Statistically, the incidence of breast cancer rose dramatically in the 1970s and 1980s. This dramatic increase was attributed to 2 main causes: the increasing use of screening mammography that started in the 1970s, and an increase in obesity and dietary fat content in the general population.

**Screening Mammography:** The use of screening mammography started in the 1970s with the Health Insurance Plan of Greater New York trial (a randomized controlled trial) and then the Swedish Two-County Trials. As a result of these studies, screening mammography was incorporated into the U.S. guidelines via the American Cancer Society and the National Institutes of Health. As we began to regularly screen for breast cancer, the incidence appeared to rise dramatically.

**Prevalence:** Since the 1970s when screening mammography was incorporated into our practices, the incidence of breast cancer in the U.S. appears to have decreased. This has happened for 2 main reasons. (1) When a screening program is initiated, you have a high pickup rate in what is called the “incidence phase.” Then, after a while, all the preexisting cases are eliminated, and you begin picking up just new cases. So the screening program’s pickup rates begin to drop into what is called the “prevalence rate.” Therefore, in 2013, we have passed beyond the pickup rates and dropped into the prevalence rate, giving us the impression that the number of breast cancers is leveling off or decreasing. However, breast cancer is still the most common cancer in women, but it is one of the cancers where the incidence is beginning to decrease. (2) In the U.S., there has been a focus on improving diet and exercise and controlling obesity, which is an important risk factor for breast cancer. As we continue to tackle the obesity problem, we may see the incidence of breast cancer decrease even further; particularly as we start to modify Western diets.
Card 2
Current Controversies in the Use of Screening Mammography

The use of screening mammography started in the 1970s and 1980s after several trials showed benefit for detecting breast cancer. Because we now regularly screen for breast cancer, we are detecting breast cancer at earlier and earlier stages. This has brought up several controversial issues. Are some cases detected at such an early stage that we really do not need to do anything about them? Are there ages at which the detection of early stage breast cancer will not affect life expectancy? At what age should we stop screening for cancer? How aggressively should we treat early stage breast cancer? Other somewhat related and controversial questions are: What should we do about ductal carcinoma in situ (DCIS). Is this really a cancer? Should we be treating it aggressively? I do not think the answers to all these questions are known, but they are good questions to consider as people live longer.

**Age vs Screening Benefit:** As our society ages, should there be cutoff ages for when we discontinue mammographic screening? This continuing area of controversy is associated with 2 different schools of thought. According to the U.S. Preventative Services Task Force, the use of screening mammography should be discontinued when women reach age 75 years. However, the American Cancer Society (ACS) says that there should not be a cutoff age for mammographic screening, but, rather, this decision should be discussed on an individual basis between a woman and her provider. Therefore, on one hand, we have a controversial but clear age-related guideline for discontinuing breast cancer screening. On the other hand, the ACS gives us a more individualized but labor-intensive approach in which every woman must come to her own decision. The ACS approach perhaps better accounts for the fact that we are really talking about physiology and not chronology. Depending on what conclusion we finally reach, we may find ourselves extending breast cancer screenings further out as our population continues to age. A risk is that early stage breast cancers will be detected and, despite treatment, life expectancy will not be extended.
Card 3
Z11 Trial: Changing Our Beliefs About Axillary Dissection

The recently published American College of Surgeons Z0011 trial (or the Z11 Trial) looked specifically at the subset of women who underwent lumpectomy and radiation therapy for early stage breast cancer. In this trial, early stage breast cancer included T1 (tumor <2 cm) and T2 (tumor ≤5 cm) cancers. The average patient had a T1c cancer (size ranging from 1 to 2 cm) and was clinically node-negative (lymph nodes cannot be felt on palpation). These patients were staged with sentinel lymph node biopsy (SLNB) and were found to have 1 to 2 SLNs that were positive for micrometastatic disease. In the Z11 trial, these women were randomly assigned to either axillary dissection or observation only. At the end of the trial, the 5-year disease-free survival rate, the 5-year overall survival rate, and the axillary recurrence rates did not differ significantly between the 2 groups.

**Conclusions:** For women with early stage breast cancer who have micrometastatic axillary SLN-positive disease, a completion axillary dissection is not beneficial in those patients treated with a combination of lumpectomy and radiation therapy. In this population, completion axillary dissection does not contribute to either survival or local control.

**Comments:** When this study was published, the results and conclusions were considered to be quite significant because most general surgeons held the erroneous belief that all women with a positive SLN needed a completion lymph node dissection. However, the authors gave a rather simple explanation for their new recommendation. Residual axillary disease must be treated somehow, and the addition of radiation therapy does just that. Radiation therapy treats any residual disease that may be in the axilla because whole-breast radiation fields typically extend into at least the lower axilla. What the authors of this trial were saying was that, as long as the patient completes her whole-breast radiation, she is getting adequate axillary therapy and does not benefit from additional operation.
The recently published American College of Surgeons Z0011 trial (or the Z11 Trial) investigated the value of completion axillary dissection in women with early stage breast cancer and axillary node-positive disease that was treated with the combination of lumpectomy and whole-breast radiation. The results showed that completion axillary dissection did not benefit either survival or local control and should not be performed in this population. Did this study impact the actual practice standards of most surgeons?

**Survey:** After hearing several of the first reports on the trial, I put together a survey for general surgeons in the Pacific Northwest. The response rates were relatively good. The survey showed that general surgeons in the Pacific Northwest were fairly early adopters of the Z11 Trial’s recommendations. After the surgeons in this region had heard about the trial, they quickly changed their practice: they were decreasing the practice of performing an immediate axillary dissection for SLN positivity for patients undergoing lumpectomy and radiation. Therefore, just months after publication of the Z11 Trial, we were already seeing changes. Of course, there were some conservative surgeons (a small percentage) who said they were not going to change their practice based on the Z11 Trial. I believe that if we now repeated the survey, the number of surgeons who are not following the trial’s recommendations would be even lower.

**Practice Concerns:** On review of the survey data, I became concerned because some surgeons were already omitting axillary dissection for patients who were not included in the Z11 study population. For any clinical trial, the results should never be extended to populations that were not studied. Plus, in the Z11 Trial, the axilla was being treated: whole-breast radiation was believed to provide adequate treatment to the lower axilla where most residual micrometastatic disease is found. This point is important because the trial excluded patients who did not receive adequate radiation treatment, such as those who had total mastectomy and generally do not get radiation, those who received only partial breast radiation, those who had neoadjuvant therapy, those who refused radiation, and those who had radiation in a prone position (radiation fields did not reach the axilla). The Z11 Trial’s authors were very careful to point out that the data could not be extended to patients who were not getting low axillary radiation. Therefore, I became concerned when the survey revealed that some general surgeons were no longer performing axillary dissection for those patients who were excluded in the Z11 Trial, which is a serious overextension of the data.
Triple Negative Breast Cancer vs Axillary Dissection: Did the Z11 study’s conclusions apply to women with clinically negative axillary sentinel nodes and triple negative breast cancer (TNBC)? TNBC is the term used to describe a breast cancer that lacks estrogen and progesterone receptors and HER2/neu. Because only a few TNBC patients were found in the Z11 Trial, there was not enough power in the data to suggest that they should not have an axillary dissection. For one thing, these patients are often node-positive, and it is well known that they have higher risks of recurrence after lumpectomy/radiation. Therefore, we would consider TNBC patients to be an exclusion to the recommendations of the Z11 Trial.

TNBC vs Ovarian Cancer: The author of a recent report in Science commented that, genetically, TNBCs look more like and maybe behave more like an ovarian cancer than like a breast cancer. Personally, I consider TNBC to be a systemic disease — a very bad systemic disease because it lacks targets (estrogen receptors, progesterone receptors, and HER2/neu). If the cancer is missing all 3 targets, it seems to be particularly aggressive. Accordingly, TNBCs have a basic biological aggressiveness and cannot be treated with targeted hormonal therapy or antibody therapy against HER2/neu. Like ovarian cancer, TNBC lacks targets, requires aggressive chemotherapy, and must be treated like a systemic disease.

TNBC vs Basal Cells: TNBCs are sometimes called “basal-like cancers” because they lack the same hormone receptors and HER2/neu expression as seen with the normal basal cells of the ducts. Ducts have a basal layer (the outermost layer) of cells that do not proliferate under the influence of estrogen and progesterone when a woman is pregnant. Really, their only function is to hold the ducts together. TNBCs, or basal-like cancers, are most common in younger women and women who are BRCA1-positive. However, BRCA2-positive patients tend to have more of a sporadic profile, so BRCA2 incurs an increased risk but the same prognosis as sporadic breast cancer. BRCA1 incurs increased risk and a worse prognosis because the cancers tend to be more of these TNBCs and the patients tend to be younger. Younger patients get more basal cancers, which may explain the long-recognized phenomena that younger women tend to get worse cancers. This is probably because, biologically, they are getting more basal-like cancers or TNBCs.
Card 6  
Sentinel Lymph Node Biopsy: Technique Issues and Notes

A sentinel lymph node biopsy (SLNB) is used to determine if cancer has spread from the breast tissue (the original cancer site) to surrounding lymph nodes.

**Dual-Agent Technique:** Much of the available data show that SLNB is most accurate with the dual-agent technique that uses both isofluran blue (Lymphazurin™ 1%) and technetium sulfur colloid radioactive material. In SLNB, the biopsy will almost always be performed in the axilla, so many general surgeons believe Lymphazurin is not necessary. Rather, they can just use the gamma scintillation detector to identify the radioactive colloid. For me, the blue dye sometimes works, but the radioactivity almost always works. In a few patients, neither of the agents work, and these are known as “nonvisualization” cases. These patients tend to be older, to be obese, and to have had prior axillary or breast surgery. However, in about 97% of the remaining cases, the node will be identified on SLNB and can then be removed. In my practice at Oregon Health and Science University in Portland, Oregon, and the Knight Cancer Institute, I use both agents.

**Anaphylaxis:** Among the patients receiving Lymphazurin, 1% will have an anaphylactic reaction. I personally have never seen one of these reactions in the >1000 SLNBs that I have performed. However, I have seen a patient get hives. But these patients are under general anesthesia and can quickly be treated with Benadryl® and fluids.

**Teratogenic Potential:** Lymphazurin is a Category C teratogen. Therefore, it cannot be used in pregnant women who are undergoing SLNB.

**False Oximetry Readings:** As a colormetric dye, Lymphazurin can interfere with the pulse oximeter and cause falsely low pulse oximetry readings. At our institution, this is not a big deal: not everybody has a pulse oximeter because these are often minor cases in otherwise well patients. Nonetheless, if the saturation levels sag, it may be falsely related to the dye.

**Internal Mammary Nodes:** Another issue in SLNB comes about when lymphoscintigraphy shows uptake in the internal mammary (IM) nodes. IM node status correlates very well with the axillary status. Usually, when you see an IM node, you will also see an axillary node. Therefore, the current thinking is to perform the axillary SLNB, and if it is negative, then the IM node is probably negative. If the axillary SLNB is positive, then you alert the radiation therapist and make sure that radiation fields are extended into the IM nodes.

**Good Technique:** SLNB is a good technique. It works with everybody. It even works in males, in multifocal tumors, and after neoadjuvant therapy.
A controversial topic in sentinel lymph node biopsy (SLNB) is whether it should be performed in cases of ductal carcinoma in situ (DCIS). Not all DCIS is created equal: DCIS is a range of diseases with different grades and different risks. Therefore, there are some accepted indications for SLNB in DCIS.

**Node Positivity in DCIS:** Data from the 1970s and 1980s taught us that about 5% to 10% of DCIS cases are node-positive. Now in 2013, we know that node-positivity in DCIS is more likely when a palpable mass is present, when microinvasion is seen on the core needle biopsies, when the extent of DCIS is >2 cm, and, particularly, when DCIS is high-grade or if comedo necrosis is present. If more than a few of these indicators are present, the risk of node positivity can be up to 20%. When a core needle biopsy shows DCIS, you often go on to perform the needle-localized lumpectomy and discover invasion, which is most likely to occur if there is microinvasion, if a big area is involved, if DCIS is high-grade, or if comedo necrosis is present. Then, the most likely scenario is that you perform the lumpectomy and get the rest of the DCIS out. But when you see the invasion, you will then wish you had done the SLNB. I have a very low threshold for doing SLNB in DCIS because I do not want to be in the position where I wish I had done it. In my experience, most DCIS has at least some of those factors related to node positivity, so we commonly do SLNB for DCIS.

**Side Effects:** SLNB is not a free lunch — there is a small but real risk of lymphedema. In some series, the lymphedema rate is as high as 7%. It can be temporary. There is numbness. There is a risk of an axillary lymphocele because these are typically not drained. Therefore, we limit the patient’s activity for a week after SLNB.

**Patient Warning:** It is important to remind the patient that SLNB is a minor procedure, but it does come at some cost. I think those costs are outweighed by the information obtained from the staging, particularly in this higher-risk DCIS group and in invasive cancers.
Open Biopsy Being Replaced by Core Needle Biopsy

Today, breast lesions are generally sampled with a needle biopsy or core biopsy. The question often asked is whether there is still a role for open biopsy for breast lesions.

**Triple Test vs Open Biopsy:** In the 1980s, my partners and I wrote a lot of papers on the triple test for breast lesions, which is the combination of clinical exam, imaging, and needle biopsy. Prospective trials that compared the triple test with open biopsy found 100% concordance when all the elements suggested cancer or when all the elements were benign. In other words, you would always find cancer on open biopsy if all 3 parts of the triple test indicated a cancerous lesion. Or, you would always find a benign lesion on open biopsy if all 3 parts of the triple test indicated a benign lesion. As a result of these studies on triple testing in the early 1990s, we were able to lower our open biopsy rates to about 8%.

**Current Approaches:** Today, it is very uncommon to do an open biopsy. I will do an open biopsy if I truly suspect inflammatory breast cancer and I am not reaching the diagnosis any other way, but that situation probably comes up only once a year. Therefore, today, most palpable lesions are sampled with a handheld core biopsy, and most nonpalpable lesions are sampled with either an ultrasound-assisted or mammographically assisted core biopsy. Cores biopsies are now being done with vacuum-assisted devices such as Mammotome® that, in many cases, allow removal of the entire radiographic abnormality. Therefore, it is very important to place a clip (tissue marker) to identify the location of the target tissue. We recently had a case in which the patient refused the clip, and the core biopsy showed ductal carcinoma in situ (DCIS). When we went back, the procedure was a difficult without having the clip to direct us. Placing the clip is very important when you do these types of core biopsies, particularly if the patient will undergo a neoadjuvant therapy, because, if there is a good radiographic response, you need to know where the original lesion was located.

**Lumpectomies:** The ongoing use of screening mammography will continue to push the diagnosis of breast cancer to the left where we are finding smaller and smaller tumors, which are usually nonpalpable and radiographically detected. As we find smaller tumors, we are seeing all sorts of things on the core biopsies that may require needle-localized open lumpectomies for follow-up and treatment, not for diagnosis.
Card 9
Risk Lesions of the Breast: Their Significance and Treatment Options

In the breast, “risk lesions” are those lesions that appear to indicate that a patient has an increased risk for the eventual development of breast cancer. Risk lesions include lobular carcinoma in situ (LCIS) and its counterparts, such as the atypical hyperplasias (either ductal or lobular), and other lesions like flat epithelial atypia and papillomatosis with atypia. These risk lesions are not site-specific, and they are not precursors. Instead, they are markers for an increased risk of breast cancer. Compared to the risk found in the general population, the risk of breast cancer is about 4 times higher when atypical hyperplasias are present and about 8 times higher when LCIS is present, which translates into a risk of about 1% per year for at least 30 years. For example, when LCIS is identified on biopsy, the risk of breast cancer is about 35% at 30 years. For other lesions, the lifetime risk may be a little less, but the risk is still elevated.

Important Indications: These risk lesions are not site-specific. The cancer will develop in 30% of women. We do not know when it is going to come: the average time is about 8 to 12 years, but it can extend out over 30 years. The cancer can come in either breast, and it can come in some other part of that same breast. When the cancer does develop, it might be a ductal cancer or it might be a lobular cancer. Therefore, the presence of a risk lesion only tells us one thing: this patient is at risk for the development of breast cancer.

Treatment Options: When a woman is identified with one of these risk lesions, there are only 3 really rational treatments: One is to just observe her and make sure she gets her annual mammograms for at least out to 30 years. For many women, following this approach will take them up to 75 years of age, at which time screening may be discontinued at the discretion of the physician. The second option is to perform a bilateral prophylactic mastectomy, often with a reconstruction. This approach is often chosen in women who have other risk factors, such as family history or gene positivity. And the third option is to do chemoprevention per the P01 and P02 breast cancer prevention trials which showed that that the 20% to 30% risk could be cut in half with 5 years of tamoxifen or raloxifene therapy.
Card 10
Risk Lesions of the Breast: Coexisting DCIS and Invasive Cancer

The presence of a risk lesion found on biopsy of the breast indicates that the patient is at increased risk for the eventual development of breast cancer. Risk lesions include lobular carcinoma in situ (LCIS), the atypical hyperplasias (either ductal or lobular), and other lesions like flat epithelial atypia and papillomatosis with atypia.

Diagnosis: In the past, many of these lesions were diagnosed on open breast biopsy. When the only thing seen on open biopsy was a risk lesion, it was referred to as a “pure risk lesion.” Remember, with open biopsy, the lesion was identified using a relatively large tissue sample. Today, most risk lesions are diagnosed on core biopsy using a relatively small tissue sample. Because risk lesions can sometimes coexist with either ductal carcinoma in situ (DCIS) or an invasive cancer, we may wonder if any other lesions are present in the breast when a risk lesion is seen on core biopsy. Therefore, when you see a risk lesion on a core biopsy, should you go back with a needle-localized lumpectomy and take that out to make sure you have not got something coexisting with the core biopsy. We know from the core biopsy data that, on lumpectomy, you will find either DCIS or an invasive cancer in 10% to 30% of the risk lesions diagnosed on core biopsy.

Indications for Needle-Localized Lumpectomy: For biopsies that demonstrate pure risk lesions (and nothing else), when should you go back in to look for DCIS and invasive cancer? I think you should go back in certain cases (such as those with LCIS) because the risk of finding an invasive cancer or DCIS is as high as 30%. The risk of finding invasive cancer or DCIS can be as high as 20% for a papilloma with atypia and is about 10% to 20% for the atypical hyperplasias.

No Lumpectomy Needed: Are there patients for whom the core biopsy is satisfactory and you do not need to go back in to look for DCIS and invasive cancers? I believe you do not need to follow up with a lumpectomy when the patient has normal risk, when this was a screening mammogram, when the lesion was completely removed by aspiration biopsy, when there were very low numbers of foci (typically <4), and most importantly, when there is concordance (lesion seen on mammogram was not a BI-RADS 5 and the radiologist believes that the risk lesion explains or is concordant with what was seen on mammogram). But, if the radiologist has concerns about this lesion and the core biopsy shows only a risk lesion, you probably should go back and perform the lumpectomy.
Card 11
Risk Lesions of the Breast: Chemoprevention

Among breast lesions, those identified as “risk lesions” on core biopsy indicate an increased risk for the eventual development of breast cancer. Compared to the risk found in the general population, the risk of breast cancer is about 4 times higher when atypical hyperplasias are present and about 8 times higher when lobular carcinoma in situ (LCIS) is present, which translates into a risk of about 1% per year for at least 30 years. One treatment option for patients with a risk lesion is to do chemoprevention per the P01 and P02 breast cancer prevention trials, which showed that the 20% to 30% risk could be cut in half with 5 years of tamoxifen or raloxifene therapy.

The 5-Year Requirement: This 5-year treatment requirement is based on old data showing that 5 years of tamoxifen therapy seemed to be ideal for breast cancer prevention. Because the 5-year standard was used to derive the data, that is the way the Food and Drug Administration approved the drug. In addition, some data suggested that giving tamoxifen for 10 years actually increased the incidence of receptor-negative cancers. Regardless, these data are being revisited to assess their accuracy. But, meanwhile, we must stay with the data based on the original prevention trials.

Risk Reduction: The other issue with prolonged hormonal therapy is that it comes with risk. When the P01 (observation versus tamoxifen) and the P02 (tamoxifen versus raloxifene) trials came out, we learned that many patients with a Breast Cancer Risk Assessment Tool score of >25% had lobular carcinoma in situ (LCIS), which is a risk lesion for the eventual development of breast cancer. In the P01 trial, tamoxifen was associated with a 50% reduction in this cancer risk in patients with risk lesions. In the P02 trial, both tamoxifen and raloxifene provided that effect, and their efficacies were found to be equivalent.

Side Effects: At that point, we thought we would be writing prescriptions for tamoxifen or raloxifene for everyone. But, in fact, that did not happen. Instead, chemoprevention proved to be the treatment measure chosen least often of the 3 available options for patients with risk lesions (observation, bilateral prophylactic mastectomy, or chemoprevention). Why? Because the drugs have side effects, and people are understandably shy of them. Tamoxifen causes hot flashes, increases the risk for thrombosis, and is associated with a 1% risk of low-grade endometrial cancer and a smaller risk of liver cancer. Raloxifene has similar effects and is actually less tolerated by younger women. Arimidex® is used to treat breast cancer in postmenopausal women. Because it is an aromatase inhibitor, it is not tolerated at all by younger women and, in older women, it can cause severe musculoskeletal problems, bone loss, and fractures.
Neoadjuvant therapy has been around for many years as part of the treatment regimen for breast cancer. It has been extensively studied by the National Surgical Adjuvant Breast and Bowel Project, and it has been shown in prospective randomized trials to be associated with a number of benefits.

**Buying Time:** First, it buys time to get the results of genetic testing. When the results arrive, then the woman can make an informed decision about whether she is a candidate for lumpectomy/radiation (if the tumor shrinks adequately during neoadjuvant therapy) or whether she is a better candidate for bilateral mastectomy.

**Biologic Tests:** In the past, we have always used adjuvant therapy after the tumor was gone, and we hoped the drugs were effective against any remaining microscopic disease. But with neoadjuvant therapy, we can see the drugs working as the tumor shrinks. In a few patients, the tumors do not shrink, which indicates that these tumors are not sensitive to those particular drugs and different agents are needed.

**Breast Conservation Rates:** Neoadjuvant therapy increases the number of women who can have their breasts preserved via lumpectomy/radiation therapy. In most women, there is a very real partial response to neoadjuvant therapy. The tumors shrink and, in some cases, patients who previously could not have had their breasts preserved are converted to patients who can. This is an important reason to have a clip (tissue marker) in place because, in some cases, very large tumors can shrink and become nonpalpable after neoadjuvant therapy.

**Survival:** Most randomized trials have not shown an improvement in overall survival or disease-free survival with neoadjuvant therapy. However, survival is improved for a small subset of patients who have a “pathologic complete response” (tumor shrinks and no tumor present on lumpectomy). Pathologic complete responders (13% to 26% of patients) tend to be the worst patients: they are younger, have higher-grade tumors, and have triple negative or HER2/neu cancers. Therefore, for this particularly high-risk group, neoadjuvant therapy may actually improve survival.

**Expanded Trials:** The next generation of randomized trials for neoadjuvant therapy is the I-SPY TRIALS (Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging And moLecular Analysis). The I-SPY 2 TRIAL is the second-generation trial in which women undergo scheduled standard follow-up studies, and then, by a certain time, undergo surgery. This trial is unique because it is open — it incorporates new chemotherapy regimens as they come along. Most agents used in neoadjuvant therapy are the same agents used in adjuvant therapy, such as Cytoxan®, Adriamycin®, and the taxanes. But as newer agents come along, they can be incorporated into the I-SPY 2 TRIAL.
Card 13
Genetic Testing in Breast Cancer: NCCN Guidelines

Genetic testing is the new-wave approach for breast cancer. We know that all breast cancers are probably hereditary, but we still call some breast cancers “sporadic” when we cannot identify the particular gene that may have driven that cancer. We have identified breast cancer syndromes that appear to be driven by particular mutations, usually germline mutations. For example, PTEN is associated with the Cowden syndrome, which is found in a minority of patients, and p53 is associated with the Li-Fraumeni syndrome in which breast cancer plays a major role. The most prevalent genes are BRCA1 and BRCA2, which control the Hereditary Breast and Ovarian Cancer syndrome, indicating that these genes are associated with a link between breast cancer and ovarian cancer. Overall, BRCA1 and BRCA2 increase the risk of these cancers about tenfold. Of the 2 genes, BRCA1 is probably the most egregious because it increases the breast cancer risk up to 80%, it increases ovarian and fallopian tube cancer risk up to 46%, and it increases the risk of a triple negative breast cancer that is often found in young women with histories of breast/ovarian cancer in their family.

Guidelines for Genetic Testing: I use the National Comprehensive Cancer Network Clinical Practice Guidelines (NCCN Guidelines®) to determine who should undergo genetic testing. For every 100 women, about 22 will meet NCCN Guidelines for genetic testing, meaning that about 25% of our breast cancer patients should undergo genetic testing. Of the original 100 women, about 10% will be gene-positive. Some companies that market these tests are placing pressure on general surgeons to bypass the genetic counselor and order the test themselves. This trend worries me, because if we do not follow the guidelines, we may be testing all women rather than the 25% who meet the guidelines for testing to identify the 10% who will ultimately be gene-positive. Therefore, I recommend that we follow the NCCN Guidelines. I still use the genetic counselors to order the tests because they have the best understanding of the NCCN Guidelines, they have the time to counsel patients about the meaning of positive and negative tests, and they have the expertise to develop a treatment plan for either outcome. They can also take the time to sort through the family history, make detailed pedigrees, and determine what genes we should be looking for in addition to BRCA1 and BRCA2.
The National Comprehensive Cancer Network Clinical Practice Guidelines (NCCN Guidelines®) are useful for helping us determine which breast cancer patients should undergo genetic testing. According to these guidelines, about 25% of breast cancer patients should undergo genetic testing. The most prevalent breast cancer genes are BRCA1 and BRCA2, which control the Hereditary Breast and Ovarian Cancer syndrome. Overall, BRCA1 and BRCA2 increase the risk of these cancers about tenfold. The NCCN Guidelines indicate that a breast cancer patient should undergo testing for BRCA1 and BRCA2 when (1) there is a known gene carrier in the family, (2) there is a personal history of breast cancer plus another risk factor, and (3) the patient has a ≥25% risk as calculated by a mathematical model.

**Germline Mutations:** BRCA1 and BRCA2 are germline mutations, so the risk of getting them from an index parent is 50%. For example, in families with a known mutation, if there are 4 girls in the family, the odds are that 2 will have the gene and 2 will not. These women should be tested for that particular mutation because it is extremely rare that a family has more than 1 type of mutation. If the index relative has a known mutation, then the genetic counselor can cut right to the chase and order testing for that particular mutation.

**Risk Factors:** The second guideline is that BRCA1 and BRCA2 testing should be performed for the patient with a personal history of breast cancer plus another risk factor. These risk factors include diagnosis before age 45 years, Ashkenazi Jewish heritage (1 in 40 Ashkenazic women carry BRCA mutations), and if there are 2 breast cancers (1 before age 50 years). In addition, the presence of certain other cancers in the family may be tip-offs to the presence of Hereditary Breast and Ovarian Cancer syndrome, which would include fallopian tube cancers, ovarian cancers, and male breast cancer, which is strongly linked to BRCA2.

**Mathematical Models:** Another indication for BRCA1 or BRCA2 testing is if someone has a ≥25% risk as calculated by a mathematical model. Genetic counselors have access to software tools that predict the genetic risk. Several very sophisticated mathematical models are available that can predict breast cancer risk. The most commonly used models are BRCAPRO, the Claus model, and the Cuzick-Tyrer model. These models can be used to justify testing for BRCA1 or BRCA2, and they can also be used to put women on chemoprevention trials.
Card 15
Breast MRI: General Indications

MRI of the breast is not a substitute for a screening mammogram. Instead, breast MRI should be used as an addition to mammography in selected patients. MRI is not useful for detecting ductal carcinoma in situ (DCIS) or for detecting risk lesions, such as lobular carcinoma in situ, the atypical hyperplasias (either ductal or lobular), and other lesions like flat epithelial atypia and papillomatosis with atypia. Therefore, MRIs should not be used as a substitute for a mammogram and they should not be used routinely for women with DCIS and when looking for risk lesions.

Good Indications for MRI: A good indication for breast MRI is when the patient is node-positive or has a multifocal or multicentric tumor in the breast. MRI is also a good way to follow response after neoadjuvant chemotherapy in some patients, although the mammogram works just fine in some patients. MRI has been used to screen women who are at high risk (>25% lifetime risk), particularly if they are positive for BRCA1 or BRCA2. This was studied in the MAMMA trial in Europe in which women underwent both a mammogram and MRI. The results demonstrated that MRI was more of an adjunct to mammography. In other words, MRI seemed to add to the sensitivity of mammography.

Occult Primary Tumors: I think probably the best indication for MRI is for that small subset of women with occult primary tumors. These women present with axillary adenopathy, which is biopsied. After immunohistochemistry is performed, the lesion is determined to be breast cancer. However, the breast exam and the mammogram are normal. What do you do in these cases? The old teaching was that a mastectomy should be performed. But MRI can detect the primary tumor with a very high accuracy in these patients. Among patients with axillary disease and a normal mammogram, about 50% will have an occult primary found on the MRI. But if you do not see the tumor on mammogram, MRI, and clinical exam, then I am very comfortable leaving the breast intact. I have several patients for whom we have avoided mastectomy for occult primaries, and they are doing just fine.
Card 16
Breast MRI: Breast Tissue Density as an Indication

We often hear about the patient with a negative mammogram but, clinically, has “lumpy breast syndrome.” They immediately go to MRI. Is this a legitimate use of MRI?

**Breast Density vs MRI:** This question of whether breast density is an indication for MRI has been investigated. A recent paper was presented at a regional meeting that I attended where the authors tried to make a case for using breast density, which can be measured by various objective scales, as part of risk assessment. I think this issue is multifactorial. The old term for a lumpy breast was “mazoplasia,” which means nodular lumpy breast tissue often painful, usually found in younger women, often cyclic and associated with cyclic mastodynia, and most commonly found in the upper outer quadrant where 60% to 70% of breast tissue is located. Because of the lumpy breast tissues, these women and their providers are concerned that something is hiding in the breast. Should we be using MRI on these patients?

**Guidelines:** Neither the American Cancer Society’s guidelines nor the American Society of Breast Surgeons’ guidelines suggest that breast density is an indication for breast MRI. Remember, these are young women for whom the risk of breast cancer is lower. In addition, mammography does improve with patient age: as their risk for breast cancer increases, breast density decreases and mammography becomes a better test because there is more fat in the breasts. Besides, at that point, most things found on the MRI are going to be false-positives that do not require biopsy. Therefore, breast density is not currently in the guidelines as an indicator for breast MRI.
A mammogram is a wonderful test because, as the breast cancer risk increases with age, the mammography’s pickup rate also improves as the patient ages. In a sense, mammography is a test that grows with the patient.

**Discontinuing MRI Screening:** Let’s say that, for some reason, you add MRI to a patient’s annual mammogram, and the results of both come back negative. Should both tests be used for the following year’s screening? Because the mammogram’s pickup rate improves with patient age, our radiologists discontinue the use of the MRI if, year after year, it is not adding much. That issue always comes up because, per the guidelines of the American Society of Breast Surgeons and the American Cancer Society (ACS), MRI is added for women with known mutations or a lifetime risk >25%. But the guidelines do not tell us when to discontinue the MRI. In my practice, we have a mutual discussion between me, the radiologist, and the patient to determine when to stop MRI screening — when the mammogram is so good that the MRI is not adding any benefit.

**Very High Risk vs Breast MRI:** Patients who had mantle radiation for lymphoma between the ages of 10 and 30 years have a particularly high risk of breast cancer. These patients are now nearing the ages of 50 and 60 years, or older. For these patients, radiologists often continue the breast MRIs because the patients’ risks are so incredibly high. Breast MRI is also provided for patients who refuse testing for BRCA although they have relatives who are known BRCA1 or BRCA2 carriers. According to the ACS guidelines, these patients should have mammograms because they have a 50% chance of also being carriers. If you use MRI screening in this group, you are probably overscreening 50% of the women because they may be gene-negative. Therefore, in this particular group, I agree with the ACS that, if the patient absolutely refuses BRCA testing, you should treat them as if they are gene-positive. Although you are not worried about radiation exposure with MRI, you are worried about a lot of false-positive findings that would result in unnecessary biopsies. From the patient’s standpoint, it makes more sense to get tested for BRCA, but there continues to be a small group of women who simply do not want to get tested even though they have a 50% chance of being BRCA-positive.
Ultrasound (US) is a relatively standard diagnostic approach for the workup of breast lesions. Women who present with a mass in the breast will often undergo both a mammogram and US. US of the breast is very critical for differentiating cystic lesions from solid lesions. For young women, the US provides significantly more information than does a mammogram. Even in patients with tumors, US measurements are often far more concrete if a well-defined mass is seen. Compared to a mammogram, the US will often give you a much clearer picture of the lesion if you can see exactly where the mass starts and stops on the US and if you can get a good look at the location in relation to the underlying chest wall and the overlying skin.

**Axillary US:** For patients with an invasive breast cancer, US of the axillary lymph nodes (LN) has become an important part of the clinical workup. For most patients, axillary US is performed to determine whether the LNs look normal or abnormal. When the LNs look normal, there is usually no percutaneous biopsy, and staging of the LNs is recommended via sentinel LN biopsy. If the US identifies worrisome LNs (enlarged or morphologically different in appearance), then a percutaneous biopsy is recommended. That biopsy is usually an US-guided biopsy, often either a core needle biopsy or, frequently, a fine-needle aspiration biopsy. The sampled tissue is then sent to pathology or cytology for evaluation. If the LNs contain malignancy, then we know that the patient is node-positive prior to therapy. This information is helpful for guiding neoadjuvant therapy, for anticipating the need for axillary LN dissection if the patient is taken to surgery, for providing the indications for postmastectomy radiation, and for determining whether immediate reconstruction is a reasonable consideration.
The use of MRI for breast cancer screening is increasing, especially as more women at high risk for the eventual development of breast cancer are being identified. As we have become more comfortable with genetic testing, we are identifying more people who are carriers of or who may be family members of carriers for a deleterious mutation in the BRCA1 or BRCA2 gene. For these women, screening MRI, as an adjunct to the screening mammogram, is very important to allow early detection of any breast malignancy.

**Atypia & LCIS**: Breast MRI is sometimes considered as a screening tool for women with atypia or lobular carcinoma in situ (LCIS), both of which indicate a significantly increased risk for the eventual development of breast cancer. Data from the American Cancer Society has classified atypia and LCIS in the “in-between category” which has insufficient evidence to recommend for or against MRI screening. However, these women have a 4- to 8-fold increased risk for the development of breast cancer, so breast MRI may be recommended.

**Recommendations for Screening MRI**: Breast MRI is still considered to be an adjunct to mammography — it is not considered to be a stand-alone test. Although many of my patients would like to have the breast MRI without the mammogram, that day has not yet arrived. According to the current guidelines, annual breast MRI screening is recommended for (1) patients who carry a known mutation in the BRCA gene or who have a first-degree relative that is a BRCA carrier when the patient herself is untested; (2) patients with a lifetime risk ≥20% to ≥25% that was estimated using some of the genetic risk prediction models available online; and (3) patients with previous radiation to the chest, such as for Hodgkin disease, between the ages of 10 and 30 years.

**Effect of MRI Screening on Lifetime Risk**: For patients with a 15% to 20% lifetime risk of developing breast cancer, the evidence is insufficient to recommend either for or against MRI screening. However, quite a few women in this category undergo MRIs for screening. Women who have a diagnosis of atypia or those who demonstrate a strong family history but multiple benign breast biopsies will often request the MRI to ensure that, if they do develop a breast cancer, it is detected at an early stage.
Card 20
Mayo Clinic’s Indications for Breast MRI

A hotly debated topic, especially when managing a patient with newly diagnosed breast cancer, is whether we should routinely perform a bilateral breast MRI to assess for any additional disease. However, we have no good solid data showing that a bilateral breast MRI prior to surgery for breast cancer significantly improves the outcomes in terms of long-term local recurrence or number of re-excisions. Many centers routinely do an MRI on all women with newly diagnosed breast cancer. I practice at the Mayo Clinic in Rochester, Minnesota, and we have not adopted this protocol to date. Instead, we tend to have an open discussion with the patient about the potential for false positives and for detecting additional lesions that may or may not be malignant but will prompt an additional biopsy.

**Mayo’s Indications:** In our practice at Mayo, we do not immediately send everyone who has breast cancer to MRI. We tend to provide breast MRI for (1) women with very dense breasts, especially those cases in which the primary tumor is relatively difficult to detect; (2) women who present with disease in the lymph nodes but no disease in the breast; and (3) patients with an invasive lobular cancer for which it is much harder to determine the true size of the lesion on mammogram and ultrasound. We also use breast MRI to monitor response to therapy for patients undergoing neoadjuvant chemotherapy.
Card 21
Fibroadenomas of the Breast: Management

Case 1: A 25-year-old woman presents with a palpable breast mass. Ultrasound shows that it is a solid mass, and suspicion is high for fibroadenoma. What should happen next?
Recommendations: In my practice at the Mayo Clinic, I tend to have a low threshold, in most of these cases, for performing a biopsy confirming that this is truly a fibroadenoma. If the patient agrees, I perform an ultrasound-guided percutaneous needle biopsy, and in most cases, I leave a clip (tissue marker) to show where the biopsied lesion was located. If the pathology report shows fibroadenoma, I tell the patient that observation is a very good management approach. If the mass increases in size or if it is already relatively large (>2 cm), then I recommend excision. Therefore, if we ultrasound the mass 1 year later and find that it has increased by ≥1 cm, then I would lean toward excision just to rule out any abnormality. The diagnostic question at that point is whether the lesion is a phyllodes tumor.

Case 2: The patient above is diagnosed with a fibroadenoma. She is found to have multiple masses that are painful, especially during menses.
Recommendations: If 1 dominant lesion is causing most of the issues (this is usually the largest lesion), then I would consider excising that lesion. But, often, these women have multiple lesions, and we want to avoid excising 4 or 5 fibroadenomas from a single individual. Therefore, I recommend a good baseline ultrasound to determine the size of each lesion and treating the patient with oral pain medications or cold/warm compresses to provide symptomatic relief. Repeat the ultrasound at 1 year to ensure that none of the lesions is changing significantly.

Case 3: The patient presents with a cystic lesion of the breast.
Recommendations: Usually, aspiration is done on ultrasound-guided percutaneous needle biopsy so you can watch the simple cyst collapse. If the aspirated fluids are completely clear, we usually discard them. But, if there is anything about the cyst that does not look simple (any irregularities in its wall or does not completely collapse on aspiration), I tend to be a bit more concerned. Surgical excision is never a bad option for lesions that cause us concern, but we want to avoid overuse of this option. If the aspirated fluids are bloody and the lesion appears to be a completely simple cyst, then everything is most likely fine. I would probably send the bloody fluids to the cytology lab, but if that cytology comes back negative and the cyst completely disappears on aspiration, then I would not be concerned.
A young woman presents with a palpable breast mass, and ultrasound shows a solid mass. If the lesion is well circumscribed and has very smooth margins, then it is most likely a fibroadenoma. However, we should be suspicious of a phyllodes tumor when the ultrasound shows a complex lesion (poorly defined margins; shape lacks a smooth, oval contour). If the lesion has been stable for many years, then it is most likely a fibroadenoma. If it has been growing over time, you may want to consider surgical excision because the lesion is most likely a phyllodes tumor.

**Biopsy:** Percutaneous needle biopsy is our big friend in this situation. If pathology comes back as a fibroadenoma, then we are usually comfortable with the diagnosis. If the pathology comes back as a phyllodes tumor, then the patient needs to be surgically treated for the tumor. However, we commonly receive an “in-between” pathology report, such as a “fibroepithelial lesion,” which means that the pathologist needs more tissue.

**Treatment:** For phyllodes tumors, the mainstay of treatment is surgical excision with decent margins. Phyllodes tumors can be categorized as low-, intermediate-, or high-grade tumors. Others categorize them as benign, intermediate, or malignant phyllodes. For the malignant phyllodes, a 1-cm margin is needed at surgical excision. However, for any phyllodes tumor, you need a good 1-cm surgical margin with a nice sample of the normal tissue surrounding the tumor to ensure that the margins are widely free. The biggest issue with phyllodes tumors tends to be local recurrence within the breast. Therefore, the strongest component of treatment is good adequate surgery of this area. Depending on the size of the phyllodes tumor and the size of the breast, this can be achieved with a lumpectomy. But if the breast is small and the tumor is large, then a mastectomy may be required to excise the tumor with adequate margins.

**Axillary Lymph Nodes:** The axilla is not involved in the treatment scheme of phyllodes tumors. Neither nodal staging nor lymph node sampling are required at surgery.
Card 23
Pathologic Nipple Discharge

When a patient presents with nipple discharge, we must differentiate between benign and malignant discharge. The features of physiologic discharge are a bilateral discharge that occurs on manipulation of the breast, the fluid is often milky or greenish in color, and the discharge comes from multiple ducts within the nipple/areolar complex. The features of pathological discharge are that of a unilateral discharge that comes from a single duct; the fluid is either bloody or clear; and the discharge occurs spontaneously (without manipulation of the breast). Unfortunately, most patients do not fit 100% into either list.

**Ductoscopy:** A few years ago, we had a flurry of activity about ductoscopy for individuals presenting with nipple discharge. Some centers are still very interested in ductoscopy, but at Mayo Clinic where I practice, we have not used it very much. Some centers also use a ductogram in which dye is injected and imaging is performed. This is not a very accurate test.

**Recommended Workup:** For me, the standard workup of nipple discharge is (1) a good history, (2) a good physical examination, and (3) ultrasound particularly focused on the tissue in the subareolar region, looking for any dilated ducts and any growths within the ducts.

**Periductal Mastitis:** Periductal mastitis most commonly occurs in smokers, and it can occur in men. This is often a chronic and recurring problem. In the acute phase, when patients present with an abscess collection associated with their mastitis, we need to treat them with incision and drainage or, if it is small and early, oral antibiotics and percutaneous aspiration. The issue with periductal mastitis is that, even once the acute abscess or mastitis resolves, there are often chronic changes in that tissue underneath the nipple-areolar complex. Therefore, the recurrence rate from this process is very high. Patients often come back with repeated episodes of infection. In this situation, the ideal thing is to get everything to subside and then to operate in the elective setting to (1) resect the offending duct, which is essentially the central ductal system behind the nipple-areolar complex, and (2) excise those central ducts to remove the chronic tissue causing these recurrent episodes. This can often be done without removing the nipple, but in the worst cases, the nipple must be excised.

**Idiopathic Granulomatous Mastitis:** Idiopathic granulomatous mastitis is a somewhat similar but different condition. It tends to occur in younger women and is not associated with smoking. The diagnosis requires a percutaneous biopsy in which, typically, a noncaseating granuloma is seen on histology. In this disease, it is best to avoid surgical intervention, and treatment is challenging. Steroids are often effective. Sometimes, the mastitis will burn out over 6 to 12 months.
To manage patients with atypical ductal hyperplasia (ADH), I recommend that we consider 2 things. **Excisional Biopsy:** First, we must perform a surgical excisional biopsy to ensure that no malignancy exists in that area. In published retrospective series, the surgical excision rates show upstaging to malignancy in 15% to 20% of these cases. Therefore, the safest approach is to perform surgical excision anytime the core needle biopsy shows ADH. I believe that ADH and ductal carcinoma in situ (DCIS) are not very different from each other. ADH is essentially a very small extent of a lesion that, under the microscope, looks very similar to DCIS. Because there is significant potential for sampling error, the surgeon needs to excise more tissue for pathologists to examine under the microscope so they can decide whether this patient actually has DCIS, invasive cancer, or just ADH. **Annual Screening & Chemoprevention:** The second aspect of care is to counsel patients with ADH regarding their increased risk of breast cancer. Patients with ADH, as well as those with atypical lobular hyperplasia, have about a fourfold increased risk of breast cancer. Therefore, we must ensure that, annually, these patients have both screening mammograms and good clinical breast exams. We also need to discuss some chemopreventive medications with them, such as tamoxifen or raloxifene. **Chemoprevention:** In premenopausal patients with ADH, we mainly consider the use of tamoxifen for chemoprevention. In studies that monitored women with ADH for approximately 30 years after their biopsy, the risk of developing breast cancer ranged from 25% to 30%. The use of chemoprevention decreased this risk by 50%. In the P01 breast cancer prevention trial, chemoprevention was associated with an 86% reduction in breast cancer risk in the subgroup with atypia. In short, the chemopreventative options are very good. Often patients are reluctant to use chemoprevention because they do not have an actual diagnosis of breast cancer. Therefore, I recommend discussing the risks and benefits of chemoprevention with the patients. If the patient elects not to take the chemoprevention, or even if they do elect to take chemoprevention, they should be monitored closely with annual mammograms and clinical breast exams.
Card 25
Other Breast Pathologies: Papilloma, Sclerosing Adenosis, and Pleomorphic LCIS

After the biopsy of a breast lesion, the pathology report may come back with any number of findings, including papilloma with atypia, intraductal papilloma, sclerosing adenosis, and pleomorphic lobular carcinoma in situ (LCIS).

**Papilloma With Atypia:** Papilloma with atypia is similar to atypical ductal hyperplasia (ADH). Like ADH, we must perform an excisional biopsy of papilloma with atypia because the upstage rates range from 20% to 30%. On the pathology report, papillary lesions can range from being “just atypia” to an intraductal papillary carcinoma and invasive papillary carcinoma. Identifying these papillary lesions on a core needle biopsy is sometimes very challenging. Therefore, being able to remove the full lesion for evaluation under the microscope is important.

**Intraductal Papilloma:** A patient presents with a bloody nipple discharge that is diagnosed as intraductal papilloma. But on biopsy of the excised tissue, the pathology report that says “papilloma with atypia.” The lesson here is, although we usually think of intraductal papilloma as a benign lesion, it can harbor some atypia or there could be a malignancy associated with it.

**Sclerosing Adenosis:** After examining a breast biopsy specimen, the pathology report says “sclerosing adenosis.” I essentially classify sclerosing adenosis without any atypia as benign with no need for surgical excision. Although this is predominately a benign lesion, the patient should be monitored with annual screening mammograms.

**Pleomorphic LCIS:** Pleomorphic LCIS is a slightly newer term being seen on pathology reports of breast biopsy samples. Most people treat pleomorphic LCIS similarly to ductal carcinoma in situ (DCIS). Because pleomorphic LCIS is on the nasty end of the LCIS spectrum, it must be excised to negative margins, but staging of sentinel lymph nodes is not necessarily required.
A woman presents with a diffuse red, erythematous breast and what appears to be inflammatory nodes in her axilla. She is afebrile. Initially, the top 2 conditions on my list of differential diagnoses are mastitis of the breast and inflammatory breast cancer (IBC).  
**Mastitis:** Taking a good history and performing a good examination are important. I would consider an infective process when the patient reports having fevers and redness, the breast presents with something that looks like an abscess or a mastitis, and the patient has a history of recent lactation or injury to the breast. In that situation, I would treat with oral antibiotics. I think it would be reasonable to consider an ultrasound examination for any underlying abscess cavity, especially for larger breasts in which I am not always able to detect the underlying abscess cavity on the physical examination alone. If the ultrasound identifies a fluid collection, then I have a clear-cut answer.  
**Inflammatory Breast Cancer:** The bigger question is “How do you not miss IBC?” Sometimes when we see IBC, the patient has been on antibiotics for 1 to 2 weeks and the redness has not subsided. The affected breast appears to be diffusely enlarged (rather than focally enlarged), and its skin is thickened (orange peel phenomenon). I often see a line where the bra has indented the skin, which is not seen on the contralateral side. The best tests are mammogram and ultrasound followed by core needle biopsy of any underlying solid mass within the breast. Punch biopsy of the skin can help diagnose IBC. If we see diffuse skin changes and the skin biopsy shows changes consistent with IBC, then that would be another indication to consider an MRI to evaluate for any underlying lesions if you are unable to see them on the mammogram or ultrasound.  
**Treatment:** To treat IBC, first administer neoadjuvant chemotherapy. After the patient completes chemotherapy, then a straightforward old-fashioned modified radical mastectomy with primary closure of the skin is needed. The patient completes the treatment with postmastectomy radiation therapy. A lymph node dissection should be performed — there is really no role for sentinel lymph node biopsy in these patients.
Role of Neoadjuvant Chemotherapy in Breast Cancer

Neoadjuvant chemotherapy is increasingly being used in the treatment of breast cancers of all size and stages. It has 2 main roles in the treatment of breast cancer. (1) One role is to take the patient with inoperable disease, such as inflammatory breast cancer, and make her a candidate for mastectomy. (2) The next role is to take patients with operable disease (such as a resectable 5-cm tumor that requires a mastectomy) and shrinking the tumor to the point where breast conservation may be considered.

**Evaluating Tumor Response:** Increasingly, we are administering chemotherapy in the neoadjuvant setting to evaluate the tumor’s response to chemotherapy. The old approach required that we excise all of the disease, make the patient disease-free, and then give them chemotherapy. But with this approach, we never really knew how the chemotherapy affected the tumor. So today, if a patient will definitely require chemotherapy after surgery, we are asking whether we should administer chemotherapy before surgery. Obviously, for patients with a 1-cm node-negative tumor that is positive for both estrogen and progesterone receptors, neoadjuvant chemotherapy is not used. But for a triple negative tumor or a HER2-positive tumor in a very young lady with node-positive disease, administering chemotherapy before surgery is very reasonable.

**Survival Benefit:** We have not clearly shown a survival advantage from the use of neoadjuvant chemotherapy, but neither have we shown any survival disadvantage. Currently, it appears that the survival rates are similar for neoadjuvant chemotherapy and non-neoadjuvant chemotherapies. However, when we look at those patients with the most aggressive tumor types, such as triple negative disease, neoadjuvant therapy may shrink the disease in some cases to the point that there is no disease remaining by the time they get to surgery. These patients have better survival rates than do those patients who have significant residual disease at surgery. Therefore, if we can tailor the therapy and get the right drugs on board in the neoadjuvant setting, I believe we will eventually be able to see improved survival rates with neoadjuvant therapy.
Card 28
Whole-Breast Radiation Versus Partial-Breast Radiation

Whole-breast radiation is our conventional 6-week course of radiation that we give Mondays through Fridays for patients with breast cancer after they have undergone a lumpectomy. Many centers around the country offer it. The issue with this treatment is that women are unable to come to the radiation facility Mondays through Fridays for 6 weeks for their radiation therapy. As a result, many women are not following through with the recommended adjuvant radiation therapy. This fact has prompted us to find alternatives.

**Partial-Breast Radiation:** After lumpectomy, the cancer tends to come back in the region around the lumpectomy cavity, which we classify as “tumor-bed recurrences.” The incidence of having a new tumor that comes back in a different quadrant of the breast is reasonably low. With this knowledge, we began to investigate the efficacy of partial-breast radiation, which delivers radiation only to the area of the lumpectomy cavity and not to other portions of the breast. By radiating the smaller area, we are able to deliver the radiation over a shorter time — sometimes only a 1-week course of radiation therapy is required.

**Delivery:** Partial-breast radiation can be delivered in several different ways. One method is with external beam radiation, which is a very good approach. The other way to deliver partial-breast radiation is via intracavitary radiation. This requires placement of a balloon or some kind of brachytherapy catheter into the lumpectomy bed and then delivering the radiation to the area around the lumpectomy bed from within. Studies that evaluate partial-breast radiation may include external beam radiation, intracavitary radiation, or both of these modalities.

**Guidelines:** Currently, 3 different sets of guidelines for the use of partial-breast versus whole-breast radiation have been published by 3 different groups, including The American Brachytherapy Society, the American Society of Breast Surgeons, and the American Society of Radiation Oncology. These various sets of guidelines have many similarities and just a few differences.

**Main Indications:** Partial-breast radiation tends to be the standard approach. It is indicated for elderly ladies with small node-negative breast tumors. This newer technique should not be used in a 31-year-old woman with a 5-cm breast tumor. When deciding between whole-breast versus partial-breast radiation, I tend to look at patient age (partial-breast radiation indicated in those aged >50 or >60 years). I also will consider partial-breast radiation in invasive ductal tumors because we tend to know exactly where these tumors start and stop. However, I would not recommend it for invasive lobular tumors or for pure ductal carcinoma in situ. Partial-breast radiation may also be considered for smaller tumors (usually a T1 tumor <2 cm in size) with negative margins and negative lymph nodes.
Axillary Lymph Node Sampling: The Dual-Tracer Technique

Most patients who undergo a lumpectomy for a breast lesion will also undergo some kind of axillary lymph node sampling. In early breast cancer, the status of the axillary nodes is a major prognostic factor. In addition, staging with sentinel lymph node biopsy (SLNB) can provide important information needed to help tailor treatment.

**Dual-Tracer Method:** I practice at Mayo Clinic in Rochester, Minnesota, and my approach to doing SLNB is to use a dual-tracer method. Most papers published in the literature demonstrate that the identification rate is higher and the false-negative rate is lower if 2 tracers are used. Therefore, for my lumpectomy patients, I tend to use both a radiolabeled colloid and a blue dye.

**Radiotracer:** For SLNB, the injected Tc-99m–labeled colloid enters the lymphatic system and is engulfed by histiomonocytic cells of the sentinel node. As a result, the sentinel node can be visualized before surgery using a gamma camera or during surgery using a handheld gamma-ray probe. The radiolabeled colloid is injected either the day before or the morning of surgery.

**Blue Dye:** The blue dye is generally injected in the operating room once the patient is asleep. For the blue dye, some surgeons elect to use Lymphazurin™ 1% (isosulfan blue dye), and others elect to use methylene blue. In Europe, the blue dye of choice tends to be Patent Blue V dye (sodium salt). These dyes work by binding weakly to interstitial proteins (mostly albumin) as they pass slowly through the sentinel node. It should be noted that there is a risk of allergic reactions to blue dye. Regardless, I find that this 2-tracer technique is the best modality for performing SLNB.
Axillary Lymph Node Dissection: Impact of ACOSOG Z0011 Trial

The American College of Surgeons (ACOSOG) Z0011 trial (also called the Z11 trial) concluded that axillary lymph node dissection may be omitted for select women undergoing breast conserving treatment and having only 1 or 2 positive axillary sentinel lymph nodes (SLNs). This study probably instigated more debates on breast surgery than any other study I have encountered in my career. This great study has been critiqued, criticized, and pulled apart several times because it was closed early and did not meet the predefined goal in terms of the number of patients the researchers were planning to accrue. However, because researchers were seeing a highly significant reduction in the event rate in all patients included in the study, they believed that leaving the study open for many more years would not have demonstrated any significant differences in the results seen to date.

Results: The Z11 trial opened the door for breast surgeons to consider omitting an axillary lymph node dissection for those patients who meet the specific criteria of Z11. These criteria include patients with a T1 or T2 tumor (size <5 cm) who were clinically node-negative by physical examination of the axilla, did not receive any neoadjuvant chemotherapy, had estrogen-receptor–positive disease, underwent a successfully completed lumpectomy with negative margins, and had 1 or 2 positive SLNs at the time of SLN biopsy. Essentially, the local recurrence rate and the 5-year overall survival were not significantly different for patients who underwent dissection of only the SLNs versus patients who underwent a completion axillary lymph node dissection.

Impact on My Practice: For patients in my practice who meet the criteria for the Z11 study, I definitely discuss the potential for not having an actual lymph node dissection and for conserving their axillae if only 1 or 2 SLNs are positive. I am more likely to consider axillary dissection for the 30-year-old patient, for triple negative tumors, for ≥3 positive lymph nodes, or for mastectomy patients.
Lymphedema: Prevention and Treatment

Lymphedema is one of the complications of axillary lymph node dissection and sentinel lymph node biopsy (SLNB) that concerns most surgeons and patients. The risk of lymphedema ranges from 7% to 8% with SLNB and is approximately 25% with an axillary lymph node dissection. The risk can be as high as 35% when axillary dissection is performed in women with node-positive disease who also undergo radiation therapy.

**Prevention:** There are some myths regarding the prevention of lymphedema. In general, I tend to recommend that patients try to minimize the risk of any injury to the involved extremity. I definitely do not want my patients to stop living life. Therefore, if they are gardeners and they want to get outside, I say “Go tend your roses, but wear a protective glove.” All patients should take the precautions needed to prevent any kind of injury that could introduce bacteria or infection through the skin and cause a flare-up of the underlying lymphedema. For all our Mayo Clinic patients scheduled for axillary dissection, we first have them see a physical medicine and rehabilitation physician for guidance regarding lymphedema prevention.

**The Question of Compression:** There has been a lot of debate regarding the use of compression sleeves. Should you wear them every time you fly versus only wearing a compression garment if there is evidence of lymphedema? In my experience, I am not sure whether the prophylactic compression garments are truly helpful.

**Therapy:** I believe that the most helpful approach is patient education, early recognition, and early therapy in the event that lymphedema should develop. Therapy for lymphedema is generally manual drainage with massage and physical therapy and the use of compression garments. I do not have much experience with upper extremity lymphedema pumps. A relatively new procedure that I am seeing a bit more of is the reanastomosis of some lymphatic vessels, although I still have little experience with this procedure.
Card 32
Genetic Testing and Counseling for Breast Cancer

Approximately 10% of all breast cancers have some genetic component. As more women become aware of their family history, more are becoming interested in genetic counseling.

**Indications for Genetic Testing:** When deciding if I should refer a patient for genetic counseling and testing, I tend to consider several factors. First, the patient’s age at diagnosis is important. Next, the number of family members who have a history of breast cancer, ovarian cancer, or other cancers is another important risk factor. The number of first-degree relatives with a cancer history really grabs my attention. For example, the patient whose family history shows that 1 of 8 sisters developed breast cancer is very different from the patient who has only 1 sister who has not developed breast cancer. For male breast cancer, a strong indication for genetic testing is a family history in which a male family member has had breast cancer. Finally, two other important factors include Ashkenazic Jewish descent and whether anyone in the family has undergone genetic testing for breast cancer.

**Genetic Testing Panel:** Most genetic testing for the BRCA genes is done through a single laboratory, Myriad Genetics, Inc, although this may be changing soon. Therefore, regardless of whether you get tested in 1 cancer center versus another cancer center or in 1 state versus another state, the tests will be sent to a single central laboratory. There is a slight variation in the depth of the panels that they perform at Myriad. They offer BRACAnalysis®, which is the standard test for the BRCA1 and the BRCA2 genes. For patients who test negative for BRCA1 and BRCA2, there is the BRACAnalysis Large Rearrangement Test (BART™) to look for genomic rearrangements in BRCA1 and BRCA2 that are not detected on BRACAnalysis. As more research is done to investigate genetic predispositions to breast cancer and other malignancies, I am sure that more and more potential genetic mutations will be identified and eventually added to the genetic testing panel.

**Triple Negative Breast Cancer:** In the last 2 years, we have seen a heightened awareness of patients with triple negative breast cancer. If you see a patient who is in her 40s and has a tumor that is triple negative, you may want to consider genetic testing because BRCA1 carriers tend to have a much higher rate of triple negative tumors.
Two Big Lessons: Percutaneous Biopsy and Excisional Specimens

Percutaneous Biopsy: The big campaign among breast surgeons is to convince all of us that the practice of excisional biopsy should be highly limited and percutaneous needle biopsy should always be the first consideration. Previously, a patient with a palpable lump would have it excised for pathologic evaluation. If cancer was present, the patient returned for a mastectomy or nodal staging in a second operation. Instead, we now know that, for anything seen on mammogram, ultrasound, or MRI, percutaneous needle biopsy should be performed before we rush to the operating room. The information gained from percutaneous biopsy leaves us much better informed, even to the point of having our patients aware of the need for nodal staging before going to surgery. The information gleaned from biopsy means that the procedure itself can be planned, anticipating the need to obtain negative margins. The data show that performing margin-negative excision and nodal staging in a single operation (instead of two separate operations) results in higher rates of achieving negative margins and getting the whole procedure done.

Excisional Tissue Specimens: Anytime you remove breast tissue, always orient your specimens, even if you are 100% certain the lesion is a fibroadenoma. If the initial diagnosis was benign, but the specimen shows cancer with a positive margin knowing mass orientation is imperative for further treatment. If the specimen has not been marked for orientation, re-excision must include a 360° margin around the lumpectomy cavity.
The Breast Imaging Reporting and Data System (BI-RADS) sorts mammogram findings into categories numbered 0 through 6, allowing the breast imager an accurate and consistent way to communicate the results of the mammogram or other breast imaging to us. This system provides us with an accepted lexicon of terms regarding what the imagers are observing on the studies, which are then correlated with specific recommendations about what follow-up or responses are appropriate for lesions in each BI-RADS category. I adhere very closely to the recommendations in the BI-RADS system. For example, if the patient has a BI-RADS 4 (an “indeterminate finding”), then a biopsy is indicated. If the lesion is found to be benign on biopsy, then the patient can then be followed up without any treatment other than a biopsy.

**Biopsy of Nonpalpable Masses:** In general there are three ways to biopsy a nonpalpable breast lesion that is detected on mammography, breast MRI, or ultrasound (US). The easiest biopsy technique is a freehand US-guided biopsy, which is the fall-back position for most practitioners who do image-directed biopsies. If a mass is seen on a mammogram, then the next usual step is to get an US. If the mass can be seen on US, then typically either an US-guided core biopsy or an US-guided vacuum-assisted core biopsy is performed, which essentially uses a cannula that is similar in size to an 18F Foley catheter. Therefore, a 0.5 cm skin incision must be made to perform the biopsy, and local anesthesia is essential for this procedures. The type of anesthesia used depends on the preferences of the individual doing the biopsy. Under US guidance, we can watch our needle and inject local anesthesia around the tumor as well as the skin and the track we take to reach the tumor. In addition, US guidance shows us which way the local anesthetic displaces the area to be biopsied. We avoid epinephrine in our local anesthetic because it has been associated with skin necrosis, so our standard practice is to use 1% lidocaine without epinephrine. A stereotactic core needle biopsy is much more complicated in terms of injecting the local anesthetic and visualizing how things are displaced at the biopsy site. Generally, we inject anesthetic in the skin and then along the track toward the lesion when performing a stereotactic core needle biopsy.
After performing a biopsy of a nonpalpable mass in the breast, several pathologic findings can be problematic for the surgeon. In general, there are regional variations in how biopsies that demonstrate some of these findings are to be followed up, but the approach to atypical ductal hyperplasia (ADH) is fairly straightforward.

**ADH:** When the pathologic diagnosis is ADH, we know that this patient has a significant likelihood of having a malignancy adjacent to the biopsy site. When a core biopsy demonstrates ADH, the standard practice is to remove that area via an excisional biopsy, usually in the form of a needle localized lumpectomy.

**LCIS:** When a core biopsy demonstrates lobular carcinoma in situ (LCIS), the risk of an adjacent malignancy ranges from 3% to 15%. Pleomorphic LCIS is a subtype of LCIS that is known to be more aggressive and, thus, presents a higher risk of malignancy, but this is a fairly rare finding. For most other subtypes of LCIS, we typically see LCIS (rather than malignancy) in tissue adjacent to the area that was biopsied. Remember, LCIS generally has no imaging findings. Instead, it is usually an incidental finding seen on a biopsy done for other reasons. For example, a patient with calcifications in the breast undergoes mammography, and the findings are classified as BI-RADS 4 (indeterminate, needs biopsy). So, we perform a stereotactic core biopsy of those calcifications, and, on final pathology, we get two results: (1) the calcifications are present in benign breast tissue, and (2) LCIS was found incidentally. What did we learn from this biopsy? First, we answered the question regarding the source of the BI-RADS 4 calcifications: the calcifications were seen in benign breast tissue. Second, we learned that the patient also has LCIS, so they have a high risk for eventually developing breast cancer, meaning that careful follow-up is warranted.
Case: A patient with a red breast is referred to the surgeon. How should we manage this patient?

Clinical Presentation: The patient with a red breast is generally referred to the surgeon because there is a concern for inflammatory breast cancer (IBC). The red breast is associated with several different conditions, and only a few patients with a red breast have IBC. Nonetheless, we want to rule out IBC, which is generally a clinical diagnosis.

Clinical Features: When we see a patient with a red breast, the classic finding associated with IBC is “peau d’orange,” which is lymphedema in the skin. Unfortunately, other conditions can also cause peau d’orange, but we generally suspect either IBC or a rip-roaring cellulitis with these skin changes. When cellulitis is the cause of a red breast, the breast is generally painful and the patient is febrile and feels ill because they are toxic from an infection. With cellulitis, the physical exam often shows a fluctuating area, the entire breast is usually not red, and there is usually less dermal inflammation than is seen with IBC. In contrast, patients with IBC generally feel normal: are afebrile, and have a painless breast with generalized redness.

Imaging: On routine imaging of a patient with IBC, the primary tumor is not always found. However, with our augmented imaging abilities through MRI and breast-specific gamma imaging, we are now finding the primary tumor with increasing frequency.

Skin Biopsies: Some people perform skin biopsies in the hopes of finding dermal lymphatic plugging, which is pathognomonic for IBC. However, most often, this is not found, and we must return to making the diagnosis based on clinical findings.

Workup of the Red Breast: After physical examination, the next step is to order imaging. An ultrasound (US) is usually the best choice, especially if an infection is suspected because the patient will not be able to tolerate the compression of a mammogram. The other benefit of an US is, if an abscess is found, then needle drainage of that abscess is the first step in the treatment, both for therapeutic purposes and to obtain fluid for culture to select the best antibiotic therapy for concomitant treatment.
Mondor disease is the thrombophlebitis of a vein that enters the breast either anteriorly from the abdominal wall or laterally from the axilla. It is quite painful. Sometimes there is erythema, but it is localized over the thrombosed vein, unlike inflammatory breast cancer in which the erythema is more generalized. The etiology of Mondor disease is varied, but it usually is associated with an infectious cause, but the infection is generally a low-grade underlying occult inflammation of which the patient may or may not be aware. Unfortunately, Mondor disease can sometimes be precipitated by an occult malignancy, which we must keep in mind when we see a patient with Mondor disease.

**Presentation and Clinical Findings:** Most typically, these patients present with an acute onset of localized breast pain. Because the affected vein is just beneath the skin, we can see a tubular structure just underneath the skin of the breast, and we can feel a tender tubular structure either coming up from the mid-axillary line on the abdomen or laterally from the axilla.

**Treatment:** Treatment is with NSAIDs and time. There is no reason to treat with antibiotics because the cause is thrombophlebitis and not a bacterial infection. However, we also want to ensure that the patient gets good routine cancer screening, like a mammogram, to make sure that there is no obvious malignancy in the breast. But, looking for a mammographically occult lesion is probably not warranted in a patient with Mondor disease. Ordering an ultrasound can be reassuring because, on it, the thrombosed vein is visible and everyone feels good about the diagnosis. Remember, when these patients present to us, they are quite alarmed and their primary care doctor is uncertain about the diagnosis. Therefore, giving them a definitive diagnosis and telling them it is a benign condition can make everyone happy.
In general, 5% to 10% of breast cancers are due to an inherited genetic predisposition to develop breast cancer. Although a number of different genetic mutations are associated with breast cancer, we do not have a clinical test for all of them. But we can test for the \textit{BRCA1} or \textit{BRCA2} mutations, and they are among the most common mutations we detect at this time. Once we have tests available for the other associated genetic mutations, we may find that >10% of breast cancers are inheritable.

\textbf{BRCA Genes:} \textit{BRCA1} and \textit{BRCA2} genes are tumor suppressor genes, and a mutation in either one is associated with a high lifetime risk for developing both breast and ovarian cancer. The difference between these two genes is just the site of the mutation on the chromosome.

\textbf{Indications for Genetic Testing:} When a woman requests genetic testing, we must first look at her family history. Genetic testing is strongly indicated for women who have (1) two first-degree relatives diagnosed with breast cancer at <50 years of age; (2) three or more first- or second-degree relatives diagnosed with breast cancer at any age; (3) a combination of first- and second-degree relatives diagnosed with breast cancer and ovarian cancer; (4) a first-degree relative who has had bilateral breast cancer; (5) a family history of both breast and ovarian cancer, especially in the same patient, and (6) a male relative who has had breast cancer. Men and women of Ashkenazic Jewish ancestry are at a higher risk of harboring a \textit{BRCA1} or \textit{BRCA2} mutation, so genetic testing is strongly indicated for these women who have (1) a first-degree relative with breast or ovarian cancer or (2) two paternal or two maternal second-degree relatives with breast or ovarian cancer.

\textbf{Testing/Referral:} At our hospital, we refer patients who want/need genetic testing to our High-Risk Breast and Ovarian Cancer Program where they will meet with a genetic counselor and people who specialize in mitigating breast cancer and ovarian cancer risk. If you do not have access to such a program, I recommend that you refer patients to a genetic counselor rather than directly submitting the test and then interpreting the results yourself. In the United States, only one company provides genetic testing for \textit{BRCA1} and \textit{BRCA2}, but they do not offer any counseling. Certified genetic counselors devote their careers to determining if a patient should undergo testing and, more importantly, to interpreting those test results, which is quite complicated. Obviously, a genetic counselor is not be available in all practice settings, which means the surgeon may have to learn about genetic testing and the interpretation of those results so they can appropriately counsel the patient.
Watching the literature, we can see that tests are now available to help us predict breast cancer recurrence, which, in general, is known as “molecular testing for prognostication.” Two tests are clinically approved to help predict the risk of breast cancer recurrence, and these tests are performed on paraffin-embedded tissue. The Oncotype DX® is a 21-gene array for testing patients with early stage estrogen-receptor-positive (ER+) breast cancer. The second test is MammaPrint®, which was once a 50-gene array and is now a 70-gene array. Both have been shown to be more accurate than any other prognostication technique currently available for predicting the risk of systemic failure during the 10 years following initial treatment.

**Testing vs Therapy:** These two tests have changed the way that adjuvant treatment is recommended. Previously in the United States, adjuvant chemotherapy was recommended for all relatively healthy women diagnosed with breast cancer who had a tumor >1.0 cm in size. However, with the use of these two molecular tests, we can now subdivide these women into one of three groups: low-risk, intermediate-risk, or high-risk of systemic failure. We have also learned that giving adjuvant chemotherapy to women with low to intermediate risk did not appear to change their prognosis. For these women, the prognosis is good while receiving hormonal therapy (tamoxifen or Arimidex®), and the added benefit of adjuvant chemotherapy is very small. However, adjuvant chemotherapy is efficacious for women in the highest risk group. Therefore, these molecular tests have given us the ability to stratify the recurrence risk, resulting in far fewer women receiving adjuvant chemotherapy compared to our previous protocols.
Bilateral Prophylactic Mastectomies: Risk Reduction

The prophylactic mastectomy rate is increasing among women at high risk for developing breast cancer. Traditionally, a “prophylactic mastectomy” has referred to a contralateral prophylactic mastectomy when a patient with breast cancer on one side elected to undergo a bilateral mastectomy. According to the Surveillance, Epidemiology and End Results (SEER) data, the rate of this type of prophylactic mastectomy has increased substantially during the past 10 years.

Risk-Reducing Bilateral Mastectomy: As our abilities to perform breast reconstruction have improved, we have seen an increasing number of women who are undergoing pure risk-reducing bilateral mastectomies. For example, a high-risk patient without breast cancer, such as one who carries the BRCA1 or BRCA2 mutation, elects to undergo a bilateral mastectomy. Carriers of the BRCA1 or BRCA2 mutation have a lifetime risk of breast cancer that ranges from 60% to 80% (average lifetime risk for women without the mutation, about 12%). Ideally, if these very-high-risk patients are going to consider surgery, they should undergo a bilateral prophylactic surgery before developing breast cancer. The level of risk reduction achieved by performing a bilateral prophylactic mastectomy is about 95%. Therefore, after surgery, the risk of developing breast cancer is not zero for that patient, but it approaches zero. For example, if the woman has an 80% lifetime risk of developing breast cancer before surgery, then the postoperative risk is reduced to about 2%.

The Decision: Deciding to undergo a prophylactic bilateral mastectomy is a very complex and personal decision. Ideally, it would be based only on a risk assessment. Certainly women with a lifetime risk of 60% to 80% should at least be apprised of this option and, it is not surprising that some choose to undergo bilateral risk-reducing mastectomies. But many patients with a lesser degree of lifetime risk also elect this option. At the end of the day, this option is available for women to reduce their risk, but the threshold for the level of risk reduction achieved before electing this surgery is for the patient to decide, not the surgeon. Therefore, this is often an emotional decision as well as a medical decision.
Card 41
Bilateral Prophylactic Mastectomies: Technique

Risk-reducing bilateral prophylactic mastectomies are performed on high-risk patients who do not have breast cancer. The primary goal of this surgery is to reduce the patient’s risk of developing breast cancer. To achieve this, we need to remove almost all the breast tissue. This can be done in one of three ways: (1) a simple mastectomy removing the nipple and much of the breast skin; (2) a skin-sparing mastectomy removing the nipple but preserving most of the breast’s natural skin envelope; and (3) a total skin-sparing mastectomy, also known as a nipple-sparing mastectomy.

Nipple-Sparing Mastectomy: Because the nipple remains after nipple-sparing mastectomy, there are concerns about diminished risk reduction because a little more breast tissue stays with the patient compared to the other procedures. However, preliminary studies demonstrate that the post-op risk for developing breast cancer in those who undergo nipple-sparing mastectomy are similar to the post-op risk of those undergoing skin-sparing mastectomy. Admittedly, these data are preliminary (follow-ups are <5 years). In experienced hands, a total nipple-sparing mastectomy will give the best cosmetic appearance, but the nipple is likely to have a loss of sensation, a less-than-ideal position, and, as the result of some nipple necrosis, a change in color and shape. While the level of risk reduction is comparatively small when the nipple is spared during the surgery, this type of surgery still substantially reduces the lifetime risk and gives the patient the best cosmetic appearance. Nonetheless, nipple-sparing mastectomy is not an option for all patients, especially for those with very large breasts or significant breast ptosis.

Reconstruction: When doing a nipple-sparing or skin-sparing mastectomy, immediate reconstruction is also performed. If the patient does not intend to undergo reconstruction, then we perform a routine simple mastectomy so that the postoperative appearance of the chest is relatively flat. Therefore, if the woman chooses to, she can easily be fitted with a breast prosthesis.
Card 42
Brachytherapy

Brachytherapy provides radiation to the breast from within the breast to reduce the risk of breast cancer recurrence. Its primary benefit is that it delivers the needed radiation in a much shorter time than does telotherapy (external beam radiation therapy). Brachytherapy is for patients undergoing breast-conserving therapy (lumpectomy plus an axillary procedure combined with radiation therapy) and is not for those needing postmastectomy radiation therapy.

Procedure: During brachytherapy, a balloon catheter is placed through the skin into the biopsy cavity. The balloon ensures that the walls of the biopsy site conform to a spherical shape, which can be used for treatment planning, and affixes the catheter in place. Then a radiation source, usually a small radioactive seed, is placed into the balloon either as a single source or through multiple tracks through different positions in the balloon. This is done twice daily for 5 days. When radiation is provided in this manner, the radiation dose at the balloon-breast tissue interface is quite high, which can be associated with fat necrosis that eventually (over many years) results in the development of a mass in the breast. Because of this, these patients are followed up with regular physical exams to ensure that no breast mass is developing. Newer devices that have multiple catheters within the balloon catheter now allow the radiation oncologist to do better treatment planning, thus reducing the surface dose and, hopefully, reducing the incidence of fat necrosis.

Intraoperative Radiation Therapy: Probably the newest thing in brachytherapy is intraoperative radiation therapy. After lumpectomy and while the wound is open, the radiation therapy device is placed within the lumpectomy cavity, treatment planning is done, the patient is treated, the skin is closed, and they are done. With an experienced team and the right device, the whole thing is accomplished within 30 minutes. Patients prefer this one-time intraoperative radiation therapy rather than the protocol associated with whole-breast radiation therapy (5 days/week for 6.5 weeks).

Indications: In our practice, about 5% to 8% of our patients were receiving brachytherapy, and then within a 3-year span, we saw significant fat necrosis and became less eager to provide this treatment. However, in the past year, we have once again been providing brachytherapy to about 5% to 8% of our patients. The American College of Radiation Therapy has guidelines for selecting patients for brachytherapy. In general, brachytherapy is not recommended for younger patients with larger tumors or a significant intraductal component. However, it is recommended for older patients with a relatively small tumor and a small intraductal component. In properly selected patients, the breast cancer recurrence rate is similar for brachytherapy and whole-breast radiation therapy.
Primary Occult Breast Cancer: Diagnosis and Treatment

A patient who presents with a clinically enlarged axillary lymph node and no obvious breast lesion on physical exam and routine breast imaging is said to have a primary occult breast cancer. Because breast imaging has improved significantly during the past 15 years, we are now often able to find the primary tumor within the breast on follow-up imaging. Therefore, for a patient who presents with a normal mammogram and an obvious palpable tumor or enlarged lymph node underneath the arm that demonstrates adenocarcinoma on biopsy, I recommend that we first make sure that their mammogram is up-to-date. If it is, review it closely: make sure there is no obvious tumor. Next, order a breast MRI, which will usually demonstrate the lesion within the breast. If so, then the patient can undergo an MRI-directed US to look specifically at the involved area of the breast to determine if the tumor can be seen on US. If so, then the patient undergoes an US-guided core biopsy of that area. However, if the MRI does not demonstrate a lesion or demonstrates a lesion that cannot be seen on US, then the patient can undergo an MRI-guided biopsy of the breast. But if the MRI shows absolutely nothing, then we must order breast-specific gamma imaging, which is a sestamibi scan of the breast that is approved for clinical use. The resolution of this scan is thought to be <1.0 cm in size. This nuclear medicine study is a completely different method of screening for cancer within the breast than is an MRI, x-ray, or US study. Because we have all these different modalities that look for different physical characteristics of the tumor, we are almost always able to find the primary tumor in the breast.

True Primary Occult Breast Cancer: There will always be a few true cases of primary occult breast cancer. For these cases, we generally do not go on any exhaustive process beyond the breast imaging rubric mentioned above. Instead, because the patient has known axillary disease, we assume that they have breast cancer for which three treatment options are available. (1) We can perform a modified radical mastectomy during which we remove that breast and the axilla. (2) We can perform breast preservation during which the patient undergoes an axillary dissection followed by routine whole-breast radiation therapy with or without axillary radiation, depending on the number of involved lymph nodes identified in the axillary specimen. (3) We can give the patient neoadjuvant chemotherapy followed by either breast preservation or a mastectomy with radiation therapy.