Innovations in Breast Oncology 2017
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2017
Dear Colleagues and Friends,

At the OHSU Knight Cancer Institute, we see a world without cancer. As pioneers in personalized cancer medicine, we continue to change the way the world understands and fights this disease. As Oregon’s only Comprehensive Cancer Center designated by the National Cancer Institute, we are committed to partnering with physicians from across the region to care for patients with cancer.

The beginning of 2018 represents a season of unprecedented growth at OHSU Knight Cancer Institute. Cranes dominate Portland’s South Waterfront landscape, all engaged in the construction of buildings to support our efforts to understand and treat cancer. Work on the new OHSU Knight Cancer Institute Research Building, the future home for our growing community of OHSU Knight Cancer Institute scientists and translational researchers, is proceeding on schedule and set to open this fall. Also under construction, the Center for Health & Healing South building will consolidate most of OHSU Knight Cancer Institute’s clinical oncology services in one area, facilitating patient-centered multidisciplinary care. Next door, building is underway for the Gary and Christine Rood family pavilion, which will provide much needed lodging and support services for patients and families that require long-term care at OHSU.

Although the daily progress in construction is exciting, the real story is the development of our people and the pursuit of our mission. One of OHSU Knight Cancer Institute’s primary aims is the early detection of cancer at its most curable stages. Under the direction of Dr. Sadik Esener, the Cancer Early Detection Advanced Research Center (CEDAR) is gaining momentum, recruiting outstanding scientists from around the country. In 2017, Dr. Gordon Mills, previously of MD Anderson Cancer Center, joined OHSU Knight Cancer Institute. Dr. Mills is one of the most frequently cited researchers in oncology. He will lead OHSU Knight Cancer Institute programs in Precision Oncology, and will serve as a mentor for many developing scientists across the institution.

The pace of development is exhilarating for all of us at OHSU Knight Cancer Institute. Given our dual focus on Early Detection and Precision Oncology, our aim is to fundamentally change the game in cancer — across prevention, diagnosis, treatment and cure. For this 2017 OHSU Cancer Committee Annual Report, we focus on breast cancer, highlighting some of the progress in the field of breast oncology.

Sincerely,

Kevin G. Billingsley, M.D.
Chief, Division of Surgical Oncology
Chair, Cancer Committee
Medical Director, OHSU Knight Cancer Institute
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In the U.S., about one in eight women receives a breast cancer diagnosis sometime in her life. More than 3.1 million U.S. women are living with or have survived breast cancer. Based on the National Cancer Institute’s most recent data (2010–2014), breast cancer incidence in Oregon has decreased by 2.4 percent. However, Multnomah County (the highest population at nearly 800,000) is slightly above the national average at 137 cases per 100,000 women, based on statistics from the Centers for Disease Control. That’s why at OHSU Knight Cancer Institute we are focusing on putting an end to breast cancer and working to better understand the disease to personalize treatment for each patient.

National Cancer Institute-designated Comprehensive Cancer Center

In 2017, the National Cancer Institute awarded the OHSU Knight Cancer Institute Comprehensive Cancer Center status, an honor earned only by the nation’s top cancer centers. Today, OHSU is the only NCI-designated Comprehensive Cancer Center between Seattle and Sacramento.

The OHSU Knight Cancer Institute has been an NCI-designated center since 1997. It is the headquarters for one of the NCI's largest research collaboratives, SWOG, a cancer research cooperative group that designs and conducts multidisciplinary clinical trials to improve the practice of medicine in preventing, detecting and treating cancer and enhancing quality of life for cancer survivors.

Plus, the National Cancer Institute awarded a research team at the OHSU Knight Cancer Institute $9.2 million over five years to serve as a Research Center in the NCI’s Cancer Systems Biology Consortium, or CSBC. The OHSU Knight Cancer Institute's project aims to develop strategies for improving treatment-resistant triple-negative breast cancer, an aggressive form of breast cancer that lacks key receptors known to fuel most breast cancers: estrogen receptors, progesterone receptors and human epidermal growth factor receptor 2 (HER2).

In addition, U.S. News & World Report ranked OHSU as No. 1 in Oregon in Best Hospitals 2017–18. The report also ranked OHSU Knight Cancer Institute as 26th in the nation for cancer treatment.
MULTIDISCIPLINARY CARE FOR TREATING BREAST CANCER AT OHSU

Individualized evaluation

No routine cases

Each breast cancer diagnosis belongs to a unique person, who deserves the best approach for her medical circumstances. To provide truly personalized treatment, OHSU's comprehensive breast cancer team has significant expertise in all the options currently available, including potential opportunities to join clinical trials. OHSU’s collaboration through a multidisciplinary approach ensures that each patient receives an individualized evaluation and clear recommendations.

Tumor board reviews every case

Choosing the best methods to treat each patient requires everyone on the breast team to collaborate on an individualized plan for every patient. Experts from all the key disciplines review and evaluate cases together, discussing strategies and therapy options. These weekly tumor boards include physician representatives from:

- Medical genetics
- Medical oncology
- Surgical oncology
- Plastic surgery
- Radiation therapy
- Pathology
- Oncology nursing
- Patient advocacy
- Supportive services experts, such as fertility, nutrition and counseling

Unlike typical tumor boards that meet only to discuss complex or rare cases, the OHSU Knight Cancer Institute’s comprehensive breast cancer team holds a tumor board for all cases each week. Through this conference, OHSU’s physicians work together to develop a consensus to provide patients with clear recommendations for cancer treatment through survivorship.

“Because of our multidisciplinary team review, we are ideally getting the patient the best outcome possible,” said surgical oncologist Arpana M. Naik, M.D. “Through advance discussion, we may uncover a treatment that might be a better fit for a particular patient, or we may identify if a patient is a candidate for a clinical trial.”

Genetic risk assessment

The OHSU Knight Cancer Institute is the only Oregon cancer center with board-certified medical geneticists specifically trained to determine the risk of hereditary cancer syndromes, including HBOC syndrome linked to mutations in the BRCA1 and BRCA2 genes. The OHSU team includes American Board of Medical Genetics certified medical geneticists and American Board of Genetic Counseling certified genetic counselors.
Collaborative care in hematology and oncology

OHSU specialists provide the best care possible for patients with cancer and blood disorders. Services include:

- Full consultative services for patients with any type of cancer or hematologic disease.
- Expert care for acute and chronic blood conditions, including anemias, abnormal blood counts, bleeding and clotting disorders.
- Autologous and allogeneic bone marrow transplantation for leukemia, lymphoma and bone marrow failure.
- Special DNA diagnostic studies in molecular oncology and hematology.

Coordinated single-day evaluations

The comprehensive breast cancer program provides a same-day assessment and consultation for patients diagnosed with breast cancer. In one appointment, patients can meet with the entire multidisciplinary team of specialists who design a personalized treatment plan specific for them and their type of breast cancer. The breast cancer nurse navigator, Debra Harris, R.N., M.S.N., arranges every step of treatment and scheduling to ease the process for patients and their caretakers.

Debra Harris, breast cancer nurse navigator, consults with a patient.

Top-tier screening and diagnosis technology

The state-of-the-art Breast Center at OHSU provides the latest technology to help in the fight against cancer. This technology includes:

- 4D-CT motion imaging
- Brachytherapy
- Cypsa® 4D Localization System™ — GPS for the body
- CT-driven simulation
- Intensity-modulated therapy (IMRT)
- Intrabeam
- Latest-generation linear accelerators with onboard cone-beam CT capability
- Mobetron
- Specialized procedures for comprehensive radiation services
- Stereotactic body radiation therapy (SBRT)
- Stereotactic radiosurgery
- Time-of-flight PET/CT
- TomoHD treatment system
Expertise in breast imaging and diagnostics

Imaging is often the entry point of a woman’s journey to a breast cancer diagnosis, and it can critically influence detection and treatment. The three faculty members in radiology at the Breast Center at OHSU have specialized fellowship training in women’s imaging.

As an integral part of the weekly Breast Cancer Program tumor board, OHSU radiologists review all patient history and outside imaging before a patient’s first consultation with oncology. Often, based on their expertise, the radiologists identify additional imaging beneficial for the rest of the team to review before considering treatment decisions.

“Our radiologist team is breast-specialized, increasing our level of proficiency,” said diagnostic radiologist Karen Oh, M.D. “We also believe our expertise in reading breast imaging creates fewer false positives, sparing stress and inconvenience for patients.”

In fact, OHSU’s percentage of recalls of all breast screenings (7–9 percent) is below the national requirement to maintain accreditation (12 percent). At the same time, OHSU breast cancer detection rates are on the high end of the range.

The Breast Center at OHSU is accredited by the American College of Radiology (ACR) and certified by the Mammography Quality Standards Act (MQSA) of the Food and Drug Administration. In addition, the facility uses all-digital mammography equipment.

ACR-certified services:
- Mammography (conventional digital and three-dimensional breast tomosynthesis)
- Breast ultrasound
- Breast MRI

Additional services:
- Breast biopsies, including MRI-guided, ultrasound-guided and stereotactic
- Ductogram

The greatest change in breast imaging in the last five years has been the inclusion of breast tomosynthesis to the diagnostic options. Dr. Karen Oh said multiple trials in the intervening years show the readings from 2D and 3D are comparable for accuracy, but that 3D gives additional beneficial information and leads to fewer recalls. Unfortunately, some insurance providers will not cover the 3D option. However, breast tomosynthesis is superior for patients with dense and/or complex tissue, who are often younger and premenopausal. Two years ago, OHSU added to the tomosynthesis unit, allowing for 3D-guided biopsies.
Expanding options in personalized therapies

In the last 20 years, scientists and clinicians have made major breakthroughs in fighting this cancer that affects nearly 250,000 U.S. women a year. Because no two breast cancers are alike, the goal is a more personalized approach to therapy for each patient. Several developments in the last couple of years will bring us closer to that goal. For example, sophisticated genomic testing helps predict which patients will benefit from chemotherapy, and which patients we can spare the side effects of an unnecessary treatment. A variety of targeted therapies now available also give oncologists a greater arsenal to fight this cancer.

For patients with metastatic, incurable disease, OHSU is at the forefront of individualized treatment.

“We have established a platform that allows for deep genomic, molecular and immune characterization of a patient’s tumors,” Mitri said. “This information will allow us to understand mechanisms of resistance to therapy, and to develop rational treatment combinations to overcome treatment resistance. These can be evaluated in OHSU clinical trials investigating novel treatment strategies aimed at improving outcomes in patients resistant to the standard of care.”

OHSU currently has 12 clinical trials open related to breast cancer. OHSU is the only site in the Northwest participating in the I-SPY 2 trial (Neoadjuvant and Personalized Adaptive Novel Agents to Treat Breast Cancer), which uses preoperative chemotherapy for high-risk breast cancer patients. OHSU is also an enrolling site for the SMART study (Sentimag along with routine technique in detection of sentinel node biopsy).

Advances in personalized therapies

Who needs chemotherapy?

Mounting evidence shows that some patients don’t benefit from chemotherapy. In 2007, the Food and Drug Administration (FDA) approved a genomic test, MammaPrint, that measures the activity of 70 genes and delivers a prognostic score of either high or low risk of recurrence. In 2016, the prospective MINDACT (Microarray In Node-negative Disease may Avoid Chemotherapy) Trial validated the use of MammaPrint in the adjuvant setting to determine the likely benefit of chemotherapy. The results showed that among women with early-stage breast cancer at high clinical risk but low genomic risk for recurrence, the five-year rate of survival was similar with or without chemotherapy. Based on those findings, 46 percent of women with breast cancer who are at high clinical risk can avoid toxic chemotherapy. These results led the American Society of Clinical Oncology to update the guidelines on genomic biomarkers to include the use of MammaPrint in 2017.

Oncotype DX is another genomic test approved for hormone receptor-positive breast cancers. Oncotype calculates a recurrence score based on 21 genes, ranging from zero to 100, divided into low-risk (<18), intermediate-risk (18–30), and high-risk (≥31) categories. Studies show that patients with low risk do not benefit from adding chemotherapy to anti-estrogen therapy, but high-risk patients derive a significant
The concept of decreasing blood flow to the hair follicles during chemotherapy by cooling the scalp is not new, but previous methods were cumbersome and ineffective, explains Michael A. Savin, M.D., the clinical medical director of the OHSU Knight Cancer Institute. “What has changed is that this new machine circulates a coolant through a tight-fitting cap that maintains a fixed temperature through the whole course of treatment,” he said. “The data available show cooling the scalp does not make the adjuvant therapy less effective, as scalp metastasis in breast cancer is very rare. Based on a randomized multicenter study, the process reduces — but does not eliminate — hair loss in some patients, with results tied in part to which chemotherapy they receive.”

About half the patients in the study benefited, experiencing less than 50 percent hair loss. The process was significantly more effective among patients on taxanes regimens, with 60–65 percent experiencing less hair loss. Only 25 percent of patients on anthracycline showed equivalent results.

Savin said there is some discomfort (degree of cold, tightness of fit) for the patient, but the study participants tolerated the process. Also, scalp cooling will be an out-of-pocket expense for women who want to try it, anticipated to cost $2,000 or more.

Even with mixed chances of success, OHSU is willing to offer this process to give patients options. “Hair loss occurs in most women who have breast cancer chemotherapy, and it is often an emotionally painful experience,” Savin said. “Hair loss is a kind of scarlet letter, a constant reminder of the disease. Hair is a critical element of a person’s self-image. I have known patients to refuse treatment that could determine their survival because of fear of losing their hair. By offering scalp cooling, we will give breast cancer patients the option to try to minimize hair loss if they are willing to accept the conditions and odds.”

Emerging study: neoadjuvant anti-estrogen therapy

OHSU is developing a study related to neoadjuvant anti-estrogen therapy for the treatment of ER-positive breast cancer patients. This study will use an adaptive design to allow OHSU investigators to evaluate innovative anti-estrogen treatment strategies to improve pathologic response to neoadjuvant therapy, allow more patients to undergo breast conserving therapy, and ultimately improve long-term outcomes. This study will also allow for the identification of biomarkers of sensitivity to therapy, and subsequently personalize future trials for the appropriate patient population.

Who needs bone-strengthening agents?

Some of the medications to treat breast cancer and suppress estrogen have adverse effects on bones. Also, many women with breast cancer are postmenopausal, thus more likely to be at increased risk for osteoporosis. A study published in 2017 showed that adjuvant bisphosphonate treatment in postmenopausal patients showed benefits in minimizing fractures and decreasing risk of death from breast cancer. This past summer, the National Comprehensive Cancer Network updated their guidelines to include a recommendation to consider adjuvant bisphosphonate therapy in postmenopausal (natural or induced) patients with ER-positive breast cancer receiving adjuvant endocrine therapy.

Who benefits from two newly approved drug therapies?

In treating HER2-positive breast cancer, two clinical trials announced conclusions in 2017 that added two more strategies for response. Last June, a trial involving 4,800 women with HER2-positive breast cancer showed that the addition of a second HER2-targeted medicine, pertuzumab (Perjeta), to standard-of-care trastuzumab (Herceptin) after surgery may improve outcomes.
Specialty-trained surgical oncologists

OHSU’s surgical oncologists all completed their training with intensive fellowships at Memorial Sloan-Kettering Cancer Center, one of the world’s top cancer centers. They all have a specialized focus on treating breast cancer patients.

Breast cancer surgeries typically offered at OHSU:
- Lumpectomy
- Mastectomy
  - Simple or total mastectomy
  - Modified radical mastectomy
  - Radical mastectomy
  - Prophylactic mastectomy
- Nipple- and skin-sparing mastectomy
- Lymph node surgery
- Sentinel lymph node biopsy
- Axillary lymph node dissection

Going wireless

OHSU anticipates offering an alternative method to presurgical wire localization early in 2018, using technology involving either radiofrequency waves or magnetic seeds. Radiologists can place these very tiny devices in the breast up to 30 days before surgery, streamlining scheduling and drastically cutting wait times on the day of surgery.

Modern techniques in breast reconstruction

When it comes to treating breast cancer, curing the cancer is only one component of making women feel whole again, according to plastic surgeon Juliana E. Hansen, M.D.

“At OHSU, we offer the full arsenal of breast reconstruction options to help every single patient get the right match,” she said. “It starts with our comprehensive clinic, where we evaluate patients together and create a long-term plan, which is a huge advantage. We pride ourselves on our ability to guide patients to their best choice, because women want to have confidence in their appearance and intimate relationships.

For breast reconstruction, OHSU not only offers breadth in options, but is also on the leading edge of the newest techniques that are oncologically appropriate and reduce complications. Simultaneously, OHSU providers are academically minded, constantly analyzing results to improve patient outcomes. Some of the most innovative techniques OHSU currently offers include deep inferior epigastric perforator (DIEP) flaps, oncoplastic breast reduction and prepectoral prosthesis.

DIEP flap evolution provides superior results.

In the autologous tissue reconstruction arena, the current evolution of the DIEP flap procedure that OHSU surgeons provide sacrifices no muscle.

“The operation is complex and technically challenging,” Hansen said. “We take the skin and fat from the lower abdomen, with the blood vessels, leaving behind the structures for abdominal wall function, including fascia and muscles. When I was training, this method didn’t exist. Perforator flaps have significantly added to the field of plastic surgery over the last decade. Patients who have opted for this newer
Mueller identified three key developments that have led to this technique as an option for breast reconstruction in recent years:

1. Development of acellular dermal matrices to better control the position of the implants.
2. Development of a highly cohesive gel implant to reduce contour problems.
3. Improvements in autologous fat grafting for refining appearance and natural breast enhancement.

This form of breast reconstruction is a two-step process for most patients, Mueller explained. The surgeon first places a tissue expander, usually at the time of mastectomy. Over one to three months, the surgeon adjusts the size of the expander (or “fills”) until the patient is satisfied. Then in an hourlong, outpatient procedure, the surgeon replaces the expander with an implant and uses fat grafting to complete the reconstruction. Some women may not need the expander phase, and others may choose additional surgery for nipple reconstruction.

Utilizing fat grafting in breast reconstruction is a recent enhancement. The surgeon harvests the patient’s own fat from the stomach, buttocks or thighs using liposuction. The fat is then injected back into the breast to improve results and patient satisfaction. Most women will be candidates for this method, but one contraindication is very thin patients with insufficient fat.

“I see prepectoral reconstruction as the primary method for most women going forward,” Mueller said. “Over time, it will become more widely utilized, but has not been part of traditional teaching for plastic surgeons. OHSU is one of a handful of institutions with a prominent level of experience in this method.”

Patients also generally appreciate getting a tummy tuck as part of the results, Hansen added, with tissue that is ideal for creating a natural-looking and -feeling breast.

OHSU also offers alternative perforator flap procedures using autologous tissue from areas other than the abdomen, including the thigh (ALT and PAP flaps). Tram and LAT flaps utilize a combination of tissues from the abdomen or back.

**Reshaped breast at time of lumpectomy**

With oncoplastic breast reduction in conjunction with lumpectomy, the surgical oncologist can be more liberal with the margins around the tumor, because the plastic surgeon will perform a breast reduction and lift to remove any distortion in the breast’s shape. The procedure uses only autologous tissue without an implant to reshape the breast and provide symmetry.

**Latest implant technique has multiple benefits**

The majority of breast reconstruction surgeries utilize prostheses. In recent years, major improvements in products and techniques allow surgeons to use prepectoral breast reconstruction to improve aesthetic results with less trauma to the patient.

“Traditionally, surgeons have placed implants fully or partially under the pectoralis muscle, an abnormal position,” said plastic surgeon Reid V. Mueller, M.D. “Now, we are able to position the implants on top of the chest muscle in the natural position of the breast. Early studies of this technique show that capsular scarring around the implant, overall discomfort and narcotic use is lower for patients, all while avoiding effects on mobility and strength because we are no longer cutting through the pectoralis muscle and detaching the muscle from the rib.”

**Novel method for tracing blood profusion**

**Indocyanine green dye-based fluorescent angiography**

OHSU was the first in the region to introduce indocyanine green dye (ICG) SPY Elite device angiography to evaluate blood flow in the breast. During breast reconstruction, ICG is added to the intravenous fluids. Using an infrared laser and advanced imaging techniques, surgeons can measure the blood flow in the tissues to detect poorly perfused areas of the mastectomy flap. Having this tool allows surgeons to make intraoperative decisions about the reconstruction technique to avoid later complications.
Progress in radiation oncology for breast cancer

Nearly 60 percent of patients receive radiation therapy as part of their breast cancer treatment. At OHSU, physicians provide seamless care through the Breast Cancer Program for access to all appropriate options. One of OHSU’s key goals is to achieve the best treatment outcome with the least amount of toxicity. Through some newer techniques and research study efforts, OHSU radiation oncologists are constantly making progress toward that goal.

Protective technique for the heart

OHSU was an early adopter of the deep inspiration breath hold (DIBH) technique, a proven method to reduce the heart’s radiation exposure for all left-sided breast tumors.

“Starting in 2014, we have been able to significantly reduce radiation dose to the heart, making it safer for anyone with cancer in her left breast,” said radiation oncologist Charlotte Kubicky, M.D., Ph.D.

Single-dose option for select patients

OHSU is the first and only provider in the Pacific Northwest that offers intraoperative radiotherapy (IORT) in early-stage breast cancer.

Patients receive coaching and support to consistently hold a deep breath for 20–30 seconds during the radiation delivery, effectively pushing breast tissue away from the heart. Using the Active Breathing Coordinator (ABC), patients breathe in enough air to reach a predetermined volume. Then a small valve closes, preventing air from leaking during the breath hold. The radiation will only begin at the predetermined volume. If the patient can no longer hold her breath at any time during the process, she can release a button to open the valve to breathe freely, and the radiation will stop immediately.

“We recently published the results of 127 patients who received IORT at OHSU between 2009–2016,” Kubicky said. “Our outcome is excellent, with 97 percent local control and only 3–5 percent acute and late grade 3 skin toxicity. We believe IORT is a safe and effective alternative to whole breast radiotherapy, though we will continue to follow our patients to accumulate data on efficacy and toxicity.”

Patient selection is key, according to Kubicky. For the specific patients who qualify, one dose of IORT (which adds approximately 30 minutes in the operating room) can replace weeks of daily radiation.

“Obviously the convenience is good for all patients who qualify for IORT, but for the significant percentage of our patients who live in rural areas with no access to daily radiation, it is especially beneficial,” Kubicky said. “Having IORT allows them to complete their treatment in a short amount of time and go back to their lives with minimal side effects.”

Clinical trial for lymph node surgery paired with radiation

OHSU is currently participating in the national trial ALLIANCE A011202, a comparison of axillary lymph node dissection with axillary radiation for patients with node-positive breast cancer treated with neoadjuvant chemotherapy.

The goal of this multiyear trial is to help determine the optimal combination of surgery and radiation for the management of axilla.
Transitions Program for breast cancer survivorship

The OHSU Transitions Program for breast cancer patients aims to ease the passage from treatment to survivorship by making sure patients have any needed services and support for themselves and/or family members and caretakers. Led by Christine Kemp, N.P., the program consists of:

- A review of care summary and follow-up care plan.
- Arranging appointments for the first year following treatment.
- Review of five-year follow-up plan.
- Support for coping with fears, grief and other social and emotional effects.
- Wellness strategies for nutrition, fitness and lifestyle.
- Connecting with an OHSU social worker for practical help with transportation, financial issues and communication with employers and insurance companies.

Transitions participants also have access to OHSU’s Oncology Rehabilitation team. This team consists of physical therapists, occupational therapists and speech therapists who provide specialized services to patients with cancer. This group of specialists works with people through all phases of disease and/or treatment to improve quality of life and function. Treatment is based on a patient’s individual needs and issues, grounded in science and evidence-based treatment approaches. The team can support a patient with side effects such as:

- Pain
- Cognitive issues
- Balance
- Fatigue
- Neuropathy
- Lymphedema

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What we discovered is that a breast cancer diagnosis during pregnancy doesn’t increase the risk of mortality; however, a postpartum diagnosis carries a double to triple risk of aggressive metastasis versus women who haven’t given birth,” said Pepper J. Schedin, Ph.D., of OHSU’s School of Medicine. “Further, we find that this increased risk endures to up to 10 years after childbirth. We find that about 50 percent of all young women with breast cancer are diagnosed within 10 years of having a child.”

The research culminating in the latest findings began many years ago as Schedin studied the biologic changes of breast tissue during lactation and weaning. In that work, her lab accidentally challenged three long-held beliefs:

1. That pregnancy is protective in young women,
2. That the hormones of pregnancy fuel the rare breast cancer diagnosed in young mothers, and
3. That breast cancers associated with pregnancy are rare.

“Our data showed the opposite,” Schedin said. “Rather than being protective, the tissue remodeling in the breast after lactation promoted early-stage tumor cells to metastasize. Also, these postpartum cancers aren’t rare, but occur in almost half of all young women’s breast cancer cases.”

In reviewing patient clinical charts, Schedin’s lab found that the metastasis link in these patients is to the liver. The lab group then proved that in a rodent model, the liver doubles in size during pregnancy and lactation, involuting within days of weaning. In testing the rodent samples, tumor cells preferred the involuting environment. These data were the first to show connections between the liver and breast during pregnancy, lactation and weaning, as well as showing relationships to breast cancer.

Schedin and her collaborators published the liver involution-metastasis research in 2017. Now they are working to determine a similar link in women. Through fortunate happenstance, Schedin’s team is benefiting from an inter-institutional study between Kaiser Permanente Northwest and OHSU already underway to determine if a woman’s liver health while pregnant imprints the child’s liver health. This maternal-fetal medicine team has collected MRIs of participants at two early stages in pregnancy. These scans support the hypothesis that women’s livers show volumetric growth in pregnancy.

Though there is much more research ahead, the existing data are predicting a breast cancer metastasis link to the liver in postpartum women.

“Our work makes predictions about how we may be able to use therapeutics to target breast metastasis in the liver,” Schedin said. “We recently received a Department of Defense-funded grant to obtain liver biopsies of breast metastasis to investigate if the same molecules found in the rodent model support liver metastasis in humans.”

Clinical trial outreach in community-based programs

By nature, clinical trials are exclusive. Not only are there physical criteria to meet, but patients must also have practical and financial access to the trial, including transportation to the participating site. OHSU’s Community Hematology and Oncology (CHO) providers are expanding that access for breast cancer patients by offering adaptive and innovative clinical trials in the community hospital setting.

“Very few patients can leave their communities to participate in clinical trials, so what we bring to them is our OHSU faculty with access to the full-breadth of the Knight Cancer Institute’s investigations,” said Jacqueline Vuky M.D., an OHSU medical oncologist based at Legacy Good Samaritan Medical Center in Portland. “We offer our patients trials ranging from early phase one to practice-changing phase three trials in the community setting, collaborating with pharmaceutical companies, OHSU faculty and our Legacy and community physicians. Our goal is to expand the possibilities for treatment in our patients’ home communities without the added expense and hassle of traveling.”

The CHO teams placed at five community hospitals in the Portland metro area have had significant success in accruals for trials over the past few years. As 2018 begins, there are currently 10 breast cancer trials open in the community.

“We’ve recently increased the number of trials available to our breast cancer patients because our patient demographic is motivated and interested in improving the standard of care,” Vuky said. “By conducting research at the community level, my goal is for the results to reflect and benefit the patient population we care for.”
Triple-negative breast cancer is a particularly difficult form of the disease to treat, as it lacks the key receptors known to fuel most breast cancers. Beginning in 2018, OHSU Knight Cancer Institute will target this treatment-resistant disease with a study led by principal investigator Joe Gray, Ph.D., director of the OHSU Center for Spatial Systems Biomedicine (OCSBB) and the OHSU Knight Cancer Institute associate director for biophysical oncology.

“Our goals are to identify the mechanisms by which these cancers evolve and adapt to become resistant to treatment, and to develop new strategies to counter these mechanisms,” Gray said. “Our multidisciplinary approach treats these cancers as adaptive systems that can be controlled using multiple drug combinations.”

Using advanced microscopy, Gray’s research team will leverage tools for quantitative analysis and visualization of images generated, together with computational approaches for integrating diverse molecular data types. Through analysis of core cell lines, patient-derived cultures and primary tumors, the team aims to uncover molecular networks that underlie disease progression and therapeutic response.

The OHSU Knight Cancer Institute is one of nine research institutions nationwide participating as a Research Center in the National Cancer Institute’s Cancer Systems Biology Consortium. NCI awarded OHSU Knight Cancer Institute a $9.2 million grant over five years for the study.

**MRI method that enhances diagnostic accuracy and predicts response to therapy**

With one advanced, quantitative MRI technique, investigator Wei Huang, Ph.D., of OHSU’s Advanced Imaging Research Center and his colleagues have shown promising applications for reducing unnecessary biopsies and for predicting a patient’s response to neoadjuvant chemotherapy. According to Huang, the challenge now is to translate this MRI method involving complicated data analysis into clinical practice and integration into clinical workflow.

“In terms of collecting MRI images, the process is like a breast MRI exam ordered for clinical care,” Huang said. “The difference is how we analyze the data. Our technique involves advanced mathematical modeling.”

Huang’s team published the results of a National Institutes of Health-funded study using the Shutter-Speed Model dynamic contrast-enhanced (DCE) MRI technique to improve breast cancer diagnostic accuracy in 2011 and 2012.

“Of course there is a high false-positive result in standard breast cancer screening using mammography,” Huang said. “For example, of 100 women referred for biopsy following a suspicious mammogram, the pathology report on 60 to 70 of them will come back benign. If our MRI technique can be commercialized and FDA-approved for clinical use, we could potentially spare those women an invasive biopsy procedure, along with the associated stress and cost.”

In partnership with a company, Huang and his colleagues have obtained an NIH small business grant to develop a commercial product using the OHSU MRI method. Meanwhile, Huang is also participating in a Quantitative Imaging Network consortium sponsored by the National Cancer Institute studying various advanced imaging methods to evaluate cancer response to treatment.

Using the Shutter-Speed Model dynamic contrast-enhanced (DCE) MRI technique after the first chemotherapy cycle (of a six- to eight-cycle treatment course), investigators can predict with high accuracy whether a breast cancer patient is responding to neoadjuvant therapy, Huang said.

“The current standard is to assess chemotherapy’s effect by measuring change in tumor size,” he explained. “By the time a patient has finished the entire chemotherapy treatment, the difference in size is clear for responders and nonresponders, but we lose time for taking actions, such as changing drugs and/or treatment plan, for the nonresponders. After the first cycle, there often isn’t much difference in tumor size changes between responders and nonresponders, but with our MRI method, which measures a tumor’s underlying biologic functions, we can tell a responder from a nonresponder by the conclusion of one cycle of chemotherapy.”

Huang started this NIH-funded study in 2012 and has accrued about 70 patients at OHSU.
ACCOUNTABILITY AND QUALITY IMPROVEMENT MEASURES

As a Commission on Cancer-accredited facility, OHSU Knight Cancer Institute has a cancer committee that reviews the quality of patient care using select accountability and quality improvement measures. Accountability measures are designed to promote improvements in the delivery of care while quality improvement measures are designed to monitor the need for quality improvements.

Below, please find OHSU's 2015 performance rates for three accountability measures and six quality improvement measures from five primary sites, including breast, colon, rectum, gastric and lung.

<table>
<thead>
<tr>
<th>MEASURE NAME AND DEFINITION</th>
<th>2015 PERFORMANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STANDARD 4.4 ACCOUNTABILITY MEASURES</strong></td>
<td></td>
</tr>
<tr>
<td>RECRTCT</td>
<td>Preoperative chemo and radiation are administered for clinical AJCC T3N0, T4N0 or stage 3; or postoperative chemo and radiation are administered within 180 days of diagnosis for clinical AJCC T1-2N0 with pathologic AJCC T3N0, T4N0 or stage 3; or treatment is considered for patients under the age of 80 receiving resection for rectal cancer.</td>
</tr>
<tr>
<td>LNoSurg</td>
<td>Surgery is not the first course of treatment for cN2, MO lung cases.</td>
</tr>
<tr>
<td>G5RBN</td>
<td>At least 15 regional lymph nodes are removed and pathologically examined for resected gastric cancer.</td>
</tr>
<tr>
<td>MASTRT</td>
<td>Radiation therapy is considered or administered following any mastectomy within 1 year (365 days) of diagnosis for breast cancer for women with ≥ 4 positive regional lymph nodes.</td>
</tr>
<tr>
<td>HT</td>
<td>Tamoxifen or third-generation aromatase inhibitor is considered or administered within 1 year (365 days) of diagnosis for women with AJCC T1c or stage 2 or stage 3 hormone receptor-positive breast cancer.</td>
</tr>
<tr>
<td>G15RLN</td>
<td>At least 15 regional lymph nodes are removed and pathologically examined for resected colon cancer.</td>
</tr>
<tr>
<td>LCT</td>
<td>Systemic chemotherapy is administered within 4 months to day preoperatively or of day of surgery to 6 months postoperatively, or it is considered for surgically resected cases with pathologic, lymph node-positive (pN2) and (pN2) NSCLC.</td>
</tr>
<tr>
<td>nBx</td>
<td>Image- or palpation-guided needle biopsy (core or FNA) is performed to establish diagnosis of breast cancer.</td>
</tr>
<tr>
<td><strong>STANDARD 4.5 QUALITY IMPROVEMENT MEASURES</strong></td>
<td></td>
</tr>
<tr>
<td>OHSU</td>
<td><strong>2015 PERFORMANCE RATES</strong></td>
</tr>
<tr>
<td>OHSU KNIGHT CANCER INSTITUTE LEADERSHIP TEAM</td>
<td></td>
</tr>
<tr>
<td><strong>OHSU Cancer Committee Program Activity Coordinators</strong></td>
<td></td>
</tr>
<tr>
<td>Kevin Billingsley, M.D.</td>
<td>Cancer conference coordinator</td>
</tr>
<tr>
<td>Melissa Alvarado, M.P.H., C.T.R.</td>
<td>Cancer registry quality coordinator</td>
</tr>
<tr>
<td>Susan Hedlund, M.S.W., L.C.S.W., O.S.W.-C.</td>
<td>Psychosocial services coordinator</td>
</tr>
<tr>
<td>Ellen Distefano, R.N., M.N., C.E.N.</td>
<td>Quality improvement coordinator</td>
</tr>
<tr>
<td>Katie Hennis, M.S.</td>
<td>Community outreach coordinator</td>
</tr>
<tr>
<td>Mindy Roberts, M.A.</td>
<td>Clinical research coordinator</td>
</tr>
</tbody>
</table>

OHSU Cancer Committee

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Cancer Registry Manager
Connie Ames, M.S.
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Margy Bertoldi, R.N., M.P.H., B.S.N.
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Cancer Registrar
Lorraine Colwell, C.T.R.
Tumor Registrar
Claudia Cooksie, C.T.R.
Tumor Registrar
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