



National Accreditation Program for Breast Centers  
American College of Surgeons

# Incorporating Genetics and Genomics into Practice: Breast Cancer

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ACS Cancer Program Meeting

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Chair, NAPBC





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## Genomic and Genetic Testing for Breast Cancer

- Newly diagnosed breast cancer patients
  - Impact adjuvant therapy decisions
  - Impact surgical recommendations
- 7 genomic tests
- Multigene panel genetic testing-12 pathogenic variants





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| <b>Genomic Tests<br/>Invasive disease</b> | <b>Number of<br/>genes</b> | <b>Indication</b>                                                               | <b>Info given</b>                                                |
|-------------------------------------------|----------------------------|---------------------------------------------------------------------------------|------------------------------------------------------------------|
| OncotypeDx                                | 21                         | N1(1-3nodes) and N0 ER+ breast cancer                                           | Overall recurrence risk, benefit from adjuvant chemotherapy      |
| Mammaprint                                | 70                         | N1(1-3nodes) and N0 ER+/- breast cancer                                         | Overall recurrence risk, benefit from adjuvant chemotherapy      |
| Prosigna                                  | 50                         | N1(1-3nodes) and N0 breast cancer, postmenopausal                               | Need for adjuvant chemotherapy                                   |
| EndoPredict                               | 12                         | N1(1-3nodes) and N0 breast cancer                                               | Predict distant disease at 10yrs, need for adjuvant chemotherapy |
| Breast Cancer Index                       | 11                         | ER + early stage breast cancer, N0 and N1(1-3nodes), on hormone therapy 4-5 yrs | Benefit of extended adjuvant endocrine therapy                   |



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| Genomic Tests<br>DCIS            | Number of<br>genes                 | Indication        | Info given                                                                                                     |
|----------------------------------|------------------------------------|-------------------|----------------------------------------------------------------------------------------------------------------|
| PreludeDx                        | 7 biomarkers<br>4 clinical factors | ER+ DCIS patients | DCIS recurrence risk at<br>10yrs-invasive and<br>noninvasive disease<br>Need for adjuvant<br>radiation therapy |
| Oncotype Dx Breast<br>DCIS Score | 12                                 | ER + DCIS         | DCIS recurrence or<br>invasive cancer<br>recurrence risk at 10<br>yrs                                          |





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## Cases:

64yo woman

2.8cm, node negative

ERpos/PRpos/Her2neu neg

Oncotype score → 22

48yo woman

2.8cm, node negative

ERpos/PRpos/Her2neu neg

Oncotype score → 22





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| Patient scenario                                         | Oncotype score for chemotherapy                     |
|----------------------------------------------------------|-----------------------------------------------------|
| Postmenopausal women N0<br>Postmenopausal N1 (1-3 nodes) | $\geq 26$                                           |
| Premenopausal women N0                                   | 16-25 Maybe chemo/Ovarian suppression<br>$\geq 26$  |
| Premenopausal women N1 (1-3 nodes)                       | $< 26$ Maybe chemo/Ovarian suppression<br>$\geq 26$ |



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## Cases:

64yo woman (postmenopausal)

2.8cm, node negative

ERpos/PRpos/Her2neu neg

Oncotype score → 22 → No chemotherapy rec'd

48yo woman (premenopausal)

2.8cm, node negative

ERpos/PRpos/Her2neu neg

Oncotype score → 22 → Consider chemotherapy





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## Case:

38yo woman

2.0cm, node negative

ERpos/PRpos/Her2neu neg

Genetic testing shows a BRCA 1 pathogenic variant





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## High Penetrance Breast Pathogenic Variants

|       | Adjuvant treatments?    | Consider bilateral mastectomy? | Consider prophylactic oophorectomy? |
|-------|-------------------------|--------------------------------|-------------------------------------|
| BRCA1 | PARP inhibitor          | Yes                            | Yes                                 |
| BRCA2 | PARP inhibitor          | Yes                            | Yes                                 |
| PALB2 | None                    | Maybe                          | Yes                                 |
| TP53  | Avoid radiation therapy | Yes                            | No                                  |





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## Low-Moderate Penetrance Breast Pathogenic Variants

|           | Adjuvant treatments? | Consider bilateral mastectomy? | Consider prophylactic oophorectomy? |
|-----------|----------------------|--------------------------------|-------------------------------------|
| ATM       | No                   | Maybe                          | No                                  |
| CHEK2     | No                   | Maybe                          | No                                  |
| BRIP      | No                   | No                             | Yes                                 |
| BARD1     | No                   | No                             | No                                  |
| NF1       | No                   | No                             | No                                  |
| RAD 51C/D | No                   | No                             | Yes                                 |





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## Breast Pathogenic Variants Associated with Syndromes

|                                           | Adjuvant treatments? | Consider bilateral mastectomy? | Consider prophylactic oophorectomy? |
|-------------------------------------------|----------------------|--------------------------------|-------------------------------------|
| STK11<br>Peutz-Jeghers syndrome           | No                   | Yes                            | No                                  |
| PTEN<br>Cowden syndrome                   | No                   | Yes                            | No                                  |
| CDH1<br>Hereditary diffuse gastric cancer | No                   | Yes                            | No                                  |



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## Case:

38yo woman

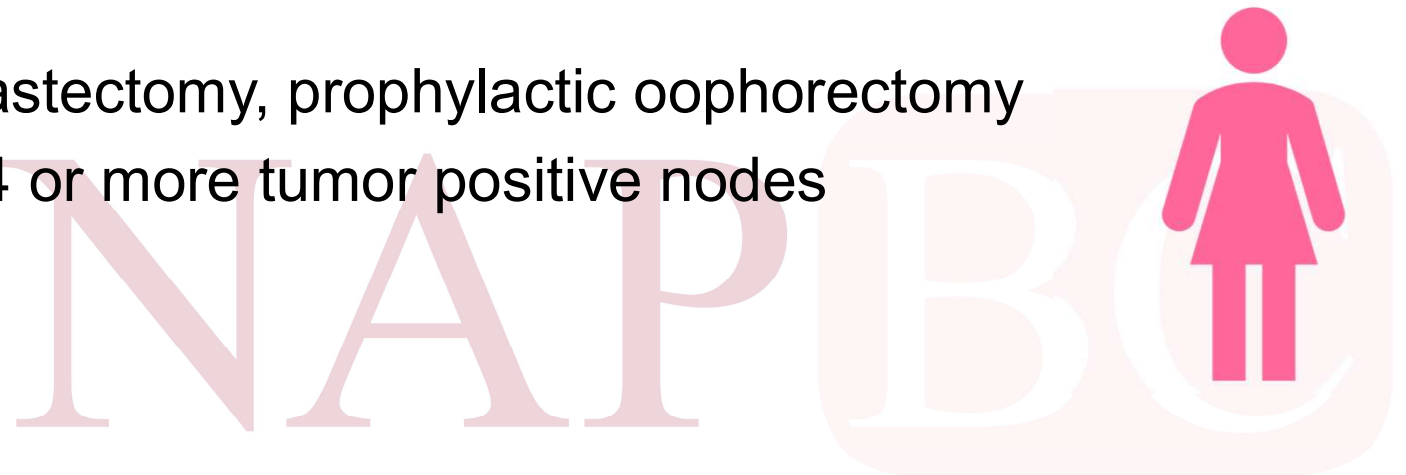
2.0cm, clinically node negative

ERpos/PRpos/Her2neu neg

Genetic testing shows a BRCA 1 pathogenic variant

Rec'd bilateral mastectomy, prophylactic oophorectomy

PARP inhibitor if 4 or more tumor positive nodes



# Cases

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|       | Contralateral breast cancer risk                                                              | Consider bilateral mastectomy? | Any other treatments?                                           |
|-------|-----------------------------------------------------------------------------------------------|--------------------------------|-----------------------------------------------------------------|
| BRCA1 | 30-40% 20 yr cumulative risk<br>Premenopausal women<br>>20% at 15yrs<br>Men: 0.2-1.2% by 70yo | Yes                            | PARP inhibitor-Olaparib<br>Prophylactic oophorectomy at 35-40yo |
| BRCA2 | 25% 20 yr cumulative risk<br>Premenopausal women<br>>20% at 15yrs<br>Men: 2-7% by 70yo        | Yes                            | PARP inhibitor-Olaparib<br>Prophylactic oophorectomy at 40-45yo |
| PALB2 | 5-8% at 10yrs<br>Men: 0.9% by 70yo                                                            | Yes                            | Consider oophorectomy 45-50yo                                   |
| TP53  | 18-49% at 10yrs                                                                               | Yes                            | Li-Fraumeni syndrome surveillance, avoid xrt                    |



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|           | Contralateral breast cancer risk | Consider bilateral mastectomy? | Any other treatments?         |
|-----------|----------------------------------|--------------------------------|-------------------------------|
| ATM       | 4% at 10 yrs                     | Maybe                          |                               |
| CHEK2     | 6-8% at 10yrs                    | Maybe                          |                               |
| BRIP      | ?                                | No                             | Consider oophorectomy         |
| BARD1     | ?                                | No                             |                               |
| RAD 51C/D | <2% at 10 yrs                    | No                             | Rec'd oophorectomy at 45-50yo |

NAP

