

**Authors:** Alvarado M<sup>1</sup>, Carter D<sup>2</sup>, Guenther JM<sup>3</sup>, Hagans J<sup>4</sup>, Leonard C<sup>5</sup>, Manders J<sup>6</sup>, Sing AP<sup>7</sup>, Chang E<sup>8</sup>, Cherepanov D<sup>8</sup>, Schultz M<sup>9</sup>

**Affiliations:** <sup>1</sup>University of California, San Francisco, CA; <sup>2</sup>Rocky Mountain Cancer Centers, Aurora, CO; <sup>3</sup>St. Elizabeth Healthcare, Edgewood, KY; <sup>4</sup>The Surgical Clinic of Central Arkansas, Little Rock, AR; <sup>5</sup>Rocky Mountain Cancer Centers, Littleton, CO; <sup>6</sup>The Christ Hospital, Cincinnati, OH; <sup>7</sup>Genomic Health, Inc., Redwood City, CA; <sup>8</sup>Partnership for Health Analytic Research, LLC, Beverly Hills, CA; <sup>9</sup>St. Joseph Medical Center, Towson, MD

**Title:** Clinical utility of the 12-gene Ductal Carcinoma *in situ* (DCIS) Score Assay: Impact on Treatment (tx) Recommendations

**Background:** About 20% of breast cancers are DCIS. Rates of subsequent ipsilateral breast events (IBE) with surgery alone are 15-60%; about 50% are invasive. Clinicians and patients (pts) must choose from a wide range of locoregional and systemic options (and combination of these txs): lumpectomy or mastectomy; whole breast radiotherapy (XRT), partial breast XRT, or no XRT; and whether to add hormonal therapy (HT). XRT reduces IBE by 50-75%, HT by 25-50%, but neither tx has impacted survival. Traditional clinicopathologic (CP) factors provide an average IBE risk derived from population studies. The *Oncotype DX*<sup>®</sup> assay for DCIS (DCIS Score<sup>™</sup>) has been validated in E5194 (Solin, et al) as a predictor of 10yr risk of any IBE and invasive IBE, provides information independent of traditional factors and is potentially valuable for reducing over- or under-treatment. This study is the first assessment of the impact of the DCIS Score assay on tx recommendations.

**Materials/Methods:** Pts with DCIS were enrolled at 11 U.S. sites from 9/12-1/14 by 5 radiation oncologists (RO) and 6 surgeons (SO). Pts with any invasive disease, LCIS without DCIS, or planned mastectomy were excluded. CP factors and physician estimates of 10yr IBE risk and tx recommendations pre- and post- assay were prospectively collected.

**Results:** 110 patients were enrolled; 39.1% by ROs and 60.9% by SOs. CP characteristics are summarized in the Table including size, margin width and necrosis. 85% of pts were ER+ compared to 97% in E5194. The median pre-assay physician estimate of 10yr risk of IBE was 20.8 % (range, 6-40) for any IBE and 10.9% (range, 3-25) for invasive IBE. Physicians correspondingly recommended XRT in 72.7%, HT in 93.6%, and additional surgery in 18.2% of the cases. Post-DCIS score estimates of IBE risk and analysis of change in tx recommendations from pre- to post-assay will be presented at the meeting.

**Conclusions:** Establishing the impact of the DCIS Score on tx recommendations is critical to understanding the utility of this genomic assay in clinical practice. Of note, the CP factors differ from the validation study (E5194) in proportions of younger pts (< 50 yr), ER+ margins < 3 mm. The pre-assay IBE risk estimates and the corresponding pre-assay tx recommendations are consistent with current practices, including the recommendation of XRT ~ 73% of the time. The full analysis will report the impact of incorporating the DCIS Score result into clinical practice.

<b>Characteristic</b>		<b>Current Study</b> <i>n</i> = 110	<b>E5194</b> <i>n</i> = 327
Age ( <i>years</i> )	Median (Range)	61 (36-83)	
	< 50	15.5%	20.2%
DCIS Size ( <i>mm</i> )	Median (Range)	8 (1-115)	7
Nuclear Grade	Low	20%	8.9%
	Intermediate	46.4%	57.2%
	High	33.6%	33.9%
Closest Margin ( <i>mm</i> )	Median (Range)	3 (0-20)	
	< 3	48.1%	3.0%
Necrosis	Present	63.6%	34.9%