DCISionRT®

# The American Society of Breast Surgeons 2024

**Title:** Limitations in Utilizing Clinicopathologic Factors Alone in Identifying Patients with DCIS who Benefit from Radiotherapy after Breast-Conserving Surgery


**Background:** Breast conserving surgery (BCS) with or without radiotherapy (RT) is a mainstay of ductal carcinoma in situ (DCIS) management. Long-term breast cancer-specific survival rates are remarkably high, exceeding 95%, with this approach with over 70% of women not having a local recurrence with BCS alone, and therefore not benefitting from the addition of RT. Thus, there is growing interest in appropriately de-escalating treatment for DCIS. Traditionally, clinicopathologic (CP) factors have been used to identify low-risk DCIS patients. However, prospective trials have failed to consistently identify a truly low-risk CP group that did not benefit from RT with respect to local recurrence rate, or a clear high-risk CP group that consistently benefits from RT. The present study assessed the re-classification of patients with high-risk CP factors into Low and High Risk groups defined by a 7-gene predictive biosignature and associated rates of ipsilateral breast recurrence (IBR).

**Methods:** Women (n=926) from four international cohorts treated with BCS had samples analyzed at a CLIA lab (Laguna Hills, CA). CP low-risk patients were identified using a) RTOG-9804-like criteria [Nuclear Grade 1-2 & Size ≤2.5cm & non-Palpable & Screen Detected & margin negative (no-ink on tumor)] and b) MSKCC-like criteria [low-risk score< 220, determined using nomogram weighted factors (excluding: number of re-excisions and RT treatment), and using no-ink-on-tumor instead of close margin]. High-risk CP was defined as not meeting these criteria. The 7-gene biosignature combined seven biomarkers with the four CP factors (age, size, palpability, margin status) using an algorithm reporting a Decision Score (DS) and Residual Risk subtype (RRt). Women with high-risk CP were classified into biosignature Low Risk (DS≤2.8, no RRt) or High Risk (DS>2.8 +/- RRt). 10-yr IBR (DCIS/invasive) rates with and without RT were estimated with Kaplan-Meier and Cox proportional hazard analyses.

**Results:** Overall, 49% and 65% of patients were initially classified into the CP high-risk groups by RTOG-9804-like and MSKCC-like criteria, respectively. CP high-risk groups had 10-yr IBR rates of 24% and 21% after BCS without RT with an absolute 16% (p<.001) and 13% (p< 0.01) IBR rate reduction with RT. The biosignature High-Risk group (63%, n=588) had a 10-yr IBR risk of 25% after BCS alone with a significant RT benefit (10-yr IBR 8%,p<.001). The biosignature reclassified 23% and 36% of CP high-risk patients into the biosignature Low-Risk group respectively; these reclassified patients had low IBR rates without RT (5.9% and 6.8%) and a minimal, nonsignificant (2.9%, p=.5; 2%, p=.5) absolute IBR rate reduction with RT. CP high-risk patients with concordant biosignature High-Risk demonstrated significant RT benefit (Table 1). The 10-year IBR rates for CP high-risk patients in the Biosignature Low and High-risk groups were comparable to the 10-year IBR rates of Biosignature Low and High-Risk groups for all patients.

**Conclusion:** The 7-gene predictive biosignature more reliably identified patients who benefited from RT compared to using traditional high risk CP criteria (RTOG-9804-like, MSKCC-like). Importantly, CP high-risk patients who were re-classified as biosignature Low-Risk had low 10-yr IBR rates and no significant difference with versus without RT.


**Table 1.**

| | All Patients | | | | | Classified as DCISionRT Low Risk (DS≤2.8 without RRt) | | | | | Classified as DCISionRT High Risk (DS>2.8 +/- RRT) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 10-yr IBR rates | | | | | 10-yr IBR rates | | | | | 10-yr IBR rates | | | | |
| | | BCS No RT (95% CI) | BCS+ RT (95% CI) | HR | $P_{LR}$ | | BCS No RT (95% CI) | BCS + RT (95% CI) | HR | $P_{LR}$ | | BCS No RT (95% CI) | BCS + RT (95% CI) | HR | $P_{LR}$ |
| **All Patients** | n=926 | 17.3% (13%,23%) | 6.9% (5,10%) | 0.4 | <0.001 | 338/926 (37%) | 5.6% (3%,12%) | 4.8% (3%,9%) | 0.8 | 0.7 | 588/926 (63%) | 25.7% (19%,34%) | 8.0% (6%,12%) | 0.3 | <0.001 |
| **MSKCC-like high-risk (≥220)** | n=606 (65%) | 21.1% (15%,29%) | 8.0% (5%,12%) | 0.3 | <0.001 | 220/606 (36%) | 6.8% (3%,16%) | 4.8% (2%,11%) | 0.6 | 0.4 | 386/606 (64%) | 30.2% (22%,41%) | 9.2% (6%,15%) | 0.3 | <0.001 |
| **RTOG-9804 like high-risk** | n=453 (49%) | 23.6% (16%,33%) | 7.6% (5%,12%) | 0.3 | <0.001 | 106/453 (23%) | 5.9% (2%,22%) | 3.0% (1%,12%) | 0.5 | 0.5 | 347/453 (78%) | 30.5% (21%,43%) | 8.7% (6%,14%) | 0.2 | <0.001 |

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