Kathmandu, Bir Hospital visit,
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Pathology North

BRCA2 mosaicism as a cause of young onset breast cancer

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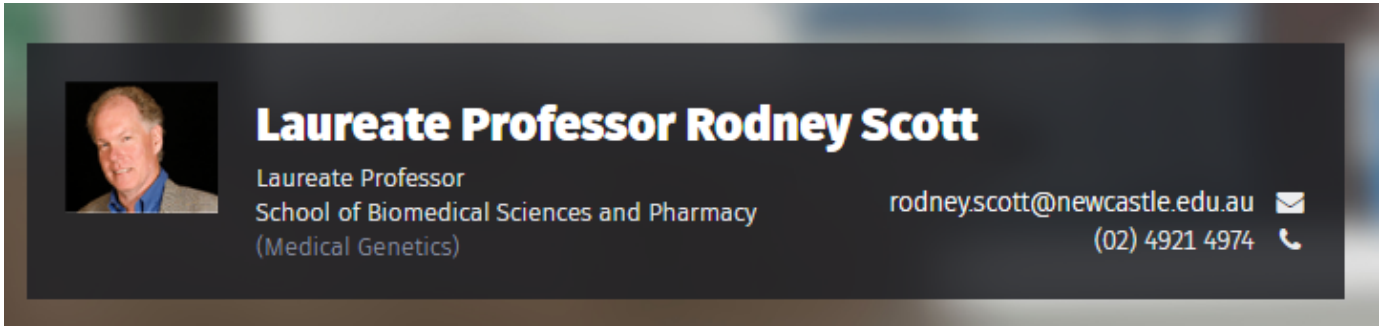


Mosaicisim is recognized as a cause of de novo disease in several cancer syndromes such as FAP, LFS and VHL

De Novo mutations in BRCA2 are extremely uncommon

BRCA1 mosaicism has previously been reported as a cause of young onset breast cancer but not BRCA2[1]

While difficult to identify using traditional Sanger Sequencing, mosaicism is readily identified with the better dynamic range of NGS

MG is a 29 year old previously well nulliparous woman

Diagnosed with a 16mm invasive ductal breast cancer, ER positive, PR positive, Her2 negative.

Underwent wide local excision and sentinel node biopsy

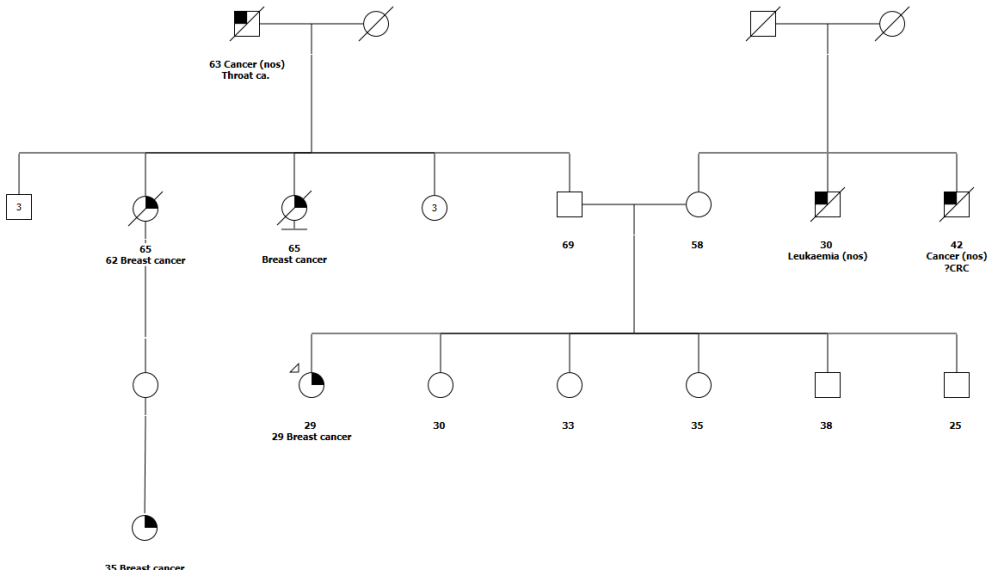
Had egg harvesting and freezing of embryos

Completed 6 cycles of chemotherapy.

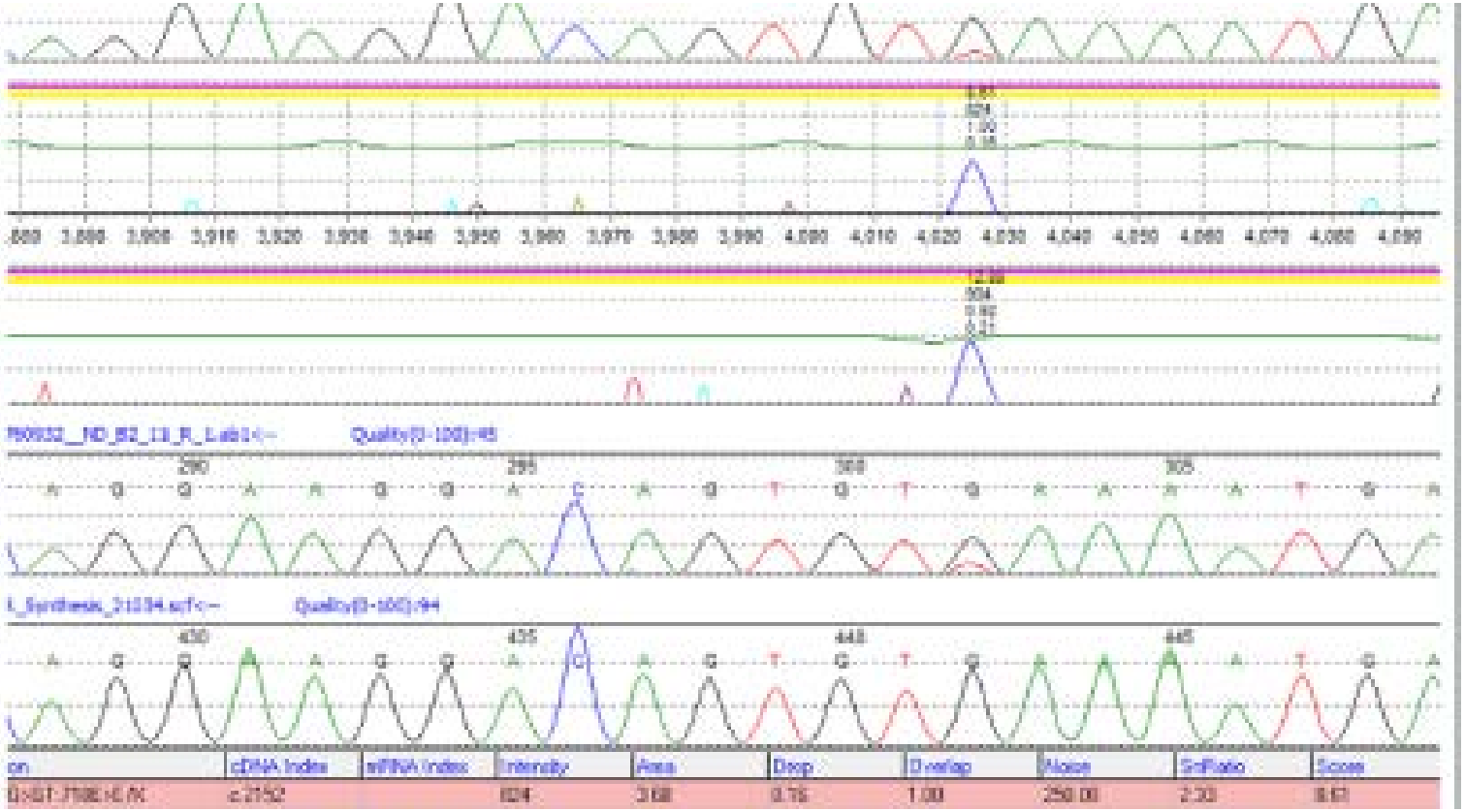
Initially undecided but proceeded with bilateral mastectomies

No evidence of in-situ or further invasive malignancy in either breast

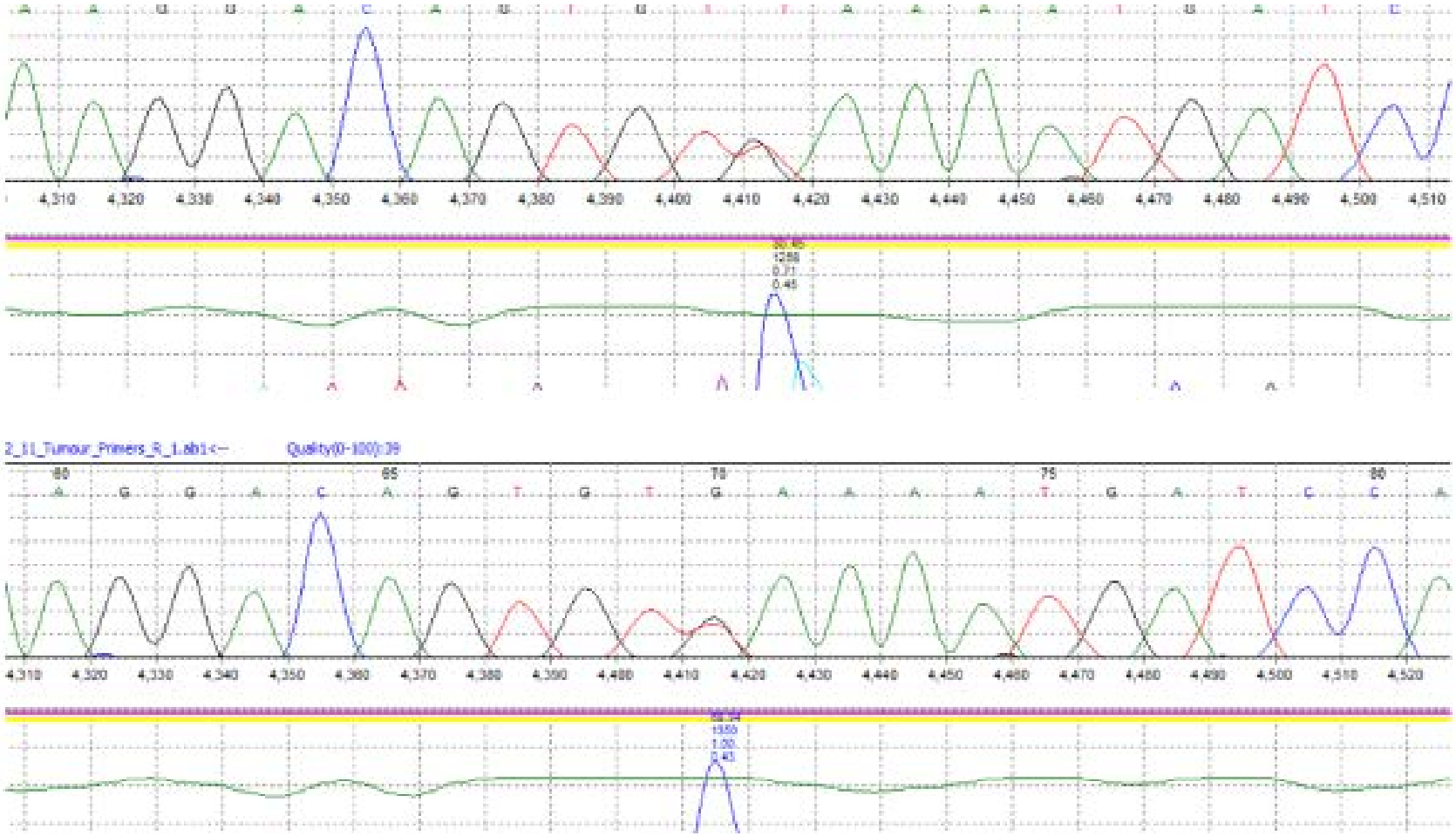
3 healthy sisters aged 30,33 and 35
Parents aged 58 and 69 with no history of cancer
No maternal history of relevant cancers
2 paternal aunts diagnosed with breast cancer at 65 and 62 and second cousin at 35



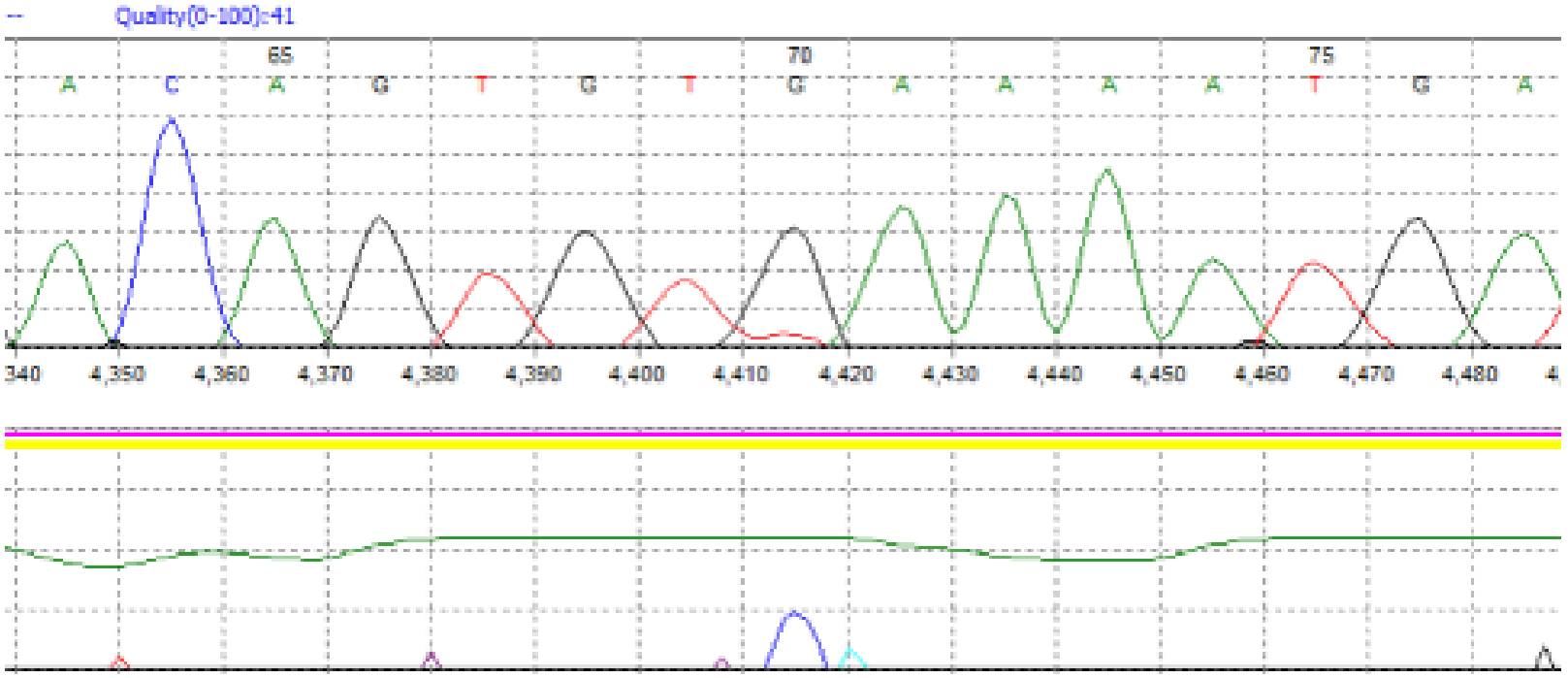
Leucocyte DNA (confirmation analysis performed using Sanger Sequencing)



Tumour DNA

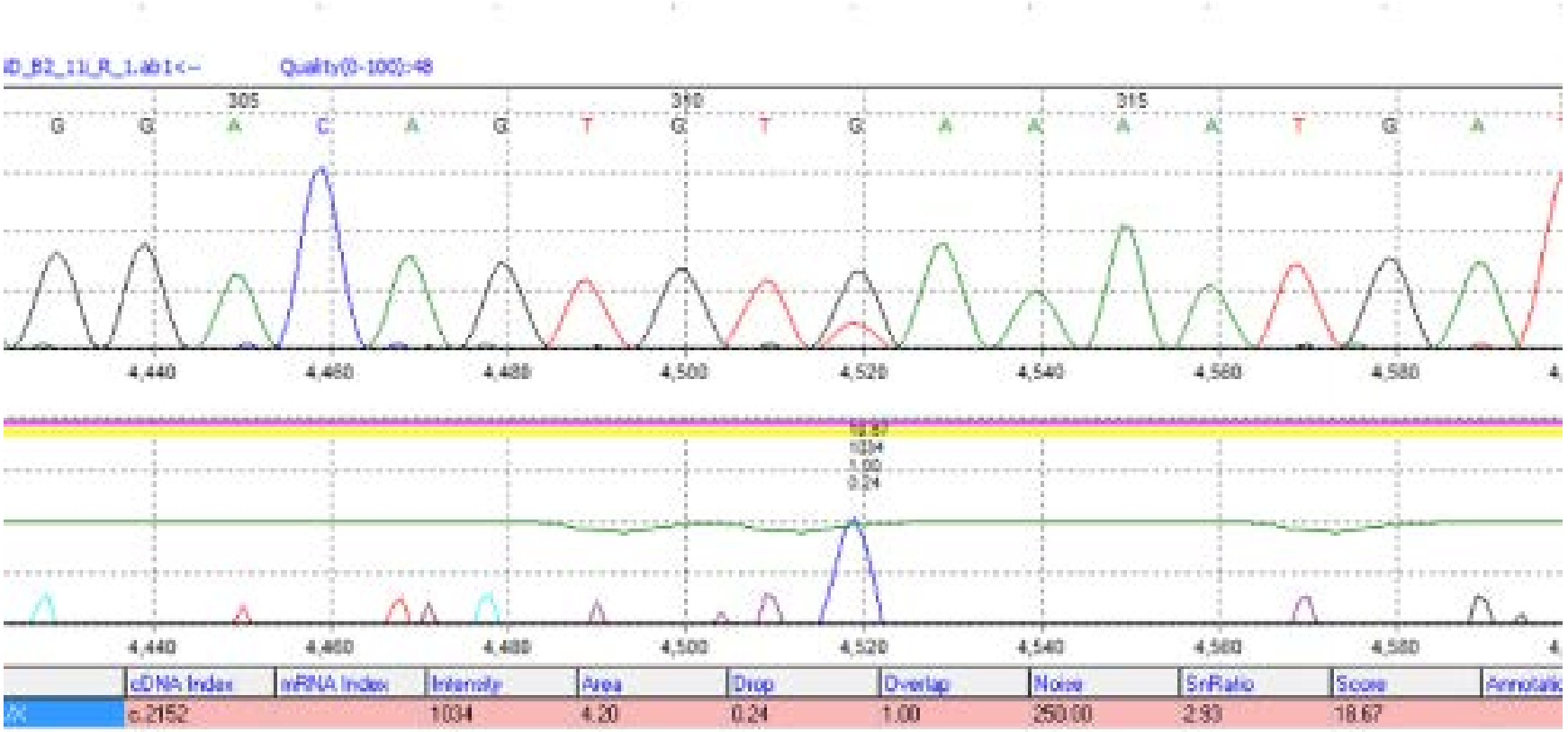


Normal adjacent breast tissue



breast adjacent to tumour

Contralateral breast DNA

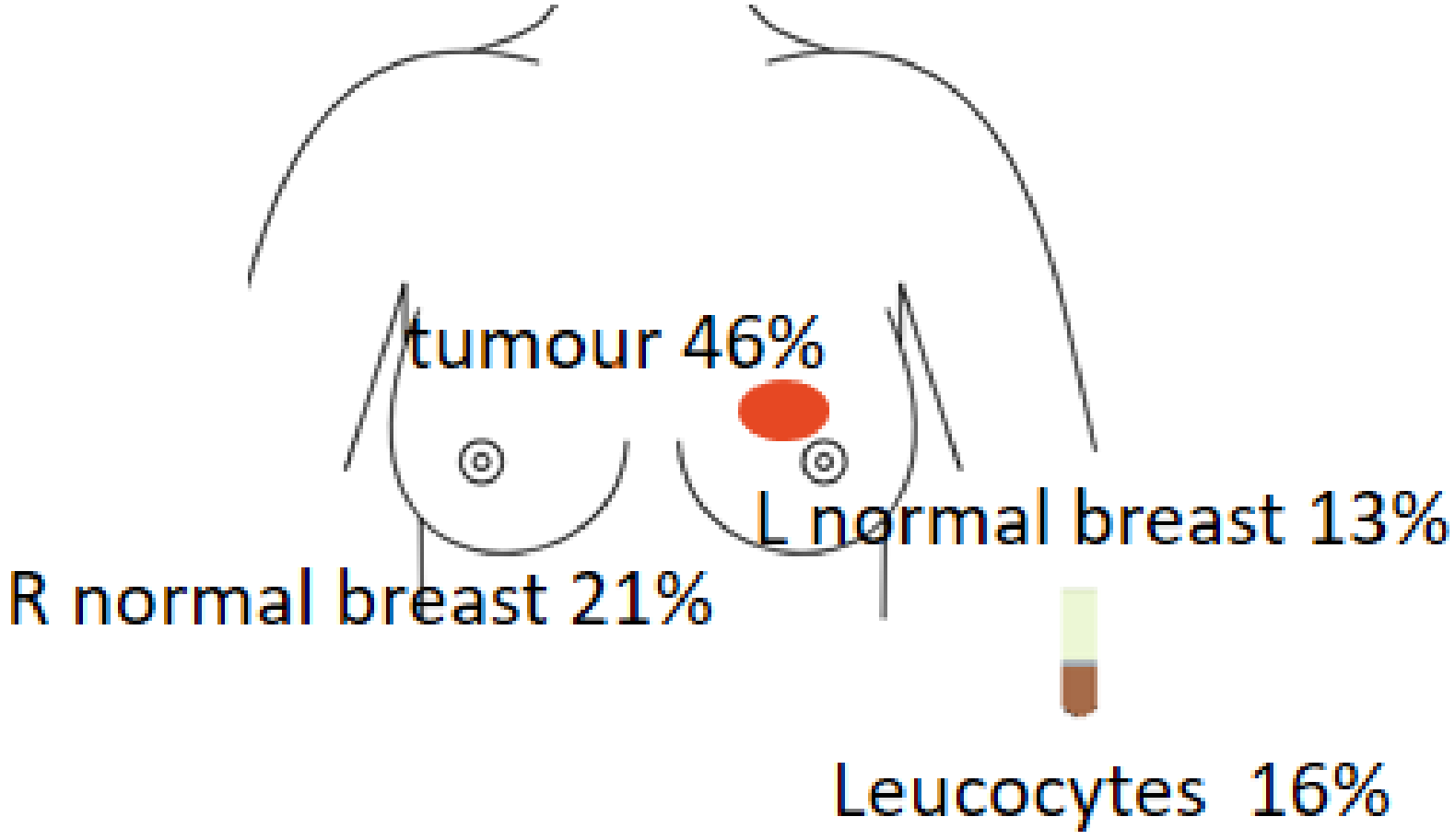


iteral breast 21%

- NGS for BRCA1, BRCA2, TP53,PALB2, PTEN

- BRCA2 c.2152G>T; p.(Glu718*) identified in:-
- 16% reads of leucocyte DNA
- 46% reads of breast cancer
- 13% reads of normal breast tissue adjacent to cancer
- 21% reads of normal contralateral breast

- As expected, the mutation was **not** identified in leucocyte DNA from either parent


tumour 46%
L normal breast 13%
R normal breast 21%
Leucocytes 16%

Risk of contralateral cancer if she had not had bilateral mastectomies

Risk for offspring: it is impossible to know if the mutation occurred before or after differentiation of founding germ line cells.
Risk ranges from 0-50% [2].

Risk of ovarian cancer: is pre-menopausal risk reducing surgery justified, given that HRT is contraindicated after a diagnosis of breast cancer.