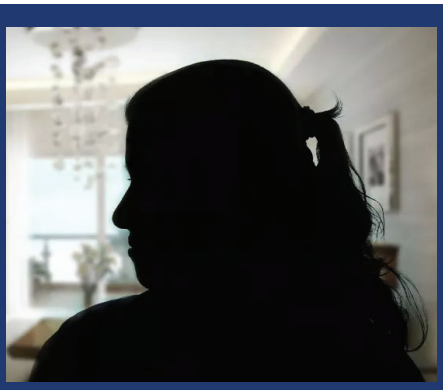
Early Genetic Diagnosis Safeguards Family from Ovarian and Breast Cancer



Gender: Female

Age: 60 years

Location: Pune, Maharashtra

Diagnosis: Ovarian Cancer

Strand Test: Germline

Conclusion:

Eligibility for PARP inhibitor therapy established

Identification of other family members at risk

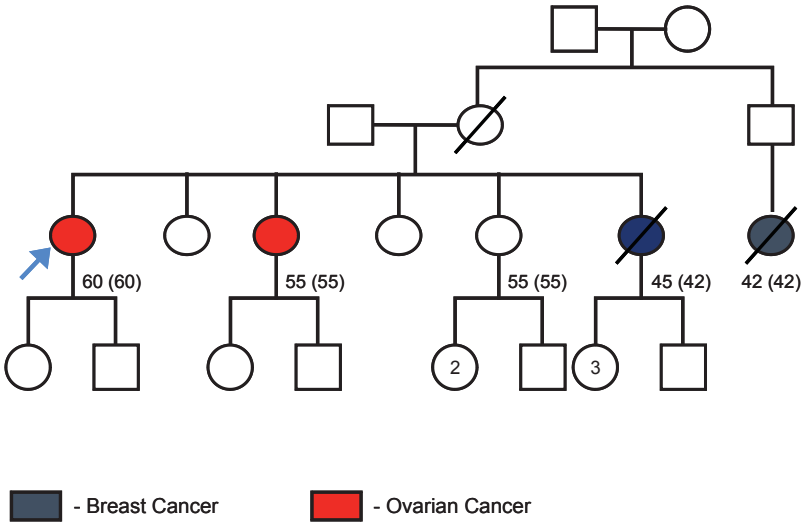
Patient Profile

Sunita*, a 60-year-old woman from Pune, was referred to a renowned oncology clinic in Pune in 2016.
She showed symptoms of ovarian cancer that were confirmed during the initial diagnosis stage. She was referred to a genetic counselor. A detailed conversation and risk profile analysis found that she has a family history of cancer.

A deeper analysis of the family history lead to the following disclosures:

- Younger sister aged 55 years was diagnosed with ovarian cancer.
- Another younger sister had been diagnosed with breast cancer at the age of 42 and had succumbed to the disease at the age of 45 years.
- A maternal side cousin sister had also lost her life to breast cancer at the age of 42 years.

Family Tree – Pre-test Genetic Counselling



A risk assessment conducted by a Strand Genetic Counselor using BRCAPRO software suggested that there was a 64.53% probability of finding a hereditary *BRCA1* or *BRCA2* mutation in this family.

*Name changed to protect patient privacy

Genetic Testing

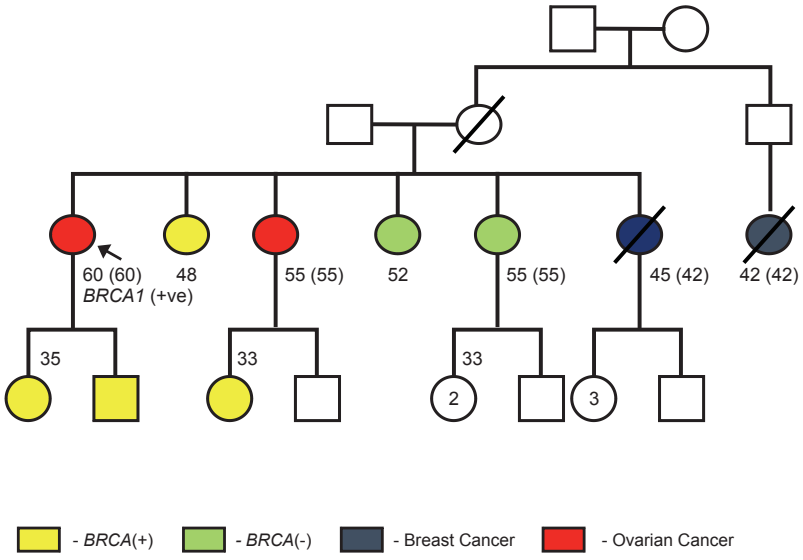
Sunita's DNA was examined using the Strand Germline Cancer Panel. She was found to be positive for a heterozygous pathogenic variant, which was detected in exon 2 of the *BRCA1* gene.

RESULT Positive for a heterozygous '**pathogenic**' variant, which was detected in exon 2 of the *BRCA1* gene.

Key Findings

Gene	Variation	Zygosity	Clinical significance
BRCA1	chr17:41276045_41276046delCT c.68_69delAg p.Glu23ValfsTer17	Heterozygous	Pathogenic

In addition to Sunita, mutation specific tests were conducted on tissue samples provided by 6 other family members. Four of these individuals were found to be carriers of the same *BRCA1* mutation, whereas two tested negative for this mutation.



Family Tree – Post-test Genetic Counselling

Strand Germline Test reports from Sunita's relatives indicated the following:

- Younger sister aged 48 years was a carrier of the *BRCA1* mutation.
- Two other younger sisters aged 52 and 55, respectively, were negative for the *BRCA1* mutation.
- Her son, daughter, and affected sister's daughter were found to be heterozygous for the same mutation.

Treatment Recommendations

Sunita was not eligible for treatment with PARP inhibitors prior to the genetic test. However, since her ovarian cancer has recurred, and her status as a *BRCA1* heterozygous carrier has been confirmed, she is now eligible to receive PARP inhibitor therapy[1–3].

Conclusion

- Two of the proband's sisters have been found to be negative for this mutation. Hence, the risk of breast and ovarian cancer for their children has been estimated to be considerably lower than that for other family members.
- Sunita's son, daughter, niece, and another sister have been advised of their risk for hereditary breast and ovarian cancer and can now take appropriate preventive measures.

References

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3. *Crafton, S. M., Bixel, K. & Hays, J. L. PARP inhibition and gynecologic malignancies: A review of current literature and on-going trials. Gynecol. Oncol. 142, 588–596 (2016).*
4. *Oza, A. M. et al. Olaparib combined with chemotherapy for recurrent platinum-sensitive ovarian cancer: a randomised phase 2 trial. Lancet Oncol. 16, 87–97 (2015).*
5. *Mirza, M. R. et al. Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. N. Engl. J. Med. 375, 2154–2164 (2016).*

Strand Germline Panel

The Strand Germline Cancer Test is designed to identify genes that are involved in several inherited cancers. The following genes are analyzed in samples from breast and ovarian cancer patients, as per international genetic testing guidelines.

ATM, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, NBN, PALB2, PTEN, RAD51C, RAD51D, TP53

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