

Familial Breast Cancer

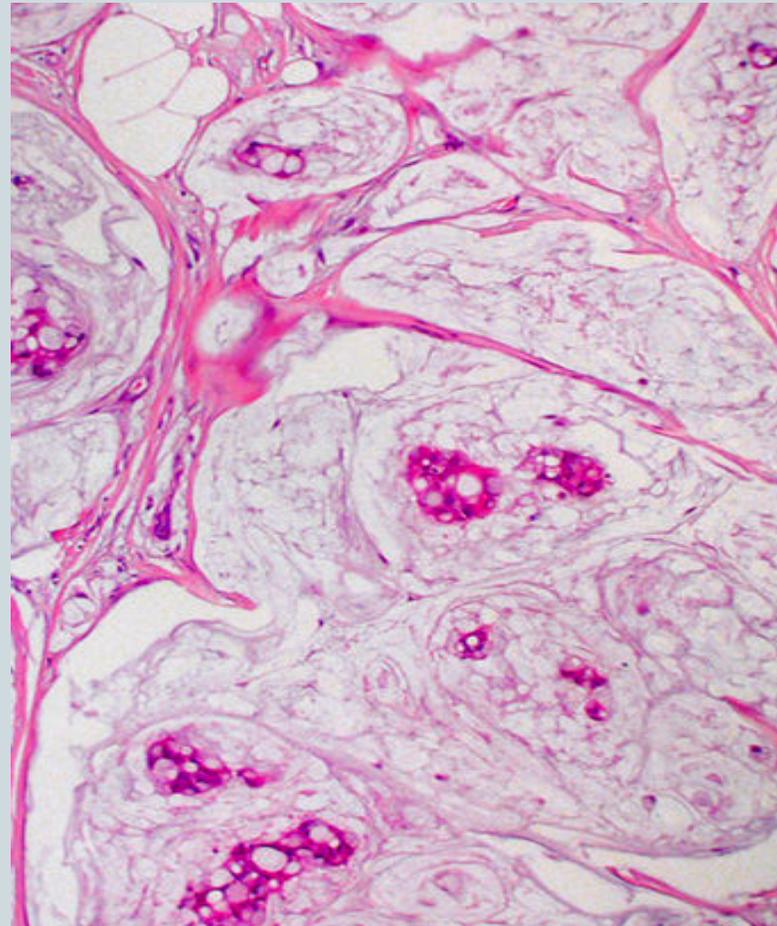
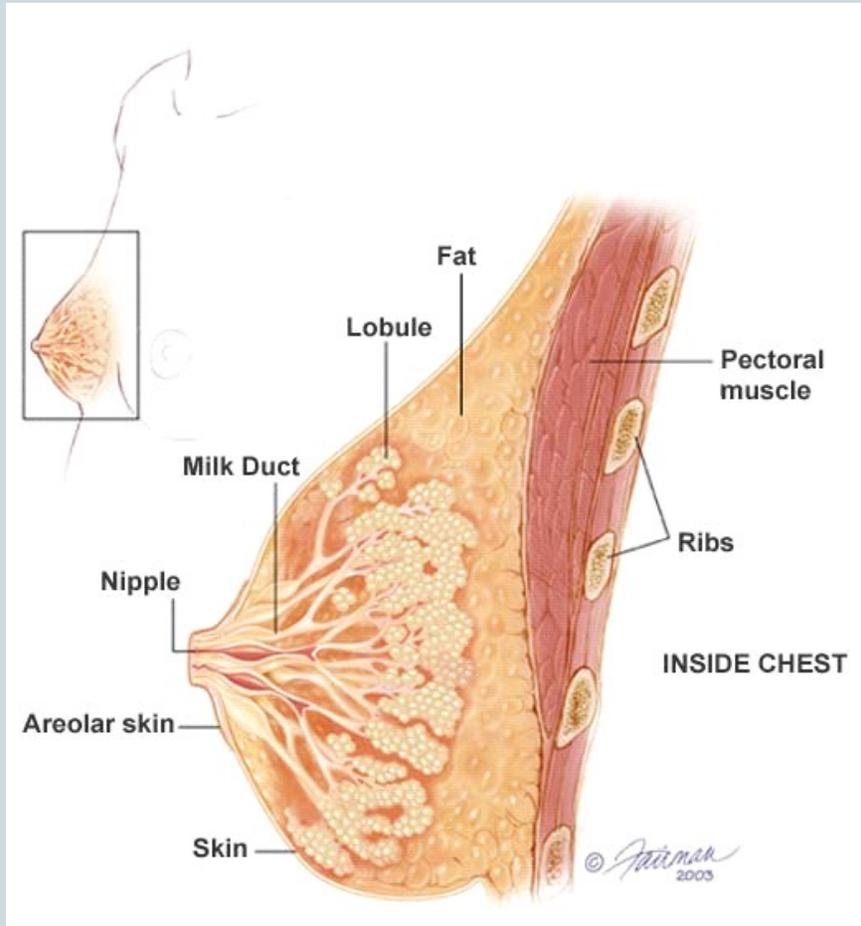


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Definitions



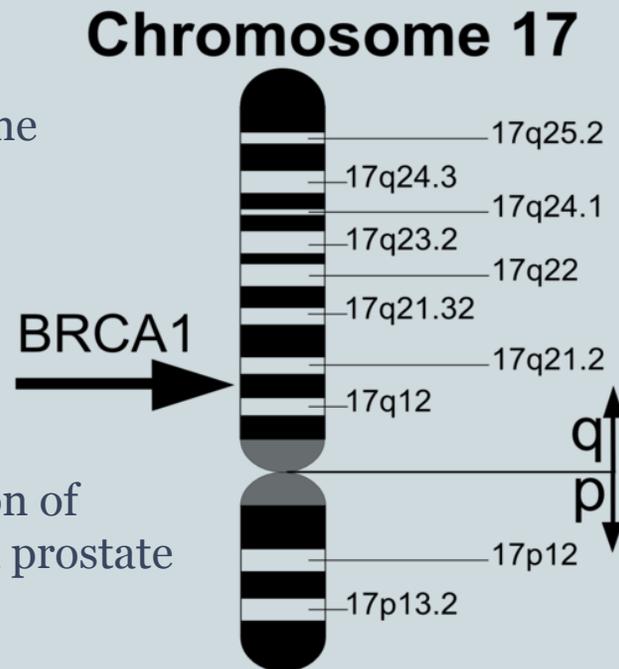
- **What is Cancer?**
 - “Cancer is a disease in which a group of cells display uncontrollable growth (division beyond normal limits), invasion (intrusion on and destruction of adjacent tissues), and sometimes metastasis” – Wikipedia.com
- **What is Breast Cancer?**
 - Breast Cancer is a disease in which the uncontrollable growth and division of malignant cells in the tissue of the breast lead to the formation of a “lump”. These cells can invade the healthy surrounding tissues through the lymph or blood vessels and result in the formation of secondary metastases. This is how cancer ‘spreads’.
 - 2 major types include :Invasive ductal carcinoma in situ, Invasive lobular carcinoma in situ.
- **What is the difference between familial and sporadic Breast Cancer?**
 - Sporadic Breast Cancer is non-hereditary and represents 85-90% of Cancer cases.
 - Familial Breast Cancer is hereditary and represents only 10-15% of Cancer cases.



The Genetics of Breast Cancer



- Fewer than 1 in 20 cases of Breast Cancer is familial and only about 1 person in 1000 carries the genes responsible.
- Genes responsible for familial Breast Cancer:
 - **BRCA1** : located on long (q) arm of chromosome # 17, at band 21.
 - **BRCA2** : located on long (q) arm of chromosome # 13 at position 12.3.
 - **TP53** : a tumor suppressor gene
 - **ATM** : Antaxia Telangiectasia Mutated gene, a recessive gene that increases the risk of developing certain types of cancer and rare genetic diseases.
 - **P65** : the altered P65 leads to an overproduction of certain hormones that help to cause breast and prostate cancer.



HBOC Basics

Why Test?

How Do I Get Tested?

Payment and Insurance

How to Be Ready

Understanding My Results >

Frequently Asked Questions >

Resources >

BRCA[®]Analysis can only be ordered by a qualified healthcare provider.

Find a Provider



sure exactly how you're related to a particular family member, or whether they had breast or ovarian cancer, discuss it with other family members. If you know your family history of cancer, your discussion with your doctor will be that much more valuable.

Take the *Be Ready Quiz*

Consider both your mother's and father's side of the family. Do you have a family or personal history of any of the following (check only if your answer is Yes):

- Breast cancer before age 50?
- Breast cancer in 2 or more relatives?
- Breast cancer in a male relative?
- Breast cancer in both breasts or twice in the same breast?
- Breast cancer and Ashkenazi, or Eastern European Jewish, ancestry?
- Ovarian cancer at any age?

You did not check any of the boxes above that identify common features of hereditary breast and ovarian cancer. If those responses are correct, your doctor may not recommend testing.

If you still have concerns about your family or personal history of cancer, print this page, which includes your quiz questions and answers, gather more information about cancers in your family, and be ready to talk with your doctor.



Watch the Video

"If I can reach a patient before she has cancer, it's ideal."

— Kevin S. Hughes, MD, FACS

President, National Consortium of Breast Centers

The importance of BRCA1



- A recent study in the yeast protein has indicated that the gene BRCA-1 is directly involved with the repair of breaks in the double stranded DNA. These breaks can be induced by radiation or by the exchange of genetic material during meiosis (crossing over). BRCA1 has the ability to directly bind to the DNA and can inhibit the nuclease activity of the MRN complex (a protein directly involved with DNA repair in mammals).
- The altered BRCA1 gene appears in only 5% of the 182000 breast cancer cases. Thus, not having the altered gene does not necessarily mean that the individual will be free of breast cancer during her lifetime.
- “Mutations in the gene BRCA1 could result due to a change in one or a very small number of DNA base pairs, or in certain cases can be caused by the rearrangement of segments of the DNA (deletion or duplication). A mutated BRCA1 gene makes a protein that cannot function efficiently due to its abnormal short length, and this defective BRCA1 protein in its turn is unable to repair mutations in other genes. The accumulation of these defects results in the uncontrollable division of the cancerous cells.”

The Classical Diagnosis Methods



- Breast Self Examination
- The Triple Test:
 - Breast examination
 - Mammography: digital or conventional
 - Biopsy: Needle Core biopsy, Fine Needle Aspiration and Cytology, Excision Biopsy
- “One stop shops” – rapid assessment of breast lumps
- Magnetic Resonance Imagery (MRI)
- Ultrasonic Imagery
- Genetic Testing (relatively new)
- Blood Test
- CT scans
- Chest X-rays

The Classical Treatment of the Disease



“The key to successful treatment is early diagnosis”

- **Surgery** – Lumpectomy , Mastectomy, underarm glands (axillary lymph nodes), axillary node clearance
- **Chemotherapy** – Cytotoxic chemotherapy: neoadjuvant therapy (before surgery), adjuvant therapy (after surgery)
- **Radiotherapy** - to destroy microscopic tumors that might have escaped surgery
- **Drugs** - Tamoxifen, which acts as an estrogen antagonist
- **Hormonal Therapies**
- **Monoclonal Antibodies** - bind to a substance and help to detect and purify it

Novel Diagnostics



- Polymerase Chain Reaction (PCR) and DNA sequencing are two techniques that can now be used to determine mutations in the gene BRAC-1
- Genetic testing
- Online genetic testing - BRCA1 Analysis: *“BRCAAnalysis® assesses a woman's risk of developing breast or ovarian cancer based on detection of mutations in the BRCA1 and BRCA2 genes. This test has become the standard of care in identification of individuals with hereditary breast and ovarian cancer and is reimbursed by insurance.” – Myriad.com*



1. The Prevalence of Deleterious Mutations in BRCA1 and BRCA2 (Excludes Individuals of Ashkenazi Ancestry)

Patient's History	Family History (Includes at least one first or second degree relative)					
	No breast cancer <50, or ovarian cancer, in any relative. [†]	Breast cancer <50 in one relative; no ovarian cancer in any relative.	Breast cancer <50 in more than one relative; no ovarian cancer in any relative.	Ovarian cancer at any age in one relative; no breast cancer <50 in any relative.	Ovarian cancer in more than one relative; no breast cancer <50 in any relative.	Breast cancer <50 and ovarian cancer at any age. ^{††}
No breast cancer or ovarian cancer at any age	2.8%	4.5%	8.7%	5.6%	9.6%	12.2%
Breast cancer ≥ 50	2.9%	5.3%	11.4%	6.4%	12.2%	15.9%
Breast cancer <50	6.8%	15.8%	30.1%	16.9%	27.3%	39.2%
Male breast cancer	12.8%	21.8%	41.9%	20.0%	40.0%*	61.9%
Ovarian cancer at any age, no breast cancer	8.8%	23.1%	42.3%	21.1%	33.2%	46.5%
Breast cancer ≥50 and ovarian cancer at any age	17.6%	26.1%	46.2%	30.3%	46.2%	60.0%
Breast cancer <50 and ovarian cancer at any age	39.1%	53.9%	67.2%	66.0%	70.8%	79.0%

[†] May include families with breast cancer ≥50 (in women or men).

^{††} Includes family members with either or both diagnoses.

Number of observations in Table 1 is 49149

*N<20



- Synthetic Lethal Screening looks for new drug targets in yeast and fruit flies.
- **“Breast Cancer gene discovery most important for 20 years.”** – Scientists have found a new gene, called NRG1, that is linked to half of all breast cancers. This new finding will help scientists have a greater understanding of the way cancer develops and lead them towards new treatments.
October 5th 2009

Acknowledgements



- BBC - http://www.bbc.co.uk/health/womens_health/issues_breastcancer2.shtml
- NCBI - <http://www.ncbi.nlm.nih.gov:80/books/bv.fcgi?rid=gnd.section.99&ref=sidebar>
- NICE - <http://www.nice.org.uk/nicemedia/pdf/CG41fullguidance.pdf>
- OMIM - <http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=114480>
- LBL Genetic Testing- <http://www.lbl.gov/Education/ELSI/Frames/cancer-genes-f.html>
- Myriad - <http://www.myriadtests.com/benefits.htm>,
<http://www.myriadtests.com/provider/doc/BRCA-Mutation-Prevalence-Percentages.pdf>, http://www.myriadtests.com/risk_brac.htm
- The Telegraph - <http://www.telegraph.co.uk/health/healthnews/6261309/Breast-cancer-gene-discovery-most-important-for-20-years.html>
- Wikipedia - http://en.wikipedia.org/wiki/Breast_cancer ,
<http://en.wikipedia.org/wiki/BRCA1>