

## Medical Breast Training Program

### Session Three: Breast Cancer Risk Assessments and Genetics

**Course Description:** This part of the course will focus on risk assessment, including the basics of hereditary cancer, identifying those with inherited syndromes, and estimating risk in those with family history who do not carry pathogenic variants (or mutations) in highly penetrant or moderately penetrant genes. The polygenic risk score and its potential applications will be introduced. Management guidelines will be reviewed for the identified syndromes depending on risk, supplemented by illustrative and challenging case discussions.

#### Learning Objectives:

- Develop a consistent and comprehensive approach to identification of those at hereditary cancer with knowledge of NCCN guidelines, American Society of Breast Surgeons' guidelines and those of USPSTF.
- Perform risk modeling in those without hereditary predisposition and understand the strengths and limitations of the various risk models (Gail – BCRAT, Tyrer-Cuzick, and BOADICEA/CanRisk)
- Appreciate the role that single nucleotide polymorphisms (SNPs) and the polygenic risk score (PRS) may play in breast cancer risk assessment, sub-stratification of gene carriers, estimation of contralateral risk in the newly diagnosed and identification of lower risk individuals.

30 Minutes	Breast Cancer Risk Factors – Non-modifiable <i>Dawn M. Mussallem, D.O.</i>
	<b>Objectives:</b> <ul style="list-style-type: none"> <li>• Describe how endogenous hormones affect risk – early menarche, late menopause and circulating estrogen levels (and are these all truly non-modifiable?)</li> <li>• Reinforce the importance of taking an extended family history at intake, ideally prior to age 30, and updating it annually recognizing the influences of age at diagnosis of affected members, race, ethnicity and family size in risk assessment. Breast and other breast cancer-related cancers should be assessed.</li> <li>• Explain the influence that breast density has on risk. Is this modifiable?</li> </ul>
30 Minutes	Risk Estimation Tools <i>Ruth Heisey, M.D., Aletta Poll, MSc.</i>
	<b>Objectives:</b> <ul style="list-style-type: none"> <li>• Review models that can be used to identify individuals appropriate for genetic counseling.</li> <li>• Demonstrate use of the most common breast cancer risk models used in clinical practice, the BCRAT and Tyrer-Cuzick models, highlighting limitations with each.</li> <li>• Outline how 5-year, 10-year and lifetime risk estimates can be used in risk management per USPSTF, ASCO, NCCN, and ACR recommendations both for enhanced surveillance and chemoprevention.</li> </ul>
30 Minutes	Genetics 101 - Assessment <i>Holly Pederson, M.D.</i>

	<p>Objectives:</p> <ul style="list-style-type: none"> <li>• Provide a high-level overview of the incidence and function of gene changes predisposing to hereditary cancer syndromes, and carrier identification strategies.</li> <li>• Discuss highly penetrant genes, moderately penetrant genes and SNPs, with suggested general pillars of risk management.</li> <li>• Touch on the differences between germline and somatic tumor testing and implications.</li> </ul>
30 Minutes	<p>Hereditary Breast, Ovarian and Pancreatic Cancer  <i>Allison W. Kurian, M.D., M.Sc.</i></p>
	<p>Objectives:</p> <ul style="list-style-type: none"> <li>• Provide a deeper and more specific approach to understanding tumor suppressor gene function with BRCA1, BRCA2 (and PALB2?) and how PARP inhibitors act selectively on the vulnerability of these cells.</li> <li>• Outline management strategies for highly penetrant genes with specific suggestions for communication of risk and options in an effective but non-directive manner.</li> <li>• Discuss special situations such as the importance of correct interpretation of circulating TP53 variants, management of CDH1 in families without gastric cancer, and RRM following ovarian cancer in BRCA carriers</li> </ul>
30 Minutes	<p>Single Nucleotide Polymorphisms and Polygenic Risk  <i>Holly Pederson, M.D.</i></p>
	<p>Objectives:</p> <ul style="list-style-type: none"> <li>• Describe how single nucleotide polymorphisms (SNPS) were discovered, how polygenic risk scores (PRS) have been validated and potential directions for further validation in non-European populations.</li> <li>• Discuss potential clinical uses for PRS – substratification of risk in both gene carriers and non-gene carriers, estimation of contralateral breast cancer risk in newly diagnosed patients, decision making in high risk patients and identification of low risk patients.</li> <li>• Review validation studies integrating PRS with traditional risk modeling (Tyrer-Cuzick and BOADICEA)</li> </ul>
30 Minutes	<p>Guidelines and Position Statements: Genetics, Counseling and More!  <i>Juliana (Jewel) M. Kling, M.D., M.P.H.</i></p>
	<p>Objectives:</p> <ul style="list-style-type: none"> <li>• Compare and contrast guidelines for when to refer for genetic counseling <ul style="list-style-type: none"> <li>• USPSTF, NCCN and ASBrS</li> </ul> </li> <li>• Discuss criteria consistent with Lynch syndrome with an emphasis on colon or endometrial cancer &lt; age 50</li> <li>• Examine general recommendations for care with different genes associated with an elevated breast cancer risk (e.g. when to offer MRI screening, risk reducing medications, etc...)</li> </ul>
<p><b>Livestream</b>  <b>June 4, 2022</b>  <b>9:00 a.m. –</b>  <b>12:00 p.m. CT</b></p>	<p>Risk Assessment, Genetics, Management of High-Risk Patients Case Discussions (5)  <b>Melinda Wu, M.D.,</b> <i>Holly Pederson, M.D., Juliana (Jewel) M. Kling, M.D., M.P.H., David W. Lim, M.D., Aletta Poll, M.Sc., Sandhya Pruthi, M.D.</i></p>