Accuracy of the BRCAPro Risk Assessment Model in Males Presenting to MD Anderson for BRCA Testing

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Hereditary Breast and Ovarian Cancer (HBOC) syndrome is due to mutations in *BRCA1* and *BRCA2* genes. Women with HBOC have high risks to develop breast and ovarian cancers. Males with HBOC are commonly overlooked because male breast cancer is rare and other male cancer risks such as prostate and pancreatic cancers are relatively low. *BRCA* genetic testing is indicated for men as it is currently estimated that 4-40% of male breast cancers result from a *BRCA1* or *BRCA2* mutation (Ottini, 2010) and management recommendations can be made based on genetic test results. Risk assessment models are available to provide the individualized likelihood to have a *BRCA* mutation. Only one study has been conducted to date to evaluate the accuracy of BRCAPro in males and was based on a cohort of Italian males and utilized an older version of BRCAPro.

The objective of this study is to determine if BRCAPro5.1 is a valid risk assessment model for males who present to MD Anderson Cancer Center for *BRCA* genetic testing. BRCAPro has been previously validated for determining the probability of carrying a *BRCA* mutation, however has not been further examined particularly in males.

The total cohort consisted of 152 males who had undergone *BRCA* genetic testing. The cohort was stratified by indication for genetic counseling. Indications included having a known familial *BRCA* mutation, having a personal diagnosis of a *BRCA*-related cancer, or having a family history suggestive of HBOC. Overall there were 22 (14.47%) *BRCA1*+ males and 25 (16.45%) *BRCA2*+ males. Receiver operating characteristic curves were constructed for the cohort overall, for each particular indication, as well as for each cancer subtype. Our findings revealed that the BRCAPro5.1 model had perfect discriminating ability at a threshold of 56.2 for males with breast cancer, however only 2 (4.35%) of 46 were found to have *BRCA2* mutations.

These results are significantly lower than the high approximation (40%) reported in previous literature. BRCAPro does perform well in certain situations for men. Future investigation of male breast cancer and men at risk for *BRCA* mutations is necessary to provide a more accurate risk assessment.

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