Managing the Complexities of DCIS Treatment: The Oncotype DX® Breast DCIS Score™ Test
DCIS Treatment Decisions Are Driven By Multiple Considerations

Goals of DCIS therapy are varied
  - Prevention of any LR and particularly an invasive LR is a primary consideration
  - Cosmetic outcomes: mastectomy vs. breast conserving surgery

Multiple factors influence treatment decisions
  - Estimated risk of LR based on clinical and pathological features
  - Estimated risk of invasive LR (approximately 50% of recurrences)
  - Patient preference

Treatments include1:
  - Surgery: Mastectomy vs. BCS
  - Radiation: Partial or Whole Breast
  - Preventive Hormonal Therapy

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LR: local recurrence
BCS: breast-conserving surgery
Better Prognostic Tools Are Needed to Guide Therapy

- Better tools to provide an individualized risk estimate that is based on the underlying tumor biology are needed.
- There is a need for tests that:
  - Provide an individualized estimate of local recurrence risk.
  - Provide confidence that you are making the right treatment recommendation.
  - Identify patients thought to be low risk based on clinical and pathological features but actually have higher-risk disease.

Genomics Can Address This Need

The Oncotype DX® Breast DCIS Score™: A Genomic Risk Stratification Tool
Oncotype DX® Breast DCIS Score™ Result: Gene Selection

- The Breast DCIS Score result is a continuous variable that provides an individualized and quantitative estimate of the chance that the DCIS will return within the next 10 years (prognosis) as DCIS or invasive breast cancer.

7 Breast Cancer-Related Genes

- Ki-67
- STK15
- Survivin
- Cyclin B1
- MYBL2

5 Reference Genes

- Beta-actin
- GAPDH
- RPLPO
- GUS
- TFRC

Proliferation

Hormone Receptor Group

Others

PR

GSTM1

PR: progesterone receptor

Clinical Validation of the Oncotype DX® Breast DCIS Score™: The ECOG E5194 Analysis
ECOG E5194 Validation Study: Prespecified Study Objectives (n=327)

**Primary**
- To determine whether there is a significant association between the Breast DCIS Score™ result and local recurrence risk

**Secondary**
- To determine whether the Breast DCIS Score result provides value beyond standard clinical and pathological factors

ECOG E5194 Validation of the Oncotype DX® Breast DCIS™ Score

- E5194 study validated the Breast DCIS Score™ result as a strong independent predictor of local recurrence (LR) risk
  - Any (DCIS or invasive) LR
  - An invasive LR

- The Breast DCIS Score result quantifies the 10-year risk of LR
  - As a continuous variable or a categorical variable by 3 pre-specified risk groups
Second Validation of the Oncotype DX® Breast DCIS Score™:
The Ontario Provincial DCIS Cohort Analysis
(Breast-Conserving Surgery Alone)
Ontario Cohort: Prespecified Study Objectives (n=571)

**Primary Objective**
- To evaluate if the Breast DCIS Score™ result is associated with the risk of local recurrence (DCIS or invasive) in patients treated with BCS alone with clear margins (no tumor on ink) and no XRT

**Main Secondary Objectives**
- To evaluate if the Breast DCIS Score result is independently associated with local recurrence adjusting for other clinical and pathological factors
- To evaluate if the Breast DCIS Score result is associated separately with the risk of DCIS or invasive local recurrence
Consistent Spectrum of Risk Across Breast DCIS Score™ Validation Studies

ECOG E5194

Ontario Cohort

Breast DCIS Score™ Result Reflects the Underlying Tumor Biology and Can Help Guide Treatment Decisions

• The Breast DCIS Score is:
  – Validated in over 1,500 patients in two studies with consistent results
  – Provides independent prognostic information beyond traditional clinical and pathological factors
  – Able to risk stratify patients regardless of treatment with or without XRT

• Studies confirm the continuous Breast DCIS Score result is significantly associated with risk of:
  - Any Local Recurrence
  - Invasive Local Recurrence
  - DCIS Local Recurrence

Breast DCIS Score™ Result Provides Information Beyond Clinical and Pathological Factors

• Within two validation studies there was a consistent and broad range of Breast DCIS Score results across clinical and pathological features.

• Age, grade, tumor size, comedonecrosis, and DCIS pattern alone cannot predict the Breast DCIS Score result.

Some clinical and pathological factors are prognostic but cannot be used as a surrogate or predictor of the Breast DCIS Score result.

Integrating the Oncotype DX® Breast DCIS Score™ Result with Prognostic Clinical and Pathological Factors:
A Patient-Specific Meta-Analysis
Integrating Genomic, Clinical, and Pathological Information Improves Risk Stratification

- A patient-specific meta-analysis was conducted by combining data from ECOG E5194 and the Ontario DCIS Cohort (BCS alone group only) to provide refined risk estimates of local recurrence after BCS alone (n=773 patients)

- Pre-specified covariates included in the patient-specific meta-analyses were:
  - Breast DCIS Score™ result
  - Age at Diagnosis (<50 years, ≥50 years)
  - Tumor Size (≤1 cm, >1-2.5 cm, >2.5 cm)
  - Year of Diagnosis (before year 2000, year 2000 or later)

BCS: breast-conserving surgery

Rakovitch et al. ASCO 2017.
Patient-specific Meta-analysis
Contribution of Biology and Clinicopathologic Features to Risk of Local Recurrence

- Integrating the Breast DCIS Score™ and clinicopathologic characteristics provides more value versus the clinical characteristics alone ($p<.002$) or the Breast DCIS Score alone ($p<.009$)

- The final model including both tumor biology and clinicopathologic characteristics is a better representation of the risk of local recurrence than a model without one or the other component
More Patients Have Risk Estimates for Local Recurrence Below 10% in Patient-specific Meta-analysis

70% of patients in this clinical subgroup will receive risk estimates below 10%
Oncotype DX® Breast DCIS Score™ Test Can Help to Personalize Each Patient’s Treatment Plan with a Refined Risk Assessment

- Oncotype DX® Breast DCIS Score™ test:
  - Quantifies 10-year risk of any local recurrence or an invasive local recurrence
  - Confirmed in a patient-specific meta-analysis involving 773 patients
  - Refined risk estimates with specified clinicopathologic features
  - Increases clarity and confidence in your patient’s personalized treatment plan

A refined risk assessment reflects tumor biology, tumor size, and patient’s age:

- Patients with a low risk of recurrence may be candidates for BCS alone
- Patients with a high risk of recurrence may require additional local therapy

## DCIS Breast Case Study

<table>
<thead>
<tr>
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<th>66 Year-Old Female Patient</th>
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<tr>
<td><strong>Tumor Size (cm)</strong></td>
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<tr>
<td><strong>Submitted By</strong></td>
<td>Kathryn Zerback, MD, Los Alamos Surgical Associates, Los Alamos, NM</td>
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DCIS Breast Case Study

CLINICAL INFORMATION
The Breast DCIS Score validation was derived from two studies, E5194 with 327 patients and the Ontario DCIS Cohort Study with 571 patients. The studies consisted of diverse DCIS patient populations treated with breast-conserving surgery alone. The results below reflect a meta-analysis with 773 patients of the two studies incorporating patient age and tumor size with the Breast DCIS Score result to estimate 10-year risk. The meta-analysis excluded patients whose tumors were multifocal and/or had positive margins.\textsuperscript{1,3}

![Graphs showing risk of any local recurrence and risk of invasive local recurrence based on Breast DCIS Score result.]

13% 10%

TREATMENT GIVEN Not Provided
**DCIS Breast Case Study**

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<thead>
<tr>
<th><strong>PATIENT</strong></th>
<th>44 Year-Old Female Patient</th>
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</table>

**SUBMITTED BY**: Charles Leonard, MD, Rocky Mountain Cancer Centers, Littleton, CO
DCIS Breast Case Study

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![Risk of Any Local Recurrence (DCIS or Invasive)](image1)

- **8%** with treatment given

- **4%** without treatment given

![Risk of Invasive Local Recurrence](image2)

- **4%** with treatment given

- **4%** without treatment given

TREATMENT GIVEN | Not Provided