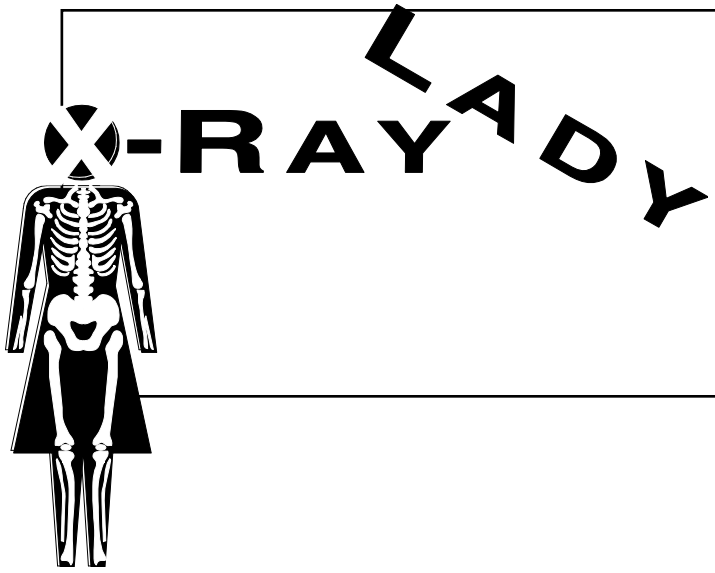


Fleitz Continuing Education
Jeana Fleitz, M.E.D., RT(R)(M)
"The X-Ray Lady"
6511 Glenridge Park Place, Suite 6
Louisville, KY 40222
Telephone (502) 425-0651
Fax (502) 327-7921
Website www.x-raylady.com
Email address xrayladyce@gmail.com

Imaging Male Breast Cancer

Approved for 6 Category A CE Credit

Please contact our office for course approval status.

A Continuing Education Course for Radiation Operators

Course Directions

Completing an X-Ray Lady® homestudy course is easy, convenient, and can be done from the comfort of your own couch. To complete this course read the reference corresponding to your posttest and answer the questions. If you have difficulty in answering any question, refer back to the reference. The test questions correspond with the reading and can be answered as you read through the text.

How Do I Submit my Answers?

- **Transfer** your answers to the blank answer sheet provided and fill out your information. Make a copy of your answer sheet for your records
- **Interactive Testing Center:** Get your score and download certificate immediately! Sign up on our website by clicking on the "Online Testing" tab or contact our office.
- **Online Answer Sheet:** Visit our website and click on the "Online Testing" tab. Answer sheets will be graded in-office daily and certificates emailed within 1-2 business days.
- **Snail Mail:** Mail a copy to X-Ray Lady, 6511 Glenridge Park Place Suite 6, Louisville, KY 40222. Allow up to 10 days turnaround time.
- **Fax:** If your license expiration date is within 2 weeks of submitting your answers, fax a copy to (502) 327-7921. Please be sure to verify that we received your answer sheet.

Certificate Issuance

Your certificate will be scored the same day or next business day. You must score at least a 75% to pass the course. The Interactive Testing Center generates your certificate upon successful completion—please print and save your certificate for your records. If you mail, email, or fax your answer sheet certificates will be emailed unless otherwise noted. Allow five to seven business days for mailed certificates.

Reporting Completed Credit

Verification of awarded continuing education will be submitted to the radiation control boards of Florida and Kentucky. For the ARRT and all other state licensure agencies, please self-report your earned credits.

X-Ray Lady CE®
Jeana Fleitz, M.Ed., RT(R)(M)
6511 Glenridge Park Place, Suite 6 Louisville, KY 40222
Phone: (502) 425-0651 | Email: xrayladyce@gmail.com
Website: www.x-raylady.com

X-Ray Lady® Refund & Exchange Policy

Updated March 2015

By placing an order and/or completing a course with X-Ray Lady®, you agree to our refund & exchange policy. The following applies if you **do not want your course and have no plans of completing it for credit**:

Returns or exchanges on unused materials may be made up to **30 days** from the original order date. After 30 days, customers may receive a credit to use toward future purchases. Credits expire one year from issue date. All refunds and exchanges are subject to a $5 re-stocking fee per course. Refunds will be issued in the same tender as the original order. Materials purchased with a check will be refunded with a cashier's check once payment has cleared.

Expiring Courses
Due to the nature of our courses, no refunds or exchanges are issued for courses expiring within one month of the course approval end date.

Courses via USPS
No refunds or credits are made for shipping and handling charges once the course has shipped to you. Customer is responsible for all shipping charges to return or exchange course materials. Refunds and exchanges are issued when the materials are received and determined to be in excellent condition. X-Ray Lady® claims no responsibility for any goods lost or stolen in transit or delivery by the U.S. postal service.

eBook Courses
No refunds will be issued once the materials have been sent. Customers wishing to return an unwanted eBook will have 30 days from the original order date to receive a credit towards a future purchase minus a $5 processing fee. You cannot order a "test only" at a later date for an eBook that you have received a credit for.

We do not "buy back" used books. If you return your used materials you will not receive a credit and the materials will be discarded. Requests for lost or deleted eBook links after course completion will be fulfilled up to 6 months after the course completion date.

X-Ray Lady CE®
Jeana Fleitz, M.Ed., RT(R)(M)
6511 Glenridge Park Place, Suite 6 Louisville, KY 40222
Phone: (502) 425-0651 | Email: xrayladyce@gmail.com
Website: www.x-raylady.com

Earning CE Credit

This activity may be available in multiple formats or from different sponsors. Continuing education credit can be awarded only once for the same activity in the same or any subsequent biennium.

This course has been evaluated and approved for a specified amount of continuing education by the agencies listed on the course cover. X-Ray Lady CE® does not imply or guarantee that completion of this course automatically ensures renewal or initial issuance of any state, national, or federal x-ray certification or licensure requirements.

It is the responsibility of the individual completing this course to understand and to comply with state, national, and federal x-ray certification and licensure regulations regarding initial and continuing requirements. Further, X-Ray Lady CE® claims no responsibility for determining if the topic or amount of continuing education credit is appropriate for the person completing the course.

The field of medical imaging and medicine is ever changing. Readers are advised to check the most current product information provided by equipment and supply manufacturers. X-Ray Lady CE® does not assume any liability for any injury and/or damage to persons or property arising from information contained in this course. The information contained in this course should not be used for medical diagnosis or treatment. Users of this information are encouraged to contact their physician or health care provider for any health related concerns. The X-Ray Lady CE® is neither responsible nor liable for any claim, loss, or damage resulting from the use of this course.

Copyright Notice

X-Ray Lady CE®
Jeana Fleitz, M.Ed., RT(R)(M)
6511 Glenridge Park Place, Suite 6 Louisville, KY 40222
Phone: (502) 425-0651 | Email: xrayladyce@gmail.com
Website: www.x-raylady.com

Imaging Male Breast Cancer

Approved for 6 Category A CE Credits

Course Description

This homestudy course titled *Imaging Male Breast Cancer* provides current information about imaging breast cancer in men. Specific parts of this course include a historical overview of breast cancer, an introduction to breast cancer, benign and malignant breast disease, imaging examinations, and radiation protection in mammography. Also provided is information about *BRCA1* and *BRCA2* cancer risk and genetic testing. Imaging modalities are discussed with indications and contraindications for imaging breast masses in men. Radiation protection considerations in breast imaging are a necessary component of any imaging course and are included. The major parts of the course include:

Part 1	Historical Overview of Breast Cancer
Part 2	Introduction to Breast Cancer in Men
Part 3	Benign and Malignant Breast Disease
Part 4	Imaging Examinations
Part 5	Radiation Protection

Objectives: Upon completion of this homestudy course, the participant will

1. Recall historical facts about breast cancer.
2. Identify current statistics and facts concerning breast cancer in men.
3. Differentiate between the signs and symptoms of breast cancer in men as compared to women.
4. Discuss reasons for late diagnosis of breast cancer in men.
5. Identify ethnic and geographic differences and disparities in breast cancer detection.
6. State facts about genetic testing for breast cancer and recall psychosocial information concerning testing and disclosure of test results.
7. Compare and contrast signs and symptoms of benign and malignant breast masses in men.
8. Discuss the advantages and disadvantages of mammography, ultrasonography, magnetic resonance imaging, and related imaging procedures used to diagnose breast cancer in men.
9. Given facts or questions concerning radiation protection during imaging procedures, select the best response.

Imaging Male Breast Cancer

"Believe you can and you're halfway there"
Theodore Roosevelt

Part 1 Historical Overview of Breast Cancer

"May we, then, infer that, as has more than once been contended, cancer, like insanity, follows in the wake of civilization."

Walter Hayle Walshe, Professor of Pathological Anatomy, University College, London, 1846

There is a commonly held viewpoint that cancer is a product of industrialized societies. Jean Jacques Rousseau noted that with "…Civilization, humans have lost touch with nature, and are paying a price in terms of common diseases." Historically, cancer has plagued the human race. It is not a new disease, but has been endemic throughout the natural world, and has been present in all human societies. Artifacts recovered from Greek temples indicate that in the years prior to Hippocrates, Greeks would place clay models of breast tumors in temples as votives, in the hope that an illness of supposed supernatural cause might be cured by supernatural intervention. The first written description of breast cancer was done on ancient papyrus. In this early account, the doctor described inflammatory breast cancer, stating that treatment was futile, and that the woman should be left alone.[1] Ancient Greeks, around 200 AD, thought an excess of black bile caused cancer. It was thought that the monthly menstrual flow naturally relieved women of this excess, which explained why breast cancer was more common after menopause.[2]

Prominent European surgeons and physicians of the 18th and 19th centuries regarded cancer not only as a modern, stress-related disease, but also as an illness predominantly of women. Some of them also thought they knew why this was the case.[3]

Women are more subject to cancerous disorders than men, especially such women that are of sedentary, melancholic disposition of mind, and meet with such disasters in life, as occasion much trouble and grief. (Richard Guy, 1759)

The speculation by early physicians that focused on constitutional melancholy as the underlying link to cancer persisted into the 20th century. John Hunter and James Paget, 18th and 19th century surgeons, proposed that breast and other cancers could develop

after a person who was constitutionally predisposed to melancholy experienced trauma or a physical blow. In the 17th century, the Dutch surgeon Adrian Helvetius performed both lumpectomy and mastectomy for breast cancer, claiming both procedures were curative. Historical surgical texts provide a graphic illustration of the instrumentation and methods used to treat breast cancer. In 1811, Fanny Burney wrote an account of her mastectomy, in which she chronicled the pain and indignity suffered from the procedure. It is documented that Ms. Burney lived 30 years following the surgery. Mastectomy has been the primary breast cancer treatment for over 2000 years. The first hospitals dedicated to cancer were built in Rheims in 1740 and in London (the Royal Free Cancer Hospital now Royal Marsden Hospital), in 1828.

Breast cancer has been a predominant type of cancer for centuries, with steady increases in incidence in westernized countries throughout the 20th century, long before environmental factors such as man-made DDT, radiation, or the petro-chemical industries came under consideration. Regardless of the speculations surrounding the cause of cancer, there is much early information documented about the incidence levels of the disease. Knowledge about the relative frequency of breast and other cancers 200 years ago comes from the first statistical analysis of deaths from cancer in men and women in Verona (1760-1839) by Rigoni-Stern. It is reported that there were 944 female deaths compared with only 142 males.

Approximately one-third of the female cases reported were breast cancers, and one-third were uterine cancers. It is not known whether there was any strong bias in recording these mortality data, but the number of diagnosed female cancers is remarkable. Within this number, it must be presumed that cancer was underdiagnosed, and that most individuals would have died at a relatively young age. These data still suggest a low rate compared with more recent times. Rigoni-Stern made a significant observation when he noted that "…Whereas nuns were much more likely to die of breast cancer than married women, the opposite was true of uterine cancer."[3] In 1700, Bernardion Ramazzini made further reference to this in a statement "…You can seldom find a convent that does not harbor this accursed pest, cancer, within its walls."[3]

In Paris and Geneva, during the same period in which the Verona study (1837-1842) was conducted, a similar female cancer ratio of over 3 to 1, in comparison to men, was also noted. Detailed records of cancer subtypes in men and women at the Middlesex Hospital in the mid-19th century reveal a marked predominance of breast and uterine cancers. In the records there is no mention of prostate cancer, and only a brief mention of a low significant number of cancers in men that might be

attributed to smoking. Such cancers were of the lip, mouth, and tongue, however; few lung cancers were reported, possibly because cigarettes had yet to replace the pipe.

Part 2 Breast Cancer

Introduction to Breast Cancer in Men

Breast cancer in men is a rare disease (accounting for 1% of breast cancer cases in the United States). [4] The incidence of male breast cancer has remained relatively stable over the past decade with only a 1% annual increase between 1975-2004.[4] The American Cancer Society (ACS) estimates that about 2,240 new cases of invasive breast cancer will be diagnosed among men in the United States in 2013.[4] For men, the lifetime risk of getting breast cancer is about 1/10th of 1% (1 in 1,000).[4] Breast cancer is about 100 times less common among men than among women, but is often not detected at an early stage, when treatment can be most effective in reducing mortality.[4] According to the ACR, the reasons for the 1% annual increase in the diagnosis of male breast cancer are unknown, and are not likely to be attributable to increased detection.[4]

The mortality rate of breast cancer is higher for men than for women for several reasons. Unlike for women, screening mammography is not recommended for males because breast cancer in men is rare. Males also do not have the same amount of breast tissue that women do, so by the time the cancer has been detected, it has often spread into the chest cavity, thus a late-stage diagnosis. Occasionally male breast cancer is misdiagnosed as gynecomastia, thereby causing a delay in cancer diagnosis.[5] A lack of public awareness about male breast cancer is often cited as another reason that those affected do not seek prompt medical care. The medical community has also been criticized for improperly diagnosing male patients who present with breast tenderness, a palpable mass, or overt symptoms of breast cancer.[6] Personal stories about male breast cancer patients are abundant on the Internet.[6] However, one such tragic story, about a man named John Nick, had a positive outcome. After Mr. Nick's untimely death, his family formed a foundation (John W Nick Foundation, Inc.) that is dedicated to male breast cancer awareness.[6]

John Nick died of breast cancer at the age of 58.[6] Approximately 6 years before his death he had consulted with his physician about nipple inversion on his right breast. The physician told Mr. Nick not to worry about the nipple inversion.[6] About two years later, Mr. Nick consulted yet another physician, who also dismissed the signs and symptoms of breast cancer.[6] Four years after the first symptoms appeared, Mr. Nick was finally diagnosed with breast cancer, and 20 of his lymph nodes sampled at surgery were positive for malignancy.[6] Although Mr. Nick underwent an immediate mastectomy

and subsequent chemotherapy, the cancer metastasized to his bones, and he died in June 1991.[6]

The ACS estimates that in 2013 about 410 men will die from breast cancer in the United States.[4] Each year the ACS publishes current key statistics about breast cancer in both men and women, and this information is available on the ACS Web site at www.acs.org. Fortunately, although only about 1% of men are diagnosed with breast cancer, results from a study released in 2007 found that men with the disease may be at higher risk than women of dying from the disease.[7] There have been several studies of male breast cancer, but their conclusions indicate that further investigation is needed. One of the most significant findings of these studies was that the treatment of male breast cancer is based upon research conducted primarily on breast cancer in women.[8] Studies suggest that there may be biological differences between male and female breast cancers that could affect survival rates.[5] For example, in one study, researchers found that men with even small breast cancer tumors, or tumors that had not yet metastasized to the lymph nodes, tended to die before females with similar diagnoses (6 years for men versus 15 years for women).[7] The study found no difference in survival for men with advanced stages of breast cancer compared to similarly diagnosed women.[7] Also, the study found that men were less likely than women to receive chemotherapy or radiation therapy for breast cancer.[7]

The Breast

The breast consists mainly of lobules (milk-producing in women), ducts, and stroma. The stroma consists of fatty and connective tissue surrounding the ducts and lobules, blood vessels, and lymphatic vessels. The breast of both males and females are identical at birth, remaining quiescent until hormonal influence takes place at puberty.[9] Until puberty (usually around age 13 to 14), young boys and girls have a small amount of breast tissue consisting of a few ducts located under the nipple and areola. At puberty, the female ovaries produce estrogen, which stimulates breast tissue, causing breast ducts to grow in size, lobules to form at the ends of the ducts, and the quantity of stroma to increase. In males, hormones produced by the testicles inhibit growth of breast tissue.

During the peripubertal period in males there is an increase in estrogen level, and a 30-fold increase in testosterone.[9] As the hormonal balance is shifting, there is a brief proliferation of the breast ducts and stroma, followed by involution and ultimate atrophy of the ducts. Subcutaneous fat and a remnant of subareolar ductal tissue characterize the normal male breast. Development of the breast lobules requires both

estrogen and progesterone, which are usually not present in sufficient levels in males. Cooper's ligaments, found in the female breasts, are absent from the male breast.

The external landmarks of the breast include the nipple, inframammary fold, and axilla.

> ***Inframammary fold*** *refers to the most inferior aspect of the breast where it meets the anterior abdominal wall.*

Of the structures mentioned, the only fixed point of reference in the breast is the nipple, and it is an important landmark in describing any breast abnormality (Figure 1).

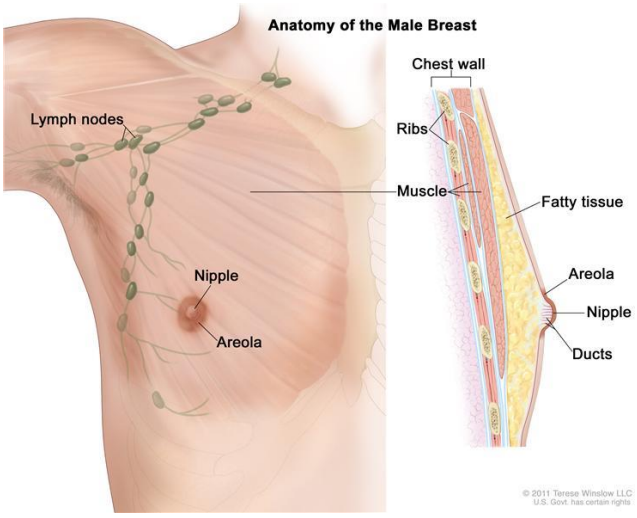


Fig. 1. External landmarks of the breast. Retrieved from www.cancer.org.

Two methods are used to subdivide the breast into smaller areas for localization of lesions. The quadrant method divides the breast into four areas (Figure 2).

- Upper-outer quadrant (UOQ)
- Upper-inner quadrant (UIQ)
- Lower-outer quadrant (LOQ)
- Lower-inner quadrant (LIQ)

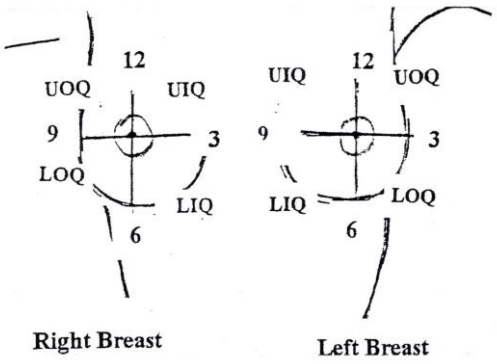


Fig. 2. Quadrant and clock method.

The clock method, as illustrated in Figure 2, is also used, and helps to describe the location of abnormalities in the breast. The clock method can be confusing since the 4 o'clock position in the right breast represents the LIQ while 4 o'clock in the left breast represents the LOQ.

Skin

The skin at the base of the breast is about two millimeters (mm) thick and becomes thinner as it approaches the nipple (0.5 mm).[10] The skin covering the breast contains sweat glands, sebaceous glands, and hair follicles that open to form skin pores. Sebaceous glands are oil-secreting glands located in the skin.

The sebaceous glands are prone to infection, and the inflammatory process may mimic carcinoma on the mammographic image.[11] The skin pores may also be visualized on mammography as tiny multiple lucencies.[11]

Nipple-Areola Complex

The nipple and areola are located at the most distal point (apex) of the breast. The areola contains erectile and smooth muscles, and the Montgomery glands surround the nipple.

The size and characteristics of the nipple vary, but the nipple is the center point of the breast and provides a reference to describe the location of normal anatomy and pathology. The shape of the nipple can be flat, round, or cylindrical, and it generally protrudes from the breast. Males may present with developmental variations such as inversion, retraction, or enlargement of the nipple, which may be caused by either a benign or a malignant condition. Any sudden change in the nipple itself, or to the skin around the nipple, is significant and indicative of an underlying malignancy, and requires thorough investigation.

> ***Inversion*** *refers to a case in which the entire nipple is pulled inward. The turning inward may be far enough so that the nipple lies below the surface of the breast.*

> ***Retraction*** *of the nipple means that only a slitlike area is pulled inward. Both inversion and retraction may be either congenital or acquired, and may be either unilateral or bilateral.*

Supernumerary nipples, or polythelia, can affect both sexes. These accessory nipples are more commonly found just below the normal breast, but can be located anywhere along the milk line that runs from the axilla to the groin. Those with polythelia may have associated breast tissue that undergoes physiological and pathological change like that observed in normal breast tissue. The condition is associated with other congenital disorders such as renal agenesis, renal cell carcinoma, supernumerary kidneys, and cardiac abnormalities.

The breast is situated anteriorly to the pectoralis major muscle and the pectoralis minor muscle. These muscles aid in controlling upper arm movements.

> *The **pectoral muscles** consist of the pectoralis major and the pectoralis minor. The pectoralis major muscle is a large, thick, fan-shaped muscle that covers the upper parts of the chest. The pectoralis minor muscle is a thin, flat, triangular muscle lying below the pectoralis major.*

Adipose tissue and connective fascia separate these muscle layers from breast tissue, creating the retromammary space.

Breast Lymphatics and Sentinal Node Mapping

The lymphatic system is an essential part of the immune system. The lymph network is made up of fine capillaries that merge to form lymph vessels. Cellular waste and lymph fluid is transported via lymph nodes, ducts, and specialized organs to the bloodstream. Lymph nodes are usually present in clusters in the axilla, on either side of the neck, and in the groin (Figure 3).

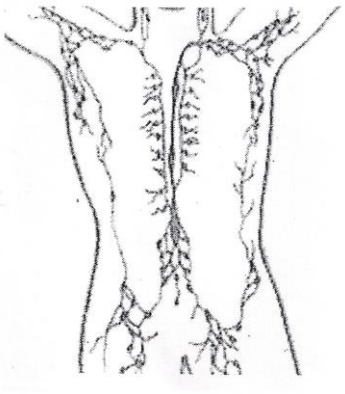


Fig. 3. Lymphatic system. Courtesy National Institutes of Health. National Cancer Center.

In the embryo, the breast and its lymphatic system develop from a central breast bud. Lymph fluid is a clear white-yellow fluid that contains white blood cells

(lymphocytes), proteins, and some red blood cells. Lymph nodes are usually located in the upper outer quadrant of the breast and tend to follow the route of the blood vessels, but can be located anywhere in the breast, including in the medial and inferior portions.[12] Lymph nodes can vary in size, but most normal lymph nodes are less than two centimeters in length and have a kidney-bean shaped appearance.[7] Superficial lymphatic drainage beneath the skin of the breast goes to the pectoral and infraclavicular lymph nodes, and to the deep plexus. Deep drainage goes to the pectoral nodes and the subscapular nodes, and then to the lateral axillary and apical nodes. Deep drainage also goes to the apical and deep cervical nodes. The lateral half of the breast tends to drain into the pectoral group of axillary lymph nodes, and the medial half of the breast drains into the internal mammary lymph node. The internal mammary nodes drain toward the mediastinal nodes (Figure 4).

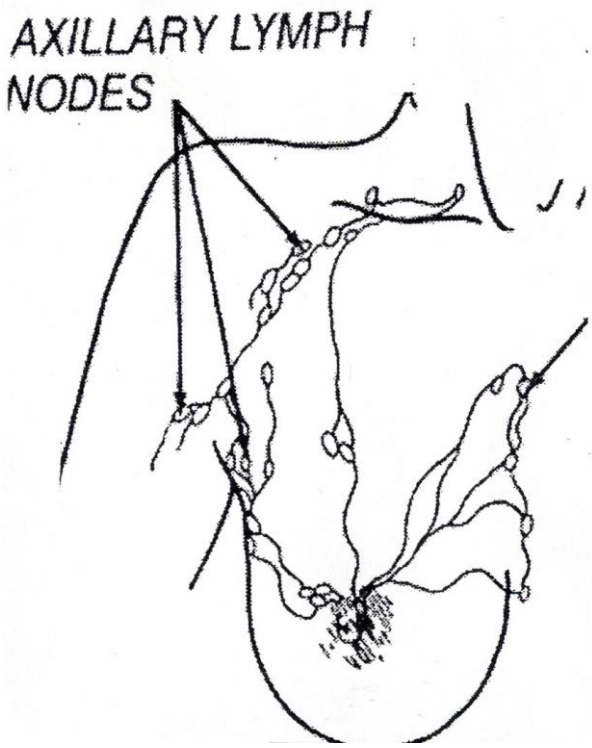


Fig. 4. Axillary lymph nodes. Courtesy National Institutes of Health. National Cancer Institutes.

Approximately 97% of the lymphatic drainage of the breast passes to the axillary nodes, and about 3% drains to the internal mammary nodes.[7] Lymph drainage from the breast is significant because it is by this route that malignant cells may leave the breast and spread to other areas of the body.[4] Because the lymph drainage routes are similar to those through which blood flows, the breast has a predictable pattern for lymphatic drainage.[12]

Lymph nodes can vary in size between mammographic examinations, appearing and disappearing on various studies and sometimes disappearing completely.[7] If a benign appearance is maintained, lymph nodes that demonstrate small increases in size can be followed mammographically.[7] There is a high correlation between dense lymph nodes that are ill-defined, or have spiculated margins, and malignancy.[7] If, in mammography, there is a loss of the fatty hilum around a lymph node, loss of margin definition, spiculation, rounding, and/or increasing density, a biopsy should be considered.[7]

The term "sentinel lymph node" (SLN) has been coined to describe the condition in which certain lymph nodes are first in line to receive lymphatic drainage from a tumor. SLN mapping is a diagnostic procedure used to locate and mark the SLN before biopsy, and to confirm the presence of cancer in the lymph nodes. Once a malignant tumor has been identified, the primary drainage for the entire breast can be determined via sentinel node mapping. The procedure consists of injecting the breast with either a radiocolloid preparation or a blue dye. When radiocolloids are used, SLN mapping is referred to as lymphoscintigraphy. After the tracer has been administered, a gamma detector is used to identify areas of radioactive uptake, and a computer is used to create images of the lymph flow.

The SLNs are identified, excised, and examined by a pathologist for the presence of cancer. Just because a lymph node shows uptake of the tracer material does not mean that the lymph node contains cancer cells. SLN mapping is recognized as an acceptable alternative to axillary node dissection, and can establish which patients require node dissection and additional treatment.[12] The procedure is not indicated in patients who are known to have high-risk lesions, non-invasive cancer, and non-palpable breast masses.[12] Other poor candidates for the procedure, according to Health Canada's Canadian Breast Cancer Initiative, include individuals with:

- Palpable lymph nodes;
- Locally advanced breast cancer;
- Multifocal breast cancer;
- A record of previous breast surgery; and,
- A record of previous radiation therapy.[13]

Blood and Nerve Supply to the Breast

Blood is supplied to the breast via the anterior cutaneous, or perforating, branches of the internal mammary, and the lateral mammary branch of the lateral thoracic arteries. The thoracic branches of the axillary artery, the posterior intercostal

branches of the descending thoracic aorta, and the internal mammary artery also supply blood to the breast.

Perforating branches from the 2nd through the 4th intercostal arteries supply blood to deep portions of the breast. A branch of the internal thoracic artery supplies the medial portion of the breast. The lateral portion of the breast receives its blood supply from branches of the subscapular artery, which arises from the 3rd portion of the axillary artery. The superior thoracic artery, arising from the first part of the axillary artery, supplies the pectoralis major muscle.

The breast is supplied with sensory and sympathetic nerves by the anterior and lateral cutaneous branches of the 4th through 6th intercostal nerves.

Introduction to Pathology and Risk

Pathology is defined as the anatomical or functional manifestation of disease. Breast pathology may be either benign or malignant. A benign breast condition is any non-cancerous breast abnormality. Although not life-threatening, benign conditions may cause pain or discomfort for some patients. Not all-benign breast conditions signal an increased risk for breast cancer. Depending on the type of benign breast condition, and the patient's medical history, clinical presentation, and associated risk factors, treatment may or may not be necessary.

> ***Risk*** *refers to the probability of a person developing or dying from a particular disease, and is discussed as absolute and relative.*
>
> ***Absolute risk*** *refers to a person's chance of developing a specific disease over a certain time period. The absolute risk of disease is estimated by examining a large number of people who are similar in some respects (in terms of age, for example), and counting the numbers of individuals in this group who develop the disease over the specified time period.*
>
> ***Relative risk*** *(RR) is computed by comparing the number of persons in an exposed population showing an effect with the number in an unexposed population who show the same effect.*
> *While relative risks are useful for comparisons, they do not provide information about the absolute amount of additional risk experienced by the exposed group. Relative risk (RR) also refers to the rate of cancer in women with a given condition or diagnosis divided by the rate of cancer in the reference population.*

The reference population should be defined since this alters the calculated RR. Additional factors that affect RR include the age of the patient at the time of biopsy and the number of follow-up years.

The etiology of breast cancer in men is not fully understood but hormonal and genetic factors appear to play a role. As with female breast cancer, increasing age is an important risk factor for the development of breast cancer in men. Men with breast cancer average about 67 years old at the time of their diagnosis.[14] Breast cancer risk is increased if other members of the family (blood relatives) have had breast cancer, and this will be discussed in detail later in this course.

Klinefelter Syndrome

Klinefelter syndrome, also known as the XXY condition, is a term used to describe males who have an extra X chromosome in most of their cells. Instead of having the usual XY chromosome pattern that most males have, these men have an XXY pattern. This is a congenital condition that affects about 1 of 1,000 men.[14] This condition causes the testicles to be smaller than usual thus rendering approximately 95% to 99% of XXY males infertile.[15] Compared with other men, those with Klinefelter syndrome have lower levels of androgens and estrogens, which puts them at a higher risk of developing gynecomastia and breast cancer.[16] Males with Klinefelter syndrome have a 20-fold increased incidence of breast cancer, and are more likely to have bilateral breast cancer.[16] Bilateral mammography should always be performed on males with Klinefelter syndrome.[16]

Males whose chest areas have been exposed to radiation for the treatment of disease have an increased risk of developing breast cancer. Observations of survivors of the atomic bombings of Hiroshima and Nagasaki, and of women who have received therapeutic radiation treatments to the chest and upper body, document an increased breast cancer risk as a result of radiation exposure.[17] The significance of this risk in those having a genetic susceptibility to breast cancer is unclear. Preliminary data suggest that increased sensitivity to radiation could be a cause of cancer susceptibility in carriers of BRCA1 and BRCA2 mutations, and in association with ATM and TP53 mutations, all of which will be discussed later in this course.[17]

Heavy alcohol consumption increases the risk of breast cancer in both men and women.[18] The risk of breast cancer increases by approximately 10% for each 10-gram of daily alcohol intake (equivalent to one drink or less) in the general

population.[17] The liver plays an important role in sex hormone metabolism by producing binding proteins that carry the hormones in the blood. These binding proteins affect the hormones' activity. Men with severe liver disease, such as cirrhosis, have relatively low levels of androgens and higher estrogen levels, and therefore may have an increased risk of developing breast cancer.[18]

Prostate cancer is sometimes treated with estrogen-related hormonal therapy. This treatment may slightly increase the risk of breast cancer. Also, men taking high doses of estrogens as part of a sex change procedure may have a higher risk of breast cancer. Some studies have suggested that certain conditions that affect the testicles, such as having an undescended testicle, having mumps as an adult, or having one or both testicles surgically removed, may increase breast cancer risk; however, more research is needed in this area.[4]

Recent studies have shown that a woman's breast cancer risk is increased by obesity during adult life. Obesity is assumed to be a risk factor for male breast cancer as well.[4] This assumption is based on the fact that fat cells in the body convert male hormones into female hormones. This means that obese men have higher levels of estrogen in their body.[4]

Because the research into the etiology of male breast cancer has not received the same attention as that of females, little data about causative factors currently exists. In a recent study involving the large U.S. Veterans Affairs computerized medical care system database, researchers were able to calculate relative risks and 95% confidence intervals for male breast cancer associated with conditions occurring one or more years after initial hospitalization.[8] The database consisted of 4,501,578 men whose medical conditions were significantly related to breast cancer risk.[8] Such conditions included diabetes, obesity, orchitis/epididymitis, Klinefelter syndrome, and gynecomastia.[8] Additionally, among African American males, cholelithiasis emerged as a significant risk predictor of breast cancer.[8] Diseases that have previously been related to male breast cancer risk that were not supported by the study outcomes included thyroid disease, smoking-related conditions, liver cirrhosis, prostatic hyperplasia, and fractures.[8]

The data supports such known significant male breast cancer risks as Klinefelter syndrome, gynecomastia, obesity, and orchitis/epididymitis.[8] Previous speculations that male breast cancer is influenced not only by tissue at risk, but also by hormonal and inflammatory factors, were substantiated by the study data.[8]

Dietary Habits and Relationship to Geographic Patterns

Diet has been indicated as a factor in the development of breast cancer. It is known that the metabolism of food affects the production and secretion of hormones, which are regulated by enzymes under genetic control. Epidemiologists searching the world for discrepancies in breast cancer incidence have found that in areas where breast cancer is common, diets are high in fat and animal protein. Americans, for example, consume three times as much fat (and more animal protein) than the Japanese, and the incidence of breast cancer in the United States is noticeably greater than in Japan.[19] It has been noted that as countries assume a more "Western" diet, in which fat constitutes 40% of the calories consumed, breast cancer incidence rises. This connection between diet and breast cancer has been documented in the rising breast cancer rate in Iceland, as that nation's diet shifts from predominately fish and sheep to more western fare.[20]

Socioeconomic status is considered to be an interrelated factor in the dietary link to breast cancer. As one's economic status increases, one's risk of developing breast cancer also increases; this supports a connection between income and a diet rich in fat and animal protein, which, as previously stated, has been tied to increased breast cancer rates. It is important to note that when large populations move from a low-incidence area to a high-incidence area, they tend to assume the cancer risk patterns of the new geographic location. This has long been documented among immigrants from Asia to the United States. Typically, breast cancer rates increase somewhat in the first generation following immigration, then continue to increase in subsequent generations until they approach those of the country in which the immigrants are living.[21]

Animal experiments also indicate that high-fat diets encourage the development of breast cancer by augmenting the production and release of certain hormones.[22] It is thought that dietary fats do harm by serving as a vehicle for fat-soluble environmental carcinogens, by providing a source for co-carcinogens, or by depressing the immune response.[23] Almost anything a woman ingests can be detected in fluids secreted within the breast ducts. For example, five minutes after a woman smokes a cigarette, nicotine appears in her breast secretions.[19] Studies of breast fluids have found that breast secretions contain much higher levels of cholesterol than the blood does. Moreover, breast fluids can also contain a potentially cancer-causing by-product of cholesterol metabolism.[24]

Several studies have looked into the roles of specific dietary components. One found that breast cancer mortality is highest in areas of the United States where the per capita consumption of milk is high, and, less expectedly, where that of eggs is low.[25] Other studies have found that vegetarians have lower rates of breast cancer than non-

vegetarians.[26,27] Also, there is an interesting geographic link between breast cancer and the selenium levels found in water, soil, and local cuisine. Regions known to have high selenium levels in the water, soil, and diet have lower breast cancer rates. In Japan, where dietary selenium levels are around 300 micrograms a day, mortality from breast (and colon) cancer is much lower than in the United States, with an average dietary selenium level of 70 micrograms a day.[28,29]

Carcinogens

A number of cancer-causing agents, or carcinogens, have been identified. These include chemical carcinogens (such as ingredients in tobacco smoke), physical carcinogens, products like asbestos fibers, radiation, and certain viruses. Chemical carcinogenesis is considered to be a multi-step process. During a preliminary stage, a carcinogen known as an initiator causes irreversible damage to the genetic material of one or more normal cells, and permanently alters their behavior.[30] At some later time, these damaged (or initiated) cells undergo further transformation, perhaps from exposure to one or more chemical agents known as promoters, beginning to reproduce themselves continuously, forming a tumor.

Some chemical carcinogens act indirectly, since they must be activated by enzyme systems within the body before they can produce cancerous changes.[30] In addition, there are co-carcinogens, materials that enhance carcinogens. Alcoholic beverages, for instance, augment the power of tobacco smoke, and have been suggested as agents in the development of cancer of the esophagus.[30]

Various studies indicate a link between breast cancer and a common environmental contaminant called polycyclic aromatic hydrocarbons (PAH).[30] Polycyclic aromatic hydrocarbons have been found to be carcinogenic in experimental studies. This chemical is produced during the combustion of oil and gas, and is commonly found in cigarette smoke and broiled meat. In one study involving tissue samples from 104 women with early stage breast cancer and 105 women with benign breast disease, the women with breast cancer were twice as likely to have elevated levels of PAH-DNA their breast tissue as compared with women with benign breast disease.[30] The association between PAH-DNA damage and breast cancer remained after other breast cancer risk factors had been considered.[30]

Two possible interpretations of the data from these studies have been given. First, women in the study who had breast cancer may have been more sensitive to PAH exposure, which played a role in the development of their breast cancer.[**30**] Second, changes in cancer cells might have contributed to the development of PAH-DNA

damage, which suggests that the PAH exposure may have factored into the progression of cancer but not directly caused it.[30]

Some studies have suggested that there is an increased risk of breast cancer in men who work in hot environments such as steel mills. It is thought that this correlation could result from the fact that long-term exposure to higher temperatures can affect the testicles, which in turn affect hormone levels.[4] Men who are heavily exposed to gasoline fumes may also have a higher risk of breast cancer; however, additional research is needed to confirm environmental workplace exposure and increased risk of breast cancer.[4]

In the United States the National Toxicology Program (NTP) is responsible for the identification and evaluation of carcinogens; the International Agency for Research on Cancer (IARC) has a similar role internationally.[30] The NTP is responsible for producing the *Report on Carcinogens,* an informational scientific and public health document that identifies agents, substances, mixtures, and exposure circumstances that may increase the risk of developing cancer.[30] The current NTP report may be found at the NTP's Website, which is http://ntp.niehs.nih.gov/ntp/roc/toc11.html.[30]

Genetic Influence on Male Breast Cancer

Nearly every cell in the body contains 46 chromosomes, which are tightly packed bundles of deoxyribonucleic acid (DNA), half of which came from the biologic mother and half from the biologic father. While the DNA of any two people is more than 99% the same, the fraction of DNA that varies among individuals can play an important role in risk of disease.[31] The most common type variation, called a single nucleotide polymorphism (SNP), affects just a single building block of DNA.[31] SNPs are used in genome-wide association studies to identify chromosome regions that are related to certain diseases. By studying large populations of individuals with and without disease, researchers can provide indicators as to which SNP variations are associated with breast cancer.[31] In gaining an understanding about altered genetic pathways, researchers will ultimately be able to turn knowledge of genetic variations and risk into targets for drug development, which may help prevent and/or control diseases such as breast cancer.[31]

About 1 out of 5 men with breast cancer has close male or female relatives with the disease.[4] Definite familial tendencies are evident in cancer risk assessment, with an increased incidence seen in men who have a number of female relatives with breast cancer. An increased risk of male breast cancer has been reported in families in which the *BRCA2* gene mutation on chromosome 13q has been identified.

BRCA1 and *BRCA2* are human genes that belong to a class of genes known as tumor suppressors. In normal cells, *BRCA1 and BRCA2* genes help ensure the stability of the cell's genetic material, and help prevent uncontrolled cell growth. Mutation of these genes has been linked to the development of both hereditary breast and ovarian cancer. Not all gene changes, or mutations, are deleterious. Some mutations may be beneficial, whereas others may have no obvious effect. Harmful mutations can increase a person's risk of developing a disease, such as breast cancer. In women, mutations of the BRCA1 and BRCA2 genes are responsible for about 5% to 10% of breast cancers.[32] Women with either of these altered genes have a lifetime breast cancer risk of up to 80%.[32]

In men, changes in the *BRCA2* gene seem to be responsible for about 10% of breast cancer cases.[32] The lifetime breast cancer risk for men with *BRCA2* mutations is about 5% to 10%, which is much higher than the risk for other men.[32] Men with harmful *BRCA1* mutations also have an increased risk of breast cancer, and possibly of pancreatic cancer, testicular cancer, and early-onset prostate cancer as well.[32] However, male breast cancer and pancreatic cancer appear to be more strongly associated with *BRCA2* mutations.[32] The likelihood that a breast cancer is associated with a harmful mutation in *BRCA1 and BRCA2* is highest in families with:

- A history of multiple cases of breast cancer, or cases of both breast and ovarian cancer;
- One or more family members who have had two primary cancers (original tumors that develop at different sites in the body); or,
- Ashkenazi (Eastern European) Jewish heritage.[32]

Not every person in such families carries a harmful *BRCA1* or *BRCA2* mutation, and not every cancer in such families is linked to a harmful mutation in one of these genes. Also, not everyone who has a harmful *BRCA1* or *BRCA2* mutation will develop breast cancer (or an associated cancer). According to the National Cancer Institute, risk estimates related to *BRCA1* or *BRCA2* mutations are based on families with many affected members, and may not accurately reflect the levels of risk for *BRCA1* or *BRCA2* mutation carriers in the general population.[32]

Specific gene mutations are more common in certain populations. For example, two specific mutations in the *BRCA1* gene, and one in the *BRCA2* gene, are most commonly found in the Ashkenazi Jewish population.[32] The frequency of the genetic mutations in this specific population is about five times higher than that found in the general population.[32] Other ethnic and geographic populations around the world, such as

the Norwegian, Dutch, and Icelandic peoples, also have higher frequencies of specific *BRCA1* and *BRCA2* gene mutations.[32] Limited data also indicate that the frequencies of specific *BRCA1* and *BRCA2* gene mutations may vary among individual racial and ethnic groups in the United States, including African Americans, Hispanics, Asian Americans, and non-Hispanic whites.[32] The likelihood of a harmful *BRCA1* or *BRCA2* mutation is increased with certain familial patterns of cancer. These patterns include the following:

For males of Ashkenazi Jewish descent:

- Any first-degree relative diagnosed with breast or ovarian cancer; and,
- Two second-degree relatives on the same side of the family diagnosed with breast or ovarian cancer.[32]

For males who are not of Ashkenazi Jewish descent:

- Two first-degree relatives (mother, daughter, or sister) diagnosed with breast cancer, one of whom was diagnosed at age 50 or younger;
- Three or more first-degree or second-degree relatives (grandmother or aunt) diagnosed with breast cancer, regardless of their age at diagnosis;
- A combination of first- and second-degree relatives diagnosed with breast cancer and ovarian cancer (one cancer type per person);
- A first- or second-degree relative diagnosed with both breast and ovarian cancer regardless of age at diagnosis; and,
  breast cancer diagnosed in a male relative.[32]

Genetic Testing for BRCA1 and BRCA2

Genetic testing is highly specialized and only a small number of laboratories are capable of providing the array of molecular tests currently available.[17] The many molecular testing methods available each have its own costs, strengths and weaknesses.[17] Thus, the selection of the appropriate genetic test for a given individual requires extensive knowledge of genetic diagnostic methods, correlation between clinical and molecular findings, and access to information about rapidly changing test options.[17] Government regulation of genetic tests to date remains extremely limited, however, the Centers for Medicare and Medicaid Services under the Clinical Laboratory Improvement Act (CLIA) regulates all clinical human laboratory tests performed in the United States for the purposes of generating diagnostic or other health information. CLIA assurance standards, as well as documentation and validation of tests and procedures.[17] Genetic

tests are considered to be highly complex, which indicates that a high degree of knowledge and skill is required to perform or interpret the test. Laboratories conducting such complex tests must undergo proficiency testing at specified intervals but CLIA has yet to establish specific proficiency testing of laboratories offering genetic testing.

Several methods are available to test for *BRCA1* and *BRCA2* gene mutations. A blood sample is required for these tests, and the laboratory results are available within several weeks. Genetic counseling is generally recommended before and after a genetic test. The genetic counseling usually involves a risk assessment based on the individual's personal and family medical history, discussions about the appropriateness of genetic testing, and the medical implications of a positive or negative test result.

Currently, there are no standard criteria for recommending or referring an individual for *BRCA1* or *BRCA2* mutation testing. In a family with a history of breast and/or ovarian cancer, it may be most informative to first test a family member who has the disease.[32] If that person is found to have a harmful *BRCA1* or *BRCA2* mutation, then other family members can be tested to see if they also have the mutation.[32] A male who has a relative with a harmful *BRCA1* or *BRCA2* mutation, and who appears to be at increased risk of breast cancer because of that family history, should consider genetic counseling to learn more about his potential risk.[32] The cost for *BRCA1* and *BRCA2* mutation testing usually ranges from several hundred to several thousand dollars.[32]

A positive test result generally indicates that a person has inherited a known harmful mutation in *BRCA1* or *BRCA2,* and therefore has an increased risk of developing certain cancers.[32] A positive test result provides information only about a person's risk of developing cancer, and cannot predict whether (or when) an individual will actually develop cancer.[32] A positive genetic test result may have important health and social implications for family members, including future generations.[32] Genetic tests can reveal information not only about the person being tested, but also about that person's relatives.[32]

How a negative test result will be interpreted depends on whether or not someone in the tested person's family is known to carry a harmful *BRCA1* or *BRCA2* mutation.[32] If someone in the family has a known mutation, testing other family members for the same mutation can provide information about their cancer risk. If a person tests negative for a known mutation in his or her family, it is unlikely that he/she has an inherited susceptibility to cancer associated with *BRCA1* or *BRCA2.* This type of test result is called a "true negative," and does not mean that a person will not develop cancer; it means that the person's risk of cancer is probably the same as that of people in the general population.[32]

For those who have a positive *BRCA1* or *BRCA2* genetic test result, there are several options available for managing cancer risk.[32] Such options include increased surveillance, prophylactic surgery, risk avoidance, and chemoprevention. Surveillance means screening, such as mammography and magnetic resonance imaging (MRI). Prophylactic surgery involves removing as much of the "at-risk" tissue as possible in order to reduce the chance of developing cancer. Risk avoidance refers to modifying certain behaviors that have been associated with an increased risk of breast cancer in the general population. Research results on the benefits of modifying individual behaviors to reduce the risk of developing cancer among *BRCA1* or *BRCA2* mutation carriers are limited.[32] Chemoprevention is a therapeutic approach that involves the use of natural or synthetic substances to reduce the risk of developing cancer, or to reduce the chance of cancer recurrence. For example, the drug Tamoxifen has been shown in numerous clinical studies to reduce the risk of developing breast cancer by about 50% in women who have an increased risk of the disease, and to reduce the recurrence of breast cancer as well.[32] Tamoxifen is also used to treat certain types of breast cancer in men.[32]

Other Genetic Mutations & Predisposition Cancer Syndromes

There are several other mutations in genes that have been associated with hereditary breast cancer. These include *TP53, PTEN, STK11/LKB1, CDH1, CHEK2, ATM, MLH1, and MSH2.* [32] Although mutations in these additional genes have been found to increase the risk of breast cancer, the majority of hereditary breast cancers can be accounted for by inherited mutations in *BRCA1* and *BRCA2.* [32]

About 1-2% of all cancers is associated with hereditary cancer syndromes; these syndromes are associated with very high lifetime probabilities of developing certain cancers. Individuals with hereditary cancer syndromes have a heritable mutation in every cell, which may have been inherited from a parent or arisen early in development. For example, retinoblastoma, a rare childhood cancer in the retina of the eye, is an example of hereditary cancer that is associated with a specific gene mutation in about 35% of all cases. Two additional examples of genetic cancer syndromes include familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC). Both of these syndromes confer a high risk of colorectal cancer at an early age, and at multiple sites within the colon and rectum. Individuals with HNPCC are also predisposed to endometrial and ovarian cancers. Heritable cancer syndromes should be suspected when several generations of a family are diagnosed with certain cancers at a relatively young age, or when several individuals in a family develop multiple primary cancers.

Ataxia-telangiectasis (AT) is a disorder characterized by increased malignancies, ataxias, and radiation hypersensitivity. The gene that is mutated in this syndrome is called ATM. The risk of cancer for individuals with 2 AT mutations is 60 to 180 times greater than that for the general population. Individuals with one ATM mutation are 5 times more likely to develop breast cancer than a mutation-free individual is.[33]

Cowden's disease (sometimes known as multiple hamartoma syndrome), also contributes to an increased risk of developing breast cancer. Individuals with Cowden's disease often have benign tumors made up of one or more normal skin or thyroid tissues or mucus membranes. Other abnormalities of the breast, such as fibroadenomas, areolar and nipple malformations, ductal epithelial hyperplasia, and fibrocystic lesions, have also been identified as related to Cowden's disease.[34]

Muir-Torre syndrome is a disorder thought to be associated with mutations in the MHL1 and MSH2 genes. Studies show that these genetic mutations confer an increased risk of developing breast cancer, especially for postmenopausal women. Muir-Torre syndrome is characterized by multiple benign and malignant tumors occurring in the skin, gastrointestinal tract, and genitourinary tract.[35]

First described in 1969, the mutations of the p53 gene have been linked to some families with the rare Li-Fraumeni syndrome. Such mutations are associated with soft tissue sarcoma, osteosarcoma, leukemia, brain tumors, multiple pulmonary neoplasms, and adrenocortical carcinoma. Individuals with p53 germline mutations are presumed to have a 50% risk of developing breast cancer; 25% of these are more likely to develop bilateral breast disease.

In 2002, researchers identified an altered gene, called CHEK2 or CHK2, which can double the estimated lifetime risk of breast cancer. About 1% of the United States population is believed to be carriers of the mutated gene. As with other gene mutations, carrying the gene does not necessarily mean that the carrier will develop breast cancer; however, his or her increased risk is comparable to individuals who have a mother or sister with breast cancer. The CHEK2 and CHK2 genes were identified in a United Kingdom and Netherlands study of 1,071-breast cancer patients who had not inherited the BRCA1 or BRCA2 gene. In this group, 5.1% of women and 13.5% of men had inherited a faulty version of CHK2, compared with 1.1% overall in the control group.

Peutz-Jeghers syndrome is an early-onset autosomonal dominant disorder characterized by both melanocytic macules on the lips, perioral, and buccal regions, and multiple gastrointestinal polyps, both hamartomatous and adenomatous.[17] Mutations in the STK11 gene at chromosome 19p13.3, which appears to function as a tumor suppressing gene, have been identified as one cause of PJS.[17] A large series of 419

patients with the syndrome have been reported to have a cumulative incidence of cancer of 85% by age 70 years, the cancer commonly affecting the gastrointestinal tract.[17] In addition, the cumulative risk of breast cancer was 31% by age 60 years; only 2 ovarian cancers were seen in this series.[17]

BRIP1 (also known as *BACH1)* encodes a helicase that interacts with the BRCT domain of *BRCA1***.**[17] This gene also has a role in *BRCA1*-dependent DNA repair and cell cycle checkpoint function.[17] Biallelic mutations in *BRIP1* are a cause of Franconi anemia, as are similar mutations in *BRCA2*.[17] Inactivating mutations of *BRIP1* are associated with an increased risk of breast cancer. [17] Over 3,000 individuals from *BRCA1/BRCA2* mutation-negative families were examined for *BRIP1* mutations.[17] PALB2 (a partner and localizer of *BRCA2*) interacts with the *BRCA2* protein and plays in role in DNA repair.[17] One of the ten families identified as having a *PALB2* mutation included a case of male breast cancer, raising the possibility that male breast cancer is included in the spectrum of *PALB2.*[17] Similar to *BRIP1 and CHEK2*, there was incomplete segregation of *PALB2* mutations in families with hereditary breast cancer.[17]

Psychosocial Issues in Inherited Cancer Syndromes

Psychosocial research in the context of cancer genetic testing helps to define psychological outcomes, interpersonal and familiar effects, and cultural and community responses.[17] It also identifies behavioral factors that encourage or impede surveillance and other health behaviors. [17] Information obtained through psychosocial research can enhance decision-making about risk-reduction interventions, evaluate psychosocial interventions to reduce distress and/or other negative sequelae related to risk notification and genetic testing.[17] Decisions about whether to pursue breast cancer genetic testing involve complex biologic, behavioral and social elements. [17] Factors that may influence uptake of testing include:

- Cost of genetic testing;
- How informative testing would be (e.g., presence of a known mutation in the family or ethnic group versus lack of identified mutation); and,
- Extent to which the genetic test results are likely to influence clinical decision-making.[17]

Motivations for testing include the belief that testing positive would increase one's motivation to get regular clinical breast examinations, to do breast self-exams, and to get recommended imaging studies (i.e., mammography, MRI, or US).[17] Additional motivations for testing is to receive information that would benefit other family members

and it may be recommended by a physician.[17] Limited data is available about the characteristics of at-risk individuals who decline to be or have never been tested. Although a majority of test decliners/deferrers in one study felt that their health was at risk, they reported learning about their status would cause them to worry about the following:

- Their children's health (This was reported as the main reason for worry.);
- Their life insurance;
- Their own health;
- Loss of their job; and,
- Receiving less screening if they did not carry a *BRCA1* or *BRCA2* mutation.[17]

Apprehension about the impact of the test result was a more important factor in the reason to decline than concrete burdens.[17] The literature in the area of risk perception, health beliefs, and personality characteristics is not extensive; however, the information available indicates that these are important factors in decision-making about breast cancer genetic testing. Women more so than men tend to be the prime communicators within families about the family history of breast cancer. Higher numbers of maternal versus paternal transmission cases are reported. This is likely due to family communication patterns, to the misconception that breast cancer risk can only be transmitted through the mother, and to the greater difficulty in recognizing paternal family histories because of the need to identify more distant relatives with cancer.[17] Physicians and counselors taking a family history are encouraged to elicit paternal as well as maternal family histories of breast, ovarian, or other associated cancers.[17] The NCI has found that the accuracy of reported family history of breast cancer varies; some studies found levels of accuracy above 90%, with others finding more errors in the reporting of cancer in second-degree or more distant relatives, or in age of onset of cancer.[17] A NCI study evaluated communication of test results to first-degree relations at 4 months post-disclosure and found women with a *BRCA* mutation more often share their results with their mother and adult sisters and daughters than with their father and adult brothers and sons.[17] Participants also were more likely to inform brothers of their test results if the *BRCA* mutation was inherited through the paternal line.[17] Another NCI study also concluded that women may find it difficult to communicate about inherited cancer risk with their partners and with certain relatives, especially brothers, because of those persons' own fears and worries about cancer.[17]

A study of Dutch men at increased risk of having inherited a *BRCA1* mutation reported a tendency for the men to deny or minimize the emotional effects of their risk

status, and to focus on medical implications for their female relatives. Men in these families, however, also reported considerable distress in relation to their female family members.[17] Some had increased distress and feelings of responsibility if their daughters developed breast cancer; however, more than half of male carriers of mutations did not adhere to the screening guidelines recommended after disclosure of genetic test results.[17] These findings are consistent with those for female carriers of *BRCA1/2* mutations.[17]

Counseling for breast cancer risk typically involves individuals with family histories that are potentially attributable to *BRCA1* and *BRCA2* mutations. It also may include individuals with family histories of Li-Fraumeni syndrome, ataxia-telangiectasia, Cowden syndrome, or Peutz-Jeghers syndrome. Management strategies for carriers may involve decisions about the nature, frequency, and timing of screening and surveillance procedures, chemoprevention, risk-reducing surgery, and the use of hormone replacement therapy.[17] Some of the psychosocial outcome studies involve specialized, highly selected research populations. Also, the few studies conducted to date about the psychological outcomes associated with genetic testing for mutations in breast cancer predisposition genes have shown low levels of distress among those found to be carriers and even lower levels among noncarriers.[17] A 1999 study found that an individual's response to learning his or her own *BRCA1/2* test result was significantly influenced by his or her gender and by the genetic result status of other family members.[17] Adverse, immediate outcomes were experienced by male carriers who were the first tested in their family or by noncarrier men whose siblings were all positive.[17] In another study, depression rates of post-disclosure were measured and also found that the distress of male subjects was highly correlated with the status of their siblings' test results or lack thereof.[17] Further, case descriptions have supported the importance of family relationships and test outcomes in shaping the distress of tested individuals.[17]

The Medical Record and Documentation

The medical record, health record, or medical chart is a systematic documentation of a patient's medical history and care.[36] Medical records are uniquely personal documents and there are many ethical and legal issues surrounding them, such as who has access to them and the proper storage and disposal of the records.[36] The medical record allows communication among health care providers, and contains critical evidence of the type and quality of care provided to the patient.[37] The 3 most recognized reasons for the medical record are:

- To document the diagnosis, treatment and progress of the patient;
- For business purposes; and,
- To use as legal documents.

According to a recent article in *Mayo Clinic Women's HealthSource,* electronic personal health records are likely to replace handwritten notes.[38] During Barack Obama presidency, his goal was to make electronic medical records a priority.[39] One of the major roadblocks is finding the right technology to handle the transition to paperless medical records. Among the many challenges are the storing, accessing, and updating of records so that the patient's privacy is maintained yet the information is accessible across a wide network of medical providers.

The medical record serves as the basis of the quality and timeliness of the care provided to the patient. The record also serves as a legal document, and is often cited in malpractice litigation. In the first two-thirds of the 20th century, the most common reasons for malpractice were negligent acts of commission (i.e., physicians did something wrong).[40] Medical care providers were often charged with the failure to order radiologic studies in a timely manner. The litigation involved what is referred to as "omission of care." Defensive medicine, in which medical care providers ordered tests and procedures that were not indicated medically, but which if absent might render the physician vulnerable in malpractice litigation, became the norm.[40,41] The annual cost to the nation for defensive medicine has been estimated to range from $25 billion to $126 billion.[40]

Radiologists specializing in breast imaging are subject to litigation for "failure to diagnose cancer" and "failure to follow up," or failure to obtain additional diagnostic studies to clarify or confirm the tentative diagnosis, when appropriate.[40] It is anticipated that as the sophistication of radiologic and nonradiologic procedures and tests continues to expand, the errors caused by physicians' omission in ordering or using this technology will increase.[40] Radiologists can expect to be more frequently sued not only for failing to recommend imaging tests, but for failing to recommend other diagnostic procedures as well.[40] One may also speculate that in the not-so-distant future, radiologists will likely be subject to litigation for errors in omitting the use of technology that is not yet the standard of care, such as computer-assisted detection (CAD) and teleradiology, when obtaining expert consultations.[40] Conscientious review of the patient's medical history and clinical findings in conjunction with the mammography request is a first step in providing quality patient care, and hopefully, in reducing future litigation.

The mammographer plays a critical role in reviewing the patient's medical history and clinical symptoms prior to mammography. The mammographer documents information in the patient's medical record and is the liaison between the patient and the radiologist. Radiologists have a duty to acquaint themselves with the pertinent clinical information concerning patients whose mammograms they will be interpreting.

In many breast imaging centers, it is the mammographer who questions the patient and completes a preprinted questionnaire form.[41] If this is the procedure used, the mammographer should have the patient or her advocate review, sign, and date the questionnaire form. Risk management experts recommend that a written form on which the patient must provide (i.e., write) pertinent clinical information is the most reliable source document.[40,41] Although it is acceptable practice for the mammographer to complete the information on the questionnaire form, there may be less likelihood of misunderstanding if the patient herself fills out the form.[40] The mammographer can then go over the completed form and obtain additional verbal confirmation from the patient. If the patient fills out the form, the mammographer should document that the completed questionnaire was reviewed, and that the patient confirmed the answers. Such notations in the record should be signed and dated.

A system that ensures that every patient undergoing mammography provides a complete medical history, possible symptoms, and clinical signs is critical to obtaining high quality breast images. Risk management experts also suggest that the questionnaire form have a question about the patient's understanding of why she is having the mammography procedure.[40] By asking these pertinent questions, the mammographer is able to determine if the mammography request properly matches the patient's clinical signs and symptoms, or if the procedure is merely a screening examination. To reduce the possibility of a missed cancer, every effort must be made to distinguish diagnostic patients from screening patients. Risk management experts suggest that this should be done repeatedly, beginning at the appointment setting, when the patient arrives at the reception desk, and finally by the mammographer before the examination begins.

In the *Practice Standards for Medical Imaging and Radiation Therapy: Mammography Practice Standards*, the American Society of Radiologic Technology (ASRT) provides guidance about the mammographer's involvement in the documentation. Standard One Assessment states that the practitioner (i.e., the mammographer) should collect pertinent data about the patient and the procedure.[42] The ASRT Standard Two, Analysis/ Determination, and Standard Eight, Documentation, further address the mammographer's role and responsibility.[42] The mammographer is

generally the first to review the reason for the mammography examination and to determine if the request is appropriate based on the presenting facts. In this capacity, the mammographer has a professional responsibility to confer with the radiologist about the appropriateness of the imaging request, and to decide if additional projections are required. There are 3 recognized ways that a mammography examination can be designated diagnostic rather than screening. These include:

- History from the referring physician;
- History from the patient; or,
- Conversion of a screening mammogram into a diagnostic mammogram by the radiologist because of the presence of abnormal findings.[41]

When taking the patient's medical history or confirming what the patient has written, the mammographer should be able to use the information about risk factors, as well as the "red-flag" indicators of breast disease and initiate further health history questions. Such factors include a family history of breast and ovarian cancer, previous breast surgery or interventional procedures, previously diagnosed benign or malignant breast lesions, skin changes, or changes in the palpable consistency of the breast. During the mammography procedure, the mammographer should be attentive to visible breast changes in the skin, nipple and breast texture. Any unusual signs or symptoms should be documented and conveyed to the radiologist. The following section covers commonly encountered and unusual benign breast conditions and lesions.

Genetic Information Nondiscrimination Act (GINA)

In 2008, the Genetic Information Nondiscrimination Act (GINA) became federal law.[32] GINA prohibits discrimination based on genetic information related to health insurance and employment, but the law does not cover life insurance, disability insurance, and long-term care insurance.[32] Genetic discrimination occurs when people are treated differently by insurance companies or employers because they have a gene mutation that increases their risk of a disease.[32] Certain parts of GINA relating to health insurers will take effect between May 2009 and May 2010, and those relating to employers will take effect by November 2009.[32] Some of the protections available under GINA include:

- Premiums or contributions to a group health plan cannot be increased based on the genetic information of an individual enrolled in the plan;
- Insurers cannot require an individual or family member to undergo a genetic test before enrollment in a group health plan;

- Insurers cannot request, require, or purchase genetic information about an individual before the person's enrollment in a group health plan, or in connection with that person's enrollment in the plan;
- Health insurers cannot use genetic information as the only basis upon which to claim a pre-existing condition is present and therefore deny coverage;
- Employers cannot refuse to hire, and cannot fire, individuals based on their genetic information;
- Employers cannot discriminate against employees with regard to salary, terms and conditions of employment, privileges, and opportunities for the future because of their genetic information;
- Employers cannot request, require, or purchase genetic information about an employee except under specific conditions; and,
- Employers cannot disclose an employee's genetic information except under specific circumstances.[32]

Basic Facts about Cancer

The occurrence of cancer increases with age, generally affecting adults beginning in their middle years. Nearly 77% of all cancers are diagnosed at age 55 or older.[30] Cancer is the body's loss of control over cellular growth. This loss of control results from an increase in growth-stimulating signals, or from a decrease in either growth inhibiting or growth differentiation-inducing signals. All cancers involve the malfunction of genes that control cell growth and division. About 5% of all cancers are strongly hereditary, with the remainder resulting from damage to genes during one's lifetime.[30] Cancer usually begins in a single cell and progresses through three distinct stages that includes initiation, promotion, and progression.

Initiation of cancer occurs when the cell's deoxyribonucleic acid (DNA) sustains irreversible damage. Hyperplasia and excessive multiplication of the cells characterize promotion, the second stage. Progression occurs when the cell is subject to genetic mutations and malignant replication by its descendents.[43] Cancer researchers explain risk by using terms such as lifetime risk and relative risk. Lifetime risk refers to the probability that an individual, over the course of a lifetime, will develop cancer or die from it. In the United States, men have slightly less than a 1 in 2 lifetime risk of developing cancer; for women, the risk is a little more than 1 in 3.[18] Relative risk is a measure of the strength of the relationship between risk factors and the particular cancer; it compares the risk of cancer developing in persons with a certain exposure or trait to the risk in persons who do not have this exposure or trait.[18]

Over the past 3 decades, the development of screening tests that prevent and detect some cancers at an early, more treatable stage, and treatment advances have increased the 5-year survival rate for all cancers combined from 50% in 1975-1977 to 66% in 1996-2004.[18] The National Cancer Institute (NCI) estimates that approximately 11 million Americans with a history of cancer were alive in 2005, more than 3 times the number in 1970.[18] Some of these individuals were considered cancer-free, while others still had evidence of cancer, and may have been undergoing treatment.[18] About 1,479,350 cancer cases are expected to be diagnosed in 2009 (statistics for any current or prior years may be found on the website www.acs.org).[18] This estimate does not include carcinoma *in situ* (non-invasive cancer of any site except urinary bladder, and does not include basal and squamous cell skin cancer).[18]

Cancer is the second leading cause of death in the U.S., exceeded only by heart disease.[18] In the United States, nearly 1 of every 4 deaths is cancer related.[18] The 5-year relative survival rate for all cancers diagnosed is 60%.[18] After adjusting for normal life expectancy, the 5-year relative survival rate represents persons who are living five years after diagnosis, whether disease-free, in remission, or under treatment with evidence of cancer. While 5-year relative survival rates are useful in monitoring progress in the early detection and treatment of cancer, they do not represent the proportion of people who are cured permanently, since cancer can affect survival beyond five years after diagnosis.[18]

Because of the increasing number of cancer survivors the medical community have expressed concerns about how to best meet the survivor's unique needs.[30] Examples of these include the need for regular medical surveillance, continuity of care, and dissemination of information about how a particular cancer and its treatment may affect future health.[30] Of the 11 million cancer survivors living in the United States as of January 1, 2005, approximately 880,300 had been diagnosed with more than one cancer.[30] Most of these second or more cancers would be expected to occur even if cancer survivors had the same risk of cancer as the general population. The ACS uses the following to determine the definition of multiple primaries.[30]

- A cancer of a different site and histologic (microscopic composition of cells and/or tissue) type than the original cancer is considered a separate primary.
- Cancers of a different histologic type in the same site are considered separate primaries regardless of whether they are diagnosed at the same or different times.
- A new cancer of the same site or with the same histology as an earlier one is considered the same primary cancer if diagnosed within 2 months, or a separate

primary cancer if diagnosed after 2 months, unless the medical record specifically states that it is recurrent or metastatic disease.

- If an organ is paired, each member of the pair is generally considered to be a separate site.
- Important exceptions to these general rules include most histological types of cancer in the prostate and urinary bladder, for which multiple tumors are reported as a single primary with the date of the first invasive lesion.
- A different set of rules is used to determine multiple primaries of the lymphatic and hematopoeitic systems.[30]

A recurrence of cancer can be distinguished from a second primary cancer in the following ways. A second (or multiple) primary cancer is the occurrence of a new cancer that is biologically distinct from the original primary cancer.[30] The determination of whether a new cancer is a separate primary or a recurrence, or metastasis, of the original cancer is important clinically, because it influences staging procedures, prognosis, and treatment.[30] This determination usually involves a combination of pathological, clinical, and in some cases, additional laboratory studies. Physicians may also use information about typical patterns of recurrence and common sites of metastases for the first cancer in making a diagnosis. When the analysis is unclear, molecular and cellular laboratory tests may be used to analyze the DNA of cells from both the original and the new tumor to determine if they have a common origin. Tumor registries rely on the information in the medical record to determine whether a cancer is a recurrence, or metastasis, of a previously treated cancer, or a new cancer. [30]

The ACS estimates that 880,300 cancer survivors who have been diagnosed with more than one cancer were living in the United States as of January 1, 2005.[30] Among men who have been diagnosed with more than one cancer, the 10 most common are prostate, colon and rectum, urinary bladder, melanoma, kidney and renal pelvis, oral cavity and pharynx, lung and bronchus, non-Hodgkin lymphoma, leukemia and thyroid cancer.[30] Among women who have been diagnosed with more than one cancer, the 10 most common are breast, colon and rectum, uterine corpus, melanoma, lung and bronchus, thyroid, ovary, urinary bladder, non-Hodgkin lymphoma, and uterine cervix cancer .[30] Two of the factors that are strongly related to the development of a second primary cancer include the site of the first primary tumor and the person's age at initial diagnosis.[30]

Aside from familial cancer syndromes and genetic susceptibility factors, some of which have been discussed previously, there are other factors that have been implicated

in the development of multiple primary site cancers.[30] Individuals may be at increased risk of developing multiple primary cancers due to exposure to several risk factors, such as the use of tobacco and alcohol. Hormonal factors play an important role in the development of female breast cancer and several cancers of the female reproductive system. Immunodeficiency syndromes, either acquired or inherited, are associated with an increased risk of non-Hodgkin lymphoma and some other cancers.[30] Patients receiving immunosuppressive therapy after kidney transplants are at increased risk of developing non-Hodgkin lymphoma, Kaposi sarcoma, and squamous cell cancer on sun-exposed areas of their skin. Suppression of the immune system may predispose a person to other forms of skin cancer, including malignant melanoma. Individuals with human immunodeficiency virus (HIV)-related immunodeficiency are at increased risk of non-Hodgkin lymphoma, Kaposi sarcoma, and cervical and anal cancer.[30]

Human papillomavirus (HPV) infections are the main cause of cancer of the uterine cervix, and have been implicated in other cancers of the anogenital tract (vulva, vagina, perineum, anus, and penis) for which there is evidence for mutually increased risk.[30] There is also a growing body of evidence supporting the theory that HPV, especially HPV-16, may be one of the causes of oropharyngeal cancers.

Cancer treatments can damage normal cells resulting in short-term and long-term side effects, including an increased risk of subsequent cancer years or decades later.[30] When weighing the risks and benefits of treating the first cancer, the physician must consider the risks of developing a second cancer. The second cancers associated with radiation therapy include acute leukemia, chronic myelogenous leukemia, breast, lung, thyroid, and non-melanoma skin cancers.[30] Second cancers of the bone and connective (soft) tissues occur within or adjacent to the irradiated area among patients treated with high-dose radiation. Several factors are related to the risk of radiation-induced cancers including the dose and type of radiation, radiosensitivity of exposed tissues, and individual inherent susceptibility factors. The risk is generally higher when developing tissue is exposed at a young age. Both radiotherapy and chemotherapy can cause treatment-related leukemia.

Recommendations exist for identifying men and women with primary breast cancer who have hereditary syndromes that increase their risk of developing multiple primaries.[30] Both the American Society for Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) have published guidelines for follow-up with men and women after treatment for breast cancers. These guidelines recommend regular physician visits, including history and physical examination and annual diagnostic mammography. MRI, US, positron emission tomography (PET), and bone

scan examinations may also be indicated for specific individuals, following their breast cancer treatment.[30]

The National Institutes of Health (NIH) estimate that overall cancer treatment costs in the year 2008 were $228.1 billion. The distribution of this cost was $93.2 billion for direct medical costs (total of all health expenditures), $18.8 billion for indirect morbidity costs (cost of lost productivity due to illness), and $116.1 billion for indirect mortality costs (cost of lost productivity due to premature death).[30] Lack of health insurance and other barriers prevent many Americans from receiving optimal treatment.[18]

The American Cancer Society has issued a 2015 challenge, which seeks to eliminate disparities in the cancer burden among different segments of the United States population. The ACS recognizes that the causes of health disparities are complex and interrelated, but likely arise from socioeconomic disparities in work, wealth, income, education, housing, and overall standard of living. Economic and social barriers to high-quality cancer prevention, early detection, and treatment services, as well as the impact of racial and ethnic discrimination, are all factors related to these disparities.[18] Some of the facts regarding these disparities include the following:

- African Americans are more likely to develop and die from cancer than any other racial or ethnic group;
- Hispanics have lower incidence rates for all cancers combined, as well as lower incidence rates for the most common types of cancer, in comparison to whites, but have higher rates of cancers associated with infection, such as uterine, cervix, liver, and stomach cancers;
- Asian Americans and Pacific Islanders have lower incidence rates than whites for the most common cancer types, but have a higher incidence of many of the cancers related to infection;
- American Indians and Alaska Natives have mortality rates for kidney cancer that are higher than those in any other racial or ethnic population; and
- Socioeconomic status is highly correlated with both cancer risk and outcomes from prevention to palliative care.[18]

The ACS states that scientific evidence suggests that about one-third of the cancer deaths that occur in the United States each year are due to nutritional and physical inactivity factors, including excess weight.[18] Furthermore, for the majority of Americans who do not use tobacco, dietary choices and physical activity are the most important modifiable determinants of cancer risk.[18] The ACS's most recent guidelines

emphasize the importance of weight control, physical activity, and dietary patterns in reducing cancer risk. To review, the ACS recommendations for individual choices include the following:

- Maintain a healthy weight throughout life;
- Adopt a physically active lifestyle;
- Limit alcohol consumption; and,
- Consume a healthy diet, making sure to consume vegetables and fruits.[18]

The American Cancer Society provides a 24-hour information cancer resource network and can be accessed online at cancer.org and through a call center (1-800-227-2345).

General Cancer Facts

Cells that form cancerous growths are characterized by uncontrolled growth. Cancer cells do not necessarily reproduce more rapidly than normal cells, but they fail to respond to the normal signals to stop reproducing. They also do not respect tissue boundaries, and invade adjacent areas. Cancer cells tend to be less well-developed, or differentiated, than normal cells; they are unable to perform the functions of normal, mature cells. The nuclei of cancer cells appear irregular and enlarged, and grow in a disorderly fashion, with no regard for the spatial patterns typical of healthy tissue.

A key characteristic of cancer cells is their ability to break off from the tumor, travel through the bloodstream or lymph vessels, and establish a new growth at remote sites, a process referred to as metastasis. Not every abnormal growth is cancerous, however; benign tumors, unlike cancer, do not infiltrate neighboring tissue and do not metastasize. If a benign tumor creates a health problem because of its bulk or location, it can usually be removed completely, and it is not likely to recur.

The specific cellular events that trigger the transformation of a normal cell into a cancerous cell are still unknown, but the development of cancer within an individual appears to depend on a complex interplay of genetic and environmental factors. As mentioned previously, genetic factors might make some persons particularly susceptible to cancer-causing agents, influencing critical internal factors such as hormonal responses and the overall responsiveness of the immune system. The etiology of male breast cancer remains virtually unknown. Both genetic and environmental factors appear to contribute to its development. In females, one explanation may be hormones, which induce changes in breast tissue, also influencing the course of female breast cancer. However, in males the hormonal influence is less distinct. Breast cancer can take many forms and follow many different paths. Tumors developing from one type of

breast tissue do not necessarily look or act like those from another type of breast tissue. Some breast cancers grow rapidly; others evolve over many years. Breast cancer is almost always a disease of women, with less than 1% of all breast cancers occurring in men.

Signs and Symptoms

Breast changes can be either benign or malignant, and must be thoroughly investigated before being designated as benign.

Specifically, the term benign breast lesion refers to any palpable lump or image-detected abnormality that has been biopsied and found not to contain cancer cells. Benign breast conditions are very common in women but are very rare in men. Unlike malignant breast conditions, benign lesions are never life-threatening.[17]

In males, cases have been reported where mammograms were interpreted as normal, but where the pathologic diagnoses were lipoma, fat necrosis, adipose tissue, and hematoma.[43] Other benign breast lesions that have been reported to occur in males include epidermal inclusion cyst, subcutaneous leiomyoma, subareolar abscess, intraductal papilloma, pseudoangiomatous stromal hyperplasia, and lymph nodes.[44]

Most men referred for breast imaging have palpable masses, breast enlargement, or tenderness.[13] All suspicious breast masses and complaints are usually first evaluated with mammography, and for lesions that are difficult to image with mammography, ultrasonography (US) is often helpful for additional characterization.

Although the appearance of the margins and shape of the lesion are important indicators of whether the lesion is benign or malignant, they are just indicators until proven otherwise. Many benign lesions, such as radial scars, abscesses, postoperative scars, fat necroses, and hematomas, can mimic malignant lesions. Likewise, some malignant lesions, such as invasive ductal carcinoma (IDC), medullar carcinoma, mucinous carcinoma, fibrosarcoma, lymphoma, primary or secondary pseudolymphoma, and metastasis, can mimic benign lesions.[45]

A capsule appears on mammography as a thin radiopaque line surrounding a mass. An encapsulated mass is most often benign.[45] The silhouette sign is another indicator of a benign process. A silhouette sign appears as lines running through the middle of a suspicious area of the breast. If the lines are seen to run into, through, and out of the lesion, this represents silhouetted structures in front of or behind the lesion. Recognizing a true silhouette sign also can help determine if a suspicious lesion has a spiculated border. If a mass is spiculated, the lines radiating from it will disappear in the middle of the abnormality, which is a strong indicator of malignancy.[45]

> ***Spiculation*** *of a lesion usually represents a malignancy. A lesion with spiculations has a distinct solid center and sharp lines of variable lengths radiating in all directions away from the center. Usually the spicules are not bunched together, and the larger the central core of the tumor, the longer the spicules.*

A halo is a sign that appears as a thin, radiolucent curved line on the mammographic image. A halo represents the edge of a mass which is compressing the surrounding fatty tissue.[45] A halo sign is strongly indicative of a benign process. Although rare, the halo sign can occur in certain malignant processes.[45]

Nipple discharge or pain physically discloses many of the benign breast diseases, while some are only detected during mammography, MRI, or US. Any history of nipple discharge and pain should be investigated.[7] Depending on the imaging modality, breast lesions will manifest with skin thickening, calcifications, asymmetric densities, or circumscribed masses.[45] Both benign and malignant breast lesions can be placed in one of 5 categories:

- Circular or oval;
- Stellate or spiculated;
- Calcifications;
- Thickened skin syndrome; and,
- Any combination of the 4 listed above.[45]

Certain types of benign breast conditions have been labeled as risk markers. Investigators have suggested that individuals with risk marker lesions have an increased associated risk of developing breast cancer.[12] Until recently there was insufficient epidemiological data to prove or disprove this association. Findings from a study of 9,087 women, led by the Mayo Clinic Cancer Center (July 21, 2006 issue *of The New England Journal of Medicine*) adds evidence to a growing body of knowledge that shows that individuals with benign breast disease have a higher risk of breast cancer. The researchers suggest that the evaluation of benign lesions include such considerations as age at benign biopsy, family history of breast cancer, and the pathologic findings of the benign lesion.[10,46]

Symptoms of male breast cancer may include a breast lump, swelling, skin dimpling or puckering, nipple retraction, redness or scaling of the nipple or breast skin, and nipple discharge.

The physical appearance of the breast can aid in the diagnosis of both benign and malignant lesions, and the following summarizes the diagnostic implications of various physical presentations:

Erythema (redness) and edema (skin thickening) are both physical skin changes. Erythema of the skin may be localized to one area of the breast or include the entire breast. Erythema is associated with infection, abscess, and inflammatory carcinoma; however, it is also associated with other types of carcinomas and benign conditions.[11] Edema is caused by the development of fluid within the skin and interstitial spaces, and causes the skin to develop the appearance of an orange peel (‘peau d’orange).

> ***Peau d’orange*** *describes the skin of the breast when it thickens and develops prominent pores causing it to resemble the skin of an orange. The condition is caused by obstruction of the axillary lymphatics, and may be either a benign or malignant condition (i.e., inflammatory carcinoma).*

The presence of edema can indicate an infection, carcinoma, or systemic disease which manifests by fluid retention in the breast.[11] Both erythema and edema may be present following radiation treatment for breast cancer. Nipple inversion can be developmental; however, sudden inversion can indicate the presence of a tumor.[11] Eczematous changes such as reddening, flaking, and crusting of the nipple may be benign, but are also symptoms associated with Paget’s disease of the nipple.

> ***Paget’s disease*** *is an inflammatory disease of the nipple. The actual appearance of the nipple varies with the extent and stage of the disease. Paget’s disease accounts for approximately 1-5% of all breast carcinomas.*[11]

Nipple discharge may vary in color from yellow to white to green to brownish. The color of the discharge is less important than its occurrence in one or both breasts, and whether it occurs spontaneously or is expressed.[11] Bloody or clear, watery discharge may be indicative of either papilloma (benign tumor) or carcinoma.[11] A clear, watery discharge is more indicative of carcinoma than any other color.[11] Any spontaneous nipple discharge always requires further investigation.

Normal architecture of the breast consists of ductal structures. These structures, while not individually evident mammographically, present a pattern of radial lines that converge at the nipple. Architectural distortion may be present with benign and

malignant disease processes, occurring with both masses and calcifications.[45] Breast surgery, injury, resolving hematoma, and radial scar may also be evident as architectural distortion.[45] The parenchyma of both breasts should be smooth in outline, devoid of asymmetric bulging or "pulling in".[45] The contour, or shape, of both breasts should be symmetrical. Any bulging, dimpling, or retraction of the skin can indicate an underlying pathological process, either benign or malignant.[45] The breasts should move symmetrically when the patient slowly raises the arms. Any differences in breast movement can indicate an underlying pathological process and require further investigation.

Breast pathology is seen in mammography as a mass, calcification, or diffuse accentuation of the glandular tissue.[10] These manifestations may only be made apparent by indicators such as asymmetry, architectural distortion, and/or changes in contour of the parenchyma.[10] Secondary mammographic signs may include dilated ducts, dilated veins, and skin thickening.[10] Their presence is an important diagnostic marker, and requires further investigation. Asymmetry of the parenchyma is the greatest aid in determining breast abnormalities, both benign and malignant.[45] The breasts are mirror images, and the distribution of glandular tissue should appear the same with only minor variation. A disproportionate amount of tissue in any area of the breast requires further investigation.

Findings of breast asymmetry often are seen during screening and diagnostic mammography. Because there has been some confusion about the proper use of the term "asymmetry" in describing this deviation, the 4th edition of the American College of Radiology Breast Imaging and Reporting and Data System (BI-RADS) has incorporated changes. In the BI-RADS lexicon for asymmetric breast findings, in order to correct any misuse and improve clinical standardization of reporting, the 4th edition has replaced the following:

- Asymmetric breast tissue with global asymmetry;
- Density seen in only a single projection with asymmetry; and,
- Focal asymmetric density with focal asymmetry.[47]

> ***Focal asymmetry*** *is visible as a confined asymmetry with a similar shape on two views but does not fit the criteria of a mass (i.e., lacks convex outer borders and conspicuity).*
>
> ***Global asymmetry*** *occupies a volume of less than one quadrant of the breast. This finding is almost always benign and requires no additional evaluation if there*

are no corresponding palpable abnormalities, architectural distortions, significant calcifications, or masses. This type of asymmetry may indicate the presence of an underlying breast cancer if it corresponds to a palpable abnormality.[47]

Developing asymmetry *is a focal symmetry that is new, larger, or denser at current examination than at previous examinations. To identify such lesions, comparison with at least 2 years previous mammograms is critical. A developing asymmetry that cannot be accounted for by differences in imaging technique, positioning, or weight loss, HRT, surgery, trauma, or infection at the site should raise suspicion.*[47]

The American College of Radiology (ACR) recommends that once an asymmetric finding is seen, it should be determined whether that finding is due to a definite lesion.[47] Additional imaging studies such as straight lateral views, rolled views, and spot compression views at mammography, MRI, or US should be applied in a logical manner.[47]

Exact breast positioning will vary from one examination to the next, but regions of asymmetry should be seen in at least one view on later examinations. The concern is that not all breast cancers form a mass visible at mammography, and there is the potential for the radiologist to dismiss asymmetries because a mass is not evident. Conventional breast positions may not provide sufficient information for the proper evaluation of asymmetry findings.

For additional evaluation of asymmetry seen on one projection, it is recommended to return to that projection and alter it slightly to determine whether the finding is real. A real lesion is unlikely to change its appearance.[47] A straight lateral view should be obtained for an asymmetry seen only on a mediolateral oblique (MLO) view. A rolled view should be taken for an asymmetry seen only on a craniocaudal (CC) view. Spot compression views, rolled views, or views with altered x-ray tube angles may help spread or reorient tissue structures to help define and characterize asymmetries.[47]

To obtain a rolled view, the mammographer should gently rotate the breast around the axis of the nipple and recompress it in this new orientation. Using the rolled view to determine the presence of a lesion, the mammographer should direct the roll so that the area in question is rolled toward and projected over an area of fat and not over dense tissue, which may obscure the lesion.

A spot compression view with and without magnification is a common method used for evaluating asymmetry. By applying vigorous compression to a target area,

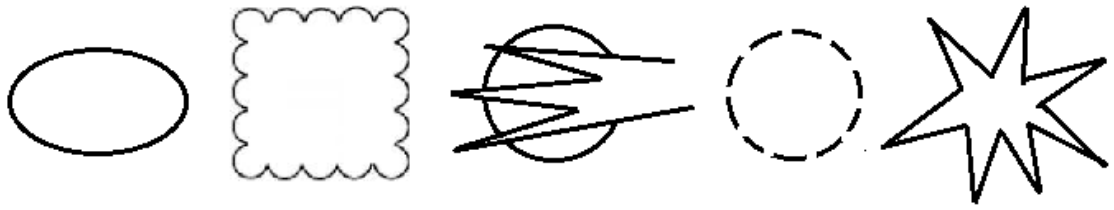
normal fibroglandular tissue is more likely to spread apart whereas a true abnormality will retain its characteristics. It is always advisable to obtain spot compression in two projections since even true abnormalities may spot compress away. There are some disadvantages to using the spot compression view and these include the following:

- It is generally obtained in the same projections as are used in standard mammography, and may produce the same superimposition of structures; and,
- The focal compression can roll or squeeze the abnormality out of the field of view.

When mammography or palpation can determine the location of a lesion, targeted US is indicated and valuable. If the location cannot be established, ultrasonography is unreliable in evaluation of areas of breast asymmetry. The role of MRI for assessment of asymmetric breast findings has not been established.[47]

Characteristics of Benign and Malignant Breast Lesions

The Breast Imaging Reporting and Data System™ (BIRADS™), defines a mass as a space-occupying lesion seen in two different projections, and a possible mass as a lesion seen in only one projection. Borders, margins, and the overall shape of breast masses are important diagnostic indicators of whether the lesion is benign or malignant. The margins of a lesion may be circumscribed, microlobulated, obscured, indistinct, or spiculated (Figure 5).



Circusmscribed Microlobulated Obscured Indistinct Spiculated

Fig. 5. Examples of lesion margins. Courtesy drawing DG Moore Consulting.

The shape of a lesion can be round, oval, lobulated, or irregular (Figure 6). A circumscribed border on a lesion strongly indicates a benign condition, whereas a spiculated border is an indication of malignancy.

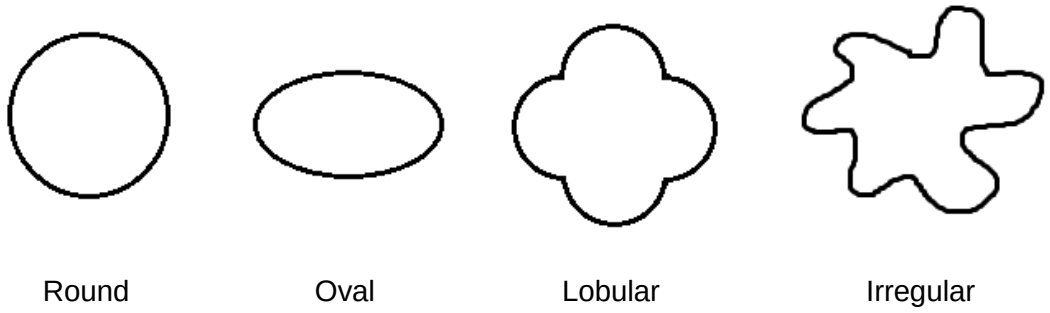


Fig. 6. Common shapes of breast masses. Courtesy drawing DG Moore Consulting.

Part 3 Benign and Malignant Breast Disease

Disclaimer *concerning facts and statistics in the following discussion of benign and malignant breast diseases and conditions. Males are subject to both benign and malignant diseases and conditions of the breast. Because male breast cancer is rare, there has been minimal investigation into its etiology, diagnosis, and treatment. Most guidelines for the treatment of male breast cancer are based on research gathered about female breast cancer. The facts and statistics presented about benign breast diseases and breast cancer are based on cancers in women unless otherwise specifically stated as cancers which have occurred in men. Every attempt was made to find the most recent information about the male breast; however, in some areas, very little information exists.*

Benign Breast Disease

Recognizing that certain breast conditions are associated with breast changes is important for careful correlation of the patient's history with the breast images and cytological examination of tissue. Benign breast diseases, in some cases, may be clearly grouped into well-defined categories, such as benign calcifications, benign cysts, inflammatory and reactive breast disorders, masses and tumors, disease processes, and common and unusual diseases of the nipple-areola complex. Some benign breast diseases cross-definitional boundaries and may easily be recognized in more than one category. Then there are the rare and unusual breast diseases and conditions that elude all categories. Benign breast conditions that have been documented in men include gynecomastia, lipoma, fat necrosis, hematoma, epidermal inclusion cyst, subcutaneous leioyoma, subareolar abscess, intraductal papilloma, and pseudoangiomatous stromal hyperplasia.[16]

Gynecomastia

Gynecomastia is the most common benign breast condition in males, and affects about a third of all males at some point over the course of their lifetimes.[16] Gynecomastia is not a tumor, but rather refers to an increase in the amount of breast tissue. The amount of breast tissue that can be palpated is normally much smaller in men than in women. A male with gynecomastia has a button or disk-like growth under the nipple and areola that can be palpated and may be visible. Gynecomastia is much more common than breast cancer in men; however, any increase in breast tissue must be evaluated before being diagnosed as benign.

Gynecomastia is common among teenage boys and older men due to changes in the balance of hormones in the body. In rare cases, gynecomastia occurs because tumors or diseases of certain endocrine glands result in the abnormal production of

estrogen. Certain diseases of the liver can also create imbalances in male hormonal levels and lead to gynecomastia.[16] As previously mentioned, obesity, Klinefelter syndrome, and certain medications leading to male hormonal imbalances can also cause gynecomastia.

Although gynecomastia may mimic (and even mask) malignancy, in mammographic images it usually appears as benign nodular lesions. In mammography, all lucent lesions of the male breast appear to be benign. Three mammographic patterns of gynecomastia have been identified: nodular, dendritic, and diffuse.[44] Nodular gynecomastia appears mammographically as a fan-shaped density emanating from the nipple and gradually blending into surrounding fat. The nodular appearance may be symmetric or more prominent in the upper, outer quadrant of the breast.[44] Dendritic gynecomastia appears on the mammographic image as a retro-areolar soft-tissue density, with prominent extensions that radiate into deeper adipose tissue.[44] Diffuse gynecomastia appears in mammography to be similar to that of a heterogeneously dense female breast.[44]

Benign Calcifications

Breast calcifications play a primary role in the detection of first-time breast cancers, and also in evaluating women who have had breast-conserving therapy.[48] Breast calcifications are rare in males; however, incidences have been reported to occur in this population. Mammography is the first imaging modality of choice to screen the entire breast for calcifications. Ultrasound is capable of demonstrating calcium deposits within the breast, but is used only as a diagnostic examination after an abnormality has been identified mammographically.[48]

Calcifications must be thoroughly investigated before being pronounced benign or malignant. This includes review of the medical history, comparison with prior imaging studies, and if necessary, biopsy, cytology, and pathology examinations. Benign calcifications include those resulting from fat necrosis, radiation therapy, and a number of disease processes.

Dermal Calcifications

Dermal calcifications are also referred to as skin calcifications, and are actually calcifications within sweat glands.[49] Generally the patient is asymptomatic, but if the calcifications are of significant size, they may be palpable.[49]

Dermal calcifications classically appear with a lucent-center, and they may be grouped, scattered, polygonal, or spherical.[49] Skin calcifications are located within the

cutaneous sweat glands, most commonly along the medial aspect of the breast, and may range in size from 1-2 mm.[49] Dermal calcifications are very common, and have no clinical significance.

Dystrophic Calcifications

Dystrophic calcifications are also referred to as heterotopic or postoperative calcifications. They are generally benign and may be very extensive.[48]

General imaging clues are large, irregular calcifications with lucent centers located adjacent to a scar (from a previous surgery). Dystrophic calcifications may also be subcutaneous. Imaging recommendations should correlate with the clinical history for an accurate diagnosis. Magnification views may aid characterization of the calcifications. Post-lumpectomy mammographic findings include focal skin tethering and distortion (scarring) with irregular, large calcifications. Post-radiotherapy mammography images usually show limited, small numbers of dystrophic calcifications that may be very extensive, involving the chest wall and subcutaneous tissues.[49]

Ultrasound findings illustrate dense echogenic foci associated with hypoechoic scar. Large calcifications may show posterior shadowing in ultrasound images. No specific findings are demonstrated in MRI, but there may be moderate enhancement with post-operative scarring. Additional investigation of dystrophic calcifications is suggested if there is a suspicion of malignancy; however, there is no known increased potential for malignancy.[49]

Fat Necrosis

Fat necrosis is defined as a benign, nonsuppurative, inflammatory process of the breast related to trauma or surgery.[48] Examples of such accidental trauma include a direct hit to the thorax, or seatbelt injury. Iatrogenic trauma includes breast surgery, radiation therapy, and direct injection of silicone into the breast. Spontaneous development has been reported in those with diabetes and collagen vascular disease.[49] Fat necrosis most commonly occurs in the subareolar and superficial areas near the skin. It can occur at any age and has been documented to occur in males.

Patients with breast fat necrosis may be asymptomatic, with the condition being discovered only in screening mammography. Symptomatic patients may present with a tender, palpable mass or masses; the mass may be firm and fixed, with associated skin thickening and retraction.[48] Ecchymosis and/or edema of the breast may also be present. Fat necrosis may resemble infiltrating ductal or lobular carcinoma, ductal carcinoma in situ (DCIS), lipoma, or steatocystoma multiplex.[48]

Mammographic findings show a spiculated area of increased density with prominent fibrosis. Calcifications may be either pleomorphic (branching, rod-like, angular) or dystropic (coarse, lucent-centered, eggshell-like).[49] Ultrasound is beneficial if the mammographic findings are negative or inconclusive. Ultrasound imaging generally reveals an irregular, hypoechoic mass with a variable enhancement pattern. An anechoic mass will be circumscribed, round to oval, with variable posterior acoustic features.[49] There may also be distortion in the normal breast architecture.
No treatment is necessary for fat necrosis. If the mass is painful, excision may be a suggested treatment. The prognosis for fat necrosis is excellent, with no malignancy potential.[49]

Benign Cysts

A simple breast cyst is a fluid-filled round to oval structure containing an epithelial cell lining and eosinophilic contents.[48] The peak prevalence for breast cysts occurs between the ages of 35-50, and are rarely found in males.[48] The etiology of cysts is thought to arise from obstructed ducts, dilatation of terminal ducts within lobules, or imbalance between secretions and absorption.[48] Cysts may contain calcifications.[48]

On physical examination, a cyst will be soft and freely movable. The patient may complain of tenderness or may be asymptomatic, with the cyst first being detected in screening mammography (in females). Cysts may enlarge, remain unchanged for several years, or resolve spontaneously.[48] A cyst may be solitary or multiple, and ultrasound is useful in determining whether a cyst is cystic or solid. Simple cysts have no potential to become malignant, but may proliferate under estrogen stimulation. Complex cysts have a malignancy rate of 0.3%.[48] The treatment for painful cysts is aspiration performed under US guidance and cytological examination of the fluid. Biopsy is recommended for complex cysts having an intracystic mass.

Epidermal Inclusion Cyst (EPI)

The epidermal inclusion cyst is the most common epithelial cyst of the breast.[49] It arises from skin and adnexa and can be either cutaneous or subcutaneous. There is no age predilection for EPI, and it has been reported to occur in males. On clinical examination, EPI is a smooth, round, palpable mass that is movable and often visible. It most commonly arises from obstructed hair follicle(s), and may occur along embryonic lines of closure; however, it may also be caused by squamous metaplasia of a sweat duct. EPI is also associated with the traumatic downward implantation of epidermal fragments during reduction mammoplasty, fine needle aspiration (FNA), or core biopsy.[49]

Prior to mammography, the EPI lesion should be marked with a BB. A tangential view is helpful in viewing the cyst, and when using US a standoff pad may be necessary with lower frequency transducers.[49] Mammography findings demonstrate a well-circumscribed mass with some borders being ill-defined. The mammographic image may appear normal due to superficial cysts being "burned out" by exposure factors required for denser breast areas. Approximately 20% of EPI lesions will contain heterogeneous calcifications.[49] Ultrasound findings show a well-defined, round mass that is usually hypoechoic, with low-level internal echoes. The dermal extension will be evident with posterior acoustic enhancement, with occasional anechoic or hyperechoic areas.[49]

Treatment of EPI is controversial because some advocate complete resection, while others recommend no intervention unless the lesion is inflamed or painful. The prognosis of EPI is excellent, with malignancy potential being extremely low.[49]

Inflammation, Infection, and Reactive Breast Disorders

Inflammatory (noncurrent) diseases and infection involving breast tissue is rare.[50] Resulting lesions often clinically resemble malignant processes, requiring additional diagnostic investigation and usually a biopsy.

Abscess

A breast abscess is also referred to as a focal breast infection, with localized pus collection within the breast tissue.[49] It presents clinically as a firm mass of variable shape and size; and the patient may also present with nipple discharge, skin retraction or tethering, and axillary lymphadenopathy. The patient may complain of pain upon palpation although most do not experience pain. Approximately 50% of breast abscesses are found in the upper outer quadrant. The most common cause of a breast abscess is bacterial entry via the nipple; however, stasis and duct obstruction can also contribute to the condition.[49] *Staphyloccus aureus* and *streptococcal* species are the most common organisms isolated in puerperal breast abscesses. Non puerperal abscesses typically contain mixed flora (*S aureus*, *streptococcal* species, and anaerobes).[51]

Depending on the etiology, the abscess may resolve, but this typically requires local or systemic treatment. When a breast abscess is suspected, a complete blood count (CBC) with differential blood count can be helpful. An aerobic and anaerobic culture may be useful, but should be collected in a sterile environment.[51]

Treatment consists of aspirating the abscess cavity to determine the infectious pathogen and administering antibiotic therapy (for 7 to 10 days) based on the culture results.[51] The infection, if properly treated, generally resolves in 2-3 days.[83] Surgical excision may be required for certain cases of breast abscess. Prognosis varies from excellent to poor, with the recurrence of breast abscess being high (39-50%) when treated with standard incision and drainage.[51] The classic mammographic appearance of a breast abscess is a noncalcified, ill-defined mass. The abscess margins will appear irregular and spiculated.[49] Ultrasound imaging is the modality of choice since a breast abscess can be painful, limiting the use of compression during mammography. In US an abscess will appear as a hypoechoic mass with variable margin characteristics (irregular, circumscribed, spiculated), and it may have a fluid/debris level.[49] If MRI is used, the abscess cavity may enhance, and edema may present as high signal on T2-weighting.[49] Inflammatory carcinoma can mimic an infectious process, because it may appear to respond to antibiotics. Unfortunately, this may delay a proper diagnosis of the malignancy.

Glandular Islands

Glandular islands, also referred to as focal asymmetric glandular tissue or asymmetric density, and is defined as focal areas of glandular tissue separated from the main glandular cone. The are usually most common in postmenopausal women older than 40 years of age.[49] The condition either reduces or becomes stable on its own over time.[11] Its classic mammography appearance is an asymmetric, focal, rounded, soft tissue, low-density area, with mottled, internal, fatty deposits.[49] Using mammography, the best imaging clue is the presence of an internal fatty density, which usually has a convex contour, though in some, it may be rounded. The mass may be between 1-5 cm in diameter, and is usually located along the edge of the breast cone (upper outer quadrant). Diagnostic mammography images are generally required to obtain a diagnosis. Ultrasound and MRI findings are usually identical to normal parenchyma. Treatment rarely requires biopsy or short-term follow-up breast imaging.[49] The condition has no prognostic significance.[49]

Disease Processes

Systemic disease infrequently involves the breast, but mammography findings may be unique when it does. Some of these diseases have a characteristic appearance in mammography, whereas others may mimic cancer.[52] For example, the most common collagen disease detected by mammography is lymphadenopathy. Dermatomyositis, an

autoimmune collagen vascular disease, is characterized by chronic degeneration of striated muscle and skin. In mammography, this condition appears, as extensive dystrophic subcutaneous calcifications.[52] Vasculitis, as seen in Wegener granulamatosis, is a rare, systemic, autoimmune disorder. It may appear in mammography as an irregularly shaped high-density mass simulating breast cancer.[52] A few of the more common systemic diseases and conditions that affect the breast are covered in the following discussion.

Diabetic Mastopathy

Diabetes is a disease in which the body does not produce or properly use insulin. Insulin is a hormone that is needed to convert sugar, starches, and other food into energy required for daily life. There are 23.6 million children and adults in the United States, who have diabetes, or 7.8% of the population.[53] While an estimated 17.9 million have been diagnosed with diabetes, 5.7 million people are unaware that they have the disease.[53] Obesity is strongly associated with diabetes. The major types of diabetes include type 1, type 2, gestational, and pre-diabetes. Type 1 diabetes results from the body's failure to produce insulin, the hormone that "unlocks" the cells of the body, allowing glucose to enter and fuel them. It is estimated that 5-10% of Americans who are diagnosed with diabetes has type 1.[53]

Type 2 diabetes results from insulin resistance, a condition in which the body both experiences insulin deficiency and is unable to properly use insulin. Most Americans who are diagnosed with diabetes have type 2.[53] Gestational diabetes is a type that develops during pregnancy. Approximately 5-10% of women with gestational diabetes are found to have diabetes, usually type 2.[53] Pre-diabetes is a condition that occurs when a person's blood glucose levels are higher than normal, but not high enough for a diagnosis of type 2 diabetes. There are 57 million Americans with pre-diabetes.[53,54]

Women with long-standing insulin-dependent diabetes mellitus (IDDM) often have dense breast tissue. A condition known as diabetic fibrous breast disease (DFBD) often occurs in women who have early-onset, long-standing, insulin-dependent diabetes mellitus. Soler and Khardori first described the condition as an association between insulin-dependent diabetes mellitus and diabetic fibrous breast disease. Its etiology is thought to be an autoimmunity factor that produces the benign breast condition. According to Soler and Khardori, the following are requirements for a diagnosis of diabetic fibrous disease:

- Patient history: Early onset, long-standing, insulin-dependent diabetes mellitus which develops prior to menopause;
- Physical examination findings: Rock-hard, painless, irregularly outlined, discrete, freely movable masses; often bi-lateral, occasionally solitary;
- Mammographic findings: Dense glandular tissue;
- Ultrasonography findings: Marked acoustical shadowing of sound waves; and,
- FNAC findings: Rock-hard tissue that resists needle motion, no evidence of malignancy, 50% of aspirates reported as having "insufficient cellular material for evaluation".[55]

Diabetic mastopathy, also called diabetic fibrous breast disease (DFBD), is a self-limiting process with onset approximately 20 years after the initial diagnosis of diabetes.[49] Diabetic mastopathy is an uncommon tumor-like fibrous proliferation of the breast tissue occurring more frequently in women with type I insulin-dependent diabetes.[56] The condition occurs most frequently in premenopausal women, but has also been reported in diabetic men. It represents fewer than 1% of all benign breast lesions.[56] By the time DFBD breast symptoms are present, patients often have other complications of diabetes, such as retinopathy, nephropathy, and neuropathy.[49] Clinically, patients present with a firm, palpable, mobile, non-tender unilateral or bilateral breast mass or masses. The underlying pathogenesis of DFBD is unclear, but, as previously mentioned, it may represent an autoimmune reaction caused by hyperglycemia.[56] There has been no reported link to subsequent development of breast cancer.

Mammography findings of DFBD show dense parenchyma obscuring the masses. The increased density of the breast tissue may represent a glandular pattern, with no distinct masses, spiculation, or calcifications. On ultrasound, the masses appear to be nonspecific, irregular, and hypoechoic, but may appear with marked posterior acoustic shadowing.[49] The presence of a palpable mass, along with mammography and US findings, may be suggestive of breast cancer. Magnetic resonance imaging shows focal heterogeneous enhancement with low intensity in the early dynamic phase, with gradual enhancement over time.[49]

Investigation of masses in the diabetic patient includes core (or surgical) excisional biopsy to establish a diagnosis, and fine needle aspiration (FNA) biopsy for follow-up on recurrent lesions. Excisional biopsy is recommended because about 60-80% of all masses are bilateral or recurrent or both. Histologically, DFMB shows increased numbers of fibroblasts in a primary collagenous stroma, and periductal,

perilobular, or perivascular infiltration of B-cell lymphocytes. These findings substantiate the etiology as a form of vasculitis, an inflammatory condition of the blood vessels.[56]

Nipple-areolar Complex

The nipple-areolar complex is often evaluated as a separate region of the breast. This area may be affected by a host of disease processes, many of which have similar appearances; in men it is the area of the breast in which breast diseases most commonly develop. The nipple may be mistaken for a mass in both mammography and MR imaging. To counteract this problem, the nipple should be positioned in profile on at least one mammographic view. Common benign findings in the nipple-areolar complex include eczema, duct ectasia, periductal mastitis, adenomas, papillomas, leiomyomas, and abscesses.[57]

Many of the disorders of the nipple-areola complex are unique, and differ in important ways from those that occur elsewhere in the breast.[57] Patients may present with developmental variations that may have either a benign or malignant cause. Eczema of the nipple-areola complex may be associated with systemic conditions; however, if topical treatment does not cause the condition to resolve, it may be necessary to exclude Paget's disease of the nipple. Psoriasis may cause nipple changes, as well as other benign processes, including allergic contact dermatitis and *Canadidia* infection, which typically occurs in lactating women.[57] When skin changes are present, a clinical evaluation by the patient's primary care physician, dermatologist, or surgeon should be part of the diagnostic work-up which should include repeat mammography, US, MRI, galactography, needle aspiration and ductal lavage.[57]

Duct Ectasia (Subareolar Abscess)

Duct ectasia is also referred to as mammary duct ectasia or mastitis obliterans. It is most commonly defined as nonspecific subareolar ductal dilation. The dilated ducts may be palpable, and there may be spontaneous nipple discharge in colors ranging from yellow and green to brown.[49] The patient may present with pain and tenderness, often localized to the subareolar area, and nipple retraction. In women, the etiology is not related to parity or breast-feeding, but may be secondary to inflammation, obstruction, glandular atrophy, or stasis of the duct contents in both males and females.[49]

Mammography findings include the classic imaging appearance of enlarged tubular retroareolar structures. Calcifications may be present within or around the ducts, with punctuate, coarse, rod-like appearance, or they may appear spherical with lucent centers.[49] Ultrasonography shows the general features of dilated subareolar ducts

coursing to the nipple, with the internal matrix showing anechoic fluid and echogenic debris.[49] Periductal fibrosis may be seen as a hyperechoic area periductally.[48]

Investigation of duct ectasia includes biopsy if clinical or imaging characteristics are suspicious for carcinoma. The treatment is generally symptomatic, with no further imaging following mammography.[49] Women with duct ectasia have an excellent prognosis, with no related associated increased risk for invasive breast cancer.[49]

Masses

A mass is defined as a space-occupying lesion seen in 2 different projections. If a potential mass is seen on only one view, the term asymmetry is used until the presence of a mass is determined. Once the presence of a mass has been established, its size is usually associated with metastasis, and is an indicator of the potential disease prognosis. The following sections provide information about common and unusual breast masses.

Hematoma

A hematoma is a localized mass of extravasated blood within the breast. It may occupy a surgical cavity or traumatic tear (seatbelt injury) and may spread into the parenchyma, connective tissue, or adipose tissue.[49] It is the most common problem resulting from trauma to the breast, and generally resolves spontaneously without intervention. The presenting feature is a painful, palpable mass following reported trauma or surgery, for example lumpectomy, excisional biopsy, augmentation, reduction, core biopsy, fine-needle aspiration, or cyst aspiration. There is usually ecchymosis and skin discoloration.

Imaging studies are not required if the diagnosis is clinically obvious.[49] False positive results can be reduced if mammography is conducted two weeks after aspiration or biopsy. Early changes will appear in mammography with variable margin characteristics ranging from ill-defined to sharp as a round or an oval mass. Late changes may show that the mass has decreased in size over time, though there may be a persistent residual skin thickening.[49] Early ultrasound findings show an ill-defined mass with architectural distortion, as compared to late changes, where the mass is more sharply defined. Magnetic resonance imaging findings may show (delayed) minimal to moderate enhancement.

Treatment of hematoma includes supportive care, such as analgesic medications and an ice pack in the acute stage, and warm compresses in the later stage of resolution. Aspiration may be required for large, painful masses. A hematoma caused

by trauma usually resolves in six weeks, whereas those resulting from lumpectomy may take up to one year to resolve.[49]

Lipoma

A lipoma is defined as a benign, well-circumscribed, encapsulated, adipose tumor.[19] Clinical presentation includes a mobile, generally soft, palpable mass. A lipoma is usually unilateral but may be bilateral in 3% of women.[49,58] A lipoma must be differentiated from other fat-containing lesions such as hamartoma, galactocele, hibernoma, fibrolipoma, and oil cysts.[49]

The classic mammography appearance of a lipoma is a radiolucent, circumscribed, smooth mass surrounded by a thin, dense capsule. The presence of fat on both sides of the capsule allows the margin to be visible. Architectural distortion may be demonstrated. Ultrasound is not necessary for identification; however, the mass will be hypoechoic. No treatment is necessary.

Myoid Hamartoma

Myoid hamartoma is also referred to as leiomyomatous hamartoma or muscular hamartoma. It is defined as a benign, proliferative lesion. Clinical presentation of myoid hamartoma includes a palpable mass that is generally first detected in mammography. It is predominately located in the upper outer quadrant of the breast, ranging in size from 2-11 cm.[49]

Other lesions resembling myoid hamartoma include infiltrating lobular carcinoma, circumscribed carcinoma, and benign lesions such as cysts and fibroadenomas. Mammography findings depict a well-encapsulated round or oval mass that may have a lucent halo.[58] Ultrasound findings show a well-circumscribed mass that has internal echogenicity. There is neither a tendency for recurrence nor an increased risk for malignancy associated with myoid hamartoma.[56] Core biopsy may be required to adequately diagnose the lesion.

Papilloma

Papilloma is also referred to as large duct papilloma, intraductal papilloma, intracystic papilloma, and central papilloma. A papilloma is defined as a benign epithelial lesion characterized by a branching or lobular tumor.[48]

There are two types of papillomas: solitary intraductal and multiple peripheral. Solitary intraductal papilloma is a small (average size 3 to 5 mm), benign tumor that grows within a milk duct. A papilloma may have a trigger point (Haagensen) where a

discharge can be elicited if pressure is applied.[12] It most commonly occurs in women 30 to 55 years of age; however, it has also been diagnosed in men.[48] Intraductal papillomas are found within a dilated duct or cyst, and are usually attached to the wall of the involved duct by a stalk.[59] Multiple peripheral intraductal papillomas originate in the smallest ducts of the breast's terminal lobular unit, and occur less frequently than solitary papillomas.[48] Multiple peripheral intraductal papillomas tend to occur in younger patients, and may be bilateral. Spontaneous nipple discharge occurs in approximately 20% of all cases.[12] These lesions have a higher risk of becoming malignant, and are considered risk marker lesions.[18]

Clinically, the majority of patients present with spontaneous nipple discharge, and occasionally a palpable mass.[49] Patients with solitary intraductal papilloma typically report a bloody or clear nipple discharge of less than 6 months' duration.[48] Patients with multiple peripheral papillomas are less likely to have nipple discharge, but are at greater risk for recurrence and malignant progression.[48] Solitary papillomas are generally found in the central, periareolar area of the breast. Peripheral papillomas can occur in any quadrant of the breast. Diagnostic differentiation between papilloma, papillary carcinoma, and papillomatosis must be made.

Papilloma is usually not visible on mammography, but it may present as a nonspecific mass with large, irregular, dense microcalcifications. On US it is demonstrated as a focal hypoechoic solid mass that is well defined, usually lobulated.[56] Magnetic resonance imaging is useful in distinguishing between benign and malignant causes of nipple discharge.[48]

Papilloma lesions have a tendency to undergo spontaneous infarction. Controversy exists regarding the steps to take following after a core biopsy. The controversy involves whether surgical excision should be performed, or whether the patient should be monitored with frequent breast imaging.[49] Although a papilloma is not malignant or premalignant, its diagnosis carries a slight associated increased risk of developing breast cancer.[49]

Pseudoangiomatous Stromal Hyperplasia (PASH)

Pseudoangiomatous stromal hyperplasia (PASH) is defined as a benign, neoplastic, myofibroblastic process. It is a mesenchymal lesion that may be mistaken for angiosarcoma.[60] Clinically, it presents as a painless, palpable, unilateral, firm or rubbery mass, usually in postmenopausal women taking HRT.[49] It has also been reported in microscopic findings seen in gynecomastia, axillary tissue, and immunosuppressed patients.[49] The natural progression of the lesion may show rapid

growth, which requires biopsy for differentiation from other lesions such as low grade angiosarcoma, fibroadenoma, phyllodes, and hamartoma.[49]

Mammography findings show a round or oval, noncalcified mass that can range from 1-10 cm. The margins will be fairly well-circumscribed. In ultrasonography, PASH will appear as a round or oval mass with variable internal echogenicity and variable posterior echo pattern.[49] PASH is treated by performing wide local excision. The prognosis is excellent; however, local recurrences have been reported.

Miscellaneous Breast Conditions

Intramammary Lymph Node

Intramammary lymph node is also called intraparenchymal lymph node. It is defined as an oval, smoothly marginated, fat-containing mass. It is a common mass often found in the lateral breast, usually discovered during diagnostic mammography.[49] General pathology shows it as a lymph node or nodes completely surrounded by breast tissue. Enlargement of the lymph node(s) can result from neoplasms, regional inflammation, infection, or a reaction to a foreign body.[49] Mammography findings show a fat-containing mass usually greater than 1 centimeter (cm) in length. The size of the mass is less important than its classic appearance.[81] Ultrasound findings show a hypoechoic oval mass that is well-circumscribed. Magnetic resonance imaging studies may be done for comparison with mammography and ultrasonography findings. No treatment of the inframammary lymph node is required unless there are suspicious imaging or clinical findings. The prognosis is excellent.

Breast Cancer

According to the National Cancer Institute (NCI), the types of breast cancer most commonly diagnosed in men are similar to those found in women.[61,62] Men generally develop breast cancer at a later age than women do. Significant differences have been noted between male and female breast cancers with respect to the expression of a variety of biologic factors. The following include a few, but not all, of these factors: hormone receptors, such as estrogen receptors and progesterone receptors, proteins related to basement membrane and extracellular matrix degradation, and protooncogenes. For invasive carcinomas, female and male tumors are morphologically indistinguishable. Scientists speculate that over-or underpresentation of particular histologic subtypes in male breast cancers is a problem and suggest that this topic requires further investigation.[61]

The most common type of male breast cancer is infiltrating ductal carcinoma (IDC), also called invasive ductal carcinoma. Ductal carcinoma in situ (DCIS, also called intraductal carcinoma) has also been diagnosed in men.[62] DCIS is an early stage breast cancer confined to the breast ducts. Rare cancers, such as inflammatory breast cancer and Paget's disease of the nipple, have also been reported in men.[62] Lobular carcinoma in situ (LCIS) is a risk marker lesion for increased breast cancer risk in women, but this same tendency has not been seen in men.[62]One of the major differences between male and female breast cancers is that in males the most common location is usually subareolar and eccentric to the nipple.[62] Margins of the lesions are more frequently well-defined, and calcifications are rarer and coarser than those occurring in female breast cancer.[44]

With ultrasonography, invasive ductal carcinoma appears as a discrete, hypoechoic mass, with its margins being angulated, microlobulated, or spiculated. Since approximately 50% of males with breast cancer have enlarged axillary lymph nodes, routine US of the axillary region is recommended. Cancers are typically named for the body organ or tissue in which the cancer originates. Breast cancer originates in the tissues of the breast, and if the cancer spreads to a distant organ, the cells of the secondary cancer would be breast cancer cells. This often allows pathologists to tell whether a cancer is a primary tumor, originating in the site where it is detected, or a secondary tumor that represents a metastasis from a cancer at another location in the body.

Almost all breast cancers arise in epithelial tissues, and like other epithelial cancers are called carcinomas. Because the breast is a gland, breast carcinomas are sometimes identified as adenocarcinomas. Carcinomas arising from the ducts (ductal carcinomas) account for the greatest percentage of all breast cancers. Breast cancer may be further classified as invasive or noninvasive. Noninvasive carcinomas are confined to the ducts and acini, whereas invasive carcinomas have broken through the borders of the ducts, invading the surrounding fatty or fibrous structures. About 94% of all breast cancers are invasive.

The earliest tissue changes that can be pathologically identified as malignant are the noninvasive cancers, either noninfiltrating ductal carcinoma or lobular carcinoma in situ. Some cells may develop changes that are abnormal but not malignant. Surgically removed tissue will generally demonstrate a spectrum of abnormalities ranging from simple hyperplasia (associated with atypical cells) to cells that are clearly cancerous. If an individual presents with breast hyperplasia, it does not mean that cancer is imminent. The excessive cell accumulation that characterizes hyperplasia is

an extremely common finding in tissue samples of benign breast lesions. There is no way to identify which hyperplastic changes will actually become cancerous.

Types of Breast Cancer

Breast cancers are distinguished according to cell types because different kinds display different rates of growth and metastasis. The greatest percentage of breast cancers involves the terminal duct.

Invasive Ductal, Not Otherwise Specified (NOS) (Terminal Duct)

Invasive ductal carcinoma (IDC) accounts for approximately 85% of primary male breast cancers.[62] IDC is a cancer that has spread beyond the ducts of the breast. This cancer lacks special histology characteristics, and is designated NOS for "not otherwise specified." Clinically, these tumors are characterized by a palpable mass that is stony hard to the touch. Presenting symptoms may include nipple discharge, nipple inversion, skin retraction, and ulceration in men and women with advanced disease. Invasive ductal carcinoma (IDC) in the male breast appears on mammography images as a high-density, irregular mass with well-defined contours.[16] The margins of IDC masses are usually spiculated, lobulated, or microlobulated.[16] US imaging is valuable in identifying the relationship of the mass to the nipple. If skin thickening and retraction are present, they can easily be identified in US imaging.

Invasive ductal carcinoma is the most common type of breast cancer, accounting for approximately 65% to 75% of all breast cancers, and causes connective tissues to proliferate, producing contractures.[12] These may be fixed to the skin or chest wall, with nipple retraction. Even though these tumors may not grow large, they often spread to the axillary lymph nodes, and have a poor prognosis. The presence of an extensive intraductal component (EIC) may be of prognostic significance, as the rate of local recurrence after conservative treatment is reportedly high.[12] Architectural distortion may be isolated or associated with the mass. In ultrasound, this mass appears as a hypoechoic mass, commonly with marked hypoechogenicity.[12]

Ductal Carcinoma in Situ (DCIS) (Terminal Duct)

The ACS estimates that more than 62,000 new cases of carcinoma *in situ* (DCIS) will be diagnosed in 2009. DCIS refers to the most common type of noninvasive breast cancer, usually found in women. DCIS lesions are often microscopic, generally have not invaded adjacent tissues, and rarely produce symptoms. In earlier times, DCIS

was considered a rare type of breast cancer; however, with today's high-quality mammography images, it is no longer a rare condition.

In situ cancers are often multicentric, meaning they may develop at several locations within a single breast. Some, but not all, in-situ carcinomas will progress to become invasive carcinomas of varying types. Among those affected with ductal carcinoma in situ, more than half, and as many as two-thirds, may later develop invasive carcinoma. It is impossible to predict which of the noninvasive lesions will undergo further growth. In a morphologic study of the distribution of histologic subtypes and metastatic patterns in 778 male cases of breast cancer, the occurrence of papillary DCIS occurred with a much higher frequency (46%) than expected.[61] Also, in the same study, micropapillary and cribiform patterns occurred with a much lower frequency (22% of pure DCIS combined), with only 5 of 114 cases being comedo-type DCIS.[61] The authors of the study concluded that the predominance of papillary patterns reflected the relative abundance of ducts, and the poorly-developed terminal-ductal lobular units in the male breast.[61]

The term DCIS refers to a family of cancers that occur in the breast ducts. There are two categories of DCIS: non-comedo and comedo. The term comedo describes the appearance of the cancer. When comedo-type breast tumors are cut, the necrosis inside of them can be expressed out just like a comedo, or blackhead, on the skin. **[62]** The most common non-comedo types of DCIS are:

- Solid DCIS: cancer cells completely fill the affected breast ducts;
- Cribiform DCIS: cancer cells do not completely fill the affected breast ducts; there are gaps between the cells;
- Papillary and micropapillary DCIS: the cancer cells arrange themselves in a fern-like pattern within the affected breast ducts; micropapillary DCIS cells are smaller than papillary DCIS cells.[62]

Comedo type DCIS tends to be more aggressive than the non-comedo types of DCIS.[62] Pathologists can usually easily distinguish between comedo type DCIS and non-comedo types when examining the cells, because comedo type DCIS tends to plug the center of the breast ducts with necrosis.[62] When necrosis is associated with cancer, it often indicates that the cancer is able to multiply rapidly.[62] On mammography images, DCIS appears as calcifications that are round or oval, and variable in density in one or more clusters. DCIS may have a linear orientation, which follows a ductal-like distribution, or it may be amorphous. Architectural distortion is rare with DCIS unless associated with invasive ductal carcinoma.

Medullary Carcinoma (Terminal Duct)

Medullary carcinoma is an invasive ductal tumor accounting for about 5% to 7% of all breast cancers in women.[12] It appears as an encapsulated, circumscribed, mobile mass that is frequently mistaken for a fibroadenoma in the younger patient. Medullary carcinomas have a fast growth rate, and may grow quite large. These tumors are locally aggressive, but despite that tendency the prognosis of pure medullary carcinomas is better than that for infiltrating ductal carcinomas (NOS); if they do prove fatal, however, death usually occurs within 5 years of diagnosis.[12] On mammography images, medullary carcinoma appears as a round mass with ill-defined margins. It appears as a solid, homogeneously hypoechoic, round mass on ultrasound.[12]

Mucinous Carcinoma (Terminal Duct)

Mucinous carcinoma is an invasive ductal cancer which in its pure form represents about 2% of all breast cancers in women.[12] Mucinous carcinoma can develop at any age. It contains cells that produce mucus, which gives the tumor a glistening appearance, and is characterized by a slow growth rate. Though a mucinous carcinoma can grow to be bulky, in its pure form its prognosis tends to be highly favorable. Systemic recurrences have been reported to occur more than 10 years after initial treatment.[12] Axillary node involvement occurs in approximately 25% of patients.[12] On mammography images, mucinous carcinoma appears as a round mass with well-circumscribed to obscured margins. These lesions appear well-circumscribed and hypoechoic on ultrasound, and may be either homogeneous or heterogeneous.

Tubular Carcinoma (Terminal Duct)

Tubular carcinoma is an invasive ductal cancer constituting about 2% of total breast cancers in women.[12] Also known as orderly carcinoma, it microscopically displays characteristic tubular structures ringed with a single layer of cells. Calcification is present in up to 50% of these lesions. It carries a prognosis similar to that of invasive ductal carcinoma but less favorable than that of medullary carcinoma. If associated with pure lesions the prognosis is excellent.

Tubular carcinoma often presents as a palpable breast mass; however, most tubular carcinomas are diagnosed by mammography. This special form of invasive carcinoma is the only one that typically presents with the mammography appearance of a spiculated mass.[12]It presents as a multicentric mass in up to 28% of patients, and as a bilaterality in 12% to 38%.[12] There is a family history of breast cancer in up to 40% of

tubular carcinoma cases.[12] Tubular carcinoma appears as an ill-defined, hypoechoic mass that may have associated shadowing in ultrasound.[12]

Invasive Cribiform Carcinoma (Terminal Duct)

Invasive cribiform carcinoma accounts for 1.7% to 3.5% of all breast cancers.[12] Approximately 25% of these lesions have associated features of tubular carcinoma, with well-differentiated, cribiform DCIS present in adjacent breast tissue in about 75% of cases.[12] On mammography images, invasive cribiform carcinoma appears as a well-circumscribed to ill-defined mass, and may present with microcalcifications. In ultrasound, it appears as a hypoechoic mass with minimal posterior acoustic shadowing.[12]

Adenoid Cystic Carcinoma (Terminal Duct)

Adenoid cystic carcinoma accounts for less than 0.5% of all breast cancers.[12] In clinical examination, these lesions present with a palpable mass that is generally located in the subareolar area. Axillary nodal involvement and metastasis are uncommon, resulting in an excellent prognosis. On mammography images, this cancer may range in appearance from a partially well-circumscribed mass to one with obscured margins.

Invasive Lobular Carcinoma (Lobular)

The Burga et al study confirms that lobular carcinoma can and does develop in the male breast, a finding which was previously unreported.[61] Among the 759 cases of all lobular carcinoma, three demonstrated invasive lobular carcinoma, diagnosed purely on a morphologic basis.[61] In many cases a discrete mass may not be present; rather, the clinical signs may be areas of breast thickening, induration, and focal tenderness. These carcinomas are similar in appearance and behavior to the invasive ductal carcinoma (not otherwise specified), except that invasive lobular carcinomas arise in the small end ducts, or lobules. The prognosis for invasive lobular carcinoma tends to be unfavorable.[12] Carcinomas of the male breast have a higher rate of hormone receptor positivity than do those of the female breast when matched for tumor stage, grade, and patient age.[63]

On mammography images, the lesions may be demonstrated as a spiculated mass, and there may be parenchymal asymmetry and architectural distortion.[12] On ultrasound images, this cancer appears as a hypoechoic mass with angular or ill-defined margins.[12]

Papillary Carcinoma (Subareolar Area)

Papillary carcinoma accounts for 1% to 2% of all breast cancers, and until recently reported (Burga et al), it was not considered a type of cancer that affected the male breast.[61] Generally, in females, those affected are between the ages of 63 and 67.[12] The lesion appears as a palpable, lobulated, circumscribed mass, with the most common site of occurrence (90%) being in the subareolar area.[12] These lesions may protrude and stretch over the skin, causing erythema and occasionally ulceration. Nipple discharge has been reported in 22% to 35% of cases.[12] Most papillary carcinomas are found in a dilated duct, and are often soft, friable tumors with the tendency to hemorrhage. Papillary carcinomas may become invasive, but they grow slowly. They are estrogen-receptive, have a favorable prognosis, and with complete excision, the survival rate approaches 100%.[12] On mammography images, papillary carcinoma appears as a large, well-circumscribed mass with benign-appearing calcifications. This lesion appears as a complex cystic mass with a solid, hypoechoic mass on ultrasound.

Paget's Disease (Nipple-Areola Complex)

Paget's Disease is a cancer involving the nipple, and constitutes 1% to 5% of all breast carcinomas.[12] This cancer affects the ducts beneath the nipple. It is not always palpable, and is most frequently noninvasive; however, 50% of patients do have a palpable mass.[12] Initial presenting signs include reddening of the nipple and areola with pruritus. As the disease progresses, the tumor cells grow through the ducts onto the surface of the nipple, causing moist, scaling, eczema-type changes leading to ulceration and erosion of the nipple. The prognosis depends on whether the underlying tumor is invasive or noninvasive. Approximately 95% of patients with Paget's Disease have an underlying intraductal carcinoma that is poorly-differentiated.[12] Patients with Paget's Disease may have a normal appearing mammogram, or one that demonstrates nipple retraction, thickening, or calcifications.

Inflammatory Carcinoma (Skin)

The clinical findings of inflammatory carcinoma of the breast include erythema, edema, and breast warmth; however, in approximately 4% of women with dermal lymphatic involvement, the traditional signs are absent.[12] Ridges or wheals may appear on the skin, or the breast skin may display the pitted appearance known as *peau d'orange,* or orange peel.[12] Inflammatory carcinoma does not cause a fever or other

signs of infection; the breast's redness and warmth develop as a result of cancer cells blocking the lymph vessels in the skin of the breast. Inflammatory carcinoma is rare, representing 1% of all breast cancers.[12] Approximately 80% of patients presenting the clinical signs of inflammatory carcinoma have dermal lymphatic involvement.[12] This is one of the most malignant of all breast cancers, and has the least favorable prognosis; most patients with aggressive lesions die of metastatic disease within one to two years of diagnosis.[12]

In mammography, the affected breast is usually larger and less compressible, with trabecular thickening and architectural distortion not present in the contralateral breast. Thickening of the skin and trabecular structures may be present without an identifiable mass. This is demonstrated in ultrasound as an irregular, ill-defined, hypoechoic mass or masses, with or without posterior acoustic shadowing.[12]

Melanoma (Skin)

Primary breast skin melanomas constitute approximately 2% to 5% of all melanomas.[12] The two most common types of melanoma in the breast are superficial spreading and nodular. Breast melanoma presents as a growth with irregular borders; the growth may vary in color (tan, brown, black, pink, blue, and gray), and there may be depigmentation in surrounding areas. Other presenting clinical signs may include nodularity, induration, and ulceration.

Evaluation of male breast masses should include the possibility of metastasis to the breast, particularly if there is a history of cancer elsewhere.[61] Prostatic carcinoma has been implicated as the most frequent cause of metastatic male breast cancer.[61] In the Burga et al study, the tumor which most commonly metastasizes to the male breast was cutaneous melanoma.[61] Other common sources of metastastic carcinoma in the male breast include the lung and larynx.[61]

Angiosarcoma (Stroma)

Angiosarcoma accounts for fewer than 0.05% of all primary breast cancers.[12] It presents as a painless, discrete mass that may result in diffuse breast enlargement in approximately 12% of all cases.[12] There may be a bluish-red discoloration of overlying skin if a superficial lesion is present. Contralateral breast involvement is common, and tumor size is considered to be of value in determining prognosis of the disease. Mammography displays an irregular mass that may present with coarse calcifications.

Growth Rates of Breast Cancer

The rate at which a tumor grows is usually expressed by the phrase “doubling time”. Doubling time is the length of time it takes for a tumor to double its diameter, increasing eight times in volume in the process. The doubling time of breast cancers varies from a few days to more than a year. Furthermore, the doubling time of a tumor lengthens as the tumor grows in age and size. Once a tumor is big enough to be felt, at about 1 to 1.5 centimeters, it may have been in the breast for years, during which time it was shedding cancer cells into the bloodstream and the lymphatic system.

Clues to Breast Cancer Prognosis

Scientists have long been searching for ways to predict the likelihood that breast cancer will spread or metastasize. Numerous factors are known to play a role in determining the likelihood of metastasis, including the size of the tumor when it is discovered, the age of the patient, and certain characteristics of the tumor itself (tumor grade and estrogen receptors).

Identifying the proteins found in tumors (which are known as biomarkers), such as E-cadherin, can greatly affect the type of breast cancer treatment recommended, and may help determine the likelihood that cancer will spread. When breast cancer is diagnosed early, before there is lymph node involvement, only 20% to 30% will spread. Those individuals found to be at high risk of metastasis may be treated more aggressively with chemotherapy.

Several physical characteristics provide clues to a breast tumor’s behavior. In general, the larger a breast cancer, the greater the chances that metastases are growing elsewhere in the body. Both tumor size and the number of affected lymph nodes are correlated with prognosis; as a rule, larger tumors and tumors with numerous malignant lymph nodes are more difficult to cure or control. Another prognostic indicator is the tumor’s contour. Cancers with a smooth, rounded outline, though they account for only 25% of all breast cancers, have a markedly better prognosis than those with contours made irregular by growths protruding into adjacent tissue or vessels. The prognosis is also poorer for breast tumors that contain areas of dead or necrotic cells, and tumors made up of poorly-differentiated cells. The following is a summary of prognostic factors associated with breast cancer.

- The tumor’s size correlates with metastasis and prognosis.
- The status of axillary lymph nodes is considered the most important prognostic factor.

- The histologic examination of axillary lymph nodes following axillary dissection is considered more accurate than clinical evaluation.
- The levels of axillary lymph nodes include:
    - Level I: inferior and lateral to pectoralis minor muscle (external mammary, axillary vein, and scapular lymph nodes)
    - Level II: posterior to pectoralis minor muscle, and below axillary vein (central lymph nodes)
    - Level III: medial to pectoralis minor muscle (subclavicular lymph nodes), and adjacent to chest wall
- The significance of micrometastasis is unknown.

Breast Cancer Staging

Breast cancer staging is a critical step in determining the best treatment for the patient. The system recommended is explained in the *Manual for Staging of Cancer*, published in 1997 by the American Joint Committee on Cancer (AJCC).[64] The system uses the TNM method, in which the T describes the size of the primary tumor, N describes the regional lymph node involvement, and M describes the presence or absence of distant metastasis. Figure 7 provides a summary of the TNM breast cancer staging classification.

AJCC Classification for Tumors (T)	
TX	Tumor cannot be assessed
TO	No evidence of tumor found
Tis	Carcinoma in situ
T1	Tumor 0 to 2 cm in greatest dimension T1a tumor 0.5 cm in greatest dimension T1b tumor more than 0.5 cm but less than 1 cm in greatest dimension T1c tumor more than 1 cm but less than 2 cm in greatest dimension
T2	Tumor 2 to 5 cm in greatest dimension
T3	Tumor more than 5 cm in greatest dimension
T4	Tumor any size with extension to chest wall or skin T4a chest wall extension T4b breast skin edema or ulceration, skin nodules T4c both T4a and T4b T4d inflammatory carcinoma
AJCC Classifications for Regional Lymph Node Involvement (N)	
NX	Regional nodes cannot be assessed
NO	No regional node metastasis
N1	Metastasis to lymph node(s) in axilla, same side as breast cancer. Node(s) freely movable
N2	Metastasis to lymph node(s) in axilla, same side as breast cancer. Node(s) fixed to each other or to other structures
N3	Metastasis to internal mammary lymph node(s), same side as breast cancer
AJCC Classifications for Distant Metastasis (M)	
MX	Presence of distant metastasis cannot be assessed
MO	No distant metastasis found
M1	Distant metastasis present, including in supraclavicular lymph nodes, on the same side as breast cancer

Fig. 7. Summary of TNM breast cancer-staging classification.

Each area has subclassifications to further describe the extent of the breast cancer. For example, T4 represents a tumor of any size with extension to the chest wall or skin. A subclassification T4a further specifies that the tumor has chest wall extension. Figure 8 provides a summary of the TNM breast cancer-staging classification with subclassifications.

Breast Cancer Staging

Stage 0	**Tis**	**N0**	**M0**
Stage I	**T1**	**N0**	**M0**
Stage IIA	**T0**	**N1**	**M0**
	TI	**N1**	**M0**
	T2	**N0**	**M0**
Stage IIB	**T2**	**N1**	**M0**
	T3	**N0**	**M0**
Stage IIIA	**T0**	**N2**	**M0**
	T1	**N2**	**M0**
	T2	**N2**	**M0**
	T3	**N1**	**M0**
	T3	**N2**	**M0**
Stage IIIB	**T4**	**any N**	**MO**
	Any T	**N3**	**MO**
Stage IV	**any T**	**any N**	**M1**

Fig. 8. TNM breast cancer-staging classification with subclassifications.

Understanding the Breast Pathology Report

A pathologist will analyze the cells and tissues collected during breast biopsy to determine if the lesion is cancerous, precancerous, or benign. All invasive breast cancer reports also include a biomarker analysis, which contains an indication of the presence or absence of estrogen and progesterone receptors, and presents the results of a gene mutation test called HER2. Sections of the pathology report include:

- Demographic patient information and contact information for the physician and hospital;
- Anatomic pathology diagnosis;
  - -Histology-the type of cancer found and the arrangement of the cells;
  - -Stage-the extent of cancer-staging may not be complete until after surgery; and,
  - -Grade-the nature of the cells and their aggressiveness.
- Clinical history, including preoperative diagnosis;
- A description of what the pathologist received, and the date of the biopsy;

- Gross description, or characteristics, of the specimen; and,
- Microscopic description, or cell analysis.[14]

Depending on the type and stage of breast cancer, surgery, radiation therapy, and chemotherapy may be used. The histologic grade of the cancer helps predict the patient's prognosis. This is based on the arrangement of the cells in relation to each other, as well as features of individual cells.[4] The following gives a brief description of histologic grades 1-3, which are classifications assigned to invasive cancers: Grade 1 (well-differentiated) cancers have relatively normal-looking cells that do not appear to be growing rapidly and are arranged in small tubules. Grade 2 (moderately-differentiated) cancers have features between grades 1 and 3.[4] Grade 3 (poorly-differentiated) rating is assigned to cancers formed by cells that appear very abnormal, grow rapidly, and rarely form tubules.[4]

An additional important step in evaluating breast cancer is determining the presence of estrogen and progesterone receptors within it.[4] Cancer cells may contain neither, one, or both of these receptors. Breast cancers that contain estrogen receptors are referred to as ER-positive cancers, while those containing progesterone receptors are called PR-negative cancers.[4] Approximately nine out of ten male breast cancers have either estrogen or progesterone receptors (or both).[1] These cancers tend to have a better prognosis than cancers without these receptors, and are much more likely to respond to hormonal therapy.[4]

In a small number of breast cancers in men, the cells have too much of a growth-promoting protein.[4] Cells under the influence of the HER2/neu gene make this protein. Tumors with increased levels of HER2/neu are referred to as HER2-positive.[4] In men with HER2-positive breast cancers, there are too many copies of the HER2/neu gene (i.e., gene amplification is occurring), resulting in greater than normal amounts of the HER2/neu protein.[4] These cancers tend to grow and spread more aggressively than other breast cancers. HER2/neu testing is performed on all newly diagnosed breast cancer, because HER2-positive cancers are much more likely to respond to treatment with drugs that target the HER2/neu protein, such as trastuzumab (Herceptin) and lapatinib (Tykerb).[4]

After surgery, treatment often depends on whether cancer cells are estrogen-receptor positive or negative. The biopsy results may also provide the following information:

- **Nuclear grade:** An evaluation of how fast the nuclei of cancer cells can divide, and how the cells are arranged in relation to each other. This grade is on a scale of 1 to 3; the higher the score, the more aggressive the cancer.
- **Flow cytometry:** A measure of DNA in tumor cells. About 70% of breast cancer cells have abnormalities in their DNA.
- **S-phase fraction:** An assessment of how many cancer cells are dividing at any one time. The higher the percentage, the more aggressive the tumor.
- **Cathepsin D6:** In certain patients, high levels of this enzyme suggest that the cancer may have spread.

Survival Projections

According to the NCI, a lower stage of breast cancer correlates to a greater chance of long-term survival. The NCI estimates the 5-year survival rate to be:

- 96% when cancer is confined to the breast.
- 75% when cancer has spread to surrounding tissue.
- 20% when cancer has metastasized to distant sites. Only 6% of all breast cancers are diagnosed at this stage.

Guidelines and Information on Standard Breast Cancer Treatments

After biopsy or surgery, the pathology report will provide information for staging the cancer, a process that helps to determine whether any further treatment is needed, and predicts the outlook for a cure. There are several types of treatment available for men with breast cancer. Some of these are considered current protocols, and some are being tested in clinical trials. When clinical trials demonstrate that a new treatment is better than the current protocols, the new treatment may become the standard treatment.[67] There are 4 types of standard treatments used to treat men with breast cancer. These are surgery, chemotherapy, hormone therapy, and radiation therapy.[67]

Surgery

Surgery for men with breast cancer is usually a modified radical mastectomy (removal of the breast, many lymph nodes, and sometimes part of the pectoralis muscle). Breast-conserving surgery is also used for some men with breast cancer. A lumpectomy followed by radiation therapy may be an alternative to radical mastectomy for some. Mastectomy continues to be the primary surgical treatment; however, males can be treated with breast conservation with acceptable local recurrence. Breast-

conserving surgery in male breast cancer patients should be considered an option for patients without overt nipple/areola involvement.[67,68,69]

Axillary Nodes

Most men and women who are diagnosed with breast cancer undergo axillary, or internal, mammary lymph node assessment to determine whether the tumor has spread to these nodes. In this procedure, a surgeon removes the lymph nodes in the patient's axilla from the same side of the body in which the breast tumor resides. Ultrasound may also be used to evaluate axillary lymph node involvement, and to determine whether a total axillary lymph node dissection is necessary, or if sentinel node localization and biopsy is an option.

As previously mentioned, imaging procedures are available for identifying a sentinel node, the first node to receive drainage from a breast tumor. If a sentinel node can be accurately identified, removed, and examined for cancer cells, those patients found to have noncancerous sentinel nodes can be spared the removal of remaining lymph nodes. This means fewer surgical complications and shorter recovery time for some breast cancer patients.

Axillary lymph node dissection may cause post-surgical problems, with lymphedema being the most common. Approximately 15% to 20 % of patients undergoing axillary lymph node dissection experience lymphedema, which is an accumulation of lymph fluid. Lymphedema results in symptoms ranging from mild swelling to total immobilization and disability of the affected arm. The American Cancer Society (ACS) is so concerned that lymphedema patients receive adequate care that the organization funded the first effort to certify health workers who provide quality lymphedema treatment. The ACS has also published a lymphedema guide in its cancer journal, and a plain-English version for patients. Lymphedema experts recommend that patients observe common-sense precautions, including the following:

- Avoid vaccinations, blood pressure measurements, and skin punctures (like insect bites) to the affected arm; seek prompt treatment for any signs of infection.
- Do not wear constrictive clothing.
- Avoid being in excessive heat, including sunning, hot baths and saunas.
- Avoid lifting heavy objects with the affected arm.
- Monitor the affected arm for swelling, and seek early treatment.

According to the ACS, the best treatment for lymphedema is complete decongestive treatment (CDT). Complete decongestive treatment consists of gentle massage that

helps remove fluid from the arm, followed by application of an elastic glove and sleeve to keep the fluid from returning. Elastic garments alone help some patients, but must be properly fitted by a specialist. Elevating the arm helps mild cases of lymphedema; surgery and diuretic drugs have not proven to be effective treatments.

Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing them or by stopping them from dividing.[67] Adjuvant therapy should be considered for men with node-negative breast cancer as well as for women, because there is no evidence that response to therapy is different for men than women.[67] For men whose cancer is node-positive, adjuvant therapy may include chemotherapy plus Tamoxifen, which is used to block the effect of estrogen.[65] First-line use of aromatase inhibitors is now standard treatment for hormone-sensitive metastatic breast cancer in postmenopausal females. However, Tamoxifen continues to be regarded as first-line treatment in hormone-sensitive male breast cancer.[65] Researchers have found links between an individual's genetics and his or her response to treatment with chemotherapy.[67] They determined that the presence of a particular variant was associated with decreased survival of patients treated with chemotherapy regimens containing any of the three types of commonly-used chemotherapy drugs (i.e., doxorubicin. 5-fluorouracil, and cyclophosphamid).[67]

In another study, a team of NCI researchers identified an association between breast cancer survival and two proteins that, when present in the blood in high levels, are indicators of inflammation.[68] Inflammation has been associated with several modifiable risk factors, such as obesity, low physical activity, and cardiovascular disease, all of which can affect a cancer survivor's prognosis.[68]

Hormonal Therapy

Hormone therapy is a cancer treatment that either removes hormones or blocks their action, stopping cancer cells from growing. If laboratory tests show that the breast cancer cells have hormone receptors, drugs, surgery, or radiation therapy may be used to reduce the production of hormones, or to keep them from functioning.

Monoclonal Antibiodies as Adjuvant Therapy

Monoclonal antibody therapy is a cancer treatment that uses antibodies made in the laboratory from a single type of immune system cell.[67] Such antibodies can identify substances within both normal and cancerous cells that may help cancer cells

grow. The antibodies attach to the substances and kill the cancer cells, block their growth, or inhibit metastasis. Monoclonal antibodies are given by infusion, and may be used alone or to carry drugs, toxins, or radioactive material directly to the cancer cells. Trastuzumab (Herceptin) is a monoclonal antibody that blocks the effects of the growth factor protein HER2.[67]

Metastatic breast cancer

Treatment for men with distant metastases may be hormone therapy, chemotherapy, or both. Hormone therapy may include the following:

- Orchiectomy;
- Luteinizing hormone-releasing hormone with or without total androgen blockade;
- Tamoxifen for cancer that is estrogen-receptor positive;
- Progesterone; and,
- Aromatase inhibitors.[67]

Radiation

Radiation therapy is almost always recommended after lumpectomy to destroy any cancer cells left behind, and to prevent local recurrences in the breast. Without radiation therapy following lumpectomy, the odds of a local recurrence increase by about 25%. These recurrence odds include an increased likelihood of cancer spread to other parts of the body, especially when recurrence happens within the three years following surgery. Radiation can cause side effects such as fatigue, and reddening, darkening, and thickening of the breast.

Treatment with radiation can help prevent breast cancer from returning. Even though radiation can reduce the risk of dying of breast cancer, it may increase the risk of dying of other causes, particularly heart disease, results of a study suggest. Radiation has been shown to prevent breast cancer from returning in the short-term, but the long-term benefits of treatment have been less clear.

In 2002, the FDA approved MammoSite® brachytherapy, a targeted internal radiation by Proxima Therapeutic Inc. The MammoSite® radiation therapy system treatment requires 5 days to administer treatment instead of the 7 weeks required by external radiation. Brachytherapy requires that a balloon applicator be placed inside the tumor resection cavity. The balloon is inflated with a sterile liquid which causes the balloon to inflate, expanding to fill the cavity. A radioactive bead attached to a wire is threaded through the MammoSite® applicator shaft into the inflated balloon. After the treatment is completed, the balloon is deflated and the applicator system removed. The

FDA ordered Proxima Therapeutic Inc. to include a disclaimer with their product, stating that the MammoSite® radiation therapy system is not a replacement for the whole-breast radiation recommended following a lumpectomy.

High-Dose Chemotherapy

In breast cancer treatment clinical trials, researchers at the NIH and other health institutions are testing high-dose chemotherapy to find out if it is better than standard chemotherapy. They are trying to learn if higher doses of drugs can prevent or delay the spread or return of breast cancer better than standard doses of drugs, and which type of treatment helps patients live longer. Patients who receive high-dose chemotherapy are at greatest risk of suffering life-threatening side effects, because the treatment damages their bone marrow and they no longer are able to produce needed blood cells. To help repair the damage done by high doses of drugs, treatment may include peripheral blood stem cell transplantation and/or bone marrow transplantation.

Peripheral blood stem cell transplantation involves the removal of stem cells from the blood. Stem cells, which are the immature cells from which all blood cells develop, are needed because they are able either to divide and form copies of stem cells or to become fully mature red blood cells. The removed stem cells are frozen and stored while the patient is treated with high-dose chemotherapy. After chemotherapy ends, the stem cells are returned to the patient through a vein. Healthy stem cells can then begin to grow and produce all types of blood cells.

Autologous bone marrow transplantation is used in breast cancer treatment. In this procedure, some of a patient's own healthy bone marrow is removed with a needle before treatment begins. The bone marrow is frozen and stored while the patient is treated with high-dose chemotherapy. After the treatment ends, the healthy bone marrow is given back to the patient through a vein, and then can begin to produce blood cells. Peripheral blood stem cells and bone marrow transplantation may be used together as part of high-dose chemotherapy. High-dose chemotherapy has not yet been proven to be a better therapy than standard chemotherapy. Much research is still needed in this area of breast cancer treatment.

Complementary Alternative Treatments (CAM)

Eighty percent of the world's population relies on traditional and indigenous medical practices as an important part of their health care.[70] These practices are regarded as complementary alternative medicine (CAM), in contrast with conventional western practices. CAM is becoming increasingly popular in the United States, and

many Americans seek an alternative health care practitioner. The public uses CAM for both minor and major problems, from colds to cancer. Alternative medicine is an area of great public interest and activity, both nationally and worldwide.[70]

It is estimated that of the number of Americans diagnosed with cancer each year, at least half will seek out alternative or CAM care. These therapies range from nutritional and herbal treatments to mind/body practices. While no one therapy has claimed to find an outright cure for cancer, many leading oncologists have had such positive experiences with CAM that they have integrated them into their practices. Most CAM providers offer cancer care that utilizes different combinations of therapies in ways that are specific to the patient. This approach is often referred to as "integrative care," the goal of which is to attend to the human being as well as the cancer.[70]

The amount of research into CAM systems and practices is quite small in comparison with the analysis of conventional medicine. Research is increasing, however, at a rate of over 12% per year, and now indicates that certain CAM practices have important implications for the way patients are treated and managed, as well as for overall understanding of health and disease.[70] For example, mind/body therapies are useful for the management of pain, acupuncture for treatment of nausea and vomiting, and herbal medicines for depression and dementia. Many CAM practices, such as acupuncture, homeopathy, and meditation, are inherently low risk if offered by qualified practitioners. However, some natural products, such as herbal preparations, contain powerful pharmacological substances that can produce toxicity, herb-drug interactions, and major adverse effects.

Diet and nutritional interventions are widely used by professionals and the public. Millions of Americans use herbal and other supplements in combination with prescription medications, a combination yielding unknown effects. As credible information about CAM practices becomes increasingly available, medical schools, hospitals, insurance companies, the government, and private biomedical companies are beginning to explore and integrate these practices into the mainstream. Both science and common sense must serve as guides as these practices become increasingly common.[40]

In 1992, the Office of Alternative Medicine (OAM) was established by Congressional mandate as part of the NIH.[70] This organization uses federal funds to explore and research alternative courses of treatment, and to raise public interest about alternative options for treating a variety of diseases and disorders. The OAM has developed and grouped CAM therapies into the following broad categories:

- **Diet and Nutrition.** It has been recognized by conventional medicine that a diet rich in fruits, vegetables, antioxidants, and fiber may prevent some forms of cancer.

- **Mind-Body Techniques** include prayer, meditation and yoga. Some breast cancer support groups focus on this form of therapy.
- **Bioelectromagnetics.** The use of electromagnetic fields (consisting of low-frequency magnets) to penetrate the body and heal damaged tissue is not well understood, and is currently under study by the OAM and other groups.
- **Traditional and Folk Remedies** are similar to mind-body techniques, being based on concepts of human physiology that are different from those accepted by Western medicine. Chinese medicine and India's Ayur Veda are the two most recognized traditional folk remedies. Chinese medicine uses teas, herbal pharmacology, acupuncture, and acupressure to alleviate cancer symptoms. Ayur Veda is based on the classification of people into one of three body types, with each body type having its own specific remedies for disease, and regimens to protect against it.
- **Pharmacologic and Biologic Treatments**, which include antineoplastons, shark cartilage, and bovine cartilage, are among the most controversial of the CAM therapies. There is little scientific evidence to support the usefulness of these therapies.
- **Manual Healing Methods** are those traditionally used by osteopathic and chiropractic doctors, and are the most widely recognized CAM therapies. These therapies use therapeutic touch.
- **Herbal Medicine** is a part of both traditional and folk remedies. [70]

Part 4 Imaging Examinations

Early detection of breast cancer affords the best treatment and recovery outcomes. The regular use of mammography in the detection of breast cancer did not occur until the mid-1970s, when data proved that screening mammography could significantly reduce the mortality rate for women with breast cancer. Because breast cancer is rare in men, regular screening mammography is not currently recommended for males. There are no data available on the benefits or risks of mammographic screening for males.

When mammography is performed, it is often expected that it will be more accurate in men than women. This expectation is due to men's breast being less dense than women's, as well as the fact that their breasts do not undergo common changes that women's do.[4] Mammography is well-established as the most effective imaging method for breast cancer screening in women, with published reports of mammograms missing only 10-30% of all breast cancers.[12,18] Combined use of mammography, US, and MRI represents the most accurate diagnostic approach to curbing the breast cancer mortality rate.

Imaging the male breast is very similar to imaging small female breasts. Males with gynecomastia may have sufficient breast tissue to allow for ease in positioning for mammography. The standard mammographic views (craniocaudal and mediolateral oblique) of each breast are routinely obtained. One deviation from the standard mammography techniques is that on the mediolateral oblique position (MLO), a steeper x-ray tube angulation of 65-70º may be needed to adequately position the image receptor parallel with the pectoralis muscle. Magnification and spot compression views may also be used.

Occasionally, when imaging males with hairy chests, the compression paddle may slide. This problem may be corrected by using a technique that is used for small female breasts. This technique uses a spatula to aid in compression of the tissue. An alternative solution would involve rescheduling the imaging appointment after instructing the male patient to shave off chest hair in the area of clinical interest. When mammography yields suspicious findings not characteristic of gynecomastia, US is effective for evaluating the male breast.[16] Stereotactic-guided biopsy is usually not possible in the male breast because of its small size, so US guidance is performed instead.[16]

Today mammography is the gold standard imaging modality for the early detection of breast cancer. Full film digital mammography (FFDM) is widely accepted,

and is rapidly being integrated into breast imaging centers. While in December 2006 only 15% of accredited mammography units were FFDM units, as of April 1, 2009, FFDM units comprised 50.3% of all accredited units, with 6,577 in use in the United States.[71] The United States Food and Drug Administration (FDA) approved the first FFDM unit for marketing in January 2000, and there are currently 10 different FFDM units that have received FDA approval.[71] Dose measurements performed as part of the Mammography Quality Standards Act (MQSA) show overall lower average glandular doses for FFDM units than for screen-film units.[71] Additionally, phantom image scores are generally higher for FFDM units.[71]

Both screen-film and FFDM examinations involve the exposure of the breast to x-ray energies. A major difference between them is that in digital mammography, the image is acquired as an electronic signal in digital format. The decoupling, or separation, of the functions of image acquisition, display, and archival allow independent optimization of each process. Routine clinical application of any digital approach to screening or diagnostic mammography requires that the images obtained be substantially equivalent to, or better than, high-quality screen-film mammograms in portraying clinically significant image detail.[72] A major feature of digital mammography that may ultimately prove to be advantageous is its ability to provide improved image contrast over all regions of the female breast. In addition, the ability to display, archive, and transmit digital mammography images may facilitate:

- Telemammography: Transmission of digital images to remote sites for the purposes of off-site monitoring of diagnostic work-ups, interpretation, consultation, and conferencing;
- Computer-aided detection (CAD) and diagnostic assistance for radiologists;
- Reduction in the number of repeat scans for technical reasons;
- More efficient storage and retrieval of images;
- Interventional techniques; and,
- Digital tomosynthesis.[72]

Breast Tomosynthesis

Screen-film and FFDM mammography have surpassed all expectations in being effective imaging tools for the detection of early-stage breast cancer; however, the appearance of overlapping tissue on mammograms poses a significant obstacle to image interpretation.[24] Breast tomosynthesis is expected to relieve this problem by reducing or eliminating tissue overlap.[73]

If screening mammograms indicate a questionable finding, a follow-up is essential. This may include several studies, such as diagnostic mammography, MRI, and US. Biopsy may be required to further confirm the diagnosis. Breast tomosynthesis technology is a modification of a digital mammography unit that allows a volume of images to be obtained from thin-slice data in a three-dimensional (3D) format.[73] Algorithms similar to those used in CT are used to reconstruct the images into conventional image orientations.[73]

Magnetic Resonance Imaging

MR imaging of the breast is a dynamic imaging technique that uses gadolinium–DTPA to improve sensitivity and image enhancement for the detection of breast cancer.[74] MR breast images effectively reveal multifocal breast disease, aid in staging and follow-up after breast cancer, and help determine which treatment options are most appropriate for a particular case.[74] In breast MR imaging, nearly all malignancies of the breast appear enhanced on the image after intravenous contrast injection.[74] Breast MRI data provide information based on the signal intensity of breast tissue in the presence of gadolinium DTPA. Malignant breast lesions produce a pattern of enhancement that is mapped onto a visual spectrum and delineated by contrast uptake and washout. When a confirmed diagnosis of malignancy is made, the contralateral breast can also be evaluated with MRI.[24] The American College of Radiology (ACR) list of current indications for breast MRI includes, but is not limited to:

- Screening of high-risk patients;
- Screening of the contralateral breast in those with a new breast malignancy. MRI has been shown to detect occult malignancy in the contralateral breast in at least 4-5% of breast cancer patients;
- Determining the extent of breast disease (i.e., metastasis, etc.); and,
- Evaluating clinical or imaging findings.[74]

The ACS concurs with the ACR in its recommendation that certain males with especially high risk of developing breast cancer should get MRI scans.[18,74] MRI is used to determine the extent of disease more accurately than standard mammography and physical examination of the breast. The imaging modality allows a better understanding of the relationship of the breast tumor to the fascia, and its extension into the pectoralis major, serratus anterior, and/or intercostal muscles. Demonstration of the relationship between tumor and other tissues provides useful information in determining candidates for mastectomy and breast-conserving surgery.

MRI may also be useful before, during, and/or after chemotherapy to evaluate treatment response and the extent of residual disease prior to surgical treatment. MRI of the breast is not recommended, as a screening modality for the general population.[74] MRI is more sensitive than mammography, having a reported sensitivity to breast cancer rate of close to 96%. This increased sensitivity may not always be a good attribute, since it detects abnormalities that may or may not be clinically significant.[74] This may lead to higher false positive results than other breast imaging modalities. Surgical decisions should not be based solely on MRI findings, because not all suspicious lesions found during MRI are cancers. All suspicious lesions should be biopsied before a surgical plan is developed.[75]

MRI has the following advantages:

- It acquires patient information without the use of ionizing radiation;
- It produces excellent soft tissue contrast;
- It can acquire images in the transverse (axial), sagittal, coronal, and oblique planes; and,
- The quality of the images is not affected by bone.[76,77]

MRI has the following disadvantages:

- It may present contraindications that would be detrimental to the patient or health care personnel;
- It has a long scan time compared to CT; and,
- Its cost may be prohibitive, and it may be unavailable in certain geographical areas.[76,77]

Current Considerations

Today, breast MR imaging offers the advantage of greater sensitivity than either mammography or US. Breast MRI is excellent for imaging dense breasts, small lesions, and multifocal breast cancer, and may also be useful as an aid in staging and follow-up on breast cancer therapies. Breast MRI also plays a decisive role in determining the course of treatment for breast cancer. For example, a MRI-guided breast biopsy can help determine whether a lumpectomy or mastectomy is the most appropriate course of treatment, after the initial breast cancer diagnosis has been rendered. MRI has also proven effective in identifying residual disease following lumpectomy or chemotherapy, and in distinguishing between postoperative scarring and an active disease process.[78]

MRI cannot always distinguish between benign and malignant lesions. This is because MRI relies on the high vascularity of malignant lesions, and some benign lesions also have high vascularity. Fibroadenomas, radial scars, and areas of inflammation can all appear enhanced on the MR images. MRI is also unable to adequately represent microcalcifications. Yet because MRI has a very high sensitivity, it has proven beneficial in reducing inaccurate cancer diagnoses, and in reducing the number of biopsies due to false positive mammograms.

The high sensitivity of MRI gives it the leading edge in detection of abnormal areas of tissue; the low specificity, however, results in a high false positive rate. Most breast MRI examinations are conducted as an adjunct to other imaging modality examinations. MRI does not really qualify as a standard breast-screening tool because the ideal screening modality must have sensitivity, specificity, reproducibility, and be cost-effective.

> ***Sensitivity*** *in breast imaging refers to the probability of detecting breast cancer when cancer is present. The goal of mammography is that sensitivity should exceed 85%. Sensitivity is often difficult to calculate, because in most clinical settings an accurate false negative rate is difficult to obtain. Access to tumor registry data helps determine the false negative result rate.*
>
> ***Specificity*** *in breast imaging is the quality of being precise rather than general. An imaging system that is highly specific can effectively differentiate between normal and abnormal changes within the breast.*
>
> ***False negative*** *refers to a missed diagnosis. This occurs when the mammography results do not detect any breast disease even though the disease is actually present (i.e., often found during cytology and histology examinations).*
>
> ***False positive*** *refers to a mammography result that indicates the presence of a breast condition when that breast condition is not present.*

Since the current state of breast MRI does not satisfy all of these requirements, it is currently only recommended as a screening examination for very high-risk men and women, and as a diagnostic tool for those with dense breast tissue or suspected breast abnormalities previously demonstrated by other imaging modalities. Breast MRI is a costly procedure compared to mammography or US examinations; it is not widely

available, especially in rural areas, and may not be accessible to certain minority populations.

MRI Safety

Most MRI magnets are superconductive, and their magnetic fields are always on. Because of this, ferromagnetic materials such as an oxygen tank, wheelchair, scissors, etc., may become projectile objects. Before entering a high magnetic field, individuals should be screened for contraindications; these would include biomedical devices/implants and devices that are electronically, magnetically, or mechanically activated, such as pacemakers, cochlear implants, certain intracranial aneurysm clips, and orbital metallic foreign bodies. These devices may move, undergo a torque effect in the magnetic field, overheat, produce an artifact on the image, or become damaged or functionally altered. There is always a concern about claustrophobia. Due to the construction of closed MRI scanners, they are potentially unpleasant for someone who fears the feeling of being closed within a structure.

Ultrasonography

Breast ultrasonography (US) is an adjunctive test, not a replacement for high quality mammography. According to Dr. Deborah Levin in a recent article published in the Radiological Society of North America (RSNA) magazine (*RSNA News)*, radiology practices should ensure that their laboratories have US accreditation.[79] She further states that US is the ultimate "image gently" modality, because there is a total absence of radiation exposure with US.[79] Dr. Levin also states that US is a patient-centered modality; an approach to the delivery of radiology services that many health care professionals advocate.[79]

Breast US has an important recognized role in the detection and evaluation of breast disease. It has become the preferred method for differentiating between solid and cystic breast lesions, and is also commonly used in image-guided breast biopsy procedures. A major advantage of US is that images are produced without radiation exposure. The accuracy of US in distinguishing between a solid and cystic lesion is between 96-100%.[12] Like MRI, US is more sensitive than mammography for dense breast tissue. MR imaging is dependent on contrast uptake by the lesion, while US is not. Also, US is less expensive than MR imaging, but is highly dependent upon operator expertise.

Some of the known strengths of US:

- It images muscle and soft tissue very well, and is particularly useful for delineating the interfaces between solid and fluid-filled spaces;
- It renders “live” images, where the operator can dynamically select the most useful section for diagnosing and documenting changes, often enabling rapid diagnoses;
- It shows the structure of organs;
- It has no known long-term side effects, and rarely causes any discomfort to the patient;
- The equipment is widely available and comparatively flexible;
- Scanners are small and easily carried, and examinations can be performed at the bedside; and,
- The procedure is relatively inexpensive compared to other modes of investigation (e.g., CT, x-ray tomography, and MRI).[80]

Some of the weaknesses of US imaging:

- US devices have trouble penetrating bone;
- US performs very poorly when there is gas between the transducer and the organ of interest;
- The depth penetration of US is limited, even in the absence of bone or air, making it difficult to image structures deep in the body;
- The method is operator-dependent. A high level of skill and experience is needed to acquire diagnostic quality images; and,
- There are no scout images, so once an image has been acquired there is no exact way to tell which part of the body was imaged.[80]

The ACR has published guidelines for the performance of US examination of the breast. In these guidelines, the ACR provides that appropriate indications for breast US include, but are not limited to:

- *Evaluation and characterization of palpable masses and other breast-related signs and/or symptoms;*
- *Evaluation of suspected or apparent abnormalities detected on other imaging studies, such as mammography or MRI;*
- *Detection of an underlying mass that may be obscured on the mammogram;*
- *Guidance for breast biopsy and other interventional procedures; and,*
- *Preparation of treatment plans for radiation therapy.*[80]

The ACR also suggests that breast US images be correlated with clinical signs and/or symptoms, and with other prior examinations (i.e., mammography, MRI).[80] The images under investigation should be viewed in two perpendicular projections, and real-time scanning by the interpreter should be considered. The ACR Breast Imaging Reporting and Data System® (Bi-RADS®) US categories should be used in characterizing breast masses.[80] These include the categories of size, shape, orientation, margin, echogenicity, lesion boundary, attenuation, special cases, and surrounding tissue.

Image-Guided Interventional Breast Procedures

Introduction

Image-guided breast biopsy is recognized as a reliable alternative to surgical biopsy for the histopathologic diagnosis of breast lesions. Breast abnormalities and overt lesions must be thoroughly investigated before a report is prepared presenting the pathologic status (i.e., benign or malignant). Image-guided breast biopsy can be performed with mammography, US, or MRI.[81,82]

In the past, patients with a breast mass had only one choice, a one-step surgical intervention procedure.[83,84] Today, however, image-guided biopsy provides a two-step method that allows time for consultation and decision-making choices after the biopsy, but before the next step. “Studies have shown that the emotional burden of breast cancer is easier to bear if biopsy and treatment are performed at separate times.”[34] “Imaging guided fine-needle aspiration (FNA) and core needle biopsy (CNB)…are alternatives to excisional biopsy for mammographically-depicted breast lesions that require tissue sampling for diagnosis.”[85] For lesions visible on mammography stereotactic-guided biopsy is an option.[85] Presurgical needle localization can also be performed with stereotactic guidance.[85]

Breast Specimen Imaging

One method that helps to increase the accuracy of breast biopsies is breast specimen imaging, which consists of imaging the excised tissue. Introduced in 1966, the technique has been used to gauge the success of image-guided interventional breast procedures.[86] The ACR and other advocates of breast health support the concept of breast specimen imaging as an adjunct to the breast cytology and histology report.

The main goals in imaging excised breast tissue are verifying and documenting that the lesion in question has been removed. Breast specimen imaging has been shown to be 89% accurate for this purpose.[86] Specimen imaging provides two permanent records, the image and the dictated report. It also has an important role in

verifying lesion removal and providing an image sample that can guide the pathologist in the examination. The image from an excisional biopsy specimen can show the size and shape of the lesion, as well as whether it consists of calcifications, a mass, or architectural distortion. Specimen imaging in needle localization breast biopsy procedures is conducted to document that the localizing device has been removed from the patient.

Studies have shown that when specimen images demonstrate that calcifications (or a mass) extend to the borders of the tissue block, an interpreted report stating that the margins are involved is accurate more than 95% of the time.[86] Margins are considered to be clear if histological examination shows that at least 1 millimeter (mm) of tissue on all surfaces edges of the specimen is free of cancer. Pathology results for all breast biopsies should be compared with mammograms and specimen-imaging reports to make certain there is concordance. Post-operative follow-up may be necessary if the pathology findings are not as originally forecast by the mammography and specimen image examinations. The images of a breast specimen can often reveal previously undetected pathology because the tissue is viewed without superimposition of other breast tissue. The ACR recommends imaging tissue from all core biopsies when the lesion contains calcifications. When the abnormality is a mass, specimen imaging is not usually performed.

Medical Outcomes Audit

The Mammography Quality Assurance Act (MQSA) requires certified mammography facilities to perform a medical outcomes audit. Each facility is required to establish and maintain a mammography medical outcome audit program to follow up positive mammography assessments, and to correlate pathology results with the interpreting physician's findings. The objective of the program is to ensure the reliability, clarity, and accuracy of the interpretation of mammograms. Analysis of the outcome data should be made individually and collectively available to all interpreting physicians at the facility. Additionally, any cases of breast cancer among women imaged at the facility that subsequently become known to the facility should prompt the facility to initiate follow-up on surgical and/or pathology results, and to review the mammograms taken prior to the diagnosis of a malignancy. The FDA requires that the audit analysis shall be initiated no later than 12 months after the date the facility becomes certified. Each facility is required to designate at least one interpreting physician to review the medical outcomes audit data at least once every 12 months. This individual is also responsible for documenting the results, and for notifying other interpreting physicians of

both audit and facility aggregate results. If follow-up actions are taken, the audit-interpreting physician is also responsible for documenting the nature of the follow-up.

Ductography or Galactography

Ductography or galactography is an imaging procedure that often helps define the cause of unilateral, single-pore, spontaneous nipple discharge. Conventional ductography is a mammographic examination performed after retrograde filling of the lactiferous ducts with contrast material. Being invasive, conventional ductography has various complications and contraindications. Contraindications to ductography include a significant history of severe allergy to iodinated contrast material, debilitating anxiety, a disorder that precludes patient cooperation during the procedure, or a history of prior nipple surgery that would cause a complete disconnect of the nipple pores from the underlying ducts. MRI hydrography is a non-invasive depiction of the fluid-filled tubular structures. Both conventional and MRI ductography provide information about the interface between a lesion and the fluid filled duct. MRI ductography does not require the use of a contrast agent.

Part 5 Radiation Protection in Mammography

Obligations to Protect

The mammographer has moral, ethical, and legal obligations to protect the public, patients, co-workers, staff, and self from harm while in the service of providing imaging services. "From harm", is an all-encompassing concept that sometimes may seem overwhelming to the individual mammographer; however, when put into perspective, one realizes that he/she is part of a healthcare team, where each member shares a portion of the burden of safety. Mammography technologists are provided guidelines about safe practices, professional behavior, and the scope of imaging practice by the American Registry of Radiologic Technologists (ARRT), American Society of Radiologic Technologists (ASRT), American College of Radiology (ACR), and the Mammography Quality Standards Act (MQSA).

The ARRT *Standards of Ethics* is a professional document that provides registered technologists (i.e., mammographers), registered radiologist's assistants, and candidates with guidelines for acceptable ethical conduct in ensuring protection, safety, and comfort while providing imaging services.[87] Specifically, item 7 of the ARRT *Code of Ethics* states that a "radiologic technologist uses equipment and accessories, employs techniques and procedures, performs services in accordance with an accepted standard of practice, and demonstrates expertise in minimizing radiation exposure to the patient, self, and other members of the healthcare team."[87]

ASRT, the premier organization for imaging professionals, provides further guidance to mammographers in the form of practice standards. For example, Standard 4 of the ASRT *Radiography Clinical Performance Standards* section states that quality patient services are provided through the safe and accurate performance of a deliberate plan of action.[88] Specific criteria associated with this standard further emphasize that radiographers use radiation shielding devices and set "…technical factors according to equipment specifications to minimize radiation exposure to the patient."[88] Additionally, ASRT Standard 8 is based on the specific criteria that radiographers document fluoroscopy time and radiation exposure parameters.[88]

The *Radiography Quality Performance Standards* component of the ASRT *Practice Standards* also highlights several actions that the mammographer must accomplish; these state that the mammographer must:

- Maintain controlled access to restricted areas during radiation exposures;
- Follow federal and state guidelines to minimize radiation exposure levels;

- Maintain and perform quality control on radiation safety equipment such as aprons, thyroid shields, etc.;
- Develop and maintain a technique chart for all equipment; and,
- Participate in radiation protection, patient safety, risk management, and quality management activities.[4]Additional information about the ASRT *Practice Standards for Medical Imaging and Radiation Therapy* is available on the ASRT Web site (www.asrt.org).[88]

For all diagnostic imaging procedures there are universal practices that must be followed by all personnel.[89,90] The ACR has issued detailed universal practice guidelines that support personnel actions during imaging procedures.[90] The ultimate goal of the practice guidelines is to minimize radiation exposure to patients, staff, and the public while delivering high-quality diagnostic images. The ACR practice guidelines for general radiography that relate to breast imaging procedures are paraphrased in the following broad statements:

- *The written or electronic request for mammography should provide sufficient information to demonstrate the medical necessity of the examination, and to allow for the proper performance and interpretation of the examination.*
- *All breast imaging studies should be permanently labeled with patient identification and the date of the examination.*
- *All facilities performing breast imaging should have protocols for standard views of each anatomic area that will be imaged.*
- *All facilities performing breast imaging should have technique charts listing exposure factors that will reliably produce diagnostic radiographs, in order to minimize the need for repeat exposures.*
- *Repeat rates should be part of the routine quality control process.*
- *All breast images should be reviewed for positioning and diagnostic quality at the facility before the patient is released.*
- *All facilities producing breast images should have policies and procedures for the appropriate shielding of patients.*
- *All facilities should have immobilization and assistance procedures that are appropriate for the age and size ranges of patients to be imaged. These should be available to ensure that images of diagnostic quality can be obtained in patients who are unable either to cooperate or to be positioned in an usual manner due to age or physical limitations, and without unnecessary irradiation of healthcare workers.*

- *Reporting should be in accordance with the ACR Practice Guideline for Communication of Diagnostic Imaging Findings.*
- *The diagnostic imaging equipment and facility should meet all applicable federal and state radiation standards.*
- *In facilities where digital imaging is used, the equipment should meet the specifications described in the ACR Technical Standard for Digital Image Data Management.*
- *Automated processing is preferred.*
- *Radiologists, mammographers, and all supervising physicians have a responsibility to minimize radiation dose to individual patients, staff, and society as a whole while maintaining the diagnostic quality.*
- *Facilities, in consultation with the medical physicist, should have policies and procedures in place and adhere to them in accordance with ALARA. They should also have documented policies and procedures related to quality, patient education, infection control, and safety. These should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety Infection Control, and Patient Education Concerns appearing in the ACR Practice Guidelines and Technical Standards Handbook.*[90]

Radiographer Non-Compliance

The philosophical concepts of radiation safety and ALARA become real when, in everyday practice, radiography personnel implement universal practice standards. Although ALARA universal practice standards are easy to perform, there exists widespread concern that radiological personnel are not performing them on a consistent basis. Variations have been found to range from strict adherence to shielding and collimation to no compliance.[91] Several studies (i.e., Tilson and Lemley) and national reports (i.e., *The Challenges and Potential for Assuring Quality Health Care for the 21st Century)* have provided information about the reasons for lack of ALARA compliance.[91] Data from a study conducted in 2003 (i.e., Slechta and Reagan) of the factors related to radiation protection practices indicate that there is poor compliance with radiation safety practices, especially safety practices designed to reduce unnecessary exposure to personnel.[91] Slechta and Reagan based their research on variable factors such as the type of initial professional education, work site type, and years of employment.[91] The results showed that the type of initial professional education was not significantly related

to compliance with ALARA practices, although it had a small, significant association with knowledge of safety practices.[91] The type of work site and years of employment in medical imaging were found to be the more important variable factors in determining compliance with ALARA practices. Specifically, a higher rate of ALARA compliance was found to exist in large hospitals than in any other type of work site.[91]

Factors Impacting ALARA

Recognized ALARA practices consist of simple yet effective measures that can be applied in all imaging procedures. These include those items directly related to the imaging procedure, such as patient communication, examination preparation, motion control, and reduction in repeat examinations. Other items that contribute to the overall goal of ALARA include the design of the x-ray room, structural protective shielding, protective barrier requirements, and equipment design.

Patient Communication & Examination Preparation

Communication between the mammography staff and the patient is vital for ensuring the successful outcome of an imaging procedure. Also, mammographers have a professional and ethical obligation to accurately explain radiation protection principles to patients and the public so that the risks and benefits of using ionizing radiation in medical imaging can be understood. The ASRT refers to the radiographer's responsibility to educate in Practice Standard 3, which states that the "…radiographer educates the patient, public, and other health care providers about procedures, along with the biological effects of radiation, sound waves, magnetic fields, and protection."[88]

Patients present for imaging procedures with various levels of apprehension and knowledge. Patients have the right to know the details of their imaging procedure, and have the legal right to be informed about the potential risks and benefits. Most facilities providing diagnostic imaging services will require the patient or his/her legal guardian to complete an informed consent form. Patients have a right to know about the imaging procedure, and if adequately informed may be more at ease and cooperative. If the imaging procedure requires that the patient disrobe, clear directions and privacy are important. Retake examinations often become necessary when the patient has not properly disrobed, or has failed to remove jewelry, zippers, hairpins, etc during the initial examination. While the patient is preparing for the imaging examination, the mammographer can use the time to extend a welcome, and to explain to the patient how he/she may be of help during the procedure. If positioning or immobilization devices are

needed, the mammographer should briefly explain why they are needed and how they will be used.

Successful communication also includes critical listening skills. If the patient provides details about his/her medical history or chief complaint, the mammographer should be attentive and determine how the information may impact the selection of technical and related imaging factors.

Retaking Radiographs

When a breast image must be retaken, the radiation dose received by the patient increases. The ultimate goal of all imaging procedures is the production of high quality images. A retake may be required whenever the image quality fails to provide adequate diagnostic information. The reasons for retakes range from simple mammographer forgetfulness to complex technical errors. The most common causes of retakes include improper positioning of the part or patient, inaccurate selection of the technical factors (over or underexposure of the image), patient motion (voluntary and involuntary), and improper film processing techniques. The observant mammographer can correct many of these errors beforehand, thus minimizing the number of retakes and reducing the patient radiation dose.

If in doubt about the need for a retake, the mammographer should consult with a supervisor to determine whether the image provides sufficient diagnostic information. Since retakes result in increased radiation dose to the patient, each image should be thoroughly evaluated for diagnostic integrity prior to the decision to perform a retake. Factors such as whether either the patient's condition or the technical factors can be improved upon during the retake examination must also be considered prior to actually taking the retake. In many cases, these factors cannot be easily changed, and the outcome of the retake may not yield any improvement in image quality, so a retake should not be attempted.

A retake analysis program can easily be incorporated into the overall quality control program. Whether performed by an individual or the supervisor, analysis of the number and causes of retake examinations can result in heightened awareness of areas needing correction. Such information can be used to design staff in-service training and customized continuing education. Further, information about an individual mammographer can be used during personnel evaluations as a way to begin a self-improvement plan, or at worst, to begin the documentation for punitive action and eventual termination of employment.

ALARA in Action

The concept of ALARA is best explained as actions the mammographer performs in every imaging examination to provide maximum radiation protection to the patient, public, and self. Some of the simplest ALARA actions performed by the mammographer can be the most effective. Examples of these include when the radiographer:

- Uses the lowest exposure factors that will produce a high-quality diagnostic image;
- Performs the procedure correctly the first time to avoid retake examinations;
- Properly shields the patient with gonadal shields; and,
- Limits the primary radiation beam to the area of clinical interest.

There are many factors contributing to the overall goal of ALARA. Each of the following will be briefly reviewed: cardinal principles, structural design, protective apparel, primary beam limitation, filtration, selection of technical exposure factors, film-screen combinations, grids, and equipment design.

The **cardinal principles** of radiation protection are time, distance, and shielding (TDS). If used together, these principles can effectively minimize radiation exposure. The cardinal principles were first introduced for nuclear-energy employees who had the potential to be exposed to high levels of radiation in the workplace. The mammographer employed in breast imaging is not expected to receive such high levels of radiation; however, the cardinal principles have practical application to everyday medical imaging and special procedures.

The T in TDS refers to the fact that radiation exposure is proportional to the length of time exposed to radiation. A five-minute radiation exposure would result in a radiation dose five times as great as a one-minute radiation exposure. This has several implications that can be related to minimizing radiation exposure. The mammographer has a responsibility to:

- Reduce the amount of time exposed to radiation. The mammographer should stand behind the protective barrier during the exposure, and should not allow visitors in the room during the exposure.
- Make the x-ray exposure only when the imaging room doors are closed. This practice provides a substantial degree of protection for patients and staff who may be walking past the imaging room.
- Reduce the amount of time that the patient is exposed to radiation. The mammographer should reduce retake examinations, which subsequently reduces the total quantity of radiation dose received.

- Use a fast exposure-time whenever possible. A fast exposure time helps minimize patient motion. Motion results in image blurring, which reduces image quality and increases the need for retake examinations.

Exposure Control

There are many factors that influence the amount of radiation that the patient receives. Of these, there are only a few within the mammographer's control. The correct selection of exposure factors is under the direct control of the mammographer, and if performed consistently can reduce radiation exposure to patients and staff. There are various systems available for the selection of technical exposure factors; these include both manual and automatic variables on computed and direct mammography equipment. Automatic exposure control (AEC) systems limit the length of the exposure, and thereby have some impact on overall radiation dose. AEC devices are also referred to as phototimers, and are programmed to terminate the radiographic exposure time at a predetermined value. Mammographers are advised to continually review current technical and positioning references in regard to proper selection of AEC chamber(s), and correct positioning when using them.

The D in TDS is for distance as it relates to the distance between the patient, mammographer, and the radiation source. One of the most effective methods that radiographers can use is to put as much distance between themselves and the radiation source as possible. The inverse square law applies to point sources of radiation, and can be used to demonstrate the effect of distance on radiation intensity. The distance principle as applied to patient protection refers to the fact that every breast imaging procedure should be performed with the x-ray tube or source positioned at the proper distance from the patient or part being examined.

The S in TDS is for shielding. When x-ray travels through living tissue, the quantity and energy of the x-ray decreases as a result of attenuation by the tissue. The degree to which the quantity and energy of the x-ray beam is decreased depends upon the following three factors:

- Original quantity and energy of the x-ray;
- Type of absorber material, or atomic number of the tissue; and,
- Thickness of the absorber material in centimeters or inches, and consideration of any existing pathology.

Structural Design for Radiation Protection

A breast imaging room must be designed to ensure that placement of the equipment is proper, and that the structural protective shielding meets recommended protective guidelines. A qualified medical physicist must survey the prospective room design and determine the exact requirements for structural shielding. Whether the prospective breast imaging room is already in existence or is part of a new construction, appropriate thickness of lead structural shielding must be installed according to the physicist's specifications, which are usually mandated by state and/or federal laws. The physicist provides recommendations for both primary and secondary protective barriers.

Primary structural protective shielding provides protection from the primary x-ray beam. Primary radiation emerges directly from the x-ray tube window, and moves without deflection toward a wall, door, etc. A wall in the path of the primary radiation requires the most protective shielding. For equipment capable of operating up to 150 kVp, protective primary structural shielding should consist of 1/16th inch of lead and extend as high as seven feet from the imaging room floor.[92] Primary structural protective shielding is installed perpendicular to the primary x-ray beam.

Secondary radiation occurs when the primary x-ray beam is deflected or re-directed by the object being irradiated. Radiation leakage around the x-ray tube and scatter radiation generated by the patient and other objects receiving radiation comprise secondary radiation. Secondary protective structural shielding should consist of 1/32nd inch of lead, extend to the ceiling, and be located parallel to the primary beam.[92] Secondary protective shielding is also installed in the control console shield and structural barrier window through which the mammographer can observe the patient. The window is required to contain 1.5mm of lead equivalent.[92]

Protective apparel for Radiation Protection

Protective apparel is used for the patient and mammographer whenever additional protection is desired or necessary. Protective apparel consists of lead-impregnated vinyl gloves and aprons. If the x-ray tube operating capacity is in the 100-kVp range, the lead gloves and aprons should contain at least 0.25-mm of lead equivalent; however, a lead apron is typically lined with 0.5-mm of lead or its equivalent.

Gonadal shielding protects the patient's gonads from direct exposure to the primary radiation beam. Gonadal shields should be used in addition to collimation. Gonadal shielding should be provided for all persons having reproductive potential, including adults of reproductive age and children. The anatomic location of the testes in the male generally allows for adequate shielding while not obscuring important anatomic

structures; however, the ovaries are located near the vertebral spine, ureters, and the small and large intestines, and pose a shielding challenge. Gonadal shields should meet the following specifications based on the kilovoltage range of the radiography equipment being used:

- 0.25 mm of lead equivalent for 100 kVp or less;
- 0.5 mm of lead equivalent for 100 to 150 kVp; and,
- 1.0 mm of lead equivalent for 150 kVp and above.[92]

Protective gloves, aprons, and lead gonad shields impregnated with lead should be handled and stored with care. Protective apparel should not be folded during storage since cracks may result from bending. If cracks occur, radiation may leak through and diminish the protective characteristic. Protective apparel should be checked at least every three months for cracks.

Primary beam limitation

Primary beam limitation is one of the most effective methods that can be employed to reduce unnecessary radiation exposure to the patient. Limitation of the primary x-ray beam has a twofold benefit: it reduces the amount of radiation dose to the patient by reducing the amount of scatter radiation while also producing a high quality image. As the amount of primary radiation is reduced, the quantity of secondary scattered radiation is also reduced.

Filtration

Filtration of the primary radiation beam is another method that contributes to the overall goal of ALARA. A radiographic filter removes low-energy, long-wavelength photons from the primary radiation beam. The two major functions of a radiographic filter are (1) protecting the patient's skin and superficial tissue, and (2) improving the quality of the radiation beam.[92] The filter removes the longer wavelengths, or the lower energy photons, from the primary radiation beam, resulting in a primary radiation beam that is more homogeneous in nature. Specific mammography x-ray tube filtration requirements and the use of grids will be discussed later in this course.

A Review of Facts

To review, the following facts are presented regarding radiographic image-quality factors:

- Kilovoltage (kVp) is under the direct control of the mammographer. The penetration ability and quality of the primary beam is controlled by kVp. The higher the kVp, the greater the penetrating ability of the primary radiation.
- mA and mAs are under the direct control of the mammographer. These factors affect the quantity of radiation in that the quantity of radiation is proportional to the mA.
- Filtration affects both the quality and quantity of radiation in the primary beam.
- Source to image distance (SID) is under the direct control of the mammographer. The SID affects the quantity of x-ray photons but has no effect on the quality of the radiation beam. The quantity of x-ray photons is affected by the inverse square law, which states that the intensity (quantity) is inversely proportional to the square of the distance.

Quality assurance and quality control are very important aspects of an active ALARA-based radiation safety program. Quality assurance consists of all the activities that support the delivery of high-quality breast imaging and patient care. Quality assurance is the broad umbrella of evaluation and monitoring which encompasses all the systems that affect the delivery of breast imaging services and patient care. This includes the patient information data systems, personnel policies and procedures, and overall operating procedures (clerical, technical, support, administrative, etc).

All imaging systems and accessory equipment, such as cassettes, viewboxes, and darkroom environmental features, are subject to regular required inspection, maintenance, and testing protocols that must be performed to assure the integrity of the system. Mammographers are encouraged to continue to expand their knowledge and understanding of quality assurance and quality control by consulting specific references on these subjects.

Imaging Equipment Design for Radiation Protection

Digital Mammography

The greatest advantage of digital radiography is that the steps of recording, displaying, and archiving an image are decoupled, providing the radiologist and radiographer the opportunity to optimize each task independently. Screen-film radiography, computed radiography (CR), and digital radiography involve exposure of the body to x-ray energies. A major difference in digital mammography is that the digital image is acquired as an electronic signal in digital format.

Use of computerized software in digital mammography allows for post-processing and optimization of the digital images that is not possible in screen-film radiography. For example, images that may be underexposed or overexposed can be corrected with software applications. Because of ongoing innovations in digital mammography software programs, system manufacturers typically issue updates or revisions to the system software.[45] These must be installed and tested to ensure ongoing compliance and quality. Such software upgrades are considered part of the ongoing quality control program in digital mammography, and are often highly specific to a particular system.[45]

Sharing of digital breast images is important in the timely delivery of radiology services, and in the delivery of high-quality medical care.[93] The ability to share prior images may result in fewer imaging examinations for the patient, and ultimately, a reduction in radiation exposure.

Computer Aided Diagnosis (CAD)

CAD is defined as a diagnosis made by a radiologist who considers the output of a computer analysis of an image when making an interpretation. With CAD, radiologists use the computer output as a "second opinion," but make the final decision themselves.[94,95] CAD is a concept established by taking into account the roles of physicians, whereas automated computer diagnosis is a concept based on computer algorithms only.[94] CAD is a technical method for the automated detection of lesions and various pathologies. With CAD, the performance by computers does not have to be comparable to or better than that of physicians, but needs to be complementary to diagnosis made by those physicians. [94,95]

The radiologist interprets and analyzes the image findings; if necessary the patient is recalled for further work-up, or the findings may be dismissed as insignificant.[48] Suboptimal quality images result in poor CAD output. CAD has the potential to increase detection of cancer; however, it is the radiologist's knowledge and interpretive skill that determine the final decision.[94,95]

Picture Archiving and Communication Systems (PACs)

Successful and efficient diagnostic imaging reporting must bring together the current and prior images, prior reports, orders, and other clinical information, as well as the reporting or declaration systems used to create the reports. The information travels via a pathway in the following order:

- Images are acquired and sent to an image display, along with prior examinations retrieved from storage; and,

- Current images are stored for future use as “priors”.

A PACS system serves as the image-handling aspect of this process; the five principle functions of a PACS include:

- Image acquisition: interfacing the digital imaging equipment and receiving the digital image data;
- Image storage: securely storing the image data, which may contain thousands of gigabytes of information;
- Image communication: rapidly communicating image data over computer networks;
- Image display: formatting and displaying images on workstation screens sufficient for primary diagnosis or other clinical tasks; and,
- Image management: properly identifying and indexing the data in terms of its clinical content. [96]

Images that must be transmitted to other locations are sent by clear and well-accepted standards, which exist because of the Digital Imaging and Communication in Medicine (DICOM) standard.[97] DICOM images are labeled with the modality code and a specialization of the digital x-ray image object. Some of the pressing issues of the current state of digital imaging are the security of patient information, image data storage requirements, and disaster recovery of data.

Mammography

Currently, mammography is the only radiation examination fully regulated by the federal government. As mentioned previously, the federal MQSA Act went into effect on April 28, 1999. With the passage and implementation of this act, machines, staff, and interpreting physicians came under strict requirements intended to promote the consistent production of high-quality breast images, and to control radiation dose.
In reviewing data gathered, since 1992, during the MQSA on-site facility inspection program, the FDA concluded that the quality of image interpretation, which depends on human factors, is difficult to measure in practice. In preparation for reauthorization of MQSA, Congress commissioned a study from the Institute of Medicine (IOM) to determine whether additional steps could be taken to increase the accuracy of mammography interpretation, and whether the current regulations should be modified to improve the oversight process. The committee was also asked to evaluate mammography services, and to identify steps that could be taken to ensure the safe and

effective use of other screening or diagnostic tools; these recommendations are shown in Figure 9.

Improve Mammography Interpretation

- Revise and standardize the required medical audit component of MQSA.
- Facilitate a voluntary advanced medical audit with feedback.
- Designate specialized Breast Imaging Centers of Excellence and undertake demonstration projects and evaluations within them.
- Further study the effects of continuing medical education (CME), reader volume, double reading, and computer-assisted diagnosis (CAD).

Review MQSA regulations, inspections, and enforcement.

- Modify regulations to clarify their intent and address current technology.
- Streamline inspections and strengthen enforcement for patient protection.
- Ensure an adequate workforce for breast cancer screening and diagnosis.
- Collect and analyze data on the mammography workforce and service capacity.
- Devise strategies to recruit and retain highly skilled breast imaging professionals.
- Make more effective use of breast imaging specialists.

Improve breast imaging quality beyond mammography.

- Mandate accreditation for "non mammography," or breast imaging methods that are routinely used for breast cancer detection and diagnosis, such as ultrasound and magnetic resonance imaging.

Fig. 9. Summary of the IOM Committee Recommendations to Improve Breast Imaging Quality. Adapted from Improving Breast Imaging Quality Standards. Institute of Medicine and National Council of the National Academies. The National Academy Press. Washington, DC 2005.[98]

The recommendations of the Committee represent a consensus that was developed through review and discussion of published literature as well survey and modeling results. It was understood that the recommendations could not be implemented immediately without waiting for the next MQSA reauthorization in 2007; however, the group stressed that the recommendations are interconnected, and that implementing the entire set will be important in achieving further improvements in the effectiveness of breast cancer detection. Additional information can be found in the document titled *Improving Breast Imaging Quality Standards,* published by the Institute

of Medicine and the National Research Council of the National Academies, available at www.nap.edu.

The MQSA requires personnel to receive specific training in digital mammography in addition to meeting the initial MQSA mammographic training qualifications. Interpreting physicians and mammographers are required to obtain eight hours of initial training related to FFDM prior to first using the technology. The MQSA specifies that this should include practical (hands-on) training in any aspects of FFDM systems which are unique to those systems, and fall under the responsibility of the radiologic technologists or interpreting physician.[93] The FDA strongly recommends that interpreting physicians and radiologic technologists whose eight hours of FFDM training did not include any training in soft copy interpretation obtain such practical training under a qualified instructor before beginning to independently manipulate and interpret soft copy images.[93]

Specialized mammography equipment is much different than conventional x-ray equipment. Two major differences include the ranges of kVp and mA used for mammography. The kilovoltage used during mammography varies between 25 and 28 kVp, and the mA, depending on the equipment manufacturer, may vary from about 2 mA to as high as 180 mA.[99] Automatic exposure control settings allow for the production of high-contrast breast images over a wide range of breast thickness, thus reducing the amount of retake examinations due to this variable. Another specific design feature that helps prevent over-penetration of breast tissue is the composition of the anode. The anode of the mammography x-ray tube is made of molybdenum, which allows for the low energy range of x-ray energies needed for mammography.

All mammography x-ray tubes require filtration in the port. Beryllium is the material of choice for mammography tube filtration because it allows the low-energy x-rays to exit. Some mammography x-ray tubes are equipped with an interchangeable rhodium filter designed for use with the molybdenum anode. This combination allows for the production of the higher energy x-ray beams that are needed for larger or denser breast tissue.

Scatter radiation produced by breast tissue is controlled with the use of a grid. Since the introduction of grids in 1978 on dedicated mammography units, the amount of scatter and secondary radiation has been reduced. This not only decreases the radiation dose, but also improves image quality, specifically radiographic contrast. A grid is used on all mammography procedures except in magnification views of the breast. The radiation dose to the breast significantly increases in specialized methods such as magnification, but provides improved visualization of breast tissue. Increased radiation

dose during magnification imaging of the breast also results from the additional exposure required because of the failure of the reciprocity law.[99]

Compression of breast tissue and selection of slow speed, single emulsion screens and compatible film are additional features that have provided a reduction in radiation exposure during mammography. Compression of breast tissue during mammography serves to decrease the thickness of the breast tissue, improve image quality, and decrease radiation exposure.

As with any imaging procedure, by limiting the number of projections taken, and by reducing retake examinations, the amount of radiation dose to both the patient and the radiographer is reduced. Radiographers are encouraged to be ever vigilant with regard to observing all radiation protection measures at all times.

Radiation Detection and Monitoring

Radiation detection and monitoring are important to the overall radiation protection program in any facility. Monitoring of personnel provides important information regarding the amount of radiation exposure received. Information gathered from personnel monitoring is generally reviewed by the radiation safety officer (RSO) to determine if it is within the acceptable exposure guidelines. After review, corrective actions may be required to reduce or eliminate the radiation exposure. It should be noted that monitoring is not considered a protective method; rather, the data gathered from monitoring provides information about the wearer's personal radiation safety habits and the imaging environment.

Radiation monitoring is recommended for those who are exposed occupationally on a regular basis to ionizing radiation, and who are at risk of receiving 10% or more of the annual occupational effective dose limit of 5 rems in any single year.[100] Regardless of the company supplying personnel radiation monitors and reporting, there is a certain amount of information that is commonly contained in a report. This information is listed as follows:

- Personnel identification, usually by a number (name, birthdate, and sex);
- Type of dosimeter;
- Radiation quality (e.g. X-rays, beta particle, neutron, combined radiation exposure);
- Equivalent dose data for the entire reporting period; and,
- Notation of the starting date that the monitoring company began keeping records for the individual.

Radiographers should maintain a copy of their accumulated permanent equivalent dose record. This information can then be conveyed from employer to employer throughout the person's work life. The optically-stimulated luminescence (OSL) dosimeter combines the best features of the traditional film badge monitor and thermoluminescent dosimeter, while eliminating some of their disadvantages. The OSL dosimeter can be worn for up to one year, but in actual practice is usually only worn for a two month period.[92] A disadvantage of the OSL dosimeter is that it must be shipped to the radiation monitoring company for reading, so determination of exposure is delayed.[92] The OSL dosimeter has a sensitivity reading as low as 1 mrem for x-ray and gamma ray photons, and is considered the monitor of choice for monitoring both personnel working in low-radiation exposure environments and pregnant workers.[92]

The Safety Manual from the Office of Safety and Environmental Health at Johns Hopkins offers the following additional tips regarding personnel radiation monitoring:

- *Individuals who may receive an occupational radiation dose in excess of 10% of the allowed limits shall be required to use a personnel monitor.*
- *The monitor is a measure of the individual's personal exposure. It should not be given to other people to wear.*
- *Once a month, the films within the monitor must be changed. Failure to change the film at the proper time negates the monitor's usefulness.*
- *Monitors should not be put in radiation sources for experimental purposes.*
- *The personnel radiation monitor is issued to document exposure to the head and trunk of the body. The monitor should be worn at the waist or chest level, never at the extremities. When wearing a protective apron, the personnel radiation monitor should be worn outside the apron at the collar level.*
- *If a monitor is lost or damaged, a new monitor must be obtained before continuance of activities involving possible radiation exposure. There is a charge for exchange of damaged holders.*
- *Technologists should take care of the personnel radiation monitor as it is also sensitive to heat, moisture and pressure. Appropriate precautions should be observed.*
- *A personnel radiation monitor should never be worn when receiving radiation exposure as a patient.*
- *An annual record of radiation exposure should be provided to the technologist at his/her request.*[100]

Radiation protection procedures for patients, staff, and the general public require that radiography personnel be knowledgeable about the nature of ionizing radiation, and constantly attentive to all safety measures. Radiography personnel are challenged to apply a variety of methods, techniques, skills, and knowledge in an effort to practice ALARA in every imaging procedure.

Conclusion

Mammographers and medical care providers have a unique opportunity to communicate the facts about male breast cancer to patients, the public, and the community at large. Most patients receiving mammography services will be female. If each female patient could be challenged to educate relatives, friends, and co-workers about male breast cancer, the number of lives saved could be substantial. To promote this idea, the mammographer, with permission, could distribute literature about male breast cancer to each patient, or include such information in waiting room reading resources. The American Cancer Society is an ideal source for literature on male/female breast cancer, and the materials are often free or low-cost.

In the process of soliciting the patient's family breast cancer history, the mammographer has an opportunity to provide male/female breast health information to the patient, and ask them to share it with others. Breast cancer in men often grows undetected until a late-stage diagnosis is rendered. Some of the reasons cited for this include a lack of public awareness, failure of medical professionals to act on breast complaints from males, or just inattention on the part of males to possible signs of disease in their breasts. Regardless of the reasons, many men could be saved from this deadly disease with early detection and intervention. Awareness of the signs and symptoms of breast cancer is the first step in reducing its current mortality rate for men.

Consider the following personal stories from people across the United States who have been affected by male breast cancer.

- Hello, my name is Brent. I am a breast/chest cancer survivor of 4 years and I did not know that men could have breast cancer;
- Hello, my name is Winston; I am 35 years old and didn't think much about it when I noticed my left nipple had inverted. I just though it was a sign of growing older;
- Hello, my name is Steven, and when I was a teenager, I noticed a lump in my right breast just behind the nipple. My doctor said it was normal for this to happen, but now, several years later, I just found out I have stage IV breast cancer;

- Hello, my name is Susan, and my father recently died from breast cancer. Now my family and I are meeting with a genetic counselor to decide if we should have genetic testing for breast cancer.[6]

In a moment of decision, the best thing you can do is the right thing.
The worst thing you can do is nothing.
Theodore Roosevelt

Citations for Imaging Male Breast Cancer

1. Breasted, J.H. The Edwin Smith Papyrus. Chicago: University of Chicago Press, 1930; 403-406.
2. Baum, M. Breast cancer 2000 BC to 2000 AD-Time for a paradigm shift? ATCA Oncologica, 1993; 32(1): 3-8.
3. Greaves, Mel. *Cancer the Evolutionary Legacy*. Oxford University Press; New York, 2000.
4. American Cancer Society. Detailed guide: breast cancer in men. What are the key statistics about breast cancer in men? Retrieved from http://www.cancer.org on June 22, 2009.
5. Bio-Medicine. Breast cancer in men often underestimated and Under-treated. Retrieved from http://www.bio-medicine.org on June 22, 2009.
6. John W Nick Foundation, Inc. Personal stories. Retrieved from http://wwwjohnwnickfoundation.org on June 21, 2009.
7. Imaginis. Study: breast cancer may be more deadly in men (dateline June 3, 2007). Retrieved from http://www.imaginis.com on May 3, 2009.
8. Brinton LA, Carreon JD, Gierach GL, McGlynn KA, Gridley G. Etiology factors for male breast cancer in the U.S. Veterans Affairs medical care system database. 29 March 2009. Retrieved from http://www.springerlink.com on June 22, 2009.
9. American Cancer Society. Breast cancer in men. Retrieved from http://www.acr.org on May 29, 2009.
10. Hartman L. Benign breast disease and the risk of breast cancer. *New England Journal of Medicine.* 2006;353:229-237.
11. Andolina V, Lillé S, Willison K. *Mammographic Imaging: A Practical Guide, 2nd ed.* Philadelphia, PA: Lippincott, Williams & Wilkins; 2001.
12. Cardenosa G. *Breast Imaging Companion, 2nd ed.* Philadelphia, PA: Lippincott, Williams & Wilkins; 2001.
13. Canadian Breast Cancer Research Alliance. Retrieved May 2, 2009 from www.breast.cancer.ca/WebNET.
14. American Cancer Society. What is breast cancer in men. Retrieved from http://www.cancer.org on May 1, 2009.
15. National Institute of Child Health and Human Development: National Institutes of Health. Klinefelter syndrome. Retrieved from http://www.nichd.nih.gov on May 3, 2009.
16. Chen L, Chantra PK, Larsen LH, Barton P, Rohitopakarn M, Zhu E, Bassett LW. Imaging characteristics of malignant lesions of the male breast. RadioGraphics 2006;26:993-1006.
17. National Cancer Institutes. U.S. National Institutes of Health. Genetics of breast and ovarian cancer (last modified 04/24/2009). Retrieved from http://www.cancer.gov on May 3, 2009.
18. American Cancer Society. Breast cancer facts & figures 2007-2008. Retrieved from http://www.cancer.org on May 1, 2009.
19. Earnst L. Wynder. Dietary factors related to breast cancer. *Cancer* 45:899-904, 1980.
20. T. Hirayama. Epidemiology of breast cancer with special reference to the role of diet". Prevention Medicine 7:173-195, 1978.
21. MacMahon, B. Dietary hypotheses concerning the etiology of human breast cancer. Nutrition and Cancer 1:38-41, 1979.
22. Carroll, K.K. Experimental evidence of dietary factors and hormone-dependent cancers. Cancer Research 35:3374-3383, 1975.
23. Vorherr, H. Breast cancer in relation to overnutrition. Klin Wochenschr 58:167-171, 1980.

24. Petrakis, N., C.A. Maack, R.E. Lee, and M. Lyon. Mutagenic activity in nipple aspirates of human breast cancer. *Cancer Research* 40:188-190, 1980.
25. P. Hill, E.L. Wynder, L. Garbaczeqski, et al. Diet and menarche in different ethnic groups. European Journal of Cancer 16:519-525, 1980.
26. S.P. Gaskill, W.L. McGuire, C.K. Osborne, and M.P. Stern. Breast cancer mortality and diet in the United States. Cancer Research 39:3628-3637, 1979.
27. R. L. Phillips. Role of lifestyle and dietary habits in risk of cancer among seventh-day adventists. Cancer Research 35:3513-3522, 1975.
28. Brenner, A.J., Aldaz, C.M. The genetics of sporadic breast cancer. Prog. Clin. Biol. Res. 1997;396:31-51.
29. Ryan, K.M., Bernie, G.D. Myc onogenes: the enigmatic family. Biochem. J. 1996, 314:713-721.
30. American Cancer Society. Cancer facts & figures 2009. Retrieved from www.acs.org on June 15, 2009.
31. National Cancer Institute. Identifying genetic variations that may increase use risk of breast cancer (posted 03/29/2009). Retrieved from www.nci.org on June 19, 2009.
32. National Cancer Institute: U.S. National Institutes of Health. *BRCA1* and *BRCA2:* cancer risk and genetic testing. Retrieved from http://www.cancer.gov on June 20, 2009.
33. Baron, R. H., Borgen P. I. Genetic susceptibility for breast cancer: testing and primary prevention options. Oncol News Forum. 1997; 24:461-468.
34. Muir, E. G, Yates-Bell, A.J., Barlow, K.A., Multiple primary carcinomas of the colon, duodenum, and larynx associated with keratoachnthomata of the face. Br J. Surg. 1997; 54: 191-195.
35. Starich, T.M., Vanderveen, J. P., Awert, F. et. al. The cowden syndrome: a clinical and genetic study in 21 patients. Clinical Genetics. 1986; 29: 222-223.
36. Wikipedia, the free encyclopedia. Medical record. Retrieved May 15, 2009 from www.wikipedia.org.
37. Hendricks MM. Documentation for mammographers. *Radiol Tech*. May/June 2007.;78:396M-412M.
38. RT Image. (In the News)Managing health information efficiently. February 2, 2009. 22;5:9.
39. Schultz A. The paperless workflow: mammography embraces electronic reporting. *RT Image.* February 2, 2009. 22;5:20-22.
40. Berlin L. Errors of omission. *AmerJRad.* 2005;185:1416-1421. Accessed May 1, 2009 from www.ajronline.org..
41. Homer MJ, Berlin L. Mammography and the patient information form. *AmerJRad.* 2002;178:397-310. Accessed May 1, 2009 from www.ajronline.org..
42. American Society of Radiolgic Technologists. The practice standard for medical imaging and radiation therapy. 2007. ASRT. Accessed May 1, 2009 from www.asrt.org.
43. Greenwald, P., Kelloff, G., Burch-Whitman, C. Kramer, B. Chemoprevention. CA Cancer J. Clin. 1995; 45:31-49.
44. Applebaum AH, Evans GFF, Levy KR, Amirkhan RH, Schumpert TD. Mammographic appearances of male breast disease. RadioGraphics 1999;19:559-568.
45. Thompson-Hoffman T. Radiologic appearance of uncommon breast diseases. *Radiol Tech*.2005;76:217M-229M.
46. Benign breast disease an important cancer risk factor. Available at www. the doctorslounge.net/print.php. Accessed May 11, 2006.
47. Youk JH, Kim E, Ko KH, Kim MJ. Asymmetric mammographic findings based on the fourth edition of BI-RADS: types, evaluation, and management. *RadioGraphics*. 2008, 10.1148. RSNA, 2008.

48. Monda LA. Differentiation of breast calcifications. *Radiol Technol* 2005;76(3):532-543.
49. Birdwell, R, Morris L, Wang EA, Shi-Chang, Parkinson, BT. *Pocket Radiologist Breast Top 100 Diagnoses.* Philadelphia, PA:Saunders;2003.
50. Sabate JM, Clotet M, Gomez A, De la Heras, P, Torrubia S, Salinas T. Radiologic evaluation of uncommon inflammatory and reactive breast disorders. *RadioGraphics.* 2005;25:411-424. Accessed May 1, 2009 from www.rsna.org.
51. Blumstein Howard A, Rontal Amy K. Breast abscess and masses. Available at www.emedicine.com/emerg/topic68.htm. Accessed June 22, 2006.
52. Feder JM, De Paredes ES, Hogge JP, Wilken JJ. Unusual breast lesions: radiologic-pathologic correlation. *RadioGraphics.* 1999;19:S11-S26.Accessed May 1, 2009 from www.rsna.org.
53. American Diabetes Association. All about diabetes. Retrieved May 25, 2009 from www.diabetes.org.
54. American Diabetes Association. Type 2 diabetes. Retrieved May 25, 2009 from www.diabetes.org.
55. Westinghouse W, Hoffman NY. Diabetic fibrous breast disease. *Radiol.* 1989;172:667-670.
56. Thompson-Hoffman T. Radiologic appearance of uncommon breast diseases. *Radiol Tech*.2005;76:217M-229M.
57. Nicholson BR, Harvey JA, Cohen MA. Nipple-areolar complex: normal anatomy and benign and malignant processes. *RadioGraphics.* 2009;29:S509-S523. Accessed May 1, 2009 from www.rsna.org.
58. Fibrocystic breast disease. Available at health.allrefer.com/health/fibrocystic-breast-disease-info.html. Accessed May 11, 2006.
59. Benign breast disease an important cancer risk factor. Available at www. the doctorslounge.net/print.php. Accessed May 11, 2006.
60. Goel NB, Knight TE, Pandey S, Riddick-Young M, de Pareded ES, Trivedi A. Fibrous lesions of the breast: imaging pathologic correlation. *RadioGraphics.* 2005;25:1547-1559. Accessed May 1, 2009 from www.rsna.org.
61. Burga AM, Fadare O, Lininger RA, Tavassoli FA. Invasive carcinomas of the male breast: a morphologic study of the distribution of histologic subtypes and metastatic patterns in 778 cases. Virchows Arch. 2006 November; 449(5): 507-512. Retrieved from www.pubmedcentral.nih.gov on July 1, 2009.
62. Imaginis. Breast cancer in men. Retrieved from http://www.imaginis.com on May 3, 2009.
63. Erhan Y, Zekioglu O, Erhan. Invasive lobular carcinoma of the male breast. Retrieved from www.cma.ca on July 1, 2009.
64. American Joint Committee on Cancer. *Cancer staging manual.* 6th ed. New York, NY. Springer. 2002.
65. National Cancer Institute. Genetic variant associated with resistance to chemotherapy drug in women with breast cancer. Retrieved from www.cancer.gov on June 16m 2009.
66. Nordman IC, Dalley DN. Breast cancer in men-should aromatase inhibitors become first-line hormonal treatment? *The Breast Journal*: 2008:14(6);562-569.
67. National Cancer Institute. Male breast cancer treatment. Retrieved from www.cancer.gov on July 1, 2009.
68. National Cancer Institute. Researchers identify biological markers that may indicate poor breast cancer prognosis. Retrieved from www.cancer.gov on June 16, 2009.
69. Golshan M, Rusby J, Dominquez F, Smith BL. Breast conservation for male breast carcinoma. Retrieved from www.sciencedirect.com on July 1, 2009.
70. Dr. Wayne B. jonas. “An Overview of Complementary and Alternative Medicine” presented Friday, October 20, 2000, in a Medical Review of Complementary

Therapies. Sponsored by the Jewish Hospital Heart and Lung Center, Louisville, KY.
71. U.S. Food and Drug Administration. Center for Devices and Radiological Health. Mammography. Retrieved May 10, 2009 from http://www.fda.gov/cdhr/mammography/facilities-rev.htm.
72. American College of Radiology. ACR Practice Guideline for the Performance of Screening and Diagnostic Mammography. (2008 Res.24) Available at: www.ACR.org/secondarymainmenucategories/quality-safety/guidelines/breast/screening-diagnostic.ASPX. Accessed December 26, 2008.
73. Park JM, Franken EA, Garg M, Fajardo LL, Niklason LT. Breast tomosynthesis: present considerations and future applications. *RadioGraphics.* 2007;27:S231-S240. Accessed May 1, 2009 from www.rsna.org.
74. American College of Radiology. ACR practice guideline for the performance of contrast-enhanced magnetic resonance imaging (MRI) of the breast. Revised 2008. Retrieved May 14, 2009 from www.acr.org.
75. Diagnostic Imaging. Study offers updated guideline on use of breast MR imaging. The newsmagazine of imaging innovation & economics. CMP Medica Journals. April 2009 (25).
76. Grey ML, Ailiani JM*. CT & MRI Pathology: A Pocket Atlas*. New York, NY: The McGraw-Hill Companies, Inc.; 2003.
77. Roth CK. Rad Tech's Guide to MRI: Imaging Procedures, Patient Care and Safety. Oxford, England: Blackwell Science, Inc.;2002.
78. Duffy E. Best for the breast: looking for MRI's place. *RT Image*. 2009;22:50-51.
79. Levin D. (My Turn). Sound advice: use ultrasound. *RSNA News.* May 2009.19:4.
80. American College of Radiology. ACR practice guideline for the performance of a breast ultrasound examination. Revised 2007. Retrieved May 14, 2009 from www.acr.org.
81. Sentinel lymph node biopsy. Accessed May 23, 2009 from www.imaginis.com/breasthealth/sentinelnode2.asp.
82. Siemens Medical. Magnets, spins, and resonances: an introduction to the basics of magnetic resonance. Siemens Medical Solutions. Erlangen: 2003.
83. Johnson Marlene. Breast biopsy techniques and breast pathology. *Rad Tech.* September/October 2007, Vol. 70/No.1.
84. Homer Marc J. Mammmographic interpretation: a practical approach, 2nd Ed. 1997. McGraw-Hill Companies. New York, NY.
85. ACR practice guideline for the performance of stereotactically guided breast interventional procedures. American College of Radiology. Accessed at ACR.org. June 25, 2008.
86. Monda LA. Breast specimen imaging. *Radiol Tech*. November/December. 2005;77:121M-543.137M.
87. American Registry of Radiologic Technologists. *Standards of Ethics.* Retrieved from www.arrt.org on June 18, 2009.
88. American Society of Radiologic Technologists. *Radiography Clinical Performance Standards.* Retrieved from www.asrt.org on June 12, 2009.
89. North Carolina University Health and Safety, Radiation Safety Division. *Radiation safety and alara.* Retrieved from www.ncsu.edu on May 17, 2007.
90. American College of Radiology. *ACR guidelines and standards, ACR practice guideline for general radiography.* 2006;17-20. Retrieved from www.acr.org on June 1, 2007.
91. Slechta AM, Reagan JT. An examination of factors related to radiation protection practices. Radiol Tech:79 (March/April 2008):297:308.
92. Sherer MA, Visconti P, Ritenour ER. *Radiation Protection in Medical Radiography*. 5th Ed. St. Louis, MO. Mosby; 2006.

93. Mammography Quality Standards Act. MQSA inspection procedures: V6.01.8.1.0. Information for mammography facility personnel, inspectors and consumers about implementation of the mammography quality standards act of 1992 (MQSA). Retrieved from www.fda.org on June 15, 2009.
94. Kunio, D. Computer-aided diagnosis in medical imaging: Historical review, current status and future potential. Comput Med Imaging Graphy 2007;31(4-5): 198-211. Available at: www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrex&artid=1955762. Accessed December 7, 2008.
95. Norris T. Computer-aided detection in mammography. Radiol Tech Vol. 73, NO. 3. Jan/Feb 2002.
96. Dryer, KH, Hirschorn DS, Thrall JH, et. al. PACS: A Guide to the Digital Revolution, 2nd Ed. Springer Science + Business Media. New York, NY: 2006.
97. Wikipedia, the free encyclopedia. DICOM. Available at: http://en.wikipedia.org/wiki/DICOM. Accessed July 18, 2008.
98. Institute of Medicine. National Research Council. 2005. *Improving Breast Imaging Quality Standards*.
99. Rothenberg LN. AAPM Tutorial: Patient dose in mammography. Available at: http://www.rsnajnls.org.cgi/reprint/10/4/739?maxtoshow&hits. Accessed November 1, 2008.

Additional References

1. Shagam JY. Positron emission tomography. *Radiol Tech*. July/August 2001;72:551-569.
2. National Cancer Institute: U.S. National Institutes of Health. Male breast cancer treatment: health professionals version (last modified 09/25/2008. Retrieved from http://www.cancer.gov on May 1, 2009.
3. Feig S, Hendrick R. *Radiation risk from screening mammography of women aged 40-49 years.* Jnatl Cancer Inst Monogr: 119-24. PMID 9709287.
4. Johns Hopkins Safety Manual. *Personnel monitoring*. Retrieved from www.hopkinsmedicine.org/hse/policies/HSE_policies/indiv_sections/HSE913.pdf on June 5, 2007.