BRCA1 and *BRCA2* Prevalence Tables for Mutations Detected by Sequencing, the 5-site Rearrangement Panel (LRP) and the BRAC*Analysis*® Large Rearrangement Test (BART™) in High Risk Patients

The table below represents observations of deleterious and suspected deleterious mutations by Myriad Genetic Laboratories, Inc. through its clinical testing service. Data obtained through testing performed under specific research protocols are not included here. The information included in these tables was obtained from a routine laboratory requisition and has not been independently verified. Patients for whom relevant information was not provided were not included in this tabulation.

This table shows the outcome of testing for patients for whom the test ordered was Comprehensive BRAC*Analysis* and the patient met Myriad's current criteria for concurrent complementary BART testing (for a description of the criteria used to identify these high risk patients, please see https://www.myriadpro.com/BRAC_BART). The total is based on 25,535 patients. The data broken down by ancestry is based only on patients for whom a single unambiguous ancestry was indicated on the Test Request Form and includes 17,558 individuals distributed across the listed ancestries.

The table shows the percentage of high risk patients who were positive for a mutation in *BRCA1* or *BRCA2*, and the percentage of all of the mutations detected that were found with sequencing, the LRP (5-site Rearrangement Panel) and BART (BRAC*Analysis* Large Rearrangement Test). The number of patients in each cell is provided in parentheses. Note that BART detects all 5 of the mutations included in the LRP, but for the purpose of the table below, the mutations detected by the LRP are listed separately from any other large rearrangements detected solely with BART.

Prevalence Table

Ancestry	Percentage positive for any mutation	Percentage of all mutations detected that were detected with sequencing	Percentage of all mutations detected that were detected with the LRP[1]	Percentage of all mutations detected that were detected with BART[2]	Percentage of all mutations detected that were large rearrangements (LRP + BART)
African	29.9% (515)	91.6% (472)	0.2% (1)	8.1% (42)	8.3% (43)
Asian	25.4% (109)	93.6% (102)	None (0)	6.4% (7)	6.4% (7)
Central/Eastern Europe	24.4% (400)	92.0% (368)	2.2% (9)	5.8% (23)	8.0% (32)
Latin American/ Caribbean	31.3% (399)	79.4% (317)	0.2% (1)	20.3% (81)	20.5% (82)
Native American	17.7% (49)	95.9% (47)	None (0)	4.1% (2)	4.1% (2)
Neareast/ Mideast	26.6% (41)	80.5% (33)	None (0)	19.5% (8)	19.5% (8)
Western/ Northern Europe	23.3% (2651)	90.3% (2394)	3.6% (96)	6.1% (161)	9.7% (257)
Ashkenazi Jew[3]	12.8% (86)	95.3% (82)	1.2% (1)	3.5% (3)	4.7% (4)
TOTAL[4]	23.8% (6084)	90.1% (5479)	2.4% (147)	7.5% (458)	9.9% (605)

(Footnotes)

1 The LRP (*BRCA1* 5-site rearrangement panel) has been included as part of all Comprehensive BRAC*Analysis* tests since August 12, 2002.

2 This column does not include the 5 large rearrangements that are also detected with the LRP.

3 This group includes Ashkenazi Jewish patients receiving Comprehensive BRAC*Analysis* + BART, either as their original test, or as a reflex to Multisite 3 testing for the 3 founder mutations prevalent in patients of this ancestry.

4 This group contains everyone who received Comprehensive BRAC*Analysis* + BART, including those patients for whom no ancestry or multiple ancestries were listed. Therefore, the number of patients in this category (25,535) is greater than the sum of all of the patients included in the individual ancestries (17,558).

FAQs for BART™ Prevalence Table

These numbers are based on patients who met Myriad's high risk criteria and who have had BART included as part of Comprehensive BRAC*Analysis*®. What are the numbers for patients who have other clinical histories, and for whom BART was ordered separately?

It is more challenging to draw conclusions from patients for whom BART was ordered as an elective test because there are a wide range of factors that can influence a provider's decision to order BART as a billed test. Therefore, it is difficult to establish the overall pattern of mutations in the population of patients for whom BART was ordered separately from Comprehensive BRAC*Analysis*. Fewer patients from the lower risk category are positive on BART testing. Of all of the mutations that are found in lower risk patients, it does appear that a smaller percentage are detected with either the LRP or BART. We are currently examining different possible explanations for this difference, but it is likely that it is at least partially due to the observation that the majority of large rearrangements are in *BRCA1* (approximately 87%). Since the cancer risks associated with *BRCA1* mutations are higher than those associated with *BRCA2*, there are more *BRCA1* mutations in patients with high risk clinical histories overall, and this is reflected in the higher proportion of mutations that are large rearrangements in *BRCA1*.

These data seem to indicate a very high prevalence of large rearrangements detected with BART in patients of two ancestries, Latin American/Caribbean and Near/Middle Eastern.

The high percentage of large rearrangements as a proportion of all mutations detected in patients of Latin American/Caribbean descent is statistically significant. The apparently high percentage of large rearrangements among patients of Near/Middle Eastern descent does not meet statistical significance due to the relatively small number of observations. Providers should factor this into their clinical decision when deciding the appropriate test to order.

The previously described *BRCA1* mutation del exons 9-12 (Weitzel et al., 2007, *Cancer Epidemiol Biomarkers Prev* 16, 1615-20) made up one third of the large rearrangements detected in patients of Latin American/Caribbean descent.

What is the chance that a mutation will be found if BART is now ordered for a patient who did not meet the criteria to have the BART test included as part of their Comprehensive BRAC*Analysis*?

According to the most recent data from our entire clinical testing population, 92.5% of all mutations in *BRCA1* and *BRCA2* are detected with Comprehensive BRAC*Analysis* (full sequencing of both genes and a screen for 5 specific large rearrangements in *BRCA1*), and the remaining 7.5% of mutations are detected with BART. Therefore, the chance of finding something with BART is a small fraction of the chance of finding something with the standard testing. Overall, less than 1% of all BART tests ordered on patients who have already had negative results on Comprehensive BRAC*Analysis* are positive for a deleterious mutation.

One important consideration that has emerged from this most recent data is the significance of considering the ancestry of the patient, particularly for patients of Latin American/Caribbean ancestry. In this group, only 80% of all *BRCA1/2* mutations were found with the standard testing and 20% of all mutations were found with BART. Since a higher percentage of mutations in this group are of the type that are detected only with BART, these patients are more likely to be positive if BART is ordered. This recent data also shows a similar finding for patients of Near/Middle Eastern descent, but the numbers in this group are so small that we can't be sure if this is reliable information. Earlier findings of an increased frequency of large rearrangements in patients of African descent, based on data presented at the 2007 meeting of the American Society of Human Genetics, are not supported by this more recent analysis on a much larger group of patients.

Can I order BART only for patients who have had Comprehensive BRAC*Analysis* in the past?

Yes. BART is available as a reflex test at the time of Comprehensive BRAC*Analysis* testing or can be ordered as a standalone test for patients who have had comprehensive BRAC*Analysis* only in the past. Insurance coverage of this test may vary based on payor policy.