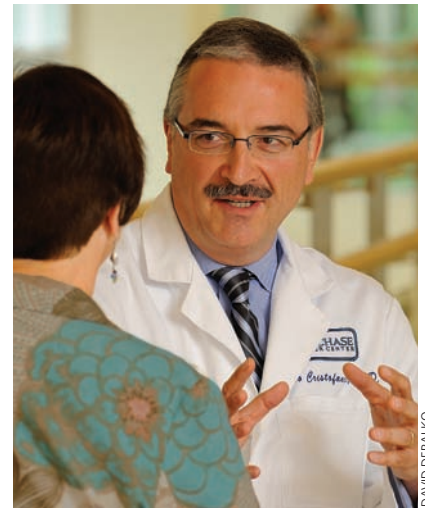
"Patients with inflammatory breast cancer often face challenging odds—first to be promptly and accurately diagnosed and then to receive the most effective treatment," Cristofanilli says. "With the opening of this clinic, Fox Chase is dedicating itself to improving both diagnosis and care for inflammatory breast cancer patients."

Cristofanilli comes from the Univer-

sity of Texas M.D. Anderson Cancer Center, where he founded and led the Morgan Welch Inflammatory Breast Cancer Program and Clinic, which treats more cases of the disease than any other facility in the world.

Inflammatory breast cancer accounts for only about 1 percent of breast cancers in the United States and can be difficult to diagnose, as it rarely causes a lump and may not appear on a mammogram.

Pat Halpin-Murphy, president and co-founder of the Pennsylvania Breast Cancer Coalition, and Patti Bradfield, president of the Inflammatory Breast Cancer Foundation, were among the guests who celebrated the opening of the clinic at the Women's Cancer Center at Fox Chase.



DAVID DEBALCO

Clinic founder Massimo Cristofanilli



## ROOM TO GROW

*Facility Makes Space for Research, Patient Care*

A newly expanded building that supports Fox Chase research and treatment programs was dedicated in honor of a former Center president in May. The Robert C. Young, M.D., Pavilion houses the Women's Cancer Center, the department of radiation oncology, the research program in cancer control and prevention, and the Institute for Personalized Medicine.

The event drew elected officials including Philadelphia City Councilman Brian O'Neill, U.S. Rep. Allyson Schwartz, and state Rep. Brendan Boyle to the Pavilion's sun-drenched "campus corridor," where they mingled with employees, board members, donors, and the building's namesake, who served as president of Fox Chase for 18 years before stepping down in 2007.

"While this honor is immensely flattering as well as humbling," Young said, "it is not so important what is on the building as what takes place within it. The unique blend of science and medicine facilitated by the building's design will serve cancer research and our patients well into the future."

The Young Pavilion subsumes the 108,000 square feet of the former Prevention Pavilion. With 116,000 square feet of new space, the 224,000-square-foot building is the largest on Fox Chase's campus.

PHOTOS: SCOTT H. SPITZER



## Scientist, Survivor, Supporter Staffer Reflects on Half-century at Fox Chase

In 1959, NASA selected the first seven American astronauts, Charlton Heston's epic film *Ben-Hur* debuted, and on August 1, Anna O'Connell was hired as a research technician at Fox Chase. As she prepared to retire earlier this year, O'Connell reflected on the career of a lifetime.

**A**nna O'Connell came to Fox Chase as a recent graduate of Temple University seeking a job that would help ready her for graduate school and a Ph.D. At the time, Fox Chase consisted of one building and 125 employees—a far cry from today's multi-building complex and nearly 2,500 employees. Then-director Timothy R. Talbot Jr. "sent me a personal letter offering me the job," she recalled.

She started off in pathology before moving on to chemotherapy research and, eventually, virology, where she worked for Baruch S. Blumberg. When Blumberg received the Nobel Prize in medicine in 1976 for the discovery of the hepatitis B virus, he invited O'Connell and a handful of other colleagues to join him and his family for the ceremony in Stockholm.

"We had a marvelous time," O'Connell recalled with a smile. "We stayed in the Grand Hotel on the waterfront—it was magnificent."

But O'Connell faced her share of adversity, including a diagnosis in 1965 of metastatic thyroid cancer. She was 28. "Five physicians told me I had nothing wrong with me, and I decided, 'No, that's not true,'" she said. She insisted on having a node removed from her neck. Tests showed it to be cancerous. Her instinct—and the ensuing treatment at Fox Chase—likely saved her life.

After that, "I became very active in raising money for patients, and I also talked publicly about being a cancer victim," she said.

**O'Connell faced her share of adversity, including a diagnosis of metastatic thyroid cancer.**



Scientist Anna O'Connell

Although the experience derailed her plans for graduate school, it also strengthened her dedication to Fox Chase. She passed on other job offers, even turning down higher salaries.

O'Connell moved up the ranks to research associate and, eventually, staff scientist (a position that, she was quick to point out, she probably couldn't achieve today without a doctorate). She came to be the go-to person for information and lab equipment. As editor of *The Scientific Report*, an annual compendium of Fox Chase research, she became known for her merciless pursuit of scientists tardy with their contributions.

Retirement elicited mixed emotions for the veteran staffer, who said it was the people she would miss most. Though she officially left Fox Chase at the end of January, it's a likely bet she will stay connected to the Center, which she readily admitted has been "a second family."

At one of the last meetings she attended as an employee, O'Connell expressed an optimistic view of the future of the institution she has watched grow and change: "I believe that we will survive, and I believe that we will change for the better."

She should know.

### Fox Chase President Chairs Federal Committee

**P**resident and chief executive officer Michael V. Seiden was named chairman of the integration panel of the Department of Defense's Ovarian Cancer Research Program, a position responsible for helping to direct funding from the Congressionally Directed Medical Research Program, in May.

The panel oversees the peer review of

grant proposals and recommends overall strategies and resource allocations for the program, which is known for funding innovative research. Members are selected based on expertise and interest. Seiden will serve for fiscal year 2011.

The Department of Defense is a major source of funding for biomedical research.

## HONORS & AWARDS

### Nobelist Earns Recognition in Asia, Europe

Researcher Baruch S. Blumberg, who won the Nobel Prize in medicine in 1976 for discovering the hepatitis B virus, recently received two international honors.

In Bangladesh, a lecture was named in Blumberg's honor. The first Blumberg Lecture was held in Dhaka on World Hepatitis Day—May 19—at a conference attended by more than 400 hepatologists, gastroenterologists, internists, and surgeons.

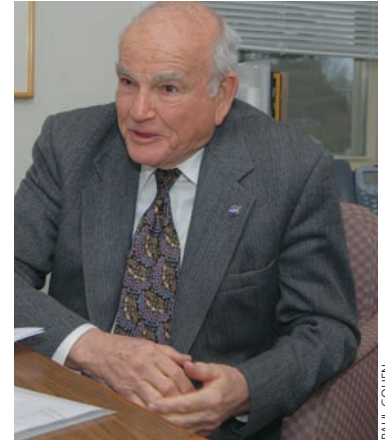
"It is a great honor to have this important event include my name," Blumberg says. "Disease does not know boundaries, and cooperation between many nations

has been effective in achieving widespread relief from sickness and death."

Separately, Blumberg was elected an honorary member of the Romanian Academy, a cultural forum founded in 1866 that covers the scientific, artistic, and literary domains.

In March, he traveled to Bucharest to deliver a presentation to the Academy on the prevention and control of liver cancer, of which hepatitis is a leading cause.

Blumberg co-invented a vaccine against hepatitis B that has become one of the most widely used in the world, with billions of doses administered.



Baruch S. Blumberg

PAUL COHEN

### Oncologist Honored for Work in Prevention

Paul F. Engstrom, an oncologist specializing in gastrointestinal cancers and senior vice president of the Center's extramural research programs, earned the American Society of Preventive Oncology's Distinguished Achievement Award for his work in cancer prevention and control.

Engstrom accepted the award at the society's annual meeting in March, at which he delivered a talk on the progress made in cancer prevention over the past 40 years.



Paul Engstrom

### Veteran Nurse Receives National Award for Patient Education

The Oncology Nursing Society selected Kathy Smith, clinical coordinator of the infusion room, to receive the Excellence in Patient/Public Education Award, which she accepted at the society's 35th annual congress in San Diego in May.

Smith was honored for her work in educating patients about undergoing chemotherapy. She co-developed and teaches a class on the topic at Fox Chase and developed a video for those unable to attend.

"Patients tended to be anxious when they came to the infusion room for their first treatment because they didn't know what to expect," Smith says. "We wanted to create an environment where patients and their loved ones could get information about managing the physical and emotional effects of chemotherapy. Our goal is to prepare them by letting them know what to expect and helping them develop a support system."

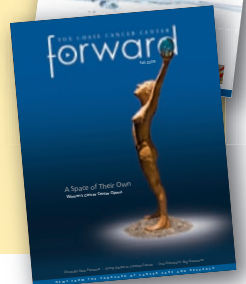
A 34-year veteran of nursing, Smith is in her 20th year with the Center.

#### 'Self Congratulations'

**FORWARD** magazine recently earned several awards in national and international communications contests:

- Silver award of distinction—Communicator Awards, judged and overseen by the International Academy of the Visual Arts
- Silver award, best overall medical publication—Magnum Opus Awards, sponsored by *ContentWise* in conjunction with the Missouri School of Journalism
- Award of excellence, best new magazine/journal—APEX contest, sponsored by Communication Concepts

In addition, *Connect*, the Center's employee magazine, received the grand award for best internal magazine in the Magnum Opus contest, and "Wag," the video that launched the "Love Versus Cancer" initiative, earned a silver in the Communicator Awards program.





# The Gift of Gab

RETIREE COUNTS HER BLESSINGS AFTER RECONSTRUCTIVE SURGERY

By Jill M. Ercolino

**S**tories bubble out of Karen Williams. The retired secretary talks about her family, her friends, and her job at Sesame Place, a theme park in Langhorne, Pennsylvania, 20 miles north of Philadelphia, where Williams greets children, teens, and the young-at-heart.

Her candid chatter is endearing and self-deprecating. And that's why it's so hard to believe that eight years ago, this single mom, now 62, faced the prospect of never speaking again.

It all started when Williams, a casual smoker for 40 years, noticed a white, pimple-like bump on her tongue. "It was getting more and more uncomfortable and felt like it was inflating," she recalls.

A biopsy confirmed that Williams had carcinoma of the tongue, a disease she trudged through with humor. "I always thought that if I got cancer," she says, "I would get it in the mouth because I'm so sarcastic, and look what happened."

Friends urged her to go to New York City for treatment, but Williams chose Fox Chase. "I didn't like the idea of going to a large teaching hospital," she says. "I wanted to go somewhere that specialized in cancer. Fox Chase was my kind of place."

Treatment would require the removal of part of her tongue. When she met John A. Ridge, the head-and-neck surgeon who would perform the procedure, and Neal

Topham, the reconstructive surgeon who would rebuild her tongue using tissue and blood vessels from her left wrist (*for more on Topham, see page 17*), she knew she had made the right decision. Known as experts in their fields, the pair inspired confidence.

"With them," Williams says, "I just knew everything was going to be OK...that I would be OK."

Her 12-hour surgery was followed by weeks of recovery—some of it spent attached to a feeding tube—as well as radiation treatments and speech therapy. Williams appreciated the help of Fox Chase social

workers with navigating her questions and fears. Equally meaningful were small gestures of kindness from her doctors.

"Dr. Topham would come in every day and change the dressings on my wrist," she says, recalling the Saturday afternoon he stayed a bit longer to cheer on her favorite college football team, Notre Dame, on TV.

Today, Williams (no longer a smoker) sometimes counsels others with tongue cancer and continues to count her blessings—

even if she can't eat spaghetti. "I can't curl my tongue because it used to be my arm," she explains with a laugh.

But she's willing to make that sacrifice. "To be where I am today, it's a miracle—it's my miracle, and I'm very grateful." 🍀

*"To be where I am today, it's a miracle."*

PHOTO BY TOMMY LEONARDI

## IT'S ALL IN YOUR PERSPECTIVE.

Karen Williams, right, displays the sense of humor she maintained during her recovery from tongue cancer. Joining the Sesame Place employee are Kristen Harrell of Wilmington, North Carolina, and her daughter Kendall.





# CLOSING IN ON A KILLER

RESEARCHERS ADVANCE  
TREATMENT, UNDERSTANDING  
OF OVARIAN CANCER

By Kristine M. Conner

Ovarian cancer kills nearly 15,000 women in the United States each year. Fewer than half of those diagnosed with the disease survive five years.

Those grim statistics reflect, in part, the lack of a reliable means to detect ovarian cancer early: More than 80 percent of patients are diagnosed after the disease has traveled beyond the ovary. Finding better treatments is essential to improving survival, as is unlocking clues to the disease's development. Studies by Fox Chase researchers released this spring made major contributions on both fronts.

## [A new strategy](#)

Robert A. Burger, director of the Women's Cancer Center, led an international Phase III clinical trial that found that adding bevacizumab (known by the trade name Avastin) to standard frontline chemotherapy for advanced ovarian can-

## Women diagnosed with advanced ovarian cancer have ANOTHER FRONTLINE TREATMENT STRATEGY TO DISCUSS WITH THEIR DOCTORS.

cer, then continuing treatment with it alone, extends patients' progression-free survival—the time before the disease returns or worsens. Women receiving chemotherapy alone had a median progression-free survival time of 10.3 months, but those receiving bevacizumab, 14.1 months.

“This finding represents a 28-percent reduction in the risk of disease progression over time,” Burger notes. “This is a fairly high-risk population, so a four-month improvement is significant.”

Bevacizumab interferes with angiogenesis, the process by which new blood vessels form to supply a tumor's growth. Although the drug has been found to extend progression-free survival for other cancers, this is the first Phase III trial showing it to be effective against advanced ovarian cancer.

Researchers will continue to analyze quality of life and overall survival among the study's nearly 1,900 participants. In the meantime, Burger says, women diagnosed with advanced ovarian cancer have another frontline treatment strategy to discuss with their doctors. He hopes the study's results will be confirmed by another Phase III trial under way in Europe, which might hasten FDA approval of the treatment regimen. “We believe this drug can be valuable in the treatment of this disease,” he says.

### Where it all begins

Another key to improving ovarian cancer treatment will be finding ways to diagnose it at an earlier stage. In a separate

study, researcher Jeff Boyd, chief of the division of molecular pathology, and colleagues from Memorial Sloan-Kettering Cancer Center produced groundbreaking evidence of how and where ovarian cancer originates.

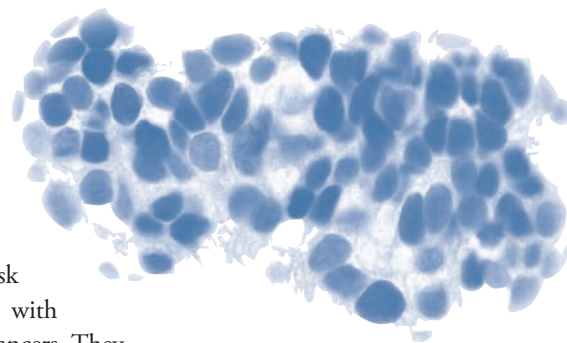
“Unless you understand where cancer begins—what the precursor lesions might be—it is hard to develop an early-detection or screening test,” Boyd says. “We have known precursor lesions in other cancers, such as cervical, colorectal, and breast. None of that knowledge has existed for ovarian cancer.”

Over six years, the researchers used a combination of microscopic and molecular imaging to examine ovarian tissue from three groups:

women with mutations in BRCA tumor-suppressor genes, who have up to a 40-percent lifetime risk of ovarian cancer; those with no known genetic risk factors; and others with early-stage ovarian cancers. They found that most ovarian cancers develop inside cysts that form in the epithelium, the tissue that lines the ovary's surface, and were able to identify early genetic events in the cells' transformation.

All evidence pointed to inclusion cysts, which fold into the ovary from its surface, as the site of origin, and to dysplasia—early structural changes—and aneuploidy—having too many chromosomes—as key factors in the cell, Boyd says. “We could actually see the progression from completely normal epithelium through dysplasia to cancer,” he says.

The findings will be critical in the search for a reliable screening test, he says: “We're at a place now where we can focus our efforts on looking for early lesions and early biomarkers, before cancer develops.”



Ovarian cancer kills nearly 15,000 women in the United States each year, in part because of difficulty in detecting the disease early.

### TERMS DEFINED

**Frontline therapy:** The medical therapy recommended for the initial treatment of a disease.

**Clinical trial:** Study of a drug, diagnostic, or other tool in humans. Clinical trials have four phases. Phase I assesses the product's safety; subsequent phases assess efficacy.

**Biomarker:** A biological substance—often a protein—whose concentration reflects the presence or severity of a disease.

“the big C”  
fight  
love  
war  
battle  
victim  
win  
therapy  
cope  
partner  
victory  
treatment  
survivor  
conquer  
individual  
support  
join  
heal  
brave  
share  
cure  
team  
killer  
lose

# WHAT'S IN A WORD



## THE CHANGING LANGUAGE OF CANCER

By Nancy Ross-Flanigan

With a cancer diagnosis comes a whole new vocabulary for patients. First, there's the medical jargon: terms like *prognosis*, *metastasis*, and *remission* suddenly become part of everyday conversation. Then other words, less clinical but no less capable of evoking strong emotional reactions, are added to the mix. Talk turns to “brave” folks who “battle” cancer and to those fortunate legions of “survivors” whose “positive attitudes” help get them through.

But how appropriate are these clichés for cancer as we currently know and experience it? And how do such words and metaphors affect patients, their families, and others who seek to understand the disease and its impact? ▶

## From 'The Big C' to the War on Cancer

In talking about cancer, we've come a long way from the days when even speaking the word was taboo outside the medical arena. People used euphemisms like "the big C" or concocted elaborate stories to explain protracted illnesses and deaths from cancer. Cowed by cancer's reputation as a sure killer, patients—described in those days as "victims"—reacted with resignation when informed of their diagnosis. That's if they were told at all; some physicians thought delivering the dreadful news could be so detrimental they told the patient's family, but not the patient.

Then in 1971, President Richard Nixon signed the National Cancer Act, the opening volley in what came to be called "The War on Cancer," elevating the disease with a pen stroke from a shameful secret to a national priority. In the years that followed, as new treatments and early detection began improving the odds of survival, previously passive patients needed to know it was possible to soldier on and conquer the foe, and battleground analogies seemed appropriately empowering.

But today, at least for some cancers, the focus has shifted from annihilating an acute illness once and for all to managing a chronic disease that flares up from time to time, with periods of respite between episodes. At the same time, some people with cancer—and those who care for them—are chafing at the limitations of the old clichés and searching for new language that more accurately reflects cancer's complexity and the various ways people experience the disease.

### Changing the conversation

Early this year, Fox Chase kicked off "Love Versus Cancer," an initiative that uses relatively gentle language and imagery to frame the cancer experience and recognize the unifying role of love in that experience.

support ~~victim~~ partner  
"The Big C"  
love

"The message we're trying to communicate to patients is, 'You're not alone; there are people who will be going through this with you,'" says Fox Chase president and chief executive officer Michael V. Seiden. "Being diagnosed with cancer shouldn't immediately equate with battle and catastrophe. That's not to say the experience won't be profound, but we want to call attention to the care, compassion, bright minds, and big hearts that will surround and partner with you at a place like Fox Chase."

The initiative isn't about banning particular words or forcing people to talk about cancer in any particular way, stresses Luanne Chynoweth, director of the Center's social work services department. At Fox Chase, the emphasis is on being sensitive to patients' individual needs, in language as in other aspects of care.

"As social workers, we try to listen for what someone is making of the whole experience," Chynoweth says. "Some want to embrace the warrior concept; for others it's a softer, warm and comforting thing, defined by the love and support of the people around them."

Physicians, too, are becoming more conscious of the words they choose and the ways they communicate with patients. In some cases, it's a matter of avoiding medical lingo that patients may misconstrue.

"People with cancer take great offense when a clinician says, 'The patient failed drug X,' and will point out that the *patient* didn't fail it; the cancer failed it," says clinical geneti-

<< *The message* we're trying to communicate to patients is, 'You're not alone; there are people who will be going through this with you.' >>



cist Mary B. Daly. “It’s as if patients think the caregivers are ascribing blame to them for not responding to the therapy. I don’t think the caregivers really intend that; it’s just medical terminology that takes on a different meaning to patients.”

Good communication—about cancer or any other subject—involves more than just being careful not to offend, Daly adds. “There are techniques you can learn to make sure you’re really giving the patient an opportunity to speak in their own words,” she says. “Listen carefully and repeat back what they say to make sure you understand their perspective. Then, going forward with that patient, if you know what kinds of words are relevant to them, you try to couch things in those terms.”

When appropriate to the patient and situation, analogies and often-used figures of speech can simplify complex information and help patients and physicians find common ground for communication. But there’s a danger in oversimplification, says Richard Penson, a gynecologic oncologist at Massachusetts General Hospital and lead author of the paper, “Cancer as Metaphor,” published in 2004 in the journal *The Oncologist*.

“When you feel like you understand something, but you really don’t understand it completely, that’s a vulnerable way to be informed, and that’s a big risk with these metaphors,” Penson says. Once-powerful expressions also may become diluted through overuse, and even worse, they may stigmatize, frighten, or confuse the very people they’re intended to comfort and inform.

A pediatric oncologist quoted in Penson’s paper relates the story of a 6-year-old girl who took her mother’s admonitions to “keep on fighting” a bit too literally, kicking and punching the nurses and doctors who were trying to carry out a procedure. Battle analogies also may scare children, who associate war with horrific injuries and death. And the emphasis on “fighting” or “beating” cancer, while surely countering the image of a patient as a passive ▶

## (No longer) a time for war?

Nearly 40 years ago, the call for a “War on Cancer” rallied the nation behind a cause and reinvigorated cancer research. Is a battle cry still the best way to build such support? Does militaristic language capture what’s going on today in research laboratories and hospitals throughout the nation?

These are important questions to consider, says Otis Brawley, chief medical officer of the American Cancer Society. “As a famous politician said, ‘Words matter.’ Language sets our view and determines the path we’re going to take as we deal with any issue, be it cancer or some other social or health issue.”

While battle imagery once had the power to galvanize, it may be undermining anti-cancer efforts now, says Fox Chase president and chief executive officer Michael V. Seiden.

“We’ve made a lot of progress with a lot of different cancers, but when we use vocabulary like ‘war,’ people want to know, ‘Did we win or lose?’” Seiden says. “What ends up happening is, as the public—through sources such as foundations and the National Cancer Institute—invests billions of dollars in cancer research and treatment and sees that their neighbors are still dying of cancer, that counts in the war vernacular as a loss. They might think, ‘We’re spending all this money and we’re still losing; why should we keep trying? Let’s pull the troops out.’ ”

But that’s a short-sighted view, Seiden says. Instead of talking about combat with a foe that must be conquered if we’re to be considered successful, we would be better served by looking at cancer as a complex tapestry that we’re unraveling strand by strand, increasing our understanding as we see how each thread fits into the whole.

“Consider that modern humans have existed on the planet for, say, 100,000 years,” Seiden says. “We made no progress against cancer in the first 99,950, but in the last 50 years we tripled survival for some cancers, increased it tenfold for others, and even cured some cancers. We’re doing all kinds of things that were unimaginable even 25 or 30 years ago. Because of this progress, life is going to look totally different for our children, grandchildren, and great-grandchildren.”

Language sets our view and determines the path we’re going to take as we deal with any issue.

<< I believe that choosing my own word, creating my own metaphor, helped. It gave me a critical feeling of control.>>

## At the heart of cancer care

The Fox Chase initiative “Love Versus Cancer” invites those affected by cancer—from patients and their families to physicians and scientists—to join in recognizing the power of love to bring strength and hope to the challenge of confronting the disease.

The initiative launched earlier this year with the release of the three-minute video “Wag,” set to the lilting notes of Nat King Cole’s “L-O-V-E.” The video, which can be viewed at [LoveVersusCancer.org](http://LoveVersusCancer.org), stars pet-therapy dog Mary Margaret and her canine colleagues, along with Fox Chase’s human caregivers.

In dealing with cancer, the importance of scientific and clinical expertise cannot be overstated, says Joanne Hambleton, head of nursing and a former Fox Chase patient. But she believes the initiative speaks to another important piece of the equation.

“Love Versus Cancer really gets to the core of what we do,” she says. “We’re going to use our brains, but we’re going to give you our hearts.”

### Visit [LoveVersusCancer.org](http://LoveVersusCancer.org) to:

- ▶ Watch the “Wag” video, featuring Fox Chase’s canine and human caregivers
  - ▶ Stock up on Love Versus Cancer gear, including T-shirts, wristbands, and buttons
  - ▶ Send a Love Versus Cancer e-card
  - ▶ Post a public thank-you note
- ...and more!



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recipient of medical care, may leave patients of all ages feeling unduly responsible for the outcome.

“Sick people do not need the implication that better strategizing and fighting harder would lead to victory,” wrote syndicated columnist Judith Martin, also known as Miss Manners, in 2005. “What they need is the recognition, expressed in countless different ways, that they are still the same individuals they were before they got sick.”

During treatment for breast cancer, one writer and retired professor came up with a solution that neutralized the pugilistic imagery, expressed her individuality, and kept her from shouldering the entire responsibility for recovery.

“At the start of each chemotherapy infusion, I imagined hundreds of miniature fairy godmothers wielding tiny magic wands, floating through my bloodstream searching for cancer cells,” wrote Elaine Whitman, professor emeritus at the University of Utah School of Medicine, in an essay published in *Pulse* magazine. “Whenever they discovered one they would gaily call out ‘Bibbidi-bobbidi-boo!’ and transform it into ... a rose.”

Extending the metaphor, Whitman flipped through a book of beautiful rose photographs the night before each infusion and wore a ring adorned with a gaudy rose. Friends got onboard, sending her rose soap, lotion, and greeting cards. Mindful of the power of words, she also decided early on not to use the harsh-sounding term “chemo,” but to refer to her treatments as *chemotherapy*, emphasizing the life-saving potential.





“Did any of this make a difference? I have no proof, but I’m convinced that it did,” Whitman wrote. “I believe that choosing my own word, creating my own metaphor, helped. It gave me a critical feeling of control.”

### Survivor: Cancer Island

Sometimes words construed as positive and intended to convey a sense of control can have unintended effects. Take “survivor.” Initially promoted by the National Coalition for Cancer Survivorship as a substitute for “victim” and now defined as anyone with a current or past cancer who is still living, as well as family, friends, and caregivers affected by the diagnosis, the label has been embraced by countless men, women, and children who have lived with cancer and its aftermath. The word connotes strength and resilience, qualities that certainly come in handy when one must deal with cancer, but while it can serve the laudable purpose of making people feel part of a hardy tribe, the survivor identity also can cause distress.

“Particularly for people who have poor prognoses and probably won’t survive, they may feel they have to put on a brave face or be Lance Armstrong. It puts pressure on them,” says Stanford University anthropologist Sarah Lochlann Jain, whose current research project is titled “Cancer Culture in the United States.” “I’m sure that happens with other diseases, not just cancer, but with cancer there’s that particular rhetoric of the survivor.”

Speaking of “brave,” that’s another word some would like to expunge from the cancer lexicon.

“We call cancer patients ‘brave,’ perhaps, because the very word ‘cancer’ makes most of us tremble in fear. But there is nothing brave about showing up for surgery or radiation sessions,” wrote Dana Jennings, who was diagnosed with prostate cancer in 2008 and blogs about cancer for *The New York Times*. “Bravery entails choice,” he wrote in March, “and most patients have very little choice but to undergo treatments.”

“To me it falls more into squaring your shoulders and going to do what has to be done,” he added in an interview. “You do what you need to do to cope.”

Of course, it’s precisely because friends and family members want to help loved ones cope that they often use words like “brave” and “survivor” in an effort to boost spirits. Jennings understands and appreciates that. “I know people are trying to be kind, and I know what they’re trying to get at,” he says. But sometimes, rather than struggling to find the appropriate language, it’s good to remember that words may not be needed at all.

“A lot of times we forget that being quiet, but present, can really be a powerful thing,” Jennings says. “Just to show that you cared enough to show up and look the patient in the eye is a good thing. There’s not necessarily a need to fill up the silence.”

*Nancy Ross-Flanigan has been writing about science and medicine for more than 25 years. The former science writer for the Detroit Free Press, she also has written for The Dallas Morning News and the magazines Health, Fitness, and More. She has had cancer three times, most recently 20 years ago, but she’s never been fond of the “survivor” label.*

# ‘IN SHORT...’

FOX CHASE recently welcomed eight new members to its board of directors. These leaders in business, academia, and the community have no doubt learned a thing or two on the road to their achievements. We asked them to share their most important life lessons—in 10 words or less.



## Surviving makes you stronger.

Andrew Bodnar, M.D., J.D.\*  
Retired executive, Bristol-Myers Squibb Company  
*\*former board member who returned to service after a brief hiatus*

## Reputations take a lifetime to build and seconds to destroy.

Michael J. Heller, Esq.  
Attorney, Cozen O'Connor

## 'The perfect is the enemy of the good.'—Voltaire

Jill M. Michal  
President and chief executive officer,  
United Way of Southeastern Pennsylvania

## Listen carefully, and only then speak.

Thomas E. Shenk, Ph.D.  
Chairman, department of molecular biology, Princeton University

## You can't change people. You must instead change your expectations.

Lindy Lou Snider  
Founder and chief executive officer, Lindi Skin Inc.

## Identify things within your control/influence—let everything else go.

Pamela A. Strisofsky  
Chief financial officer and managing director, TL Ventures

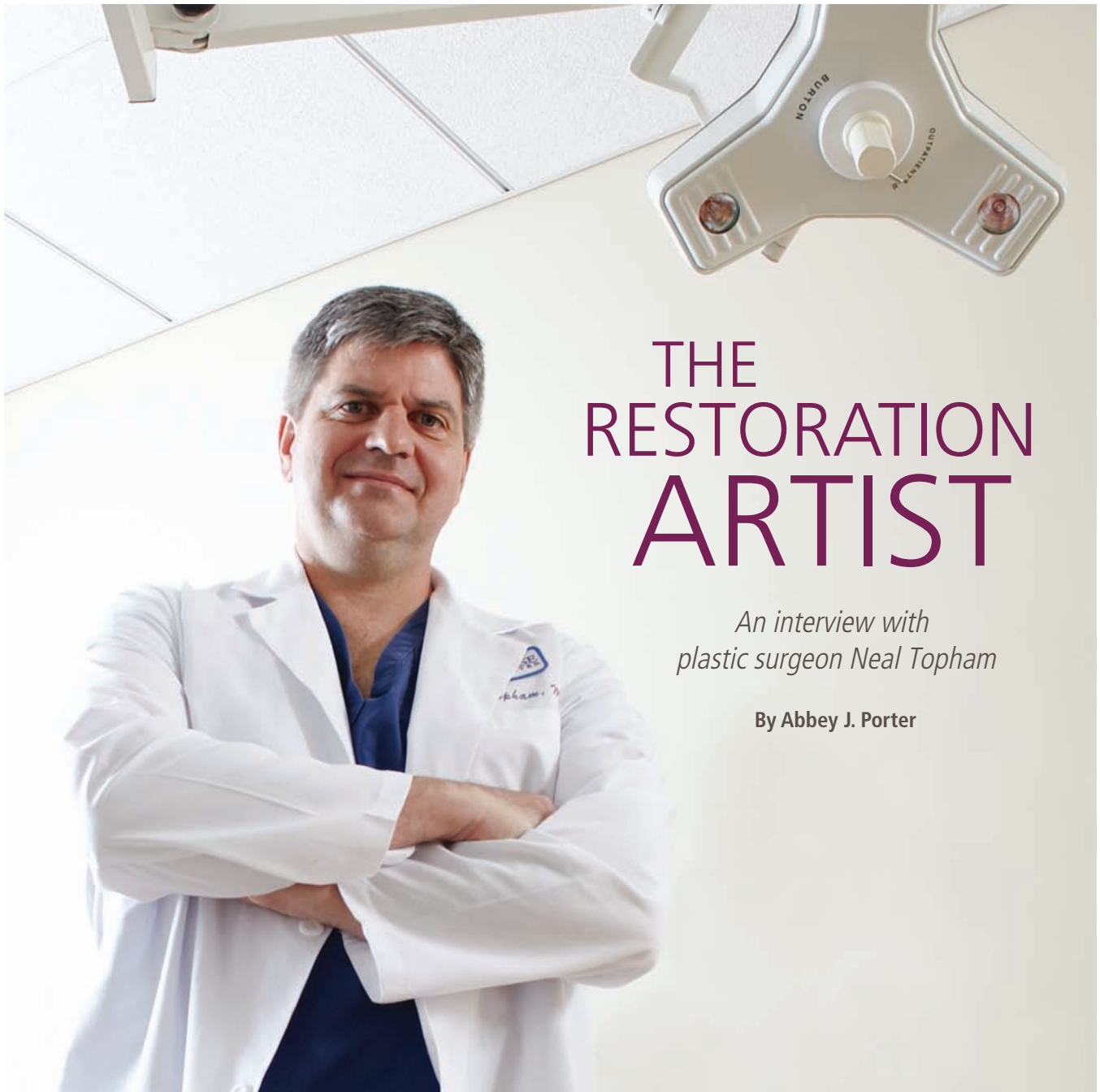
## Keep life in balance: Find time for family, friends, yourself.

William L. Stulginsky  
Retired partner, PricewaterhouseCoopers, LLP

## Caring for others brings many intangible gifts over a lifespan.

Zane R. Wolf, Ph.D., R.N.  
Dean, School of Nursing and Health Sciences, La Salle University





# THE RESTORATION ARTIST

*An interview with  
plastic surgeon Neal Topham*

By Abbey J. Porter

**T**he term “plastic surgery” might bring to mind cosmetic procedures like nose jobs and tummy tucks, but the work of **NEAL S. TOPHAM**, chief of plastic and reconstructive surgery, couldn’t be more vital to his patients. A specialist in microsurgery—using tissue from one part of the body to rebuild another—Topham helps erase the marks of cancer, both physical and psychological, and restore patients to wholeness.

**What is the role of plastic surgery in the cancer world?**

The plastic surgeon’s job is to fix the defect that’s sometimes created when a tumor is removed. With microsurgery, you go to an unaffected part of the body for tissue to use for the repair. If you had to remove part of a patient’s jawbone, for instance, you might use tissue from his leg to rebuild it. ▶

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**When you perform a surgery, what are your goals?**

Well, it's not just about restoring form; it's about function as well. If someone has an intact jawbone, they can talk and eat. If someone loses their tongue, is it possible to make it so they can swallow again? These are normal activities that, if you lose them, leave huge holes in your life. And there is an aesthetic concern as well; once you restore the patient's form and function, you can come back and make refinements so their appearance is as palatable as possible to the rest of the world.

**What role does the aesthetic part play in the patient's recovery?**

It plays a huge role. Take breast reconstruction, which is about 50 percent of the cases I do. That doesn't have a functional role, but it has a psychological one. If a patient has a mastectomy and walks around the rest of her life with a scar across her chest, it can be a reminder of what she went through. If I can restore her so she has a breast that is aesthetically pleasing, she can heal and eventually say, 'Oh, that's in my past. It's a big part of what I've gone through, but I don't dwell on it.' There are studies that show that patients do better, psychologically, when they are restored.

**UNTANGLING THE TERMS**

**Plastic surgery** comes from the Greek *plastikos*, meaning to mold or shape; it has nothing to do with plastic. While best-known for aesthetic, or cosmetic, procedures, plastic surgery also includes subspecialties such as burn surgery and microsurgery. (See below.)

**Reconstructive surgery**, as its name suggests, is the rebuilding of a part of the body that has suffered a physical defect—whether from cancer, trauma, or another cause—to restore its form and function.

**Microsurgery**, a subspecialty of plastic surgery, involves the transfer of tissue from one part of the body to another—the part being rebuilt—and reattaching blood vessels.



**"YOU WANT PEOPLE'S HOPES AND DREAMS TO STAY ALIVE."**

—Neal Topham, chief of plastic and reconstructive surgery

**How did you become interested in this line of practice?**

After medical school, I started in general surgery and when I rotated with plastic surgeons, as soon as I saw some of the things they did... You know how sometimes something speaks to you? I realized that's where I wanted to go. In my mind's eye, that's what I always envisioned surgery being. I liked the creativity of it; no two procedures are the same.

**When it comes to your work, what are you most proud of?**

The satisfaction comes from, basically, not seeing the patient anymore—when they are healthy enough and restored to a point that they're just another person out there. I think that's the best achievement. It would be nice to say that they remembered you and everything, but hopefully they are just out there functioning. Ideally, they've overcome it and been fixed to a point where they just move on.

**What is it like to see people negotiate the experience of having cancer, day after day?**

I see patients take a lot of different approaches. Some people are just huge pioneers, amazing people that can take on this problem and push right through it. Some people, it can be overwhelming for them, so it's important to basically walk them through it.

**What's the hardest part?**

The hardest part is the failure—when what we try to do doesn't work out. I had a patient recently who was undergoing breast

reconstruction, but her tumor came back and totally overcame her, and she is going to succumb to it. It was hard to see, when she knew it had come back and we had to stop the reconstruction, which was very important to her. It was like the cancer had become real to her, because she was not going to progress and have a family and do the things that normal people do, and the realization that this was basically it for her came during one particular conversation we had... You want people's hopes and dreams to stay alive, and that day, she was seeing that she was going to lose this battle.

**Does it get easier over time?**

It has gotten easier. I think the more experience you gain, the more you accept that sometimes in this battle against cancer, you can't win—and sometimes victory can be really sweet. I think I prepare myself a lot better than when I started out and if something didn't work I was really distraught and frustrated. You learn to roll with it more, and I think that comes with being more seasoned.

It used to be more up and down for me. Now it's more level, in terms of understanding what my role is and where I can actually do what I need to do and where I can't. Learning that—where you can and can't—is probably the toughest lesson.

**It sounds like this work can be pretty difficult to handle.**

Yeah, there are times you go home and feel like crying. You can't sleep, and you're worried about what's happening. There are times when you question how long you can do it. Historically, there is a huge

attrition rate in microsurgery. People start off in it and gradually move to other areas; a lot move into aesthetics. The cases are long, and they can be grueling—a surgery can go 16 hours. I think some surgeons can't fight that battle forever, and they turn it over to the next generation.


### What keeps you coming back?

Part of it is that you just have to. That's one thing; you just kind of have to. And part of it is that it's a worthy goal. The people who come in—if you don't do it, who is going to help them? If you give up, it helps nobody. Eventually, the times when you are frustrated or disappointed will wear off and something good will happen.

### Do you have to coordinate a lot with your patients' other caregivers?

That's right. Mainly, I'll coordinate with a surgeon in another specialty. I work with head and neck surgeons, breast surgeons, gynecological surgeons, surgical oncologists—all of them. That makes our specialty unique. All the other specialties rely on us to come in and be like "the closer" in a baseball game. Of course, I work with medical oncologists and radiation oncologists, too, to plan chemotherapy and radiation therapy. It's nice to be part of a group of physicians who are working together and aren't just in our own practices, not communicating. That's one of the advantages of being here at Fox Chase.

### How aware are patients, at the outset, of the reconstructive aspect of their treatment?

People don't necessarily consider the plastic surgeon who's going to fix them, but I think it's important for them to think about. In the end, that's one of the things that can be most important. You want the cancer gone, of course, but you also want everything done that can be done to restore you and help you move forward. 

*To read about Karen Williams, a patient treated by Topham, see page 7.*

## Picture This: SIMULATED SURGERY

You don't have to talk with Neal Topham for long before a couple of things become clear: One, the soft-spoken plastic surgeon is someone you'd want at your bedside, should the need arise; and two, he is at the top of his game.

The day of his *Forward* interview, Topham had recently returned from lending a hand with a complex case at Temple University: A man who had been shot in the face had lost his entire jawbone, plus soft tissue and skin.

The surgery, which involved rebuilding the patient's jaw using a bone from his lower leg, plus skin and fat from his thigh, took 16 hours. It might have taken longer, but for the benefits of new technology Topham had brought: virtual, or computerized, surgical planning. By providing detailed three-dimensional images and simulations, the system allows surgeons to plan a surgery ahead of the actual event.

"It shortens operating time, because you shift what you would do in the operating room to what you can do outside it," Topham explains. "When you come to the operating room, you can just proceed through the steps without having to stop in between and plan and think about it."

In addition to reducing "time on the table" by up to two hours, the system improves surgeons' precision by allowing them to determine ahead the exact cuts required for newly matched bones to line up correctly—the first time. Overall, the system should mean lower costs and better outcomes, Topham says.

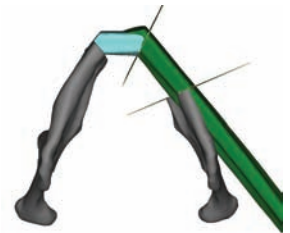
"What we're doing represents a paradigm shift in the way we think about reconstructing patients," he says. "All the planning is done before surgery, and then the plan is brought to surgery and carried out, whereas before we had to do more of that work on the fly."

Topham has been working with the Colorado-based Medical Modeling Corporation, which produces the customized 3-D models used during surgeries, to further refine and improve the system. He also collaborates with Synthes, a medical device company in West Chester, Pennsylvania, to investigate next steps for the technology.

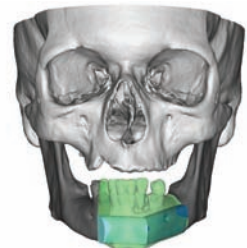
Fox Chase is the first in the Philadelphia region, and among just a handful in the nation, to use virtual surgical planning. "We're definitely on the leading edge of this technology, and we're just beginning to discover what these tools can offer," Topham says. "I think we're going to see a rapid change in how patients are cared for."



1 "Virtual surgery" removes the cancerous portion of the patient's jawbone, which will be rebuilt using the fibula (in green).



2 The fibula is shaped and inserted into the jaw. (The precise, three-dimensional bone models are generated from CT scans of the patient.)



3 The anticipated results of the planned surgery.

IMAGES: MEDICAL MODELING CORPORATION



#### ON THE WEB

To read more about Neal Topham and the reconstructive surgery program at Fox Chase, visit [www.fccc.edu/topics/topham](http://www.fccc.edu/topics/topham).

# RADIATION THERAPY: Risk *vs.* Reality



HOW A 'PHANTOM'—  
AND A CULTURE OF VIGILANCE—  
HELP KEEP PATIENTS SAFE

By Matt Steinmetz and Abbey J. Porter

PHOTO BY JUSTIN HUNT

*Since recent media stories shone a spotlight on errors made in radiation therapy, patients might question the risk of undergoing such treatment. Experts at Fox Chase and elsewhere talk about the realities of this valuable therapy and how to ensure that patients—and practitioners—play it safe.*

It's 10 p.m., but Alain Guemnie Tafo's workday isn't over. In a room on a lower floor at Fox Chase, the tall postdoctoral researcher leans intently over a form lying on a treatment table. He rests one hand on it lightly while adjusting a handheld controller with the other. A turn of a knob brings a red light beaming from the open eye of the machine arching over him: a new, state-of-the-art linear accelerator, one of just a few of its kind in the country.

Guemnie Tafo doesn't have to remind his patient to stay still. As on many evenings, his subject tonight is "the phantom," a sophisticated dummy, of sorts, that's shaped like a human torso and contains an array of radiation sensors.

A postdoctoral researcher training to become a medical physicist, Guemnie Tafo is running a quality control test—essentially, a dry run of a treatment a real patient will receive the following day. A computer printout verifies that the regimen is executed precisely as specified by the treatment plan.

It's one of many steps in a system designed to ensure the safety of patients undergoing radiation treatment at Fox Chase.

## **PUBLIC CONCERNS**

The safety of radiation therapy has come under public scrutiny since recent high-profile media coverage revealed treatment errors that led to patient injuries, and even some deaths. A February *New York Times* story drew attention to incidents of radiation errors in New York, detailing the harrowing stories of severely overradiated patients. The preceding

June, the newspaper had reported on a Philadelphia veterans' hospital that administered incorrect radiation doses to 97 of 114 veterans with prostate cancer.

Such disturbing cases might prompt some patients to wonder whether they should undergo treatment. Eric Horwitz, chairman of radiation oncology at Fox Chase, has an answer: Yes. "Radiation therapy is safe more than 99.9 percent of the time," he says, adding that while he applauds the *Times* articles for bringing attention to lapses in safety, "it would be tragic if they led patients to fear needed therapy."

Even the *Times* attests to the rarity of errors: It identified 621 mistakes in the state of New York, which it described as "a leader in monitoring radiotherapy and collecting data about errors," between 2001 and 2008. According to the American Society for Radiation Oncology, 13.6 million radiation treatments were performed in the state during that period, which means errors occurred just .0046 percent of the time. Moreover, the *Times* noted that of the errors, "most were minor, causing no immediate injury."

Make no mistake: Radiation oncology is a rapidly evolving, highly technical field populated by increasingly powerful, complex equipment. The good news is that those tools deliver more precise treatment, often in a shorter time and with fewer side effects. But it's imperative, experts say, that they are operated by a properly trained staff, that patients are appropriately monitored, and that treatment facilities have safety checks in place. ▶

## Safety of CT Scans Examined

Among clinicians' most powerful tools for detecting and monitoring cancer are computed tomography exams, or CT scans, which provide detailed cross-sectional pictures of the body. But the recent publication of studies suggesting that radiation from the scans might *cause* cancer has generated concern and confusion.

The diagnostic capability of CT scans, which has vastly reduced the need for exploratory surgery, has led to a dramatic rise in their use over the past few decades. It is estimated that people receive seven times the dose of diagnostic radiation each year, on average, that they did in 1980, due mostly to CT scans.

Studies published in December in *Archives of Internal Medicine* assert that the scans may cause thousands of cases of cancer each year in the United States. But there is considerable disagreement among radiologists regarding the validity of those conclusions, says Rosaleen B. Parsons, head of diagnostic imaging at Fox Chase. The primary criticism: that the study's conclusions are based on an inappropriate extrapolation of data from survivors of the Hiroshima and Nagasaki nuclear bombing. Calculating CT-scan-related cancer incidence from that population, Parsons says, is

like expecting the results of eating fast food occasionally to be the same as eating it for three months straight.

Parsons is certain of one thing: "For our patients, the immediate benefits of CT scans far outweigh any uncertain risk that may be out there, many years in the future."

Among CT scans' benefits to cancer patients:

- Detecting small abnormalities more effectively than other tests
- Providing information about the size and location of a tumor and whether it has spread
- Guiding a biopsy or planning for radiation therapy or surgery

Parsons advocates caution, and common sense, in employing the tests. "I think they should be used judiciously," she says. "But if you need a CT scan, you need a CT scan. They give you information that other tests cannot."

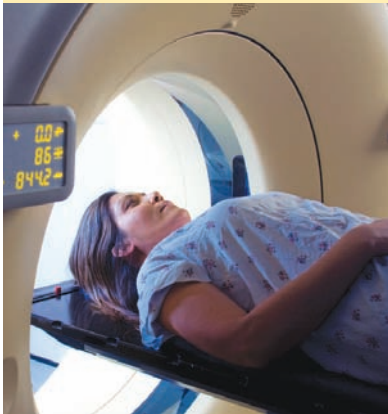
Healthcare providers can take steps to safeguard patients from unnecessary radiation exposure, she adds.

"We are very proactive about making sure the doses are as low as possible at Fox Chase, and consider alternative imaging exams where feasible," she says, noting that a system built into the modern scanners used at the Center minimizes the dose while maintaining image quality.

Ultimately, Parsons says, "these studies should inspire patients to ask questions about the tests they are getting, and to be their own advocates."

### TIPS FOR PATIENTS:

- Keep records of your radiological exams to help avoid unnecessary repetition of tests
- Ask your doctors about alternative tests that don't involve radiation
- Inquire whether your treatment facility has been accredited by the American College of Radiology



## AN ISOLATED INCIDENT

A staple in cancer treatment for more than 100 years, radiation therapy consists of high-energy radiation from sources such as X-rays, gamma rays, neutrons, and protons that kills cancer cells by damaging their genetic material. Today, about half of all cancer patients receive radiation therapy, often in combination with chemotherapy or surgery. Three primary types are in use:

- **External beam radiation therapy**, the most common form, uses a machine such as a linear accelerator to direct beams at the tumor from outside the body. Methods such as three-dimensional conformal radiation therapy, or 3D-CRT, and intensity-modulated radiation therapy, or IMRT, target tumors precisely with the help of sophisticated computer software.
- **Brachytherapy** involves implanting tiny radioactive "seeds" in or near the tumor, where they deliver a continuous dose of radiation. The practice is commonly used to treat cervical, prostate, and skin cancers.
- **Systemic radiation therapy** entails the patient swallowing or receiving an injection of a radioactive substance such as iodine. It is typically used to treat or manage thyroid or bone cancer.

While no single agency oversees all aspects of medical radiation, it is nonetheless a highly regulated field, with state and federal agencies setting safety standards for hospitals and physicians. In Pennsylvania, for instance, the Department of Environmental Protection (DEP) requires biannual site inspections and has rigid standards for reporting mistakes.

Problems like those at the veterans' hospital occur when safety regulations aren't followed, says W. Robert Lee, a professor of radiation oncology at Duke University School of Medicine, who testified on the matter in July 2009 before the U.S. House of Representatives' Committee on Veterans' Affairs.

"I agree with the federal investigators who concluded that quality management practices were 'deficient,'" he says. "In short, the 'culture of safety' that we in radiation treatment strive for was not accomplished. My hope is that patients...will recognize that the situation at the Philadelphia VAMC is an isolated incident."

In contrast, Horwitz says, some institutions go "above and beyond what's required when it comes to assuring patient safety." He places Fox Chase—home to one of the largest academic radiation therapy departments in the country—firmly in that category.



So does Fox Chase radiation safety officer Karen Sheehan, who characterizes the Center's safety record as "stellar—among the cancer treatment community's best."

"We're wholly committed to maintaining patient safety," Sheehan says.

Fox Chase has been recognized as one of the top NCI centers in the country for radiation therapy and safety standards, and Horwitz and his colleagues consult on safety issues at other institutions.

The Center's recipe for success? A culture of vigilant, proactive monitoring, and multiple layers of safety checks.

Take the phantom. Whenever a patient is to undergo intensity-modulated radiation therapy, an advanced and highly precise form of external beam therapy, a phantom serves as test subject. While most hospitals employ the practice only when first using a new machine, Horwitz says, Fox Chase is dedicated to the practice. "Fox Chase has done it for every single one of our 5,000 IMRT patients for the past 11 years," he says, "and we will continue to do so."

The department also voluntarily developed its own internal tracking and reporting system to identify errors, catching any small mistakes—the kind that have no impact on the patient—before they can develop into anything serious. The department uses the system, which has earned praise from the DEP, as an educational tool, revisiting any missteps to ensure they don't occur again.

In addition, multiple radiation therapists must be present at all times during treatments. "We never have people treating patients by themselves," says Robert A. Price Jr., chief clinical physicist, who oversees the technical aspects of treatment planning and delivery. "One person could think '4' and enter '8' that day; the other person is there to guard against that type of human error."

And while Fox Chase is a longtime leader in the advancement and use of leading-edge radiation technology, Price says, it is also committed to adopting those technologies carefully and sensibly. He recalls a recent case in which the Center obtained a new machine that promised faster, more precise treatment. Despite urging by the manufacturer to begin using it immediately, the department waited until several months of testing and dry runs had proven the equipment sufficiently reliable and efficient for use with patients.

## DOING YOUR HOMEWORK

Radiation therapy is, on the whole, a safe practice. As Lee puts it, "Your odds of beating cancer with the help of treatments like radiation therapy are significantly greater than being harmed by a mistake."

## "YOUR ODDS OF BEATING CANCER WITH THE HELP OF TREATMENTS LIKE RADIATION THERAPY ARE SIGNIFICANTLY GREATER THAN BEING HARMED BY A MISTAKE."

Nonetheless, it's worth paying attention to safety. Analysis of the tragic cases detailed in *The New York Times* reveal they did not happen purely by chance, just as Fox Chase's safety record is no accident. Patients can do more than cross their fingers and hope they're not among the unlucky; Horwitz suggests they use a critical eye when selecting a treatment provider.

"The key is for patients to select an institution with multiple checks and balances, adequate staffing, and technical staff onsite to assure the equipment is functioning correctly," he says.

He suggests patients ask questions such as:

- Does the radiation therapy team radiate a test "phantom" before administering treatment?
- How are implanted brachytherapy seeds monitored to ensure proper placement and delivery of therapy?
- Do multiple radiation therapists attend the machines so that no one is treating the patient alone?
- Are there full-time physicists, engineers, and information technology staff onsite to ensure that equipment functions properly?

And with a radiation oncology department, as in other areas of medicine, staff experience, patient volume, and department size are also relevant.

Once they're comfortable that they're in an environment committed to safety, patients should be confident in their radiation therapy and be able to focus on the matter at hand: becoming well. 📍

## LEARN MORE

For more information on radiation therapy:

**Fox Chase Radiation Oncology**

[www.fccc.edu/physicians/radiation](http://www.fccc.edu/physicians/radiation) • 1-888-FOX CHASE (1-888-369-2427)

**American Society for Radiation Oncology**

[www.rtanswers.org](http://www.rtanswers.org) • 703-502-1550

**National Cancer Institute**

[www.cancer.gov](http://www.cancer.gov) • 1-800-4-CANCER (1-800-422-6237)



# GETTING A CLEAR READ

## THE SKINNY ON SCREENING TESTS

By Katrina Woznicki

Screening tests are vital to the early detection—and successful treatment—of cancer, but the rules about who should get screened, and when, can be murky. Fox Chase experts cut through the confusion.

**D**eaths from cancer have declined in recent decades, thanks to better treatments, reduced smoking rates, and yes—screening. And there's more good news: Overall death rates from cancer continue their steady decline in the United States, while screening rates appear to be on the rise.

The ability of screening tests to prevent and detect cancer—and save lives—seems clear.

“The value of screening is that it can find most cancers at their most treatable stage,” says Mary B. Daly, chairwoman of the department of clinical genetics. “The bottom line is to detect the cancer at a point when we can make a difference.”

What's less clear are the rules about who should get screened, and for which types of cancer and when, with even the experts struggling to reach consensus.

Last fall, the U.S. Preventive Services Task Force set off a firestorm of controversy when it issued new recommendations that instead of starting to get mammograms at 40, women should wait 10 years longer, till age 50—and then have the test every two years instead of annually. Several months earlier, the American Urological Association had recommended that men as young as 40 undergo prostate-specific antigen, or PSA, screening for prostate cancer—a significant departure from the position of organizations like the American Cancer Society, which no longer recommends routine PSA testing at any age.

Why the controversy? Cancer can be as unique as each patient, and testing equally as nuanced—which means coming up with a one-size-fits-all rule for screening is a challenge. Plus, evolving testing technologies have raised new dilemmas. All those factors make it more important than ever to turn to experts on the front lines of cancer treatment who understand the biological complexities of cancer.

#### HOW EARLY IS TOO EARLY?

Timing is everything when it comes to cancer, a disease that can progress slowly or quickly depending on a person's biology. Cancer is the abnormal division of cells; when cells grow uncontrollably, they invade healthy tissue and organs, leading to tumors. Screening tests such as mammography or the PSA test for prostate cancer pick up on those shifts in cell behavior, allowing physicians to find cancers in their earliest stages.

As screening technology evolved and became more sensitive, the ability to detect a greater variety of cancers—even abnormal cell growth that is not yet cancerous—improved. But that advantage brought new challenges: No two cancers are exactly alike, which means one screening test may not work for everyone. Extremely sensitive tests also can lead to false-positive and false-neg-

ative results. A suspicious spot on an X-ray might suggest abnormal cell growth but turn out to be nothing, whereas tumors might develop so gradually that they go undetected.

Moreover, if cancer is found, treatment may cause more health risks than the disease, particularly if it is a slow-developing cancer. A major dilemma facing physicians today is that, for some cancers, there is no definitive way to determine which tumors pose a threat sufficient to warrant treatment. The more experienced the physician, however, the greater his or her ability to discriminate.

#### CHALLENGE AND PROMISE

Despite its imperfections, screening is a vital tool when used appropriately by people who understand its limitations, says J. Leonard Lichtenfeld, deputy chief medical officer of the American Cancer Society. “We can substantially reduce deaths from cancer in this country just by doing what we already know,” he says, “and that includes getting the tests that are proven to reduce the risk of cancer death.”

Robert A. Burger, director of the Women's Cancer Center at Fox Chase, points to the success of the Pap smear, a test for cervical cancer put into widespread use shortly after World War II, as an illustration of the power of screening to save lives.

“This was the first example where implementing screening dramatically reduced the incidence of death from cervical cancer,” Burger notes. “The incidence of invasive cervical cancer has dropped dramatically in the past 40 years.” ▶

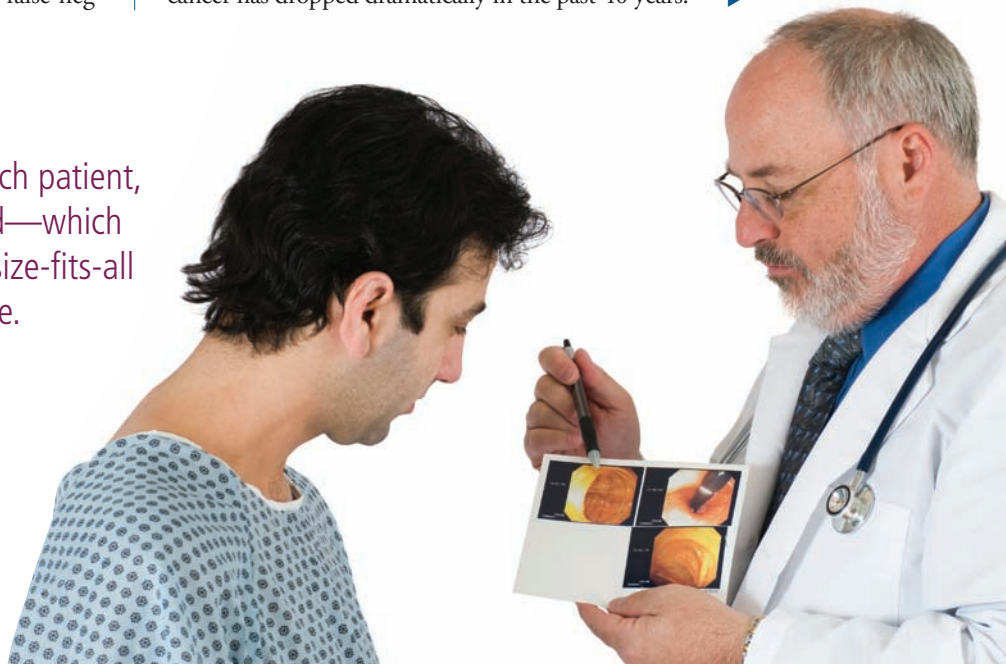
#### TESTING TIPS

**A**sk the experts. Cancer centers aren't just for treatment; Fox Chase offers risk assessment, genetic counseling, and screening, as well as the ability to map the genetics of individual patients and tumors.

**B**e in the know about screening recommendations and guidelines. Being proactive is one of the best lines of defense against cancer.

**C**ontact Fox Chase at 1-888-FOX CHASE (369-2427) with questions or to schedule an appointment.

Cancer can be as unique as each patient, and testing equally as nuanced—which means coming up with a one-size-fits-all rule for screening is a challenge.





KARL SEIFERT

Analyzing a prostate tissue sample image are Veda N. Giri, director of prostate cancer risk assessment, and colleague Taylor Kim. Giri recommends seeking screening services and cancer risk counseling from a comprehensive cancer center like Fox Chase, which offers the latest techniques and a faculty with specialized medical and scientific expertise.

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Nearly 80 percent of women 18 and older report undergoing a Pap smear in the past three years.

For other types of cancer—such as colorectal—the screening rate is not as high. “We’re screening a little over 60 percent of the U.S. population who should be getting screening for colorectal cancer, and that’s an improvement from years past,” says Minhuyen T. Nguyen, director of clinical gastroenterology at Fox Chase. The challenge, she says, is that the idea of colorectal screening—in the form of a colonoscopy—makes many people squeamish. It also requires time off from normal activities, and sedation. Scientists are trying to develop more patient-friendly screening methods, such as allowing patients to send a fecal sample from home as an initial step.

### FROM THE GET-GO

People may think expert cancer care is needed only for treating advanced cancers, but that’s a misunderstanding, says Veda N. Giri, director of prostate cancer risk

## SCREENINGSCAN

PROCEDURE	WHAT IT IS	WHO SHOULD HAVE ONE
<b>MAMMOGRAPHY</b>	A mammogram is a low-dose X-ray image of the breast used to detect the development of tumors in breast tissue.	The National Cancer Institute recommends women undergo a mammogram every one to two years beginning in their 40s, and possibly earlier if they have a family history of the disease.
<b>PAP SMEAR</b>	The Pap smear tests for cancerous or precancerous conditions in the cervix. During a pelvic exam, a swab is used to collect cells from the cervix that are then examined for abnormalities.	The National Cancer Institute recommends women have Pap tests at least once every three years after they become sexually active, beginning no later than age 21.
<b>PROSTATE-SPECIFIC ANTIGEN (PSA) TEST</b>	The test measures levels of PSA, a protein produced by prostate gland cells, present in the blood. High PSA levels indicate possible prostate cancer.	The American Cancer Society recommends that men at average risk discuss screening with their doctors beginning at 50. Men at heightened risk, such as African-Americans and those with a family history of the disease, should start this process at 45. Men at higher risk, such as those with multiple family members diagnosed at an early age, should start at 40.
<b>COLONOSCOPY</b>	Designed to screen for colon cancer, a colonoscopy involves a tiny camera on a thin, flexible tube, called a colonoscope, being inserted into the rectum to capture images of the interior of the large intestine. It also provides an opportunity for biopsy or removal of suspected lesions.	The American Cancer Society and the American College of Gastroenterologists recommend beginning screening at age 50 and repeating every 10 years if results are normal.

assessment. A National Cancer Institute-designated comprehensive cancer center like Fox Chase, for example, offers the latest screening techniques and diagnostics and has specialized medical and scientific expertise, such as knowing a disease's molecular pathways or noticing subtle differences in tumor behavior.

"A patient needs to seek expertise from the beginning from a risk assessment team that is involved with cancer on a day-to-day basis and therefore has a more sophisticated approach," Giri says. At a comprehensive cancer center, she adds, medical oncologists, surgeons, radiologists, pathologists, and biologists work together under one roof. That combined expertise can be critical when it comes to testing and interpreting results.

Prostate cancer, for example, "is a very heterogeneous disease, meaning that it behaves differently in each man," Giri explains. At the heart of the debate about prostate cancer screening is the possibility of catching a cancer so early that it would not have progressed during a man's natural lifetime, thereby causing undue stress. Experts don't necessarily know whether a tumor caught by a screening test

will develop aggressively and become life-threatening or develop so slowly that treating it would cause more harm than good by producing side effects.

"An expert cancer center will perform ongoing research into the genetics and biology of different tumors to determine how we can predict who is most at risk for aggressive cancer and screen in a more tailored fashion in the future," Giri notes. "Such research is vital to improving screening and early cancer-detection methods."

Her colleagues echo her sentiments. Cancer centers are able to stay informed of the latest screening technologies and protocols, as well as treatments, Burger says.

"Oncology experts have a sophisticated knowledge base about the disease and the disease process, and a great deal of experience in knowing what the disease looks like," he says. "It's erroneous to think a specialized cancer center is only for patients who have advanced cancers or who have failed standard therapy. A comprehensive cancer center is not a last resort; it's really a first resort, to help avoid a last-resort situation. Why wouldn't you want the expertise there at the get-go?"

## WHO IS AT RISK

Risk factors include a family history of the disease, obesity, not having children by age 30, use of oral contraceptives, alcohol consumption, and genetic factors. Risk increases with age; at 40, a woman's risk of developing breast cancer is 1 in 257. By 80, it's 1 in 24.

Infection with certain types of human papilloma virus (HPV), as well as smoking, a compromised immune system, and poor diet may increase a woman's risk of cervical cancer.

The risk of prostate cancer increases with age. Race is also a factor; African-American men are particularly vulnerable. Family history, genetics, and diet—particularly one high in red meat—also have been associated with increased risk.

Risk factors include a family history of the disease or a personal history of polyps or ulcerative colitis, as well as smoking and eating a diet high in red meat and low in fiber.

## ACCURACY

Mammograms are 85 to 90 percent accurate at detecting benign or malignant breast tissue abnormalities.

While the Pap smear is not 100-percent accurate, it is capable of detecting the vast majority of cervical cancers and abnormalities. Between 60 and 80 percent of American women diagnosed with invasive cervical cancer have not had a Pap smear in the preceding five years.

While exact percentages are uncertain, the PSA test is not 100-percent accurate. False positives and false negatives are known to occur.

Colonoscopy is considered the gold standard for colorectal cancer screening, though recent studies suggest that instead of preventing 90 percent of cancers, as previously thought, the actual number may be closer to 60 or 70 percent.

## Enzyme May Help to Guide Treatment for Head and Neck Cancer

*Findings pave way for personalized approach*

Research from Fox Chase may lay the groundwork for providing more personalized treatment for advanced head and neck cancer. Most treatment for advanced head and neck cancer involves chemotherapy with a drug called cisplatin, an inorganic platinum agent that inhibits cell growth. Although many patients do not respond well to the drug, oncologists typically don't prescribe alternatives because they don't know which patients will respond and which won't.

Recent research from Fox Chase suggests that levels of ERCC1—an enzyme that helps repair cisplatin-related DNA damage—can predict which patients are likely to respond to platinum therapy. ERCC1 levels correspond with the likelihood of survival for patients with squamous cell carcinoma, a common type of head and neck cancer that originates in the

mucous membranes. The findings might eventually help guide treatment selection for patients with recurrent and metastatic disease.

"These results open avenues to testing other agents that could be more effective in specific patients and cause fewer side effects," says medical oncologist Raneer Mehra, who presented the findings in April at the annual meeting of the American Association for Cancer Research.

Mehra and her colleagues studied the tissues from tumors of the head and neck taken from more than 100 patients treated at Fox Chase, comparing those treated with cisplatin and surgery to those treated with surgery alone. They found that low ERCC1 levels were associated with increased survival among those receiving the drug. In the 33 patients treated with surgery alone, there was no association between ERCC1 status and survival.

"This is definitely a step toward personalized medicine," Mehra says. "When we saw there was a survival difference in patients who received the cisplatin treatment based on this biomarker, we were very excited. These findings support the idea that personalized medicine is possible in treating these cancers."

The analysis could not have been conducted without Fox Chase's extensive tissue biorepository, Mehra notes.

"As an investigator, I see a great opportunity in these results," she says. "Our goal now will be to validate these results, reproduce them with tumors from a different source, and design a prospective study to test a patient's tumor and treat it accordingly based on ERCC1 level."

*Funding for the research was provided by Fox Chase's Keystone Program in Head and Neck Cancer.*

## Scan Could Aid Kidney Cancer Diagnosis, Treatment

Many of today's imaging tools can alert doctors to abnormalities such as a lump but can't provide more precise information, such as whether the lump is cancerous, and if so, what type. Now a diagnostic scan may become available that is capable of distinguishing one of the most common and deadly forms of kidney cancer. As one of the first scans capable of providing information on tumor type, such a tool would help physicians and patients make more informed decisions.

Kidney cancer is often diagnosed radiographically, when a mass is detected on a CT or MRI scan—tests that cannot distinguish among cancer types, which carry varying levels of risk. As more Americans undergo scans as part of evaluation for a vari-

ety of ailments, the number of kidney tumors detected incidentally has increased, such that up to 70 percent are now discovered that way.

Many of the patients whose scans show kidney masses undergo surgery, and in some cases their tumors turn out to be benign, meaning they wouldn't necessarily have required immediate surgery. But in the absence of a definitive presurgical diagnosis, surgeons often operate to be safe.

Fox Chase surgeons and nuclear medicine physicians recently participated in a national, Phase III clinical trial that demonstrated that the use of an antibody called 124I-girentuximab, or G250, combined with PET or CT imaging, can distinguish clear-cell renal cell carcinoma from other types of kidney masses. If approved by the Food and Drug Administra-

tion, the test would be one of the first disease-specific molecular scans capable of not only identifying a tumor's origin and location but also providing data on its cell type, arming physicians and patients with critical information.

"The ability to distinguish preoperatively between aggressive and less aggressive kidney masses is a critical challenge," says Robert G. Uzzo, chairman of the department of surgery, who presented the findings in June at the annual meeting of the American Urological Association. "Such information has a significant impact on the patient by giving physicians the ability to match tumor biology to the most appropriate treatment."

The antibody, which binds to a unique protein expressed on the cells of clear-cell renal cell carcinoma, is injected intravenously as part of a PET or CT scan. The scan holds promise for earlier detection and treatment of advanced disease.

The new diagnostic tool could help patients and doctors pick the most appropriate treatment.

## Study Links Smoking with Estrogen, May Shed Light on Lung Cancer in Women

While the rate of lung cancer in men has decreased in recent decades, the rate for women has continued to grow. Research at Fox Chase may provide an explanatory piece of the puzzle.

Cell biologist Margie Clapper and her colleagues recently set out to examine the effects of tobacco smoke on the lungs of female mice, hoping to identify cellular changes that lead to cancer.

The researchers found that the smoke triggers rapid changes in gene expression in the lungs, including an increase in the expression of genes involved in estrogen metabolism. Ten genes were differentially expressed within the lungs of smoke-exposed mice at three, eight, and 20 weeks of exposure, compared to control animals. The gene most affected, known as *Cyp1b1*, activates toxins in tobacco smoke and metabolizes estrogen to a form believed to be carcinogenic.

"We found a link between hormones, tobacco smoke, and lung cancer when we weren't even looking for it, which is very exciting," says Clapper, who co-leads the Cancer Prevention and Control Program.

"Previous work has suggested that estrogen may play a role in lung cancer, but no one has shown that smoke can actually accelerate the metabolism of estrogen within the lungs, as suggested by our data."

The observation that estrogen can be detected within the lungs and that its metabolism is upregulated in the lungs of smoke-exposed female mice may provide new insight into the rise of lung cancer among women, Clapper says.

The investigators hypothesize that estrogen plays a role in the formation and progression of lung cancers similar to the role it plays in some breast cancers. The idea is consistent with previous studies indicating that women with lung cancer who take hormone replacement therapy have a poorer prognosis than those who do not, regardless of smoking history.

Based on the data, which were published in June in *Cancer Prevention Research*, the team further hypothesizes that estrogen metabolism may also contribute to lung cancer in nonsmoking women. Since only female mice were studied, it isn't known how males—whose lungs also produce estrogen—would react.



By looking at gene expression changes after short-term smoke exposure, the investigators hope to find ways to intervene in or reverse the process. "If we can identify the earliest events that happen within the lungs when you begin to smoke, we might be able to use drugs or naturally occurring substances to block them," Clapper says.

## Protein Plays Critical Role in Development of Aggressive Breast Cancers

Fox Chase scientists have identified a potentially significant molecular player in the development of aggressive breast cancer. In studies of mice, the team found that the protein NEDD9 is critical in the formation of breast tumors that are induced by high levels of the protein HER2/neu, a cell-surface receptor involved in cell growth. HER2-driven breast cancer, which accounts for about one in five cases of breast cancer in people, is one of the most aggressive forms of the disease.

Molecular biologist Erica A. Golemis and her colleagues found that 89 percent of mice with an intact NEDD9 gene developed HER2-

induced tumors over an 18-month period, compared to only 29 percent without the gene. The findings indicate a novel role for NEDD9 in tumor initiation.

"There is a lot of research describing genes that contribute to cancer formation, but it is truly exciting when a study shows that the loss or absence of a single gene prevents cancer from occurring," says Joy L. Little, a postdoctoral fellow on the Golemis team who presented the findings in April at the annual meeting of the American Association for Cancer Research. "The fact that HER2-driven tumors usually don't form without NEDD9 is new information that may help us identify

which type of cancer a patient has or choose the best treatment. If tumors show higher levels of NEDD9, it could be they are more aggressive."

The researchers plan to further investigate the biology of the protein and what makes it crucial in the formation of HER2-driven tumors. NEDD9 also may provide a target for drug development.

*Funding for this research was provided by the National Cancer Institute, National Institutes of Health, Israel Cancer Association, Stanley Abersur Research Foundation, Ben-Gurion University of the Negev, Pew Charitable Fund, and the Commonwealth of Pennsylvania.*

## Viral 'Fossils' Found in Vertebrate Genomes

In an unexpected discovery, researchers have found that the genomes of humans and other vertebrates contain ancient genetic sequences from two deadly virus families.

It was known previously that retroviruses—RNA viruses that insert DNA copies of their genetic material into their hosts' genomes when they replicate—have left behind bits of that material in vertebrate genomes. However, neither of the nonretroviral RNA families in question integrates their genetic material into their host, making the discovery especially surprising. The conservation of the sequences over time, however, suggests that they give the host some selective advantage.

"This was a surprise for us," says virologist Ann Skalka. "It says that the source of our genetic material is considerably wider than we thought."

In comparing thousands of viral genes from non-retroviral families to the genomes of 48 vertebrate species, including humans, the research team uncovered 80 viral sequence integrations into 19 species. Nearly all of the sequences come from ancient relatives of the Ebola/Marburg and Borna virus



Ann Skalka

families, which include deadly pathogens that cause hemorrhagic fevers and neurological disease, respectively. The findings were published in July in *PLoS Pathogens*.

Skalka explains the unexpectedness of the find: "These viruses replicate their RNA and are not known to make any DNA. They have no known mechanism for getting their genetic material integrated into the DNA of

the host genome."

It is remarkable, she adds, that the sequences, some of which may have been integrated into the host genomes more than 40 million years ago, have been largely conserved—in a form that suggests they provide or provided some active benefit, such as protection from infections by related viruses. "One might even think of these integrations as genomic vaccinations," Skalka says.

The research team included investigators at the Institute for Advanced Study in Princeton, where Skalka was on sabbatical when she initiated the study.

Demonstrating conclusively that the viral sequences have a biological function will take additional research. However, the team noted that expression of some of the viral genetic material has been detected in human tissues, supporting the possibility that they are active in host species.



### ON THE WEB

To read more about Skalka's research and link to a discussion of her work on NPR's "Science Friday," visit [www.fcc.edu/topics/fossils](http://www.fcc.edu/topics/fossils).

## Some Clinical Trials Exclude Gay, Lesbian Participants

Researchers at Fox Chase have found evidence that some clinical trials exclude gay and lesbian individuals from participating based on their sexual orientation.

All clinical trials are conducted under guidelines developed by the investigators stating who may participate. Typical criteria include factors such as age, gender, previous treatment history, type and stage of disease, and other medically relevant factors. However, the researchers found that some trials exclude individuals based on sexual orientation.

In reviewing a clinical trial database for criteria that required participants to be in heterosexual relationships, biostatistician Brian Egleston, biologist Roland Dunbrack, and medical oncologist Michael Hall found that the exclusion of lesbians and gay men from

clinical trials is not uncommon in the United States, particularly in studies related to sexual function or couples counseling.

"Most gay and lesbian patients are probably unaware that their sexual orientation is being used as a screening factor for clinical trial participation," Egleston notes. "This is a potentially significant issue, both for patients and the medical research community."

The researchers searched ClinicalTrials.gov, a website that provides information on more than 80,000 trials sponsored by the National Institutes of Health, other governmental agencies, and private industry.

The searches, which included only trials with sites in the United States, showed that 15 percent of identified studies using the terms "erectile dysfunction," "couples," and "hypoac-

tive" (related to hypoactive sexual disorder) included language exclusionary of gays and lesbians. In addition, industry-sponsored trials, multi-region trials, and Phase III trials were more likely to exclude lesbians and gay men.

The exclusionary language was not detected in studies unrelated to sexual function.

The findings were published in a research letter in the March 18 issue of *The New England Journal of Medicine*.

*Following publication of these findings, U.S. senators led by John Kerry requested that Secretary of Health and Human Services Kathleen Sebelius investigate the alleged exclusionary practices. Their letter to Sebelius and a press release issued by Kerry can be found at [fcc.edu/topics/excluded](http://fcc.edu/topics/excluded).*



# Engineered Antibody Targets Ovarian Cancer Cells

## Research points to potential new treatment

Healthy and stubborn, ovarian cancer is a particularly vexing malignancy, difficult to diagnose in its early stages and difficult to treat once it progresses. However, research at Fox Chase is focusing on one of the most promising new approaches to dealing with the disease—using engineered antibodies to target tumor cells while leaving healthy cells intact.

Gregory P. Adams, co-leader of the research program in developmental therapeutics, and his colleagues recently isolated a small, antibody-like molecule called GS45 that is capable of zeroing in on a red flag, of sorts, that distinguishes ovarian cancer cells from normal ones.

The molecule targets a receptor called the Müllerian Inhibiting Substance Type II Receptor, or MISIIR, which is scarce in normal tissue but more abundantly present on the surface of human ovarian cancer cells.

"A problem with targeted therapies is that many of the targets found on cancer cells are also found on normal cells," says Tatiana Karakasheva, a member of the Adams lab who presented the research in April at the annual

American Association for Cancer Research meeting. "When you direct cell-killing drugs at those targets, you get side effects. The great thing about this target is that it's primarily restricted to the reproductive system, and its expression dramatically increases in ovarian cancer."

But finding antibodies that would home in on and bind to the receptor was a challenge. Using a method in which human antibody fragments are expressed and selected on the surface of viruses that infect bacteria, Karaka-

Research at Fox Chase is focusing on a promising new approach to dealing with ovarian cancer.

### The Mighty Mouse

With the exception of clinical trials—studies of drugs or other tools that have undergone extensive preliminary testing—scientists do not experiment on humans. Instead, they rely on plant, animal, fungal, and bacterial "models" for their studies. Perhaps none has proven as indispensable to studying and developing treatments for cancer as the mouse, the most widely used research mammal.



Mice are genetically more similar to humans than any mammal other than primates: 95 percent of their DNA coding sequence is the same, and they share nearly all the same organs. They are unusually easy to breed for specific traits, allowing researchers to create strains ideal for studying particular cancers. And because mice develop quickly, scientists can track tumor growth in a short time.

Research leading to 21 Nobel Prizes has included mice, and in recent years, mouse studies have helped investigate a breast cancer vaccine, study the origins of testicular cancer, and develop a drug that appears to stop the growth of lung cancer.

Mice tend to adapt well to laboratory life, and institutions have a vested interest in the health and well-being of their charges, which can cost thousands of dollars each. Researchers using laboratory animals must provide funders with detailed descriptions of their research and comply with federal regulations on the animals' care.

Fox Chase's laboratory animal program has voluntarily earned accreditation from the Association for Assessment and Accreditation of Laboratory Animal Care.

sheva and Adams managed to isolate a group of candidates, including GS45.

The researchers then engineered the fragments into full-size antibodies that can be used in further experiments. They plan to first demonstrate that GS45 does, indeed, selectively target ovarian cancer cells; then explore its potential for cancer treatment by attaching a drug to it.

The scientists will be working with mice, but as Adams explains, "because mouse and human MISIIR are almost identical, whatever the mouse experiments reveal about targeting and toxicity is likely to apply to humans. That puts us in a powerful position to move this work forward through additional pre-clinical studies and, if it continues to show promise, to clinical trials."

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# Science at the Sea

Early Outpost Looked to Marine Life for Clues to Cancer Growth

By Abbey J. Porter and Matt Steinmetz

In Fox Chase's formative years, the researchers who helped chart the Center's scientific course reached far beyond Philadelphia to start a tradition of pioneering investigation into cancer's origins.

In 1930, Stanley P. Reimann, founding director of the Lankenau Hospital Research Institute—a precursor of the Institute for Cancer Research that would form the scientific arm of Fox Chase—financed the construction of a one-room laboratory in North Truro, Massachusetts, with a \$1,000 gift from his father-in-law.

Perched on a bluff overlooking the Cape Cod Bay, the Marine Experimental Station operated under the direction of Frederick S. Hammett, the Institute's first scientific director and a "high-spirited man full of interesting ideas," according to a 1975 journal article by Temple Uni-



Christened the Marine Experimental Station, the tiny lab in North Truro, Massachusetts, was the site of lively scientific activity during the 1930s and '40s.

versity physician Fred B. Rogers. The laboratory's mission: to investigate the biological basis of cancer.

Reimann believed that basic cancer research didn't necessarily mean studying cancer, but studying normal cell growth—a revolutionary idea. The area's teeming sea life provided excellent test subjects for the dozen or so Institute scientists who traveled to North Truro each

summer to spend the year's warmest months in the serene, unspoiled environment, where they were sometimes joined by collaborators from other institutions.

"The work at the Marine Station provides the foundation on which progress of the Institute in its studies of [cell] growth may be had," wrote Hammett to Reimann in a letter dated February 14, 1936. Dozens of such letters, archived in the Talbot Research Library at Fox Chase, chronicle the 18 summers that Ham-



mett—a full-time New Englander—oversaw the outpost while Reimann ran the Institute in Philadelphia.

For the first several years, the North Truro crew crowded into a single small, dark laboratory that resembled a Cape Cod cottage. In 1935, Reimann purchased the land on which the lab stood, which had previously been rented, as well as surrounding acreage on which a new building was constructed in 1938.

Experiments at the outpost included Hammett's multi-year study of tiny, jellyfish-like creatures called *Obelia*, in which he documented the effects of amino acids and carcinogens on growth and life cycle. Other scientists studied brown and red marine algae. The researchers published papers in journals including *Nature* and *Protoplasma* and in 1937 launched their own journal, *Growth: A Journal for Studies of Development and Increase*, with Hammett as editor-in-chief.

In 1939, Hammett organized the first Symposium on Development and Growth at North Truro, drawing some 400 scientists from across the country and around the world for what would become an annual event. The symposium led to the establishment of what is today known as the Society for Developmental Biology.

As time passed, the station's equipment became outdated and faculty participation dwindled. Hammett, who struggled with the effects of tuberculosis for much of his adult life, lobbied Reimann frequently for additional scientists and resources.

The lab faced another challenge as well: By 1947, the surrounding area had become so populated that the marine life

*"The work at the Marine Station provides the foundation on which progress of the Institute in its studies of [cell] growth may be had."*

—Frederick S. Hammett, in a letter to Stanley P. Reimann (February 14, 1936)

was dying out. The formerly pristine landscape "had become covered with numerous buildings and cottages," recalled Reimann in the book *Reimann's History*. "Much of the flora and fauna in the front of the laboratories had disappeared. Apparently the more delicate creatures did not like human contact."

As work at the Institute in Philadelphia increased, fewer scientists migrated to North Truro. "I do not know what to say at the moment about the summer," wrote Reimann to Hammett on January 20, 1947. "There is no one who can profitably go up to the Cape and work. All of the possible people are full up with their own programs and we really should not interrupt them."

Work at the scientific outpost ceased in 1948. In 1953, Hammett died of prostate cancer.

The Marine Experimental Station seems to be largely relegated to history, but a crumbling *Philadelphia Record* article about Hammett, dated December 1943, testifies to a spirit of commitment that helped launch the Fox Chase of today:

"When storms from the North Atlantic buffet the Cape, the slight figure of the Philadelphia scientist will be seen making his way through the snow drifts to his Truro laboratory. ... Dr. Hammett has made Truro a mecca of scientists...and is sending throughout the world the fame of Philadelphia's Lankeau Hospital." 📍



The Cape Cod research outpost, overseen by Frederick S. Hammett, far left, drew scientists from Philadelphia and beyond for 18 years to study cell growth in the pristine environment.



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