

BRCA_{Analysis} Rearrangement Testing (BART)

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As you recall, *BRCA1* and *BRCA2* gene mutations cause hereditary breast and ovarian cancer syndrome (HBOC). *BRCA1* and *BRCA2* gene mutations are the most common cause of hereditary breast cancers and hereditary ovarian cancers. BRCA_{Analysis} Rearrangement Testing (BART) is a newer test that can detect *BRCA* gene mutations that may have been missed by traditional testing.

What is traditional *BRCA* testing?

For nearly the past decade, traditional *BRCA* testing has been used to detect mutations in the *BRCA* genes. Traditional *BRCA* testing works by 'spell checking' the genes. Thus each letter of DNA is checked letter by letter to determine if any letters are missing, added, in the wrong order, or swapped out for different letters. It is believed that traditional testing is able to detect about 95% of *BRCA1* and *BRCA2* gene changes.

What is BART?

BART is an additional test that also detects mutations in the *BRCA1* and *BRCA2* genes. However, this testing can detect large deletions, duplications, and rearrangements in the genes that traditional testing cannot detect. Therefore, even though a patient may have tested negative using traditional testing, it is still possible that they have a mutation in the *BRCA1* or *BRCA2* genes. BART has been available since August 2006.

What are the cancer risks?

There is not thought to be a difference in cancer risks among patients who test positive with traditional testing versus those who test positive using BART. Therefore, females who test positive for a *BRCA1* or *BRCA2* gene mutation using BART have a 40-65% chance to develop breast cancer and a 20-40% chance to develop ovarian cancer. These patients are also at high risk to develop second breast cancers. *BRCA* mutations are also associated with an increased risk for cancers of the male breast, prostate, pancreas, colon, and melanoma.

Who should receive BART?

Until now, BART was ordered reflexively on patients who were considered high risk to have HBOC based on their personal and family histories, but who tested negative with traditional testing. High risk was defined as greater than 30% by BRCApro or as outlined by Myriad's high risk criteria. However, the NCCN recently updated their guidelines to include BART on all patients who qualify for traditional *BRCA* testing. Some private insurance companies have already begun to cover BART. Since it is believed that most all insurance companies will cover BART by then end of the year, Myriad Genetics will hold DNA until 12/31/2012 in situations where BART is not currently covered.

The risk to test positive for a *BRCA* gene mutation by BART depends largely on the individual's ancestry. Myriad Genetics, which is the only lab that can offer *BRCA* gene testing clinically, has published some of this data. Of all patients who are at high risk to have a mutation *and* are of Latin American/Caribbean or Neareast/Mideast ancestry, about 20% who tested positive had a mutation that was detectable only by BART. On average, about 5% of *BRCA* mutations belonging to people at high risk who are of other ancestries have a mutation that can only be detected by BART. Even though these numbers sound high,

they apply to 'high risk' individuals only. Myriad has reported that if a person tests negative with traditional *BRCA* testing, their risk to test positive by BART is less than 2%, regardless of ancestry.

How is this test performed?

For the patient, the experience is the same as traditional *BRCA* testing. A sample of blood is collected in a purple-top tube and sent to Myriad Genetics for testing. At UT Southwestern, we are in the process of calling back patients who had tested negative by traditional testing and who have not had BART. Additionally, we have set up an additional clinic at John Peter Smith (JPS) for patients needing BART who qualify for Myriad's Financial Assistance Program who have already tested negative by traditional *BRCA* testing. Myriad now performs BART routinely on all patients who qualify for *BRCA* testing through Myriad's Financial Assistance Program. All patients receiving BART will meet with a genetic counselor before their blood draw.

What is the bottom line?

BART is an additional test that is able to detect mutations that would have otherwise been missed by traditional *BRCA1* and *BRCA2* gene testing. In accordance with NCCN guidelines, this test should be run in conjunction with traditional *BRCA* gene testing on all patients who meet criteria for *BRCA1* and *BRCA2* gene testing.