Brighter Picture for Endometrial Cancer

Delivering Women’s Cancer Care Closer to Home

Living Well with Advanced Breast Cancer
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New director, honoring Susan F. Smith, leadership updates

ASK AN EXPERT
How do clinical trials advance treatment for women’s cancers?

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TURNING POINT 2017 is published for supporters of the Susan F. Smith Center for Women’s Cancers. To learn more about the center, call 617-632-2675.

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About the cover
Young woman faces breast cancer with support from her husband. See page 23.

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Membership listing current as of August 1, 2017.
Dr. D’Andrea Appointed Susan F. Smith Center Director

Dana-Farber’s Alan D’Andrea, MD, an internationally recognized basic scientist and expert in the faulty DNA damage and repair mechanisms that can drive certain ovarian cancers, was appointed director of the Susan F. Smith Center for Women’s Cancers in early 2017.

In his new role, Dr. D’Andrea leads a team of basic and translational researchers dedicated to discovery and to the rapid integration of findings from the laboratory to the clinic to benefit patients with breast and/or gynecologic cancers. He succeeds Dirk Iglehart, MD, who was director of the center from 1999 until 2016. Ursula Matulonis, MD, director of Gynecologic Oncology, served as interim director, investing countless hours in educational and research efforts. Dr. Matulonis, Eric P. Winer, MD, chief clinical strategy officer at Dana-Farber and director of Breast Oncology, and Judy Garber, MD, MPH, director of Dana-Farber’s Center for Cancer Genetics and Prevention, will continue to lead in their respective areas.

Dr. D’Andrea is also director of the Center for DNA Damage and Repair at Dana-Farber and the Alvan T. and Viola D. Fuller American Cancer Society Professor of Radiation Oncology at Harvard Medical School. He leads a Stand Up To Cancer Dream Team focused on ovarian cancer – specifically, therapies such as PARP inhibitors that exploit cancer’s vulnerability in the area of DNA repair.

His career at Dana-Farber began in the department of Pediatric Oncology, then shifted to Radiation Oncology, where he directed the division of Genomic Stability and DNA Repair. As he investigated the genetic causes of an uncommon pediatric cancer syndrome called Fanconi anemia, he and his colleagues discovered that their work related to the larger issue of how cells repair damaged DNA – and what happens when such repairs fail to be made. The research had a direct bearing on new approaches to the diagnosis and treatment of women’s cancers.
Dr. Winer Earns Two Major Honors

Eric P. Winer, MD, was honored at the San Antonio Breast Cancer Symposium (SABCS) in December 2016 with the William L. McGuire Memorial Lecture Award and, in June 2017, with the Gianni Bonadonna Breast Cancer Award from the American Society of Clinical Oncology (ASCO). Both awards acknowledge his leadership in advancing science, improving clinical care, and mentoring the next generation of breast cancer researchers and clinicians.

Excerpts from Dr. Winer’s McGuire Memorial Lecture

“Moving forward there are three areas that need focus: resistance to therapy, overtreatment, and health equity.”

“I want to remember and thank the Dana-Farber breast oncology group as well as all breast cancer patients I have cared for and their families. One very special aspect of being a medical oncologist, specifically a breast cancer doctor, is you’re given this door to walk into people’s lives, and if you go in, you have an experience that is like few other experiences. My patients have really been my teachers.”

Dr. Garber named Susan F. Smith Chair

Judy Garber, MD, MPH, is the first incumbent of the Susan F. Smith Chair. The chair, created by Josh and Anita Bekenstein in honor of Susan F. Smith, is designated to be filled by an exceptional senior faculty member at Dana-Farber who embodies the unwavering commitment to excellence and passion for conquering cancer that Mrs. Smith brought to every aspect of her work at the Institute.

Dr. Garber is director of Dana-Farber’s Center for Cancer Genetics and Prevention and founder of the Institute’s Cancer Risk and Prevention Clinic, one of the first devoted to the identification and management of individuals at highest cancer risk. Her research activities include the study of breast cancer risk assessment and communication, breast cancer genetics, and pharmacogenetics. More recently, her research has expanded to the study of basal-like breast cancer, the most common form in women with \textit{BRCA1} mutations.
Drs. Shapiro and Zhao Awarded Program Project Grant

Dana-Farber’s Geoffrey Shapiro, MD, PhD, and Jean Zhao, PhD, are the first recipients of a new program project grant in breast and gynecologic cancer research sponsored by the Susan F. Smith Center. The grant of $500,000 annually for three years is intended to foster research in both breast and gynecologic malignancies – particularly studies that could lead to clinical trials. Drs. Shapiro and Zhao’s project aims to develop novel targeted and immunotherapy combinations to treat triple-negative breast cancer and high-grade serous ovarian cancers with certain molecular characteristics.

Dr. Goel Named First Recipient of Iglehart Fellowship

Dana-Farber’s Shom Goel, MD, PhD, is the first recipient of the J. Dirk Iglehart, MD, Breast Cancer Term Fellowship. Established by donors in Dr. Iglehart’s honor, the two-year fellowship was created to support the work of a physician-scientist who shares the passion for education and collaboration of the Susan F. Smith Center’s longtime director who retired in 2016.

In addition to caring for patients, Dr. Goel plans to focus his fellowship on targeted therapies – including a promising new class of drugs called CDK4/6 inhibitors. He is currently investigating which breast cancers may respond best to CDK4/6 blockers, and how these drugs might be combined with other agents. He hopes to translate his results into clinical trials.

Dr. Matulonis’ Research Leads to New Drug

Women with relapsed ovarian cancer who are sensitive to platinum-based chemotherapy can now benefit from the newly approved drug niraparib, thanks to research co-led by Ursula Matulonis, MD, director of Gynecologic Oncology at the Susan F. Smith Center. The drug won approval from the Food and Drug Administration in March 2017, after an international clinical trial showed it can lengthen the period in which the disease is held in remission.

The findings of the trial, dubbed ENGOT-OV16/NOVA, were published in the New England Journal of Medicine and presented at the European Society for Medical Oncology 2016 Congress in Copenhagen. Dr. Matulonis was senior author and led the U.S. arm of the trial.

Known as a PARP inhibitor, niraparib works by hindering DNA repair in cancer cells that are particularly vulnerable because of malfunctions in DNA-repair pathways. In clinical trials, PARP inhibitors have shown promise against cancers that carry mutations in the DNA-repair genes BRCA1 or BRCA2.
Clinical trials are the fulcrum of cancer research – the means by which progress in the laboratory receives a real-world testing in patients. Like all tests, clinical trials are designed to answer questions – namely, is the new treatment or technique safe? Is it effective? How does its performance compare to standard approaches?

“Trials are important for all patients who are being treated for a cancer diagnosis,” says Erica Mayer, MD, MPH, of the Susan F. Smith Center for Women’s Cancers, who has led and participated in numerous trials of new breast cancer treatments. “Every day in the clinic I’m reminded that the treatments we have available today exist because of the work that has been done in clinical trials, and because of the women who have participated in them.”

**New Drugs Prove Themselves**

To appreciate the importance of clinical trials in women’s cancers, one need merely read a list of therapies approved for patient use in the last few years: niraparib and olaparib for certain ovarian cancers, and palbociclib for breast cancer, to name a few. Each was declared safe and effective by the Food and Drug Administration (FDA) only after proving itself in a series of trials involving hundreds or thousands of patients.

“Clinical research is one of the main engines for the continual improvement of cancer treatment,” says Ursula Matulonis, MD, director of Gynecologic Oncology at the Susan F. Smith Center. “Trials not only provide patients with access to the latest potential therapies, but enable researchers to evaluate the agents for safety and effectiveness.”

Since 2012, six new medications for breast cancer have come “off trial” – approved by the FDA as standard therapies on the basis of
their performance in clinical testing. The same has been true for four drugs targeting gynecologic cancers. Physician-scientists from the Susan F. Smith Center have played key roles in the development and testing of several of these agents.

Impressive as the figures are, they only hint at the current extent of clinical research into women’s cancers. Advances in basic science, and the alacrity with which researchers have seized on them to improve existing therapies, have led to a significant expansion in the number and range of clinical trials.

**Nearly 100 Trials**

That energy is very much in evidence at the Susan F. Smith Center, where investigators are leading or participating in nearly 100 open trials. Of the more than 60 trials for breast cancer, the majority are focused on metastatic disease.

Such research is particularly meaningful for women with advanced cancers, who may benefit from new treatments or participation in clinical trials. For example, Linda Dziobek, who has advanced ovarian cancer, has been enrolled in several clinical trials.

“One of the reasons that Dana-Farber and the Susan F. Smith Center are leaders in clinical research is that pharmaceutical firms see us as partners in the quest to improve patient treatments,” says Ian Krop, MD, PhD, chief of Breast Medical Oncology and clinical research director for Breast Oncology. “Our track record and reputation for quality have made us a go-to place for testing the next generation of breast cancer therapies.”

**Support Clinical Research**

Your gift helps make it possible for doctors to test new drugs and drug combinations in patients through clinical trials. To learn more or make a gift, contact Suzanne Kouri at 617-632-4055 or suzanne_kouri@dfci.harvard.edu.

www.susanfsmith.org
Drug Shown to Block Progression of HER2 Breast Cancer

Researchers at Dana-Farber’s Susan F. Smith Center for Women’s Cancers and other institutions have found that a type of breast cancer that often develops resistance to targeted therapies can be driven back into remission in mice by a drug that blocks the division of cancer cells.

For patients with HER2-positive breast cancers, drugs such as Herceptin often halt the growth of tumors but many patients’ cancers become resistant. This study demonstrates the potential of agents known as CDK4/6 inhibitors to overcome this resistance.

Researchers created a strain of genetically modified mice that carry a switch for turning production of the HER2 protein on and off in breast tissue. With the switch on, the mice developed human-like HER2-positive breast tumors. With the switch off, the tumors shrank, only to return months later about two-thirds of the time.

Researchers examined tissue samples from original and recurrent tumors to see how they differed, and found that genes that control cell division and the cell cycle were overactive in recurrent tumors. Notably, these tumors had abnormally high levels of two proteins associated with the cell cycle: cyclin D1 and CDK4.

“In HER2-positive breast cancer, cyclin D1 partners with CDK4 to drive cell proliferation,” says the study’s first author, Shom Goel, MD, PhD, of the Susan F. Smith Center. “We learned that drugs targeting CDK4 can also overcome mechanisms of drug resistance, and reinstate tumors’ original susceptibility to HER2 blockers.

“In cells, we found that the drug abemaciclib – which inhibits CDK4 and the related protein CDK6 – was active against HER2-positive breast tumor cells that were resistant to standard treatments. Strikingly, when we added a HER2-targeting drug to abemaciclib, we saw even greater efficacy. Studies in mouse models showed the same benefit.”

Senior co-authors were Jean Zhao, PhD, and Ian Krop, MD, PhD, chief of Breast Medical Oncology. Co-authors included Sara Tolaney, MD, MPH, associate director of Clinical Research for Breast Oncology, and Eric P. Winer, MD, director of Breast Oncology and chief clinical strategy officer.

A randomized clinical trial that builds upon these findings is now open across the U.S. and Europe.

Chemical structure of the CDK4/6 inhibitor abemaciclib
Do Low-Risk DCIS Patients Need Treatment?

A new clinical trial is exploring whether the principle of less-is-more applies to treatment of the most common type of non-invasive breast cancer.

The trial, dubbed COMET (Comparison of Operative to Monitoring and Endocrine Therapy), will examine whether patients with low-risk ductal carcinoma in situ (DCIS) fare as well with careful monitoring, with or without hormone therapy, as they do with surgery, with or without radiation therapy.

The COMET trial, co-led nationally by Ann Partridge, MD, MPH, director of the Susan F. Smith Center’s Young and Strong program, is open to women age 40 and older with low-risk DCIS that tests positive for receptors to the hormones estrogen or progesterone. Participants will receive either standard therapy or active surveillance with or without hormone therapy. Investigators will track them over time and compare survival rates and quality of life of members of the two groups.

The foundation of the trial was supported by research at Dana-Farber/Brigham and Women’s Cancer Center by Mehra Golshan, MD, FACS, a breast surgeon in the Susan F. Smith Center for Women’s Cancers, and others, which suggested that surgery for DCIS does not improve a patient’s already excellent chances of survival. Golshan is the site principal investigator of the trial at Dana-Farber.

DCIS involves the presence of abnormal cells inside a milk duct of the breast. Although not life-threatening in itself, DCIS can increase the future risk of developing an invasive breast cancer. Well over 99 percent of women with DCIS are alive a decade after diagnosis. Most undergo standard treatment, but in those who don’t, the condition often doesn’t spread beyond the milk duct to become invasive.
Can a Vaccine Prevent DCIS from Becoming Invasive?

In a multi-site clinical trial, researchers are studying whether a NeuVax vaccine can rouse the immune system to recognize and target abnormal cells in the milk ducts of the breast in patients with ductal carcinoma in situ (DCIS), also known as non-invasive breast cancer. The phase 2 trial, dubbed the VADIS trial (for VAccine in women with DcIS of the breast), is a preliminary exploration: If NeuVax proves successful in generating an immune response to DCIS cells, and does so safely, the door would open for further testing of vaccines as ways to prevent invasive breast cancer.

The vaccine has two components: GM-CSF, a drug that increases the number of disease-fighting white blood cells, and a piece of HER2, a protein expressed (and over-expressed in HER2-positive breast cancers) in most breast cancer cells. When these two substances are injected into the skin, the immune system may be able to target breast cancer cells and attack them with the white blood cells.

The trial, led at Dana-Farber by Tari King, MD, chief of Breast Surgery at the Susan F. Smith Center, and Judy Garber, MD, MPH, director of Dana-Farber’s Center for Cancer Genetics and Prevention, is open to pre- and postmenopausal women diagnosed with DCIS on core breast biopsy. Participants will receive the vaccine during the waiting period before surgery. At the time of surgery, a section of breast tissue will be examined for signs of an immune system attack on the DCIS cells.

“The VADIS trial brings this novel and important immune research to women with DCIS and may help to move the immunotherapy field toward prevention,” Dr. Garber says.

Exploring a Method for Ovarian Cancer Detection

Currently there are no screening tests for ovarian cancer, and it is often diagnosed at a late stage. To help address this, Dipanjan Chowdhury, PhD, chief of Radiation and Genomic Stability in Dana-Farber’s department of Radiation Oncology, hypothesized that ovarian cancer may contain a unique set of microRNAs that be detected in a patient’s blood.

Chowdhury has analyzed blood samples from 179 women who were being treated for a pelvic mass to see if the micro RNAs could indicate which masses were benign, borderline, or malignant. On the strength of these results, he is now expanding this effort to further analyze the samples. While there is much to be learned about the role that microRNAs play in ovarian cancer, identifying a unique signature for the disease may one day lead to a diagnostic test.
New Program Addresses Breast Cancer Risk

A program to educate women about their risk of breast cancer and provide personalized screening recommendations for those at elevated risk has opened in the Comprehensive Breast Health Center at Brigham and Women’s Hospital, in collaboration with Dana-Farber. The program, called B-PREP (Breast cancer Personalized Risk assessment, Education, and Prevention), explores how certain factors contribute to risk and will develop new approaches for surveillance and prevention.

“Our estimates suggest that 10-20 percent of women are at increased risk of developing breast cancer, either because of an inherited genetic mutation, a family history of the disease but no known mutation, or because they’ve had a breast biopsy that showed abnormal cells,” says Tari King, MD, chief of Breast Surgery at the Susan F. Smith Center for Women’s Cancers. “Among the other 80 percent, some may also be at increased risk secondary to other factors such as obesity or increased breast density. By developing a comprehensive program for all women at risk, we hope to learn more about how these and other non-genetic factors impact risk and educate women about risk-reducing strategies.”

The B-PREP team includes surgeons, oncologists, breast imagers, nurse practitioners, social workers, and other breast specialists from Brigham and Women’s and Dana-Farber. Led by Dr. King and Daniel Morganstern, MD, a medical oncologist at Dana-Farber, B-PREP is open to all women, whether or not they have a breast condition. Women whose assessment indicates an elevated level of risk will be invited to continue in the program and will receive personalized screening and risk-reducing recommendations.

Research is a key component of the program. B-PREP staff will refer eligible women to cancer-prevention clinical trials, and patients will be invited to donate blood, saliva, or tissue from biopsies that will be used to study new approaches to risk stratification and breast cancer prevention.
Metastatic breast cancer has not stopped Kim Delling, Lola Baltzell, and Michael Kovarik (left to right) from living life to the fullest.
In early 2015, Kim Delling had put her 2009 bout with breast cancer behind her. Then, at a routine checkup, her doctor ordered an additional test. “I knew something was up,” recalls Delling, a 50-year-old real estate agent in Wilmington, Mass.

The cancer had come back. It had spread to her lungs, liver, and lymph nodes and was, according to her local doctor, incurable.

A visit with Erica Mayer, MD, MPH, a breast oncologist at the Susan F. Smith Center for Women’s Cancers at Dana-Farber, softened the news. “Dr. Mayer said she had a toolbox full of tools for me,” says Delling. “Just because this disease is incurable doesn’t mean I can’t live with it.”

That shift in perspective – looking at metastatic breast cancer as a chronic disease rather than an immediate near-term death sentence – is the result of a transformation in the way doctors treat it. New medicines and improvements in supportive care are making it possible for many patients to live with the disease for many years, and live relatively well.

Approximately 250,000 women and 2,000 men are diagnosed with breast cancer in the U.S. each year according to the National Cancer Institute. In about six percent of those cases, the cancer has already spread to liver, lung, bone, or brain tissue. Metastatic disease, however, also occurs in those who were treated for early stage disease, like Delling. Researchers estimate that 20 to 25 percent of patients with early breast cancer will develop metastatic cancer eventually, despite advances in early-stage care.

For patients with metastatic disease, currently numbering about 200,000 in the U.S., the disease is not curable. But individual experiences vary widely. While the disease can occasionally move rapidly, more patients are living longer than ever before. About 26 percent of women with metastatic breast cancer are still living five years after diagnosis and some continue to do well 10 or 15 years after diagnosis.

“We’ve taken steps forward, and for certain
types of metastatic breast cancer, large steps forward, so more patients are living longer than ever before,” says Eric P. Winer, MD, director of Breast Oncology and chief strategy officer for Dana-Farber. “But it is still a disease women ultimately die from, so these steps make it so more women can live a long time with the disease and be, essentially, symptom free.”

Drivers of Change

Targeted therapies that block the molecular drivers of cancer growth have helped extend life expectancy for metastatic breast cancer patients. For instance, Herceptin, which is used to treat women with HER2-positive breast cancer, frequently extends survival for women with metastatic disease. In the past few years, even more potent medicines that target HER2 have been approved, adding to the success. “The more we target HER2, the better people with this disease do,” says Nancy Lin, MD, clinical director of Breast Oncology at the Susan F. Smith Center, and director of the Metastatic Breast Cancer Program.

For estrogen receptor (ER)-positive breast cancer, a similar story may be unfolding. Palbociclib and ribociclib, which target cancer drivers called CDK4 and CDK6, were recently approved for routine use, and a similar drug, abemaciclib, is currently in late-stage trials.

Women with metastatic triple-negative breast cancer have been the hardest to treat. Just five years ago, there were few trials of new drugs for this condition, but that has started to change. Trials are currently testing antibody-drug conjugates, so-called smart bombs that attack the cancer but leave healthy tissue relatively untouched, and immunotherapy drugs, which have shown dramatic success in melanoma and lung cancer, and early promise in breast cancer. “There are a lot of exciting drugs in late stage trials, so there’s more hope than ever before that at least one of them will be a breakthrough,” says Dr. Lin.

Currently, Dana-Farber has dozens of open clinical trials testing new drugs and new treatment regimens for all sorts of metastatic breast cancer, including cases in which the cancer has spread to the brain. In the past, few trials were open to patients with brain metastases, but Dana-Farber offers several. “This is no longer the forgotten corner of metastatic breast cancer,” says Dr. Lin.

For Delling, supportive care and her doctor’s thoughtful treatment approaches have kept her active and working for the two years since she learned her cancer was metastatic. Over time, she’s participated in three trials and tried five treatments. Her current regimen, which is not part of a trial, is working extremely well. “People would never in a million years know that I have stage 4 cancer,” she says.

But she does have to live with side effects, such as neuropathy, which causes numbness in her hands and pain in her feet. “At times, it’s like walking on broken glass,” she says.

Delling takes medications to minimize the nerve damage, and her care team at Dana-Farber watches her closely. “It’s another layer of care that helps people feel better and maybe even do better,” says Dr. Lin.

Embracing Care

With so many treatment options and potential side effects, patients need extra support to track and manage their symptoms and care. To provide this support, Lin and colleagues at Dana-Farber launched the EMBRACE (Ending Metastatic BReAst Cancer for Everyone) program. “Taking care of metastatic breast cancer patients has become increasingly complicated,” says Dr. Lin. “We wanted to make sure we provide consistent support for our patients.”

EMBRACE started out as a research program to help Dana-Farber clinical researchers learn more about metastatic breast cancer from their patients. Now, it is also a clinical program with outreach, educational
programs, and coordinated care. Patient coordinators support oncology teams by knowing what is going on with patients, tracking tumor test results, and identifying potential clinical trials. They also connect patients to the resources available to them, such as support groups, palliative care, and nutritionists.

EMBRACE also remains a research program that has so far enrolled over 1,700 patients. In December 2016, data collected with support of the EMBRACE study revealed genetic alterations in metastatic ER-positive breast cancer that are not seen in the disease before it spreads. These mutations could help the cancer evade therapies, so they could point to promising new targets for drugs that could beat drug-resistant cancer.

In the long run, combinations of new therapies could, conceivably, eradicate metastatic cancer or prevent it from becoming metastatic in the first place. “As we understand which drugs overcome resistance, our ultimate goal will be to try to cure metastatic breast cancer,” says Nikhil Wagle, MD, a medical oncologist at Dana-Farber.

Leads for new drugs are found faster by studying larger numbers of patients, so in 2015 Dr. Wagle launched the Metastatic Breast Cancer Project. It appeals to women and men with metastatic breast cancer across the U.S. to share tumor samples and medical records for research. The project, which is a collaboration between Dana-Farber and the Broad Institute of Harvard and MIT, has enrolled more than 3,400 patients to date.

Dr. Wagle’s team reaches metastatic breast cancer patients through social media, although it is patients themselves who appeal to friends, support groups, and online followers to create a self-sustaining influx of new participants. “Patients put out an impassioned plea to others, telling them that it’s easy, and if you share your information, think of how much faster progress could be,” he says.

For Delling, her husband, stepchildren, siblings, friends, and career keep her fighting to live every day. But she is also inspired by the promise of research. “Every day they’re discovering,” she says. “There are disappointments, but there are also new drugs around the corner.”
Susan F. Smith Center for Women's Cancers

TURNING POINT 2017
Human Touch Surgeries, New Therapies

Brighten the Picture in Endometrial Cancer

by Robert Levy

Although she had been fully prepped on what to expect, Barbara Losordo was a bit surprised at the ease and speed of her recovery from surgery for endometrial cancer. Discharged from the hospital the same day she had undergone the procedure, she needed no pain medication afterward. Within a week, she was driving. Within a month, she was back in the gym.

“I felt so good it didn’t seem like a major operation,” says the mother of two adult children, who lives with her husband on Cape Cod. Her experience exemplifies how an approach to endometrial cancer, championed at the Susan F. Smith Center for Women's Cancers at Dana-Farber, is helping women make a full return to their lives.

The approach includes reducing the impact of hysterectomy, the standard treatment for endometrial cancer, so patients can recover more quickly with fewer complications and shorter hospital stays. In one area, in particular, surgeons at Brigham and Women's Hospital (BWH), Dana-Farber's partner in adult care, are demonstrating that human skill can outperform robot-assisted surgery in some patients.

Endometrial cancer, which arises in the lining of the uterus, is the most common form of gynecologic cancer. This year, an estimated 61,000 women in the United States will be diagnosed with the disease. Often detected early, it can usually be cured...
by surgery and, if necessary, a combination of chemotherapy, radiation, and hormonal therapy.

While research is under way to improve cure rates even further, “the treatment of the disease is itself turning a corner, with a growing use of minimally invasive, laparoscopic procedures,” says Losordo’s surgeon, Colleen Feltmate, MD, director of minimally invasive surgery in Gynecologic Oncology at BWH.

Laparoscopic surgery uses a small camera and long instruments inserted through small incisions. Doctors began using laparoscopic surgery for hysterectomies and biopsies to detect cancer spread in the 1990s. It was an improvement over open surgery, which required large incisions and increased the chance of infections and other complications.

Around 10 years ago, hospitals around the country began acquiring technology that allows the surgeon to manipulate these tools via a robotic arm. The robotic technique is especially useful for patients who are obese or have a complicated surgical history with a lot of scar tissue in the pelvis.

Many surgeons, however, find that using conventional laparoscopic technique without robotic assistance allows them to complete the operation in less time, with fewer and smaller incisions, and with equally good results. Fewer surgeons use conventional laparoscopy because it requires more training, but the benefits – shorter operations and lower costs – are hard to argue.

At most hospitals in the United States, robot-aided procedures remain the standard for patients with endometrial cancer. At BWH, by contrast, fully 80-85 percent of such surgeries are performed laparoscopically without robotic assistance.

This approach has had a demonstrable effect on recovery times, Dr. Feltmate says. “Ten years ago, patients were usually in the hospital for three or four days and were out of work for about six weeks. Today, 70-80 percent of our patients go home the same day as surgery. Like Barbara Losordo, many can drive in a week and are often back at work in two to four weeks.”

Sparing the Nodes

Another tissue-sparing advance involves checking the lymph nodes around the uterus for cancer. Traditionally, surgeons would remove 15-20 nodes and examine them for cancer cells that may have escaped the uterus. The procedure is critical to identifying patients at risk for metastatic cancer, but the removal of so many nodes can create new problems, particularly lymphedema, a blockage of lymph flow that can cause a painful swelling of the legs and increased susceptibility to infection.

Borrowing a technique from breast cancer and melanoma surgery, gynecologic surgeons at BWH use a more selective procedure known as sentinel lymph node mapping. Before the operation, the surgeon injects a fluorescent dye at two precise locations in the patient’s cervix. Lymphatic channels carry the dye to the sentinel nodes – the first nodes that cancer cells are likely to reach if they leave the uterus.

When the uterus is removed, the sentinel nodes are also removed and immediately examined for tumor cells by a pathologist. Sentinel node removal dramatically reduces the risk of lymphedema and its morbidity as compared with more complete node removal. It usually takes a week for all the biopsies to be complete. Depending on the results of these exams, patients may require additional treatment such as chemotherapy or radiation therapy. The good news is that most patients are cured by surgery alone.

Research and Recommendations

At Dana-Farber, the approach to endometrial cancer encompasses genetics and prevention as well as a range of research studies.

On the genetic side, Huma Rana, MD, clinical director of the Center for Genetics and Prevention, and her colleagues counsel patients who test positive for Lynch syndrome, a hereditary condition that increases one’s risk of developing endometrial cancer, as well as cancers of the colon, stomach, small intestine, pancreas, liver, or other organs. “By identifying people with Lynch syndrome, who often come to us because of a strong family history of endometrial or colon cancer, we can recommend screening to find these cancers early or offer surgery to reduce chances of developing them,” Dr. Rana says.

In addition, scientists at the Susan F. Smith Center are leading several clinical trials of new agents for patients with advanced or otherwise hard-to-treat endometrial cancers. One early-stage trial is testing an immunotherapy drug called avelumab, a “checkpoint inhibitor” that seeks to unleash an immune system attack on tumor cells. The study, initiated and led
by Panos Konstantinopoulos, MD, PhD, of the Gynecologic Oncology Program at the Susan F. Smith Center, is the first to test an immunotherapy agent in patients with endometrial cancer.

The trial includes patients whose tumor cells have a flaw in the mismatch repair (MMR) pathway – a genetic system that repairs certain kinds of DNA damage. These mutations can be inherited, as in Lynch syndrome, or occur only in the tumor cells. Research by Dr. Konstantinopoulos and his colleagues suggests that such tumors may be especially susceptible to immune checkpoint inhibitors. “The study is still under way, but early indications are that several patients, including some with MMR pathway abnormalities, have responded well to the drug,” he observes.

For uterine serous cancer – an aggressive type for which there few good treatments – investigators plan to test a drug that blocks a key stage of the cell-division cycle. The cycle includes several pauses that allow the cell to “proofread” its DNA and make corrections. Many endometrial cancers barge right through one such pause because of a mutation in the gene TP53. The resulting accumulation of DNA damage, however, is often repaired during a second pause, controlled by the gene wee1.

The clinical trial, to be led by Joyce Liu, MD, director of Gynecologic Oncology Clinical Research in the Susan F. Smith Center, will examine the safety and effectiveness of a compound known as AZD1775, which inhibits wee1. The hope is that by hindering DNA repair in cancer cells already hobbled by a broken TP53 gene, the compound will create such a buildup of DNA damage that the cancer cells can no longer survive. Investigators hope to open the trial in 2017.

Support Basic Science

Before new drugs and drug combinations can be tried with patients, they must first be tested in the lab, which is called “basic science.” Help make it possible for basic scientists at the Susan F. Smith Center for Women’s Cancers to find the most effective, targeted treatments that will one day translate to patient care. To learn more or make a gift, contact Suzanne Kouri at 617-632-4055 or suzanne.kouri@dfci.harvard.edu.
Delivering Women's
Boston’s Longwood Medical Area stretches over 213 acres surrounding the quadrangle of Harvard Medical School. It includes Dana-Farber Cancer Institute, Brigham and Women’s Hospital, Boston Children’s Hospital, and a dozen other hospitals and research institutions.

In other words, Longwood is a nexus of scientific research and innovative clinical care matched by only a handful of other medical centers in the world. If you are an up-and-coming medical researcher, or a young doctor eager to train at one of the best hospitals in the world, Longwood is where you want to be.

If, however, you or someone close to you has a serious diagnosis, you may be torn between wanting to be where the cutting-edge clinical care and research are located, or enjoy an easier commute. Eric P. Winer, MD, director of Breast Oncology in the Susan F. Smith Center for Women’s Cancers at Dana-Farber, understands these circumstances. “It is very important to me, as an oncologist, to know my patient as a person,” Dr. Winer says. “I tell her that I may be the ‘cancer expert,’ but she is the expert on herself. The ultimate treatment decisions that we make together may differ from person to person. That process includes choosing the best place for her to receive care. It’s not always Longwood.”

**Breast Cancer Care Beyond Longwood**

In addition to his leadership role in the Susan F. Smith Center for Women’s Cancers, Dr. Winer also serves as Dana-Farber’s chief clinical strategy officer. In that job, he takes a broader view to see where Dana-Farber has – or should have – partnerships with community providers.

Through a combination of strategies – care collaborations, satellite centers at local hospitals, partnerships with physician practices, and community outreach – Dana-Farber’s leadership in women’s cancers is currently being felt in locations from Maine to Rhode Island, and as far away as Brazil and China.
Launched in 2005, the program was built in response to issues that Dr. Partridge and her colleagues were seeing among women age 45 and younger in the clinic. “We realized that the younger women with breast cancer were having the hardest time. One day, they have their whole lives ahead of them – career, relationships, motherhood, education – and then they see it potentially put on hold. One 32-year-old woman described her breast cancer diagnosis as a roadblock to everything else.”

Reaching Young Women

As Dana-Farber expanded its geographic reach through partnerships, the Program for Young Women with Breast Cancer was already poised to spread out. “We embraced the satellite concept,” says Ann Partridge, MD, MPH, founder and director of the program. “We imagined it as a replicable clinical service from the very beginning.”

Supporting Young Women

The Susan F. Smith Center for Women’s Cancers has a dedicated program for young women with breast cancer that offers resources, education, and opportunities to participate in research studies. Visit www.dana-farber.org/YoungWomenBreastCancer, or follow @youngstrongDFCI on Twitter.

The overarching objective of these affiliations, Dr. Winer says, “is to bring the most current approaches to treatment to various communities. The treatment of breast cancer is a good example of why this is so important for an individual patient.

“Twenty years ago or so, the options for treating a woman with breast cancer were very limited: surgery, chemotherapy and radiation,” Dr. Winer adds. “By today’s standards of precision, these are blunt instruments. We have learned so much about drug development and other newer individualized treatment options. We also know more about risk, prevention and early intervention. It is our responsibility to engage with oncologists in communities beyond Longwood so their patients have access to these options.”

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The program attracted a lot of attention and, in 2014, the Centers for Disease Control awarded the program, now called Young and Strong, a $1.75 million 5-year grant to expand its reach throughout New England. Dr. Partridge hopes to bring that multi-disciplinary and augmented supportive care approach to benefit young women with breast cancer where they live and work.

As a result, a new Young and Strong program is in the works at Lifespan Cancer Centers in Rhode Island as well as plans for partnerships in Stamford, Conn., and Worcester, Mass.
Addressing Gynecologic Cancer

Ursula Matulonis, MD, director of Gynecologic Oncology at the Susan F. Smith Center, offers her perspective on the value of community partnerships. “If a patient feels strongly that she wants to be closer to home for her treatment and she has a trusting relationship with her oncologist, then our responsibility is to partner with that oncologist in every way we can,” says Dr. Matulonis.

Dr. Matulonis visits the satellite Dana-Farber/Brigham and Women’s Cancer Center at Milford Regional Medical Center on a regular basis, where she sees some of her own patients with gynecologic cancer, and consults on others. But, she says, “I really want to work with the members of the medical team as much as possible.

“Dana-Farber has made a commitment to these communities, and to these patients, to deliver the highest standards of cancer care,” Dr. Matulonis says. “That means that we also have made a commitment to our colleagues in those communities.”

Assessing Risk

Katherine Schneider, MPH, LGC, a senior genetic counselor in Dana-Farber’s Center for Cancer Genetics and Prevention, waited a long time for the Institute’s network strategy to take shape. “About 16 years ago, I was on a task force charged with finding ways to serve individuals across a spectrum of cancer experience, including those at high risk based on family history,” Schneider says. “We realized that offering genetic counseling and testing at our satellites and affiliates would allow more people to get this important information.”

To judge by their interest, people living in those communities were ready to learn. Schneider and her team of colleagues from Dana-Farber take turns travelling to South Shore, Milford, Londonderry, and inner-city Boston 1-4 times a month for on-site genetic counseling and testing clinics for individuals who have personal and family histories of cancer. Schneider and her team also provide state of the art telehealth genetic counseling and testing services to hospitals in Concord, New Hampshire, and Bangor, Maine.

“These days, a lot of people are very aware of the role of genetics in cancer risk, especially women with a family history of breast or gynecological cancers,” Schneider said. “They really want the whole story – and that often means having a multi-gene panel test to clarify their risks.

“While learning you are at risk isn’t good news, by any means, it gives you a chance to be proactive. Armed with that knowledge, the families I’ve worked with have felt more in control of their future.”
As one saying has it, strength is not measured by how many times you get knocked down, it’s measured by how many times you get back up. By that indicator, Patty Klein is a very strong woman.

Klein was diagnosed with ovarian cancer in 2010. She received the standard treatment available at the time and responded well. Over the next three years, however, she went through several disheartening cycles of treatments and recurrences that left her eager to learn about new strategies being tested.

Klein and her husband Jay went to work. Like the successful business partners they are, they understood the importance of doing their own research. “We read everything that we could find on clinical trials,” she says. “In the process, we learned about Dana-Farber’s leadership in this field.”

That’s when they heard about a clinical trial being led by Ursula Matulonis, MD, director of Gynecologic Oncology at the Susan F. Smith Center for Women’s Cancers. The trial tested a PI3 kinase inhibitor combined with a PARP inhibitor, a type of drug that interferes with a tumor repairing itself after treatment.

Again, the trial worked well – Klein was cancer-free for more than a year – but the cancer eventually came back and she went in search of more clinical trials. Her care team at Dana-Farber helped her find and enroll in the best options at other cancer centers.

Klein took an optimistic view. “I learned that ovarian cancer is a stubborn disease,” she says. “So I knew the odds favored recurrence. I also learned that I have a genetic risk so I faced even longer odds. I saw clinical trials as opportunities to improve them.”

And not just for herself. BRCA1, a genetic mutation associated with breast and ovarian cancer, runs in families. Klein’s sister was diagnosed with breast and ovarian cancer, and two of her nieces tested positive for the BRCA mutation.

The Kleins are founders of A+ Meetings and Incentives, a full-service meeting management company that includes Fortune 500 corporations among its clients. As experts in the business of customer service, they give Dana-Farber an A+ for patient care. She is back for her fourth clinical trial – a step she views as giving her some control and the ability to make choices of her own. “I intend to be a survivor,” she says.
Survivor Spotlight

Navigating Cancer Together

Interview by Naomi Funkhouser

Joy Yang, 36, and her husband, Sam Nathan, were approaching their second wedding anniversary in October 2015 when Yang’s diagnosis of inflammatory breast cancer (IBC) sidelined the bliss and busyness of newlywed life.

For the young couple, 18 months of chemotherapy, surgery, hormone therapy, and radiation set them on a dizzying course that put their wedding vows – a promise to stand by each other in sickness and in health – into sharp focus.

When Yang, a therapist at MIT who specializes in young adult mental health, felt a lump in her breast, her local physician referred her to the Young and Strong Program at the Susan F. Smith Center for Women’s Cancers. Yang was quickly guided from diagnosis to a specialized treatment plan by her oncologist, Ann Partridge, MD, MPH, who founded the program and sees young patients, as do many other doctors in the center.

As Yang began four months of weekly chemotherapy treatments, Nathan – currently pursuing a doctoral degree in psychology – turned, with trademark scholarly focus, to books. He recalls doing “a ton of reading” during that time, whether it was Yang’s study protocol, or The Emperor of all Maladies: A Biography of Cancer. Understanding his wife’s disease gave him a sense of control during her illness, an important coping strategy as he assumed the unfamiliar role of caregiver. To be fully present for her during long days of treatment, he hired a dog walker and leaned on her family – who rented a house nearby – for support, sometimes grocery shopping with her mom.

A Dana-Farber-led study shows how critical these coping strategies are for spouses. The study found that among partners of young women with breast cancer, anxiety affected more than 42 percent of survey respondents. The study, led by Nancy Borstelmann, MPH, LICSW, director of Social Work at Dana-Farber, is one of the first to examine the psychological and social issues affecting family members of people with cancer. “Cancer doesn’t just happen to one person; it has an impact on the entire family,” Borstelmann said.

Yang completed treatment earlier this year. “Getting back to most of who I was before this started feels good,” she says. She finds joy in being able to travel once again, a passion she pursued in June on a three-week trip to Italy – one week of which she spent solo adventuring. “Sometimes in a marriage, to be stronger together means finding your way back to yourself,” she adds.

Joy Yang, with husband Sam Nathan
Liquid Gold
A Conversation with Heather Parsons, MD, MPH
by Elizabeth Dougherty

Heather Parsons, MD, MPH, a breast oncologist in Dana-Farber's Susan F. Smith Center for Women's Cancers, is exploring the value of liquid biopsies in breast cancer care. Here, Dr. Parsons explains how she learns about a patient’s breast cancer by probing the data collected through a blood draw instead of tumor tissue.

What is a liquid biopsy?
A liquid biopsy looks for tumor DNA found in the patient's blood. DNA is normally found inside cells and tells cells what to do. Cancer is, in part, a disease of changes in that DNA code.

Both normal cells and cancer cells release DNA into the bloodstream. We can figure out which DNA comes from the cancer cells because these instructions are different from the instructions in normal cells. Using DNA sequencing to analyze the tumor DNA, we can identify mutations and alterations that come from the patient's tumor. That information could help physicians choose a patient's treatment and helps researchers understand cancer better.

What are the benefits of liquid biopsies?
The problem with needle biopsies is that they may be painful. They can also be impossible to do if the tumor is not easy to access. Sometimes the tissue taken during a biopsy doesn’t yield the information we want.

A liquid biopsy gives us similar information with a blood sample, which is easier to do. We can take blood samples over and over. For instance, we can get a blood sample when someone starts on their therapy, then a month later, and a month after that. If their cancer grows, we can do it again. We can compare all those liquid biopsies to each other and it gives us a lot more information about the cancer’s progress.

How are liquid biopsies being used now?
In our care for breast cancer patients at Dana-Farber, we’re only doing these tests as part of research studies, though they are used in routine care for lung cancer patients. For a patient participating in a research study using a liquid biopsy, there is no extra effort. The sample is simply another blood tube that's collected. We use those blood samples to look at the circulating tumor DNA and learn whether the alterations we find can be used as markers of whether a given treatment will work or not.

How might liquid biopsies be used in the future?
In the near future, we hope to use liquid biopsies to help match patients to clinical trials. Currently, the sequencing tests that influence a patient’s care plan are only done on the DNA from a traditional tumor biopsy.

I’m excited about the potential for using liquid biopsies in early stage cancer. This approach would allow us to monitor these patients after treatment to let us know if they still have tiny bits of cancer that might come back and cause trouble later. We’d like to be able to do more for the patients who need more, less for those who need less.
Making a Difference

Susan F. Smith Center for Women’s Cancers
Executive Council

The Executive Council is guided by a commitment to eliminating breast and gynecologic cancers through education, advocacy, and fundraising. The council dedicates all funds raised for immediate use to the Susan F. Smith Center in pursuit of ongoing breakthroughs in women’s cancers research. Founded in 2003, the council has, to date, raised $12 million for the Susan F. Smith Center. To learn more about the Executive Council, contact Brenda Goodell at 617-632-5089 or brenda_goodell@dfci.harvard.edu.

A Legacy of Support

Thanks to the ongoing generosity of our donors, the Susan F. Smith Center for Women’s Cancers at Dana-Farber has raised more than $149 million over the past 18 years, and more than $14.5 million in fiscal year 2016 alone. To learn more about how you can strengthen our ongoing work against women’s cancers, contact Suzanne Kouri at 617-632-4055 or suzanne_kouri@dfci.harvard.edu.

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