



One

2015 Breast Cancer
Annual Report



Carolinas HealthCare System



OVERVIEW

The Breast Program at Carolinas HealthCare System's Levine Cancer Institute, offers comprehensive care. Patients with benign and malignant disease of the breast are managed through multidisciplinary care that includes medical oncology, radiation oncology and surgical oncology, reconstructive surgery, breast radiology, guidance from nurse navigators, genetic risk assessment and testing, individual and group support and counseling, and nutritional support and education services.

Levine Cancer Institute participates in both industry- and investigator-led clinical research. The Institute hosts a weekly breast conference that includes a dedicated review of radiology, pathology, staging and treatment guidelines. There is also a weekly working conference that reviews the current treatment plan of the majority of patients treated in the breast center.

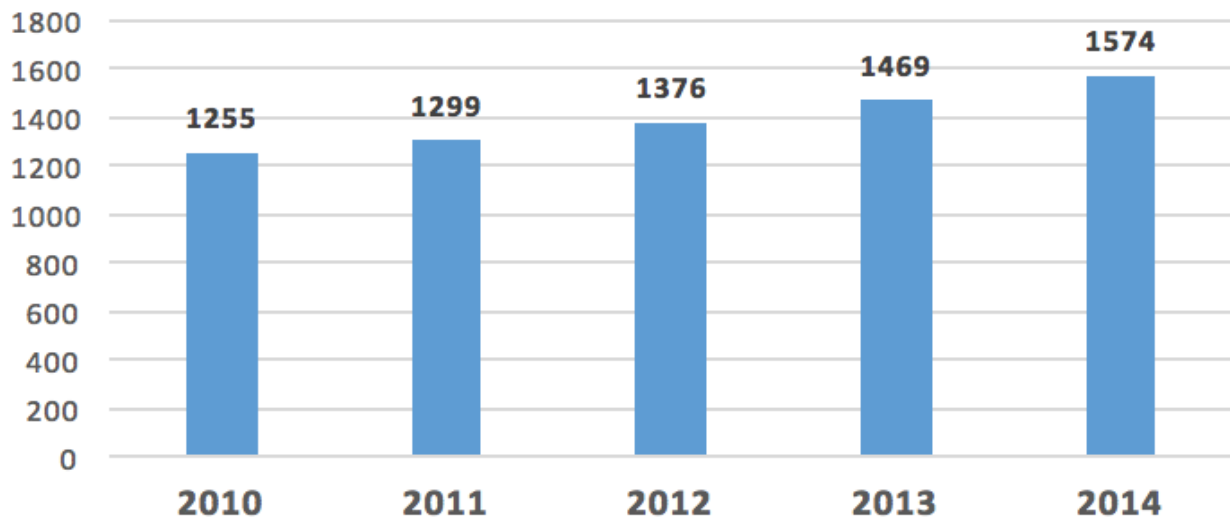
Levine Cancer Institute offers many community events to provide opportunities for patient education throughout Mecklenburg and Union counties. This report comprises data from the following eight network facilities: Carolinas Medical Center, Carolinas HealthCare System Cleveland, Carolinas HealthCare System Mercy, Carolinas HealthCare System NorthEast, Carolinas HealthCare System Pineville, Carolinas HealthCare System Stanly, Carolinas HealthCare System Union and Carolinas HealthCare System University.

INCIDENCE

Breast cancer is the most common cancer among women in the United States. It accounts for about 29 percent of newly diagnosed cancers in America.(1) The American Cancer Society estimated there would be approximately 234,190 new cases of breast cancer among both women and men diagnosed in the United States during 2015. Since 2004, overall breast cancer incidence rates have been relatively stable.(2) In North Carolina, the projected number of female breast cancer cases for 2015 is 7,820.(1)

At Carolinas HealthCare System, breast cancer is the most common female malignancy and accounts for 19 percent of all cancers reported in 2014. Since 2010, there has been a steady increase in the number of breast cancer cases seen by the System.

FIGURE 1
BREAST CANCER INCIDENCE, CAROLINAS HEALTHCARE SYSTEM 2010-2014



TYPES OF BREAST CANCER

Infiltrating or invasive ductal carcinoma (IDC) is the most common type of breast cancer, making up 70 to 80 percent of all breast cancer diagnoses. Invasive lobular carcinoma (ILC), sometimes called infiltrating lobular carcinoma, is the second most common type of breast cancer, accounting for 10 to 15 percent. Tumors may also exhibit combinations of both histological types. Breast cancer cases at Carolinas HealthCare System have similar types, when compared to other accredited hospitals in the United States.

FIGURE 2A
HISTOLOGIC TYPES OF BREAST CANCER, CAROLINAS HEALTHCARE SYSTEM 2014

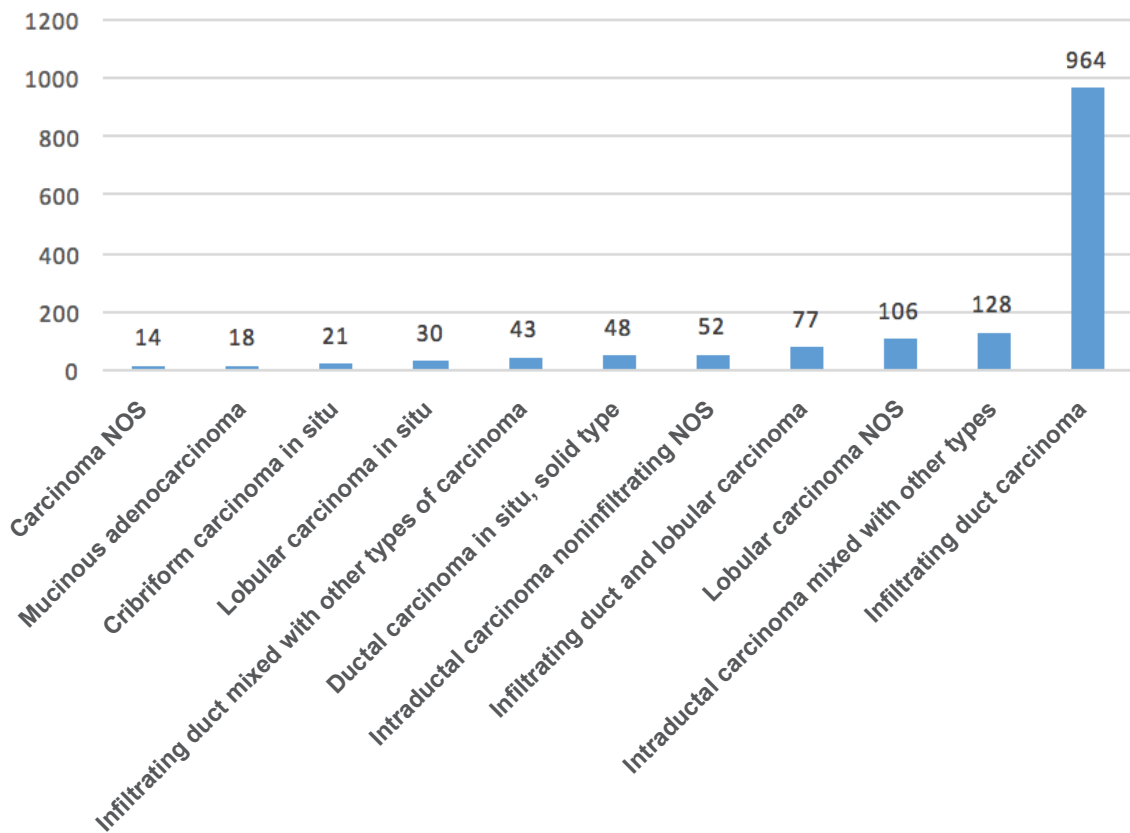
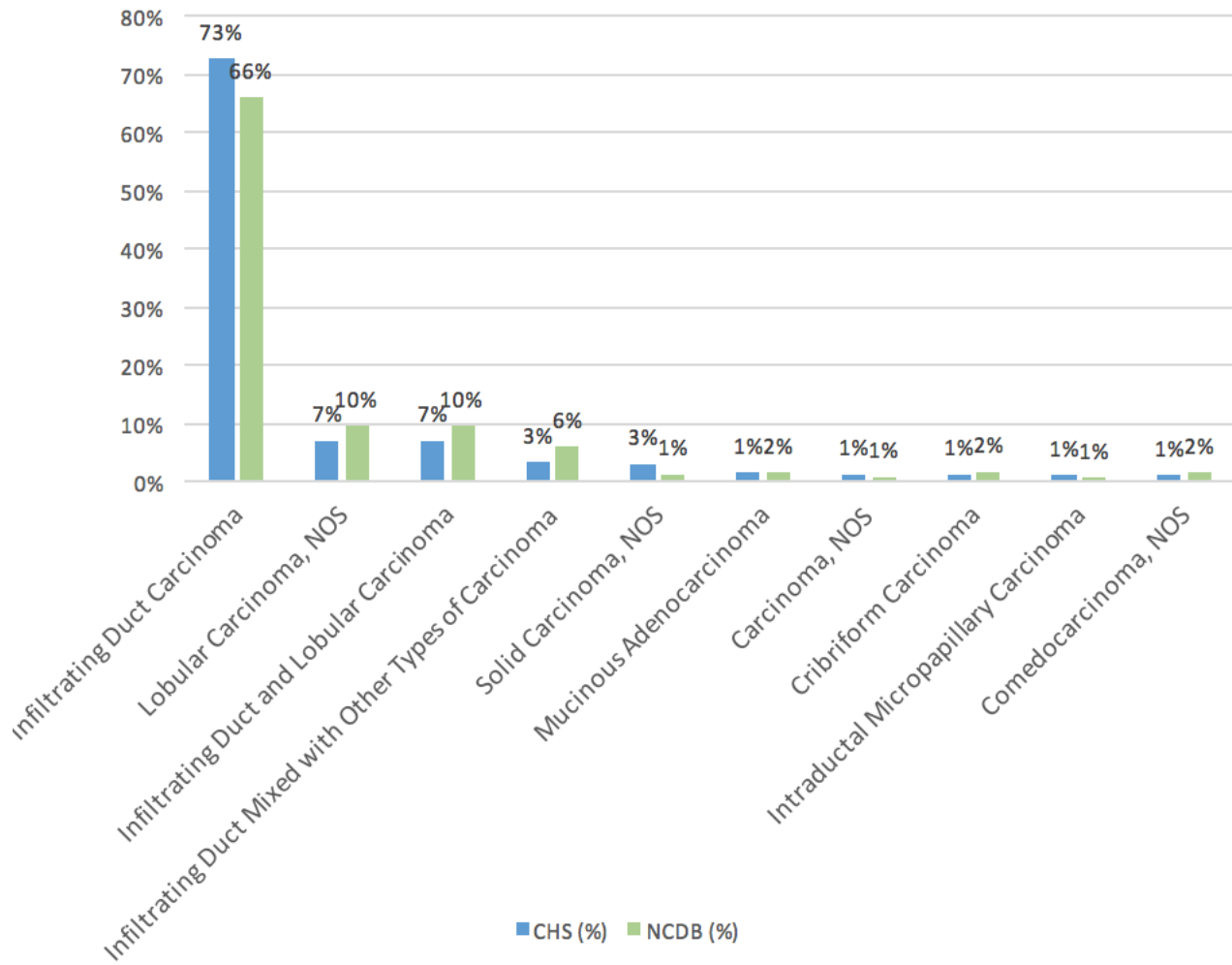


FIGURE 2B
 HISTOLOGIC TYPES OF BREAST CANCER 2003-2013 CAROLINAS HEALTHCARE SYSTEM VS
 NCDB HOSPITALS



Source: American College of Surgeons Commission on Cancer National Cancer Data Base (NCDB) Benchmark Reports

RISK FACTORS

Besides being female, increasing age is the most important risk factor for developing breast cancer. Based on the National Cancer Institute SEER statistics 2008-2012, the median age at the time of breast cancer diagnosis was 61 years. Breast cancer rates are at their highest in people aged 55 to 64. (4) At Carolinas HealthCare System, 75 percent of those diagnosed with female breast cancer were at least 60 years old. The highest volume of patients with a newly diagnosed breast cancer is reported in the 60 to 69 age group at 27 percent. The second highest age group was 50 to 59. Age comparison using analytic case from 2003 to 2013 from the American College of Surgeons Commission on Cancer National Cancer Data Base benchmark reports is shown in Figure 3B. Carolinas HealthCare System has comparable age group distribution when compared to other US hospitals.

Another non-modifiable risk factor associated with increased breast cancer risk includes a family history of breast cancer, particularly having one or more affected first-degree relative. It is estimated that 5 to 10 percent of breast cancer cases result from inherited mutations, including those in the breast cancer susceptibility genes BRCA1 and BRCA2. Other factors that increase risk include exposure to hormone replacement therapy, and treatment with radiation to the breast or chest (i.e. Hodgkin's disease). Reproductive factors that increase risk include a long menstrual history (menstrual periods that start early and end late in life), oral contraceptive use, never having children, and having one's first child after age 30.

Lifestyle-related factors that increase breast cancer risk include weight gain or being overweight (for postmenopausal breast cancer), physical inactivity and alcohol consumption.

FIGURE 3A
AGE GROUP AT DIAGNOSIS OF BREAST CANCER, CAROLINAS HEALTHCARE SYSTEM 2014

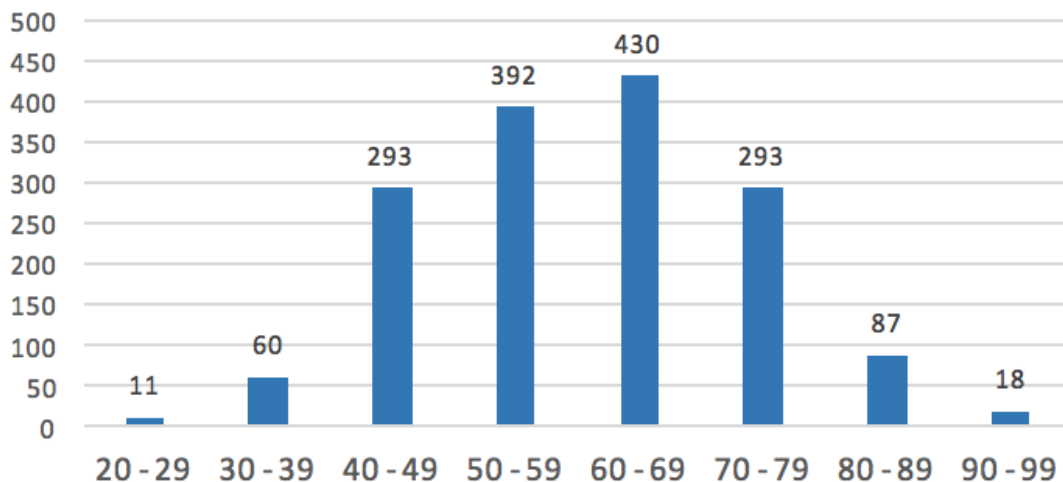
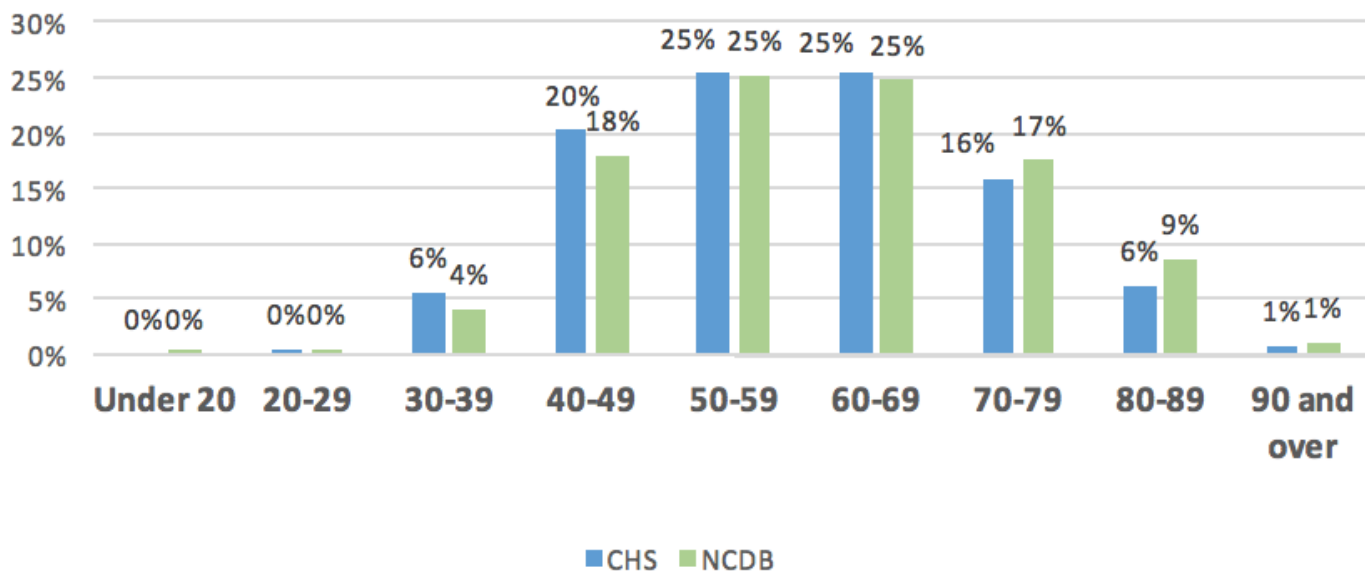


FIGURE 3B
 AGE GROUP AT DIAGNOSIS OF BREAST CANCER, CAROLINAS HEALTHCARE SYSTEM VS NCDB,
 2003-2013



Source: American College of Surgeons Commission on Cancer National Cancer Data Base (NCDB) Benchmark Reports

STAGE OF BREAST CANCER AT DIAGNOSIS

Breast cancer staging is used to determine the extent of disease. The prognosis of invasive breast cancer is influenced by the stage of the disease. The main staging system utilized for staging of cancer is from the American Joint Commission on Cancer (AJCC).(3) Non-invasive (stage 0) and early stage invasive breast cancers (stages I and II) have a better prognosis than later stage cancers (stages III and IV). In the US, about 61.1 percent of female breast cancers are diagnosed at the local stage, which corresponds to stage I and some stage II cancers in the AJCC staging system.(4) At Carolinas HealthCare System, about 68 percent of breast cancers are diagnosed at a local stage. Carolinas HealthCare System is in keeping with the national trend toward diagnosing breast cancer at an earlier stage, Stages 0, I and II.

FIGURE 4A
AJCC STAGE OF BREAST CANCER AT DIAGNOSIS, CAROLINAS HEALTHCARE SYSTEM 2014

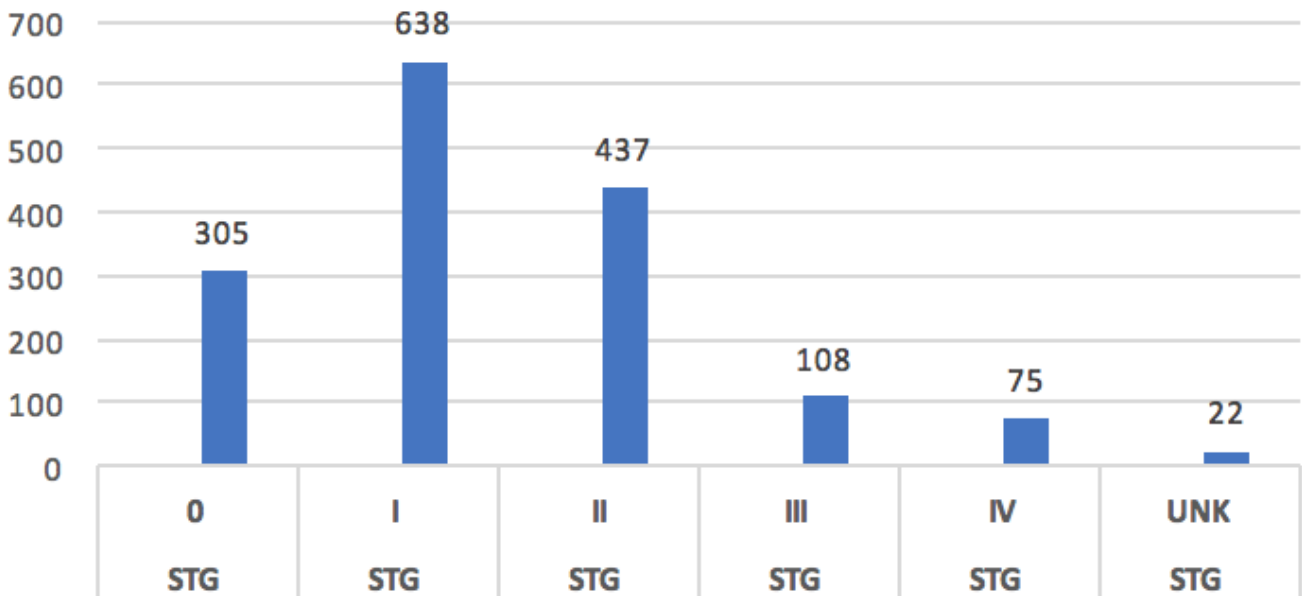
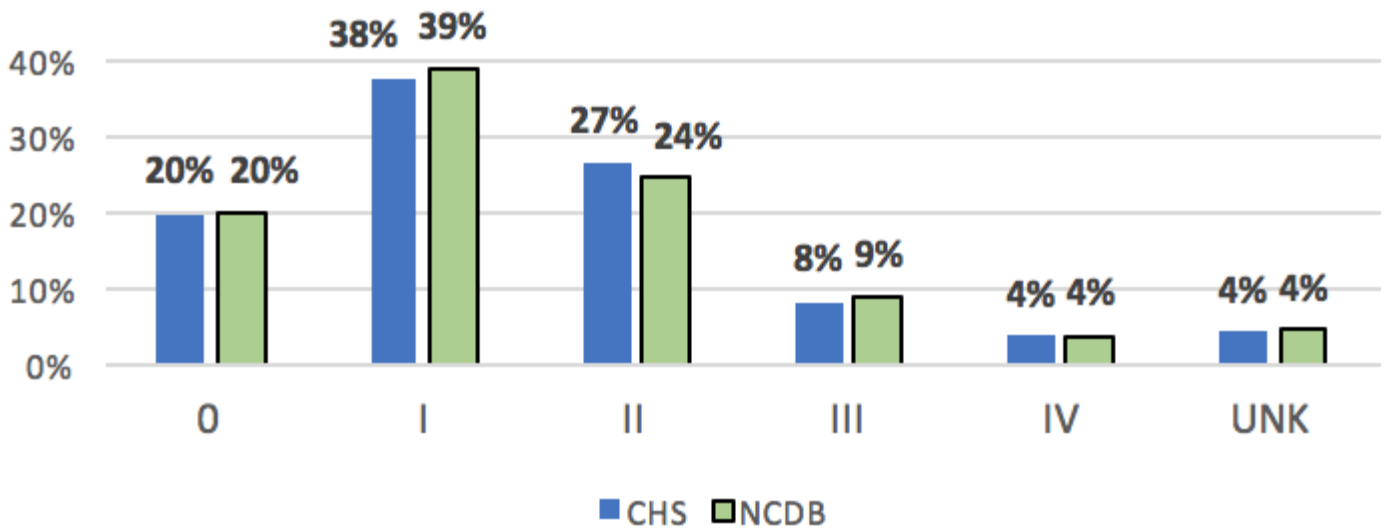


FIGURE 4B
 AJCC STAGE COMPARISONS OF BREAST CANCER AT DIAGNOSIS, CAROLINAS HEALTHCARE
 SYSTEM VS NCDB
 2003-2013

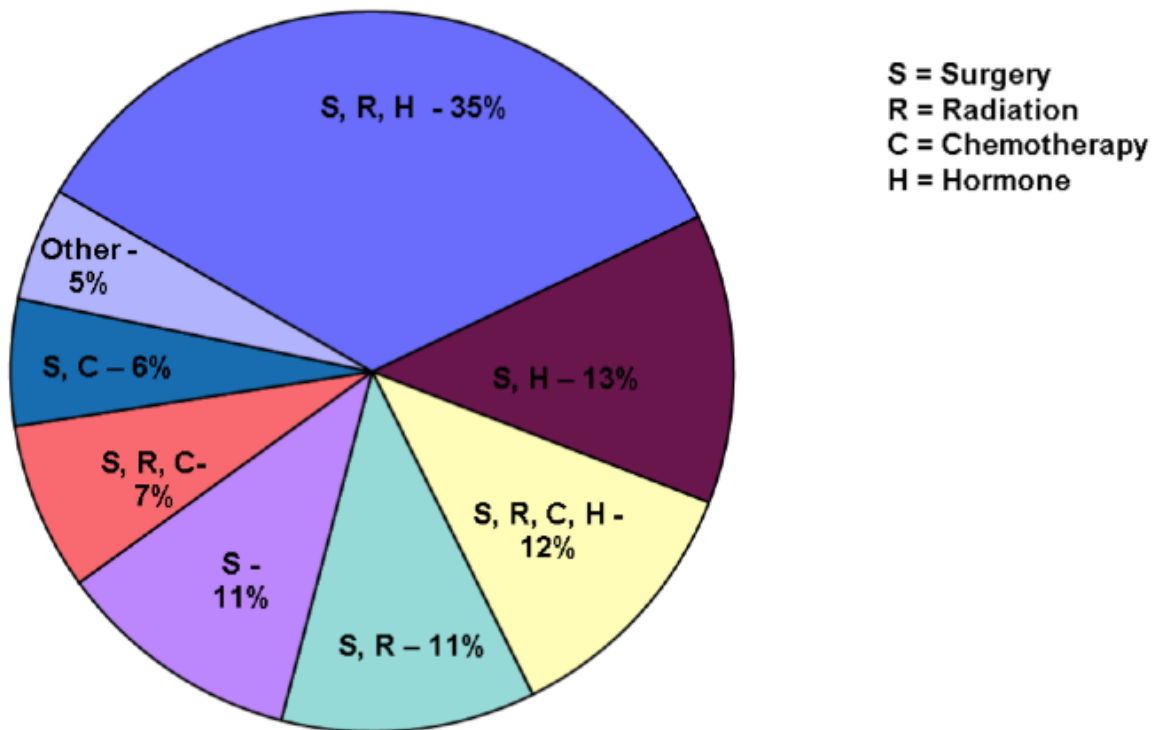


Source: American College of Surgeons Commission on Cancer National Cancer Data Base (NCDB) Benchmark Reports

BREAST CANCER FIRST COURSE OF TREATMENT

Levine Cancer Institute’s multidisciplinary breast cancer team consists of a surgeon, medical oncologist, radiation oncologist, diagnostic radiologist and pathologist. The team meets regularly at an interdisciplinary breast cancer conference to review the diagnosis and discuss treatment options based on the stage and biologic characteristics of the tumor. According to the National Comprehensive Cancer Network (NCCN) clinical practice guidelines and Levine Cancer Institute Patient Treatment Guidelines and Pathways, surgery with or without radiation is the mainstay for managing loco-regional breast cancer. The options for local treatment include lumpectomy followed by radiation therapy or mastectomy with or without reconstruction and with or without radiation therapy. An axillary procedure, either sentinel lymph node biopsy or axillary lymph node dissection is performed for axillary node staging. Additionally, systemic therapy decisions are tailored based on the hormone receptor and human epidermal growth factor receptor (HER2) status of the tumor.

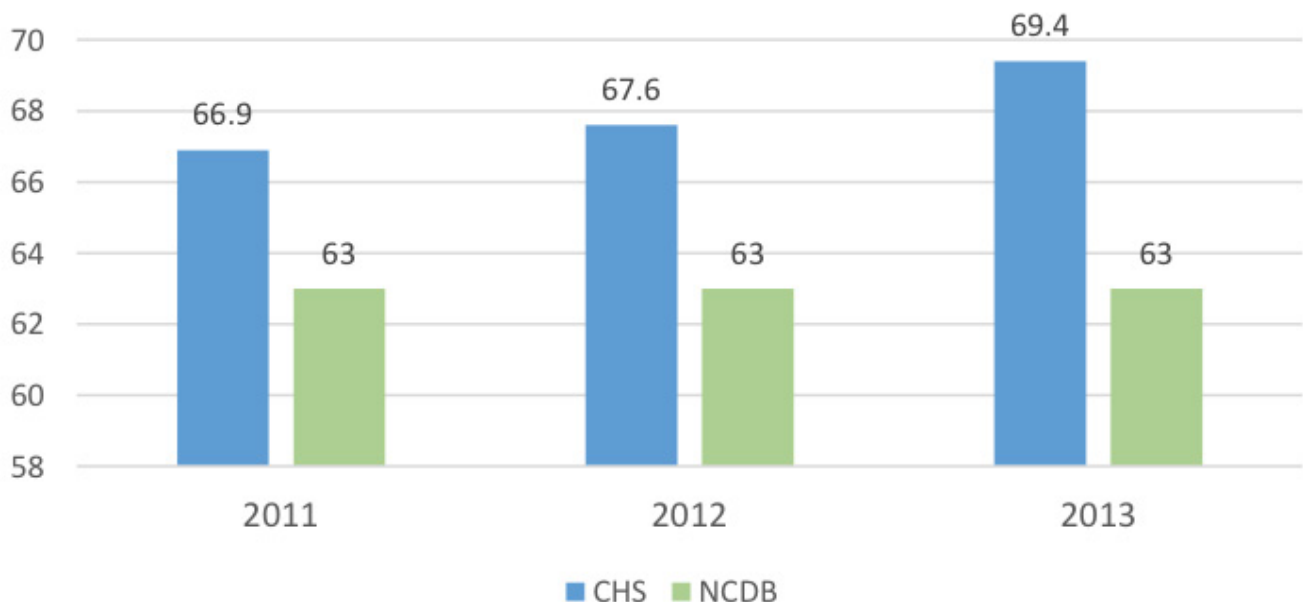
FIGURE 5
BREAST CANCER FIRST COURSE OF TREATMENT, CAROLINAS HEALTHCARE SYSTEM 2014



BREAST CONSERVATION

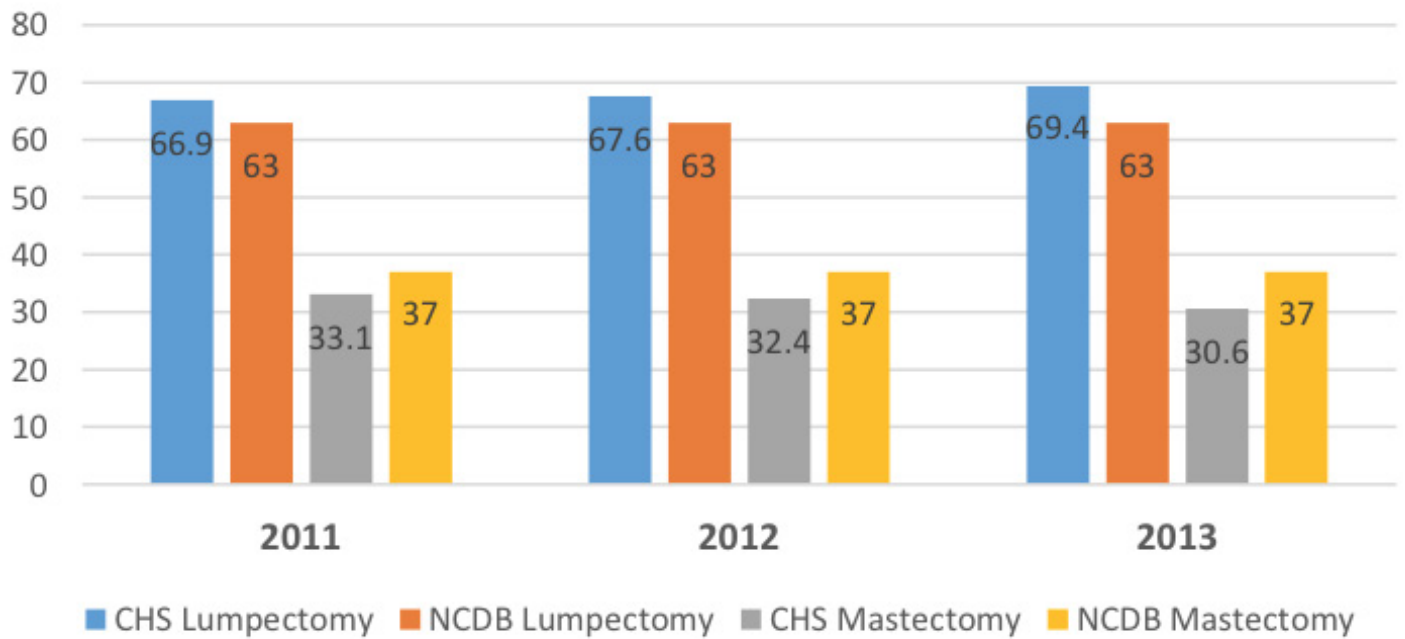
Breast conserving surgery for patients with early-stage breast cancer is a nationally accepted standard of care in appropriately selected patients. Patients are considered eligible for breast conservation if the tumor is localized and can be completely removed with negative margins, leaving an acceptable cosmetic result, and if they are candidates for radiation. The NAPBC recommends that 50 percent of all eligible patients diagnosed with early-stage breast cancer (Stage 0, I, II) are treated with breast conserving surgery. At Carolinas HealthCare System, the breast conserving surgery rate exceeds the NAPBC target and in 2011, was at 66.9 percent, in 2012, was at 67.6 percent, and in 2013, even higher at 69.4 percent as shown in Figure 6A. Additionally, Carolinas HealthCare System patients experienced a lower mastectomy rate compared to other accredited hospitals in the United States.

FIGURE 6A
BREAST CONSERVING SURGERY RATE, CAROLINAS HEALTHCARE SYSTEM VS NCDB, 2011-2013



Source: American College of Surgeons Commission on Cancer National Cancer Data Base (NCDB) Benchmark Reports

FIGURE 6B
BREAST CONSERVING SURGERY AND MASTECTOMY RATES, CAROLINAS HEALTHCARE SYSTEM
VS NCDB, 2011-2013



Source: American College of Surgeons Commission on Cancer National Cancer Data Base (NCDB) Benchmark Reports

NATIONAL CANCER QUALITY BENCHMARKS – THE LCI, CAROLINAS HEALTHCARE SYSTEM EXPERIENCE

Levine Cancer Institute participates in national cancer benchmarks for selected breast cancer quality measures as endorsed by the National Quality Forum and administered through the American College of Surgeons Commission on Cancer. The Cancer Program Practice Profile Reports (C3PR) is a quality reporting tool from the National Cancer Data Base of the Commission on Cancer (COC) that is used to measure cancer care by comparing cancer programs based on nationally accepted guideline measures.

As shown below, Carolinas HealthCare System continues to not only meet, but exceed national benchmarks. Our multidisciplinary breast cancer team understands the importance of providing comprehensive treatment services to meet the breast cancer care needs in the community.

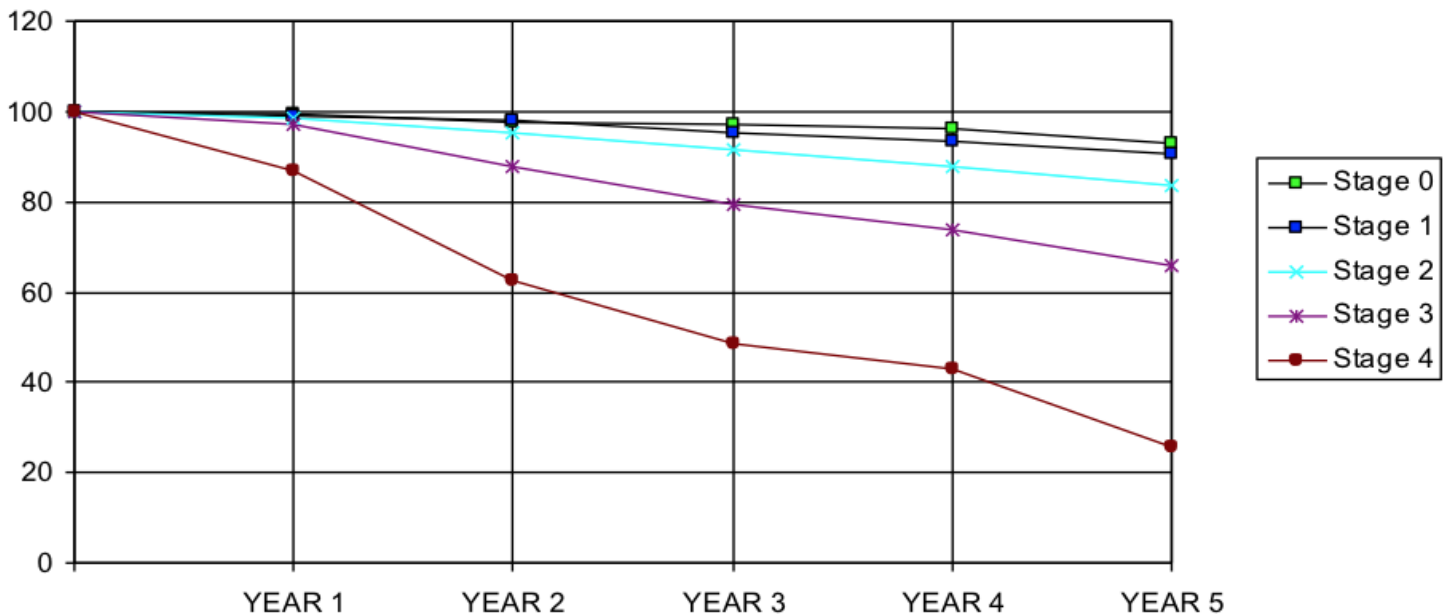
FIGURE 7
2013 CAROLINAS HEALTHCARE SYSTEM BREAST CANCER PROGRAM OUTCOMES

Select Breast Measure	COC Std	2013
Radiation therapy is administered within 1 year of diagnosis < age 70 receiving breast conserving surgery	90%	96.4%
Radiation therapy is considered after mastectomy within 1 year of diagnosis for ≥4 nodes	90%	100%
Combination chemotherapy is considered or administered within 4 mo of diagnosis < age 70 with AJCC T1cN0M0, or Stage IB-III hormone receptor-negative breast cancer	90%	99%
Tamoxifen or 3 rd generation aromatase inhibitor is considered or administered within 1 year of diagnosis for AJCC T1c or IB-III hormone receptor-positive breast cancer	90%	95.5%

BREAST CANCER SURVIVAL OUTCOMES

Breast cancer ranks second as a cause of cancer death in women. Death rates for breast cancer have steadily decreased since 1989, representing improvements in both early detection and treatment. The five-year survival for localized female breast cancer is 98.6 percent, according to the 2005-2011 SEER database.(4) Figure 8 shows unadjusted five-year observed survival rates by stage of disease at diagnosis of Carolinas HealthCare System breast cancer cases diagnosed from 2010-2014. The observed five-year survival rates for Carolinas HealthCare System during this time period are 93.1 percent for Stage 0, 90.4 percent for Stage I, 83.7 percent for Stage II, 65.7 percent for Stage III, and 25.5 percent for stage IV. The Carolinas HealthCare System survival rates are comparable to national rates for all stages.

FIGURE 8
BREAST CANCER SURVIVAL RATE BY AJCC STAGE, 2010-2014



UTILIZATION OF GENETIC COUNSELING FOR BREAST CANCER

The Cancer Genetics Program consists of a team of physicians and six American Board of Genetic Counseling board-certified genetic counselors who provide patients and their families with counseling services related to genetic risk assessment and recommendations for care. Genetic counseling services are provided at ten regional Levine Cancer Institute Cancer Center sites.

The National Comprehensive Cancer Network has specific criteria for further genetic risk evaluation in an individual with a breast cancer diagnosis.⁽⁵⁾ Specifically focusing on two criteria – namely early-age onset breast cancer, defined as a breast cancer diagnosis at 45 years of age or younger, and a diagnosis of triple-negative breast cancer at age 60 or younger – our analysis of referrals during the period from January 2014 to December 2014, showed women with newly diagnosed breast cancer, meeting these two criteria, are appropriately referred for cancer genetic counseling and testing.

FIGURE 9A
UTILIZATION OF GENETIC COUNSELING FOR BREAST CANCER, 2014

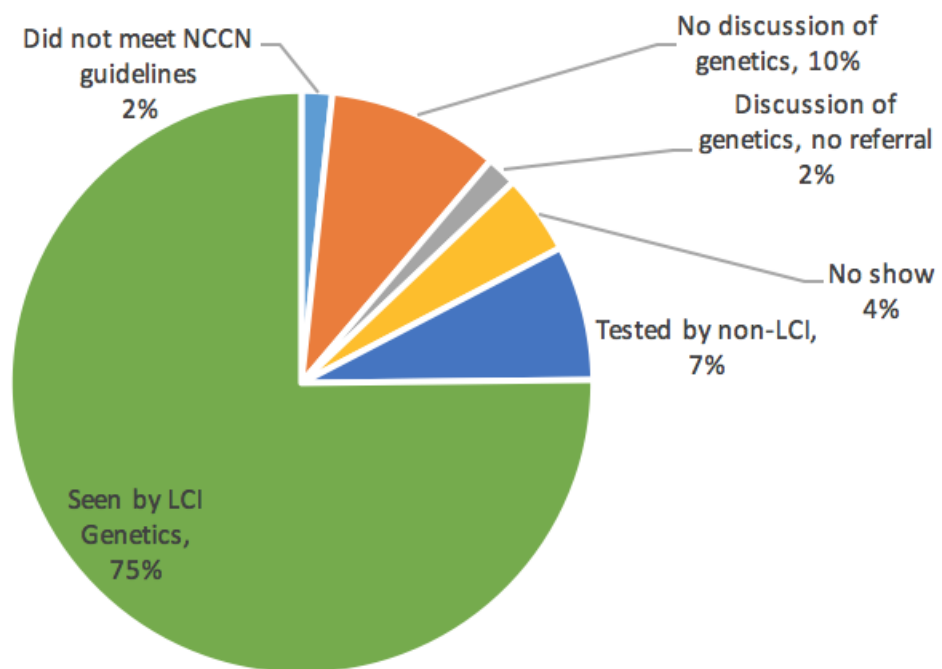
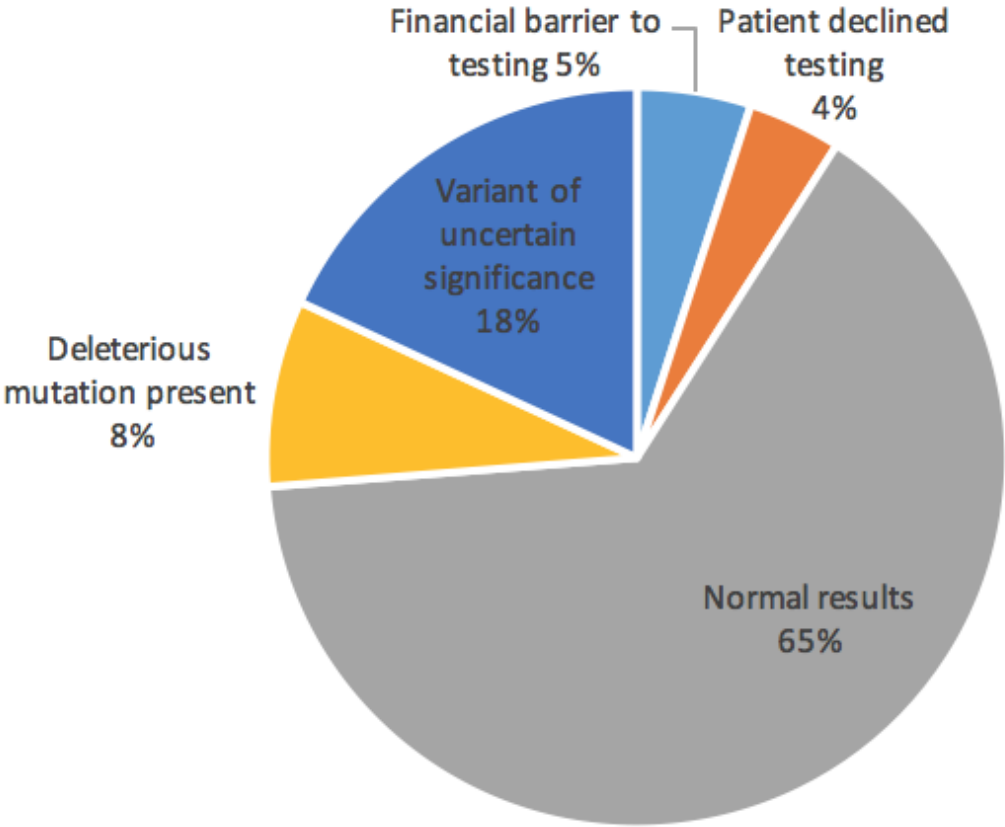


FIGURE 9B
OUTCOMES OF REFERRALS TO THE LEVINE CANCER INSTITUTE GENETICS PROGRAM



RADIOTHERAPY HYPOFRACTIONATION FOR BREAST CANCER

The Radiation Oncology Program at Levine Cancer Institute is accredited by the American College of Radiology. The best length of course and dose per radiation treatment for breast cancer is under ongoing investigation. Historically, a woman with breast cancer would receive radiation once daily for approximately six weeks. For decades this was the standard. As planning technologies advanced, it was conceivable that women could receive slightly more radiation per day, finishing all of their treatments on the order of three to four weeks. Multiple clinical trials were conducted to define the ideal candidates for this shortened course of radiation called hypofractionation.

We now have multiple clinical trials demonstrating the shorter course of radiation to be safe and effective in a well-selected group of patients who need radiation to their breasts but not their lymph nodes. Nationally, reports have suggested clinicians have been slow to adopt the change in dose fractionation. We examined our rate of adoption of this evolving treatment option. Our records indicate that we are above nationally reported rates of offering hypofractionation, and our adoption of the technique has been rapid.

When compared to prior to 2011, when national consensus guideline was issued by the American Society for Radiation Oncology (ASTRO) (6), our rates of hypofractionation have tripled, going from <10 percent to 35 percent of all women with early-stage breast cancer treated at the Institute in 2014. Considering only approximately 50 percent of the early-stage patients meet criteria for hypofractionation, it is likely 70 percent of those patients who are eligible are receiving hypofractionation here at Levine Cancer Institute. Published reports suggest implementation of this new technology to be 20 to 30 percent nationally in 2014. We are proud of the Institute's radiation oncology physicians for rapidly adopting new, safe and effective measures for women with breast cancer.

TRIPLE-NEGATIVE BREAST CANCER

Molecular subtypes of breast cancer have been identified by gene expression profiling. It has become increasingly known that breast cancer is not one disease, and treatment is not a “one-size-fits-all” approach. Recent research indicates that breast cancer is a group of diseases distinguished by different molecular subtypes, clinical behaviors and treatment. Triple-negative breast cancer (TNBC) is a term used to describe a breast cancer that lacks expression of the estrogen receptor, progesterone receptor and the human epidermal growth factor receptor 2 (HER2). It is one of the more aggressive subtypes of breast cancer. At present, chemotherapy is the main treatment for early-stage and advanced TNBC.

About 10 to 20 percent of all breast cancers in the United States are triple-negative. At Carolinas HealthCare System, 11 percent were triple-negative. The majority are diagnosed at an early stage, Stage I and II.

FIGURE 10A
MOLECULAR SUBTYPES OF BREAST CANCER, CAROLINAS HEALTHCARE SYSTEM, 2014

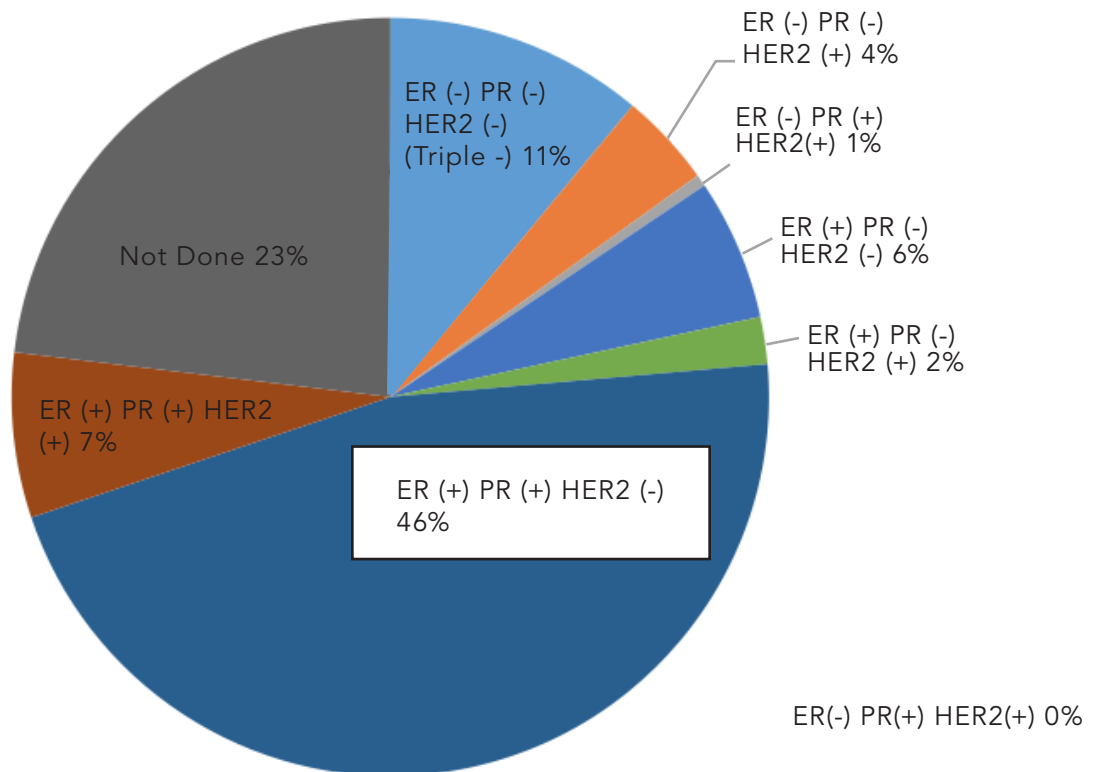
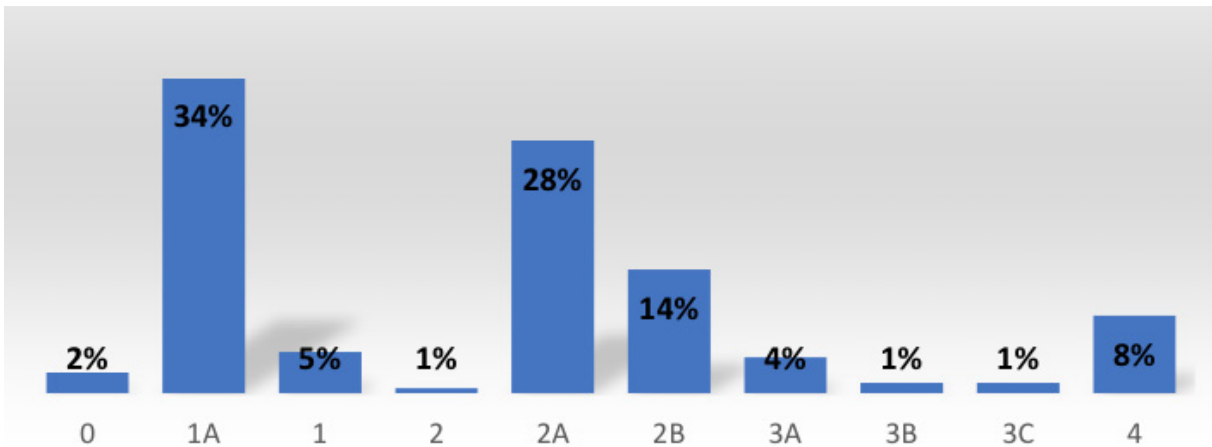


FIGURE 10B
 STAGE OF TRIPLE-NEGATIVE BREAST CANCER AT DIAGNOSIS, CAROLINAS HEALTHCARE SYSTEM 2014



Clinical trials are research studies that test new ways to prevent, detect, diagnose or treat a disease. Taking part in cancer clinical trials offers the opportunity to contribute to the knowledge of cancer and help in the goal of improving cancer treatments. At Levine Cancer Institute, there are several clinical trials that are being offered for patients with triple-negative breast cancer. Our goal is to have a menu of research studies that evaluate several types of targeted approaches to better treat this type of breast cancer more effectively. These currently include the following:

1. GO29505 (FAIRLANE): A Phase II Randomized, Double-Blind, Study of Ipatasertib (GDC-0068), an Inhibitor to AKT, in Combination with Paclitaxel as Neoadjuvant Treatment for Patients with Early Stage Triple-Negative Breast Cancer (NCT02301988)
 2. B55/BIG 6-13 (OLYMPIA): A Randomized, Double-Blind, Parallel Group, Placebo-Controlled Multi-Centre Phase III Study to Assess the Efficacy and Safety of Olaparib Versus Placebo as Adjuvant Treatment in Patients with Germline BRCA1/2 Mutations and High Risk HER2 Negative Primary Breast Cancer Who Have Completed Definitive Local Treatment and Neoadjuvant or Adjuvant Chemotherapy (NCT02032823)
 3. GO29227 (LOTUS): A Randomized, Phase II, Multicenter, Placebo-Controlled Study of Ipatasertib (GDC-0068), an Inhibitor of AKT, in combination with Paclitaxel as Front-Line Treatment for Patients with Metastatic Triple-Negative Breast Cancer (NCT02162719)
- Carolinas HealthCare System is one of the top five accruing sites for this clinical trial worldwide and the top accruer in the United States.
4. MK-3475-086 (KEYNOTE-086): A Phase II Clinical Trial of Pembrolizumab (MK-3475) as Monotherapy for Metastatic Triple-Negative Breast Cancer (NCT02447003)

HIGHLIGHTS OF THE BREAST CANCER PROGRAM

- The Breast Program of the Levine Cancer Institute at Carolinas Medical Center (CMC) in Charlotte, NC received a full three-year accreditation from the National Accreditation Program for Breast Centers (NAPBC) in 2015. Only 17 centers in North Carolina hold this distinction.
- Other locations that are NAPBC accredited include: Carolinas HealthCare System Northeast Breast Health Center, in Concord, NC, and Carolinas HealthCare System Union's Edwards Cancer Center, in Monroe, NC
- Expanded the distribution of breast cancer patient treatment summaries and survivorship care plans
- Opened several clinical research studies that are evaluating novel agents including immunotherapy

OUTREACH EFFORTS

Levine Cancer Institute provides several educational opportunities on breast health for the public and provides access to mammographic screening for the uninsured.

- Project PINK provides access to screening mammograms for underserved women who are age and risk eligible in Mecklenburg and Union counties. Free mammography days target underserved communities where we are able to serve those most in need. Our partnership with Charlotte Radiology and their Mobile Breast Center, provides "breast expertise on wheels." As a result, since 2011, this provided 1,685 uninsured women with screening and diagnostic breast exams, identifying six new cases of breast cancer.
- The Witness Project provides mammography screenings for underserved African American females in Stanly County.
- The I-CAN Ambassador program provides education on cancer prevention, screening, health and wellness strategies to school children in kindergarten through 12th grade.
- In 2005, we held 23 community health fairs to provide community education sessions regarding breast health to about 2,100 attendees.

SUMMARY

The essential components of our Breast Cancer Program that meets the growing volume of new breast cancer cases at Carolinas HealthCare System include:

- Recertification by the NAPBC in 2015 for the Breast and Surgical Oncology Center in Charlotte, NC
- Continued NAPBC accreditation for the Carolinas HealthCare System NorthEast Breast Health Center and the Carolinas HealthCare System Union’s Edwards Cancer Center
- Breast cancer specialists in the areas of surgery, medical oncology, radiation oncology, plastic surgery, radiology and pathology
- Weekly multidisciplinary breast conference
- Weekly working radiology breast conference
- Breast cancer nurse navigation
- Support services which include survivorship, integrative oncology, lymphedema and genetics

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6. Smith BD, Bentzen SM, Correa CR, et al. Fractionation for whole breast irradiation: an American Society for Radiation Oncology (ASTRO) evidence-based guideline. *Int J Radiat Oncol Biol Phys.* 2011;81:59-68