SITEMAN CANCER CENTER AT BARNES-JEWISH HOSPITAL AND WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

Jewish Health

The Jewish Community's Source for Health News About Breast Cancer

Issue No. 1 Winter 04/05

Studies find Jewish women and men at increased risk for hereditary cancer

In the last ten years genetic research has led to the identification of the genetic basis of some common diseases, such as breast cancer. Genes that contribute to a high chance of developing breast cancer have been identified, and are found more frequently among Jewish families. During this same time period, the assessment of breast cancer risk and the treatment of women with breast cancer has greatly improved. In combination, these genetic and medical advances provide the greatest opportunity to reduce the toll breast cancer can bring to a family and a community. **This newsletter provides information on the connection between family history and breast cancer risk, so Jewish families may be informed of these recent medical advances and benefit from this new wealth of knowledge.**

How is this newsletter different from other breast cancer education pieces? First, as noted by the title, it is written specifically for St. Louis Jewish families. Members of the St. Louis Jewish community have asked for, and collaborated with us, to share this information with the community at-large. Second, and in direct contrast to other breast cancer education pieces, this newsletter contains information specifically about **family based breast cancer risk**—the connection between family history and cancer risk.

During the last ten years genetic research has shown Jewish women and men have an increased frequency of mutations in two genes associated with a increased chance for breast, ovarian and other cancer types. Little information has been offered to the Jewish community preventing women and their families from beginning early cancer screening and seeking therapies to reduce cancer risk. Early surveillance can save lives.

Education has always been a core value in our community. This newsletter provides key information you may use with your physician to assess your family based cancer risk and seek medical care appropriate for your family's level of risk. **Not all families will have an increased cancer risk, but for those at high risk, use this information in your journey toward a healthier life.**

This newsletter is a collaborative project among healthcare professionals at Washington University School of Medicine, St. Louis Jewish women and St. Louis community leaders. Jewish women of all ages participated in the development of this newsletter. We are grateful for the opportunity to share this information with you.

Did You Know?

This newsletter addresses the connection between family history and breast cancer risk. A positive family history is a risk factor for other cancer types or chronic illnesses. All the more reason to learn your family medical history.

Save-a-Life

The Jewish community came together to eradicate Tay Sachs, now let's do it again to fight breast cancer

Do you have curly hair? What is your eye color? Are your fingers long and slender? Physical traits vary among families. The frequency of certain diseases also varies among groups of people. Tay Sachs disease is more common among Jewish families, while sickle cell anemia occurs more frequent among African Americans. Knowing the health risks associated with your ethnic background is important when evaluating your family history of common diseases, such as breast cancer.

A positive family history of breast cancer is one of the most important risk factors for breast cancer. For Jewish families, the significance of the family cancer history is even greater, because Jews have a higher chance to carry a gene alteration that predisposes to breast and other types of cancer. Your doctor must consider your family cancer history and ethnic background in order to make appropriate cancer screening recommendations.

Remind your health care professional of your ethnicity and your family medical history. It's a New Year's resolution with lasting benefits.

Did You Know?

Not every person who has a cancer gene mutation will develop cancer.

Family history is an important breast cancer risk

There are many factors that influence a woman's chance to develop breast cancer. The three most significant risk factors are **gender**—more women than men develop breast cancer; **age**—breast cancer risk increases with age; and **family history**—a positive family history increases a woman's risk.

Practical information about the influence of family history on breast cancer risk needs to be shared and understood. Advances in cancer genetics have occurred rapidly in the last ten years, but the education of health care professionals and the community has lagged behind. This delay has prevented families from taking advantage of these medical advances.

Jewish women with a family history of breast or ovarian cancer have a higher chance to develop breast cancer. This risk increases with an increasing number of relatives with cancer. For some women this risk is high, and they may consider earlier and more frequent breast health screening. In contrast, women who have no family history of breast or ovarian cancer do not have an increased family based breast cancer risk. The general cancer screening guidelines are appropriate for women with an average cancer risk.

See the Assessing Your Risk section on page 2 to help assess your family based breast cancer risk. Work with your physician to identify if your chance for cancer is higher and if so, should you seek screening at a younger age and repeat the screening more frequently.

You can't change your family history, but you can understand how your family medical history influences your health. Take steps now to understand the importance of your family medical history.

INSIDE

Documenting your family medical history

Physicians use family history information to calculate your family based cancer risk. Ask your family about your family's medical history so you may give your healthcare providers an accurate history. Inaccurate cancer reporting, or failing to include **all** family members with cancer, may impact the assessment of your family based cancer risk and subsequently any medical recommendations.

What information should you document?

- Document both your mother's and your father's cancer family history.
- List all your relatives, those with **and** without cancer, and their biological relationship to you.
- Document **any** type of cancer (for example, breast, ovarian or pancreatic cancer).
- Confirm the organ where the cancer started.
- Write down the age at diagnosis for any family member with cancer.

How should you verify the history?

Your family may not know the details of a relative's diagnosis. Your family may know your grandmother had "female cancer", but was it ovarian, uterine or cervical cancer? Knowing the correct diagnosis is critical in the assessment of your family based cancer risk. Collecting records allows a physician to clarify the exact cancer diagnosis and obtain important details helpful in the assessment of your cancer risk. You may ask your family members with cancer to release or collect their cancer related medical records. If the person is deceased, the closest living family member may legally release the medical records. Hospitals keep records for a variable period of time. Records may be available for several years, even decades. If medical records are no longer available, you can obtain a death certificate from the vital statistics office from the state where your relative died. The death certificate may list the primary cancer diagnosis.

What should you do with your family medical history?

- Share your family medical history with your doctor, even if he / she does not ask. This information may be useful in your family's medical care today and in the future.
- Take time to update your family medical history as needed.
- Talk with a genetics specialist about any questions regarding your family medical history.
- Include your family medical history as part of your family story. Make sure your children have access to this information.

Assessing Your Risk

All women have a chance to develop breast cancer. It is an unfortunate fact all women face. On average, women have about a 10-12% chance over their lifetime to develop breast cancer. The question is how do certain factors increase this baseline chance?

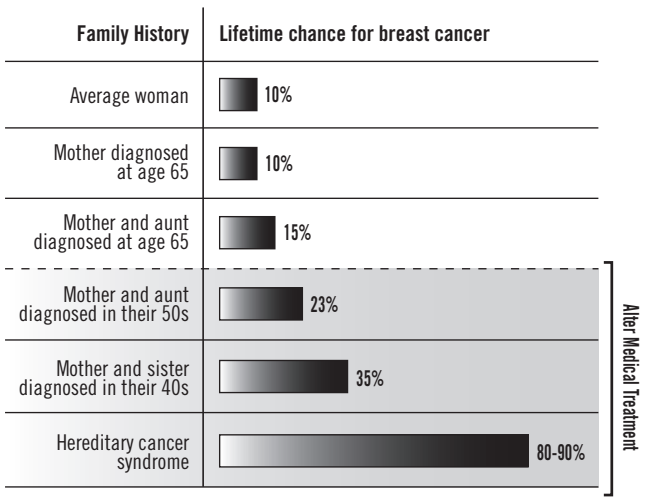
There are many factors that are known or suspected to be associated with the development of breast cancer. Our focus is on the family cancer history because a family history of breast cancer is one of the most significant risk factors. Several models are available to predict a woman's chance for breast cancer and to determine if this chance is higher than the baseline chance of 10%.

The Gail model is the most common tool used by physicians, and widely available over the Internet. This model focuses on risk factors such as a woman's age when her first child was born. However, this model includes limited family history information and is not best at predicting breast cancer risk among women with a family history of cancer.

For a woman with a modest family history of breast cancer, a different model is used, known as the Claus model. Dr. Claus showed a woman's chance for breast cancer is influenced by the number of female relatives with breast cancer, the biological relationship or closeness to her, and the age each relative was diagnosed with breast cancer. Intuitively, these data make sense. For example, a woman who has a mother diagnosed with breast cancer at 35 has a higher chance to develop breast cancer than a woman who has a grandmother who was diagnosed in her eighties.

The Claus model is based on studies of Caucasian women, of diverse ethnic background, with a modest family history of breast cancer. The model is not specific for Jewish women and may underestimate risk among some women. The Gail and Claus models are not appropriate to predict risk among women with a strong family history of cancer consistent with hereditary cancer. Read the Link Between Genes and Cancer to learn more about families with hereditary cancer.

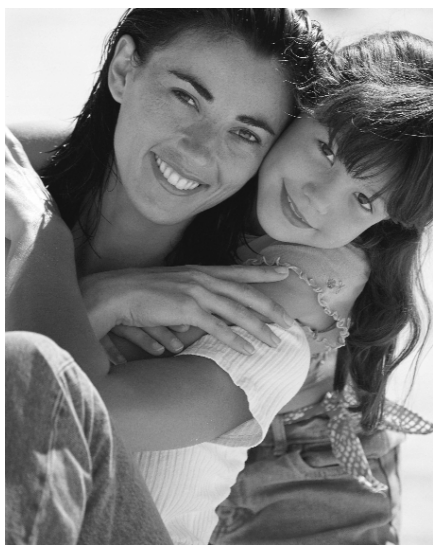
See how a family history of breast cancer influences a woman's lifetime chance.



The graph is not intended to show every family scenario; rather it is used to depict the influence of family history on the likelihood to develop breast cancer. Work with your doctor or a genetics specialist to understand your family's cancer history and the influence on your health.

The link between Genes and Cancer

All cancer is genetic but only a small percentage is hereditary.



Cancer develops from a single cell that over time accumulates multiple sporadic gene abnormalities. The cell loses its ability to control normal cell growth. Consequently, the cell transforms into a cancerous tumor. For assessing heritable risk, these cancers are considered "sporadic" and are not associated with a genetic or hereditary predisposition to develop cancer. The majority of women with breast cancer have a "sporadic" form of cancer.

About 5% of women with breast cancer have a "hereditary" form of the disease. Hereditary cancer or a hereditary cancer syndrome results from a **single** gene abnormality (mutation). The mutation disrupts the normal functioning of the gene. Any person, male or female, with a mutation has a higher chance or **predisposition** to develop certain types of cancer.

A hereditary cancer syndrome is diagnosed based on the family cancer history. Families with hereditary cancer often have multiple family members, in more than one generation, with cancer. Different cancer types may result from the same gene mutation in a family. Younger age at diagnosis is also noted in families with hereditary cancer. An inherited gene mutation is present from the time of conception and is found in all cells of the body. For this reason, people with a cancer predisposition gene mutation may develop cancer at a young age.

Not all people in a family with hereditary cancer inherit the family gene mutation. Family members who do **not** inherit the gene mutation will **not** have a high chance for cancer, even though they have a family history of cancer.

Genetic specialists evaluate the family cancer history to identify if features consistent with hereditary disease exist. When these features are present, they work to identify the specific cancer syndrome.

Several hereditary cancer syndromes have been identified which are associated with an increased chance for breast cancer. Genetic research has identified Jewish women and men have a higher frequency of mutations in the **BRCA1 and BRCA2 genes**. Abnormal alterations in these two genes are associated with an increased risk for breast, ovarian and other cancer types.

Nearly 3% of all Jewish men and women (3 in 100 people) has one of three specific mutations in the BRCA1 and BRCA2 genes. This compares to a mutation frequency of less than 1% in Caucasians (1 in 400-800 people) who are not of Jewish ancestry. As noted in the table, the likelihood of a gene mutation increases with a positive family history of cancer.

One focus of genetic research is to identify genes associated with an increased cancer predisposition. This research helps physicians identify families with a higher cancer risk and institute early screening or prophylactic medical or surgical treatments.

Jewish Family Cancer History	Likelihood of BRCA1 or BRCA2 mutation
Jewish woman with breast cancer diagnosed by 40 years	21%
Two related women with breast cancer diagnosed at any age	25%
Jewish woman with ovarian cancer diagnosed at any age	40%
Two related women with breast cancer and one woman with ovarian cancer diagnosed at any age	64%

MEDICAL RECOMENDATIONS

Options are Plenty

The American Cancer Society cancer screening guidelines are appropriate for people with an average cancer risk. However, people with a strong family history of cancer may need to begin screening at a younger age and repeat screening more frequently. Why? People with a strong family history of cancer have a much higher cancer risk, and their medical follow-up should reflect their increased cancer risk. Recommendations vary based on the level of risk and the possibility a family has hereditary cancer.

Medical recommendations for women with or at-risk for a hereditary "breast cancer" syndrome, due to a *BRCA1* or *BRCA2* gene mutation only, are listed below. Families with a different hereditary cancer syndrome should follow the guidelines for that given condition or syndrome.

Experts in cancer genetics put forth these recommendations. Not all physicians agree with these guidelines because long-term studies showing the effectiveness of these recommendations are not available. Screening and risk reducing options are discussed.

Screening Options
(looking for cancer at an early stage)

1. Begin breast health screening (usually mammography) by 25 years of age or ten years prior to the age of the youngest person who was diagnosed with cancer in the family.

- The combination of mammogram and breast ultrasound as a routine screening practice is currently being evaluated among women with a high breast cancer risk.
- MRI of the breast has recently been shown to be more sensitive in detecting breast lesions than mammography alone among high-risk women.
- Talk with your doctor about the best breast health screening for you based on the individual characteristics of your breasts and your family cancer history.

2. Begin ovarian cancer screening by 30-35 years of age or ten years prior to the age of the youngest person who was diagnosed with cancer in the family. Transvaginal ultrasound and a blood test called CA125 (a blood tumor marker) are used to screen for ovarian cancer.

- The available methods for screening for ovarian cancer are less than perfect. For this reason, not all gynecologists will recommend the screening listed above. Speak with your gynecologist about the benefits and limitations of ovarian cancer screening for you.

Prophylactic Options
(treatments to reduce cancer risk)

1. Prophylactic mastectomy (removal of the breast tissue) has been shown to reduce breast cancer risk by greater than 90% among high-risk women.

- The decision to remove healthy breast tissue is a very personal decision which requires consideration of multiple factors such as level or risk, self-image, and sexual identity, to name a few.
- Breasts can be reconstructed after mastectomy using either implants or your own fat tissue. A plastic surgeon performs this type of surgery.

2. Prophylactic oophorectomy (removal of ovaries) has been shown to reduce ovarian cancer risk by greater than 90% among high-risk women. Removing the ovaries also reduces breast cancer risk among younger women.

- The decision to remove healthy ovaries is a personal decision. The desire for children, level of risk, utility of screening, and sexual identity are some factors that should be considered.
- Women who have their ovaries removed should consult with their doctor about the long-term effect on their bone health. Weight bearing exercises or medications may be recommended for some women to strengthen the bones.

3. Prophylactic Tamoxifen (a drug used to block estrogen) has been shown to reduce breast cancer risk by 50% among high-risk women.

- Like any medication, Tamoxifen has side effects and risks, including an increased chance for blood clots and risk for uterine cancer.
- New drugs, such as Evista, are being evaluated to determine how they reduce breast cancer risk in comparison to Tamoxifen.

Currently there are no national recommendations to alter the medical management of men who have or who are at high risk to have a BRCA1 or BRCA2 gene mutation. Physicians may recommend early cancer screening for men with a gene mutation, based on the family cancer history.

All cancer screening or risk reducing options must be considered in the context of the family cancer history. Additional screening may be recommended based on the family history.

A few facts about breast cancer

Breast cancer is a common disease among women. Nearly 1 in 9 women will develop breast cancer in their lifetime. Breast cancer has the second highest cancer related mortality, second only to lung cancer. By comparison, considering all chronic illnesses, heart disease is the most common disease among American women.

In the United States, breast cancer occurs most frequently among Caucasian women. African American women have a lower overall rate of breast cancer, but have the highest rate of breast cancer in young women, and the highest breast cancer related death rate.

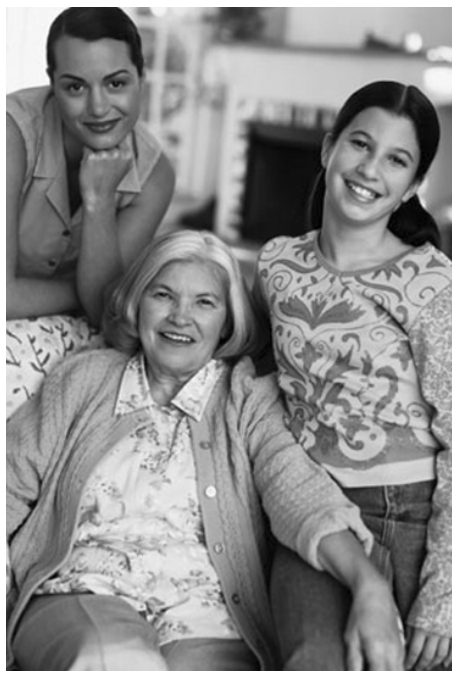
Early studies conducted to examine the frequency of cancer among different subgroups within the United States showed Jewish women had a slightly higher rate of breast cancer than other Caucasian women. This slight increase may be due in part to the frequency of gene mutations associated with a higher chance for breast cancer.

It may be decades before breast cancer is eliminated as a threat to women's health. Until then, there are positive steps you can take now to monitor your breast health.

- Ask your doctor how to perform a breast exam and perform one on a regular basis.
- Talk with your physician about what age you should begin mammogram screening.
- Learn more about your family medical history and share this information with your children.
- Remind your doctor about your family medical history and ethnic background.
- Encourage your female friends and family members to undergo breast health screening.

A PHYSICIAN'S PERSPECTIVE

Take my advice, please.



I know more than a thing or two about the subjects you see discussed on the pages of this newsletter. And my perspective comes from several vantage points. I'm a middle aged woman of Ashkenazi Jewish heritage. I'm a 15 year breast cancer survivor. I'm a mother, wife, relative, and friend to others. I'm a radiologist who specializes in breast imaging. I live and breathe these issues every day. I understand the importance of being proactive.

I didn't always know what I know now… neither as a professional, nor as a patient. We now have a much greater understanding of cancer families, who they are, what that means to the family as a whole, and what that means to the individuals in those families. But even more important, we have better strategies to deal with the issues. Professionals are available to help you understand your breast cancer risk and to make recommendations on the most appropriate surveillance methods for you, based on your family history. Medical options are available to screen for cancer early or even reduce cancer risk. And the best news of all is that we are experiencing an information explosion. Ten years from today, we'll know far more about this complex subject than we did twenty years ago, and we'll have even more refined strategies.

There are many ways we can help ourselves and others in this life. We can pay attention to what we can do for ourselves. We can have others watch out for us. We can watch out for others. But personally, I think the best strategy is to do all of these things together. There are things we can learn from each other, and admittedly, we have a lot to learn. Medical professionals make progress by basic research, but they also make progress by caring for and tracking families such as yours.

This is a field that is changing so rapidly, even the average doctor can't keep up with it. So my advice is to pay careful attention to what you see on these pages. Talk with your family members. If you think what you read here might apply to you or your family, speak with your doctor about seeking advice from the experts.

Genetic testing: Benefits and Limitations

Genetic testing is used to identify an abnormal alteration (mutation) in a specific gene. Gene alterations which are simple variations (polymorphisms) or for which the consequence on gene function is unknown (variants of unknown significance) may also be identified. Work with a genetics professional to assess your family cancer history, identify appropriate testing and to interpret the results of any genetic testing.

Some points to consider about genetic testing:

- The family cancer history must be evaluated first to determine the possibility a family has a hereditary cancer syndrome and what gene should be analyzed, before any testing is performed.
- There are benefits and limitations to every genetic testing protocol. For example, some protocols only examine for specific mutations in a gene. Before proceeding, understand what information can be gained from testing and the specific limitations of the protocol.
- With genetic testing, consider how you will use the information in your medical decision-making. Consider what choices you may consider based on the results. Is your medical decision making different with genetic testing than other medical tests you have?
- Testing is most informative when an affected family member (a relative with cancer) is tested first. If a mutation is identified, other family members may consider being tested for the same mutation. If no mutation is identified, genetic testing for that specific gene may not be informative (useful) for your family.
- Testing is not used to determine if you currently have cancer or at what age cancer may develop. Genetic testing only shows if a gene mutation is present.

Genes associated with a high cancer risk continue to be identified. Keep in touch with your physician or genetics specialist to determine if new advances in genetics may be important in your family's medical care.

Did You Know?

The U.S. Surgeon General's Family History Initiative encourages family discussion of health history. A web-based family history tool is available at **http://www.hhs.gov/familyhistory**

GLOSSARY

BRCA1: A gene found on chromosome 17. Abnormal alterations (mutations) are associated with an increased chance for breast, ovarian, and other cancer types.

BRCA2: A gene found on chromosome 13. Abnormal alterations (mutations) are associated with an increased chance for breast, ovarian, and other cancer types.

CA125: a blood tumor marker used to detect ovarian cancer. Not all physicians use this test to check for ovarian cancer because it does not always predict if a woman has ovarian cancer and in some cases suggests ovarian cancer is present when it is not.

Incidence: the frequency of a disease in relation to the group of people in which it occurs.

Mammogram: an x-ray of the breast that is used to detect breast cancer.

Mastectomy: a surgical procedure performed to remove the breast tissue.

Mutation: an abnormal alteration in a gene that disrupts a gene's ability to function properly.

Oophorectomy: a surgical procedure performed to remove the ovaries.

Predisposition: the potential or likelihood to develop a certain disease or condition based on the presence of a specific factor, such as a gene mutation.

Polymorphism: an alteration in a gene that does **not** disrupt a gene's ability to function properly. Polymorphisms are found in thousands, if not all, of our genes.

Prophylactic: any treatment that is used to prevent a disease from developing.

Syndrome: a collection of features that run together. In the context of a hereditary cancer syndrome, a collection of different cancers due to the same gene mutation.

Transvaginal ultrasound: An ultrasound in which the ultrasound probe is place in the vagina so the ovaries and surrounding area can be viewed.

RESOURCES

Hereditary Cancer Program
Washington University
School of Medicine
Alison Whelan, MD; Director
314-454-6093

The program provides cancer risk assessment and education as a clinical service. Genetic testing is coordinated for individuals who wish to pursue this option.

Siteman Cancer Center
Barnes-Jewish Hospital and Washington University School of Medicine
www.siteman.wustl.edu
314-747-7222
800-600-3606

Siteman Cancer Center provides screening, diagnostic and treatment services for people with cancer and families with a family history of cancer

Newsletter
Contact Jennifer Ivanovich, MS Genetic Counselor for questions about this newsletter. 314-454-5076

REFERENCES

1. American Cancer Society. Breast Cancer Facts and Figures, 2003-2004
2. Gail MH, et al. Projecting individualized probabilities of develop breast cancer for white females who are being examined annually. JNCI. 1989;81-1879-86
3. Rockhill B, et al. Validation of the Gail et al. model of breast cancer risk prediction and implications for chemoprevention. JNCI. 2001;93:358-366.
4. Claus EB, et al. Age at onset as an indicator of familial risk of breast cancer. Am J Epidemiol. 1990;131:961-972.
5. Claus EB, et al. Autosomal dominant inheritance of early onset breast cancer. Implications for risk prediction. Cancer. 1994;73(3)643-651.
6. Domchek SM, et al. Application of breast cancer risk prediction models in clinical practice. J Clin Oncol. 2003;21:593-601.
7. Roa BB, et al. Ashkenazi Jewish population frequencies for common mutations in BRCA1 and BRCA2. Nat Genet. 1996;14:185-187.
8. Tonin P, et al. Frequency of recurrent BRCA1 and BRCA2 mutations in Ashkenazi Jewish breast cancer families. Nat Med. 1996;2:1179-1183.
9. Thompson D, et al. Cancer incidence in BRCA1 mutation carriers. 2002; JNCI. 94(18):1358-1356.
10. The Breast Cancer Linkage Consortium. Cancer risks in BRCA2 mutation carriers. JNCI 1999;91:1310-1316.
11. King MC, et al. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. Science. 2003;302(5645): 574-5.

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Lynne Kipnis, PhD, served as our primary advisor and community advocate. Dr. Kipnis is a clinical psychologist who has worked diligently to increase community awareness on a variety of women's health issues. This program would not have moved forward without Lynne's support and enthusiasm.

Jewish leaders and community organizations partnered with us to provide avenues to distribute the newsletter, and more importantly, opportunities to meet directly with community members to share our message of good health and empowerment.

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TAKE ACTION

This information is presented to help your family understand the connection between family history and cancer risk.

- Learn your family medical history
- Share your family medical history with your family and your physicians
- Remind your doctor of your ethnic background
- Contact genetics specialists with questions about your family based cancer risk

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THE ST. LOUIS AFFILIATE OF THE SUSAN G. KOMEN BREAST CANCER FOUNDATION