



# Bay Area Breast Cancer SPORE Newsletter

Specialized Programs of Research Excellence at the University of California San Francisco

## Genetic Testing for *BRCA1* and *BRCA2* Mutations: 12 Years of Experience at UCSF By Mary S. Beattie, MD, MAS



Soon after the discovery of the *BRCA1* and *BRCA2* genes in the mid-1990s, UCSF began clinical testing for mutations in these genes at the UCSF Cancer Risk Program. In the last 12 years, the Cancer Risk Program has provided genetic counseling and *BRCA* testing to over 1400 individuals and families.

Over 95% of individuals undergoing *BRCA* testing at UCSF agree to participate in a unique study that performs follow-up of those being tested, as well as storage of their blood, DNA, and tissue. Many studies at UCSF and worldwide have used information from these 1400 individuals for research purposes. Importantly, the UCSF Cancer Risk Program has provided genetic counseling and testing services to many individuals and families at high risk of hereditary breast and ovarian cancer.

The ability to link clinical

services with creation of a research program has allowed patients and families in the Cancer Risk Program to receive state-of-the art genetic testing, and to also receive up-to-date evidence-based guidelines from experts in this field.

For families at high risk of hereditary breast and ovarian cancer, *BRCA* testing can provide accurate risk assessment, and can also potentially identify family members who are not at high risk. It is generally recommended to begin *BRCA* testing with the family member who has the highest likelihood of carrying a *BRCA* mutation. If possible, this means beginning the *BRCA* testing process with an individual affected with breast or ovarian cancer.

About 5-10% of all breast and ovarian cancers are attributable to *BRCA* mutations. Genetic counselors in the UCSF Cancer Risk Program are knowledgeable of features of a family history that indicate potential hereditary breast and ovarian cancer. These features include: breast cancer before age 40, ovarian cancer at any age, breast and ovarian cancer in the same individual, bilateral breast cancer, male breast cancer, and multiple generations affected with breast and/or ovarian cancer.

Unusual cancers, cancers at young ages, and multiple cancers in a single individual also are signs of potential hereditary cancer. In the general population, about 1 in 200-300 individuals carry harmful *BRCA* mutations. In the Ashkenazi Jewish population, about 1 in 40 individuals carry harmful *BRCA* mutations. Thus, an Ashkenazi Jewish woman with breast or ovarian cancer at any age is recommended to undergo *BRCA* testing.

For individuals who carry *BRCA* mutations, the lifetime risk of breast cancer is 50-80%. The risk of a second breast cancer diagnosis in *BRCA* carriers who have already had breast cancer is up to 50%. For *BRCA1* carriers, the lifetime risk of ovarian cancer is up to 50%; and for *BRCA2* carriers, the lifetime risk of ovarian cancer is up to 20-30%. *BRCA* mutations have been associated with prostate cancer, melanoma, gall bladder cancer, and pancreatic cancer.

*BRCA* carriers, and their first-degree relatives who have not yet been tested for *BRCA* mutation, are recommended to undergo annual screening with breast MRI and mammography starting in their mid-20s.

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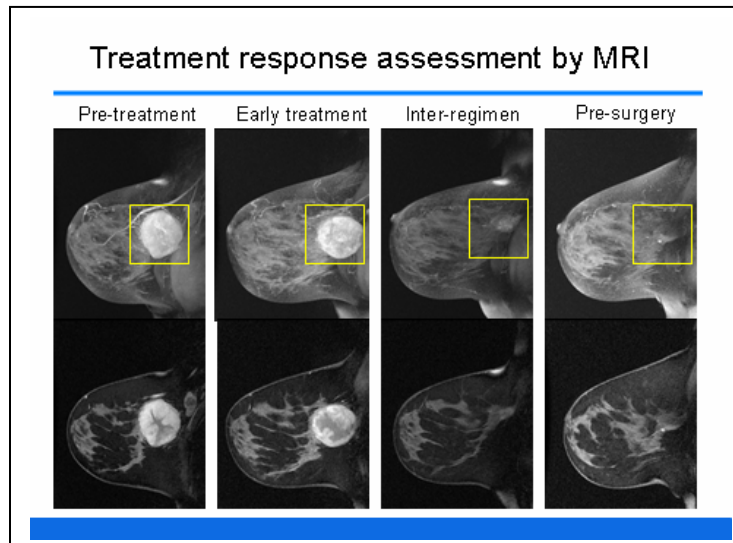
# The Role of MRI in Breast Cancer Treatment

By Nola Hylton, PhD

Magnetic resonance imaging, or MRI, is a relatively new imaging test for the breast that has both advantages and disadvantages in comparison to conventional methods (i.e., x-ray mammography, and ultrasound). Some of the advantages that have led to increased use of breast MRI are its ability to detect small cancers, its effectiveness in identifying tumors in women with dense breast tissue, and the fact that it does not use ionizing radiation. Disadvantages of breast MRI include limitations for distinguishing between early breast cancer and some benign conditions of the breast such as proliferative hyperplasia that can lead to unnecessary biopsies, escalation of surgical management (i.e., wider excisions and higher rates of mastectomy), patient anxiety, and health care cost. Our team of researchers, including imaging scientists, breast radiologists, surgeons, and oncologists, has been developing MRI methods for the breast for over 15 years. The major focus of our work has been to develop high-resolution contrast-enhanced techniques for improved breast cancer detection, diagnosis, and staging. We work closely with MRI systems manufacturers to develop instrumentation and software that can be used to detect cancers in the breast as small as a few millimeters. As part of ongoing research we are exploring more advanced MRI-based methods that can measure tissue characteristics related to extent of blood supply to a tumor and water diffusion that may reflect how fast a tumor is growing or dying as a result of treatment with chemotherapy. New MRI methods are

being evaluated as part of the national I-SPY trial led by Drs. Laura Esserman and Nola Hylton that integrates measurement of molecular markers in breast tumors and MRI imaging in an effort to maximize the effectiveness of neoadjuvant (chemotherapy before surgery) treatment for patients with breast cancer. In collaboration with the American College of Radiology Imaging Network (ACRIN) 6657 study, I-SPY is using MRI to measure tumor response during chemotherapy. In the first results from ACRIN 6657, reported at the Annual Meeting of the Radiological Society of North America held in Chicago, Illinois, in December 2008, tumor volume measured by MRI

method for imaging DCIS may help to better tailor surgical approaches, and in some cases, may allow women to choose a non-surgical option such as hormonal treatment. As part of a pilot clinical trial of hormonal treatment of DCIS led by Dr. Hwang, we are using MRI to evaluate patients before and after short-term hormonal treatment given prior to surgery. Other studies being conducted by Drs. Catherine Klifa and Catherine Park are exploring normal tissue composition by MRI as a potential marker for risk of a recurrent tumor in populations of women receiving chemotherapy. Dr. Klifa is also



was shown to be a sensitive measure of tumor response to chemotherapy treatment and was able to provide early prediction of response after only one cycle of chemotherapy. Another major component of MRI research at UCSF is the development of methods for detecting and characterizing ductal carcinoma in situ (DCIS), a non-invasive and early stage of breast cancer with excellent prognosis. Imaging researchers Drs. Nola Hylton, Bonnie Joe, and T32 fellow Dorota Wisner are working closely with breast surgeon Dr. Shelley Hwang to develop MRI methods that can accurately depict the extent of DCIS in the breast and determine if invasive disease is also present, even if not apparent by clinical or mammographic evaluation. A sensitive

interested in determining the MRI characteristics associated with mammographic breast density and is collaborating with Dr. John Shepherd to study the relationship between MRI density and tissue composition and mammographic density. These studies are examples of collaborative science with the goal of using breast imaging to accelerate our understanding and ability to treat breast cancer. As imaging methods continue to advance, we expect to use these tools to gain greater insight into both the anatomy and function of normal and cancerous breast tissue.

## Conquering Disparities

By Carolene Marks, BADco Commissioner and Organizer, UCSF Breast SPORE Advocate



In October 2007, with the support of our Breast SPORE Advocacy Core (BSAC), Susan G. Komen for the Cure, and the San Francisco Commission on the Status of Women, we convened a unique coalition of Bay Area providers of Breast Care for underserved/underinsured African American women. It was an impressive group, which spearheaded the organization of the Bay Area

Disparities Coalition (BADco).

We determined we would first concentrate on woman under the age of 40 years for whom there are few resources. BADco is a collaborative effort to increase breast cancer awareness and knowledge of African American women under 40 in the Greater SF Bay Area by connecting them to breast health resources. We are a consortium of organizations, agencies and community members who share a common vision of helping African American women in the Greater San Francisco Bay Area identify breast health resources, including the following: UCSF Helen

Diller Family Comprehensive Cancer Center, UCSF SPORE BSAC, California Health Collaborative, California Pacific Medical Center, Northern California Cancer Center, Women's Cancer Resource Center, Southeast Health Center, Arthur H. Coleman Medical Center, MCC Breast Health Center, American Cancer Society, Breast Cancer Connections, and Calvary Hill Community Church.

We implement the community service commitment of the Breast Cancer SPORE in a unique organization. We have prepared the first Breast Health Resources List for Women under 40 which has

been eagerly received. We are now going to determine the effectiveness of our work in order to know how many women have benefited.

BADco is considering other needs where we can be most effective in saving African American women's lives with regard to breast cancer. We understand there is intense research being conducted into triple negative (estrogen receptor, progesterone receptor, and HER2/neu-oncoprotein negative) tumors.

We are gratified by our results in the past year and anticipate equally effective caring activities in the months ahead.

*If you are interested in becoming a volunteer advocate with the Breast SPORE Advocacy Core, please contact Sarah Goins at 415-502-2986 or [sarah.goins@ucsf.edu](mailto:sarah.goins@ucsf.edu)*

### Lymphedema Education & Exercise Group

Free Meetings—3<sup>rd</sup> Wednesday of the Month  
5:00-6:30 pm  
Helping people understand, manage & prevent Lymphedema

Women's Health Resource Center at California Pacific Medical Center  
3698 California Street, Lobby Level  
San Francisco, CA 94118  
<http://www.AdventureBuddies.net>

### Art for Recovery

Art for Recovery provides a safe environment where adults can express the intense feelings that arise in life-threatening illnesses; nurturing the aesthetic sensibilities of patients, visitors, and medical staff at the various campuses of UCSF Medical Center and in the community.

If you are interested in learning more please go to  
<http://www.cancer.ucsf.edu/afr>  
or email  
[cynthia.perlis@ucsfmedctr.org](mailto:cynthia.perlis@ucsfmedctr.org)

# Markers of Pre-Invasive Breast Cancer

By Shelley Hwang, MD, Yunn Yi Chen, MD, PhD, and Fred Waldman, MD, PhD

The UCSF Breast Cancer SPORE and Breast Oncology Program is a perfect environment for collaborative translational research. Drs. Hwang, Chen, and Waldman have been working together on research projects for many years. Other collaborators include Drs. Karla Kerlikowske, Koei Chen and Chris Benz, Sandy DeVries (the Waldman Lab Manager), and post-doctoral scientists who have worked in the lab (Junko Suzuki, Jim Korkola, and many others).

The theme for this group's work is that breast cancer exists in a continuum, from normal-appearing cells in the breast duct and lobule, to cells that appear "hyperplastic" (more normal breast cells than usual in a duct or lobule, suggesting the cells are growing more rapidly than normal), to cells that appear "atypical" (usually because their growth patterns seen under the microscope are unusual, but not bad enough to call "carcinoma or cancer"), and finally to ductal carcinoma in situ (DCIS), which can look as abnormal as invasive cancer cells, but the cells are contained inside the breast duct or lobule. Invasive breast cancer, by definition, has invaded or grown through the breast duct.

The projects from this group of investigators use tissue samples donated from patients undergoing surgery from UCSF and CPMC, which show these "pre-invasive" patterns, either alone or in the presence of

invasive cancer. Research is aimed at determining what relationships exist between these different points along the breast cancer continuum, by examining which changes are seen in DNA, RNA, and proteins as cancer cells move along the cancer progression pathway.

DCIS and atypia are thought by many to be precancerous conditions, identified before the cancer cells have invaded the breast tissue surrounding the ducts. Because they are some of the earliest manifestations of cancerous changes detectable in the breast, many investigators including those at UCSF have been interested in discovering what causes some DCIS to

appearing changes in DCIS. We are testing this hypothesis in a group of "window trials," which are conducted in the "window" of time between diagnosis and surgery.

Currently, the treatment of DCIS is surgical excision of all DCIS cells, often followed by radiation. The goal of treatment is to prevent progression to invasive cancer by removing all precancerous cells. In our current window trials, we treat patients with DCIS with drugs that can block estrogen-dependent tumor growth. Response to these drugs is monitored by breast MRI and by examination of the treated tissue.

*"A better understanding of these factors will reduce the burden of treatment in patients with DCIS, and may identify future strategies to help prevent invasive cancer."*

Hwang, Chen, Waldman

become invasive, while others never develop this ability. Much progress has been made examining how the features of DCIS at diagnosis predict a subsequent diagnosis of invasive breast cancer.

In addition, this group is conducting studies to determine whether some drugs may reverse cancerous-

By identifying the biologic and radiographic changes in DCIS that occur with these drugs, we hope to understand whether DCIS progression can be halted or reversed without surgery. A better understanding of these factors will reduce the burden of treatment in patients with DCIS, and may identify future strategies to help prevent invasive cancer.

## Me & My Girls

### A letter from a Loving Husband

By Permission of Kelly Dietz

“OK, this is fun now. What a great opportunity to invent a whole new you. Or better yet, a whole new set of Yous. (Not that I ever think you need re-inventing, just making the best of it.)

Your shorter hair wig is your casual, quick, spunky personality. It is fun, light, and easy. She is care-free, yet smart and witty. She is a voracious reader and not always given the credit she deserves for her intelligence. She attends Burning Man every year, not with her closest group of friends, but with the local underground art crowd. She is care-free and whimsical, yet grounded by her family and strong group of friends. Her name is Renee.

The long, full chestnut wig is more sophisticated. She is a star, not in the famous sense, but in the glamour and style she exudes. She is elegant, but with attitude and spice. She is 1/4 Latina and has a bit of a

temper. She is a work-out fanatic, but never in public. Her friends think she is in shape because she dances



at the clubs 'til single-digit hours. Her casual attire always has some sewn-on sort of sparkle. Her name is Esperanza -- that's "hope" in Spanish.

The long stringy wig is a bit more complex. She comes from money but lost her way for a bit in her twenties. Ran with the wrong crowd, maybe

did a little drugs. Had a kid young and never married the father. She has now found her path and is true to herself and

has a good purpose in life, married a good man and they had a couple kids themselves. She volunteers at the local food bank. Her social life is confined to a small group of very close friends with whom she spends a lot of time. She is beautiful yet never flaunts it. She is almost always casual, preferring a contemporary pair

of jeans and an understated yet designer tee-shirt. Her name is Amanda.

Then there is the one without the wig: beautiful, smart, compassionate. The matriarch of the family - passionate about growing good kids who respect the people and environment around them.

She is a savvy businesswoman, intimidated by none. She has an innate intuition for good ideas, and the drive and determination to implement them. She is a fantastic cook and enjoys a great meal, whether it be just with her family, or a feast with 20 close friends. She is athletic, fit, and cherishes her time outdoors. She is a lovely spirit with an inspiration for life and an appreciation for what she has. Her name is Kelly. I'm glad I get the one without the wig.

I love you.”

~ Your Husband



## BreastCancerTrials.org Goes Nationwide

By Elly Cohen, PhD

We are very excited to announce that BreastCancerTrials.org (BCT.org) is now operating *nationwide!*

An online clinical trial matching service developed at the UCSF Center of Excellence for Breast Cancer Care, BCT.org enables users to learn about breast cancer research studies across the United States and to easily identify trials that might be right for them. It includes studies investigating: Breast cancer prevention, detection, treatment and quality of life.

BCT.org helps users find trials based upon their self-reported health history.

Match results are supplemented with:

- Easy-to-read trial summaries
- Information for contacting research sites
- Educational material about clinical trials

BCT.org also features a message service, allowing users to share their online health history with selected research sites. A Trial Alert Service, notifying users about newly listed trials, will be released in March.

BCT.org is an extension of a successful regional pilot co-developed by UCSF and the National Cancer Institute. Supported by The Safeway Foundation, it is a program of Quantum Leap Healthcare Collaborative, a nonprofit, public benefit company affiliated with UCSF.

BCT.org encourages all persons affected by breast cancer to help improve care by considering clinical trial participation.

Please visit us at [www.BreastCancerTrials.org](http://www.BreastCancerTrials.org)

**BRCA1 and BRCA2 article continued from page 1**

Chemoprevention with the drug tamoxifen may reduce the risk of breast cancer by about half in *BRCA* carriers. Because 80% of breast cancer diagnosed in *BRCA1* carriers is estrogen receptor negative, tamoxifen may be less useful in *BRCA1* carriers. The majority of breast cancer diagnosed in *BRCA2* carriers is estrogen receptor positive, so tamoxifen may be more effective in this population.

Mastectomy is also a way to reduce breast cancer risk, and there are many surgical and reconstruction options for women who choose it. Because screening for ovarian cancer is associated with significant false-positives and false-negatives, it is recommended for *BRCA* carriers who have completed childbearing to strongly consider salpingo-oophorectomy (removal of the tubes and ovaries). If this surgery is done before menopause, it also reduces the risk of breast cancer by approximately 50%.

Strong legal protections exist to prevent health insurance discrimination, particularly with the newly passed Genetic Information Non-discrimination Act (GINA). It is illegal for health insurance companies to drop or deny insurance coverage, or to increase insurance rates, based on a genetic test result. Many initial theoretical concerns arose when *BRCA* testing was new, but these concerns have not been bourn out. National court records have not shown any case of genetic discrimination based on *BRCA* testing.

*BRCA* testing is not generally indicated in children, and the youngest age at which UCSF would recommend *BRCA* testing is in the early-mid 20s. *BRCA* mutations are not associated with increased risks of childhood cancer, and the earliest age at which positive results would influence medical care is the mid-20s. *BRCA* testing is also not recommended in individuals with current

severe depression or other significant active mental health diagnoses. Genetic testing can be done when mental health concerns are stable and treated.

The UCSF Cancer Risk Program recently surveyed all females that had undergone a *BRCA* test at UCSF, and achieved an excellent response rate of over 80%. The main purposes of this survey were: to examine screening and prevention in all *BRCA* testers; and to examine the impact of genetic counseling and testing on both individuals and families. With over 1000 returned surveys, preliminary results suggest many women have used *BRCA* test results to make decisions regarding breast cancer screening and prevention. Furthermore, the vast majority of females that have undergone a *BRCA* test report genetic counseling and testing have had a positive impact for themselves and their family members.

In summary, for appropriate individuals and families, *BRCA* testing can provide accurate risk assessment and influence screening and prevention. *BRCA* testing is often used to assist with medical decision making, and it can help determine whether screening breast MRI is indicated. Targeted clinical trials for both treatment and prevention are being offered to *BRCA* carriers, so *BRCA* testing can facilitate entry into some clinical trials. In families with known *BRCA* mutations, negative test results can identify individuals who are not at high risk of breast and ovarian cancer.

For more information, please contact the UCSF Cancer Risk Program at 415-885-7779.



*The Bay Area Breast Cancer SPORE Newsletter is produced annually by the SPORE Advocacy and Tissue & Outcomes Core at UCSF.*

*It is mailed to all current study participants as well as breast care surgeons and oncologists at UCSF, CPMC and SFGH.*

*If you have questions or comments about the material printed in this newsletter, or if you would like to have additional copies sent, please call the Outcomes Office at 415-353-9763. More information about SPORE and related studies available at:*

**[http://cancer.ucsf.edu/breast\\_spore](http://cancer.ucsf.edu/breast_spore)**

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**About the Ida & Joseph Friend Cancer Resource Center**

The Cancer Resource Center supports wellness and the healing process by providing patients and their loved ones with information, emotional support, and community resources. The CRC maintains a multimedia library, provides access to specialized health databases, and offers research assistance. We host diverse support groups and classes, and direct people to other community resources. All CRC programs are free.

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