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SureSelect™ Hybridization

- Genomic DNA isolated using automated system (Roche MagNpure)
- DNA uniformly sheared to ~250 bp using Covaris instrument
- Fragmented gDNA ligated with bar codes and adaptors
- Samples pooled to batch sizes (currently 24 or 48)
- Bait are 120-mer biotinylated RNA molecules
- Fragmented, pooled, barcoded DNA is hybridized overnight with Bait: Each exon has >= 3 baits
- Bait/DNA hybrids captured on Streptavidin magnetic beads and washed

Bilateral Mastectomy BRCA Positive Women Reduces Breast Cancer Risk Substantially

- Prospective EMBRACE Trial¹
- 570 healthy female mutation carriers were studied including 405 BRCA1 and 165 BRCA2 women from an Institutional Family Cancer Clinic database
- 156 BRCA1 and 56 BRCA2 mutation carriers underwent Bilateral Risk Reducing Mastectomy (RRM)
- During 2037 person-years of observation, 57 cases of breast cancer occurred in the surveillance group versus NO cases in the BRRM group
- Conclusion
- BRRM reduces the breast cancer risk substantially for healthy BRCA1 and 2 mutation carriers

¹Hemminki BA et al. Substantial breast cancer risk reduction and potential survival benefit after bilateral mastectomy when compared with surveillance in healthy BRCA1 and BRCA2 mutation carriers: a prospective analysis. Ann Oncol 2013, April 10 (Epub ahead of print).

Table 2. Results and Interpretations of BRCA Analysis Genetic Tests^{1,2}

Result	Interpretation
Positive for a mutation	Mutation identified for clinically relevant, should inform management decisions regarding surveillance
Genetic variant	Variant of uncertain significance
Segment	Mutation likely, but not proven to be deleterious
Frame	Mutation will likely not impact breast cancer risk to any extent
Polymorphism	Mutation not associated breast cancer risk
Significance	Mutation or variant not deleterious to individual
Specificity	Mutation or variant not deleterious to individual
Variant/Polymorphism not identified	Region not tested or mutation not identified to any extent
Not identified	Pathogenic BRCA variant not found, but does not guarantee an absence of breast cancer risk to any extent

NICE Guidelines

- A family member with a known BRCA mutation
- Personal history of breast cancer (BRCA)
- Age 40 years old at time of diagnosis (BR)
- 2 relatives with 1 diagnosed BRCA gene
- Age 40 years old + 1 relative with breast cancer or prior family history
- Age 40 years old + 1 close relative breast cancer
- Any age + any family member diagnosed at 40 years old
- Any age + 2 or more family members breast cancer at any age
- Any age + breast cancer family history with pathogenic variant carrier
- Any age + 2 or more relatives with ovarian cancer
- Any age + family history suggestive with breast cancer
- Any age + high risk ethnicity (Ashkenazi Jewish) can be considered

Consider annually for women: 50 ~ 59 years. Felize annually to women: 40 ~ 59 years old at high risk for breast cancer but with a 30% or less chance of being a BRCA or TP53 carrier. Family breast cancer: Classification, care, and management of breast cancer and related risks in people with a family history of breast cancer CG164. Not assuming the same FH side, there is no significant difference in the rate of development of breast cancer between the PR and SR groups from 40 to 49 (P^a = "0.431). When interpreted as requiring an FH on the same side, empirical criteria do not detect this difference. It is recognized that the moderately higher risk of breast cancer observed in some families may be due to a multifactorial and polygenic risk model. The patients were being narrowed by the nice criteria, identifying patients who subsequently developed breast cancer. The UK National Institute for Health and Care (NICE) provides guidance for the classification and management of people with a FH of breast cancer (CG164) [3]. Kuchenbaecker KB, McGuffOG L, Barrowdale D, et al. The BRCA test result was also considered for appropriate risk categorization. Patients are stratified into population risk (PR, 10-year risk 8%). DOI: A 10.1038 / SJ.BJC.6602175. Future routine clinical practice is likely to require the analysis of genetic variants contributing to polygenic risk in order to achieve better performance of risk estimation models. It would seem beneficial to refine risk stratification methods to focus resources on women who will benefit most from early assessment. We would like to recognize the recently retired Simon Ojston, statisticians at the Department of Science of the Population, the University of Dundee. The authors state that they declare that they have no conflict of interest. PUBLIBLE'S NOTE: Springer's nature remains neutral with respect to jurisdictional claims on published institutional and institutional maps Milne RL, Burwinkel B, Michailidou K, et al. The frequency and percentage of 10 at absolute risk are shown in Table 2, or other ovarian cancer at any age, or three first-degree or RDS, diagnosed with breast cancer at an average age of more than 60 years. In the smallest place of the following female breast cancers only in the family: Two first-degree or SDRS diagnosed with breast cancer at an average age of 50 years (at least one must be a FDR.). Assuming the same FH side, a similar pattern³ absolute risk is observed, with no group reaching the detection threshold³ suggested by Nice.Table "3 shows KMSA results. There is evidence that other approaches such as Boadicea may be effective in risk stratification³ [7], although there is no direct published comparison³ the pleasing empAic criteria. This study has used a simple methodology to evaluate current classical practice in the cancer gene of the United Kingdom. There was a significant difference between the ages of 40 and 49 years between women PR and HR (p^{*} = "0.036), but not in the exclusion³ of BRCA mutation³ (P^a ° = "0.136). The impact of a panel of 18 SNPs on the risk of breast cancer in women attending a single screening class³ a family member in the UK: a case control study. Using only one side FH, there were 554 (39.3%) PR, 490 (34.8%) MR, and 365 (25.9%) Female human resources. Thirty women developed invasive cancer before May 2016. Not assuming the same side, the MR/HR Group (excluding BRCA carriers) had a significantly higher breast cancer rate of 50 to 59 aAaos (P^{**} = "0.049). The boadicea model of gene susceptibility to breast and ovarian cancer. 30 à 49 aAaos with a known BRCA1 or BRCA2 mutation³ Mastectomydo reductor not offered. It should be considered as a strategy option³ of risks with all women at high risk. Women who consider that this should have a etaredoM597.0111.0599.0812.0185.0381.0823.0472.0hgih & etaredoM131.0171.0713.0 720.0 541.0631.0580.0 910.0 Jdedulcxe sreirrac ACRB(hgih & noitalupoP360.0 240.0 823.0 500.0 941.0 630.0 190.0 300.0 hgih & noitalupoP11.0197.0382.0431.0 730.0 134.0143.0 840.0 etaredom & noitalupoPraey 95AAAc05sraey 94AAAc04sraey 93

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