

Screening for common BRCA1/BRCA2 pathogenic variants using in-house SNaPshot panel

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Introduction

To date, the most important and best characterized genetic risk factors for breast and ovarian cancer are germline pathogenic variants (PV) in the *BRCA1* and *BRCA2* genes. The prevalence of *BRCA1/BRCA2* PV carriers in the general population is approximately 0.2%, but this may vary considerably by variant, between countries or between some ethnic groups due to the founder effect¹. Testing for population specific founder PVs could be reasonable in countries where full *BRCA1* and *BRCA2* gene sequencing and copy number variant detection is not reimbursed by country. Here we are sharing our experience in long term screening for Latvian frequent founder PVs of *BRCA1* and *BRCA2* by our own laboratory developed test.

Aims and Objectives

Develop a good test for the current economic situation in Latvian healthcare that will be able to detect the largest number of frequent pathogenic variants in the population.

Materials and Methods

SNaPshot, Sanger sequencing, statistical analysis.

Results

The SNaPshot (minisequencing) panel was developed for the detection of founder *BRCA1* and *BRCA2* pathogenic variants (PVs) specific to the Latvian population according to published data for 2016^{2,3}. The panel included 11 PVs – Latvian founder PV, common population PV. Recently (in 2024) the panel was changed – one PV was removed and 10 PVs were added due to the availability of new data of *BRCA1* and *BRCA2* PVs⁴. Currently 4407 women and 79 men have been tested using both tests (old and new). Overall, 8.87% of women tested positive for one of the pathogenic variants.

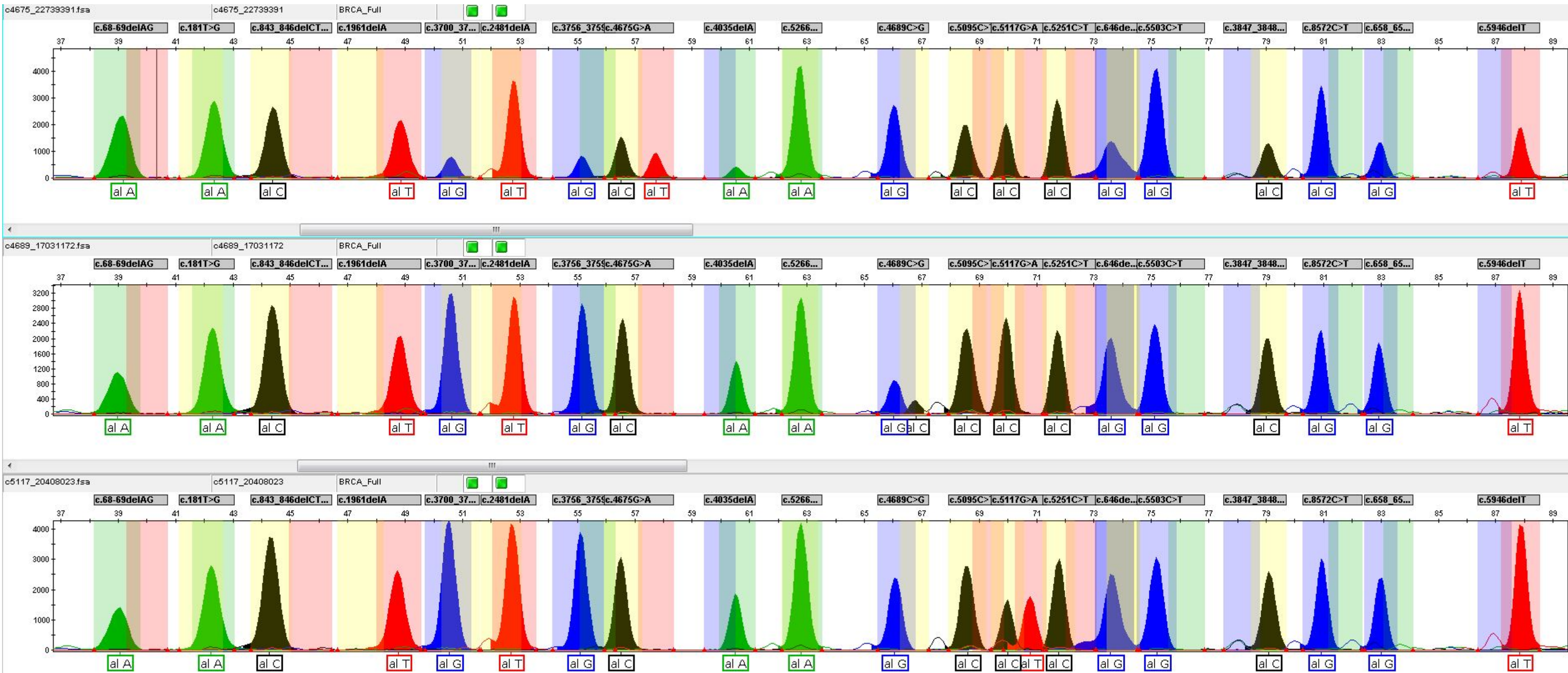


Figure 1. Typical view of SNaPshot results using GeneScan analysis software. Samples positive for different pathogenic variants are shown.

Discussion

The *BRCA1* and *BRCA2* PV positive rate in breast and ovarian cancer varies between studies using new generation sequencing (NGS) panels, depending on cohort selection, and is typically in the range of 9–12%. Our developed targeted PV test positive variant rate of 8.87% is an excellent result comparing to studies performed using the NGS method. Positive PV and breast or/and ovarian cancer diagnoses for female patients are represented in Figure 2. The most prevalent PVs in patients tested are *BRCA1 c.5266dup c.4035del*, which is in agreement with other studies^{2,4}. Surprisingly *BRCA2 c658_c659del* was the 3rd most frequent PV in our samples. Data were analyzed on unique patients – excluding repeated tests. As we are the biggest private clinical laboratory in Latvia, we can conclude that our data is representative of the frequency of *BRCA1/BRCA2* PVs in Latvia.

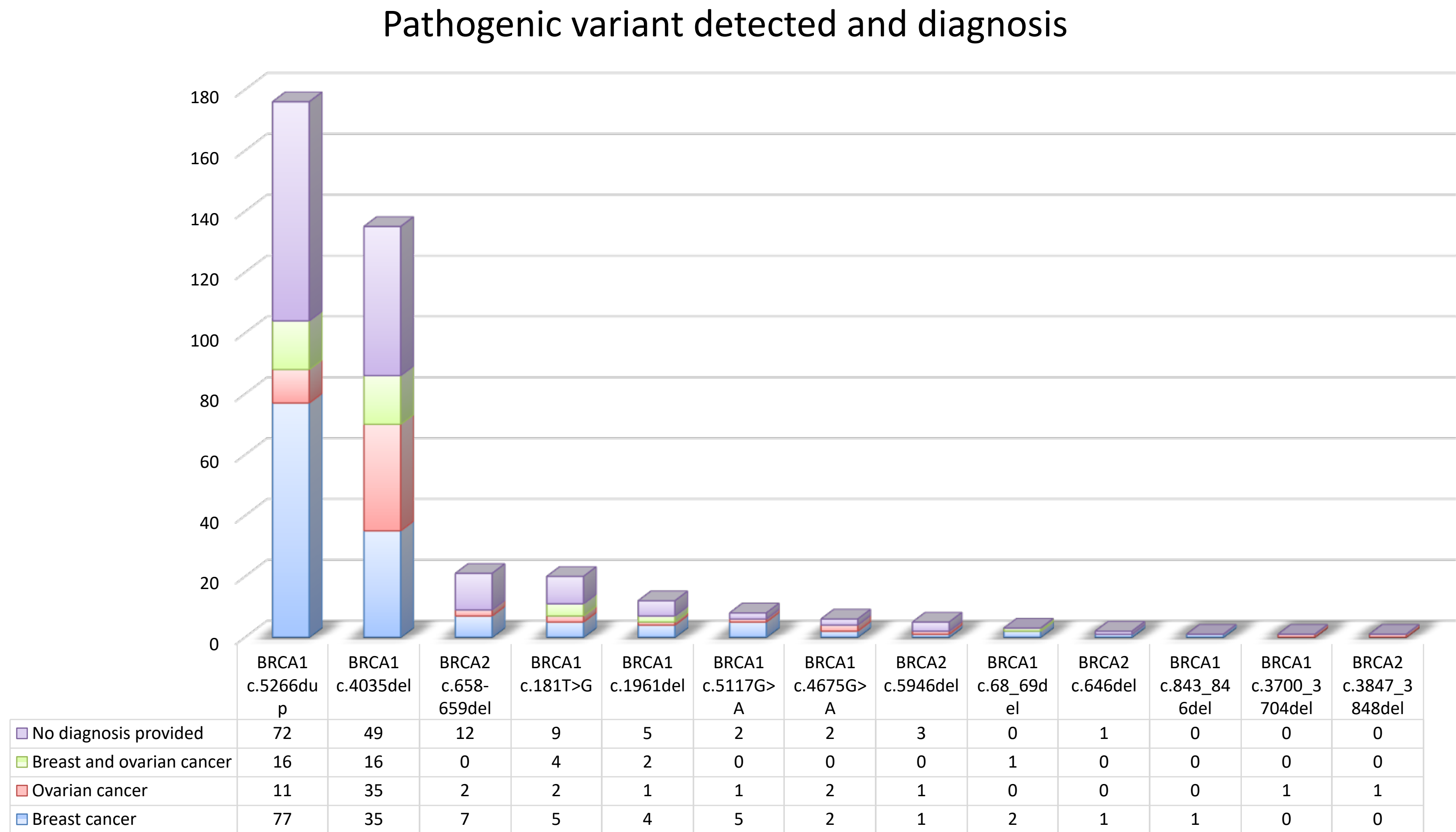


Figure 2. Pathogenic variants detected in female patients and diagnoses. Some patients are diagnosed with both breast and ovarian cancer.

Conclusion

Given the economic situation of our healthcare, an appropriate test has been developed that can give results relatively quickly and at low cost. The methodology allows for modifications – reducing or expanding the number of variants to be tested, and confirming suspicious results with Sanger sequencing. A positive PV rate of 8.87% is an excellent result for a targeted non NGS panel.

References

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