

Advancing Breast Cancer Research and Clinical Innovation

More than 2.4 million women worldwide, including more than 250,000 in the United States, will be diagnosed with breast cancer this year. Despite remarkable advances in prevention, detection, and treatment, breast cancer continues to be one of the leading causes of cancer deaths for women in this country.

While we now know that there are many distinct subtypes of breast cancer, numerous questions persist. For instance, risk assessment remains imprecise, creating uncertainty about a woman's risk for developing some breast cancer subtypes, which impacts physicians' ability to recommend prevention strategies. When patients are diagnosed, limited information exists to offer tailored local therapy based on their tumor biology. Importantly, the comparative benefits of local treatment approaches, including long-term impact, are still not fully known. Answers to questions like these are central to developing more precise treatments for patients.

The Breast Surgeons at the Dana-Farber/Brigham and Womens Cancer Center are at the forefront of this effort. In collaboration with colleagues in medical oncology, radiation oncology, cancer pathology, and diagnostic imaging, our clinicians and scientists have established a breast cancer research program that spans the entire continuum of the disease, uniquely positioning us to expand the boundaries of what is currently known about breast cancer.

An Opportunity to Change the Status Quo

The Dana-Farber/Brigham and Womens Cancer Center has pioneered advances in surgery, imaging, and targeted therapies that have dramatically improved outcomes for many women with breast cancer. Today, the country's foremost breast surgical oncologists lead the breast surgery efforts. Tari King, MD, directs breast surgery and has nationally recognized expertise in lobular carcinoma in situ (LCIS). Elizabeth Mittendorf, MD, PhD, oversees breast surgery research and is a national leader in the development of immunotherapy for breast cancer.

Under their direction, our breast cancer surgeons are collaborating on research across the continuum of care—from prevention and diagnosis to treatment and survivorship. Their discoveries will drive clinical innovation focused on four key priorities: prevention and early disease, patient-centered outcomes, tailored local-regional therapeutic strategies, and tumor immunology. These efforts will rely on a foundation of quality and value; the importance of training and educating

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the next generation of breast surgical oncologists; and rigorous stewardship of our comprehensive biospecimen collection, which is essential to all our research.

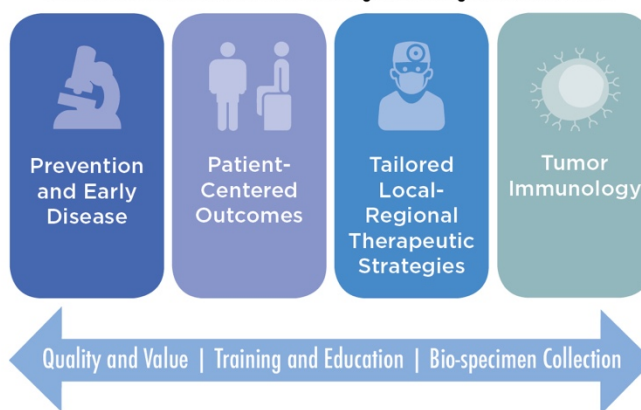
Prevention and Early Disease

The Comprehensive Breast Health Center at BWH is a long-standing outpatient clinic that cares for nearly 4,000 women and men every year with various breast-related concerns. Specialists at the BWH Breast Center are leaders in the evaluation and treatment of breast cancer as well as a variety of benign breast disorders, including lesions known to identify women at increased risk for developing breast cancer.

Serving a diverse group of patients from the greater Boston area, the Comprehensive Breast Health Center at BWH has been transformed with the advent of our **Breast cancer Personalized Risk assessment, Education, and Prevention (B-PREP)** program. With this highly individualized approach to risk assessment, screening, and preventive care, we provide every woman with a comprehensive evaluation of her risk for developing breast cancer and strategies for risk reduction.

Breast Surgery Research Program

Collaborative investigation across the continuum of care to set new standards for the evaluation and treatment of benign and malignant breast disease



Women with modifiable risk are offered a range of prevention strategies, including risk-reducing medications such as tamoxifen or new hormonal agents. For some women, lifestyle changes—including exercise, a healthy diet, and reduced alcohol use—are a better fit. B-PREP also enables women to participate in clinical trials exploring other novel prevention strategies.

Understanding Hereditary Risk of Developing Breast Cancer

The identification of a cancer-associated genetic mutation in an individual has implications for prevention, screening and treatment. This includes initiating screening at a younger age, and using supplemental imaging with breast MRI as well as mammograms. Medications that reduce breast cancer risk may be offered. Alternatively, bilateral prophylactic mastectomy provides a surgical risk-reducing option. However, many of the gene mutations associated with breast cancer risk have only recently been discovered, and the optimal management of women who carry these mutations is still being determined. Receiving this type of result may complicate the surgical decision-making process, particularly among women already facing a breast cancer diagnosis. To determine the best way to counsel patients through genetic testing and assess the

impact of counseling strategies on surgical decision making, our team is leading a large clinical trial called GET FACTS (*GE*netic *T*esting *F*or *A*ll breast *C*ancer *p*atien*TS*). This trial aims to determine the best way to counsel patients regarding their genetic testing results and will help us determine the optimal way to ensure patients are as informed as possible as they make their surgical decisions.

Learning More About Ductal Carcinoma in Situ (DCIS)

DCIS, a precancerous lesion classified as Stage 0 disease, is characterized by tumor cells confined to the milk duct. It is not invasive or life-threatening, but if left untreated it may give rise to invasive disease in roughly half of patients. Currently, breast oncologists are unable to predict who will develop invasive breast cancer and who will not.

Therefore, every patient with DCIS is offered the same treatment options: lumpectomy with or without radiation or mastectomy, which all yield the same survival rate but may be altogether unnecessary 50 percent of the time. Without clear data on the comparative benefits of these therapies—or how patients experience their long-term side effects—counseling women on the optimal treatment remains a challenge. Amidst this uncertainty, fear becomes a determining factor, with many women presuming that the most extensive surgery is their safest option.

To advance more informed—and more precise—treatment, and to address the specific needs of patients diagnosed with DCIS, the team is leading clinical trials to evaluate the efficacy of new and emerging therapies, and working to establish a formal **DCIS program** that consolidates research, education and clinical care. The combination of these efforts has the potential to transform the patient experience and create new treatment options for patients with DCIS.

Patient-Centered Outcomes

Our surgical oncologists are also focused on helping patients participate in decision-making about their own treatment. This requires educating women about their diagnosis, treatment options, and possible survivorship issues, all within the context of their own medical history, life situation, and personal values.

The Patient-Reported Outcomes, Value & Experience (PROVE) Center helps patients and physicians prepare for shared decision-making through its research on patient-reported outcomes (PRO) and patient experience. The breast surgery team is working closely with the center to study long-term clinical benefits of treatment and conduct PRO studies. These research surveys ask patients what they think about the breast surgery they had—and how it may affect their quality of life, including any impact on their self-image and intimate relationships. Recently these surveys have been made available to patients using a digital health platform allowing for their responses to be reviewed by their treating team in “real time”. This

qualitative data—gathered from a large population of women followed over several years—will provide invaluable perspectives for women facing similar treatment decisions.

Tailored Local-Regional Therapeutic Strategies

In recent years, medical oncologists have used information about tumor biology to develop more targeted systemic therapies that are proving more effective than older chemotherapy approaches. Now, breast surgical oncologists are exploring this same kind of shift, which would enable them to provide surgical recommendations based on the biology of the disease, reducing reliance on overly invasive surgeries while improving local and regional management of breast cancer. This tumor-specific approach is already having an impact on surgical removal of lymph nodes. Extensive lymph node removal often causes lymphedema, one of the most feared complications for women with breast cancer. But with some breast cancer subtypes, new systemic therapies eradicate the metastases in the lymph nodes, eliminating or reducing the need for surgery.

To more fully integrate tumor biology into surgical decision-making, our breast surgical oncologists are working closely with their medical oncology and radiation oncology colleagues to develop new guidelines for multidisciplinary treatment strategies for patients with both early and more advanced stages of disease. An example of our focused and integrated approach is the **Inflammatory Breast Cancer Program**. Inflammatory breast cancer (IBC) is one of the most aggressive forms of breast cancer. It is treated with preoperative chemotherapy, mastectomy with removal of the lymph nodes and post-operative radiation therapy. Despite this comprehensive treatment, IBC patients experience high rates of recurrence. In the IBC program, our multi-disciplinary team is testing new drugs and new strategies to evaluate the lymph nodes with the ultimate goal of minimizing lymph node surgery in patients that have a complete response to preoperative chemotherapy.

Tumor Immunology

The role of the immune system in the progression and development of cancer is of intense interest among oncologists. Against this backdrop, our understanding of cancer has changed. No longer defined as simply a disease of abnormal cell division, cancer is now viewed as a disease of abnormal relationships between cancer cells and other cells, including immune cells. The science of tumor immunology seeks to understand those relationships to allow clinicians to modulate immune cells to target tumors in treating patients with cancer.

The team has extensive experience developing vaccines to stimulate an immune response in breast cancer patients as well as in using other immunotherapy drugs called “checkpoint inhibitors” to enhance the immune response. Checkpoint inhibitors working by “taking the brakes off” the immune cells that are targeting a patient’s cancer in order to allow the immune cells to eliminate disease. A recent study led by Dr. Mittendorf demonstrated that adding a

checkpoint inhibitor to chemotherapy before surgery increases the likelihood that all of the breast cancer will be eliminated allowing us to minimize the extent of surgery performed.

We are building on this through our Breast Immuno-Oncology Program, which integrates the significant expertise that spans Brigham Health, DFCI, and Harvard Medical School, from basic immunologists to translational researchers to clinical trial investigators. Members of the Breast Immuno-Oncology Program are performing high-impact, cutting-edge research on the immunology of breast tumors to inform the development of innovative clinical trials focused on enhancing immune system response against breast tumors. Through this discovery effort, researchers will ultimately learn how to harness a patient's immune system to cure their breast cancer.

Opportunity for Impact

Philanthropic support is helping to move these vital efforts forward. Philanthropic partners play a pivotal role in realizing the tremendous potential of this breast cancer initiative through support of three key areas:

Clinical Care

Implementing the clinical care initiatives outlined depends on our ability to access the time and expertise of key personnel. In addition to a program manager, our prevention and early disease programs (i.e., B-PREP and the DCIS program) will require the ongoing support of patient navigators, social workers, and exercise and nutrition specialists to sustain our patient-centered care model.

Research

The creation of a robust research platform has allowed us to explore new lines of inquiry. This infrastructure allows our breast surgeon-scientists to collaborate with their clinical and research colleagues across the Dana-Farber/Brigham and Womens community and beyond to pursue rigorous scientific studies that promise to significantly transform breast cancer treatment. These investigations include:

- **Laboratory studies** of tumor biology and immunologic response mechanisms
- **Correlative studies** linking tumor types to clinical outcomes (e.g., invasive disease)
- **Clinical trials** to assess existing and emerging therapies
- **PRO studies** to validate new clinical care models and document survivorship issues
- **AI predictive modeling** to improve risk assessment and treatment guidelines
- **Epidemiological studies** to evaluate cancer care delivery and outcomes across understudied populations, such as older adults
- **Qualitative studies** to understand patients' lived cancer experiences and improve their decision-making support

Fueling these investigations requires strategic investment in expertise and resources. These include clinical study and research data coordinators to maintain long-term contact with patients and ensure the quality of all PRO and qualitative studies, while also ensuring proper oversight and patient consent for all bio-specimen and data collection, including blood and tissue samples, mammogram results, pathology reports, risk assessment data, and other confidential patient information. The tumor immunology lab, correlative studies, and tissue banking require technical support. A regulatory coordinator and editor each provide broad programmatic support.

Education and Training

Approved by the Society of Surgical Oncology, our Breast Surgical Oncology Fellowship Program is among the most competitive and sought-after programs of its kind in the country. The program receives nearly 100 applications for just two positions every year, underscoring how selective and coveted an opportunity it is for aspiring young breast surgeons. This rigorous one-year fellowship combines intensive, multidisciplinary clinical training, delivered in the context of focused mentorship, along with active involvement in clinical research. In addition to providing superb training, our Breast Surgical Oncology Fellowship influences the development of breast cancer research and clinical care nationally, as fellows trained at BWH often move on to become breast surgical oncology leaders at other academic medical centers.

The Power of Philanthropy

With visionary leadership from the nation's foremost breast cancer surgeons, this groundbreaking initiative—through a vital synergy between pioneering research and clinical care innovation—is dedicated to the discovery and development of new treatment approaches that will change the future for patients with breast cancer. Together with inspired philanthropic support, this transformational effort will give new hope to the many women facing this devastating disease.