

Genetic testing and management of patients with BRCA1/2-positive breast and ovarian cancers

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Assessing family history is a critical aspect of oncology consultations, especially for those related to breast and ovarian cancers. If the history indicates an increased risk of inherited malignancies, discussion, education, and genetic testing by oncologists are appropriate in developing a comprehensive treatment plan. Whether the oncologist does this or coordinates with a genetic counselor, clinicians need to be comfortable with the knowledge of risk assessment, BRCA testing, and its impact on treatment options. As the tools and technology have been developed, there are key resources for busy oncology practices to ensure practicing oncologists can provide this service with confidence.

Certain patients and families face an increased risk for hereditary breast and ovarian cancers, which may be due to the presence of specific mutations in the *BRCA1* and *BRCA2* genes. It is estimated that 5%–10% of all breast cancers are hereditary and attributable to these mutations. *BRCA1/2* mutations are found in approximately 45% of families with breast and ovarian cancers.¹ Mutations in *BRCA1* are most often seen in families with breast and ovarian cancer only, whereas *BRCA2* mutations are more common in families with male breast tumors as well as prostate, pancreatic, melanoma, and other tumors.² By age 70, patients with a germline *BRCA1* or *BRCA2* mutation have a significantly increased risk of developing breast cancer (45%–87% vs 8% in the general population; Table 1).^{3–5} The risk of ovarian cancer by this age is 60% for patients with *BRCA1* mutations and 27% for *BRCA2* carriers.^{6–8} Certain *BRCA* mutations also occur at a higher frequency in specific ethnic groups, such as those of Ashkenazi (Jewish) descent.¹

In addition, the risk for developing a second malignancy is substantially higher in *BRCA* mutation carriers than in those lacking such mutations. In women diagnosed with primary breast cancer who are *BRCA*-positive, the risk for developing a second breast cancer rises to 50% by age 50 and up to 64% by age 70, compared with 2% and 7% in the general population, respectively (Table 1).^{3,8} These women also have a 10-fold increased risk for ovarian cancer. Moreover, *BRCA* mutation carriers also have a higher likelihood of developing melanoma (relative risk [RR], 2.58), stomach cancer (RR, 2.59), gallbladder/bile duct cancer (RR, 4.97), pancreatic cancer (RR,

3.51), and cervical cancer (RR, 3.72).^{2,9}

The presence or suspicion of specific cancers or associations of certain malignancies in a given patient or family should serve as “red flags” to alert physicians to the possibility of *BRCA1/2* mutations (Table 2). Such risk factors raise the likelihood of hereditary breast or ovarian cancer and the possible need for BRCA testing. The presence of such mutations would be suggested by the combination of breast and ovarian cancers in multiple first-degree relatives, the occurrence of bilateral breast cancer in an individual, early-onset breast cancer, Ashkenazi descent, or ovarian cancer at any age.¹⁰ For example, in women who have at least four first-degree relatives with breast or ovarian cancer, the proportion that is positive for *BRCA* mutations is approximately 50%, compared with less than 1% in the general population.^{4,6,11}

Guidelines have been issued by the American Society of Clinical Oncology (ASCO) and more recently by the National Comprehensive Cancer Network (NCCN) regarding management of patients at high risk for hereditary breast and ovarian cancers, including those who may have *BRCA* mutations.^{10,12,13} These documents provide recommendations for evaluation, BRCA testing, and patient management as well as suggestions on education of patients and their families. The NCCN guidelines for BRCA testing and

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management for at-risk patients are summarized in Table 3. Both organizations stress the need for pre- and post-test counseling by a trained oncologist or genetic counselor to thoroughly discuss the testing process, test results, and various treatment and cancer surveillance options with their patients.

BRCA testing

For patients who choose to undergo BRCA testing, three outcomes are possible. Results may be (1) conclusively positive for a *BRCA1* or *BRCA2* mutation, (2) negative, or (3) indeterminate. Patients who test positive should undergo counseling with their physician or an oncologist who is trained in hereditary cancer for evaluation of treatment options, as discussed below. Those with negative results have no identifiable *BRCA* mutation but still might have a higher cancer risk due to unknown *BRCA* mutations or alterations in other cancer-predisposing genes, such as *p53* mutations.¹⁴ In some patients, a genetic variant of uncertain significance is found; the cancer risk associated with these variants is as yet unknown. Other *BRCA* genetic polymorphisms have been identified in approximately 1% of patients but are not considered to increase the risk of cancer.¹⁵

The utility of BRCA testing in the community setting is illustrated by a retrospective study of women who had already undergone testing outside large academic centers in the United States.¹⁶ Responses to a questionnaire were obtained from 646 eligible women; 64% had a personal history of cancer and 78% had at least one first-degree relative with breast and/or ovarian cancer. Twenty-two percent were found to have a germline *BRCA1/2* mutation, whereas 16% had *BRCA1/2* variants of unknown significance. More than 75% indicated they were “very satisfied” with the counseling they received. Women without a cancer history were more likely to consider prevention strategies such as prophylactic oophorectomy, mastectomy, and chemoprevention after receiving

test results than were women with a history of cancer.

These findings support the use of BRCA testing in a community practice setting and underscore the positive impact it can have on patients’ cancer detection and treatment. Support for testing was also seen in a study that evaluated the impact of BRCA testing in 122 families in which a mutation had already been identified.¹⁷ A majority of women (87%) with breast and/or ovarian cancer chose to undergo testing, demonstrating the high demand for this knowledge. In eligible women, 35% requested bilateral or contralateral mastectomy, whereas 49% opted for oophorectomy. These choices were significantly more likely in women younger than 50 years of age and in those found to be mutation carriers before they were diagnosed with breast or ovarian cancer. Most women who chose to undergo prophylactic mastectomy or oophorectomy did so within 2 years of their genetic diagnosis.

When indicated, genetic testing should be used in the most cost-effective manner. Only those individuals who are at a significantly increased risk should undergo BRCA testing. Equally important is that the correct type of BRCA test is ordered. For cases in which the specific *BRCA* mutation is unknown or not characterized, a comprehensive sequence analysis is indicated to identify the exact mutation. In families where a specific mutation has already been identified, subsequent evaluation of other family members should test only for that mutation. This approach is considerably less costly than ordering an entire BRCA sequence analysis. Those women with an exceptionally high risk who have tested negative for sequence mutations but are highly suspect in light of a strongly positive family history should undergo BRCA^{Analysis}® Rearrangement Testing (BART) to detect possible large deletions or rearrangements in the *BRCA1* and *BRCA2* genes.¹⁸

Patient counseling

The post-test counseling process

TABLE 1

Increased relative risk of breast and ovarian cancers associated with *BRCA1/2* mutations

	Relative risk	
	Sporadic	With <i>BRCA1/2</i> mutation
Risk of primary tumor		
Breast cancer	8%	45%–87%
Ovarian cancer	4%	11%–44%
Risk of second primary tumor following breast cancer		
Breast cancer	2%–11%	50%–64%
Ovarian cancer	1%–2%	10-fold increase*

*16% lifetime increased risk

should include presenting patients with a copy of their test results along with an informational brochure regarding the interpretation. If results are positive, patients are given letters and detailed information packets to share with all biologic affected relatives. Our staff follows up with patients to ensure this information is communicated and to determine whether other family members who may be at risk desire counseling and testing.

Individuals differ in their approach to informed consent. Nearly all of my patients want a brief, straightforward discussion so they can understand the test results and available treatment options. Although some prefer to have more extensive genetic counseling, most are able to make a decision for or against testing based on the information provided in a limited session. They read the educational material given to them and follow up with specific questions to make a truly informed decision. They often ask, “Doctor, what would you do if you had the mutation?” They will then decide to have a given treatment, postpone any action until a later time, or take no action if they are uncomfortable knowing the test results. However, for most patients, this knowledge is empowering, as it significantly reduces their anxiety (particularly if results are negative) and allows them to make well-informed decisions based on best available information, and helps

TABLE 2

“Red flags” for hereditary breast and/or ovarian cancer associated with *BRCA1/2* mutations

- Family member with known *BRCA1* or *BRCA2* mutation
- Personal history of breast cancer* plus one or more of the following:
 - Diagnosed at age ≤ 40 years, with or without a family history
 - Diagnosed age ≤ 50 years or two breast primaries, with at least one close blood relative with breast cancer ≤ 50 years and/or at least one close blood relative with epithelial ovarian cancer
 - Diagnosed at any age, with two or more close blood relatives with breast and/or epithelial ovarian cancer at any age
 - Close male blood relative with breast cancer
 - Personal history of epithelial ovarian cancer
 - Specific ethnicity associated with founder mutations (eg, Ashkenazi, Icelandic, Swedish, Hungarian)
- Personal history of epithelial ovarian cancer
 - Specific ethnicity associated with founder mutations (eg, Ashkenazi, Icelandic, Swedish, Hungarian)
- Personal history of male breast cancer, particularly if more than one of the following is also present:
 - One or more close male blood relatives with breast cancer
 - One or more close female blood relatives with breast or epithelial ovarian cancer
 - Specific ethnicity associated with founder mutations (eg, Ashkenazi, Icelandic, Swedish, Hungarian)
- Family history only—close family member with any of the above criteria

* Includes invasive breast cancer and ductal carcinoma in situ

them to move forward with their lives. They can also decide how they want to share this information with their immediate family and relatives.

Testing and counseling provide patients the opportunity to be proactive in terms of their cancer risk management. Using a combination of testing, aggressive cancer screening, hormonal therapy and/or chemotherapy, and prophylactic surgery, they can take control of their care to a large extent, assuming an active role in cancer prevention, early detection, and management decisions.

Patients diagnosed with early-stage *BRCA*-positive breast cancer can undergo mastectomy or receive neoadjuvant chemotherapy prior to surgery.¹⁹ One often overlooked advantage of neoadjuvant therapy is that it provides women with additional time to decide whether and when they want to undergo surgery and what type (ie, mastectomy, breast-conserving surgery, prophylactic bilateral mastectomy in conjunction with reconstructive surgery). Patients are often

emotionally overwhelmed by the diagnosis of breast cancer and may not be able to make a rational decision regarding their treatment. For other women who have already been diagnosed with primary breast or ovarian cancer, the prospect of bilateral mastectomy or oophorectomy is too overwhelming to deal with at present. They may choose to delay any decision on prophylactic surgery until after their treatment has ended or at a later time. Physicians should respect a patient's decision to postpone testing but can raise this issue again over the next several years, as they follow the patient longitudinally. The key point to recognize is that all patients are different, so it is critical to provide information, discuss options, and determine patient preferences.

Some patients are concerned about possible discrimination by insurers or employers regarding *BRCA* testing and thus may fear being tested. A study of women undergoing genetic counseling and/or testing for breast

cancer found that fear of life insurance discrimination was negatively correlated with a decision to proceed with *BRCA* testing.²⁰ However, to date, no evidence of insurance discrimination has been documented.^{20,21} Patients' fears about such issues usually far exceed any real discrimination.²²

Risk reduction and management

If patients test positive, we discuss their options and choices. They range from increased cancer surveillance through yearly clinical breast cancer examinations and self-examination, mammograms, and MRIs (for breast cancer), or pelvic examinations, vaginal ultrasonography, and CA-125 monitoring (ovarian cancer); prophylaxis with tamoxifen or raloxifene (Evista); or prophylactic bilateral mastectomy and/or bilateral oophorectomy. Do patients want to use a selective estrogen receptor modulator to reduce their risk by 50%? They may or may not want to receive tamoxifen if they are premenopausal or raloxifene if they are postmenopausal. Do they want to undergo aggressive screening? Some may desire an immediate bilateral mastectomy or oophorectomy, whereas others may prefer to postpone that decision until the first abnormal mammogram. Not all patients choose bilateral surgery and oophorectomy as their major risk-reduction option.

Among families with a history of breast cancer, prophylactic mastectomy has been shown to reduce the risk of breast cancer by 90%.^{23,24} This approach may be an option for some women who already have been diagnosed with primary breast cancer in one breast or for those who wish to avoid undergoing multiple biopsies due to abnormal findings.

Similarly, oophorectomy can decrease the risk of ovarian cancer. Women who opted for such prophylactic surgery had a 96% lower relative risk of coelomic epithelial cancer compared with those who chose surveillance only.^{25,26} Not always appreciated is the reduc-

tion in risk of breast cancer associated with oophorectomy in *BRCA1* carriers. A 47% decrease in adjusted relative risk of breast cancer was observed in patients who underwent oophorectomy but had no history of breast or ovarian cancer and had not undergone a prophylactic mastectomy; the risk reduction was even greater (72%) for women who were followed for 5–10 years.²⁷ This option may be more relevant for women who have completed child-bearing and are entering menopause.

Family counseling

Each of our patients undergoes a three-generational family history for a complete risk assessment of hereditary cancer. This history is updated yearly to determine whether their risk profile has changed based on a recent cancer occurrence in their extended family, the impact of which may not be apparent to patients. It is not uncommon for the initial intake to require two or more visits for patients to research their family cancer history, contacting relatives and their physicians, so that a thorough assessment can be conducted. A complete family history must be obtained to identify family members who have had or who are at increased risk for cancer and to educate them about the risk to themselves and their children. In addition, a family member with cancer may have been tested previously so that the patient you are seeing could limit their testing, if appropriate, to the known familial mutation. The biologically related family members to be notified if a positive mutation is found need to be identified. This step may require working across states to contact various family members and their physicians, distributing educational brochures, and collecting test results from relatives to assemble a complete genetic cancer profile. To me, this represents a real opportunity to reach out to our primary care colleagues. Any at-risk individual identified can then be referred to a local oncologist or genetic counselor for risk assessment and medical management. I

TABLE 3

Guidelines for management of hereditary breast and ovarian cancers associated with *BRCA1/2* mutations

Women

- Breast self-examination (BSE) training and regular monthly BSE starting at age 18
- Clinical breast examination, semi-annually, starting at age 25 years
- Annual mammogram and breast MRI screening starting at age 25 years or based on earliest age of onset in family
- Discuss option of prophylactic mastectomy on a per-patient basis and counsel regarding degree of protection, reconstruction options, and risks
- Recommend salpingo-oophorectomy to reduce risk, ideally between 35 and 40 years or upon completion of child bearing, after discussing reproductive issues, cancer risk, degree of protection for breast and ovarian cancers, and management of menopausal symptoms
- For patients who elect not to have prophylactic mastectomy, concurrent transvaginal ultrasonography and CA-125 screening, every 6 months starting at age 35 or 5–10 years earlier than earliest age of first diagnosis of ovarian cancer in the family
- Consider chemoprevention options for breast and ovarian cancers, including discussing risks and benefits

Risk-reduction guidelines

- Consider investigational imaging and screening studies, when available

Men

- BSE training and regular monthly practice
- Semi-annual clinical breast examination; consider baseline mammography
- Adhere to NCCN screening guidelines for prostate cancer

Women and men

- Discuss risk to relatives, options for risk assessment, management, and consideration of genetic testing for at-risk relatives
- Education regarding signs and symptoms of cancer(s), especially those associated with *BRCA1/2* gene mutations
- Refer to NCCN guidelines for other cancer screening recommendations

Risk to relatives

- Advise relatives about possible inherited cancer risk and consider genetic consultation and/or testing

NCCN = National Comprehensive Cancer Network

From National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Genetic/familial high-risk assessment: breast and ovarian. V.1.2007. Available at: www.nccn.org. Accessed January 7, 2008.

encourage patients to mail the report of their specific mutation along with the contact letter to their family member to share with their physician.

BRCA detection in men

The risk of BRCA-associated cancer in men is often misunderstood, because the focus has been predominantly on women. *BRCA2* mutations are thought to account for 14%–20% of breast cancers in men.^{28,29} Patients should be informed that male relatives of women identified as mutation carriers have a 50% chance of inheriting the mutation.

Men diagnosed with *BRCA1/2* mutations who are at increased risk should be trained to perform monthly breast self-examination and to undergo regular mammography and a semi-annual clinical breast examination.¹⁰ For women with these mutations, counseling is advised for male carriers, their children, and other at-risk family members.

Evidence also suggests that men with *BRCA* mutations may be at increased risk for other tumors, such as prostate cancer. In one study of 251 unselected Ashkenazi men with prostate cancer, *BRCA2* mutation carriers

Patients' perspectives

Wendy—

About 2 years ago Dr. Bosserman first told me about BRCA testing, but at the time I didn't want to hear about it. My sister, however, did want more information because our mom had cervical cancer when she was younger and had subsequently died from ovarian cancer. My sister's physician informed her that a member of the family who had already had cancer should start this testing. So she called and talked to me about it, but I blocked it out then because I was sick of being tested and going to the doctor.

Two years later I called Dr. Bosserman to let her know I had decided to be tested. She totally took care of testing for me. Dr. Bosserman's office had the kit to me within a week, and I went straight over to the hospital and had blood drawn. It was a very fast and easy process, which surprised me.

My BRCA results came back positive. So then my sister went, and her test results were negative. Now I'm trying to arrange for my 21-year-old daughter to be tested. I know that she is now going to be more aggressive in monitoring and getting screened.

After I had a lumpectomy, 1 year later a (nonmalignant) tumor on my ovary was detected and I had a complete hysterectomy. I now have my yearly mammogram and an MRI of the breast.

Lynne—

Once Dr. Bosserman performed a complete family history, we determined that my dad had prostate cancer, and his mother and aunt both had breast cancer. My father's BRCA test was positive, so I was tested and was also found to be positive. After discussing the high risk of breast cancer recurrence with Dr. Bosserman, I decided to undergo a double mastectomy. My sister did the same after her test came back positive, too.

I'm definitely glad they have this BRCA test. Otherwise, my sister would probably have ended up getting breast cancer as well. I have two daughters, ages 25 and 23, who will also be tested soon. I would recommend the BRCA test for anyone who has a history of breast cancer in the family.

had an increased risk of prostate cancer (odds ratio, 4.78; 95% confidence interval, 1.87–12.25; $P = 0.001$), although those with *BRCA1* mutations did not have an increased risk.³⁰ Therefore, men who have been diagnosed with *BRCA* mutations should undergo regular prostate examinations and prostate-specific antigen (PSA) determinations. NCCN guidelines suggest that men with a deleterious *BRCA2* mutation should begin screening for prostate cancer at age 40 rather than age 50, since such mutations increase the lifetime risk of developing prostate cancer from 14% to about 20%.

A recent study indicates that men also have difficulty correctly recalling BRCA test results of a family member and understanding how this might affect risk to themselves and their children.³¹ Men may have greater cognitive and emotional distancing related to genetic testing, requiring more counseling

to ensure they fully understand the impact of these results.

Conclusion

The significant increase in risk of breast and ovarian cancers associated with *BRCA1* and *BRCA2* mutations provides an opportunity for both physicians and patients to play an active role in cancer prevention and treatment management decisions. Now that BRCA testing has become widely available, the demand for and satisfaction with this diagnostic tool are obvious from published reports and individual patients (see accompanying patient perspective). BRCA assessment is viewed by many patients as empowering, because it allows them to make more informed decisions about cancer prevention and treatment, ranging from informed denial to heightened surveillance to prophylactic surgery. Identification of ad-

ditional family members who may be at increased risk and who could benefit from testing and counseling multiplies the potential benefits of this process, greatly increasing the physician's impact on cancer detection and prevention within each family. In addition, I have often seen patients receive tremendous support from potentially affected family members who welcome the knowledge, which relieves the patient of any guilt about the shared risk. Families may also appreciate that there is a rational explanation for the excess cancers they have all seen but have had no recourse other than radical surgery.

Patients usually welcome testing as part of their cancer consultation, despite the overwhelming amount of information reviewed. Patients are processing extensive amounts of material in any new cancer consultation. Adding genetic risk assessment, which can affect treatment decisions, has generally increased the confidence patients have in their care. They come to us as experts at a time of great vulnerability. Learning that we take into consideration all aspects of their care in our treatment plan helps them feel less vulnerable and more in control of choosing the best options for their care while respecting their individuality. Tools currently available make inclusion of genetic risk assessment, counseling, consent, testing, education, and treatment planning realistic in the oncologist's office. This is yet another milestone in the field of community oncology that has pioneered the delivery of state-of-the-art care at the most convenient site for patients.

References

1. Honrado E, Benítez J, Palacios J. The molecular pathology of hereditary breast cancer: genetic testing and therapeutic implications. *Mod Pathol* 2005;18:1305–1320.
2. Cancer risks in *BRCA2* mutation carriers. The Breast Cancer Linkage Consortium. *J Natl Cancer Inst* 1999;91:1310–1316.
3. Ford D, Easton DF, Bishop DT, Narod SA, Goldgar DE. Risks of cancer in *BRCA1*-mutation carriers. Breast Cancer Linkage Consortium. *Lancet* 1994;343:692–695.
4. Struwing JP, Hartge P, Wacholder S, et al.

The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. *N Engl J Med* 1997;336:1401–1408.

5. Antoniou A, Pharoah PD, Narod S, et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history: a combined analysis of 22 studies. *Am J Hum Genet* 2003;72:1117–1130.

6. Ford D, Easton DF, Stratton M, et al. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. The Breast Cancer Linkage Consortium. *Am J Hum Genet* 1998;62:676–689.

7. Marroni F, Aretini P, D'Andrea E, et al. Penetrances of breast and ovarian cancer in a large series of families tested for BRCA1/2 mutations. *Eur J Hum Genet* 2004;12:899–906.

8. Easton DF, Ford D, Bishop DT. Breast and ovarian cancer incidence in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. *Am J Hum Genet* 1995;56:265–271.

9. Thompson D, Easton DF; Breast Cancer Linkage Consortium. Cancer incidence in BRCA1 mutation carriers. *J Natl Cancer Inst* 2002;94:1358–1365.

10. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Genetic/familial high-risk assessment: breast and ovarian. V.1.2007. Available at: <http://www.nccn.org>. Accessed January 7, 2008.

11. Grann VR, Jacobson JS. Clinical utility and genetic testing. Educational Book of the American Society of Clinical Oncology, 2007:107–112.

12. Statement of the American Society of Clinical Oncology: genetic testing for cancer susceptibility. Adopted on February 20, 1996. *J Clin Oncol* 1996;14:1730–1736.

13. American Society of Clinical Oncology (ASCO). ASCO policy statement update: genetic testing for cancer susceptibility. *J Clin Oncol*

2003;21:2397–2406.

14. Lai H, Ma F, Trapido E, Meng L, Lai S. Spectrum of p53 tumor suppressor gene mutations and breast cancer survival. *Breast Cancer Res Treat* 2004;83:57–66.

15. Bellosillo B, Tusquets I. Pitfalls and caveats in BRCA sequencing. *Ultrastruct Pathol* 2006;30:229–235.

16. Chen WY, Garber JE, Higham S, et al. BRCA1/2 genetic testing in the community setting. *J Clin Oncol* 2002;20:4485–4492.

17. Meijers-Heijboer H, Brekelmans CT, Menke-Pluymers M, et al. Use of genetic testing and prophylactic mastectomy and oophorectomy in women with breast or ovarian cancer from families with a BRCA1 or BRCA2 mutation. *J Clin Oncol* 2003;21:1675–1681.

18. Myriad Genetics, Inc. BRCA^{Analysis}® Rearrangement Test. Available at <http://www.myriad.com>. Accessed January 15, 2008.

19. NCCN Clinical Practice Guidelines in Oncology. Breast cancer. V.1.2008. Available at: <http://www.nccn.org>. Accessed January 11, 2008.

20. Armstrong K, Weber B, FitzGerald G, et al. Life insurance and breast cancer risk assessment: adverse selection, genetic testing decisions, and discrimination. *Am J Med Genet A* 2003;120:359–364.

21. Anderson RR, Haidle JL. Legal considerations in clinical cancer genetics. *Commun Oncol* 2006;3:100–104.

22. Hall MA, Rich SS. Patients' fear of genetic discrimination by health insurers: the impact of legal protections. *Genet Med* 2000;2:214–221.

23. Rebbeck TR, Friebel T, Lynch HT, et al. Bilateral prophylactic mastectomy reduces breast cancer risk in BRCA1 and BRCA2 mutation carriers: the PROSE Study Group. *J Clin Oncol* 2004;22:1055–1062.

24. Robson M, Svahn T, McCormick B, et al. Appropriateness of breast-conserving

treatment of breast carcinoma in women with germline mutations in BRCA1 or BRCA2: a clinic-based series. *Cancer* 2005;103:44–51.

25. Rebbeck TR, Lynch HT, Neuhausen SL, et al. Prophylactic oophorectomy in carriers of BRCA1 or BRCA2 mutations. *N Engl J Med* 2002;346:1616–1622.

26. Kauff ND, Satagopan JM, Robson ME, et al. Risk-reducing salpingo-oophorectomy in women with a BRCA1 or BRCA2 mutation. *N Engl J Med* 2002;346:1609–1615.

27. Rebbeck TR, Levin AM, Eisen A, et al. Breast cancer risk after bilateral prophylactic oophorectomy in BRCA1 mutation carriers. *J Natl Cancer Inst* 1999;91:1475–1479.

28. Haraldsson K, Loman N, Zhang QX, Johannsson O, Olsson H, Borg A. BRCA2 germ-line mutations are frequent in male breast cancer patients without a family history of the disease. *Cancer Res* 1998;58:1367–1371.

29. Couch FJ, Farid LM, DeShano ML, et al. BRCA2 germline mutations in male breast cancer cases and breast cancer families. *Nat Genet* 1996;13:123–125.

30. Kirchoff T, Kauff ND, Mitra N, et al. BRCA mutations and risk of prostate cancer in Ashkenazi Jews. *Clin Cancer Res* 2004;10:2918–2921.

31. Daly MB. Addressing the needs of men in BRCA1/2 families. Presented at the 30th Annual San Antonio Breast Cancer Symposium; December 13–16, 2007; San Antonio, Tex. Abstract 2039.

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Administrator's Perspective

Administrative issues in genetic counseling and testing

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Wilshire Oncology Medical Group offers genetic counseling as part of its comprehensive oncology consultative services. Administrative issues include informed consent, billing for genetic counseling services, genetic privacy considerations,

and authorization and payment for testing. We also provide post-test counseling for patients and counseling of other family members.

Genetic counseling

As part of our initial new patient intake, all patients fill out a three-

generational family history prior to their first consultation. Patients can download the intake form from our website or obtain one from the office. Data are entered into our electronic medical records, and any missing items are requested from the patients. Every history needs to be reviewed

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with patients, since other related family members with index cancers often can be identified. Commonly, breast cancer patients are found to have a significant or possibly significant family history, and inherited risk needs to be part of the initial treatment planning discussions. These patients receive informational handouts and are given the option to undergo individual, more detailed genetic counseling and testing. Consultations are billed by the physician as part of the initial comprehensive consult, usually at a level 5 consult. Follow-up counseling visits are billed with the 99213-99215 codes for physician evaluation and management visits depending on the time, complexity, and details of the services provided.

The oncologist decides which of the three types of BRCA tests is most appropriate, ie, either for a site-specific mutation previously identified in the family, a limited panel (eg, for patients of Ashkenazi descent), or the full *BRCA1/2* panel. Test kits are available in our offices, so there is no delay when a patient is identified, consents, and qualifies for testing.

Insurance coverage for *BRCA1/2* testing

Insurance coverage for BRCA testing is variable and can depend on the patient's family history and individual policy rules. The current cost (Myriad Genetics) for a *BRCA* specific site mutation is \$385 versus \$3,120 for the full *BRCA1/2* panel. Our medical assistants work with the insurance provider to determine whether a patient meets the plan's testing criteria for payments and what percentage will be covered. The patient can then decide whether or not to proceed with testing. Once the patient agrees to be tested, he or she is given a genetic testing kit with a signed consent and detailed

paperwork to take to a local laboratory for blood collection and shipment.

For Medicare patients, we use a standard list of criteria as determined by Medicare that includes personal and family histories of cancer.¹ Patients who meet Medicare criteria for genetic testing are fully covered for the cost of the test. Those who do not can still opt to pay for the test and sign a benefit waiver letter. A follow-up visit for post-counseling is scheduled for all patients 4–6 weeks later.

Pre- and post-test counseling

Once a patient has been counseled and has agreed to genetic testing, signed consent must be obtained. The patient reviews and signs the consent form, which includes a commitment to undergo post-test counseling once testing has been completed. Regardless of the findings (ie, positive, negative, or indeterminate), post-test counseling is scheduled to integrate recommendations into the treatment plan and ensure that the patient is prepared to share any relevant information with family members. We give each patient a copy of the specific genetic testing report, which provides information on the risk of primary and secondary breast or ovarian cancers as well as the risk of other cancers associated with that mutation. They appear to be well-received by patients. We also hand out a booklet that is written for those with positive, uncertain, or negative results, which further counsels patients on issues based on specific results. Additional visits are scheduled as needed. In addition, we offer individual family member consultations, if desired, to discuss with each member his or her own risk, options, issues, and choices or consent for testing. All family

members have the right to decide for themselves whether or not testing is right for them. We work to ensure complete understanding and comfort with results by patients and any interested family members. For relatives who live at a distance, we help them find the best option for genetic counseling near their homes.

Confidentiality of records

Respect for genetic privacy has been a cornerstone of our counseling program and is much appreciated by our patients with and without cancer. Our electronic medical records document what is discussed with patients at every visit, including inherited risk and consent for testing. If the patient agrees, we incorporate the test results and recommendations into our oncology consult and follow-up notes. All genetic results for cancer patients and those who may be at increased risk are stored in individual patient folders, which are filed separately from the regular medical records. We emphasize to patients that such records are confidential and would only be released with their signed consent to an outside source, including any referring or consulting doctors. This assurance is very important, particularly to patients who do not have cancer, since they are often concerned about insurance discrimination. Test results are unlikely to be used for this purpose, however, and this has not been an issue in our practice.

Reference

1. U.S. Department of Health and Human Services Centers for Medicare and Medicaid. Local Coverage Determination for Genetic Testing. Available at: <http://www.myriadtests.com/medicarecriteria>. Accessed January 18, 2008.

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